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This Week's Citation Classic

Jeffrey G A, Pople J A & Radom L. The application of *ab initio* molecular orbital theory to the anomeric effect. A comparison of theoretical predictions and experimental data on conformations and bond lengths in some pyranoses and methyl pyranosides. *Carbohyd. Res.* **25**:117-31, 1972. [Dept. Crystallogr., Univ. Pittsburgh and Dept. Chem., Carnegie-Mellon Univ., Pittsburgh, PA]

Ab initio molecular orbital calculations at the Hartree-Fock level with a 4-31G basis set on methanediol are used as a model for the hemi-acetal moiety of the pyranose sugars. The results, when extrapolated to the pyranoses, predict the energy and bond length differences associated with the ***anomeric*** and **exo*anomeric*** effects well-known in carbohydrate chemistry. [The ***SCI***® in-dicates that this paper has been cited over 135 times since 1972.]

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"This paper addresses a well-known phenomenon in organic chemistry known as the *anomeric* effect. The research was a collaboration between exponents of two physical sciences, crystallography and quantum mechanics. For this reason, the approach and the resulting insight into the electronic basis for the phenomenon was novel to carbohydrate chemistry. The crystallography was at the University of Pittsburgh and the quantum mechanics at Carnegie-Mellon University, separated by a ten minute walk. The fact that both senior authors spent their formative scientific years in England may also have helped to bridge the gap between their respective highly specialized disciplines.

"For some years, I had been trying to interest John Pople in trying to use quantum mechanics to predict and interpret some geometrical properties of carbohydrate molecules that I had been observing in their crystal structures. It was not until 1971 that the available computer power was such that meaningful theoretical calculations might be attempted on molecules which were large enough to simulate a significant part of a carbohydrate molecule.

Quantum mechanics is an 'art of approximation' and credibility is a key question. The crystallography provided precise data on differences in C-O bond lengths, which could be used as a test for the theory. The argument being that if the *ab initio* calculations on simpler model compounds could correctly reproduce these bond length differences, significant credence could be given to the extrapolation of the electronic structure thereby obtained for the larger molecules.

"The agreement between theory and experiment was better than expected in view of the simplicity of the model molecule, which was methanediol, and the approximations and assumptions separating the two disciplines. The theory provided insight with regard to the electronic structure associated with the *anomeric* effect. A special effort was made to explain this in terms which would be familiar to the carbohydrate chemist, which probably is the reason for the high citation index. This first model had 26 electrons. In 1974, computer technology had progressed to permit a more sophisticated model with 36 electrons, i.e., methoxymethanol, and in 1978 and 1979, we extended the calculations and comparisons to experiments with model compounds with 42 electrons. By 1982, we anticipate that computer technology will be such that we can compare the results of an *ab initio* M. O. geometry optimization, at the HF-4-31G level, of a complete pyranose molecule with the results of a neutron diffraction structure analysis at 10 K.

"This work probably contributed to the following recognition. G.A. Jeffrey: Hassel Lectureship, Norwegian Chemical Society, 1975; Pittsburgh Award of the American Chemical Society, 1979; Welch Foundation Lecturer, 1980; Claude S. Hudson Award of the American Chemical Society, 1980. J.A. Pople: Pittsburgh Award of the American Chemical Society, 1975; Linus Pauling Award of the American Chemical Society, 1977."