

Dalling D K & Grant D M. Carbon-13 magnetic resonance. IX. The methylcyclohexanes. *J. Amer. Chem. Soc.* 89:6612-22, 1967.
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Carbon-13 nuclear magnetic resonance (NMR) data were acquired for 13 methylcyclohexanes. Chemical shift assignments were made and were analyzed using linear regression techniques. The successful fit demonstrated that ^{13}C NMR can be used to predict the geometrical and conformational features found in this class of alkanes. [The SCI[®] indicates that this paper has been cited in over 500 publications since 1967.]

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"In the spring of 1965, being a first-year chemistry graduate student, I selected David M. Grant, a young professor at the University of Utah, as my thesis director. He had just obtained an extensive set of methylcyclohexanes from the American Petroleum Institute and was desirous to extend the previous ^{13}C nuclear magnetic resonance (NMR) studies made in his group on the alkanes¹ and methylbenzenes² to these conformationally important compounds.

"Today, most chemists, having access to a modern NMR spectrometer, often with pulsed, Fourier transform capabilities, would consider it most unusual that a full summer was required to obtain ^{13}C NMR data for a dozen compounds. At that time, resonance peaks were located by sweeping the magnetic field continuously through the spectrum, while simultaneously adjusting and reading the frequency of a less than stable proton decoupler. The decoupler frequency for each peak was laboriously determined by plotting peak height versus decoupler setting. Only then could the chemical shift be calculated from the proton shift and the carbon transmitter frequency. The same

data could be acquired now in a single day, utilizing a spectrometer under computer control.

"In the absence of a ^{13}C NMR data base, the resonances could not be readily identified with specific carbon positions. Hence, for assignment purposes the methylcyclohexanes were divided into three classes: 1) those having a highly favored conformation, 2) those averaging between conformers of equal energy, and 3) the intermediate cases having conformations of similar, but unequal, energies. Initially, assignments were made for the first class by analyzing symmetry and multiplicity characteristics and by finding similar chemical shifts in molecules having common environments. Ultimately, almost all of the chemical shifts were assigned unambiguously. The data were then subjected to least-squares, linear regression analysis, in order to refine the approximate predictive parameters developed in the assignment process. Five positional and four geometric parameters proved adequate to predict the chemical shifts within a standard deviation of 0.5 ppm, which is less than two per cent of the observed range.

"Why has this paper become one of the 'most-cited' papers? Although NMR had been known since the late 1940s, only in the 1960s did it leave the realm of physics to become firmly established in the chemistry laboratory. In 1965, due to sensitivity limitations which restricted samples to neat liquids and concentrated solutions, high resolution ^{13}C NMR was being practiced in only a handful of research laboratories worldwide. This paper took a set of conformationally well-characterized compounds and demonstrated for the first time that all of the significant geometrical features could be predicted using a small number of chemical shift parameters. It also documented clearly the large through-space, steric effect which occurs when otherwise separated molecular moieties are brought into close proximity. These seminal results turned out to be directly applicable to a wide variety of related organic systems, thus stimulating the adoption of ^{13}C NMR as a routine analytical tool in the standard organic laboratory. Recent books have been devoted solely to the topic of ^{13}C NMR."³⁻⁵

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3. Stothers J B. *Carbon-13 NMR spectroscopy*. New York: Academic Press, 1972. 559 p.
4. Wehrli F W & Wirthlin T. *Interpretation of carbon-13 NMR spectra*. London: Heyden and Son Ltd., 1976. 310 p.
5. Levy G C, ed. *Topics in carbon-13 NMR spectroscopy*. New York: Wiley, 1979. 3 vols.