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This Week's Citation Classic®

Allinger N L, Tribble M T, Miller M A & Wertz D H. Conformational analysis. LXIX. An improved force field for the calculation of the structures and energies of hydrocarbons. *J. Amer. Chem. Soc.* **93**:1637-48, 1971.
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The computational method familiarly known as "molecular mechanics" was further developed and applied to the determination of the molecular structures of a wide variety of hydrocarbons. Heats of formation and conformational energies were calculated. The accuracy and reliability of the method is high, and the method is very general and potentially of great use. [The *SCI*® indicates that this paper has been cited in over 450 publications.]

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Conformational analysis is a powerful tool for understanding much of organic chemistry, as shown by Barton in 1950.[1] The method was used in relatively simple cases to predict differences in reaction rates, equilibrium constants, and other quantities related to energies. The subject was summarized in a book in 1965[2] late in the "classical" (pre-computer) period. Our group published a series of papers beginning in 1959 illustrating the usefulness of computers in organic chemistry. Computers of the day had limited capabilities, and it was some years before this work had much impact. We published two earlier papers on molecular mechanics calculations[3,4] and outlined the power of the method. Our 1971 paper had a greater impact, however, because computers were then becoming more available, and this particular paper discussed not only simple molecules, but also details of the molecular structures of many complicated molecules as well. The method offered a quantitative extension of classical conformational analysis to molecules that were beyond the reach of older methods. Molecules studied in this paper included the cycloalkanes from C4 up to C12 and bicyclic and polycyclic systems such as diamantane, homoadamantane, binorbornane, and cubane. It was possible to determine geometries with experimental accuracies and to obtain energies that could be expressed as heats of formation or converted to conformational populations. It thus became possible to make more quantitative predictions than were possible earlier.

At this time, existing experimental methods for studying molecular structure were becoming more powerful, especially NMR and X-ray crystallography. These methods gave structures more accurately and quickly than previously possible. These were quantitative data that one would like to understand; such understanding was indeed available from molecular mechanics calculations.

This paper also contained a few other features worth noting. A method for energy minimization was discussed that was faster by a factor of 10 than the commonly used (deepest descent) earlier method. This made calculations on relatively large molecules (steroids) practical.

While this paper was one in a continuing series describing development of this method, it was selected for citation by many readers because the timing was such that many organic chemists then realized that this was a method they could indeed understand and utilize. The program for carrying out the calculations described in this paper was never widely distributed, mainly because the methods were so transient due to constant improvements. It was superseded two years later by the MM1 program,[5] and after another four years by MM2,[6] which are still distributed through the Quantum Chemistry Program Exchange. While the *programs* were probably cited much more than the *paper* under discussion, the early programs were never described in detail in a citable publication, and thus are not found as such in *Chemical Abstracts* or the *Science Citation Index*®. Hence the curious situation where the citations that actually appear most frequently in the literature are not abstracted by present literature compilations, and a paper that is cited less often becomes "most cited."

1. **Barton D H R.** The conformation of the steroid nucleus. *Experientia* 6:316-19. 1950. (Cited 250 times since 1955.)
2. **Eliel E L, Allinger N L, Morrison G A & Angyal S J.** *Conformational analysis.* New York: Wiley-Interscience. 1965. 524 p.
3. **Allinger N L, Miller M A, VanCatledge F A & Hirsch J A.** Conformational analysis. LVII. The calculation of the conformational structures of hydrocarbons by the Westheimer-Hendrickson-Wiberg method. *J. Amer. Chem. Soc.* **89**:4345-57, 1967. (Cited 165 times.)
4. **Allinger N L, Hirsch J A, Miller M A, Tyminski I J & VanCatledge F A.** Conformational analysis. LX. Improved calculations of the structures and energies of hydrocarbons by the Westheimer method. *J. Amer. Chem. Soc.* **90**:1199-210, 1968. (Cited 310 times.)
5. **Allinger N L.** MM1. *Quantum Chemistry Program Exchange* **11**:318. 1976. (Cited 75 times.)
6. **Allinger N L & Yuh Y.** MM2. *Quantum Chemistry Program Exchange* **12**:395. 1980. (Cited 200 times.)

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