

Connolly J D & McCrindle R. N.M.R. solvent shifts of methyl groups in alicyclic ketones. Reassignment of the methyl groups in camphor.  
*Chem. Ind. London* 1965:379-81.  
[Chemistry Department, University of Glasgow, Scotland]

**Substantial changes in the chemical shifts of some of the protons in the nuclear magnetic resonance (NMR) spectra of aldehydes and ketones are observed on going from chloroform or carbon tetrachloride to benzene as solvent. This paper presented a model which correlates the sign and magnitude of these changes with the geometrical relationship between the protons and the carbonyl group. [The SCI® indicates that this paper has been cited over 175 times since 1965.]**

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"In the early 1960s, the members of the natural product group at the University of Glasgow, including myself, were caught up in the almost explosive growth in the exploitation of NMR techniques in structural studies. Being keen to wring every last useful scrap of information out of our NMR spectra we were not satisfied with only chemical shift and spin-spin coupling data in a single solvent, but sought to interpret the effects produced by change of solvent, double resonance, or manipulation of the functional groups. Our 1965 article was concerned with the first of these.

"By 1964, the work of other groups appeared to indicate that changes in chemical shifts induced by aromatic solvents would be useful in structural and configurational studies. Indeed, benzene-induced shifts for compounds containing carbonyl groups appeared to be particularly promising, it being possible, for example, to distinguish between the axial and equatorial orientation of a methyl group adjacent to a carbonyl group in a steroid by running the spectrum in deuteriochloroform and in benzene. Still lacking was a generalization linking the sign and magnitude of the changes in chemical shift ( $\Delta\delta = \delta_{\text{CDCl}_3} - \delta_{\text{C}_6\text{H}_6}$ )

with the

geometrical relationship between the relevant proton and the carbonyl group. A study of molecular models of the compounds already investigated revealed that the  $\Delta\delta$ 's could be rationalized in terms of a surprisingly simple model, which involves a single reference plane drawn through the carbon-oxygen bond. (I must confess that I had not long returned to Glasgow from Professor Djerassi's laboratories at Stanford and visions of the 'Octant Rule' still danced in my head.) I discussed the model with Dr. Connolly who assuaged my doubts as to the possible utility of such an apparently naive idea and we set out to test it on a wide range of alicyclic ketones. Much to our delight, all, the examples obeyed the correlation including one in which the 'plane rule' indicated, and we were able to prove by isotopic labelling, that previous assignments had been in error.

"In the early winter of 1964 the work was presented at a meeting of the British NMR Discussion Group in London and submitted for publication to *Tetrahedron Letters*. Interestingly, the article was refused on the grounds of lack of sufficient interest. With changes only in format, it was submitted, with some haste, to *Chemistry and Industry* and accepted. Our sense of relief upon its acceptance heightened considerably when a paper proposing an essentially identical model came into print only a few months after our communication appeared.<sup>1</sup>

"Our article appears to have evoked numerous citations for two distinct reasons. First, the model proved to be very useful in structural and configurational studies of rigid systems and in conformational studies of flexible systems. Second, during the subsequent years the origin of benzene-induced shifts was under very intense investigation and various types of specific solvent-solute interactions were suggested to explain the shifts observed. The role of steric effects formed an important aspect of the arguments advanced and many authors cited our observation that bulky groups close to the carbonyl do not rule out use of the 'plane rule.' "

1. Williams D H & Bhacca N S. Solvent effects in N.M.R. spectroscopy. III. Chemical shifts induced by benzene in ketones. *Tetrahedron* 21:2021-8. 1965.