

# LONE PAIRS IN ORGANIC MOLECULES: ENERGETIC AND ORIENTATIONAL NON-EQUIVALENCE

## STEREOCHEMICAL CONSEQUENCES

O. EISENSTEIN, NGUYEN TRONG ANH, Y. JEAN, A. DEVAQUET, J. CANTACUZÈNE<sup>a</sup> and L. SALEM\*  
Laboratoire de Chimie Théorique,† Université de Paris-Sud, 91405-Orsay, France

(Received 28 January 1974)

### INTRODUCTION

#### The energetic non-equivalence of lone pairs

The conventional picture of the lone pairs of water or hydrogen fluoride is one with two (or three) localized orbitals pointing in tetrahedral directions on the oxygen or fluorine atom (Fig 1). These localized  $sp^3$  hybrid lone pairs give the proper total electron density of each molecule. They are therefore extremely convenient in discussing electrostatic properties such as dipole moments, H-bonding, etc.



Fig 1. Equivalent, tetrahedral lone-pairs.

However, it has been known for a long time<sup>1</sup> that the four lone-pair electrons of water, or the six lone-pair electrons of fluorine, are not equivalent. In both water<sup>2</sup> and hydrogen fluoride<sup>3</sup> there are two different potentials for the ionization of lone-pair electrons. Each ionization limit terminates a series of Rydberg excitations.<sup>2</sup> This *energetic non-equivalence* of lone-pairs has long been confirmed by molecular orbital calculations. In  $\text{OH}_2$  there is a relatively deep  $\sigma$  lone-pair orbital and a high-lying  $\pi$  lone-pair-orbital.<sup>4</sup> In hydrogen fluoride there is also a low-lying  $\sigma$  lone-pair and two degenerate  $\pi$  lone-pairs.<sup>3</sup> These energetically non-equivalent lone-pair orbitals are shown in Fig 2. The energy difference between  $\pi$  and  $\sigma$  lone-pairs is 2.1 eV in water<sup>2a</sup> and 4 eV in hydrogen fluoride.<sup>3</sup>

The non-equivalence of lone-pairs is an important factor, not only in spectroscopy, but also for *any property which involves interactions between lone pairs and other components (bonds, etc) of the molecule*. When, for instance, a lone-pair orbital interacts with an empty bond orbital, the *energy gap* between the interacting orbitals is a crucial factor;‡ therefore  $\pi$  lone pairs should interact more efficiently. Thus it is essential to distinguish between  $\sigma$  and  $\pi$  lone pairs in studying conformational preferences.

#### The directional non-equivalence of lone pairs

Separate consideration of  $\sigma$  and  $\pi$  lone-pair orbitals from the energetic viewpoint requires that we also assign to each lone pair the proper  $\sigma$  and  $\pi$  directions, rather than the conventional tetrahedral directions. It is convenient, in fact, to label the lone pairs according to their local  $\sigma$  and  $\pi$  character and to their orientation. For ether O or thio-ether S, the labels  $\sigma$  and  $\pi$  are sufficiently explicit. For halogens the directions of the two  $\pi$ -type lone pairs must be distinguished: an additional directional label is useful. These labels, some of which were first introduced by Jorgensen and Salem,<sup>6</sup> are

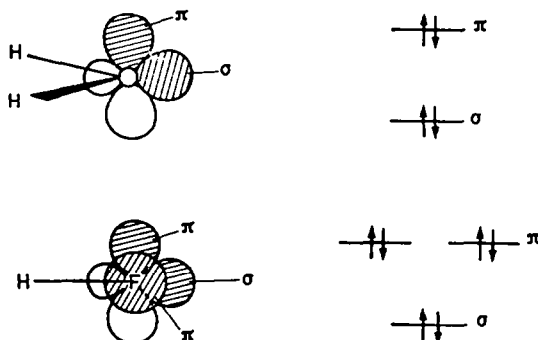


Fig 2. Energetically non-equivalent lone-pairs in  $\text{OH}_2$  and FH.

<sup>a</sup> CERCOA, CNRS 2-8 rue Henri Dunant-94320-Thiais.

†The Laboratoire de Chimie Théorique is also part of the Laboratoire de Physico-Chimie des Rayonnements, associated with the CNRS.

‡This is a well-known result of perturbation theory.

shown in Fig 3 on the model systems fluoromethane and fluorocyclohexane. In the acyclic case the labels are the same as those commonly used for a methylene group which would be placed at the position of the lone-pair orbital:  $\pi$  bisected and  $\pi$  eclipsed. In cyclic molecules the label first involves, if necessary, the nature, a (axial) or e (equatorial) of the halogen. Then the  $\pi$ -type lone pairs are distinguished as *peri*, if they are parallel to the periphery of the ring, or *hemi*, if they are directed along the major ring diagonal which bisects the ring. Thus the equatorial *peri* lone pair will be labelled (e) *peri*. The  $\sigma$ -type lone pairs are labelled respectively (a) $\sigma$  or (e) $\sigma$ .

We will now show how the energetic and directional non-equivalence of lone pairs can be applied to the interpretation of conformational properties. We first consider a simple model case which allows us to classify the different types of interaction and their electronic consequences.

### The $XCH_2$ -F molecule

*Interactions involving the fluorine lone pairs.* The pioneering attempt at quantitative analysis of the interaction between a lone pair p orbital and an empty, low-lying CX bond orbital, is probably that of Lucken.<sup>7</sup> Here we present a qualitative analysis of the interactions in  $XCH_2F$ , which draws heavily on that for hyperconjugation in  $XCH_2-CH_2^-$  anions.<sup>8</sup> Consider first the nonsubstituted fluoromethane molecule. The eclipsed and bisected  $\pi$  lone pairs of fluorine can each interact with a filled  $\pi_{CH_3}$  and an empty  $\pi_{CH_3}^*$  orbital on the methyl group.<sup>6</sup> The first interaction is 4-electron destabilizing while the second interaction is 2-electron stabilizing. If the hydrogen atom in the symmetry plane is replaced by a substituent X in such a

manner as to preserve the plane of symmetry (X=halogen,  $CH_3$ ,  $C=R$  eclipsed with F, etc), these interactions are modified in the following manner (Fig 4).

(1) First the *change in electronegativity* due to the substitution  $H \rightarrow X$  modifies the energy of the in-plane  $\pi_{CH_3}$ ,  $\pi_{CH_3}^*$  orbitals which have a significant amplitude on the hydrogen atom which is substituted. If X is more electronegative than H, both these orbitals are lowered. These are precisely the orbitals which interact with the eclipsed lone-pair  $\pi_e$  of fluorine. The 2-electron interaction between  $\pi_e$  and  $\pi_{CH_3X}^*$ , which are now close in energy, tends to become predominant, all the more so because  $\pi_{CH_3X}^*$  is strongly localized on carbon.<sup>8</sup> If X is more electropositive than H, the substituted methyl  $\pi$  orbitals rise in energy, and the 4-electron interaction between  $\pi_e$  and  $\pi_{CH_3X}$  now predominates, both because of the small energy gap and because  $\pi_{CH_3X}$  is mainly localized on carbon.

Thus the inductive effect of X is stabilizing for the eclipsed lone-pair of fluorine if X is electronegative, destabilizing for this same lone-pair if X is electropositive.

One consequence of the interactions involving the eclipsed lone-pair of fluorine is that it *tilts* slightly in the XCF plane,<sup>6</sup> and does not remain orthogonal to the CF bond. For electropositive X the upper lobe tends to tilt toward X by 2° or 3°. The tilt occurs in the opposite direction, also by a few degrees, for electronegative X (X =  $NH_3^+$ ). If X is a halogen, however, the hyperconjugative effect dominates and forces the tilt toward X. Rationalization of these phenomena is under study, in collaboration with R. Hoffman.

(2) In most cases X carries additional  $\pi$ -type orbitals, perpendicular to the plane of symmetry,

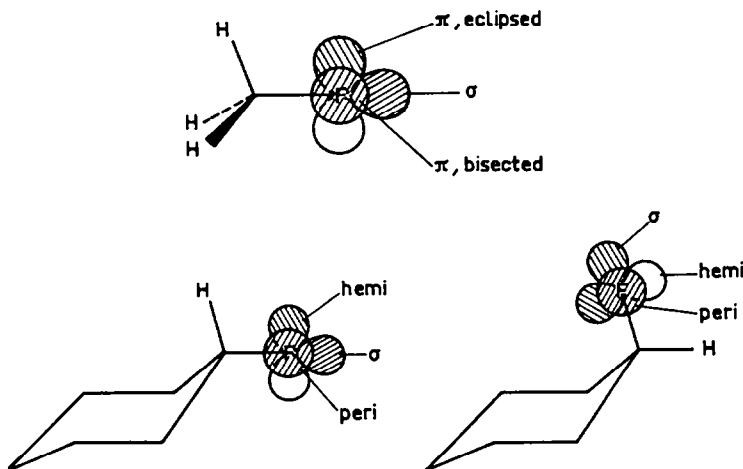
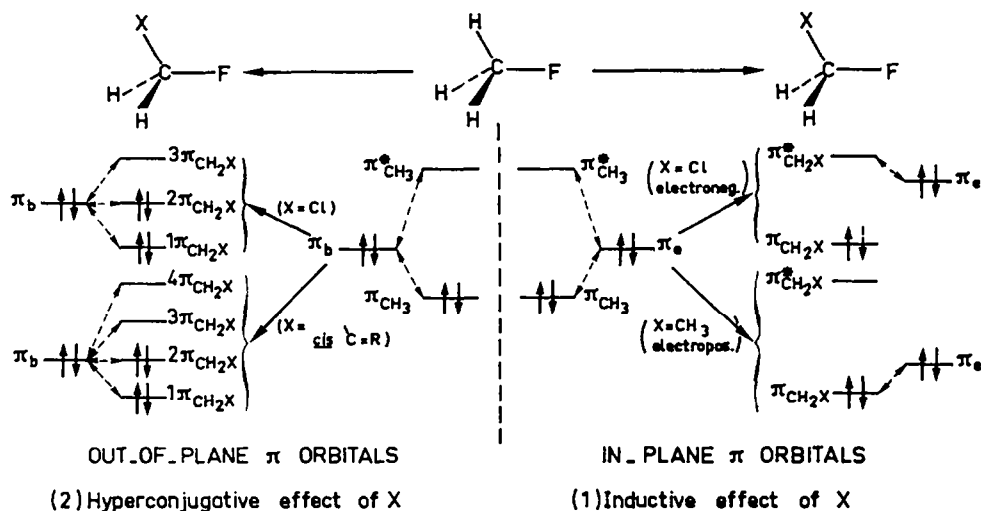


Fig 3. Labels for lone pairs.

Fig 4. Orbital interactions in X-CH<sub>2</sub>-F.

which can conjugate with the corresponding  $\pi_{CH_2}$  and  $\pi_{CH_2}^*$  orbitals of the central methylene group and with the bisected lone-pair orbital  $\pi_b$  of the fluorine atom. If X is a halogen atom, it brings one such  $\pi$  orbital with two electrons. The  $\pi$  framework of the XCH<sub>2</sub> moiety then becomes isoelectronic with an allyl anion. Thus the  $\pi_b$  lone-pair orbital interacts with *three*  $\pi$  orbitals. From the energetic point of view the major interaction should be the destabilizing interaction with the filled  $2\pi_{CH_2X}$  orbital. However  $2\pi_{CH_2X}$  is localized mainly on X, while the empty  $3\pi_{CH_2X}$  orbital, admittedly energetically further from  $\pi_b$ , has a much larger amplitude on carbon. Thus both the  $\pi_b \leftrightarrow 2\pi_{CH_2X}$  and  $\pi_b \leftrightarrow 3\pi_{CH_2X}$  interactions should be considered. If on the other hand X is a C=R double bond, it adds both a  $\pi$  orbital and a  $\pi^*$  orbital and 2 electrons to the CH<sub>2</sub>  $\pi$  system. The XCH<sub>2</sub> moiety becomes isoelectronic with butadiene. The  $\pi_b$  lone-pair orbital now interacts with *four*  $\pi$  orbitals. The two energetically nearest ones, first  $2\pi_{CH_2X}$  and then  $3\pi_{CH_2X}$ , have only small amplitudes on the carbon atom adjacent to fluorine. Thus it may be necessary in certain cases to include all four interactions with  $\pi_b$ .

To summarize, the conjugative or "hyperconjugative" influence of X appears to include a delicate balance of destabilizing and stabilizing interactions for the bisected lone-pair of fluorine. This is true whether X is a halogen or a double-bonded group.

We now turn to the application of these themes to some simple conformational problems.

#### The CHO-CH<sub>2</sub>-F molecule

The conformation of acyclic 3-halo ketones.<sup>†</sup> Let us first consider how the lone pairs of fluorine interact with a carbonyl group (X=CHO). We compare the *cis* (0°) form and perpendicular (90°) form—chosen preferentially to the 120° form because orbital effects show up more clearly—of fluoro-acetaldehyde (Fig 5). In the *cis* conformation  $n_b$  on fluorine interacts with the carbonyl  $\pi$

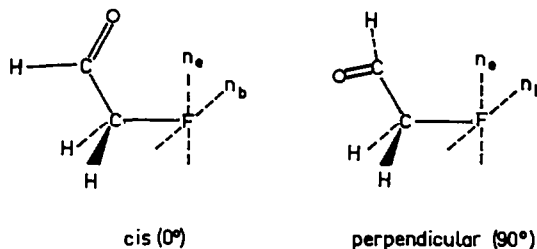


Fig 5. Conformations of fluoroacetaldehyde.

orbitals (Fig 4 (2)) while  $n_c$  interacts with the lone pair on oxygen. In the perpendicular conformation the roles are essentially reversed: now  $n_c$  on fluorine interacts with the carbonyl  $\pi$  orbitals while  $n_b$  interacts mainly with the oxygen lone pair.

Careful analysis of our *ab initio* calculations confirm that consideration must be given to the interactions between fluorine and both the carbonyl  $\pi$  orbitals and the oxygen lone pair.

The first interactions are shown schematically below in Fig 6. The interaction with  $n_b$  in the *cis* conformer resembles case (2), Fig 4, for X = C=R. (For simplicity we have restricted consideration to  $\pi_{CO}$  and  $\pi_{CO}^*$ , which correspond essentially to  $2\pi_{CH_2X}$  and  $3\pi_{CH_2X}$  in Fig 4). The interactions can be

<sup>†</sup>For a similar interpretation of the conformation of propenes, see Ref 9.

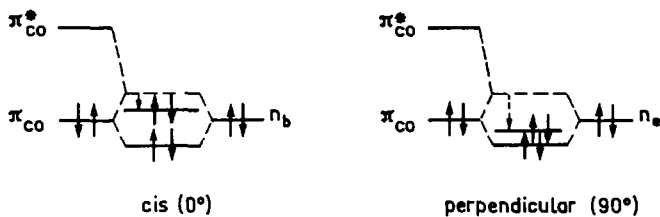


Fig 6. Orbital interactions in fluoroacetaldehyde.

decomposed into two effects:

(1) The  $n_F \leftrightarrow \pi_{CO}$  repulsive interaction which gives two levels, one slightly above the  $(\pi, n)$  pair, one slightly below the  $(\pi, n)$  pair. The  $n_b \leftrightarrow \pi_{CO}$  overlap ( $5.7 \cdot 10^{-3}$ ) and  $n_c \leftrightarrow \pi_{CO}$  overlap ( $1.3 \cdot 10^{-2}$ ) are both very small so that there is no significant difference between the top energy levels of *cis* and perpendicular conformations after this first step.

(2) The  $n_F \leftrightarrow \pi_{CO}^*$  attractive interaction, which can be considered to operate between  $\pi_{CO}^*$  and the newly formed slightly antibonding combination of  $\pi_{CO}$  and  $n_F$  which is thereby lowered (dotted arrows). Since the energy gap is the same in both conformations, the relative strength of this interaction in the two conformers depends on the relative overlaps  $\pi_{CO}^*, n_b$  and  $\pi_{CO}^*, n_c$ . These overlaps are *very different*, as the reader will easily convince himself by examining a model and by remembering that  $\pi_{CO}^*$  is essentially localized on the carbon atom. The difference is illustrated below (Fig 7). The net result of the differential overlap illustrated in Fig 7 is a much larger stabilization by  $\pi_{CO}^*$  of the two top electrons in the perpendicular conformation. One can speak loosely of a "superjacent"<sup>10, 11</sup> interaction between a non-bonding pair and a low-lying empty orbital as providing a stabilization

to the perpendicular form. An equivalent viewpoint is to speak of donation from fluorine into the carbonyl group, or simply of hyperconjugation.

The other interactions, which are not illustrated in Fig 6, are:

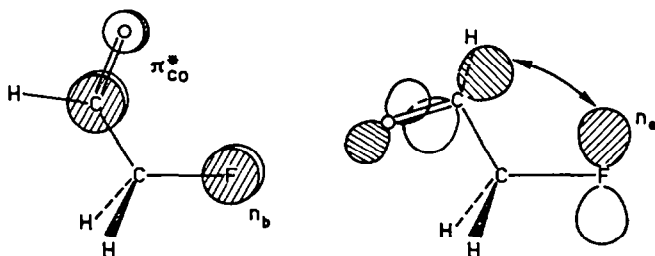
(3) The  $n_o \leftrightarrow n_c$  (*cis*) or  $n_o \leftrightarrow n_b$  (perpendicular) through-space lone pair  $\leftrightarrow$  lone pair repulsion. The relevant overlaps are very similar in the two conformations. Neither conformation seems to be favored by this effect.

(4) The interaction  $n_o \leftrightarrow n_c$  through bond,<sup>11†</sup> via the CC  $\sigma$  and CC  $\sigma^*$  orbitals. As shown qualitatively by Epiotis,<sup>9c, 12‡</sup> this through-bond interaction favors the *cis* conformation.

The relative energy of the two conformations will be determined by a balance between effect (2)—favoring perpendicular—and effect (4)—favoring *cis*. *Ab initio* calculations indicate *cis*-fluoroacetaldehyde to be 0.76 Kcal/mole more stable than the perpendicular form (in acetaldehyde this energy difference is calculated to be 0.54 Kcal/mole). *Gauche* ( $120^\circ$ ) fluoroacetaldehyde, however, is calculated to be 0.04 Kcal/mole below the *cis* form.

For experimental energy differences in chloro- and bromo-acetaldehyde (see Ref 13).

The *trend* in relative energies, however, as

Fig 7. Comparison of overlaps between fluorine lone-pair and carbonyl  $\pi_{CO}^*$  orbital.

†There is no contribution from  $n_b$  to through-bond interactions, since  $n_b$  is essentially orthogonal to  $\sigma_{CC}$  and  $\sigma_{CC}^*$ .

‡Epiotis' mechanism assumes that the conformation with the larger through-space splitting gains the larger stabilization *via* interaction with  $\sigma^*$  and that this stabilization *more than compensates* for its larger initial repulsion energy. Here the  $n_o \leftrightarrow n_c$  overlap is larger in the *cis* form.

fluorine is replaced by a more electronegative halogen atom, should be essentially determined by the variation of the superjacent interaction (2). As the lone-pair energy rises in the series fluorine, chlorine, bromine, iodine, etc the stabilization of the perpendicular and *gauche* forms is expected to increase *via* a smaller energy gap. As concerns effect (4), the competing through-bond interactions are expected to increase in parallel fashion, but

with little differential effect, particularly because of the high energy of  $\sigma_{CC}^*$ .

### The 2-fluoro-cyclohexanone molecule

*The conformation of cyclic haloketones.*<sup>14</sup> Let us now consider how the previous situation is modified in a cyclic ketone such as cyclohexanone. We compare the cyclohexanone equatorially substituted by a fluorine atom (1) to that axially substituted by a fluorine atom (2). Conformation 1 is analogous to the *cis* acyclic conformation, while 2 corresponds to the perpendicular acyclic conformation.

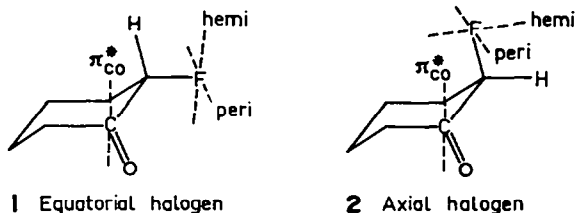


Fig 8. Conformations of fluoro-1-cyclohexanone.

The dotted lines on fluorine indicate the direction of the "peri" and "hemi" lone pairs—before interaction with the carbonyl group. Similarly the dotted line on the carbonyl carbon atom indicates the direction of the  $\pi_{CO}^*$  orbital. Clearly in 2 the *peri* lone-pair orbital of the halogen points directly at, and comes very close to, this empty carbonyl orbital.† With a much larger  $n_F$ ,  $\pi_{CO}^*$  overlap (Fig 9) the superjacent stabilization of the fluorine lone-pair should be significantly larger in 2 than in 1. In other words there is better donation from fluorine into the empty orbital of the carbonyl group. The effect, and the corresponding *axial* preference for the halogen competing with its natural *equatorial* preference should increase in the series F, Cl, Br, I, as has indeed been observed by Cantacuzène.<sup>14</sup> The

previously offered explanation<sup>14</sup> for this effect—donation from the  $\sigma_{CF}$  orbital into the  $\pi_{CO}^*$  orbital, although related, seems less likely because of the very low energy of the  $\sigma_{CF}$  bond orbital and the much larger energy gap with  $\pi_{CO}^*$ .

### The 1-chloro tetrahydropyran molecule

*The anomeric effect.* In this section we present a case where the energetic non-equivalence of the two oxygen lone-pairs, in a ring, leads to conformational preference for an electronegative substituent on carbon adjacent to the oxygen. The *anomeric effect*<sup>15</sup> is the preference of axial over equatorial C<sub>1</sub>

electronegative substituents in pyranose rings. Altona suggested<sup>16</sup> that donation from the axial lone pair of the ring oxygen into the C<sub>1</sub>X antibonding orbital stabilizes the axial conformation. It can be shown<sup>10</sup> that, if due account is made for the different energies of the two oxygen lone pairs, their interaction with the low-lying  $\sigma_{CX}^*$  orbitals leads naturally to the preference for an axial X ligand.

The two competing conformations are shown below (Fig 10) together with a Newman projection showing the relative orientation of oxygen lone-pairs. Restricting ourselves to the superjacent interactions between the two oxygen lone-pairs and the empty  $\sigma_{CX}^*$  and  $\sigma_{CH}^*$  orbitals, we obtain the interaction diagrams of Fig 11. Since calculations

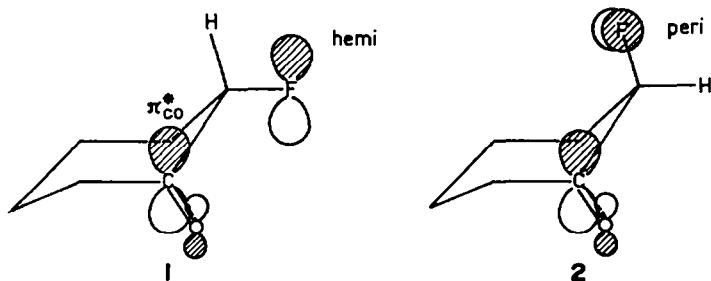


Fig 9. Comparison of overlaps between fluorine lone-pairs and carbonyl  $\pi^*$  orbital.

†In fact  $\pi_{CO}^*$  points in between  $n_{peri}$  and  $n_{hemi}$  of the fluorine atom. By analogy with the acyclic cases, one can construct an eclipsed combination of the *peri* and *hemi* lone pairs which is directed, along the CC bond, right at the  $\pi_{CO}^*$  lobe.

show the overlaps involved for  $n_F$  in both conformations to be very similar (also for  $n_O$ ), the most stabilizing interactions are those with the smallest energy gap. Simple mathematics show that the X-axial case, with one small gap and one large gap,

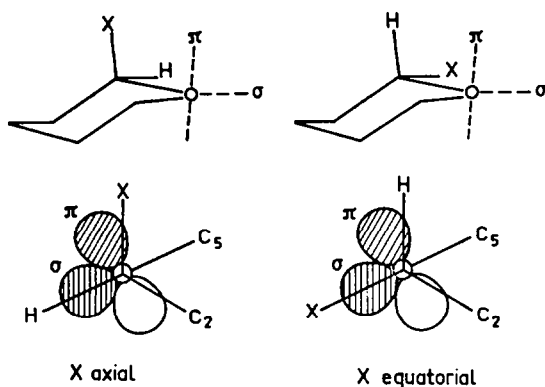


Fig 10. Conformations of 1-substituted tetrahydropyrans.

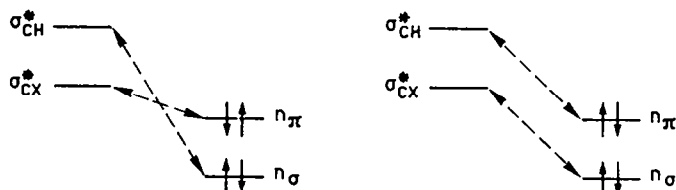


Fig 11. Comparison of superjacent interactions in halo-substituted pyranose rings. (Left: X axial; right: X equatorial)

has a larger stabilization than the X-equatorial case. The order of magnitude calculated<sup>10</sup> for the differential stabilization (3 kcal/mole) compares well with the experimental energy difference (2.7 kcal/mole)<sup>16b</sup> for X=Cl. The decrease in conformational preference with increasing solvent polarity is nicely interpreted here by an increase in the energy gaps due to a lowering of the oxygen lone-pair levels.

#### CONCLUSIONS

It is clear that we have singled out one phenomenon, namely the 2-electron stabilizing interaction between energetically and orientationally non-equivalent lone-pairs and neighboring low-lying empty orbitals. In a few cases we have also invoked the 4-electron exclusion repulsion with filled adjacent orbitals. Other effects certainly intervene in conformational properties: electrostatic dipole-dipole interactions, steric interactions,

†It has not always been clearly stated in the literature as to whether electron-electron interactions, postulated in the interpretation of conformational preferences, are purely Coulomb repulsions or also include exchange repulsion due to overlap between adjacent electron pairs. However Gillespie [*J. Chem. Ed.* **47**, 18 (1970)] did invoke the Pauli exclusion principle. Klaus Muller [*Helv. Chim. Acta* **53**, 11120 (1970)] was first to delineate clearly the exchange contribution between adjacent lone pairs which he and A. Eschenmoser labeled "conjugative destabilization".

electron-electron repulsions,<sup>†</sup> or subtle balances between electron-electron repulsion and nuclear-electron attraction.<sup>17</sup> The "superjacent" effect studied here finds its basis on undisputed photoelectron spectroscopic results which prove the energetic non-equivalence of ether and halogen lone-pairs. The application of this non-equivalence to preferential interactions with low-lying empty orbitals on neighboring groups has been shown here to allow at least a consistent interpretation of various conformational problems.

#### REFERENCES

- <sup>1</sup>R. S. Mulliken, *Phys. Rev.* **43**, 297 (1933); <sup>2</sup>J. Lennard-Jones and J. A. Pople, *Proc. Roy. Soc. A* **202**, 166 (1950); <sup>3</sup>J. A. Pople, *Ibid.* **A202**, 323 (1950); <sup>4</sup>A. D. Walsh, *J. Chem. Soc.* 2260 (1953)
- <sup>5</sup>C. R. Brundle and D. W. Turner, *Proc. Roy. Soc. A* **307**, 27 (1968); M. I. Al-Joboury and D. W. Turner, *J. Chem. Soc. B* 373 (1967)
- <sup>6</sup>H. J. Lempka and W. C. Price, *J. Chem. Phys.* **48**, 1875 (1968); H. J. Lempka, T. R. Passmore and W. C. Price, *Proc. Roy. Soc. A* **304**, 53 (1968)
- <sup>7</sup>F. O. Ellison and H. Shull, *J. Chem. Phys.* **23**, 2348 (1955); T. H. Dunning, R. M. Pitzer and S. Aung, *Ibid.* **57**, 5044 (1972)
- <sup>8</sup>P. E. Cade and W. M. Huo, *Ibid.* **47**, 614 (1967)
- <sup>9</sup>W. L. Jorgensen and L. Salem, *The Organic Chemist's Book of Orbitals* Part 1. Academic Press, (1973)
- <sup>10</sup>E. A. C. Lucken, *J. Chem. Soc.* 2954 (1959) (in particular the Appendix)
- <sup>11</sup>R. Hoffmann, L. Radom, J. A. Pople, P. v. R. Schleyer, W. J. Hehre and L. Salem, *J. Am. Chem. Soc.* **94**, 6221 (1972); <sup>12</sup>For a more mathematical digression see: L. Salem, *6th Jerusalem Symposium on Chemical and Biochemical Reactivity* (1973) in press
- <sup>13</sup>J. P. Lowe, *J. Am. Chem. Soc.* **92**, 3799 (1970); <sup>14</sup>W. J. Hehre and L. Salem, *J. Chem. Soc. Chem. Comm.* 754 (1973); <sup>15</sup>N. D. Epiotis, D. Bjorkquist, L. Bjorkquist and S. Sarkanen, *J. Am. Chem. Soc.* **95**, 7558 (1973); <sup>16</sup>Nguyen Trong Anh, *L'actualité Chimique*, p. 9 (No. 1) (1974); <sup>17</sup>On  $\alpha$ -aminoketones, see C. C. Levin, R. Hoffman, W. J. Hehre and J. Hudec, *J. Chem. Soc. Perkin II* 201 (1973)
- <sup>18</sup>S. David, O. Eisenstein, W. J. Hehre, L. Salem and R. Hoffmann, *J. Am. Chem. Soc.* **95**, 3806 (1973)
- <sup>19</sup>R. Hoffmann, *Acc. Chem. Res.* **4**, 1 (1971)
- <sup>20</sup>N. D. Epiotis, *J. Am. Chem. Soc.* **95**, 3087 (1973)
- <sup>21</sup>G. J. Karabatsos and D. J. Fenoglio, *Top. Stereochem.* **5**, 167 (1970), in particular Table 1
- <sup>22</sup>J. Cantacuzène, R. Jantzen and D. Ricard, *Tetrahedron* **28**, 717 (1972)

- <sup>15a</sup>J. T. Edward, *Chem. & Ind.* 1102 (1955); <sup>b</sup>R. U. Lemieux and N. J. Chu, 133rd *National Meeting of the American Chemical Society* Abstract No. 31N, San Francisco, Calif. April (1958); <sup>c</sup>N. J. Chu, Ph.D. Thesis p. 97. University of Ottawa, 1959; <sup>d</sup>J. T. Edward, P. F. Morand and I. Puskas, *Can. J. Chem.* **39**, 2069 (1961); <sup>e</sup>R. U. Lemieux, *Molecular Rearrangements*, (Edited by P. de Mayo) Vol II, p. 709. Interscience, New York, N.Y. (1964); <sup>f</sup>R. U. Lemieux, *Pure and Appl. Chem.* **25**, 527 (1971); <sup>g</sup>H. Booth and R. U. Lemieux, *Can. J. Chem.* **49**, 777 (1971); <sup>h</sup>E. L. Eliel, *Accounts Chem. Res.* **3**, 1 (1970); <sup>i</sup>E. L. Eliel, *Angew. Chem. Int. Engl.* **11**, 739 (1972); <sup>j</sup>S. J. Angyal, *Ibid. Int. Ed. Engl.* **8**, 157 (1969); <sup>k</sup>J. C. Martin, *Ann. Chim.* (14) **6**, 205 (1971); <sup>l</sup>N. S. Zefirov and N. M. Shechtman, *Usp. Khim.* **40**, 593 (1971); <sup>m</sup>Y. A. Zhdanov, R. M. Minyaev and V. I. Minkin, *J. Mol. Structure* **16**, 357 (1973)
- <sup>16a</sup>C. Altona, Ph.D. Thesis p. 117. University of Leiden (1964); <sup>b</sup>C. Romers, C. Altona, H. R. Buys and E. Havinga, *Top. Stereochem.* **4**, 39 (1969), in particular pp. 73–77 and Fig 18; <sup>c</sup>for a similar effect in FCH<sub>2</sub>-OH, see L. Radom, W. J. Hehre and J. A. Pople, *J. Am. Chem. Soc.* **94**, 2371 (1972); <sup>d</sup>electron delocalization, dipole-dipole interactions, and steric effects have been considered together by G. A. Jeffrey, J. A. Pople, and L. Radom, *Carbohydr. Res.*, **25**, 117 (1972)
- <sup>17</sup>S. Wolfe, *Acc. Chem. Res.* **5**, 102 (1972); S. Wolfe, A. Rauk, L. M. Tel and I. G. Csizmadia, *J. Chem. Soc. B* 136 (1971)