

ANOMERIC EFFECTS IN CARBOHYDRATES: NON EQUIVALENCE OF ENDOCYCLIC OXYGEN LONE PAIRS

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ABSTRACT.- In furanoses, a high selectivity of the axial orientation of substituents at the anomeric center is established statistically through crystallographic data studies of anomeric substructures and related hydrocarbons. This fact constitutes conclusive evidence of non equivalence of the endo oxygen lone pairs ($O = sp^2$).

We have shown (1) that the five-membered furanose ring orients polar substituents at the anomeric center in axial or pseudoaxial position much more strongly (95%) than the six-membered pyranose ring (56%). This stronger axial orientation can result from a relaxation of strain associated with the more flexible five-membered ring. It can also reveal that endocyclic oxygen is better able to contribute to a stabilizing conjugation process in five than in six-membered rings. If this is so, the torsion angle conditions for good orbital overlapping might be better fulfilled in five-membered rings.

This paper presents two types of structural arguments to support this hypothesis: the comparison with related hydrocarbons and the analysis of anomeric fragment bond lengths.

Axial orientation in pyranoses and furanoses and in related hydrocarbons

We sought to isolate the electronic effect of endocyclic oxygen from other contributing factors, e.g. ring strain or exocyclic oxygen effect (2), by comparing the axial orientation in alkoxytetrahydropyrans and alkoxytetrahydrofurans with that of the related hydrocarbons. The data, from the Cambridge Crystallographic Database, involves 208 acetoxy and methoxy tetrahydropyrans and tetrahydrofurans as well as 565 related cycloalkanes (Table I).

For the furanoses, axial or pseudoaxial selectivity is total, while for pyranoses, it is clear but limited (63-70%). We can isolate the effect of O endo oxygen on alkoxy group orientation by evaluating the ratio r of statistical percentages in the saccharides (Table I, line 2) and in the corresponding hydrocarbons (Table I, line 1) :

$$r = \frac{\text{statistical \% in saccharides}}{\text{statistical \% in related hydrocarbons}}$$

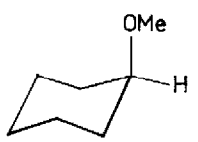
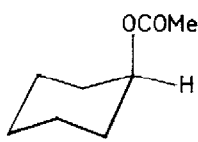
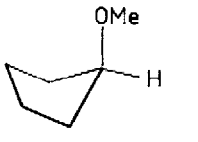
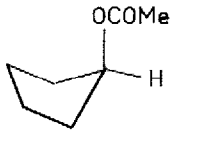
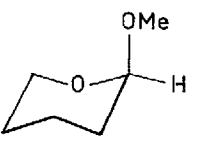
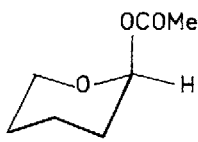
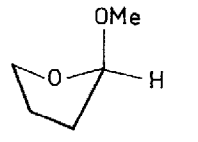
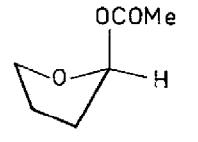
 48.3%	 37.1%	 46.2%	 25.7%
 69.8%	 62.5%	 100%	 100%

Table I : Statistical percentages of axial and pseudoaxial conformers in pyranoses, furanoses and related hydrocarbons.

This ratio shows clearly that the effect of the O endo oxygen is greater for the furanoses than for the pyranoses, i.e. 2.15 and 3.89 for five-membered rings and only 1.44 and 1.69 for six-membered rings. The O endo oxygen effect is also greater for the OCOMe substituent than for the OMe substituent ($r = 3.89$ and 1.69 respectively, as compared with $r = 2.15$ and 1.44).

These observations are related, first, to a better endoanomeric conjugation in furanoses than in pyranoses and, second, to the elimination of the competing exoanomeric effect for the OCOMe group (3), as shown by a study of the C-O lengths.

Endo, and exo bond lengths and n/σ^* stabilizing overlap

The r endo (3-4) and r exo (2-3) distances are the privileged witnesses of the n/σ^* conjugation between an oxygen lone pair orbital and the σ^* non-bonding orbitals of neighboring polar bonds. r exo $<$ r endo reveals a dominant exoanomeric effect, r endo $<$ r exo, a dominant endoanomeric effect (figure 1).

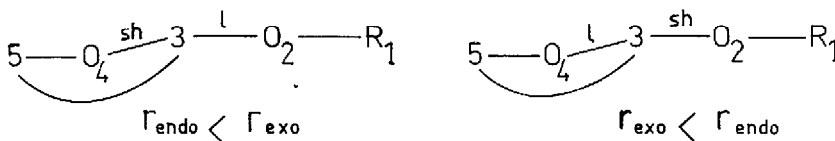


Figure 1. Dominant endoanomeric conjugation on left, dominant exoanomeric conjugation on right.

These distances are largely dependent on ϕ endo (2-3-4-5) and ϕ exo (1-2-3-4) torsion angles and on the nature of the alkoxy group:

. With the methoxy group, the exoanomeric effect is clearly seen in β pyranoses, when there is no possible endoanomeric effect ($\overline{\phi}$ endo $\approx 180^\circ$) and κ exo $\ll \kappa$ endo. The exo and endo effects coexist in α pyranoses ($\overline{\phi}$ endo = 65°) and in α' furanoses ($\overline{\phi}$ endo = 95°). The former is dominant, however, i.e. κ exo $< \kappa$ endo.

. With the acetoxy group, on the contrary, no exoanomeric effect is observed, as the n orbital concerned is, most probably, too low in energy (3). Thus, in β pyranoses, κ endo and κ exo adopt the same average value. In α pyranoses, ($\overline{\phi}$ endo = 63°) and in α' furanoses ($\overline{\phi}$ endo = 96°), the endo anomeric effect is particularly clear, with no competing exoanomeric effect. It is stronger in the α' furanoses than in the α pyranoses: the difference between κ exo and κ endo is 25% greater in this series.

sp^2 or sp^3 Oendo hybridization ?

Their investigations led FUCHS and co-workers to suggest, in certain cases, a non equivalence of the exo oxygen lone pairs (4). Moreover, the photoelectron spectra of tetrahydropyran, show a single narrow intense peak with no vibrational structure (5), i.e. a single peak that can be analyzed as an oxygen free pair: the hybridization would be sp^2 . Certain authors have discussed the anomeric effect as if sp^3 or sp^2 hybridizations were indifferent (6), but it is common practice to link this effect with an sp^3 scheme.

In fact, the nature of the hybridization is not indifferent, as the structural requirements for good overlapping distinguish clearly between the two hybridizations :

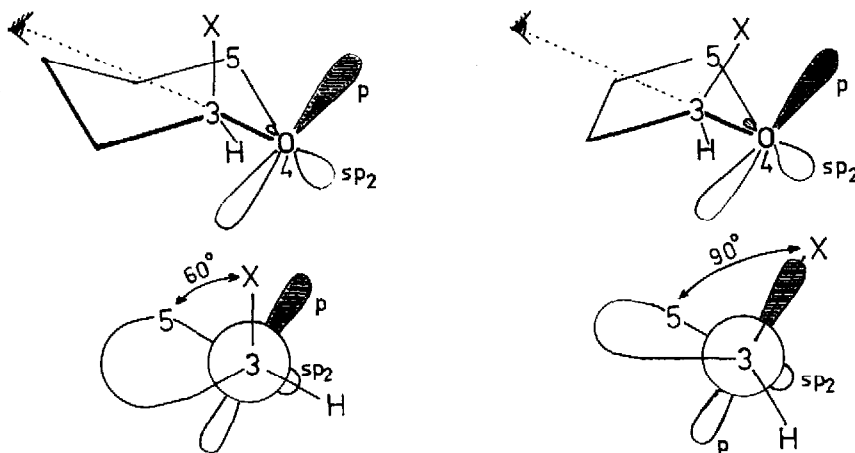


Figure 2. In furanoses (on the right) and unlike pyranoses (on the left), the torsion angles, naturally close to 90° , favor a good lone pair/ σ^* C-X overlapping for the sp^2 hybrid endo oxygen (X = OMe, OCOCH₃).

- in the hypothesis of an sp^3 hybridization, the ϕ endo torsion angles required for good n/σ^* overlapping, are close to 60° , and there is then agreement with the torsion angles, naturally close to 60° , of the rigid six-membered rings and disagreement with the torsion angles, naturally close to 90° , of the flexible five-membered rings. If this were so, the stabilizing conjugation should be better assured in the pyranoses than in the furanoses. In fact, this is contrary to our observations.
- indeed a better agreement is obtained between the natural torsion angles of furanoses (as compared with pyranoses) and those needed for good overlapping (fig. 2) if we hypothesize an sp^2 endo oxygen engaging its 2p pair in the conjugation. The enhancement of the endo-anomeric effect in furanoses, rather than pyranoses, thus solidly establishes the sp^2 hybridization of the endocyclic oxygen and extends the original suggestions made, for the exocyclic oxygen, by FUCHS and co-workers (4).

References

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