Tetrahedron Vol. 35, pp. 87–90
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0040–4020/79/0101–0087/$02.00/0

CONFORMATIONAL ANALYSIS OF TERTIOBUTYL-4, D-4, THIACYCLOHEXANE: BY PROTON NMR SPECTROSCOPY

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(*Received in UK* 12 *May* 1978)

Abstract—Proton NMR studies of tertiobutyl-4, D-4, thiacyclohexane, which has a fixed chair conformation, have allowed a direct determination of the various coupling constants. A discussion of the values of the ring torsion angles calculated from the different gauche constants ^3J shows that the most probable value is given by $J_{H\alpha e,H\beta a}$ for which there is no hydrogen atom antiperiplanar to the S atom.

Proton NMR spectroscopy is a useful method for obtaining structural information in the isotropic liquid phase. We wanted to check the accuracy of the torsion angles determined using a Karplus method in the thioethers compounds, studying the proton NMR spectrum of tertiobutyl-4, D-4, thiacyclohexane (TTCH). This molecule is interesting because of its fixed chair conformation, since the t-Bu group is confined to an equatorial position due to steric effect. The determination of the various coupling constants ^3J should provide a way to calculate an accurate value of the ring torsion angle.

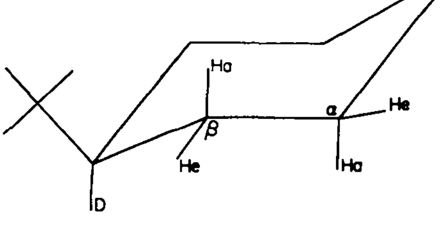
EXPERIMENTAL

The sample of TTCH was kindly provided by Dr. A. Marquet and its synthesis has been described elsewhere.[1]

NMR spectra were recorded on a high field Cameca 250 MHz spectrometer, at room temperature on carbon tetrachloride solutions. The purity of the sample has been determined by NMR spectroscopy.

RESULTS AND DISCUSSION

The proton NMR spectrum of TTCH in carbon tetrachloride exhibits different peaks (Fig. 1) which are assigned by comparison with the spectra of thiacyclo hexane and corresponding sulphoxides.[1] This preliminary approach does not give an unambiguous assignment of the β hydrogen resonances since in sulphoxide derivatives their frequencies are inverted depending on axial or equatorial conformation. The study of the different coupling constants will provide later a justification of the assignments listed in Table 1.



A complete resolution of the ABMX spins system is necessary in order to provide accurate frequency values for the two α protons. This system is easily divided into two simpler systems ABM and ABX by selective irradiation. The first ABM system ($H_{\beta a}$ being irradiated) gives a straight forward determination $J_{AM}+J_{BM} = 5.5$ Hz. The graphic resolution for this system gives $J_{AB} = -13.5$ Hz, $J_{AM} = 3.5$ Hz, $J_{BM} = 3.5$ Hz, $\nu_A = 638.1$ Hz, $\nu_B = 644.4$ Hz. The corresponding procedure on the ABX system ($H_{\beta e}$ being irradiated) gives two possible solutions:

(I) $J_{AB} = -13.5$ Hz, $J_{AX} = J_{BX} = 8.0$ Hz,
$\nu_A = 639.0$ Hz, $\nu_B = 643.9$ Hz,

(II) $J_{AB} = -13.5$ Hz, $J_{AX} = 12.0$ Hz,
$J_{BX} = 2.5$ Hz, $\nu_A = \nu_B = 641.6$ Hz.

On the other hand, J_{MX} can be measured on the multiplet corresponding to the $H_{\beta e}$ proton which is constituted by two symmetrical triplets which are reduced to a single triplet when the frequency corresponding to $H_{\beta a}$ is irradiated. The choice between the two sets of values above was achieved through iterative simulations (Fig. 1) obtained by keeping constant the resonance frequencies of $H_{\beta a}$ and $H_{\beta e}$ together with the ^2J coupling constants, since they are well established from the spectra. The new values are given in Table 2.

This assignment is consistent with the fact that the coupling constant ^3J_a must have the highest value amongst the ^3J coupling constants. Consequently this justifies the choice of the resonance frequency of $H_{\beta a}$.

A first comparison with published results concerning cyclohexane can be made.[2] As Table 2 shows, the overall effect of the endocyclic S atom is to induce a low field shift relative to the cyclohexane chemical shifts. The α protons are more shifted, but one notices that the axial α proton is more deshielded than the equatorial one. Consequently, their frequencies are practically the same, instead of being 0.48 ppm apart, as in cyclohexane.[2]

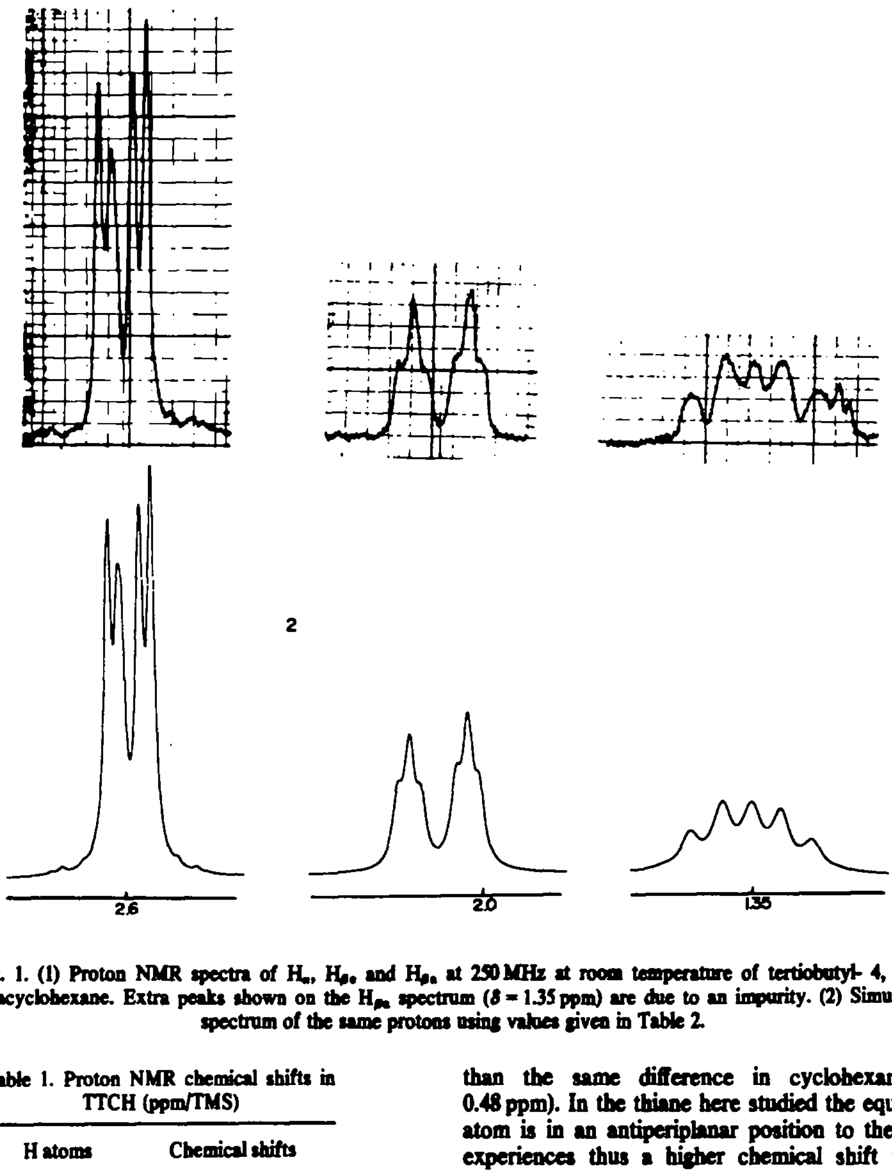


Fig. 1. (1) Proton NMR spectra of H_{α}, $H_{\beta e}$ and $H_{\beta a}$ at 250 MHz at room temperature of tertiobutyl- 4, D-4, thiacyclohexane. Extra peaks shown on the $H_{\beta a}$ spectrum ($\delta = 1.35$ ppm) are due to an impurity. (2) Simulated spectrum of the same protons using values given in Table 2.

Table 1. Proton NMR chemical shifts in TTCH (ppm/TMS)

H atoms	Chemical shifts
t Butyl	0.83
$H\beta_a$	1.35
$H\beta_e$	2.06
$H\alpha$	≃2.6

Table 2. Proton NMR spectral parameters for TTCH

	δ(ppm)		Coupling constants (Hz)	
$H_{\beta a}$	1.35	(1.14)[a]	$^{2}J_{\alpha}$	−13.5
$H_{\beta e}$	2.06	(1.62)	$^{3}J_{\alpha e\beta e}$	1.75
$H_{\alpha a}$	2.57	(1.14)	$^{3}J_{\alpha a\beta e}$	3.75
$H_{\alpha e}$	2.57	(1.62)	$^{3}J_{\alpha a\beta a}$	10.9
			$^{3}J_{\alpha e\beta a}$	3.9
			$^{2}J_{\beta}$	−13.0

(a) Values found for cyclohexane (2).

Similar observations have been made in the case of methylthianes.[3] The equatorial β proton is more deshielded than the axial one and the chemical shift difference $(\delta_{ae}/\beta) = \delta_{H\beta e} - \delta_{H\beta a} = 0.71$ ppm) is higher than the same difference in cyclohexane ($\delta_{ae(\beta)} =$ 0.48 ppm). In the thiane here studied the equatorial β H atom is in an antiperiplanar position to the S atom. It experiences thus a higher chemical shift variation in comparison with the same H atom in cyclohexane. However this interpretation does not explain the difference between the $\delta_{ae(\alpha)}$ and $\delta_{ae(\beta)}$ values going from TTCH to thiacyclohexane[4] (Table 3),

Table 3. Chemical shift differences for the Hα and Hβ protons of 6-membered rings

Compounds	$\delta_{ae(\alpha)}$ (ppm)	$\delta_{ae(\beta)}$	References
Cyclohexane	0.48	0.48	(2)
Thiacyclohexane	−0.19	0.38	(4)
TTCH	0	0.71	present work

The influence of an alkyl substituent on the chemical shifts of different protons in cyclohexane derivatives has been reported by Booth.[5] The effect of an equatorial t-Bu substituent on the neighbouring equatorial protons causes a deshielding of 0.2 ppm, while an axial α proton experiences a shielding of around 0.03 ppm. Therefore the influence of that substituent on the neighbouring methylene group must induce a chemical shift difference which can be deduced from the corresponding one in thiacyclohexane increased by 0.23 ppm. One should observe $\delta_{ae(\beta)TTCH} = 0.38 + 0.23 = 0.61$ ppm. This value is in good agreement with the value of 0.71 ppm observed here. In fact Lambert has shown that the chemical shift differences in the thiacyclohexane molecule, $\delta_{ae(\alpha)} = -0.19$ ppm and $\delta_{ae(\beta)} = +0.38$ ppm, arise from the diamagnetic anisotropy exhibited by the various endocyclic bonds.[4] However we assume that, following Booth as in the case of cyclohexanols, the influence of a t-Bu substituent on an axial or equatorial proton of the methylene group located in β position with respect to the carbon bearing the substituent is negligible, taking into account the fact that the effect of a Me substituent in the same position is very small.[5] It follows that we cannot use this argument to explain the identity of chemical shift for the TTCH α protons, since a difference of 0.19 ppm is observed for the thiacyclohexane molecule. We may assume that this is due to a different geometry because there is no reason why the effect of the tertiobutyl substituent at position 4 in the thiacyclohexane ring is higher than expected when considering the observed results in the cyclohexane homologues.[5]

The values of coupling constants $^2J_\alpha$ and $^2J_\beta$ found for TTCH (Table 2) are equal to -13.5 Hz and -13 Hz respectively. They are quite the same as those reported for thiacyclohexane ($^2J_\alpha = {}^2J_\beta = -13.5$ Hz[6]) and for cyclohexane ($^2J_\alpha = -12.6$ Hz and $^2J_\beta = -13$ Hz[7]).

It has been shown that the value of these coupling constants depends on three main contributions, electronegativity of neighbouring atoms, bond lengths and torsional angles.[8] According to this work we can see that the torsional angles of the $SC_\alpha C_\beta$ and $C_\alpha C_\beta C_\gamma$ moieties are probably around 60°. This value agrees with a chair conformation of the cycle, but it seems difficult to obtain a more accurate determination.

Concerning the ^3J coupling constants, one notices that the value of the coupling constant $^3J_{\alpha e\beta a}$ (3.9 Hz) is much higher than the value of $^3J_{\alpha a\beta e}$ (1.75 Hz). A similar difference has been noticed in the case of tertiobutyl 4-cyclohexanol.[8] This difference had been predicted by Booth in the case of heterocycles.[9] We can try to calculate the theoretical values of the ^3J coupling constants using the following equation established by Forrest:[10]

$$\text{(A)}\quad J^{g}_{1,2} = (4.1 + 0.63 \sum_i \Delta E_i) \times (1 - 0.462\,\Delta E_1)(1 - 0.462 \cdot \Delta E_2)$$

where $\sum_i \Delta E_i$ is the sum of the electronegativity differences between the substituting atoms (of the α and β C atoms) and H atom, and ΔE_1 (or ΔE_2) is the corresponding electronegativity difference of the substituent antiperiplanar to the H atom 1 (or 2). Using Pauling or Huggins electronegativity scales we see that C and S atoms have the same electronegativity.[11] Then as far as this six membered ring, having its torsion angle equal to 60° in a chair conformation, is concerned, one must observe consequently:

$$^3J_{\alpha a,\beta e} = {}^3J_{\alpha e,\beta a}$$

But this is not the case. If we assume that the torsion angle has a value not equal to 60°, we can use the method given by Forrest in order to calculate the torsion angles from the experimentally determined and theoretically calculated coupling constants.[10] These values are given in Fig. 2. The first observation concerns the fact that the projection of the $H_{\beta a}C_\beta H_{\beta e}$ angle onto a plane perpendicular to the $C_\alpha C_\beta$ axis must give an angle equal to 120° instead of the calculated 116°. Such a discrepancy must not be ascribed to a deformation of the valence angles, considering that this C atom is in β position relative to the S atom, and that rotation is allowed for the endocyclic bonds, if it is necessary, in order to take into account steric hindrance induced by the heteroatom. We conclude from this analysis that the equation (A) is inappropriate to calculate accurately the influence of the S atom on the ^3J coupling constants, at least when one of the concerned H atoms is in an antiperiplanar position relatively to the hetero...om. The conclusion which can be drawn in our case is that equation (A) does not hold to calculate gauche coupling constants as far as $H_{\beta e}$ is concerned.

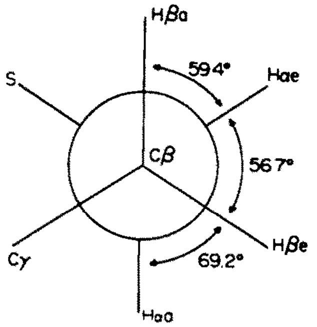


Fig. 2. Torsion angles in TTCH molecule calculated from the coupling constants ^3J given in Table 2 using the method of Ref. 10 (see text).

However we can check that it is possible to calculate the torsion angle from the $^3J_{\alpha e,\beta a}$ coupling constant since none of the concerned H atoms are antiperiplanar to the S atom, We calculate a value of 59.4° from the above coupling constant using Forrest method, which implies only a slight deformation of the ring torsion angle (which has the same value of 59.4°). This hypothesis is confirmed using the R factor:[12]

$$R = \frac{^3Jaa + {}^3Jee}{^3Jae + {}^3Jea} = 2.59.$$

This R factor value corresponds to a ring torsion angle of 60.5° which is in agreement with the preceding value.

Consequently we observe only a slight different between the value of the ring torsion angle given by the R factor method and the value given by the direct calculation using a coupling constant concerning protons for which there is no heteroatom in an antiperiplanar position. This conclusion probably means that the equation given by Forrest cannot take into account the effect of a S atom onto the coupling constants; it also means that the effect of electronegativity has probably a multiplicative effect onto the coupling constants, as recently underlined by Lambert.[13]

CONCLUSIONS

We have shown that the difference of proton chemical shifts between TTCH and thiacyclohexane could be only qualitatively explained taking into account diamagnetic anisotropy effect according to Lambert. We also have seen that the formula which has been established in order to calculate gauche coupling constants is not suitable when one of the H atoms concerned is in an antiperiplanar position relatively to a S atom. When the most accurate geometry of the TTCH conformation has to be determined, we have seen that the use of the R factor or the $^3J_{\alpha e\beta a}$ coupling constant drive us to the final result that the cycle torsion angle is close to 60°. A study of the influence of rare earth chelates onto chemical shifts has been initiated in order to compare the accuracy of such a determination of conformation to the accurate of the conformation deduced from the study of the coupling constants.

Acknowledgements—The authors are indebted to the "Groupe Grenoblois de résonance" for the spectra at 250 MHz, and to Dr. Marquet, who kindly provided the sample of TTCH on which the experiments were performed.

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