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J. Amer. Chem. Soc. **83:**4537-47, 1961.
[Dept. Chemistry, Univ. California, Los Angeles, CA]

Computation of the energies of hydrocarbon molecule conformations as a function of various geometric parameters is discussed and machine computation advanced as a means of coping with the enormous calculations necessary for their solution. New functions for non-bonded interactions are developed and compared with several previous ones. The cycloalkanes, $C_{5,7}$, are taken as examples, their conformations of minimum energy computed, and these energies compared with experimental values. [The *SCI*® indicates that this paper has been cited over 595 times since 1961.]

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"The success *of* this paper amuses me in a wry way, since I regard myself as a natural products and synthetic organic chemist, while this paper has identified me in many circles as a physical or theoretical chemist, dealing as it does with a mathematical approach to ascertaining the equilibrium conformation or shape of molecules. The paper was the beginning of a series of eight over 10 years, during which time I found myself trying to read mathematical papers and being asked to referee physical chemistry papers which often seemed out of my range. "When I arrived at UCLA as a new assistant professor, I developed an interest in sesquiterpenes. Those with six-membered rings behaved well according to Barton's recent conformational analysis. For the seven-membered ring cases, however, there was no workable conformational analysis. The only way to achieve it appeared to be by calculation of the preferred shapes of these molecules. To do this one had to calculate the energy strains associated with all kinds of deformation of the molecule, the sum of which then became the strain energy of the molecule. If these were calculated for a series of possible geometries one should find the preferred shape, of lowest energy. To do the calculations, however, required certain key parameters, constants relating molecular angles and distances to energy, and these were in short supply and of uncertain accuracy. On the other hand, the results one sought—the optimal molecular geometry and its relative energy —were known for some molecules. Hence, I set out to calculate these by varying the parameters to close in on the known results.

"I started this work with a pencil and a slide rule and was soon swamped in numbers since so many calculations were required. This must be why no one had tried before! Just at that time computers were coming into their own, so I took a one-day course in FORTRAN and was turned loose on the UCLA computer to make my own mistakes. When I was satisfied that I could sen-sibly calculate the energies and geometries of those known molecules, I had confidence to try the seven- to 10-membered rings, which I published, with equations and found parameters, in that first paper.

"The results made it possible to define the conformational analysis of these medium-ring molecules and the fascinating conformational changes they can undergo, entirely by calculation. Eventually a number of these were confirmed by experiment, in our laboratories and others, and a lot of other people began similar calculations on molecules of interest. Hence this paper opened a new field and accordingly was often cited.

"I have since left this theoretical chemistry to more sophisticated people and returned full-time to the synthesis of natural products. The pleasure of theoretical work seems not to have left, however, for I have recently returned to apply some mathematical logic to the area of systematizing organic synthesis design and expect to be happily back with the computers again soon."