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REACTIONS OF POLYSUBSTITUTED THIOPYRANS WITH PROTON ACIDS AND STRUCTURAL STUDIES OF THE RESULTING THIACYCLOHEXANES

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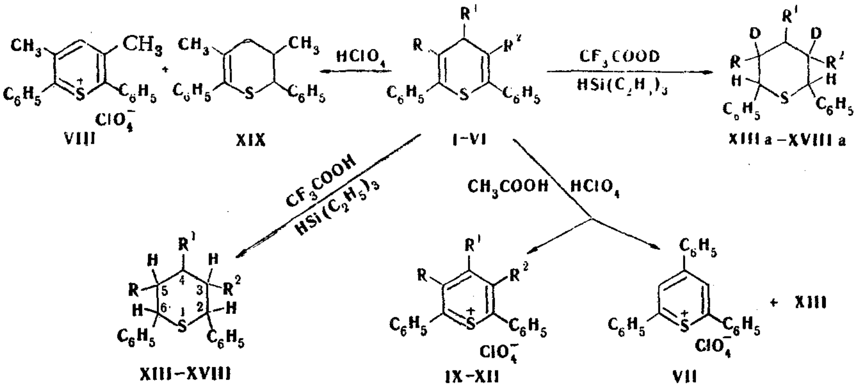
UDC 547.818:548.737:543.422.25

Depending on the number and nature of substituting groups, 4H-thiopyrans under the influence of perchloric and trifluoroacetic acids either undergo disproportionation or form thiapyrylium salts in quantitative yields with the participation of air oxygen; in the case of ionic hydrogenation with CF_3COOH—$SiHEt_3$ they are converted to thiacyclohexanes, regardless of their structure. To ascertain the reason for the difference in the mechanisms of the reaction of polysubstituted thiopyrans with proton acids the structures of the polysubstituted thiacyclohexanes were investigated jointly by NMR spectroscopy and x-ray diffraction analysis; this made it possible to form a judgment regarding the effect of the degree and character of substitution of 4H-thiopyrans on the mechanism of their reaction with proton acids. The tetrahydrothiopyran ring has a chair conformation. The phenyl substituents are equatorially oriented, while the methyl substituents are axially oriented.

We have established the existence of an effect of the degree and character of substitution of 4H-thiopyrans on the mechanism of their reaction with some proton acids. It is known that di- and triaryl-substituted thiopyrans, including sulfide I, react with 70% $HClO_4$ in acetic acid to give thiapyrylium salts and thiacyclohexanes [1], while tetrasubstituted thiopyran II undergoes disproportionation only to perchlorate VIII and dihydrothiopyran XIX [2]. For the first time we have observed that pentasubstituted (III-V) and tetrasubstituted (VI) thiopyrans react with perchloric acid in air to give only thiapyrylium salts IX-XII in quantitative yields, whereas virtually no reaction is observed in a helium atmosphere [3]. Further studies in the case of thiopyran VI made it possible to establish that both thiapyrylium perchlorate XII and thiacyclohexane XVIII are formed in a helium atmosphere when the reaction mixture is allowed to stand for a sufficiently long time (4 months), i.e., thiopyran VI undergoes disproportionation. Thus, in the reaction of thiopyrans with $HClO_4$ in acetic acid the formation of thiapyrylium salts may proceed via two



I, XIII, XIIIa R=R^2=H, R^1=C_6H_5; II, XIV, XIVa R=R^2=CH_3, R^1=H; III, IX, XV, XVa R=R^1=R^2=CH_3; IV, X, XVI, XVIa R=R^2=CH_3, R^1=C_2H_5; V, XI, XVII, XVIIa R=R^2=CH_3, R^1=C_6H_5; VI, XII, XVIII, XVIIIa R=H, R^1=C_6H_5, R^2=CH_3

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0009-3122/80/1603-0237$07.50

TABLE 1. Coordinates of the Atoms and Calculated Coordinates of the Hydrogen Atoms ($\cdot 10^4$) of the XIV Molecule*

Atom	x	y	z	Atom	X	Y	z
S	0	2050 (3)	1/2	H (2)	540	498	3017
C (2)	598 (3)	1531 (8)	3495 (14)	H (3)	927	1911	661
C (3)	572 (4)	2216 (8)	1567 (16)	H (4)	0	2482	−704
C (4)	0	1932 (12)	528 (19)	H (4′)	0	962	156
C (7)	1175 (3)	1670 (9)	4500 (13)	H (8)	978	3465	6007
C (8)	1283 (4)	2701 (9)	5773 (16)	H (9)	1919	3636	7476
C (9)	1815 (5)	2801 (10)	6678 (22)	H (10)	2646	1922	6853
C (10)	2251 (4)	1896 (14)	6273 (18)	H (11)	2465	93	4830
C (11)	2148 (4)	845 (11)	5057 (20)	H (12)	1542	−81	3183
C (12)	1612 (4)	744 (9)	4161 (16)	H (13)	800	3100	1700
C (13)	725 (5)	3775 (8)	1663 (20)	H (13′)	819	4351	497
				H (13″)	627	4378	2704

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*The numbers of the H atoms coincide with the numbers of the corresponding nonhydrogen atoms (designated by an apostrophe for the second hydrogen atom of the CH_2 group, and designated by one and two apostrophes for the second and third hydrogen atoms of the CH_3 group).

competitive pathways: 1) as a result of disproportionation of the thiopyrans; 2) via a mechanism that is realized with the participation of air oxygen. It is fully likely that the mechanism proposed for the oxidative dehydrogenation of pyrans [4] is realized in the latter case. It is apparent from the information presented above that the second pathway involving salt formation predominates for polysubstituted thiopyrans III-VI in air.

Thiopyrans II-IV and VI undergo disproportionation with trifluoroacetic acid in the usual way, and only sulfide V does not undergo disproportionation even with CF_3COOH.

In reactions involving disproportionation with CF_3COOH and ionic hydrogenation [$CF_3COOH/HSi(C_2H_5)_3$] of thiopyrans I-IV and VI the same isomer of the corresponding thiacyclohexane (XIII-XVI and XVIII) is formed [5]. Sulfide XVII was obtained by ionic hydrogenation of thiopyran V [5].

To ascertain the reasons that lead to the difference in the mechanisms of the reaction of polysubstituted 4H-thiopyrans with proton acids we attempted to accomplish the conformational analysis of thiacyclohexanes — the products of disproportionation.

In the PMR spectrum of thiacyclohexane XIVa the protons attached to C_4 form an AB system with $^2J_{AB}$ = 13.3 Hz, and this may constitute evidence for the conformational rigidity of the molecules of sulfides XIVa and XIV. The signal of the 2-H and 6-H protons in both the spectrum of thiacyclohexane XIV and the spectra of thiacyclohexanes XV-XVII, which differ only with respect to the substituents in the C_4 position is a doublet at δ 4.3 ± 0.06 ppm with $^3J_{2,3} = {}^3J_{5,6} = 2.6 \pm 0.1$ Hz. This makes it possible to assume that the molecules of thiacyclohexanes XV-XVII are symmetrical and have the same fixed conformation and the same orientation of the substituents attached to C_2, C_3, C_5, and C_6 as in the case of sulfide XIV. A comparison of the spectra of thiacyclohexanes XIII, XVIII, and XVII made it possible to express the assumption that in solution in carbon tetrachloride the molecules of sulfides XIV-XVII exist in the chair conformation and that even at room temperature the conformational equilibrium is shifted virtually completely to favor the conformer with equatorial phenyl substituents attached to C_2 and C_6 and axial methyl groups attached to C_3 and C_5.

It has been previously established [5] that the presence of an axial methyl group attached to C_3 in thiacyclohexane XVIII, which has a fixed chair conformation, leads to a decrease in the $^3J_{2a,3e}$ value to 2.8 Hz as compared with the value in the spectrum of sulfide XIII (3.3 Hz). An axially oriented methyl substituent also has a substantial effect on the chemical shifts of the axial protons of thiacyclohexane XVIII. Data from the spectra of 3,5-dideuterated tetrahydrothiopyrans XIIIa and XVIIIa are presented below. The signals of the axial 2-H and 4-H protons in the spectrum of sulfide XVIIIa (δ 4.52 and 3.05 ppm, respectively) are shifted to weak field as compared with the signals in the spectrum of thia-

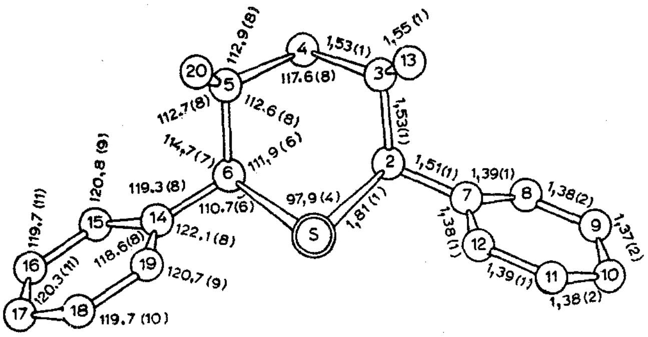

Fig. 1. Geometry of the XIV molecule: bond lengths and valence angles.

cyclohexane XIIIa (δ 4.16 and 2.83 ppm, respectively), whereas the signal of the axial 6-H proton is shifted to strong field from 4.16 ppm (XIIIa) to 4.00 ppm (XVIIIa).

Tetrahydrothiopyran XVII, the molecule of which is symmetrical and has a fixed conformation, differs from sulfide XVIII with respect to the presence of a methyl substituent attached to C_5. Taking the above information into account, the $^3J_{2,3} = {}^3J_{5,6} = 2.6$ Hz value in the spectrum of thiacyclohexane XVII makes it possible to assume that its molecules have a fixed chair conformation with equatorial phenyl substituents attached to C_2 and C_6 and axially oriented methyl groups in the C_3 and C_5 positions. Then, in conformity with the indicated effect of the axial CH_3 group on the chemical shifts of the axial protons, the 2-H signal should be shifted to strong field as compared with sulfide XVIIIa to δ 4.36 ppm, whereas the 6-H signal should be shifted to weak field to δ 4.36 ppm (as indicated, the 2-H and 6-H protons of thiacyclohexane XVII resonate at δ 4.36 ppm).

We carried out the x-ray diffraction analysis of XIV for an unambiguous solution of the problem of the conformation and configuration of polysubstituted thiacyclohexanes XIV-XVII.

Crystals of XIV are rhombic with $a = 22.882$ (8), b = 9.956 (3), c = 7.124 Å (2), M = 282.4, $d_{calc} = 1.15$ g/cm³, Z = 4, and space group Ctc 2_1.

The intensities of 531 independent reflections with $I > 2\sigma$ were measured with a four-circle Hilger–Watts automatic diffractometer guided by a PDP 8/1 minicomputer (with λCuK_α emission, a graphite monochromator, θ/2θ scanning, and a range of $1° \leqslant \theta \leqslant 57°$); no correction for absorption was introduced [$\mu(CuK_\alpha) = 16.0$ cm^{-1}]. The structure was decoded by the heavy-atom method and was refined by the method of least squares within the total matrix approximation; corrections for anomalous scattering were taken into account for the atom. The hydrogen atoms (except for two atoms of the methyl group) were exposed by differential synthesis and were included in the calculation of F_{calc}; the positional and heat parameters of the H atoms were not taken into account (it was assumed that $B_{iso} = 5.0$ Å²),* and the final R value was 0.0666 ($R_W = 0.0769$).† The coordinates of the atoms are given in Table 1,‡ while the stereochemistry of the molecule with the bond lengths and valence angles is shown in Fig. 1.

The molecule has C_S crystallographic symmetry (the m plane passes through the S and C_4 atoms of tetrahydrothiopyran ring A). The A ring has a chair conformation close to that found in the 4-amino-4-carboxytetrahydrothiopyran structure [7].

The phenyl substituents in XIV are equatorially oriented, while the methyl substituents are axially oriented. The dihedral angle between the plane of the heteroring C(2)C(3)C(5)C(6) fragment and the phenyl ring is 100.4°. The S–C bond length of 1.81 Å (1) and the endocyclic

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*The more accurately calculated coordinates of the hydrogen atoms rather than the experimental values from differential synthesis are presented in Table 1.

†For inversion of the structure with the same temperature factors $R_{inv} = 0.0681$. Thus, according to the Hamilton test [6], the coordinates of Table 1 correspond to the absolute structure and the absolute configuration of the molecule in a specifically studied individual crystal with a probability > 99.5%.

‡A table of the anisotropic temperature factors can be obtained from the authors.

CSC angle of 97.9° (4) are close to the values found in 4-amino-4-carboxytetrahydrothiopyran [7] (1.80 Å and 98.7°, respectively). The average length of the C—C single bond in the heteroring is 1.53 Å (1), i.e., it virtually coincides with the value (1.521 Å) for the C—C bond in cyclohexane [8].

It was found that in both a solution in carbon tetrachloride and in the crystalline state the molecules of polysubstituted thiacyclohexane XIV have a fixed chair conformation with equatorial phenyl and axial methyl substituents. In sulfide XIV and consequently in thiacyclohexanes XV-XVII there is a 1,3-diaxial interaction of the methyl groups, as a consequence of which the formation of the indicated thiacyclohexanes is evidently hindered. This may serve as one of the reasons for the fact that thiopyran II undergoes disproportionation with perchloric acid only to salt VIII and dihydrothiopyran XIX. Thiopyrans III-VI, which differ from sulfide II with respect to the presence of a bulky substituent attached to C_4, do not undergo disproportionation with $HClO_4$ in air but rather form perchlorates IX-XII via the mechanism that competes with disproportionation that we discussed above. The chief factors in this case are probably both the change in the electron density in the heteroring and the development of additional hindrance to hydride migration, which should be realized in the disproportionation of thiopyrans [1].

The formation of thiacyclohexanes XIV-XVI and XVIII in the disproportionation of thiopyrans II-IV and VI with trifluoroacetic acid may be associated with the higher solubilities of the starting thiopyrans and dihydrothiopyran XIX in CF_3COOH than in a mixture of perchloric and acetic acids, as well as with a change in the solvating properties of the medium.

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