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CONFORMATION OF 2-PHOSPHORYL AND 2-THIOPHOSPHORYL 1,3-DITHIANES AND RELATED COMPOUNDS. COMMENTS ON THE ORIGIN OF S-C-P ANOMERIC INTERACTIONS.

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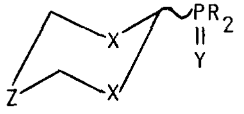
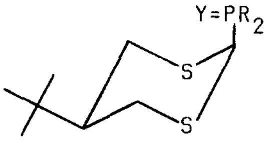
Abstract: A relationship was found between the γ-effect values in ^{13}C NMR spectra and the solution conformation of the title compounds. Base-catalyzed equilibration of anancomeric 2-phosphoryl and 2-thiophosphoryl substituted 5-t-butyl-1,3-dithianes showed that axial preference increases in the order: $Ph_2P(S) < Ph_2P(O) < (MeO)_2P(O)$. Explanation of this phenomenon is proposed,based also on the results of molecular mechanics calculations.

Significant attention has recently been devoted to the anomeric effect in 2-heterosubstituted 1,3-di- and 1,3,5-trithianes[1-5]. Juaristi et al[6] and our group[7,8] found that some 2-phosphoryl substituted compounds of this type show strong tendency to exist both in solution and in the crystal in a chair conformation with the P(O)-group being axial. However, explanation of this effect is till now far from satisfactory[9].

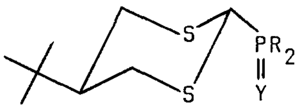
In the present paper we wish to report the results of our further studies on the conformational behaviour of 2-phosphoryl- and 2-thiophosphoryl 1,3-di- and 1,3,5-trithianes, 1,3-dioxanes (compounds 1-5) and anancomeric 5-t-butyl-1,3-dithianes (compounds 6-8) as well as to propose a new explanation for the axial preference of the phosphoryl group in 1,3-dithiane ring.



1-5



6a-8a



6b-8b

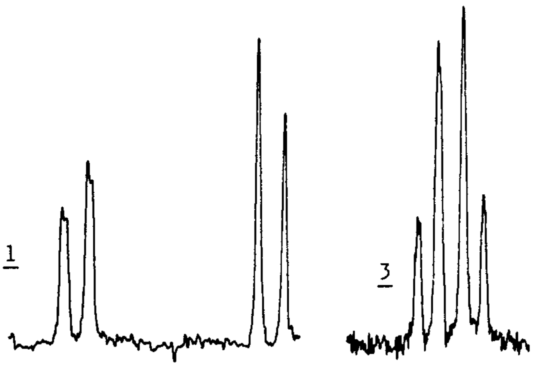
1, X=S,Y=O,Z=Me_2C,R=Ph
2, X=S,Y=S,Z=Me_2C,R=Ph
3, X=O,Y=O,Z=Me_2C,R=Ph
4, X=S,Y=O,Z=S, R=Ph
5, X=S,Y=S,Z=S, R=Ph
9, X=S,Y=O,Z=S, R=OMe
10, X=S,Y=O,Z=CH_2, R=OMe
11, X=S,Y=O,Z=CH_2, R=Ph

6, Y=O,R=Ph
7, Y=O,R=OMe
8, Y=S,R=Ph

All the compounds shown above were synthesized by the methods described by us earlier[11] and analyzed by means of ^1H, ^{13}C and ^{31}P NMR spectroscopy. Selected data from these spectral studies are collected in Table 1.

Due to the presence of the two methyl groups at C-5 or sulfur in the position 5 of the six-membered ring in compounds 1-5 the resonance signals of the geminal protons at C-4 and C-6 in the ^1H NMR spectra are simple and can be easily interpreted. However, it should be pointed out that the shape of the spectrum of these protons cannot be used for a fast and unambigous assignment of the predominant conformation in solution. For example, it was found that ^1H NMR spectra of CH_2-protons in compounds 1 and 3 are similar in shape (see Fig.1) although the $Ph_2P(O)$-group in 1 is axial while in 3[12] equatorial. As expected, in the ^1H NMR spectrum of 1 one observes the signals (doublet) of the axial methylene protons at lower field due to deshielding by the axial C-P bond. These signals are split into double doublet owing to a long--range coupling with phosphorus. On the other hand, in the ^1H NMR spectrum of 3 the resonance signals of the equatorial methylene protons are at lower field and are similarly split as a result of the W-type coupling with phosphorus. This difficulty does not appear for cis- and trans diastereomeric dithianes 6-8. Their ^1H NMR spectra are conclusive and allowed us to assign unambigously an axial and equatorial position for the P(O)- and P(S)--group at C-2[13].

Figure 1.



Methylene protons region of the ^1H NMR (80 MHz) spectra of 1 and 3.

An inspection of the ^{13}C NMR results and especially of the magnitude of γ-effect for anancomeric pairs of dithianes 6-8 and for compounds 9-11, for which conformational preferences have been established earlier, strongly suggests that the γ-effect values may be used for a fast assessment of the predominant solution conformation of the compounds under discussion. Thus, in the case of compounds 1,4,6a-8a,9-11 with the axial phosphorus substituent at C-2 γ-effect is negative and amounts some ppm. Moreover, the coupling constant between P and C-4 and C-6 observed in these compounds is nearly zero. When the phosphoryl or thiophosphoryl group is located in the equatorial position of the six-membered ring (compounds 3 and 6b-8b) the γ-effect values are positive or nearing to zero and the coupling constant $^3J_{P-C}$ is about 7-10 Hz

Taking into account this rather clear relationship between the γ-effect and axial or equatorial orientation of the phosphoryl or thiophosphoryl group at C-2 in dithianes, one may suppose that compounds 2 and 5 which contain diphenylthiophosphinyl substituent at C-2, exist in a solution as a mixture of

Table 1. Selected ^1H, ^{13}C and ^{31}P NMR data for compounds 1-11$^{a)}$

No	m.p. [^oC]	^1H NMR				^{13}C NMR			^{31}P NMR
		δH_{4ax}	δH_{4eq}	$\Delta\delta^{e)}$	$^1J_{H-P}$	γ-Effect	$^1J_{C-P}$	$^3J_{C-P}$	δ
1	263.2-263.4	3.45	2.16	1.29	5.5	-2.73	69.1	0	32.8
2	181.4-183.3	3.16	2.43	0.75	8.0	-1.43	51.5	2.9	47.5
3	142.0-143.0	3.48	3.74	0.26	5.9	-0.72	118.1	10.4	23.2
4	263.0-264.0^d	$5.23^{c,d}$	$3.87^{c,d}$	$1.36^{c,d}$	$6.9^{c,d}$	-3.97	82.4	0	47.9^c
5	176.5-178.5	4.95	3.80	1.15	11.0	-2.63	51.5	4.4	48.5
6a	262.0-262.9	3.63	2.55	1.08	3.5	-3.64	70.8	0	34.1
6b	227.0-227.8	2.55	3.07	0.52	12.9	1.21	66.2	7.1	28.5
7a	103.4-104.2	3.38	2.59	0.8	16	-4.27	159.2	0	20.4
7b	83.8- 85.4	2.69	2.96	0.27	19.0	0.67	148.0	8.7	20.6
8a	174.2-176.5	3.89	2.47	1.42	5.3	-4.49	2.9	0	49.8
8b	188.0-190.0	2.71	2.94	0.23	11.4	1.42	49.0	8.8	45.7
9	113.0-114.0	5.20	3.57	1.63	20.0	-5.0	157.4	0	18.8
10	45.0-45.5	3.54	2.56	0.98	19.0	-4.02	158.1	1.8	23.2^b
11^d	242.0-243.0	3.7	2.5	1.2	6.0	-2.93	158.1	1.8	34.1^b

a) δ values given in ppm; J values in Hz. ^1H NMR and ^{13}C NMR spectra were measured in $CDCl_3$, ^{31}P NMR spectra in $CHCl_3$ unless otherwise stated; b) in $CDCl_3$; c) in DMSO-d_6; d) data from ref.6c; e) $\Delta\delta = |\delta H_{4ax} - \delta H_{4eq}|$

axial and equatorial conformers in comparable amounts because both the γ-effect and $^3J_{C-P}$-values are mean values. This assumption was supported by our preliminary low-temperature ^{31}P NMR studies of trithiane 5. It was observed that the room temperature singlet at δ 47.9 was split at -100^{o}C into two lines of similar intensity most probably corresponding to both chair conformers, 5ax and 5eq. A lower bias of the diphenylthiophosphinyl than diphenylphosphinyl group to occupy an axial position in the 1,3-dithiane ring was also indicated by the base-catalyzed equilibration (C_6H_6, MeOH, MeONa, 25^{o}C) of the three anancomeric pairs of dithianes 6-8 followed by ^{31}P NMR spectra. The equilibrium ratios, a:b and the estimated conformational free energy differences $-\Delta G^o$(kJ/mol), are as follows: for 6: 83.4:16.6, 3.93; for 7: 88.3:11.7, 4.92; for 8: 70.2:29.8, 2.09. Thus, the greatest $-\Delta G^o$- value and hence the strongest axial preference was found for dimethoxyphosphoryl group while the lowest for diphenylthiophosphinyl group.

Finally, we should note that molecular mechanics calculations[14] of the two possible chair conformers of trithiane 4 showed that their energy is equal, if one neglects electrostatic interaction between non-bonded electron pairs on sulfur and on phosphoryl oxygen. However, if this type of repulsive interactions is taken into account, the energy of the axial conformer 4ax is smaller than that of the equatorial one, 4eq, by about 5.7-8.3 kJ/mol. This value is in a good agreement with those obtained from equilibration experiments.

As it was originally proposed in our previous paper[7], the axial position of the phosphoryl group may be additionally stabilized by attractive interactions between the phosphoryl oxygen and the axial hydrogens at C-4 and C-6. In the case of the axial thiophosphoryl group, however, the interactions of these axial hydrogens with sulfur, which is much bigger than oxygen and of lower electronegativity, may be expected to be repulsive in character leading consequently to destabilization of the axial P(S)-conformer. This is reflected in the lower $-\Delta G^0$ value for $Ph_2P(S)$-group.

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9. The generally accepted explanation of the anomeric effect in terms of delocalization of the lone pair on the endocyclic heteroatom into the antiperiplanar adjacent polar bond (in our case n_S-σ^*_{C-P} interaction) may be ruled out based on the results of X-ray data for compounds 11^{6a}, 9^7,5^{10} and $6a^{10}$. A recent proposal by Juaristi et al[6c] that through-space 3 3p-3d electron donation from sulfur to phosphorus may be responsible for the axial preference of the P-substituent is not consistent with the fact that 1,3-dithianes containing triphenylphosphonium substituent exist largely in equatorial conformation[10].
10. Unpublished results from this laboratory.
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12. Equatorial position of the $Ph_2P(O)$ group in 3 was found in the crystal[10].
13. X-Ray analysis of 6a confirmed our NMR configurational assignments.
14. We thank Prof. M.I.Kabachnik and Dr. A.P.Baranov from the Institute of Elementoorganic Compounds of the Academy of Sciences USSR, Moscow, for carrying out these calculations. The results will be published elsewhere.

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