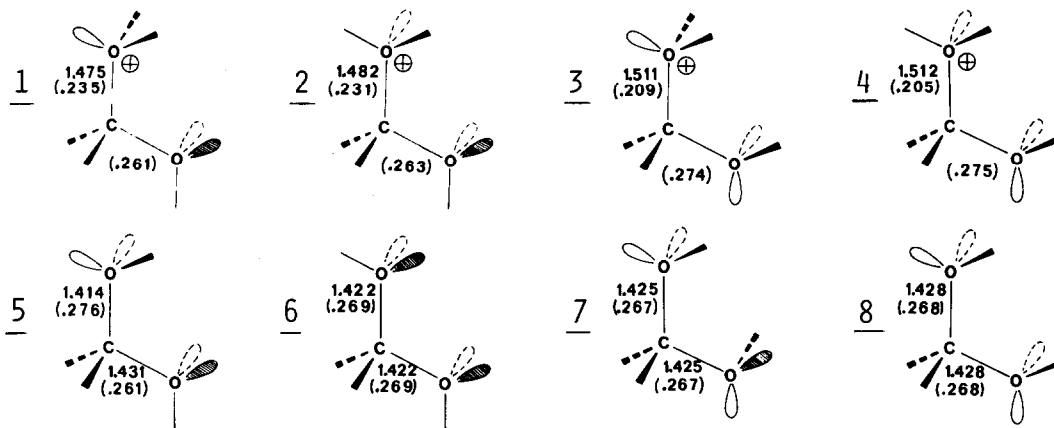


ACID CATALYZED HYDROLYSIS OF ACETALS AND ORTHOESTERS FACILITATED BY  
STEREOELECTRONIC EFFECTS. AN AB INITIO STUDY.

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Stereoelectronic control in the direction of cleavage in orthoesters, orthoamides, and acetals has been proposed by Deslongchamps: a C-O or C-N bond will be formed and cleaved the most selectively if the conformation of the molecule is such that the lone pair orbitals (lp's) on the other heteroatoms are antiperiplanar (app) to that bond [1]. We report here the results of ab initio calculations on four selected conformations of protonated dihydroxy-methanes  $\text{CH}_2(\text{OH})_2\text{H}^+$  1-4 which, when compared to the neutral species 5-8 (see also [2]) show the importance of the lp orientation on C-O<sup>+</sup> bond length (BL) and lability.



Optimization of the C-O<sup>+</sup> distances in 1-4 with C-OH=1.43 Å and of the C-O BL's in 5-8 has been performed at the STO-3G level [3], keeping all angles tetrahedral; the results are reported in the figure (in Å) together with the corresponding overlap populations (OP's, written in parenthesis). This has been followed by STO-431G calculations [3] using the optimized lengths. The following conclusions can be drawn from the theoretical results.

1) Protonation of the O oxygen in an O-C-O' fragment lengthens selectively the C-O bond ( $\Delta\text{BL} \sim 0.07 \text{ \AA}$ ,  $\Delta\text{OP} \sim -0.05 \text{ e}$ ). The C-O' bond shows on the average almost no OP variations.

2) These changes in BL's and OP's of the protonated C-O<sup>+</sup> bond show strong stereoelectronic conformational dependence and can amount to about half of the mean protonation effect

mentioned above (compare 1 and 4). The weakest C-O<sup>+</sup> bond has one app oxygen lp rather than one app O-H bond (compare 1 and 3, 2 and 4) and is found in a conformation where the O<sup>+</sup>lp is app to C-H rather than to C-OH (compare 1 and 2, 3 and 4). Clearly, the former requirement is the most important.

3) Comparison of the stereoelectronic effects in the protonated and in the neutral species respectively shows that the C-O<sup>+</sup> bond is weakened about three times more than the C-O bond by an app orientation of the O' lp; on the other hand, the C-O<sup>+</sup> bond is less strengthened than the C-O bond when the O<sup>+</sup> lp, rather than the O lp is app to the C-O' bond. In terms of the Deslongchamp's theory [1], protonation of the heteroatom of the leaving groups increases the "primary stereoelectronic control" and reduces the anomeric effect on the leaving group. These changes in the magnitude of the stereoelectronic effects on protonation agree with a qualitative perturbation scheme between an oxygen lp and the app  $\sigma_{CO}^*$  or  $\sigma_{CO}^{*+}$  bond orbital (see also [4]). Similar conclusions should hold with tetrahedral species containing other heteroatoms than oxygen (S,N,P ..) and also with other positive charges than proton surrounding one heteroatom.

The observation [1,5] or non observation [6] of stereoelectronic effects in the hydrolysis of acetals, ketals, or orthoesters is not a simple matter and depends on the whole reaction paths. The above results show indeed a substantial weakening of the C-O<sup>+</sup> bond in the conformations where the heteroatoms lone pairs are properly oriented. If the cleavage of that bond is the rate limiting step with an early transition state (TS), these orientational effects should also be operative in this TS and lead to rate enhancement or specific bond cleavage.

Further informations come from the relative energies calculated with the more reliable 4-31G basis set. They are 4.4, 10.9, 0.0 and 5.5 kcal/mole respectively for the species 5-8, and 0.0, 3.3, 6.3 and 1.4 kcal/mole respectively for the species 1-4. These results indicate first that, at least in the gas phase, the protonation energies can be conformation dependent (for example, protonation of 5 can lead to 1 or to 2 with protonation energies of 185.8 and 179.3 kcal/mole respectively). These energy results also suggest an alternative explanation for enhanced decomposition of specifically protonated species, for example in intramolecular or enzymatic catalysis. If the TS is late with a pronounced carbo-cation character, the most reactive protonated form should be that of highest energy, even if it does not correspond to the best stereoelectronic effects.

#### REFERENCES

- [1] P. Deslongchamps, *Heterocycles*, 1977, 7, 1271.
- [2] G.A. Jeffrey, J.A. Pople and L. Radom, *Carbohydr. Res.*, 1972, 25, 117.
- [3] Program GAUSSIAN 70, Q.C.P.E. n°236, University of Indiana, Bloomington, Indiana.
- [4] J.M. Lehn and G. Wipff, *Helv. Chim. Acta*, 1978, 61, 1274 and references cited therein.
- [5] O. Bouab, C. Moreau and M. Zeh Ako, *Tetrahedron Letters*, 1978, 1, 61.
- [6] S. Chandrasekhar and A.J. Kirby, *J.C.S. Chem. Commun.*, 1978, 171.

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