EFFECT OF SUBSTITUENTS ON THE NATURE OF THE PRODUCTS OF OXIDATION OF 4H-THIOPYRANS

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Depending on the degree of substitution of the thiopyran ring, either oxidation at the sulfur atom, which leads to the formation of the 1,1-dioxide, or dehydrogenation of the heteroring in the C(4) position may occur in the reaction of 4H-thiopyrans with hydrogen peroxide in acetic acid. In the case of dehydrogenation the composition of the products depends on the nature of the starting 4H-thiopyran. Some peculiarities of the structure of 4H-thiopyrans that promote their conversion to 1,1-dioxides were ascertained.

For a long time it was assumed that 4H-thiopyrans undergo profound transformations under the influence of oxidizing agents to give resinous products. It was subsequently found that it was possible to oxidize some 4H-thiopyrans to the corresponding 1,1-dioxides by means of hydrogen peroxide [1-4]; 4H-thiopyrans that are capable of undergoing conversion to 1,1-dioxides under the influence of H_2O_2 necessarily either contain two substituents in the C(4) position of the hetororing [1, 2], or else all five carbon atoms of the thiopyran ring are substituted in them [3, 4]. Di-, tri-, and tetrasubstituted 4H-thiopyrans with only one substituent in the C(4) position could not be oxidized to 1,1-dioxides. In the case of sulfides I and II we have shown that such 4H-thiopyrans are capable of undergoing conversion to thiopyrylium acetates with acetic acid in the presence of oxygen [5]. In this connection, the reaction of 2,4,6-triphenyl- (I) and 3-methyl-2,4,6-triphenyl-4H-thiopyran (II) with hydrogen peroxide in acetic acid was carried out in a helium atmosphere.

Thiopyran I, which does not form thiopyrylium salts under oxygen-free conditions with CH_3COOH, gives acetate V when hydrogen peroxide is added in a helium atmosphere. Isomerization of the 4H-thiopyran ring to a 2H-thiopyran ring with subsequent oxidation of resulting sulfide VII by hydrogen peroxide to 1,1-dioxide VIII occurs in the reaction of thiopyran II with H_2O_2. Intense absorption bands at 1128 and 1302 cm^{-1}, which are related to the SO_2 group, are observed in the IR spectrum of VIII. The singlets at 4.64 and 6.75 ppm in the PMR spectrum belong to the 2-H and 5-H protons, respectively. The protons of the methyl and phenyl substituents resonate at 1.81 and 7.27 ppm, respectively. Under the indicated conditions, thiopyran II, in contrast to thiopyran I, forms thiopyrylium salt VI in only small amounts (~1%). The different pathways of the investigated reaction for substrates I and II are evidently due to the peculiarities of the structures of the initially formed 2,4,6-triphenyl- and 3-methyl-2,4,6-triphenyl-thiopyrylium cations, which are discussed below. As a result, in the reaction of 4H-thiopyran II with H_2O_2 the formation of 2H-thiopyran ring VII with its subsequent conversion to 1,1-dioxide VIII, rather than the formation of thiopyrylium salt VI, as in the case of thiopyran I, becomes energetically more favorable.

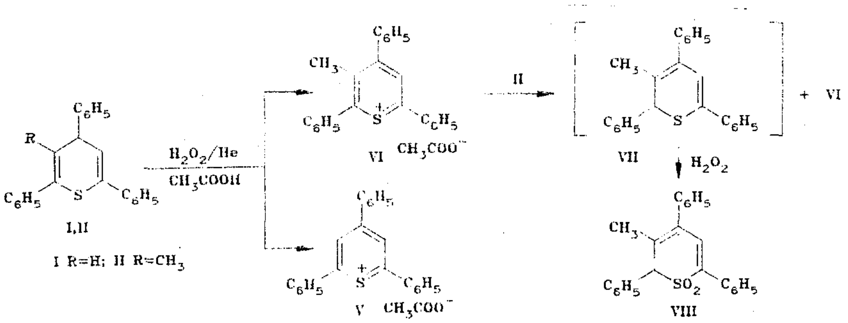

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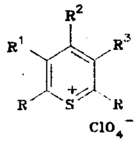
TABLE 1. PMR Spectra of Thiopyrylium Salts IX-XIII

Compound	δ, ppm					
	H_3	H_5	CH_3 attached to $C_{(4)}$	CH_3 attached to $C_{(3)}$ or $C_{(3)}$	C_6H_5	
					o-H	m-H p-H
IX	—	—	—	2,20	7,66	
X	—	—	2,78	2,54	7,60	
XI	8,89		—	—	8,10	7,71
XII	—	8,71	—	2,40	7,98	7,67
					7,7	
					7,64	
XIII [14]				2,83		

In order to ascertain the peculiarities of the structures of the 2,4,6-triphenyl- and 3-methyl-2,4,6-triphenylthiopyrylium cations we compared the PMR spectra of perchlorates XI and XII, as well as IX, X, and XIII (Table 1).



IX–XIII

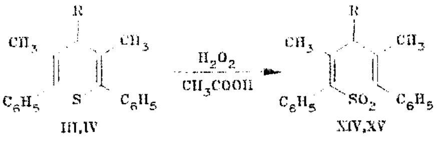
IX–XII R=C_6H_5, XIII R=H; IX, X, XII; XIII R^1=CH_3, XI R^1=H; IX, XI, XII R^2=C_6H_5, X R^2=CH_3, XIII R^2=H; IX, X R^3=CH_3, XI–XIII R^3=H

In the spectrum of salt XI the difference between the chemical shift of the signal of the ortho protons and the signal of the meta and para protons of the phenyl substituents is 0.39 ppm (Table 1). This constitutes evidence that the dihedral angle between the plane of the heteroring and the planes of each of the phenyl rings in the 2,4,6-triphenylthiopyrylium cation is small [6]. According to the results of x-ray diffraction analysis, it ranges from 15.8° to 16.6° [7], which suggests the definite effect of conjugation between the π system of the thiopyrylium ring and the π systems of each of the phenyl rings. The signals of the ortho, meta, and para protons in the spectra of penta-substituted salts IX and X virtually merge to give one peak, and the same thing is observed in the spectrum of perchlorate XII for the phenyl rings attached to the $C_{(2)}$ and $C_{(4)}$ atoms (Table 1). This indicates an increase in the dihedral angle between the plane of the heteroring and the planes of each of the cited phenyl substituents in tetra- (XII) and pentasubstituted thiopyrylium salts (IX, X), which leads to a decrease in the conjugation between their π systems as compared with triphenyl-substituted XI [6]. The magnitude of the dihedral angle can be estimated by using the results in [8] under the condition that in aryl-substituted thiopyrylium salts IX, X, and XII the principal contribution to shielding of the protons of the heteroring or the protons of the methyl substituents is due to the ring currents of the vicinal phenyl rings. The chemical shifts of the signals of the protons of the methyl groups attached to the $C_{(3)}$ or $C_{(5)}$ atom of the heteroring in the spectra of perchlorates XII and X, IX and X, and X and XIII were compared (Table 1). In the 3-methyl-2,4,6-triphenylthiopyrylium cation (salt XII), as a result of spatial interaction of the methyl group attached to the $C_{(3)}$ atom and the phenyl ring attached to the $C_{(4)}$ atom, the latter is turned 60° relative to the plane of the heteroring ($\Delta\delta_{XII,X} = -0.14$ ppm) (Table I and [8]). The same value for this angle was obtained in a comparison of the chemical shifts of the 5-H signal in the spectra of salts XII and XI ($\Delta\delta = 0.18$ ppm) (Table I and [8]). The angles of rotation of the phenyl rings attached to the $C_{(2)}$ and $C_{(6)}$ atoms in IX and X and attached to the $C_{(2)}$ atom in XII relative to the plane of the thiopyrylium ring should be identical. From a comparison of the spectra of salts X and XIII this angle is 80° [$\Delta\delta_{X,XIII} = -0.29$ ppm for CH_3 attached to the $C_{(3)}$ atom] (Table 1 and [8]). In the 3,5-dimethyl-2,4,6-triphenylthiopyrylium cation (perchlorate IX) the phenyl ring attached to the $C_{(4)}$ atom, which interacts with the two adjacent methyl groups, is turned at an angle of 90° relative to the plane of the thiopyrylium ring [$\Delta\delta_{IX,X} = -0.34$ ppm for CH_3 attached to $C_{(3)}$ or $C_{(5)}$] (Table 1 and [8]).

As we have already noted, tetrasubstituted 4H-thiopyrans, which contain two substituents attached to the $C_{(4)}$ atom [1, 2], and pentasubstituted 4H-thiopyrans [3, 4], including sulfides III and IV, are readily converted to the corresponding 1,1-dioxides under the influence of H_2O_2.

TABLE 2. PMR Spectra of 4H-Thiopyrans III and IV and 1,1-Dioxides XIV and XV

Compound	δ, ppm (in $CDCl_3$)		
	4-H	$=C-CH_3$	R attached to C
III	2,83	1,72	1,17
XIV	2,82	1,73	1,48
IV	3,88	1,58	7,23
XV	3,91	1,57	7,39



III, XIV $R=C_6H_5$; IV,XV $R=CH_3$

At the same time, oxidative dehydrogenation of the heteroring in the C(4) position occurs in the reaction of tri- (I) and tetrasubstituted 4H-thiopyran (II) with hydrogen peroxide and acetic acid in an inert atmosphere; the compositions of the products depend on the structure of the starting thiopyran. Thus the pathway of the oxidation of 4H-thiopyrans with hydrogen peroxide is determined by the number and location of the substituents in the heteroring.

A comparison of the PMR spectra of sulfides I-IV and sulfones XIV and XV made it possible to ascertain some peculiarities of the structures of the starting 4H-thiopyrans that facilitate their smooth conversion to 1,1-dioxides upon reaction with hydrogen peroxide. It is known that the 4H-thiopyran ring has the form of a compressed boat and that inversion about the S—C(4) axis occurs in solution [9, 10]. The position of the conformational equilibrium in thiopyran I and II molecules, which have a substituent attached to the C(4) atom, can be judged from the magnitude of the constant of spin-spin coupling between the 3-H and 4-H protons [10, 11]. For thiopyran I the mole fraction of the conformer with a pseudoaxial orientation of the substituent attached to the C(4) atom is 42% ($J_{3,4}$ = 4.4 Hz). In the case of thiopyran II it increased to 71% ($J_{3,4}$ = 5.8 Hz) as a consequence of spatial interaction between the substituents attached to the C(3) atom (CH_3) and the C(4) atom (C_6H_5). This provides a basis for the assumption that the presence of substituents attached to the C(3), C(4), and C(5) atoms in pentasubstituted thiopyrans III and IV will lead to an even greater shift of the conformational equilibrium to favor the conformer with a pseudoaxial substituent attached to the C(4) atom. On passing from the PMR spectra of thiopyrans III and IV to the spectra of their 1,1-dioxides XIV and XV the signal of the 4-H proton virtually retains its position, as does the signal of the protons of the methyl groups attached to the C(3) and C(5) atoms (Table 2). At the same time, the protons of the substituents attached to the C(4) atom in 1,1-dioxides XIV and XV experience the effect of the SO_2 group, since their signals are shifted to weak field as compared with those in the spectra of starting thiopyrans III and IV (Table 2). Consequently, in the oxidation of pentasubstituted thiopyrans III and IV to 1,1-dioxides XIV and XV the orientation of the substituent in the C(4) position does not change, and the equilibrium in the molecules of III, IV, XIV, and XV is shifted to favor the conformer with a pseudoaxial orientation of the substituent.

Considering the data presented above, as well as the literature examples of the oxidation of compounds that contain a 4H-thiopyran ring by hydrogen peroxide [1-4, 12, 13], it may be concluded that these compounds are readily converted to the corresponding sulfones under the influence of H_2O_2 in acetic acid only when there is no labile hydrogen atom attached to the C(4) atom of the heteroring [thiopyrans with two substituents attached to the C(4) atom [1, 2]] or when the conformational equilibrium is shifted virtually completely to favor the conformer with a pseudoaxial orientation of the substituent attached to the C(4) atom of the thiopyran ring (thiopyrans III and IV; see below). Destabilization of this conformer leads to oxidative dehydrogenation in the C(4) position of the heteroring (thiopyrans I and II). The absence of a substituent in this position complicates the oxidation of compounds that contain a 4H-thiopyran ring. Individual products of the reaction of 3,5-dimethyl-2,6-diphenyl-4H-thiopyran, as well as 2-phenyl-5,6-polymethylene-4H-thiopyrans or sym-octahydrothioxanthene, with hydrogen peroxide in acetic acid cannot be isolated [12, 13]. At the same time, 4-R-5-oxo-5,6,7,8-tetrahydrothiochromenes and 9-benzyl-sym-octahydrothioxanthene, for which it has been established that a substituent attached to the $C_{(4)}$ atom in the thiopyran ring is pseudo-axially oriented [9, 10], are readily converted to the corresponding sulfones under these conditions [4, 12].

EXPERIMENTAL

The PMR spectra of I-VI and VIII (In $CDCl_3$) and X-XIII (in d-acetonitrile) were recorded with a Varian FT-80A spectrometer with hexamethyldisiloxane as the internal standard.

4H-Thiopyrans I-III were obtained by the method in [15], and thiopyran IV was obtained by the method in [16]. Perchlorates IX-XII were obtained by the method in [17].

Reaction of Thiopyran I with Hydrogen Peroxide in a Helium Atmosphere. A solution of 2 ml of 30% H_2O_2 in 7 ml of glacial acetic acid that has been degassed by threefold freezing and thawing in vacuo (10^{-5} mm) was added to 0.6 g (1.8 mmole) of thiopyran I in a special apparatus *in vacuo*, and the reaction mixture was maintained in a helium atmosphere for 7 days. It was then worked up by the method in [5] to give 0.13 g (18.5%) of the known acetate V [5].

Reaction of Thiopyran II with Hydrogen Peroxide in a Helium Atmosphere. This reaction was realized by the method presented above. After 7 days, the precipitated crystals of 1,1-dioxide VIII were removed by filtration to give a product with mp 178-179.5°C (from alcohol) in 61% yield. Found: C 77.5; H 5.5; S 8.4%. $C_{24}H_{20}O_2S$. Calculated: C 77.4; H 5.37; S 8.6%.

3,5-Dimethyl-2,4,6-triphenyl-4H-thiopyran 1,1-Dioxide (XIV). This compound, with mp 224-226°C (from alcohol), was obtained in 57% yield by the method in [3]. IR spectrum: 1288, 1130 (SO_2); 1600 (C_6H_5); 1670 cm^{-1} (C=C). Found : C 77.6; H 5.7; S 8.4%. $C_{25}H_{22}O_2S$. Calculated: C 77.7; H 5.7; S 8.3%.

3,4,5-Trimethyl-2,6-diphenyl-4H-thiopyran 1,1 Dioxide (XV). This compound, with mp 196-197.5°C (from alcohol), was obtained in 64% yield by the method in [3]. IR spectrum: 1290, 1270, 1130 (SO_2); 1600 (C_6H_5); 1662 cm^{-1} (C=C). Found: C 74.1; H 6.1; S 9.8%. $C_{20}H_{20}O_2S$. Calculated: C 74.0; H 6.2; S 9.9%.

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