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NEW MODELS FOR CONFORMATIONAL ANALYSIS BY N.M.R.

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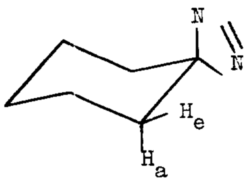
Data about the equilibrium between chair forms of cyclohexanone derivatives can be expected to disagree when they are obtained by different methods,be these chemical (1) or physical (2).The reason for this is the tacit assumption that the models can only exist in the chair conformation , or even only in the ideal chair conformation of cyclohexane itself . This is obviously not the case and it could be interesting to compare results obtained in different ways , because this can throw light on the particular geometry of the substances investigated.

The very promising P.M.R. technique usually examines a proton giving a well isolated signal and compares the results for compounds in which the same proton is exclusively in the axial or in the equatorial position.This has mostly been done for the proton of C$\underline{H}$X groupings in which X is hydroxyl (3) or halogen (4).Diazirine derivatives (I) , in which the equatorial hydrogen is shifted downfield by some 90 c/s , have also been used (5).

[♀] Aspirant of "Nationaal Fonds voor Wetenschappelijk Onderzoek".



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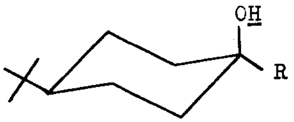

II

Another method compares not the shift , but the experimentally observed coupling with the α-protons with the the theoretical values once for the axial , once for the equatorial proton (6). In all these methods , the rather complex and broad P.M.R. pattern gives however less accurate results (7).
Substances which give sharp P.M.R. signals and which can be used as model for conformational analysis are the gem-dimethoxy cyclohexane derivatives (8).It is known that axial and equatorial methoxy groups are differently shielded (9).This has indeed enabled us to develop a new method based on the shift between the two gem dimethoxy signals . Unfortunately this shift is only about 3.2 c/s (56.4 Mc Varian spectrometer) in the best case.Improvement by a factor 1.65 could be obtained by using 100 Mc spectrometers.Although high accuracy could not be expected , detailed study was carried out and this has revealed (8b) some important aspects in this field of conformational analysis. Firstly , the chair conformation must be greatly distorted in 4-tert.butyl-1,1-dimethoxy cyclohexane in favour of a half chair form and secundly , temperature variation causes unequal shift variations for the different standard models . This suggests that data obtained by using 4-tert.butyl-1,1-disubstituted cyclohexanes as models are unreliable and one can wonder if the substrates II used by Ouellette (10) f.e. are not subjected to this phenomenon.The temperature effect illustrates the danger to use data obtained f.e. below the coallescence temperature,for the interpretation of the spectra at other temperatures.These effects are especially troublesome in our case because of the small maximal shift.

With the nuclear magnetic spectrum of gem-difluoro derivatives much better results can be expected. Fluorine is here directly bonded to the nucleus , and this should give increased shift difference between equatorial and axial position. Fluorine is also much smaller than the methoxy group and secundary steric effects should be small . In some gem-difluoro compounds the observed shift can indeed be several hundred c/s at 60 Mc (11) .

Gem-difluoro models thus turn out to be extremely promising not only for conformational studies of cyclohexane rings , but also for seven or eight membered rings , or for conformational studies in general.

Acknowledgement:

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Literature:

(1)See f.i. E.Eliel "*Stereochemistry of Carbon Compounds*", Mc. Graw-Hill , New York (1962).

(2)For I.R. study,see f.i. W.Masschelein;*Journ.Mol.Spectroscopy*; **10** , 161 (1963), *Ind.Chim.Belg.*,(review),**5** ,613 (1961)

(3) (a) E.Eliel;*Chem. and Ind.*,568 (1959)

(b) A.Lewin , S.Winstein;*J.Am.Chem.Soc.*,**84** , 2464(1962)

(c) E.Eliel,M.Gianni;*Tetr.Letters* , **3** ,97 (1962)

(4)See f.i. H van Dort , Th.Sekur;*Tetr.Letters* , 1301(1963) and ref. 3c.

(5)J.C.Martin(Univ.Illinois);private communication

(6)F.Ahet;*J.Am.Chem.Soc.*,**84** , 1053 (1962)

(7)This can be overcome by α-deuteration or using double irradiaton.

(8) (a)M.Anteunis; *Bull.Soc.Chim.Belg.*,**73** ,731 (1964)

(b)D.Tavernier,M.Anteunis;to be published.

(9)See f.i. R.Lemieux,R.Kullnig,H.Bernstein,W.Schneider; *J.Am.Chem.Soc.*, **80** ,6098 (1958)

(10)R.Ouellette;*J.Am.Chem.Soc.*, **86** ,3089 (1964)

(11)J.D.Roberts;private communication.