STEREOCHEMISTRY OF SEVEN-MEMBERED HETEROCYCLES

5*. THE CONFORMATION OF 1,3-DIOXACYCLOHEPT-5-ENES

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Synthetic methods of obtaining 1,3-dioxacyclopent-5-enes have been analyzed in all aspects because of the wide use of these compounds in practice [2]. Conclusions concerning their spatial structure [3-6] have been inadequately substantiated and are disputed, and they also do not completely agree with information which we have obtained on the conformations of seven-membered acetals based on phthalyl alcohol and 2,3-dichlorobut-2-ene-1,4-diol [7-9].

This has induced us to perform a detailed conformational study of a wide range of acetals (I-IX) using the dipole moment (DM) method and IR, Raman, and PMR spectroscopy. The aim included the elucidation of the parameters of the dynamic conformational equilibrium of the chair (C) form with an equatorial arrangement of the substituent R(e) and the twist (T) form [7]







It has been shown previously that the DM method can be used successfully for the conformational analysis of that type of unsaturated acetals [1, 7-9] where the reliability of the geometric and bond parameters adopted is confirmed experimentally by graphical treatment according to Exner. Bond parameters similar to those used in the literature [1, 7-9], taking the DM of cis-butene as 0.33 D [10], were used in the calculations.

Analysis of the DMs of compounds (II-IV) (Table 1) shows a conformational equilibrium of forms of differing polarity, as follows unambiguously from the graph (Fig. 1).

The existence of a conformational equilibrium for (II-IV) was confirmed by a study of IR spectra. A comparison of the spectra of liquids, solutions, and crystals was carried out similarly to [7-9]. When (II) crystallized, a "freezing" of the bands at 596 and 894 (and 1185?) cm⁻¹ took place, which indicates the existence of a mixture of the C and T conformations in the liquid and solutions. These bands are assigned to the C conformation, since their relative intensities rise on passing from CCl₄ solution to CH₃CN solution, and from its DM the C form is more polar. Because of the low intensity of the 596 and 894 cm⁻¹ bands no quantitative measurements were made.

The methylene protons of (I) in the 2 and 4(7) positions appear in the PMR spectra in the form of two singlets [3-6], even when the sample is cooled to -140 °C [3]. This shows a rapid (in the NMR time scale) exchange of the protons of the conformational varieties. For this reason, previous conclusions [11] about the structure of (I) are incorrect.

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TABLE 1

	Dipole moments, D			
Compound	C.	Т	$ experi-ment C_6H_6,$	
(I) (II) (III) (IV)	2,63 2,84 4,04 6,22	$ \begin{array}{c c} 0,14 \\ 0,33 \\ 1,89 \\ 4,31 \end{array} $	1,39 * 1,55 2,24 4,71	
*1.07 (C	C14),	1.14 (d:	ioxane).	

For the formal (I) a qualitative similarity with 2-aryl compounds was to be expected, as in the case of phthalyl acetals [8, 9]. In actual fact, according to the DM results in $C_{6}H_{6}$ the proportion of the C form (I) was 0.28, and for (II-IV) it was ~ 0.20 .

The crystallization of (I) was accompanied by the disappearance of the bands at 610, 940, and 1182 cm^{-1} in the IR spectra and the lines at 465, 611 (677?), 946, and 1186 cm^{-1} in the Raman spectra (Figs. 2a and 3a). This permits the conclusion that mixtures of the C and T conformations exist in the liquid and in solutions.

In the IR spectra of solutions, the relative intensities of the 610 and 642 cm⁻¹ bands depended substantially on the polarity of the medium: with an increase in polarity (from CCL₄ to CH₃CN), the intensity of the 610 cm⁻¹ band rose and that of the 642 cm⁻¹ band fell. When the temperature was lowered from +17 to -45°C, in the IR spectrum of a solution of (I) in CH₃CN the ratio of the optical densities at the absorption maxima of the 642 and 610 cm⁻¹ bands rose from 2.1 to 3.6, which indicates the higher stability of the less polar form. According to DMs, the T form is the less polar. The magnitude $\Delta H = H_T - H_C = -0.90 \pm 0.10$ kcal/mole (CH₃CN solution) was determined from the temperature dependence of D₆₄₂/D₆₁₀. In the spectrum of a solution of (I) in CCl₄, the intensity of the 610 cm⁻¹ band was low, which complicates the determination of the value of ΔH from the temperature dependence of the intensity of the bands. Consequently, ΔH for a solution of (I) in CCl₄ was determined by comparing the values of D₆₄₂/D₆₁₀ in the IR spectra of solutions in CCl₄ and CH₃CN (7.1 and 2.9, respectively). On the assumption that the molar extinction coefficients did not depend on the solvent, we obtained $\Delta H = -1.40$ kcal/mole (CCl₄).

The DMs of the 2-alkyl derivative (V-IX) are 1.19, 1.30, 1.36, 1.40, and 1.95 D (CC1₄), respectively. The use of the DM method is complicated because of the appearance of an additional "alkyl" dipole [9]. A qualitative comparison of the experimental values of the DMs with one another shows a high proportion of the C form for (IX).

It is interesting to note that the polarization of compounds (V)-(VIII) is correlated with the inductive constants of the alkyl groups (σ_I). A similar pattern for phthalyl acetals with analogous substituents in position 2 has been observed [9]. This permits the assumption in this case, as well, of close ratios of the conformation of compounds (V-VIII).

When compound (V) crystallized the 692, 872, and 1050 cm⁻¹ bands of the IR spectrum and the 404, 557, and 640 cm⁺¹ lines in the Raman spectrum were "frozen" (Figs. 2b, and 3b). The crystallization of compound (IX) led to the disappearance of the 645, 778, 920 (1055?), and (1381?) cm⁻¹ bands in the IR spectra and of the (\sim 300?), 781, 873, and (1213?) cm⁻¹ lines in the Raman spectra (Figs. 2c and 3c).

Investigations of compounds (V) and (IX) in solvents of different polarities made it possible to establish that the conformation to which the bands disappearing on crystallization related was more polar for (V) and less polar for (IX). We determined the values of ΔH for the temperature dependences of the ratios of the optical densities of the two bands assigned to the different conformations. In the IR spectra of (V) we investigated the temperature dependences of D_{677}/D_{692} (CS₂, from -10 to -105°C) and D_{1018}/D_{1050} (CH₃CN, from +20 to -40°C). The values of ΔH obtained were -0.72 ± 0.03 kcal/mole (in CS₂) and -0.35 ± 0.06 kcal/mole (in CH₃CN).

From the IR spectrum of (IX) using the D_{637}/D_{672} dependence (CS₂, from -15 to -105°C) we found $\Delta H = 0.34 \pm 0.3$ kcal/mole. The values of ΔH for solutions of (IX) in CCl₄ and CH₃CN were determined by comparing the values of D_{637}/D_{672} in the spectra of these solutions with their solutions in CS₂. This gave $\Delta H = 0.35$ kcal/mole (CCl₄) and 0.78 kcal/mole (CH₃CN).

According to NMR results, compounds (V), (VI), and (IX) have the C form [4-6], the methylene protons in the 4(7) positions being shown by an AB quartet. As a model for (VI)



Fig. 1. Comparison of the squares of the dipole moments for compounds (II) and (IV) (T - twist; C - chair; E - experimental results). Fig. 2. IR spectra of (I) (a), (V) (b), and (IX) (c) in the liquid (l) and crystalline (2) states.

we selected 2-ethyl-5-methylene-1,3-dioxane [4], which exists in the C form [12]. However, in a study of 2-tert-butyl-5,6-dichloro-1,3-dioxacyclohept-5-ene we have shown [7] that in the T and C conformations the CH_2 groups have AB systems with different magnetic nonequivalences of the protons, the bulk of them corresponding to a flexible form. Consequently, the CH_2 protons are shown as AB system even with a rapid exchange of conformational states.

We have studied the temperature dependence of the PMR spectra of compounds (V), (VI), and (IX) in CS_2 and acetone in the interval from +30 to $-80^{\circ}C$. The maximum change in the difference in the chemical shifts of the protons in the 4(7) positions was 1.3 Hz for (V), 1.0 Hz for (VI), and 5.0 Hz for (IV). These facts, at least for (IX), can be interpreted from the points of view of the existence of a conformational equilibrium. For quantitative estimates of the position of the conformational equilibrium, computer processing of the spectra within the framework of the approach suggested previously [7] is necessary.

Thus, a combination of physical methods (DM, IR, Raman, and PMR spectroscopy) has enabled us to establish that compounds (I)-(IX) exist as conformational equilibria of the C and T forms depending on the nature of the substituents in position 2. An analysis of the information obtained in the present work together with that in the literature [1, 7-9] permits a number of factors determining the conformational equilibrium of the C and T forms to be singled out.

In the first place, the possibility of the realization of the flexible form is due to the appearance of a generalized anomeric effect [7, 11], since the heterocyclic part of sucy acetals in the T form resembles the gg^1 conformation of methylal. We may note that the carbocyclic analog of (I) - cycloheptene - has a chair-like conformation according to NMR [13].

In the second place, the chair forms of (I)-(IX) are strained because of the steric repulsion of the equatorial H atoms and the vinyl hydrogens, which must be considered as a specific conformational effect of the planar fragment [7]. In the T form, the arrangement of the H atoms at C⁴ and C⁵ (C⁶ and C⁷) is close to bisectorial and is, naturally, energetically more favorable.



In the third place, the substituent in position 2 of the T form experiences considerable 1,3-syn-axial repulsion due to the volume of its R group. For this reason, the greater proportion of the C form in the series studied applied to compound (IX), where $R = (CH_3)_3C$.

We have found previously that 7,12-dioxaspiro[5,6]dodec-9-ene [1] has a T form similarly to other cyclohexanone ketals [7, 8, 11, 14]. This is a general rule of the conformational



(c) in the liquid (l) and crystalline (2) states.

organization of 2,2-dialkyl-substituted acetals. For this reason, the butenediol ketal of acetone has the T form [5], as has been found from ^{13}C NMR spectra, and is not a mixture of the C and T forms.

In the series of 2-aklyl-substituted phthalyl acetals [9] a dipole is induced in the alkyl group, the vector of which is directed from the substituent R into the ring. A failure to take the "alkyl" dipole into account, i.e., equating the C_{sp3} -H moment to the C_{sp3} -alkyl moment (as is done in the majority of cases) leads to an incorrect interpretation of the results of the DM method.

In the present investigation this appears clearly in a comparison of the DMs of (I) and (V), which scarcely differ from one another: 1.07 and 1.19 D, respectively (accuracy of the method ± 0.05 D). Ignoring the "alkyl" dipole of the CH₃ group would lead to the conclusion of an equality of the proportions of C and T for (I) and (V). However, the spectral results clearly show the existence of a shift of the equilibrium in the C direction when the H atom is replaced by CH₃.

At the same time, the experimental values of the DMs of compounds (IX) (1.95 D) and its benzo analog (2.04 D) [9] are close, with practically the same DMs of the C and T forms as those calculated from the formal: 2.63, 0.14 D and 2.67, 0.34 D, respectively. The positions of the conformational equilibria are far from identical in the two cases. For (IX) there is a \sim 1:1 mixture of the C and T forms, while for the benzo analog an anancomeric shift in the direction of the polar form was found. Consequently, alkyl dipoles induced in the (CH₃)₃C groups differ considerably. Therefore, it may be assumed with a fair degree of reliability that the field effect, and not induction through bonds, is responsible for this.

A combined consideration of IR and Raman spectra substantially supplements each of them, which provides the possibility for a broad study of spectral differences in the conformations.

For example, in the case of (V) and (IX) a "freezing" of the lines in the IR and Raman spectra relative to various vibrations is observed (see Figs. 2 and 3). It must be mentioned that the C and T forms of (I), (V), and (IX) have different vibrations in the region of the skeletal deformation vibrations of the ring (below 700 cm⁻¹), and even in the region of vibrations with a change in the lengths of the C-C and C-O bonds and of the CCH and OCH valence angles (above 700 cm⁻¹), while the bands with low frequencies (below 400 cm⁻¹) scarcely differ in the C and T conformations. In the Raman spectra of (I) and (V), in the liquid state, very strong polarized lines are observed at 864 and 811 cm⁻¹, respectively, which may relate to the pulsation vibration of the ring. In the IR spectra, very weak bands correspond to this vibration. When a t-C₄H₉ group is introduced into position 2 (IX), a very strong line in the Raman spectra at 585 cm⁻¹, to which a very weak band in the IR spectrum corresponds, can be ascribed to the pulsation vibration.

Thus, the method of vibrational spectroscopy has permitted us to determine the position of the conformational equilibrium for each of compounds (I), (II), (V), and (IX) in liquid and dissolved forms with greater simplicity and clarity than the use of ¹H NMR spectroscopy. This shows the fruitfulness of the use of vibrational spectroscopy in the conformational analysis of seven-membered cyclic acetals.

TABLE 2

Compound	α	Ŷ	P or	Solvent	DM, D
(I) (II) (III) (IV) (V) (VI) (VII) (VII) (VIII) (X)	$\begin{array}{c} 2,25\\ 2,60\\ 1,84\\ 1,40\\ 2,59\\ 11,16\\ 2,12\\ 2,39\\ 2,38\\ 2,54\\ 4,75\end{array}$	$\begin{array}{c} 0,03\\ 0,12\\ -0,09\\ -0,08\\ -0,01\\ 0,26\\ -0,25\\ -0,13\\ -0,11\\ -0,11\\ -0,11\end{array}$	23,450 40,759 39,381 49,040 102,685 453,532 28,797 38,845 37,730 39,981 76,571	CCl ₄ Dioxane Benzene » » CCl ₄ The same » »	1,07 $1,41$ $1,39$ $1,55$ $2,24$ $4,71$ $1,19$ $1,30$ $1,36$ $1,40$ $1,95$

EXPERIMENTAL

IR spectra were obtained on UR-20 spectrometer as described by Remizov and Samarina [15]. Values of ΔH were determined as descriged by Zhizhin and Sterin [16]. Optical densities D were measured at the maxima of the absorption bands. For ΔH , random errors found on treating the dependence of D_{V_1}/D_{V_2} on the temperature have been shown by the method of least squares. Raman spectra were obtained on a DFS-24 spectrometer with a He-Ne laser. Crystalline samples were obtained by freezing liquids in a capillary (d = 3 mm) in a glass cryostat cooled with liquid nitrogen. The spectra of the crystals were recorded at 100°K. The formation of crystals was determined from the appearance of the vibrations of the crystal lattice in the 20-100 cm⁻¹ region.

The PMR spectra were recorded on a Varian HA-100D spectrometer. Dipole moments were measured as described previously [17]. The coefficients of the equations for calculation were given in Table 2.

<u>2-p-Nitrophenyl-1,3-dioxacyclohept-5-ene (IV).</u> Equimolar amounts of cis-but-2-ene-1,4diol and of p-nitrobenzaldehyde were boiled in benzene containing a catalytic amount of ptoluenesulfonic acid with a Dean-Stark trap. After the theoretical amount of water had been liberated, the solution was cooled, washed with 10% NaHCO₃ solution, and dried with Na₂SO₄; mp 104-105°C (from ethyl acetate), yield 95%. Found: C 59.89; H 5.00; N 6.31%. C₁₁H₁₁NO₄. Calculated: C 59.72; H 5.01; N 6.33%, see [18].

Compounds (I)-(III) and (V)-(IX) were obtained similarly to (IV). (I) - bp 123°C (760 mm), $n_D^{2^3}$ 1.4535, see [2, 4, 19-21]; (II) - bp 86-87°C (3 mm), $n_D^{2^0}$ 1.5382, see [2, 21]; (III) - mp 63.5-64°C (from benzene), see [2, 18]; (V) - bp 71-72°C (86 mm), $n_D^{2^0}$ 1.4476, see [2, 18, 21, 22]; (VI) - bp 77°C (56 mm), $n_D^{2^0}$ 1.4500, see [2, 18, 22]; (VII) - bp 74°C (22 mm), $n_D^{2^4}$ 1.4482, see [2, 18, 22]; (VIII) - bp 104°C (104 mm), $n_D^{2^2}$ 1.4472, see [2, 18]; (IX) - bp 39-40°C (3 mm), $n_D^{2^0}$ 1.4475, see [5]. Before the physical measurements were made, the liquid samples were redistilled over Na.

SUMMARY

1. According to the results of dipole moment and IR and Raman spectroscopy methods, the butenediol acetals (I)-(IX) are characterized by a conformational equilibrium of the chair and twist forms determined by the influence of various factors.

2. In the determination of the conformational equilibrium of the 2-alkyl-substituted acetals the influence of the "alkyl" dipole must be taken into account.

LITERATURE CITED

- 1. B. A. Arbuzov, E. N. Klimovitskii, and M. B. Timirbaev, Izv. Akad. Nauk SSSR, Ser. Khim., 1799 (1980).
- C. E. Pawloski, in: Seven-Membered Heterocyclic Compounds Containing Oxygen and Sulfur (ed. by A. Rosowsky) (Vol. 26 of Heterocyclic Compounds), Wiley-Interscience, New York (1972), Chap. 5.
- 3. H. Freibolin, R. Mecke, S. Kabuss, and A. Luttringhauss, Tetrahedron Lett., 1929 (1964).
- F. Mutterer, J. M. Morgen, J. M. Biedermann, J. P. Fleure, and F. Weiss, Bull. Soc. Chim. France, 4478 (1969).
- 5. M. H. Gianni, M. Adams, H. G. Kuivila, and K. Wursthorn, J. Org. Chem., 40, 450 (1975).
- J. Soulier, M. Farines, A. Laguerre, and A. Bonafos-Bastouill, Bull. Soc. Chim. France, 307 (1976).

- 7. B. A. Arbuzov, E. N. Klimovitskii, A. B.Remizov, V. V. Klochkov, A. V. Aganov, and M. B. Timirbaev, Izv. Akad. Nauk SSSR, Ser. Khim., 1794 (1980).
- 8. B. A. Arbuzov, E. N. Klimovitskii, A. B. Remizov, and G. N. Sergeeva, Izv. Akad. Nauk SSSR, Ser. Khim., 2031 (1979).
- 9. B. A. Arbuzov, E. N. Klimovitskii, A. B. Remizov, and G. N. Sergeeva, Izv. Akad. Nauk SSSR, Ser. Khim., 290 (1980).
- A. L. McClellan, Tables of Experimental Dipole Moments, W. H. Freeman, San Francisco (1963).
- 11. A. Blanchette, F. Sauriol-Lord, and M. St-Jacques, J. Am. Chem. Soc., 100, 4055 (1978).
- 12. M. Anteunis and R. Camerlynck, Tetrahedron, <u>31</u>, 1841 (1975).
- 13. M. St-Jacques and C. Vaziri, Can. J. Chem., 49, 1256 (1971).
- 14. B. A. Arbuzov, V. V. Klochkov, A. V. Aganov, E. N. Klimovitskii, and Yu. Yu. Samitov, Dokl. Akad. Nauk SSSR, 250, No. 2, 378 (1980).
- 15. A. B. Remizov and O. A. Samarina, Zh. Prikl. Spektrosk., <u>22</u>, 870 (1975).
- 16. G. N. Zhizhin and Kh. E. Sterin, Zh. Prikl. Spektrosk., 5, 506 (1966).
- 17. B. A. Arbuzov, E. N. Klimovitskii, L. K. Yuldasheva, and G. N. Sergeeva, Izv. Akad. Nauk SSSR, Ser. Khim., 2422 (1973).
- 18. W. Kantlehner and H. Gutbrod, Synthesis, 975 (1979).
- 19. K. C. Brannock and G. R. Lappin, J. Org. Chem., 21, 1366 (1956).
- 20. M. W. Miller, Tetrahedron Lett., 2545 (1969).
- M. J. Soulier, M. M. Farines, M. A. Bonafos-Bastouill, and M. A. Laguerre, Bull. Soc. Chim. France, 1763 (1975).
- 22. V. V. Mozolis, A. I. Rutavichyus, and S. P. Iokubaitite, Trudy Akad. Nauk LitSSR, Ser. B., <u>3</u>, No. 100, 29 (1977).

STRUCTURE AND CONFORMATIONS OF STEREOISOMERIC 1, 5;2, 3-BIS-O-(N-DIETHYLAMIDOTHIONEPHOSPHATO)-β-D-RIBOFURANOSIDES FROM ¹H, ³¹P, AND ¹³C NMR SPECTRAL DATA

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We previously [1] presented a brief communication concerning the synthesis of stereoisomeric 1,5;2,3-bis-O-(N-diethylamidothionephosphato)- β -B-ribofuranosides (II) and (III) in the amidothionephosphorylation of D-ribose (I).



In this work, we present results of the analysis of ¹H, ³¹P, and ¹³C NMR spectra of compounds (II) and (III), which allow us to draw conclusions concerning their structure and preferred conformations of their component heterocycles, and also serve as a basis for establishing the configuration of the chiral phosphorus atoms [1]. In analogy with the line assignments in the PMR spectra of cyclic forms of monosaccharides, we have assigned the low-field signal with $\delta H \approx 5.75$ ppm (in CH₃CN solution) to the anomeric proton H², and the high-field

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