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DERIVATES OF 1,1,4,4-TETRAMETHYLCYCLOHEXANE

LOW TEMPERATURE NMR STUDIES

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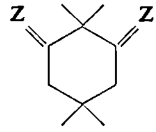
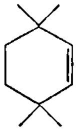
Abstract—Low temperature NMR measurements with 1,1,4,4-tetramethylcyclohexane (I) and derivatives II and III establish that chair conformations are preferred to twist boat conformations despite unfavorable axial compressions in the former.

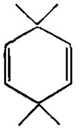
Conformational studies of 1,1,4,4-tetramethylcyclohexane derivatives should provide some interesting facts concerning chair and twist boat interconversions.[1] Thus, the parent hydrocarbon I will experience non-bonding compression interactions from two axial methyl groups in a chair conformation (Ia) while these will be alleviated in certain twist boat conformations (e.g. Ib). In this case a simple calculation indicates that the conformation stability order will still be chair > twist boat,[2] however with derivatives of I having additional axial substituents this stability order could well be reversed. With these points in mind we have examined the low temperature NMR spectra of compounds I, II and III.



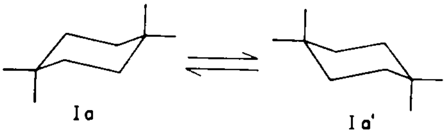
I Z = H_2
II Z = H, $OCOCH_3$ (trans)
III Z = —SCH_2CH_2S—
IV Z = O



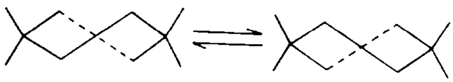
V



VI



Ia Ia'



Ib Ib'

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[1] A few examples of simple cyclohexane derivatives which prefer non-chair conformations have been reported. e.g. N. L. Allinger and L. A. Freiberg, *J. Amer. Chem. Soc.* **82**, 2393 (1960); R. D. Stolow and M. Bonaventura, *Ibid.* **85**, 3636 (1963).

[2] The principles and facts upon which such calculations are based may be found in most treatises of conformational analysis e.g. E. L. Eliel, N. L. Allinger, G. B. Morrison and S. J. Angyal, *Conformational Analysis.* (Interscience Division) J. Wiley, New York (1965). The non-bonded interactions in Ia are roughly 3·6 kcal/mole and those characteristic of the twist boat Ib probably exceed 5 kcal/mole.

The synthesis of 1,1,4,4-tetramethylcyclohexane (I)[3] began with 2,2,5,5-tetramethyl-1,3-cyclohexanedione (IV).[4] After several unsuccessful attempts to reduce the carbonyl functions of IV by modified Wolff-Kishner methods, we were pleased to find that a bis-thioketal derivative (III) could be readily prepared in high yield. Hydrogenolysis of III was accomplished by shaking a hot D.M.F. solution with Raney nickel W-2 catalsyt under 50 psi of hydrogen. The hydrogenolysis produced not only the expected I, but also the olefin V and small amounts of diene VI.[5] Evidence for the structures of I, III and V is based on the method of synthesis and the spectroscopic data presented in the experimental section. Compounds II and VI have been reported and characterized earlier.[6,7]

The NMR spectrum of I at 27° exhibited two sharp singlets (τ 9·14 and 8·76) having an area ratio of 3:2; consequently this sample must consist of rapidly interconverting chair (Ia and Ia′) and/or twist boat (Ib and Ib′) conformations. If this measurement could be made at a sufficiently low temperature the spectrum observed would be essentially that expected for a static mixture of rigid conformations with the conformation having the lowest potential energy predominating. In the event that the preferred conformation is a chair (Ia) the low temperature NMR spectrum will be characterized by a splitting of both the methyl and the methylene resonance peaks. The axial and equatorial methyl groups in Ia will give rise to separate signals of equal intensity while the methylene hydrogens will be frozen into an A_2B_2 system consisting of two equatorial and two axial hydrogens. If on the other hand, the preferred conformation is a twist boat (Ib) the methylene protons will still appear as an A_2B_2 system, however, the four identical methyl groups[8] will give a single resonance peak.

A carbon disulfide solution of I at −78° exhibited a pair of methyl resonance signals at τ 9·16 and 9·12 and a broad methylene complex at τ 8·78 and 8·72. Thus, the experimental findings confirm the earlier conclusion[2] that the preferred (lowest energy) conformation of I is a chair.

The *trans*-diacetate (II) is a particularly interesting substrate in this study. Since the chair conformation (IIa) must have an axial acetoxyl substituent, the non-bonded interactions are markedly increased over those found in Ia, while in the twist boat conformation (IIb) both acetoxyl groups may assume a pseudo-equatorial orientation. Consequently, a reduction in ΔH (chair $\rightarrow$ twist boat) is expected. A detailed calculation of the energy differences is in this case unwise; the major problem is that the non-bonded interactions associated with the axial groups in a chair conformation do not by any means vanish when the molecule changes to a twist boat, and the interactions in the latter conformation are not readily determined. Nevertheless, a crude indication of the energies involved may be of interest and is easily obtained if the previous point is ignored. Thus, the axial methyl-hydrogen interactions in IIa total 2·7 kcal,[2]

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[3] G. Chiurdoglu and A. Maquestiau, *Bull. Soc. Chim. Belges* **63**, 357 (1954) have reported the synthesis of I but do not offer convincing evidence to support the structure; F. W. Grant, R. W. Gleason and C. H. Bushweller, *J. Org. Chem.* **30**, 290 (1965) prepared I by catalytic reduction of VI.

[4] R. D. Desai, *J. Chem. Soc.* 1079 (1932).

[5] J. Fishman, M. Torigoe and H. Guzik, *J. Org. Chem.* **28**, 1443 (1963) have reported that olefins are in fact the major products when thioketals are treated with Raney Ni in solvents having carbonyl groups.

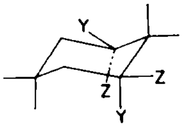
[6] A. Allen, R. Sneeden and J. Colvin, *J. Chem. Soc.* 557 (1958).

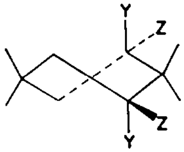
[7] W. Reusch, M. Russell and C. Dzurella, *J. Org. Chem.* **29**, 2446 (1964).

[8] In conformation Ib the two quaternary carbon atoms lie on one of the three C_2 symmetry axes.

the axial acetoxyl hydrogen interaction is roughly 0·5 kcal,[9] and the methyl-acetoxyl interaction is probably near 2·5 kcal,[10] making a total of 5·7 kcal due to non-bonded interactions in the chair conformation. This is about the magnitude of the interactions expected for a twist boat conformation and it is therefore not at all certain which conformation will predominate at low temperatures.

The NMR spectrum of II at 27° consisted of two sharp methyl resonance peaks at τ 9·0 and 9·1 a sharp acetoxyl methyl peak at 8·05 τ, a multiplet at 8·5 τ and a pair of doublets centered at 5·2 τ (area ratios are 3:3:3:2:1 respectively). At −60° a carbon disulfide solution of II displayed a very similar spectrum, but at −78° the quaternary methyl peaks were severaly broadened while the acetoxyl methyl resonance remained sharp and distinct. The methylene multiplet was also broadened, however the change here was less striking. Although our equipment did not permit additional measurements at lower temperatures, it is clear from this behavior that a chair conformation predominates as conformational interconversion is frozen. All four quaternary methyl groups are different in the chair conformation (IIa) and would therefore give four separate resonance signals; the twist boat conformation (IIb) has a C_2 axis of symmetry passing through the quaternary carbon atoms and the methyl groups would consequently appear as only two peaks in the NMR spectrum. The coalescene temperatures for the quaternary methyl resonance can be no higher than −80°, indicating that chair-chair interconversion in II has a lower activation energy than the analogous interconversion in I.[11]





II a Y=H, Z=OCOCH$_3$ II b
III a Y, Z=-SCH$_2$CH$_2$S- III b

The bis-thioketal (III) is also characterized by additional axial interactions in the chair conformation (IIIa) which are alleviated in the twist boat conformation (IIIb). Nevertheless, the low temperature NMR measurements again favor a chair conformation. The spectrum at 27° consists of four sharp singlets at τ 8·87, 8·53, 7·85 and 6·83 (area ratios 3:3:2:4 respectively).[12] When a sample of III was cooled to −78° the highest field methyl resonance was split into two peaks of equal intensity having a

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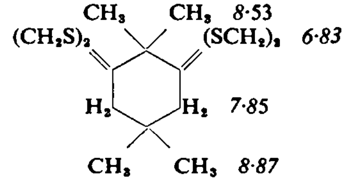
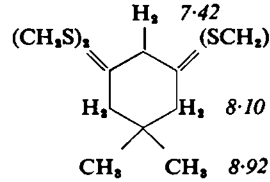
[9] The acetoxyl group is assumed to be slightly larger than a hydroxyl group.

[10] E. L. Eliel and H. Haubenstock, *J. Org. Chem.* **26**, 3504 (1961).

[11] The coalescence temp for the quaternary methyl resonance in I is ca. −65°, while methylene coalescence is observed at ca. −50°.

[12] A comparison of this NMR spectrum with that of the dithioketal derived from dimedone enables the following assignments to be made (Chemical shifts in τ).





chemical shift difference of 0·37 ppm, the cyclohexane methylene protons were similarly split with a difference of 0·22 ppm, however, the geminal dimethyl grouping located between the ketal functions remained essentially unchanged, as did the ketal methylene signal. This peculiar behavior can only be explained by assuming that a chair conformation predominates at this temperature, and that the geminal sulfur substituents bracketing the low field dimethyl grouping act to eliminate the chemical shift difference between the axial and equatorial methyls. Another unusual feature is that the high field dimethyl grouping is more strongly split than are the methylene protons. This again may be ascribed to the sulfur atoms, two of which are cis and axial with respect to the axial methyl group.

EXPERIMENTAL

The NMR spectra reported here were obtained with a Varian A-60 spectrometer equipped with a Varian variable temperature probe. Dilute solutions of the samples in CCl_4 and CS_2 with tetramethylsilane as an internal standard were employed. The temp within the probe were determined from the methanol chemical shift differences and are considered accurate to ±2°.

2,2,5,5-Tetramethyl-1,3-cyclohexanedione bisethylenethioketal (III). A solution of 2,2,5,5-tetramethyl-1,3-cyclohexanedione[4] (0·10 g) in ethanedithiol (1·0 ml) was treated with BF_3-etherate (0·8 ml). The reaction mixture deposited a white solid after standing for 10 min and was then worked up by addition of 20 ml of a 50:50 methanol:water mixture followed by ether extraction. The washed and dried ether extracts yielded a solid which was crystallized from acetone—yield 0·13 g (65%), m.p. 155–156°. The IR spectrum of III showed the absence of carbonyl absorption; the NMR spectrum is described in the text. (Found: C, 52·38; H, 7·43; S, 40·19. Calc. for $C_{14}H_{24}S_4$: C, 52·46; H, 7·53; S, 40·01%.)

Raney nickel reduction of III. A 0·5 g sample of III in 75 ml D.M.F. was placed in a 250 ml press. bottle. To this solution was added 6·0 g Raney Ni W-2, and the resulting mixture was shaken for 20 hr at 85° under 50 psi of H_2. After cooling, the mixture was filtered and the filtrate was diluted with 200 ml water and then extracted with three 100 ml portions pentane. The combined pentane extracts were washed and dried, and after carefully removing most of the solvent by distillation, the

TABLE 1

I		V	
m/e	% Base Peak	m/e	% Base Peak
41	77	48	13
43	42	50	15
55	55	67	17
56	17	69	12
57	12	77	10
69	100	79	8
70	38	81	36
71	43	82	28
83	26	91	10
125	93	95	14
140 (P)	2	123	100
		138 (P)	12

Intensity of P + 1 peaks

I. (Found: P, 10·8; Calc. for $C_{10}H_{20}$: P, 11·13%.)
V. (Found: P, 10·8; Calc. for $C_{10}H_{18}$: P, 11·09%.)

residue was examined by VPC analysis.[18] Three volatile hydrocarbons were isolated by preparative VPC and were identified as I 70%, V 20% and VI 10%. Compound VI was identified by direct comparison (VPC and IR) with an authentic sample.[7] The NMR spectrum of I is presented in the text; V exhibited resonance peaks at τ 9·05, 8·57 and 4·84 having area ratios of 6:2:1 respectively. The mass spectra of I and V are presented in Table 1.

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[18] This analysis was made with an Aerograph A-90-P equipped with a 6 ft column packed with 20% apiezon-L on chromosorb-W. At 108° the order of elution is I, V and finally VI.