Carbohydrate Research, 69 (1979) 1–26
© Elsevier Scientific Publishing Company, Amsterdam – Printed in The Netherlands

ON THE MAGNITUDES AND ORIGINS OF THE "ANOMERIC EFFECTS", "EXO-ANOMERIC EFFECTS", "REVERSE ANOMERIC EFFECTS", AND C–X AND C–Y BOND LENGTHS IN XCH_2YH MOLECULES*†

SAUL WOLFE, MYUNG-HWAN WHANGBO, AND DAVID J. MITCHELL
Department of Chemistry, Queen's University, Kingston, Ontario K7L 3N6 (Canada)

(Received November 21st, 1977; accepted for publication in revised form, April 18th, 1978)

ABSTRACT

Ab-initio molecular-orbital calculations have been performed at the STO-3G level on the series of molecules XCH_2YH in which X = H_2N, CH_3, OH, F, and Cl, and Y = O and S, and on the series of fluoromethanes CH_nF_{4-n}. The C–X and C–Y bond lengths in the gauche and antiperiplanar conformations of XCH_2YH have been optimized. In all cases, the experimental trends in the bond lengths from conformation to conformation and from molecule to molecule, and in the torsional behavior as a function of X and Y have been reproduced. Thus, the "anomeric effects" are found to be Cl > F > OH, as a function of X, and O > S, as a function of Y. Molecules in which X = CH_3 and NH_2 exhibit "reverse anomeric effects"; in methanediol, the "anomeric effect" and the "exo-anomeric effect" are equal. The results have been analyzed by a quantitative, perturbational molecular-orbital (PMO) treatment that calculates orbital interactions between XCH_2 and YH in the cases of the "anomeric" and "exo-anomeric effects", and between X and CH_2YH in the case of the "reverse anomeric effect", by using fragments and fragment orbitals generated from the ab-initio wavefunction. Attention has been focused, especially, upon the stabilizing interactions between the lone pair of Y and antibonding orbitals of XCH_2, and between the highest-lying orbital of X and antibonding orbitals of CH_2YH. The justification for this choice is that these orbitals make a dominant contribution to the highest occupied molecular orbital (HOMO) of XCH_2YH, and the stereochemical behavior of the HOMO parallels that of the total energy. In all cases, the trends in these stabilizing orbital interactions parallel the trends in the "anomeric" and "reverse anomeric effects", suggesting that, within the framework of the PMO model, such interactions may be regarded as the "origin" of these effects. Although both σ^* and π^* antibonding orbitals have to be taken into account to achieve

---

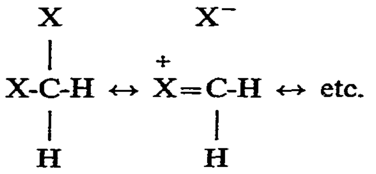
*This work is dedicated to the memory of Professor J. K. N. Jones, F.R.S., teacher, colleague, and friend.

†Portions of this work, which is Part VII in the series "Molecular Orbitals from Group Orbitals", were presented in the joint CIC/ACS Symposium on "The Origin and Consequences of the Anomeric Effect", Montreal, June, 1977.

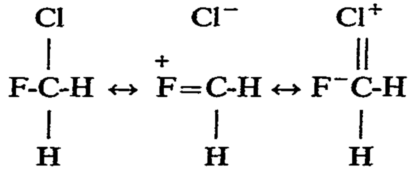
quantitative agreement between the calculated orbital interactions and the total energy-differences, only those interactions associated with σ^* vary significantly as X and Y are varied, as suggested originally by Lucken and by Altona. In the series of fluoromethanes, a linear relationship exists between the stabilizing orbital interactions and the experimental C–F bond energies, and also between the stabilizing orbital interactions and the number of double bond–no bond resonance structures. This result provides quantitative support for a description of these various effects in terms of the classical concept of double bond–no bond resonance. Finally, the trends in the C–X and C–Y bond lengths in XCH_2YH and XCH_2X molecules have been found to be the result of a combination of coulombic effects and the principle of maximization of overlap between fragments.

INTRODUCTION

In 1937, Brockway discovered that the carbon–halogen bonds in polyhalogenated methanes are shorter than those in the parent methyl halides[1]. The effect was found to increase with an increase in the number of halogen atoms, and to be greater for fluorine than for chlorine. It was suggested[1,2] that these observations are consistent with the postulate of *double bond–no bond resonance* (Eq. *1*). In terms of this postulate, the differing effects of fluorine and chlorine could be rationalized in terms of both greater ionic character in a C–F bond, and greater stability of multiple bonds involving first-row atoms.



$$\begin{array}{c} X \\ | \\ X\text{-}C\text{-}H \\ | \\ H \end{array} \leftrightarrow \begin{array}{c} X^- \\ \\ \overset{+}{X}{=}C\text{-}H \\ | \\ H \end{array} \leftrightarrow \text{etc.} \qquad (1)$$



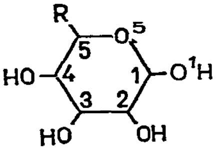
$$\begin{array}{c} Cl \\ | \\ F\text{-}C\text{-}H \\ | \\ H \end{array} \leftrightarrow \begin{array}{c} Cl^- \\ \\ \overset{+}{F}{=}C\text{-}H \\ | \\ H \end{array} \leftrightarrow \begin{array}{c} Cl^+ \\ \| \\ F^-\,C\text{-}H \\ | \\ H \end{array} \qquad (2)$$

Brockway's data were obtained by using electron diffraction. Subsequently[3], more accurate data, confirming and extending the original observations, became available from microwave spectroscopy. In the case of CH_2FCl, the relative shortening of the C–Cl bond is greater than that of the C–F bond, suggesting that each of the resonance structures shown in Eq. *2* should be taken into account.

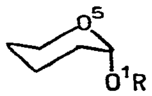
Associated with these geometrical changes is a progressive increase in the carbon–fluorine bond-energy in polyfluoromethanes with increasing fluorine substitution[4]. In the course of a detailed discussion of double bond–no bond resonance[5], Hine found a linear relationship between the number of double bond–no bond structures and resonance energies derived from the C–F bond-energies of these compounds.

The concept of double bond–no resonance was not at first accepted universally*. In terms of the structures shown in Eq. *1*, one could reasonably ask why the C–X bonds should become shorter and not longer. One might also expect valence angles about the central carbon atom to become larger than tetrahedral as double bond–no bond resonance becomes progressively more important; in fact, FCF angles in the polyhalomethanes tend to be smaller than tetrahedral. These and other difficulties were pointed out early by Burawoy[7], Hückel[8], Walsh[9], and others, and they have been summarized by Williams[10]. However, the resonance interpretation prevailed for some time, and it continues to be an important part of the language of organic chemistry, although many authors now seem to qualify its use with the phrase "or its quantum mechanical counterpart".

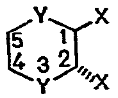
Lucken[11] appears to have been the first to suggest a molecular-orbital counterpart of double bond–no bond resonance. Livingston[12] had observed anomalously low, nuclear-quadrupole resonance-frequencies of ^{35}Cl in chlorofluoromethanes. In repeating and extending this work, Lucken observed similar effects in a number of chlorine-containing ethers, sulfides, fluorides, alkenes, and alkynes. He proposed



1



2



3

4 5

7

---

*For an interesting historical account of the emergence of these ideas, see ref. 6.

that there is an interaction between a p-orbital of the substituent (O, S, F, C=C, C≡C) and an adjacent carbon–chlorine antibonding molecular orbital, and attempted to estimate qualitatively the magnitude of this interaction.

Subsequently[13], X-ray crystallographic investigations by Jeffrey and his coworkers revealed a shortening of the carbon–*oxygen* bonds in the anomeric position (C-1–O-1) of pyranose sugars (see **1**); in the case of glycosides having an *axial* anomeric substituent (**2**), both the C-1–O-1 and the C-1–O-5 bonds appeared to be shorter than average. Jeffrey suggested that there might be some relationship between his observations and the existence of the "anomeric effect"[14], which refers to the tendency of an electronegative substituent (O, S, halogen) to favor the axial configuration when it is attached to the anomeric centre of a pyranose ring.

"Anomeric effects" are also observed in halogenated 1,4-dioxanes, dithianes, and thioxanes[15], and are accompanied by significant alterations in "normal" bond-lengths[16]. Thus, for molecules of type **3** (X = halogen; Y = O,S), C-5–Y is normal, C-1–Y is short, but, in contrast to the observations presented thus far, the C-1–X bond is *longer* than normal. These latter observations were interpreted by Altona[16] in terms of a mixing, in the manner advocated by Lucken, between a lone-pair orbital of the ring substituent and an antibonding orbital of the axial carbon–halogen bond.

An important aspect of Jeffrey's work, the work of the Leiden school[15,16], and recent publications by Paulsen[17] on aldo-pyranosyl halides, is the finding that the tendency for a *lengthening* of a C-1–X bond is uniquely associated with an *axial halogen* substituent. For example, the carbon–chlorine bond of 2,3,4-tri-*O*-acetyl-*β*-D-xylopyranosyl chloride, which is equatorial, is *shorter* than normal (1.754 *vs* 1.79 Å) and, in *cis*-2,3-dichloro-1,4-dioxane, the equatorial C–Cl bond is short (1.781 Å), but the axial C–Cl bond is long (1.819 Å).

There are extensive data[18] concerning the molecular geometries and anomeric effects associated with specific combinations of X and Y. For molecules of type **4**, with and without additional ring-substituents, the magnitude of the anomeric effect, defined as the difference between the conformational free-energy for the process **4** ⇄ **5** and the corresponding process in cyclohexane (Y = CH_2), is greater for Y = O than for Y = S for a given X; for a given Y, it is greater for X = Br than for X = Cl. We have been unable to find an accurate determination of the anomeric effect of fluorine, although there is an indication, in the work of Paulsen[17b] that it is smaller than the anomeric effect of bromine. These trends are paralleled by variations in the *geometries*[15b] of the same systems. Axial C–Cl and C–Br bonds are longer when the adjacent ring-heteroatom is oxygen than when it is sulfur; and a ring oxygen–anomeric carbon bond is shorter when the axial anomeric substituent is bromine than when it is chlorine.

There is a close correspondence between the existence of the anomeric effect in six-membered heterocyclic rings and the conformational behavior of acyclic molecules of the type X-CH_2-YH (**6**). As shown in Fig. 1, truncation of **4** leads to the gauche conformation of **6**, and truncation of **5** leads to the antiperiplanar con-

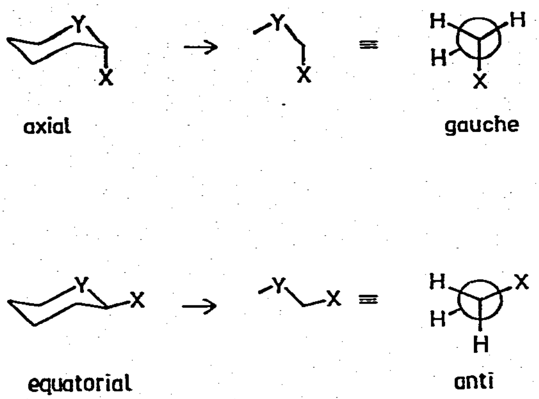


Fig. 1. The relationship between the axial and equatorial conformations of 1-substituted tetrahydropyrans and tetrahydrothianes, and the gauche and antiperiplanar conformations of XCH_2YH.

formation of **6**. In all instances[19] in which the anomeric effect is observed for a particular combination of X and Y, the gauche conformation of the truncated analog **6** is found to be more stable than the antiperiplanar conformation. In addition, it has been observed recently[20] that with $X=NH_2$ there is a "reverse" anomeric effect as, in such molecules, **5** is more stable than **4**. In this situation, as will be seen later, the antiperiplanar conformation of the truncated analog is found to be more stable than the gauche. These observations suggest that molecules of type **6** may be reasonable models for a theoretical investigation of the anomeric effect.

The interpretations of the anomeric effect that have appeared in the literature may be grouped into three types. The first[14b] emphasizes dipole–dipole and Coulombic interactions; this kind of interpretation has generally been regarded as incomplete, because it does not lead to quantitative agreement with experiment[15b], and it does not account for the observed geometries. The second invokes[21] double bond–no bond resonance, for example, **7**. Hybrid lone-pair orbitals are assumed for the ring substituent, and the interaction depicted in **7** involves specifically the lone pair that is antiperiplanar (*app*) to the anomeric substituent. Although this *app* lone-pair model rationalizes the existence of the anomeric effect, and a variant of it has been employed with considerable success to account for stereochemical aspects of ester and amide hydrolysis[22], this model, like the double bond–no bond interpretation of the bond lengths of polyfluoromethanes, does not account for both the lengthening of the C-1–X bond when X is *halogen*, and the *shortening* of this bond when X is *oxygen*.

The third kind of interpretation of the anomeric effect is based upon attempts to "explain" the results of molecular-orbital calculations. Both ab-initio[23] and semi-empirical[24] computations reproduce the "anomeric effects" exhibited by molecules of type **6**. As will be seen in the present work, ab-initio calculations also reproduce the trends in the magnitudes of the anomeric effects associated with X and Y and in the C–X and C–Y bond lengths. The available evidence indicates[24] that the Extended Hückel and MINDO/2 methods do not reproduce the anomeric effect;

CNDO/2 calculations incorrectly predict[24b] that chlorine has a smaller anomeric effect than oxygen. The reliability of explanations based upon such calculations is, therefore, less clear.

The encouraging results given by the ab-initio computational approach led to the expectation that a generally acceptable quantitative interpretation of the anomeric effect would soon follow. This has not been the case. The reason for this is that only the total energies obtained in such calculations have rigorous meaning; "explanations" or "rationalizations" of trends in computed total energies and geometries are based upon a particular mode of decomposition of the results, and such a decomposition is necessarily less rigorous than the computation of the total energy. Thus, two different interpretations of the role of the lone pairs of the atom Y in XCH_2YH have emerged, one based upon an analysis of the problem in terms of localized molecular orbitals (LMO), and the other based upon an analysis in terms of canonical molecular orbitals (CMO). The first regards the lone pairs as equivalent[23a], and it can be connected to the total lone-pair electron density, an experimental observable[25]. The second treats the lone pairs as energetically nonequivalent[26], and it can be connected to the lone-pair ionization potentials, a different kind of experimental observable[27]. In the LMO interpretation[23d], the two lone pairs *together* create a quasi-spherical potential field in which the bonding electron-pairs and nuclei are moving. This interpretation has led to the view that the anomeric effect is an example of a more general "gauche effect"[28]. As the anomeric effect is calculated to exist even when idealized bond-lengths are employed, the observed bond-length alterations were regarded as the result of the superposition of a "reflex effect"[29], namely, a relaxation of the molecular geometry caused by the molecule's adoption of the sterically unfavorable, gauche conformation.

On the other hand, the CMO interpretation of the anomeric effect focuses explicitly upon the different energies of the lone pairs of Y and the different interactions between these lone pairs and the antibonding orbitals of the XCH_2 group. This interpretation incorporates the approach originated by Lucken and Altona, and it is an example of the currently widely used "orbital interaction" or Perturbational Molecular Orbital (PMO) approach to conformational problems[30]. It is readily seen that the proposed charge-transfer into an antibonding C–X orbital may be associated with a lengthening of the C–X bond. However, there seems to be a problem in accounting for a *shortening* of this bond, when such shortening is observed, without the introduction of additional orbital interactions.

For the general case of a molecular system A–B, in which A and B are functional groups, the PMO method begins with the selection of a set of fragment or group orbitals that are appropriate for A and for B; associated with each group orbital is a specific orbital energy. The relative stabilities of the different conformations of A–B are then estimated, by allowing A and B to approach each other in different ways, and assessing the effects of these different modes of approach upon the stabilizing (that is, occupied with unoccupied) and destabilizing (namely, occupied with occupied) interactions between the orbitals of A and those of B. Eventually, the conclusion is reached that one conformation is more stable than another because it "maximizes the stabilizing interactions" or "minimizes the destabilizing interactions". The magnitude of a stabilizing interaction is proportional[30] to the square of the overlap between the interacting orbitals, and inversely proportional to the energy gap between them. The magnitude of a destabilizing interaction is approximately proportional[30] to the square of the overlap and to the mean of the orbital energies of the interacting orbitals. If the magnitude of the overlap is constant, the largest stabilizing and destabilizing orbital-interactions will be those associated with the frontier orbitals of A and of B. In addition, these frontier interactions will dominate the highest occupied molecular orbital (HOMO) of A–B, and there is extensive evidence[31] that the behavior of the HOMO parallels that of the total energy.

However, the assumption of constant overlap[32] is not valid when both stabilizing and destabilizing orbital-interactions are of interest, because different group orbitals are involved; and it breaks down completely when analogous orbital interactions of different molecules are compared, because of the different bond-lengths. Therefore, a quantitative discussion is not possible without a quantitative definition of fragment orbitals, orbital energies, overlap integrals, and the proportionality constant.

The mathematical formalism for such a quantitative treatment was developed in Part 3 of this series[33]. The principal feature of this treatment is the use of the ab-initio wavefunction of the molecule A–B as the source of the fragment orbitals A and B. Extensive tests of the method have revealed that the total energy-behavior of various molecular systems is reproduced semi-quantitatively by the behavior of the π-type orbital interactions between the fragments.

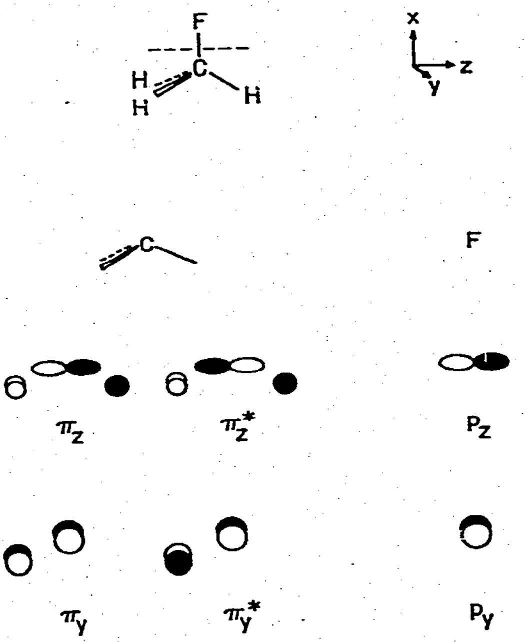
This quantitative method has now been applied to the problem of the anomeric effect. The principal objectives of the work were the following: (*i*) to determine whether the computed total energies and geometries of XCH_2YH molecules exhibit the same trends, as a function of X and Y, as is observed experimentally; (*ii*) to determine whether lone pair–antibonding interactions correlate quantitatively with the "anomeric effects" computed for these XCH_2YH molecules; (*iii*) to determine whether the orbital interaction responsible for a shortening of both the C–X and C–Y bonds in certain instances can be identified; (*iv*) to determine whether a connection can be made between the quantitative results of the present study and alternative descriptions of the anomeric effect, such as double bond–no bond resonance and the gauche effect.

In the initial formulation of the work, six molecules were examined: X = CH_3, F, Cl; Y = O, S. Later, as the implications of the reverse anomeric effect associated with X = NH_2 became clear, H_2NCH_2OH was also studied. In the final stages of the work, calculations on methanediol and the polyfluoromethanes were incorporated into the study. All computations were performed by using a locally modified version of Gaussian 70, written for the Burroughs B6700 computer of Queen's University, and the STO-3G basis set. The program for the computation of orbital interactions is implemented by specification of a particular fragmentation-mode following the

SCF calculation at a particular geometry of interest; the fragment orbitals, and all of the properties of these orbitals required for the computation of orbital interactions, are then provided by the program. Standard C–H, O–H, S–H, and N–H bond lengths were employed throughout the computations, as well as tetrahedral angles at carbon[23c].

RESULTS AND DISCUSSION

PMO Analysis of CH_3F and CH_2F_2. — It is useful to begin with a detailed consideration of the nature of group orbitals and orbital interactions in simple molecules. Fluoromethane and difluoromethane are employed to exemplify the general method. In CH_3F the analysis is based, most reasonably, upon the fragmentation $CH_3 \cdots F$; in CH_2F_2, the analysis is based upon the fragmentation $FCH_2 \cdots F$. The discussion of CH_3F takes into account the four-electron, destabilizing interactions between fluorine lone-pairs and occupied, π-type methyl-group orbitals, as well as the two-electron stabilizing interactions between fluorine lone-pairs and unoccupied, π-type methyl-group orbitals. In CH_2F_2, the interactions are between fluorine lone-pairs and the group orbitals of CH_2F. We therefore require a description of CH_3-group orbitals, and some understanding of how these are modified when one of the hydrogen atoms is replaced by fluorine.



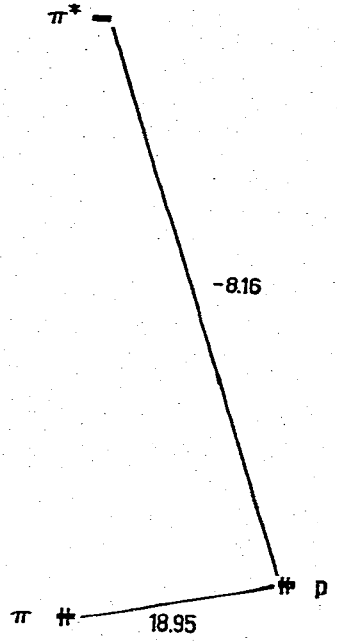


Fig. 2. Fragmentation of CH_3F into CH_3 and F, and the orbitals of these fragments that engage in π-type interactions.

Fig. 3. Orbital-interaction diagram showing the quantitative PMO analysis of CH_3F. The numbers shown here should be multiplied by two, because of the degeneracy of the x- and y-type orbitals.

The nature of the canonical orbitals of a methyl group has been discussed in a number of texts[34]. Based on our own experience, for an organic chemist or a carbohydrate chemist, the principal conceptual difficulty with the CMO description is that these orbitals are not equivalent, and they are not directed along the bonds. The latter are the more familiar *localized* molecular orbitals. Thus, in methane, there are four equivalent LMO directed along the bonds, but, in the CMO description, there are two kinds of orbitals: a low-energy orbital comprised of carbon 2s and hydrogen 1s; and a higher-lying set of three degenerate orbitals comprised of hydrogen 1s and, respectively, carbon $2p_x$, $2p_y$ and $2p_z$, the form of the combinations of carbon 2p with hydrogen 1s being dictated by the nodal properties of the individual p-orbitals. The total electron density associated with the four CMO is the same as that of the four LMO. The particular advantage of the CMO description is that it allows the total energy to be partitioned in a well defined way, so that the contributions of individual group orbitals to the final molecular orbitals may be calculated.

Fig. 2 shows CH_3F oriented with the C–F bond directed along the *x*-axis of the coordinate system. Fragmentation into CH_3 and F affords a fluorine atom having p_x, p_y, and p_z orbitals (the effects of the core electrons are ignored). The p_x orbital is used to form the bond between F and CH_3; its effect is also ignored. The π-type orbital interactions will involve the doubly-occupied p_y and p_z lone-pair orbitals of fluorine and the methyl-group orbitals having the same symmetry.

Turning to the methyl group, the low-lying s-type orbital is ignored, as is the π-type orbital constructed from the carbon $2p_x$ atomic orbital, which forms the bond to fluorine. The methyl-group orbitals that engage in π-type interactions with F are shown in the Figure as π_z, π_z^*, π_y and π_y^*. Only two of the three methyl hydrogen atoms contribute to π_y and π_y^*; the third lies in the *xz* plane, a nodal plane. All three methyl-group hydrogens contribute to π_z and π_z^*; none of the hydrogen atoms lies in the *xy* plane. This plane dictates the nodal character of these orbitals, that is, the signs on the hydrogen atoms in π_z and π_z^*.

The π_y and π_z methyl-group orbitals are degenerate; they engage in four-electron destabilizing interactions with p_y and p_z, respectively. The degenerate π_y^* and π_z^* group orbitals engage in two-electron, stabilizing interactions with p_y and p_z, respectively. Fig. 3 is, therefore, the interaction diagram required for the PMO analysis of CH_3F in terms of the π-type orbitals. For the quantitative PMO analysis, an ab-initio calculation was performed on CH_3F, and the two electron and four-electron interaction energies between CH_3 and F were computed by using Eqs. *3* and *4*, respectively[33],

$$\Delta e_{ij} = 2(\Delta_{ij} - e_i^0 \tilde{S}_{ij})^2/(e_i^0 - e_j^0) \qquad (3)$$

and

$$\Delta e_{ij} = 2\tilde{S}_{ij}[-2\Delta_{ij} + (e_i^0 + e_j^0)\tilde{S}_{ij}]/(1 - \tilde{S}_{ij}^2) \qquad (4)$$

where e_i^0 and e_j^0 are the energies of the fragment orbitals ϕ_i^0 and ϕ_j^0, and $\tilde{S}_{ij}$ and Δ_{ij} are the overlap integral and the interaction matrix-element between the fragment

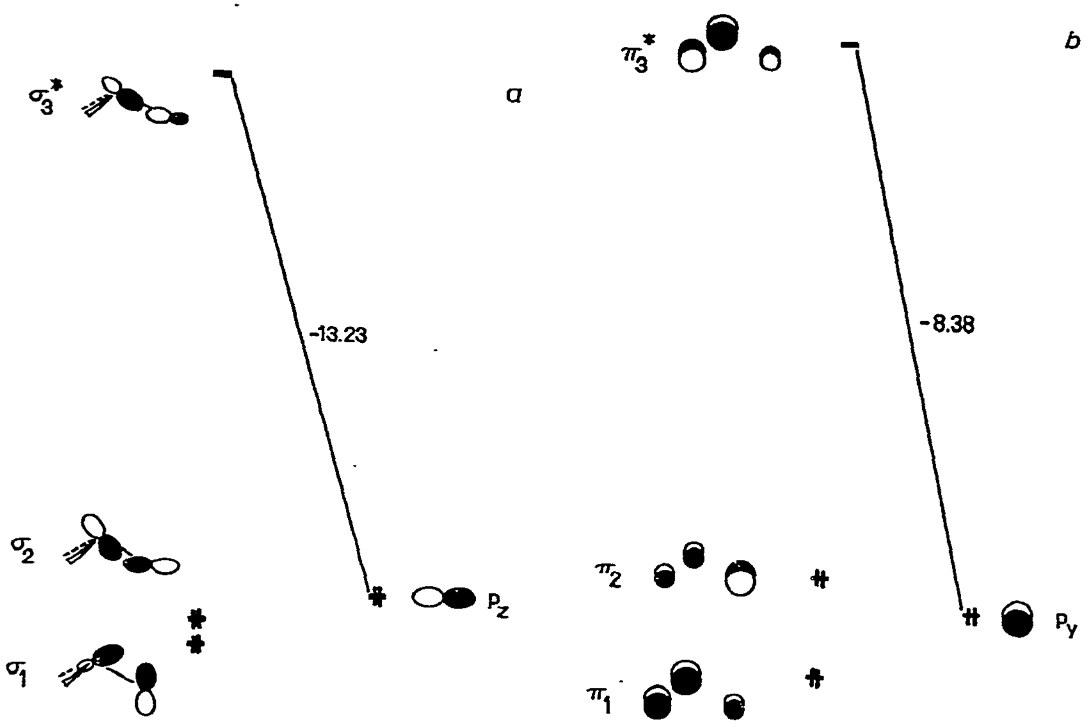


Fig. 4. (*a*) The σ-type orbitals of CH_2F, which interact with the p_z orbital of the fragmented F. The coordinate system is the same as that of Fig. 2. (*b*) The π-type fragment orbitals of CH_2F, which interact with the p_y orbital of the fragmented F.

orbitals, respectively. The numbers shown in Fig. 3 are obtained from the quantitative analysis.

Figs. 4a and 4b show the σ-type and π-type CH_2F-group orbitals that are obtained from an SCF–MO computation for CH_2F_2, with the fragmentation $FCH_2 \cdots F$. The computed stabilizing-orbital interaction energies are included in the Figures.

It may be seen that, in CH_3F, the $(p_z - \pi_z^*)$ and $(p_y - \pi_y^*)$ interaction energies calculated from Eq. *3* are -8.16 kcal/mol. In CH_2F_2, the $(p_z - \sigma_3^*)$ and $(p_y - \pi_3^*)$ interaction energies are -13.23 and -8.38 kcal/mol, respectively. Thus the stabilization associated with the p_y orbital of the fragmented F is nearly the same in both molecules, but the stabilization associated with the p_z orbital is larger in CH_2F_2 than in CH_3F. The reason for this is that the σ_3^* orbital lies lower than the π_3^* orbital. This situation causes the CH_2F group to favor σ-type stabilization over π-type stabilization. This disparity in the σ- and π-type conjugative capabilities of CH_2X groups ($X \neq H$) has been noted previously[31b,34,35], and it has been used to rationalize numerous conformational effects.

The $(p_z - \sigma_3^*)$ interaction $(n - \sigma^*)$ is the Lucken–Altona mixing between a lone-pair orbital and an adjacent antibonding orbital. However, at least five *additional* orbital interactions are also present in Fig. 4, including the $(p_y - \pi_3^*)$ π-*type* stabilizing

TABLE I

CALCULATED ORBITAL INTERACTION-ENERGIES[a] IN THE FLUOROMETHANES

Molecule[b]	*Stabilization*[c]	*Destabilization*[d]	*Total*
$H_3C \cdots F$	−16.32	37.90	21.58
$FH_2C \cdots F$	−21.61	31.62	10.01
$F_2HC \cdots F$	−24.91	25.71	0.80
$F_3C \cdots F$	−31.60	22.24	−8.36

[a] Energies are in kcal/mol. [b] In each molecule, $r_{C-F} = 1.385$Å, $r_{C-H} = 1.09$Å and all valence angles are tetrahedral. [c] $[(n - \sigma^*) + (n - \pi^*)]$. [d] $\Sigma[(n - \sigma) + (n - \pi)]$.

interaction $(n - \pi^*)$. The rationalization of the behavior of the total molecular wavefunction in terms of a specific orbital interaction would thus seem to constitute an arbitrary and incomplete description of the problem. Nevertheless, this is the essence of the PMO method. It might be justified, if it could be demonstrated, that the behavior of the chosen interaction within a given molecule and in a series of closely related molecules parallels the behavior of the total energy. Alternatively, it might be justified if it were apparent that the chosen interaction contains some readily understandable physical significance.

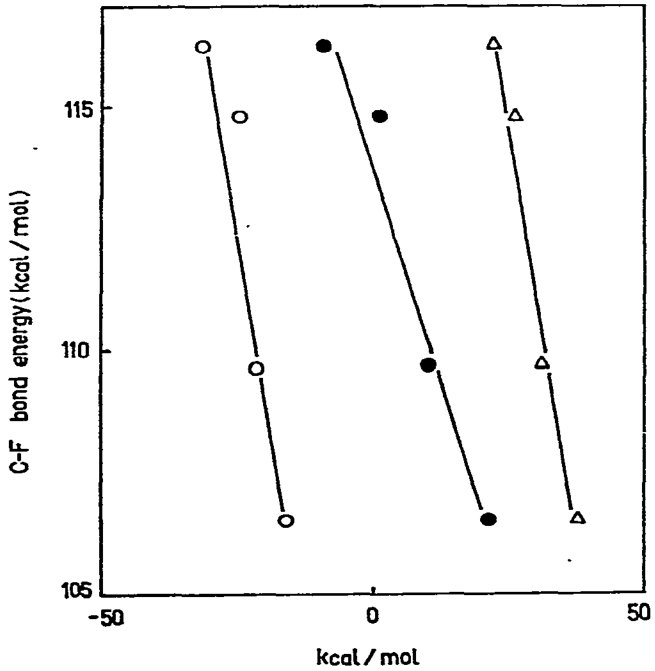


Fig. 5. Plots of the calculated stabilizing orbital-interaction energies (○), the destabilizing orbital-interaction energies (△), and the total orbital-interaction energies (●) against the experimental C–F bond-dissociation energy for the series of molecules CH_nF_{4-n}.

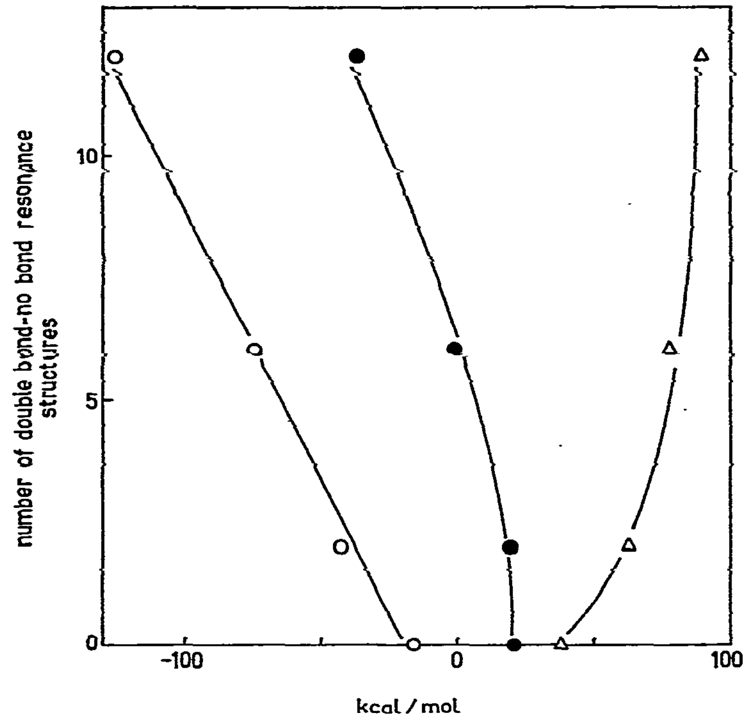


Fig. 6. Plots of the calculated stabilizing orbital-interaction energies (○), the destabilizing orbital-interaction energies (△), and the total orbital-interaction energies (●), versus the number of double bond–no bond resonance structures for the series of molecules CH_nF_{4-n}.

On the relationship between orbital interaction-energies, bond dissociation energies and double bond–no bond resonance. — Table I lists the total, calculated, orbital interaction-energies, and the separate contributions to this total of the stabilizing and destabilizing orbital interaction-energies for the series of fluoromethanes. In Fig. 5, these data have been plotted against the experimental C–F bond-dissociation energies of the four compounds[4].

We consider that the results shown here can be used to justify the view that the variations in the bond energies within the series may be rationalized by focusing upon the variations in the stabilizing orbital interactions. Alternatively, one might with equal validity focus upon the *de*stabilizing orbital interactions. However, the physical interpretations conveyed by the two choices are not the same. This may be seen upon consideration of Fig. 6, which shows the number of double bond–no bond resonance structures that can be written for the fluoromethanes, plotted against $n\Sigma\Delta e_{ij}$, where n is the number of fluorine atoms and $\Sigma\Delta e_{ij}$ is the appropriate interaction energy from Table I.

As Hine has already found[5] a relationship between resonance energies and double bond–no bond resonance in this series of molecules, Fig. 6 suggests that the stabilizing orbital interaction-energies can be connected to the concept of double bond–no bond resonance. The destabilizing orbital interaction-energies cannot. This

TABLE II

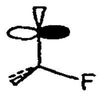
CALCULATED ENERGIES[a] OF THE FCH_2 AND OH FRAGMENT-ORBITALS OF FLUOROMETHANOL

Orbital[b]		*Conformation*	
		90°	*180°*
FCH_2	σ^*	0.5512	0.5602
	π^*	0.6535	0.6537
OH	n	−0.4124	−0.4146

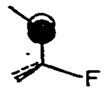
[a] In atomic units. [b] The FCH_2 orbitals are shown in Fig. 4a and 4b as σ_3^* and π_3^*, respectively.

seems reasonable, in view of the usual association of "resonance" with "stabilization". Thus the stabilizing orbital interaction-energy is seen to be both a justifiable quantity for the discussion of trends within the series and, at the same time, a quantity that can be related to a more traditional concept and computed rigorously by the quantitative PMO procedure. Whether it is possible similarly to relate the destabilizing orbital interaction-energies to some more traditional concept, such as, "steric effects", is not known, because it is more difficult to find experimental data that can be related rigorously to steric effects. Therefore, in proceeding to the analysis of the anomeric effect, we propose to focus mainly upon the stabilizing orbital interaction-energies.

The "anomeric effect" in fluoromethanol. — The analysis of FCH_2OH is based upon the fragmentation $FCH_2 \cdots OH$. The nature of the FCH_2 group orbitals is exactly the same as in Fig. 4. Table II lists the orbital energies of the σ^* and π^* orbitals of CH_2F and the n lone-pair orbital of OH, which is perpendicular to the COH plane, in the perpendicular (90°) and antiperiplanar (180°) conformations.



perpendicular



antiperiplanar

It may be noted that these orbitals are virtually transferable between the two conformations. In the 180° conformation, n interacts with π^*, and in the 90° conformation it interacts with σ^*. The ($n - \sigma^*$) and ($n - \pi^*$) interaction-energies are calculated to be −12.66 and −7.56 kcal/mol in the 90 and 180° conformations, respectively.

The orbital interactions in the 0° conformation are qualitatively the same as in the 180° conformation; they differ somewhat when computed quantitatively, because the overlap between CH_2F and OH in the two conformations is not exactly the same. At dihedral angles other than 180 and 90°, the orbital interactions consist of appropriate combinations of the interactions present at these two dihedral angles. Table III gives the stabilizing interactions associated with the oxygen lone-pair $\{(n - \sigma^*) + (n - \pi^*)\}$ in the 0, 60, 90, 120, and 180° conformations of FCH_2OH. The computed total energies of these conformations are also included. Fig. 7 shows

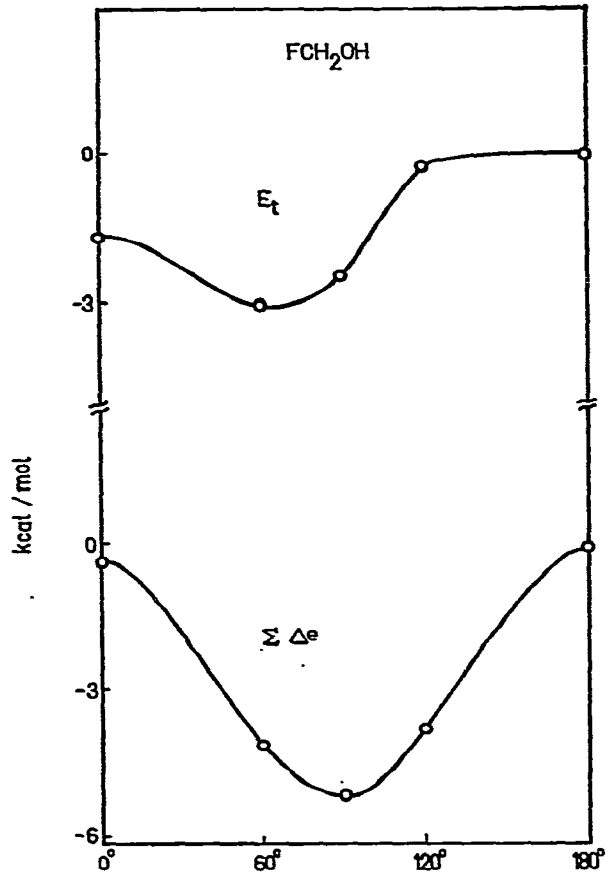


Fig. 7. The calculated total energy of FCH_2OH, and the stabilizing orbital-interaction energy associated with n_O, as a function of rotation about the C–O bond.

TABLE III

ROTATIONAL BEHAVIOR OF THE STABILIZING INTERACTIONS[a] ASSOCIATED WITH THE n FRAGMENT-ORBITAL OF FLUOROMETHANOL

Interaction	*Conformation*				
	0°	*60°*	*90°*	*120°*	*180°*
$[(n - \sigma^*) + (n - \pi^*)]$	−7.78	−11.62	−12.66	−11.28	−7.56
Total energy[b]	−211.00367	−211.00589	−211.00421	−211.00143	−211.00106

[a]Stabilizing energies are in kcal/mol. [b]Total energies are in atomic units (1 a.u. = 627.7 kcal/mol).

TABLE IV

OPTIMIZED C–X AND C–Y BOND-LENGTHS[a] OF XCH_2YH MOLECULES ($X = F, Cl; Y = O, S$)

X	*Y*	*Conformation*			
		60°		*180°*	
		C–X	*C–Y*	*C–X*	*C–Y*
F	O	1.384	1.425	1.375	1.432
Cl	O	1.827	1.419	1.803	1.431
F	S	1.388	1.811	1.383	1.821
Cl	S	1.826	1.805	1.806	1.814

[a] Bond lengths are in Å.

the total energy as a function of dihedral angle and also the stabilizing interactions associated with *n*. The shape of the total-energy curve has been noted previously[23]. For the purpose of the present, comparative investigation, we propose to define the energy difference between the 60° minimum and the 180° maximum as the theoretical "anomeric effect" in FCH_2OH.

The stabilizing interactions associated with n vary approximately in the same manner as the total energy. As noted elsewhere[31b], the HOMO of FCH_2OH, which is comprised mainly of n_O, shows the same behavior. The "anomeric effect" associated with the lone-pair interactions is 4.06 kcal/mol. This is slightly higher than the theoretical "anomeric effect" of 3.03 kcal/mol.

The "anomeric effects", bond lengths, and stabilizing ($n - \sigma^*$) *and* ($n - \pi^*$) *orbital interactions in* XCH_2YH *molecules.* — Table IV shows the optimized C–X and C–Y bond lengths in the 60 and 180° conformations of FCH_2OH, $ClCH_2OH$, FCH_2SH, and $ClCH_2SH$. In each instance, the C–X bond is longer, and the C–Y bond is shorter, at 60° than at 180°. In addition, the C–O bond of $ClCH_2OH$ is shorter at 60° than the C–O bond of FCH_2OH in the same conformation. These

TABLE V

THE TOTAL ENERGY DIFFERENCE AND THE ORBITAL INTERACTION-ENERGY DIFFERENCE BETWEEN THE 60 AND 180° CONFORMATIONS OF XCH_2YH ($X = F, Cl; Y = O, S$)

X	*Y*	$\Delta E_T{}^{a,c}$	$\Delta\Sigma\Delta e_{ij}{}^{b,c}$
F	O	3.03	4.06
Cl	O	4.44	5.53
F	S	2.64	2.14
Cl	S	2.65	2.81

[a] (Total energy at 180°) − (Total energy at 60°). [b] $[(n - \sigma^*) + (n - \pi^*)]$ at 180° − $[(n - \sigma^*) + (n - \pi^*)]$ at 60°. [c] In kcal/mol.

trends in the bond lengths are in agreement with the experimental findings on six-membered ring compounds, discussed earlier.

Table V lists the theoretically computed "anomeric effects" in these four molecules, together with the "anomeric effects" predicted by the difference in $\{(n - \sigma^*) + (n - \pi^*)\}$ at 60 and at 180°. The theoretically computed "anomeric effects" parallel the experimental findings: the effect is greater for $X = Cl$ than for $X = F$; it is also greater for $Y = O$ than for $Y = S$. Exactly the same trends are present in the stabilizing orbital interactions associated with the nonbonding lone-pair of Y. It may be concluded that not only the "anomeric effect" exhibited by a given molecule, but also the different "anomeric effects" exhibited by different molecules, are reproduced by the stabilizing lone-pair–antibonding orbital interaction.

The analysis presented here is completely general, and is not restricted to molecules in which X is a heteroatom such as halogen. This generality is illustrated by the results obtained for ethanol and ethanethiol ($X = CH_3$). In CH_3CH_2YH ($Y = O, S$), both the gauche and the anti conformations are minima on the rotational potential-energy surface. In the CH_3CH_2 fragment, two π^* orbitals are present, in addition to the σ^*_{CC} orbital, as shown here. Thus, in the 180° conformation of CH_3CH_2YH, the total $(n_y - \pi^*)$ interaction energy includes both the $(n_y - \pi^*_{CC})$ and the $(n_y - \pi^*_{CC}{}')$ interactions. As shown in Table VI, consideration of the $(n_z - \sigma^*_{CC})$ and $(n_y - \pi^*)$ interactions reproduces the fact that the difference in the stabilities of the gauche and anti conformations of CH_3CH_2YH is small.


σ^*_{CC}


π^*_{CC}


$\pi^{*\prime}_{CC}$

In terms of the lone-pair–antibonding orbital interactions examined thus far, the differences in the "anomeric effects" exhibited by the different XCH_2YH molecules may be understood upon inspection of Fig. 8 and Table VII. Fig. 8 shows the calculated n_Y, σ^*_{CX} and π^*_{CX} levels as a function of X and Y, and Table VII lists the $(n - \sigma^*)$ and $(n - \pi^*)$ interactions at their maximum values (90 and 180°, respectively). The $(n - \pi^*)$ interaction varies only slightly as X is varied. On the other hand,

TABLE VI

THE TOTAL-ENERGY DIFFERENCE AND THE ORBITAL INTERACTION-ENERGY DIFFERENCE BETWEEN THE GAUCHE AND ANTI CONFORMATIONS OF CH_3CH_2YH ($Y = O, S$)

Y	$\Delta E_T{}^{a,c}$	$\Delta\Sigma\Delta e_{ij}{}^{b,c}$
O	−0.34	−0.11
S	−0.23	−0.02

[a,b,c] See footnotes to Table V.

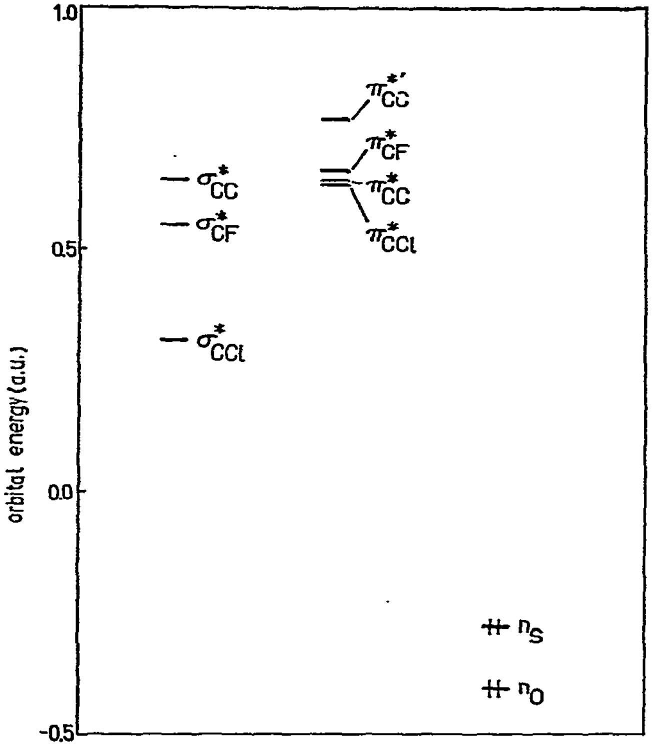


Fig. 8. The energies of n_Y, $\sigma^*_{CH_2X}$, and $\pi^*_{CH_2X}$ in various XCH_2YH molecules.

TABLE VII

MAXIMUM VALUES OF THE (n — σ^*)[a] AND THE (n — π^*)[b] STABILIZING INTERACTIONS[c] IN XCH_2YH MOLECULES

X	*Y*	*(n — σ^*)*	*(n — π^*)*
F	O	−12.66	−7.56
Cl	O	−14.48	−7.43
CH_3	O	−7.08	−7.19
F	S	−5.58	−2.77
Cl	S	−6.56	−2.81
CH_3	S	−2.80	−2.77

[a]Maximum occurs at 90°. [b]Maximum occurs at 180°. [c]In kcal/mol.

the (n — σ^*) interaction varies significantly, and in the same direction as the "anomeric effect" (Cl > F > CH_3).

For X = CH_3, the (n — σ^*) and (n — π^*) interaction energies are nearly the same. When X $\neq$ CH_3, the (n — σ^*) interaction is greater than the (n — π^*) interaction. In other words, when X is a heteroatom, the XCH_2 group favors σ-conjugation over π-conjugation, thereby leading to the preference for the gauche conformation.

As expected[36], Fig. 8 shows the sulfur lone-pair to lie higher than the lone pair of oxygen. According to Eq. *3*, the magnitude of a two orbital–two electron stabilizing-interaction is proportional to the square of the overlap and inversely proportional to the energy gap between the occupied and unoccupied orbitals. If overlap effects were ignored[32], the application of Fig. 8 to the problem would lead to the prediction of a larger anomeric effect for Y = S than for Y = O, because n_S lies higher than n_O. This is not correct. Because of the difference in the C–Y bond lengths, the overlap of σ^*_{CX} or π^*_{CX} to n_S is less than the overlap to n_O, and the "anomeric effect" is greater for Y = O, as this factor dominates*. It is, therefore, dangerous to assess the relative magnitudes of similar interactions in different molecules (such as, XCH_2OH *vs* XCH_2SH) in terms of the energy gap alone. However, within the series XCH_2OH or XCH_2SH, the trends in the interaction energies can be understood in terms of the energy gap. For example, when X is a heteroatom, the σ^* level lies lower than the π^* level, and the $(n - \sigma^*)$ interaction is larger than the $(n - \pi^*)$ interaction. Since the level ordering is $\sigma^*_{CCl} < \sigma^*_{CF} < \sigma^*_{CC}$, the $(n - \sigma^*)$ stabilizing interaction decreases in the direction $(n - \sigma^*_{CCl}) > (n - \sigma^*_{CF}) > (n - \sigma^*_{CC})$.

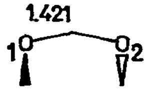
Methanediol: the relationship between the anomeric effect and the exo-anomeric effect. — It has been suggested[15b,24b] that the nature of the anomeric effect in free sugars and aldopyranosides (such as, **4** $\rightleftarrows$ **5**; X = OH, OR) may be different from that in aldopyranosyl halides, because its magnitude is less and because the C-1–O-1 bonds of **4** are short, but C-1–halogen bonds are long.

In the preceding sections of this paper it has been shown that the quantitative PMO analysis is applicable not only to molecules of the type XCH_2X, in which the C–X bonds are short, but also to molecules of the type XCH_2YH, in which C–Y is short and C–X is long. In addition, an analysis based upon the fragmentations $XCH_2 \cdots X$ or $XCH_2 \cdots YH$ leads to a satisfactory rationalization of the behavior of both systems. In view of these various observations, it seems unreasonable that XCH_2OH (X = OH) should require a fundamentally different kind of discussion.

Jeffrey, Pople, and Radom[23b] have carried out extensive calculations on methanediol as a model for the anomeric effect in free sugars, including optimization of the C–O bond lengths of various conformations. Their results are shown in structures **8**–**10**. Since their calculated C–O bond-length in CH_3OH is 1.437 Å, it is evident that the shortening of both C–O bonds has been reproduced. Inspection of molecular models reveals that **8** corresponds, in a pyranosyl compound to **11**, **9** corresponds to **12** or **13**, and **10** corresponds to **14**. The relative stabilities are **8** > **9** > **10**. This correlation suggests that **11** should represent the lowest energy conformation containing an axial C-1–OH bond, that **12** should represent the lowest energy conformation containing an equatorial C-1–OH bond, and that **13** should represent a higher energy conformation possessing an axial C-1–OH bond. The

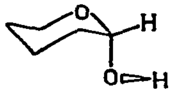
---

*The calculated $(n - \sigma^*)$ overlap in the 90° conformation is 0.1094 in FCH_2OH, and 0.0905 in FCH_2SH. In CH_3CH_2OH and CH_3CH_2SH, the values are 0.0856 and 0.0648.

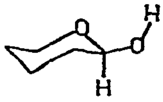


8

≡

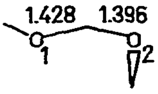


11



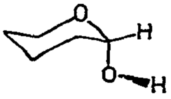
12

≡

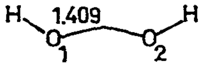


9

≡

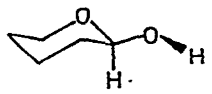


13



10

≡



14

anomeric effect in the six-membered ring is given by the energy difference between **11** and **12**. The energy difference between **11** and **13** corresponds to the *exo*-anomeric effect[37]. Therefore in methanediol, the energy difference between **8** and **9** corresponds both to the "anomeric effect" and the "*exo*-anomeric effect".

The computations on **8**–**10** were performed by using the geometries of the previous study. The PMO analysis was performed according to the fragmentation $HOCH_2 \cdots OH$. Because the X and Y groups are the same in this molecule, the

TABLE VIII

QUANTITATIVE PMO ANALYSIS OF THE CONFORMERS OF METHANEDIOL

Molecule	*Stabilization energy*[a]				*Total energy*[d]	*(rel)*[a]
	O-*1*[b]	O-*2*[c]	*Total*	*(rel)*		
8	−11.17	−11.17	−22.34	(0.0)	−187.38520	(0.0)
9	−7.64	−12.62	−20.26	(2.08)	−187.38075	(2.79)
10	−8.36	−8.36	−16.72	(5.62)	−187.37445	(6.75)

[a] In kcal/mol. [b] Stabilization energy associated with n of O-1. [c] Stabilization energy associated with n of O-2. [d] In atomic units.

TABLE IX

COMPUTED TOTAL ENERGIES AND BOND LENGTHS OF VARIOUS CONFORMATIONS OF AMINOMETHANOL

	Conformation	*C–O (Å)*	*C–N (Å)*	*Total energy (a.u.)*
	60[a] (gauche[b])			−167.85856
17	60 (syn)	1.425	1.484	−167.86340
18	60 (app)	1.439	1.477	−167.86230
	90 (app)	1.441	1.476	−167.86185
	90 (syn)	1.430	1.484	−167.86046
15	180 (app)	1.440	1.464	−167.86363
16	180 (gauche)			−167.85746

[a]Refers to the dihedral angle between the C–N and O–H bonds. [b]Refers to the dihedral angle between the nitrogen lone-pair and the C–O bond.

n — σ^* and n — π^* interactions associated with *both* oxygen atoms have to be taken into account, that is, the total interaction energy is the result of HO-1 ··· CH_2O-2-H *and* HO-1-CH_2 ··· O-2-H*. Table VIII summarizes the results. The calculated "anomeric" and "*exo*-anomeric effects" are 2.8 kcal/mol, smaller than the "anomeric effect" in FCH_2OH. The difference in the $\{(n - \sigma^*) + (n - \pi^*)\}$ interactions in **8** and **9** is 2.2 kcal/mol, also lower than the corresponding difference in FCH_2OH.

It may be concluded that the origin of the "anomeric effect" of the hydroxyl group is not fundamentally different from that of halogen. The same conclusion is reached upon comparison of the orbital interactions in CH_3OH and $CH_2(OH)_2$ with those of CH_3F and CH_2F_2, already discussed. The calculated (n — π^*) orbital interaction in CH_3OH is —8.08 kcal/mol. In conformation **9** of $CH_2(OH)_2$, the (n — π^*) interaction associated with O-1 is —7.64 kcal/mol; in conformation **10** of $CH_2(OH)_2$, the (n — π^*) interactions associated with O-1 and O-2 are —8.36 kcal/mol. On the other hand, the $\{(n - \pi^*) + (n - \sigma^*)\}$ interactions in **8** and **9** are —11.17 and —12.62 kcal/mol, respectively, indicating that the CH_2OH group, as with the CH_2F group, favors σ-type stabilization over π-type stabilization.

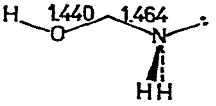
Aminomethanol. The reverse anomeric effect. — The computations on aminomethanol were performed for the 60, 90, and 180° conformations, where these values refer to the dihedral angle between the C–N and O–H bonds. The carbon valence-

---

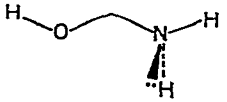
*In view of the nature of the analysis in this case, one might wonder why, in the general case of XCH_2YH, the analysis should be based entirely upon the fragmentation XCH_2 ··· YH, and not upon X ··· CH_2YH. The qualitative justification of this choice is that we are emphasizing interactions associated with the highest-lying lone-pair orbital and, in most cases, this will be the lone pair of Y. The calculated conformational stabilities associated with the n — σ^* and n — π^* interactions for the fragmentation X ··· CH_2YH do not vary in the same way as the total energy. Thus, in FCH_2OH, a PMO analysis based upon this fragmentation mode predicts the 60° conformation to be 1.11 kcal/mol *less* stable than the 180° conformation. In $ClCH_2OH$, the 60° conformation is predicted to be 0.59 kcal/mol less stable than the 180° conformation. This prediction does not change our conclusions; in fact, taking these interactions into account brings the agreement between the interaction-energy differences and the total-energy differences closer.

angles and the C–H, O–H, and N–H bond-lengths were constrained to the tetrahedral, 1.09, 0.96, and 1.014 Å, respectively. At each of the three dihedral angles, the torsional angle about the C–N bond, the angles at nitrogen and the C–N and O–H bond lengths were optimized. Table IX summarizes the principal results.

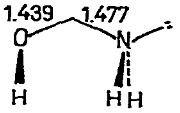
The global minimum is **15**, the 180° conformation in which the lone pair of the pyramidal nitrogen is antiperiplanar (*app*) to the C–O bond. In this conformation, the C–O bond is longer, and the C–N bond is shorter than the C–O and C–N bonds of methanol (1.433 Å) and methylamine (1.486 Å), respectively, computed with the same basis set. The 60° conformation with an *app* nitrogen lone-pair (**18**) is 0.8 kcal/mol less stable than **17**, the 60° conformation in which the nitrogen lone pair and the O–H bond have a *syn*-1,3-relationship. The preferential stabilization of this structure is probably an artifact of the model system H_2NCH_2OH associated with the presence of an internal O-H ··· N hydrogen-bond. The effect of the *app* lone pair upon the bond lengths of **17** and **18** is noteworthy: in **18**, the C–O bond is long and the C–N bond is short; in **17**, both bonds are short.



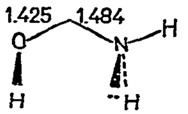
15
(180-app)



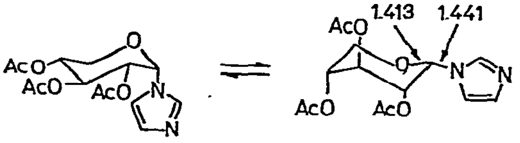
16



18
(60-app)



17



19

The quantitative PMO analysis was performed upon the 60°-*app* and the 180°-*app* conformations **18** and **15**, for the two fragmentation modes $HO \cdots CH_2NH_2$ and $HOCH_2 \cdots NH_2$, and is summarized in Table X. This Table reveals the origin

TABLE X

STABILIZING ORBITAL-INTERACTIONS IN THE 60-*APP* AND 180-*APP* CONFORMATIONS OF AMINOMETHANOL

Conformation	*Fragmentation mode*	*Interaction energy*[a]
60-*app*[b]	$HO \cdots CH_2NH_2$	−8.89
	$HOCH_2 \cdots NH_2$	−5.69
180-*app*[c,d]	$HO \cdots CH_2NH_2$	−7.17
	$HOCH_2 \cdots NH_2$	−6.36

[a]In kcal/mol. [b]Total energy −167.86230 a.u. [c]Total energy −167.86363 a.u. [d]The 180-*app* conformation is 0.00133 a.u. (0.83 kcal/mol) more stable than the 60-*app* conformation.

of the difference between X = halogen in XCH_2OH, leading to a gauche preference, and X = NH_2 in XCH_2OH, leading to an anti preference.

In the fragmentation $HO \cdots CH_2NH_2$, the anti conformation is found to be 1.72 kcal/mol less stable than the gauche, in disagreement with the trend in the total energies. In the fragmentation $HOCH_2 \cdots NH_2$, the anti conformation is found to be 0.67 kcal/mol more stable than the gauche. This is very close to the 0.8 kcal/mol difference in the total energies. In the case of X = NH_2, the appropriate fragmentation scheme is, therefore, $X \cdots CH_2OH$, in contrast to X = halogen, where the appropriate fragmentation is $XCH_2 \cdots OH$. The reason for this is that, when X = NH_2, *the lone pair on nitrogen is higher-lying than the lone pair on oxygen**, and it makes the dominant contribution to the HOMO of the molecule. The notion that the conformational behavior of XCH_2YH molecules may be discussed quantitatively in terms of the stabilizing orbital-interactions that contribute to the HOMO of the molecule is thus seen to be valid for all X examined in the present work.

An important feature of the "reverse anomeric effect" exhibited by aminomethanol is that, in the most stable conformation of this molecule, it is the C–X bond which is short and the C–Y bond which is long. This is a consequence of the dominant effect of the charge transfer from the occupied orbital of X to the antibonding orbitals of CH_2YH. It can be expected that this reversal of the bond-length trends associated with the anomeric effect will be a general property of molecules that exhibit the reverse anomeric effect.

For example, a reverse anomeric effect is observed in aldopyranosyl azides[38] and, in tri-*O*-acetyl-α-D-arabinopyranosyl azide[39], the C-1–N bond length is 1.449 Å, *shorter* than the C–N bond length of CH_3N_3 (1.47 Å ref. 40), and the C-1–O bond length is 1.422 Å, *longer* than the 1.413 Å observed[17] in methyl α-D-glucopyranoside.

---

*The energy of the oxygen lone-pair orbital, from fragmentation $H_2NCH_2 \cdots OH$, is −0.3991 and −0.3984 a.u., in the 60 and 180° conformations, respectively. The energy of the nitrogen lone-pair orbital, from fragmentation $H_2N \cdots CH_2OH$, is −0.3376 and −0.3316 a.u., in the 60 and 180° conformations. Based on these numbers, the lone pair on nitrogen lies higher by 40.3 kcal/mol.

TABLE XI

COMPUTED NET ATOMIC CHARGES (q_i) IN THE FLUOROMETHANES AND IN VARIOUS CONFORMATIONS OF METHANEDIOL

Molecule	q_C	q_F	q_{O-1}	q_{O-2}
CH_3F	−0.050	−0.149		
CH_2F_2	+0.154	−0.146		
CHF_3	+0.352	−0.152		
CF_4	+0.541	−0.135		
8	+0.114		−0.318	−0.318
9	+0.121		−0.314	−0.305
10	+0.124		−0.300	−0.300

In **19**, the C-1–N bond length is 1.441 Å, and the C-1–O bond length is 1.413 Å in the $^1C_4$ conformation.

The bond lengths. — It has been suggested throughout this paper that the conformational effects exhibited by XCH_2YH and XCH_2X molecules are closely connected to the trends in the C–X and C–Y bond lengths. The following specific questions may now be asked: (*i*) what is the origin of the progressive shortening in C–X bond lengths as the number of X substituents is increased?; (*2*) why are the bond lengths in methanediol different in the three conformations **8–10**, and why are the bonds longer in the most stable conformation **10** than in **8**, the least stable conformation?; (*iii*) why is C–X long and C–Y short when X is halogen, and why are the trends reversed when X is amino?

Table XI shows the net atomic charges at carbon and at fluorine in the fluoromethanes, and at carbon and oxygen in the three conformations of methanediol. In the fluoromethanes, the charge on fluorine is approximately the same in each instance, but the carbon atom becomes progressively more positive as the number of fluorine atoms is increased. As an increase in the ionic bond-order of a bond A–B is accompanied by a shortening of this bond[41], the present results indicate that the variations in the bond lengths of the polyhalogenomethanes are caused by coulombic effects[42].

On the other hand, the data for the methanediol conformations suggest that the bond-length variations from conformation to conformation in a CH_2X_2 molecule are the result of some additional effect superposed upon the coulombic effects, because the net atomic charges are virtually the same in the three conformations. The principal difference between **8** and **10** is that the latter contains only n — π^* stabilizing interactions between OH and CH_2OH and, as discussed earlier in Table VII, these interactions are inherently weaker than the n — σ^* interactions that are present, in addition to the n — π^* interactions, in conformation **8**. As the most stable conformation is the one that maximizes the stabilizing orbital-interactions, **8** is more stable than **10**. When the molecule is constrained to an unfavorable conformation, as in **10**, the stabilizing orbital-interactions can be increased only by an increase in the overlap between the interacting orbitals, that is, n_O and $\pi^*_{CH_2OH}$, and this increase can only be achieved by a decrease in the C–O bond length.

In terms of this argument, a *decrease* in the C–X and C–Y bond lengths of XCH_2YH molecules would be expected as a result of the coulombic effect associated with the attachment of two electron-withdrawing groups to the same carbon atom. The *increase* in the C–X bond length, in molecules that exhibit the anomeric effect, and in the C–Y bond length, in molecules that exhibit the reverse anomeric effect when X and Y are different, are regarded as the result of an overriding influence in these cases of the charge transfer to (that is, population of) XCH_2 and CH_2YH antibonding orbitals, respectively.

Summary and conclusions. — The principal results of the present work may be summarized as follows: (*1*) ab-initio SCF–MO theory at the STO–3G level reproduces the trends in the rotational behavior and in the C–X and C–Y bond lengths of XCH_2YH molecules in which X = CH_3, OH, F, Cl, NH_2, and Y = O,S; this extends considerably the earlier computations by Jeffrey, Pople, and Radom[23b] on methanediol and methoxymethanol[43]; (*2*) a quantitative analysis of the results in terms of the stabilizing orbital-interactions between the lone-pair orbital of Y and the antibonding orbitals of XCH_2, in the cases of the anomeric effect and the exo-anomeric effect, and in terms of the stabilizing orbital-interactions between the highest occupied orbital of X and the antibonding orbitals of CH_2YH, in the case of the reverse anomeric effect, reproduces not only the rotational behavior of a given molecule but also the trends from molecule to molecule; (*3*) the choice of fragmentation mode for the quantitative PMO analysis is governed by whichever of X or Y has the higher-lying highest occupied orbital, because this orbital and the antibonding orbitals with which it interacts make a dominant contribution to the HOMO of the molecule, and the behavior of the HOMO parallels the behavior of the total energy; (*4*) the stabilizing orbital-interactions computed by the quantitative PMO procedure can be connected quantitatively to the concept of double bond–no bond resonance, so that a simple and convenient classical description of the problem may be utilized with confidence; (*5*) the conformational behavior of XCH_2YH molecules and the trends in the polyfluoromethanes may also be discussed quantitatively in terms of *destabilizing* orbital-interactions; however, it is more difficult to convey this fact in a simple way; (*6*) the present results, which are based upon a CMO analysis of the ab-initio wavefunctions, cannot be connected quantitatively to interpretations based upon LMO analysis of the results; whether the trends from molecule to molecule can be discussed quantitatively in terms of the notion of equivalent lone-pairs, as has been done[23a] for FCH_2OH, will have to await a *localized* molecular-orbital analysis of the ab-initio wavefunctions; (*7*) the C–X and C–Y bond lengths in XCH_2YH and XCH_2X molecules may be understood in terms of a combination of coulombic effects and the principle of maximization of overlap between fragments.

ACKNOWLEDGMENTS

We thank the National Research Council of Canada and the donors of the

Petroleum Research Fund, administered by the American Chemical Society, for support of this research. One of us (D.J.M.) also thanks NRCC for the award of a Scholarship.

REFERENCES

1 L. O. Brockway, *J. Phys. Chem.*, 41 (1937) 185–195.
2 L. Pauling, *The Nature of the Chemical Bond*, Cornell University Press, Ithaca, N.Y., 3rd ed., 1960, pp. 314–316.
3 N. Muller, *J. Am. Chem. Soc.*, 75 (1953) 860–863; D. B. McLay and C. R. Mann, *Can. J. Phys.*, 40 (1962) 61–73.
4 C. R. Patrick, *Adv. Fluorine Chem.*, 2 (1961) 10.
5 J. Hine, *J. Am. Chem. Soc.*, 85 (1963) 3239–3244.
6 Lord Todd and J. W. Cornforth, *Biogr. Mem. Fellows Soc.*, 22 (1976) 465–468.
7 A. Burawoy, *Trans. Faraday Soc.*, 39 (1943) 79–90; 40 (1944) 537–544.
8 W. Hückel, *Structural Chemistry of Inorganic Compounds*, Vol. I, Elsevier, New York, 1950, pp. 431–437.
9 A. D. Walsh, *J. Am. Chem. Soc.*, 68 (1946) 2408–2409.
10 J. F. A. Williams, *Trans. Faraday Soc.*, 57 (1961) 2089–2098; *Tetrahedron*, 18 (1962) 1477–1486.
11 E. A. C. Lucken, *J. Chem. Soc.*, *III*, (1959) 2954–2960; see also, L. Guibé, J. Augé, S. David, and O. Eisenstein, *J. Chem. Phys.*, 58 (1973) 5579–5583; Z. Ardalan and E. A. C. Lucken, *Helv. Chim. Acta*, 56 (1973) 1715–1719; Z. de Weck-Ardalan, E. A. C. Lucken, and J. Weber, *J. Mol. Struct.*, 32 (1976) 101–110; M. Sabir, J. A. S. Smith, O. Riobé, A. Lebouc, J. Delaunay, and J. Cousseau, *J. Chem. Soc. Chem. Commun.*, (1977) 19–20.
12 R. Livingston, *J. Phys. Chem.*, 57 (1953) 496–501.
13 H. M. Berman, S. S. C. Chu, and G. A. Jeffrey, *Science*, 157 (1967) 1576–1577.
14 (*a*) C. L. Jungius, *Z. Phys. Chem.*, 52 (1905) 97; (*b*) J. T. Edward, *Chem. Ind. (London)*, (1955) 1102–1104; (*c*) R. U. Lemieux, in P. de Mayo (Ed.), *Molecular Rearrangements*, Interscience, New York, 1964, p. 709.
15 (*a*) N. de Wolf, C. Romers, and C. Altona, *Acta Crystallogr.*, 22 (1967) 715–719; (*b*) C. Romers, C. Altona, H. R. Buys, and E. Havinga, *Top. Stereochem.*, 4 (1969) 39–97.
16 C. Altona, Ph.D. Thesis, University of Leiden, 1964.
17 (*a*) H. Paulsen, *Staerke*, 27 (1975) 397–405; (*b*) P. Luger, P. L. Durette, and H. Paulsen, *Chem. Ber.*, 107 (1974) 2615–2625.
18 N. S. Zefirov and N. M. Shekhtman, *Russ. Chem. Rev.*, 40 (1971) 315–329; C. B. Anderson and D. T. Sepp, *J. Org. Chem.*, 32 (1967) 607–611; *Tetrahedron*, 24 (1968) 1707–1716; E. L. Eliel and C. A. Giza, *J. Org. Chem.*, 33 (1968) 3754–3758; W. F. Bailey and E. L. Eliel, *J. Am. Chem. Soc.*, 96 (1974) 1798–1806.
19 G. L. Bendazzoli, F. Bernardi, and P. Palmieri, *J. Chem. Soc., Faraday Trans. 2*, 69 (1973) 579–584; P. Palmieri and A. M. Mirri, *J. Mol. Struct.*, 37 (1977) 164–167.
20 J. Tesse, C. Glacet, and D. Couturier, *C. R. Acad. Sci. Ser. C*, 280 (1975) 1525–1528; G. Ricart, C. Glacet, and D. Couturier, *ibid.*, 284 (1977) 319–322.
21 J. F. Stoddart, *Stereochemistry of Carbohydrates*. Wiley–Interscience, New York, 1971, pp. 81–87.
22 P. Deslongchamps, *Tetrahedron*, 31 (1975) 2463–2490.
23 (*a*) S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc.*, *B*, (1971) 136–145; (*b*) G. A. Jeffrey, J. A. Pople, and L. Radom, *Carbohydr. Res.*, 25 (1972) 117–131; (*c*) D. G. Gorenstein, J. B. Findlay, B. A. Luxon, and D. Kar, *J. Am. Chem. Soc.*, 99 (1977) 3473–3479; (*d*) S. Wolfe, L. M. Tel, W. J. Haines, M. A. Robb, and I. G. Csizmadia, *ibid.*, 95 (1973) 4863–4870.
24 I. Tvaroska and T. Bleha, *J. Mol. Struct.*, 24 (1975) 249–259; *Tetrahedron Lett.*, (1975) 249–252.
25 D. A. Matthews and G. D. Stucky, *J. Am. Chem. Soc.*, 93 (1971) 5954–5959.
26 S. David, O. Eisenstein, W. J. Hehre, L. Salem, and R. Hoffmann, *J. Am. Chem. Soc.*, 95 (1973) 3806–3807.
27 D. W. Sweigart and D. W. Turner, *J. Am. Chem. Soc.*, 94 (1972) 5599–5603.
28 S. Wolfe, *Acc. Chem. Res.*, 5 (1972) 102–111.

29 E. L. ELIEL, N. L. ALLINGER, S. J. ANGYAL, AND G. A. MORRISON, *Conformational Analysis*, Interscience, New York, 1965, pp. 127, 345, 468 and 486.
30 See, *inter alia*: R. HOFFMANN, *Acc. Chem. Res.*, 4 (1971) 1–9; W. J. HEHRE, *ibid.*, 8 (1975) 369–376; B. M. GIMARC, *ibid.*, 7 (1974) 384–392; O. EISENSTEIN, N. T. ANH, Y. JEAN, A. DEVAQUET, J. CANTACUZENE, AND L. SALEM, *Tetrahedron*, 30 (1974) 1717–1723; G. BADDELEY, *Tetrahedron Lett.*, (1973) 1645–1648.
31 (*a*) B. M. DEB, *J. Am. Chem. Soc.*, 96 (1974) 2030–2044; (*b*) M.-H. WHANGBO AND S. WOLFE, *Can. J. Chem.*, 54 (1976) 963–968.
32 R. C. BINGHAM, *J. Am. Chem. Soc.*, 97 (1975) 6743–6746.
33 M.-H. WHANGBO, H. B. SCHLEGEL, AND S. WOLFE, *J. Am. Chem. Soc.*, 99 (1977) 1296–1304.
34 W. L. JORGENSEN AND L. SALEM, *The Organic Chemist's Book of Orbitals*, Academic Press, New York, 1973; I. FLEMING, *Frontier Orbitals and Organic Chemical Reactions*, Wiley, London, 1976.
35 R. HOFFMANN, L. RADOM, J. A. POPLE, P. v. R. SCHLEYER, W. J. HEHRE, AND L. SALEM, *J. Am. Chem. Soc.*, 94 (1972) 6221–6223.
36 F. BERNARDI, N. D. EPIOTIS, W. CHERRY, H. B. SCHLEGEL, M.-H. WHANGBO, AND S. WOLFE, *J. Am. Chem. Soc.*, 98 (1976) 469–478.
37 R. U. LEMIEUX, A. A. PAVIA, J. C. MARTIN, AND K. A. WATANABE, *Can. J. Chem.*, 47 (1969) 4427–4439; R. U. LEMIEUX AND S. KOTO, *Tetrahedron*, 30 (1974) 1933–1944; H. PAULSEN, Z. GYÖRGYDEÁK, AND M. FRIEDMANN, *Chem. Ber.*, 107 (1974) 1568–1578.
38 H. PAULSEN, Z. GYÖRGYDEÁK, AND M. FRIEDMANN, *Chem. Ber.*, 107 (1974) 1590–1613. For earlier examples of the reverse anomeric effect, see R. U. LEMIEUX AND A. R. MORGAN, *Can. J. Chem.*, 43 (1965) 2205–2213.
39 P. LUGER AND H. PAULSEN, *Chem. Ber.*, 107 (1974) 1579–1589.
40 H. J. M. BOWEN ET AL. (Eds.), *Tables of Interatomic Distances and Configuration in Molecules and Ions*, Special Publication No. 11, The Chemical Society, London, 1958.
41 M.-H. WHANGBO, S. WOLFE, AND F. BERNARDI, *Can. J. Chem.*, 53 (1975) 3040–3043.
42 G. MODENA, in S. PATAI (Ed.), *The Chemistry of the Carbon–Halogen Bond*, Wiley, New York, 1973.
43 G. A. JEFFREY, J. A. POPLE, AND L. RADOM, *Carbohydr. Res.*, 38 (1974) 81–95.