STEREOCHEMISTRY OF HETEROCYCLES.

V.* STEREOCHEMICAL PECULIARITIES OF 1,3-DIOXANES AND 1,3-DITHIANES

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The stereochemical peculiarities of substituted 1,3-dioxanes and 1,3-dithianes are discussed. The high probability of the existence of flexible conformations in these series, the considerable energy preference of the 5-C-axial position in the chair conformation of 1,3-dioxanes and 1,3-dithianes, and the definite preference of the 2-C-axial position in the chair conformation of 1,3-dithianes as compared with the axial conformations of the cyclohexane type are noted. The PMR spectra of stereoisomeric 2,5-dimethyl-5-isopropyl-1,3-dioxanes, 2-methyl-5-isopropyl-1,3-dithianes, and 2,2,5-trimethyl-1,3-dithiane are described, and their configurations and preferred conformations are proved. The results of a study of the epimerization of stereoisomers of substituted 1,3-dioxanes and 1,3-dithianes are examined, and the conformational energies of individual substituents in the 5-position of these cyclic systems are calculated on the basis of this examination.

The extension of conformational concepts to series of heteroanalogs of cyclohexane initially led to a standard approach to the study of the stereochemistry of such substances [1-4]. The necessity for taking into account those specific effects which the heteroatoms introduce into the stereochemical characteristics of the six-membered heterocyclic ring was subsequently asserted by a number of investigators [5-30]. These problems have been recently discussed most completely by Eliel [5-8], although he did not attempt to correlate the available experimental data. In a number of our papers [31-49] we also discussed several stereochemical peculiarities of 1,3-dioxanes and 1,3-dithianes but, once again, we did not make the necessary correlations. This paper is an attempt to correlate the available experimental data and contains several new experimental results.

The primary peculiarity of 1,3-dioxanes and 1,3-dithianes is that, in the majority of cases, the conformational equilibrium is shifted to favor one of the preferred conformations even at room temperature (as a rule, with the equatorial or pseudoequatorial or 5-C-axial positions of the bulkiest substituents). According to the data in [12], the percentage of axial conformers (excluding the 5-C-axial ones) usually does not exceed 1%. We have even noted the fact [35] that, on heating to +150°, the individual stereoisomers of 2,5-dimethyl-5-methoxymethyl- and -5-α-methoxyethyl-1,3-dioxanes were not substantially transformed to the conformations which are alternative to the preferred ones. This sort of effect was also observed on cooling. Similar data were also obtained by a number of other investigators [12, 22].

As follows from [6, 7] and Tables 1 and 2, one can assume that the reason for such a greater "conformational determinacy" than in the cyclohexane series consists in the nonuniformity of the magnitudes of the conformational energies of the substituents in the 2-, 4-, 5-, or 6-positions of the 1,3-dioxane or 1,3-dithiane rings.

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*See [48] for communication IV.

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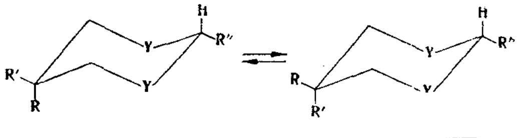
TABLE 1. Results Obtained in a Study of the Configurational Isomerization of 1,3-Dioxanes and 1,3-Dithianes



R	R	R	Y	ΔG°, kcal/mole
CH_3	H	CH_3	O	0,89±0,01
C_2H_5	H	CH_3	O	0,76±0,01
C_2H_5	H	C_2H_5	O	0,73±0,01[a]
i-C_3H_7	H	CH_3	O	0,86±0,02
i-C_3H_7	H	i-C_3H_7	O	0,83±0,01
CH_3	H	C_2H_5	O	0,74±0,02
CH_3	H	i-C_3H_7	O	0,87±0,02
CH_3	H	t-C_4H_9	O	0,80±0,02[a]
C_2H_5	H	t-C_4H_9	O	0,67±0,01[a]
i-C_3H_7	H	t-C_4H_9	O	0,98±0,01[a]
C_6H_5	H	t-C_4H_9	O	1,03±0,02[a]
t-C_4H_9	H	t-C_4H_9	O	1,36±0,01[a]
CH_3	i-C_3H_7	CH_3	O	0,36±0,02
CH_3	i-C_3H_7	i-C_3H_7	O	0,38±0,04
CH_3	CH_2OCH_3	CH_3	O	0,85±0,01
CH_3	$CH(OCH_3)CH_3$	CH_3	O	0,85±0,02
CH_3	H	CH_3	S	0,52±0,03
i-C_3H_7	H	CH_3	S	0,81±0,01
C_2H_5	H	i-C_3H_7	S	0,77±0,01
i-C_3H_7	H	i-C_3H_7	S	0,79±0,01
i-C_3H_7	H	i-C_3H_7	S	0,78±0,01[b]
CH_3	H	t-C_4H_9	S	1,04±0,01[b]
C_2H_5	H	t-C_4H_9	S	0,77±0,02[b]
i-C_3H_7	H	t-C_4H_9	S	0,85±0,01[b]
t-C_4H_9	H	t-C_4H_9	S	1,85±0,01[b]
t-C_4H_9	H	C_6H_5	S	1,94±0,02[b]

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[a] Data from [6].

[b] Data from [7].

TABLE 2. "Conformational Energies" of Substituents in a Number of Cyclohexanes, 1,3-Dioxanes, and 1,3-Dithianes*

Cyclohexane derivatives:	CH_3 — 1,70; C_2H_5 — 1,75; i-C_3H_7 — 2,15; t-C_4H_9 — 5,40
1,3-Dioxane derivatives:	2-CH_3 $\geqslant$ 3,55; 4-CH_3 — 2,90; 5-CH_3 — 0,80 (0,90); 5-C_2H_5 — 0,80; 5-i-C_3H_7 — 0,80 (1,00); 5-t-C_4H_9 — 1,40
1,3-Dithiane derivatives:	2-CH_3 — 1,77; 2-C_2H_5 — 1,54; 2-i-C_3H_7 — 1,95; 2-t-C_4H_9 $\geqslant$ 2,7; 4-CH_3 — 1,69; 5-CH_3 — 0,52 (1,00); 5-C_2H_5 — 0,80; 5-i-C_3H_7 — 0,80; 5-t-C_4H_9 — 1,80

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*In kilocalories per mole from the results in [50, 6, 7] and this paper.

This may result in the so-called "fixing" of the preferred conformation. It is known [50] that when the difference in the free energies of conformers of substituted cyclohexanes is 5.5 kcal/mole, only one molecule out of 10,000 has the alternative, disadvantageous conformation and, since the barrier to conformational conversion is usually small, there is a rapid interconversion of the conformation with the mentioned statistical result of equilibrium. This is precisely what the term conformational "fixing" means.

In the 1,3-dioxane and 1,3-dithiane series the indicated differences in free energies are less in the majority of cases, which is also responsible for the indicated statistical effect. In this case, the problem of the conversion barriers is insufficiently clear. The literature contains assumptions that a stabilizing interaction of the special hydrogen bond type may occur in such systems [51], which may increase the conversion barrier. It is possible that the observed pattern is the result of these two effects. The answers to the question of the nature of the phenomenon under discussion can be given after carrying out systematic investigations of the IR and NMR spectra of the individual stereoisomers of 1,3-dioxanes and 1,3-dithianes with a well-thought-out set of substituents in the ring over a wide range of temperatures from −100 to +150° and also after carrying out similar measurements devoted to a study of the solvent effect on the conversion process. The individual studies of this problem currently available do not contain sufficient information.

The second peculiarity of the compounds under discussion is their great tendency for assuming a flexible conformation. This peculiarity was first discussed by Foster [12, 18, 22] for the 1,3-dioxane series and subsequently by Eliel [7] for a number of 1,3-dithianes. It is interesting to note that similar data were also obtained for 1,4-dioxanes [54]. The reason for this tendency is weakening of the unbonded syn-axial interactions in both series as a consequence of replacement of the methylene groups in the six-membered ring by heteroatoms.

A quantitative estimate of the differences in the conformational energies between the chair and boat conformations in 1,3-dioxane can be made on the basis of the following reasoning. In the 1,3-dioxane molecule in the chair conformation there are two skew interactions of the butane type (α = 0.9 kcal/mole) and four skew interactions of the alkyl-oxygen type (β). This sort of interaction is estimated to be 0.35 [52], 0.38 [53], and 0.40 [14] kcal/mole for the methylene group. (The last number is the most reliable and can be taken for the β parameter.) The total energy of the chair conformation of 1,3-dioxane (E_C) in comparison with the frozen n-butane conformation (null value) is then as follows:

$$E_C = 2\alpha + 4\beta = 3.4 \text{ kcal/mole}$$

If 1,3-dioxane is in the symmetrical boat conformation, the conformation energy (E_{SB}) should be determined by the sum of the same value (there are no locked butane 1,2-interactions) and the magnitude of the bow−stern interaction (γ), which is estimated to be 3 kcal/mole [29].

Then,

$$E_{SB} = 2\alpha + 4\beta + \gamma = 6.4 \text{ kcal/mole}$$

or

$$E_{SB} - E_C = \gamma = 3.0 \text{ kcal/mole}$$

If an unsymmetrical boat conformation is assumed, the conformational energy (E_{UB}) is

$$E_{UB} = \alpha + 4\beta + \delta = 7.1 \text{ kcal/mole}$$

where δ = 4.4 kcal/mole, i.e., it is of the magnitude of a partially locked butane interaction. Hence,

$$E_{UB} - E_C = 3.7 \text{ kcal/mole.}$$

In other words, both boat conformations in the 1,3-dioxane series are close in energy and differ much less from the chair conformation than in the cyclohexane series. In the flexible conformation (the twist form), the $E_{FC} - E_C$ difference should be considerably less than $E_{UB} - E_C$ and $E_{SB} - E_C$. Considering the definite analogy with cyclohexane, the $E_{FC} - E_C$ value can be estimated to be approximately 1 kcal/mole.

The above arguments lead to the conclusion that the flexible conformation, in its various variants, is considerably more probable in the 1,3-dioxane series than in the cyclohexane series. There are data in the literature [5, 6, 9, 29], according to which the $E_{FC} - E_C$ value is estimated by considerably larger numbers. It seems to us that these calculations are less reliable, since the rotational barrier in methanol was selected as the β parameter in them. It is easy to see that this cannot be done, particularly if one takes the capacity of methanol for associations into account.

The given computational estimates serve as additional substantiation of the experimental facts found in [31-33, 36-43, 47]. We have also obtained experimental data which confirm the validity of these calculations. Thus, the configurational isomerization of both cis- and trans-2,5-dimethyl-5-methoxymethyl- and 2,5-dimethyl-5-α-methoxyethyl-1,3-dioxanes in the presence of iodine at 140° and in the presence of BF_3 at 60° leads to an equilibrium mixture with a trans to cis isomer ratio of 70 : 30. This sort of isomer ratio corresponds to a free energy difference of ΔG^* = 0.85 kcal/mole. If one considers that the cis and trans isomers are characterized, respectively, by an equatorial (pseudoequatorial) orientation of the 2-C-methyl and 5-C-alkoxyalkyl radicals and a 5-C-axial (pseudoaxial) orientation of the methyl group and also differ in ring conformation (which is the chair conformation for the trans isomer and the flexible conformation for the cis isomer [37]), the above ΔG^* value can be considered to be a criterion of the $E_{FC} - E_C$ difference. It is easy to see that it is close to the calculated value.

Even greater weakening of the syn-axial interaction should be expected in the substituted 1,3-dithiane series. In fact, the C–S bond length in 1,3-dithianes [28] is 1.80 Å, while the S–C–S angle is about 115°. This results, for example, in the fact that even the bow–stern distance in the boat conformation of 1,3-dithiane turns out to be about 2.4 Å (from the results of an examination of Stuart–Briegleb models), while in 1,3-dioxane this distance is 1.46 Å. However, qualitative calculations of estimates of the $E_{FC} - E_C$ differences in the 1,3-dithiane series are, as yet, difficult to carry out, since the β parameter for these compounds has not been precisely determined. To be sure, it follows from [20, 21] that this value should be of the order of 0.1-0.2 kcal/mole, but the indicated data require refinement. In any case, it is apparent that the fundamental possibility of the realization of a flexible conformation in the 1,3-dithiane series is completely reliable, as also acknowledged by Eliel [7].

The third conformational peculiarity of 1,3-dioxanes and 1,3-dithianes is the high advantageousness of the 5-C-axial orientation in the chair conformation as compared with the usual axial conformations of the cyclohexane type. This peculiarity is a consequence of the same reason responsible for the high degree of preferability of the flexible conformation in the 1,3-dioxane and 1,3-dithiane series as compared with the cyclohexane series. We were among the first to point out this peculiarity [31], after which it was noted by many other investigators [5].

Two conformational interactions of the β type ($2\beta = 0.80$ kcal/mole) appear on introduction of a methyl substituent into the 5-C-axial position of the 1,3-dioxane ring, which has been experimentally confirmed (0.81 kcal/mole) [14]. Consequently, for this sort of configuration of substituted 1,3-dioxane, in which the diequatorial conformation cannot be realized, the molecule may take on two alternative and, energetically speaking, almost equally advantageous forms: a flexible conformation with dipseudoequatorial orientation or a chair conformation in which one of the substituents is 5-C-axial. Selection between these two possibilities is apparently determined by the character of the 5-C-substituent.

In 1,3-dithianes the interaction of the β type in the 5-C-axial position is even less than in 1,3-dioxanes. In Stuart–Briegleb models it is seen that the 5-C–S distance is 3.1 Å [26]; in addition, it follows from [26] that the 5-C–6-C bond length in 1,3-dithiane is 1.46 Å as compared with 1.57 Å in the 4-C–5-C bond length, i.e., the 1,3-dithiane ring is extremely unsymmetrical. Hence, the entire picture of the 1,2- and 1,3-conformational interactions changes, but the considerable magnitude of the distance between the 5–C atom and the sulfur atom is a criterion of the weakening of the axial interaction in such systems.

Yet another peculiarity is manifested in 1,3-dithiane molecules. In view of the fact that the 2-C–4-C and 2-C–6-C internuclear distances in 1,3-dithiane are 2.75 Å, according to [28] (and not 2.4 Å, as in 1,3-dioxane, or 2.54 Å, as in cyclohexane), the 2-C-axial position in the chair conformation of 1,3-dithianes is also considerably more preferable than the analogous position in 1,3-dioxane and cyclohexane molecules.

We have studied the experimental evidence of the assumed advantageousness of the 5-C-axial orientation in 1,3-dioxanes and 1,3-dithianes by both NMR and by a study of the configurational isomerization of cis–trans isomeric 1,3-dioxanes and 1,3-dithianes. The NMR method gives extremely definitive information with respect to the configuration and primary conformation of stereoisomeric 2,5-dimethyl-5-isopropyl-1,3-dioxanes (Ia and Ib), which we synthesized by condensation of 2-methyl-2-isopropyl-1,3-propanediol with acetic anhydride in the presence of KU-2 cation-exchange resin [32, 34].

The PMR spectra of Ia and Ib are presented in Fig. 1. The spectra clearly demonstrate the characteristic peculiarities in the regularities of the change of the chemical shifts which emerge from the theoretical estimates of the expected changes in the proton shielding constants in substituted 1,3-dioxanes, previously published by us in [43]. The phenomenon of inversion of the chemical shifts of the α protons of the axial and equatorial substituents attached to the 5-C-atom of the ring is displayed most clearly.

An analysis of the spectra indicates that both isomers Ia and Ib exist in the preferred chair conformation, and at room temperature the equilibrium is shifted to one of the preferred conformations of each of the isomers. This conclusion follows from the considerable nonequivalency of the 4-C- and 6-C-methylene protons of the ring observed in the spectra.

The resonance of these protons in the spectra of both isomers is manifested as a typical spectrum of an AA'BB' system, which is apparent from the latent multiplicity of the AB quartet. For example, the doublet from the equatorial protons contains a poorly resolved multiplet caused by a long-range spin–spin interaction of the ${}^4J_{HH}$ type (0.4 Hz). One's attention is drawn to the great nonequivalency of the 4-C- and

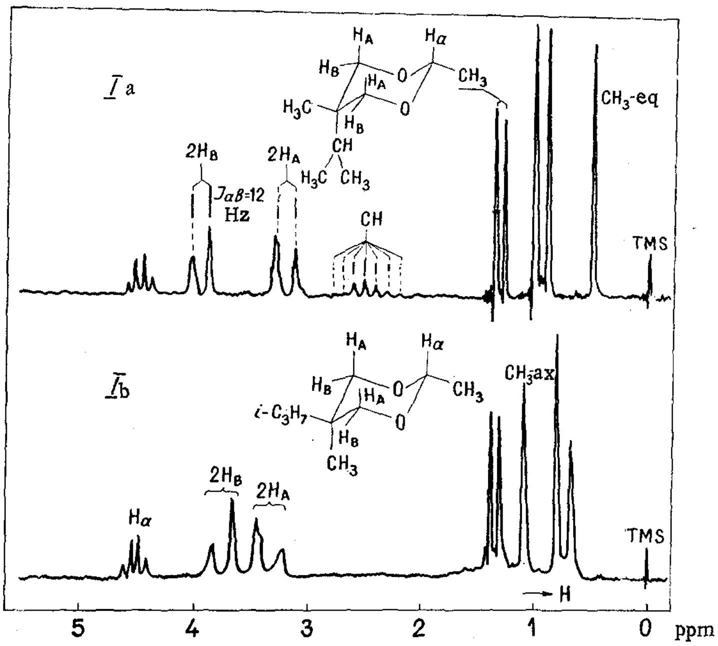


Fig. 1. PMR spectra of stereoisomeric 2,5-dimethyl-5-isopropyl-1,3-dioxanes: Ia) cis isomer; Ib) trans isomer (ν_0 60 MHz at 22°C).

5-C-axial and equatorial protons in the low-boiling isomer ($\Delta\sigma_{ae}$ = 0.70 ppm) as compared with the spectrum of the high-boiling isomer ($\Delta\sigma_{ae}$ = 0.37 ppm). Moreover, the $\Delta\sigma$ value in both cases is greater than 0.30 ppm which, according to the calculations in [43], can occur only in the chair conformation but not in the flexible conformation. These differences in the $\Delta\sigma$ values are probably due to the fact that in the high-boiling isomer, because of conformational interactions in the isopropyl group in the equatorial position, there is further deshielding of the axial protons and shielding of the equatorial protons.

The configuration of the substituents in the 2-C position is comparatively simply defined. The chemical shift of the 2-C-proton in the spectra of both isomers is the same and is δ 4.52 ppm (center of the quartet). The 2-C-methyl doublet which is displayed in the spectra of both isomers at δ 1.35 ppm also has the same chemical shift. It is known from the literature that the 2-CH_2-protons in rapidly inverting 1,3-dioxane resonate at δ 4.65 ppm [30]; the axial protons attached to 2-C, however, resonate at higher field (δ 4.43 ± 0.07 ppm). Consequently, the 2-C-hydrogen atom in isomers Ia and Ib occupies an axial position, while the 2-C-methyl group occupies an equatorial position.

The configuration of substituents attached to the 5-C-atom of the ring can be established by comparing the spectra of Ia and Ib with calculations previously made by one of us [43, 55] and also with the spectrum of standard 5-methyl-1,3-dioxane [14]. It follows from the spectrum of Ia that the methyl protons of this isomer experience a strong additional shielding and resonate at δ 0.47 ppm. The inversion of the chemical shifts in the 5-C-position of the 1,3-dioxane ring [30] indicates that this methyl radical should occupy an equatorial position; the isopropyl radical consequently occupies an axial position. This same result follows from calculations [43] and from an examination of the spectrum of 5-methyl-1,3-dioxane.

The position of the septet resonance band of the α-CH proton of the isopropyl radical is also evidence in favor of this assertion. It follows from Fig. 1 that the signal of this proton in the spectrum of isomer Ia is shifted substantially to weaker field (δ 2.51 ppm) in comparison with the position of the analogous septet in the spectrum of isomer Ib. In accordance with the calculations in [43], this should occur only for an axial orientation of the isopropyl radical.

As seen from the spectrum of Ib, the signal of the 5-C-methyl group of this isomer is displayed at δ 1.02 ppm, i.e., it is shifted to weaker field by $\Delta\sigma$ = 0.55 ppm. (The calculated shift from the data in [43] is $\Delta\sigma$ = 0.43 ppm.) This attests to the axial orientation of the 5-C-methyl group under consideration. This information is confirmed by the shift in the signal of the methylidene proton of the isopropyl radical in the spectrum of Ib to higher field. The change in the intensity ratio of the doublet of the methyl groups of the isopropyl group, in which the outer component is less intense than the inner one, also speaks in favor of this.

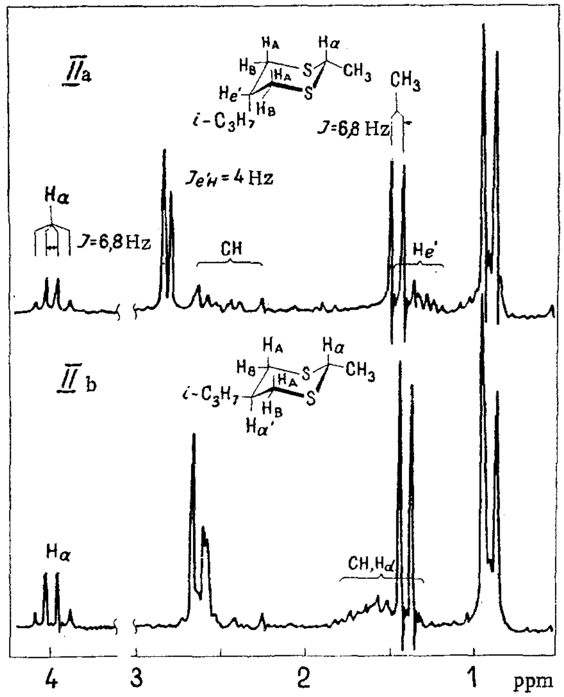


Fig. 2. PMR spectra of stereoisomeric 2-methyl-5-isopropyl-1,3-dithianes: IIa) cis isomer; IIb) trans isomer (ν_0 100 MHz at 25°C).

The NMR spectra of stereoisomers Ia and Ib hence attest to the cis configuration of the former and the trans configuration of the latter, as well as to a chair conformation for both isomers. It is easy to see that this confirms the conclusion regarding the advantageousness of a 5-C-axial orientation, for in the alternative variant the Ib isomer should have been an equilibrium mixture of two conformers, one of which (in overwhelming amounts) should have had either the chair conformation with 2-C- and 5-C-axial methyl groups and 5-C-equatorial isopropyl groups or a flexible conformation.

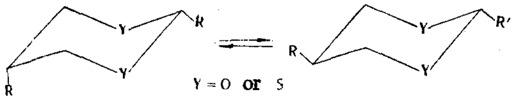
The NMR spectra of stereoisomeric 2-methyl-5-isopropyl-1,3-dithianes (IIa and IIb) are presented in Fig. 2. The signals of the 2-C-methyl group and the hydrogen atom in the 2-position of the ring appear at 1.42 ± 0.04 and 3.98 ppm, respectively, in the spectra of both isomers. This indicates that these compounds do not differ in the orientation of the substituents in the vicinity of the secondary carbon atom. The PMR spectrum of 4-methyl-1,3-dithiane [7, 26, 27] indicates that the axial 2-C proton resonates at $\delta = 4.0$ ppm, while the equatorial 2-C proton resonates at $\delta \sim 3.5$ ppm. Similar information was obtained in a study of the PMR spectrum of 2-methyl-1-3-dithiane [7, 26, 27]. The 2-C-methyl group is consequently equatorial in both isomers.

The chair conformation for both isomers follows from the symmetrical character of the spectrum and the multiplicity of the signals of the 4-C- and 6-C-methylene protons. The orientation of the substituents attached to the 5-C-atom can be judged on the basis of the following data. The signal of the 4-C- and 6-C-methylene proton in the spectrum of isomer IIb forms a typical AB quartet with a geminal constant ($^2J_{ae}$) of 13.0 Hz (which is typical for the chair conformation) and vicinal constants ($^3J_{aa'}$) 8.5 Hz and ($J_{a'e}$) 4.5 Hz. Using the Karplus graph [55], it is easy to establish that these values correspond to dihedral $H_{a'}-C-C-H_a$ and $H_{a'}-C-C-H_e$ angles of approximately 180 and 50°, thus indicating the equatorial character of the isopropyl radical. Isomer IIb is consequently a trans isomer with a diequatorial orientation of the alkyl substituents.

Correspondingly, in the spectrum of isomer IIa the 4-C- and 6-C-methylene protons are magnetically equivalent and are split under the influence of $H_{e'}$ into a doublet with a vicinal constant ($^3J_{e'H}$) of 4.7 Hz, which corresponds to a dihedral angle of ~50°. This attests to the equatorial character of the 5-C proton and, consequently, to the axial character of the isopropyl radical.

An analysis of the PMR spectrum of 2,2,5-trimethyl-1,3-dithiane (III) indicates that its molecules exist in the chair conformation. This conclusion was made on the basis of a comparison of the resonance bands of the methylene protons of the ring of the simplest 1,3-dithianes [7, 26, 27] with the analogous bands in the spectrum of III. The gem-methyl protons in the spectrum of this compound have considerable nonequivalent character ($\Delta\delta$ 0.16 ppm), which speaks in favor of the chair conformation. The 4-C- and 6-C-methylene protons are magnetically equivalent (similar to the analogous case in the spectrum of IIa) and form a doublet with a vicinal constant (^3J) of 6.25 Hz, which corresponds to an axial orientation of the 5-C-methyl radical. The spectrum of this compound graphically demonstrates the above-described conformational peculiarities of the structures under discussion, for it attests to both the considerable advantageousness of a 5-C-axial orientation and the considerable advantageousness of a 2-C-axial orientation in 1,3-dithiane molecules as compared with the usual axial orientations of the cyclohexane type.

The data obtained in a course of the study of the NMR spectra are graphically confirmed by data on the conformational energies of individual substituents in substituted 1,3-dioxanes and 1,3-dithianes. The data were obtained on the basis of a study of the equilibrium constants during a configurational isomerization of the type



This sort of isomerization was first observed by us [35, 45], and then by Eliel [6, 7], Riddell [9], and other investigators. We used such catalysts as I_2 and BF_3 in our experiments. Eliel [6,7] used only BF_3. Data on the magnitudes of the differences in the free energies of the axial and equatorial substituents obtained by us and by Eliel [6,7], Pihlaja [12], and other investigators (Table 1) as well as handbook data on the "conformational energies" of substituents (Table 2) are presented in the tables. It is apparent from these tables that the conformational energies of 5-C-alkyl substituents in molecules of substituted 1,3-dioxanes and 1,3-dithianes are substantially lower than the conformational energies of substituents in cyclohexane, as well as in the 2-C-, 4-C-, and 6-C-positions of the indicated rings. It is apparent from Table 2 that the 2-C-axial orientation in 1,3-dithiane is substantially more advantageous than the 2-C-axial orientation in 1,3-dioxane.

A fourth peculiarity of the systems under discussion is a complex set of nonsteric (in the classical understanding of this word) interactions of the "anomeric effect" type and other such phenomena [56-60]. It is well known that the anomeric effect consists in the fact that the 2-C-axial conformation is more preferred for 2-halo- and 2-alkoxytetrahydropyrans, -1,4-dioxanes, and -1,3-dioxanes. This effect is due to the dipole–dipole repulsion of the ring heteroatom and the substituent. We suppose that these effects should be considered to be limiting cases of the finer interactions described above.

Thus, an examination of substituted 1,3-dioxanes and 1,3-dithianes from the positions of conformational analysis leads to the conclusion that a greater diversity of preferred conformations is observed in these series than in the cyclohexane series. Of course, one should not consider the above list of peculiarities, which are in dialectic interrelationship with the fundamental principles of classical conformational analysis, to be absolute. However, a consideration of these peculiarities excludes the standard approach to the problem and, in addition, extends the sphere of modern configurational concepts.

EXPERIMENTAL

The 2,5-dimethyl-5-isopropyl-1,3-dioxanes (I) were obtained by the method in [31] by the reaction of 0.3 mole of 2-methyl-2-isopropyl-1,3-propanediol (mp 42-43°) with 0.9 mole of acetaldehyde in 180 ml of absolute benzene in the presence of the H form of KU-1 cation-exchange resin with azeotropic distillation of the water formed. The yield of the mixture of isomers (1 : 1) was 90%, and the mixture had bp 79° (27 mm), d_4^{20} 0.925, and n_D^{20} 1.435. Found %: C 77.2; H 8.5. $C_9H_{18}O_2$. Calculated %: C 77.0; H 8.3.

Mixture I was separated into stereoisomers Ia and Ib by rectification with an efficient, total condensation column with a glass packing and 40 theoretical plates. Isomer Ia had bp 75° (25 mm), d_4^{20} 0.9255 and n_D^{20} 1.4350. Isomer Ib had bp 81° (25 mm), d_4^{20} 0.9237, n_D^{20} 1.4330.

The isomer ratio, as a result of configurational isomerization via the methods in [6, 7] in the presence of I_2 and BF_3 (after equilibrium was reached), was Ia : Ib = 25 : 75. The purity of the isomers was 97-98%.

The synthesis of II and III, as well as the isolation of isomers IIa and IIb and their properties, were described in [44, 48]. The NMR spectra of Ia and Ib were obtained with an RYa-2303 spectrometer from the Special Design Office of Analytical Instrument Making of the Academy of Sciences of the USSR (ν_0 60 MHz) under conditions similar to those described by us in [31-33]. The spectra of IIa, IIb, and III were obtained with a Varian-A-100 spectrometer and also with a JNM-4H-100 spectrometer (ν_0 100 MHz) with stabilization of the resonance conditions with respect to a benzene internal standard.

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