# THE OXIDATION REACTIONS OF THIOPYRANS

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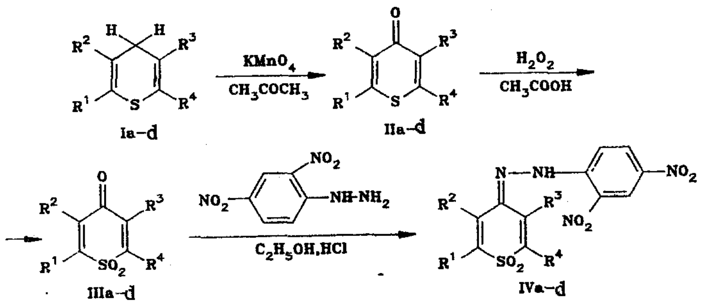
A method was developed for the preparation of compounds with 4H-thiopyrone structure by the oxidation of the corresponding 4H-thiopyranes and their condensed analogs by potassium permanganate.

4H-Thiopyrans were long considered unstable compounds and hence the study of their chemical properties has not been extensive. However, recent studies have shown the availability of these compounds and their satisfactory stability, and some of the transformations of these compounds have been studied [1, 2]. In particular, 4H-thiopyrans and their condensed analogs upon the reaction of acids were found to be disproportionate to salts and the corresponding saturated compounds, while polysubstituted 4H-thiopyrans are oxidized by hydrogen peroxide to form sulfones.

Especial interest is found in the oxidation of thiopyrans and their condensed analogs. Depending on the nature of the oxidizing agent, this reaction may proceed by three pathways: 1) at the sulfur atom to form sulfones, 2) at the double bond, and 3) at the $C_{(4)}$ atom of the heterocycle (when there is no substituent at this position) with the possible formation of thiopyrones. Great interest is found in thiopyrones in light of their use as intermediates in the manufacture of dyes, photosensitizers and biologically active compounds [3]. The reported methods for the preparation of thiopyrones involve many steps or are limited in nature.

In the present work, we attempted to obtain compounds with 4H-thiopyrone structure by the oxidation of 4H-thiopyrans and their condensed analogs.

Hydrogen peroxide, manganese dioxide and potassium permanganate in various media including acetone, 2-butanone, acetonitrile and chloroform were used as the oxidizing agent. The oxidation of thiopyrans Ia-d to the corresponding thiopyrones IIa-d proceeds most smoothly by the action of potassium permanganate in acetone at 20-60°C.



I—IV a,b $R^1=R^4=Ph$; a $R^2=R^3=CH_3$; b $R^2=R^3=H$; c $R^1+R^2=-(CH_2)_4-$, $R^3=CH_3$, $R^4=Ph$; d $R^1+R^2=R^3+R^4=-(CH_2)_4-$

The use of the other oxidizing agents leads either to the formation of tars or complex mixtures which cannot be separated.

The purity of products IIa-d was shown by thin-layer chromatography and their characteristics are given in Table 1. The IR spectra of IIa-d show a very strong band at 1590-1600 $cm^{-1}$ lacking in the initial thiopyrans, which is assigned to the carbonyl stretching band in structure A which is in resonance with the bipolar ion B. This is in accord with the literature data on the IR spectra of several monocyclic thiopyrones obtained by a different method [6].

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TABLE 1. Characteristics of Thiopyrones IIa-d

| Comp. | mp, °C (from ethanol) | $R_f$ | IR spectrum, C=O cm$^{-1}$ | PMR spectrum, δ, ppm | Found, % |  |  | Chemical formula | Calculated, % |  |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  |  |  |  | C | H | S |  | C | H | S |  |
| IIa | 97—98 | 0,47 | 1600 | 7,36 (M, 10H, $C_6H_5$); 2,04 (C, 6H, $CH_3$) | 78,1 | 5,7 | 11,2 | $C_{19}H_{16}OS$ | 78,1 | 5,5 | 11,0 | 76 |
| IIb | 128,5—131* | 0,35 | 1605 | 7,47 (M, 10H, $C_6H_5$); 7,03 (C, 2H, H vinyl) | 77,0 | 4,3 | 12,1 | $C_{17}H_{12}OS$ | 77,3 | 4,6 | 12,1 | 72 |
| IIc | 99—100 | 0,58 | 1590 | 7,36 (M, 5H, $C_6H_5$); 2,57 (M, 4H, $H^7$, $H^{10}$); 1,95 (C, 3H, $CH_3$); 1,83 (M, 4H, $H^8$, $H^9$) | 75,1 | 6,6 | 12,0 | $C_{16}H_{16}OS$ | 75,0 | 6,3 | 12,5 | 75 |
| IId | 119—121 | 0,6 | 1592 | 2,47 (M, 8H, $H^7$, $H^{10}$, $H^{11}$, $H^{14}$); 1,76 (M, 8H, $H^8$, $H^9$, $H^{12}$, $H^{13}$) | 70,7 | 7,2 | 14,5 | $C_{13}H_{16}OS$ | 70,9 | 7,3 | 14,5 | 73 |

*From benzene—hexane.

TABLE 2. Characteristics of Thiopyrone Sulfones IIIa-d

| Comp. | mp, °C (from ethanol) | IR spectrum, $cm^{-1}$ | | Found, % | | | Chemical formula | Calc., % | | | Yield (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | C=O | S=O | C | H | S | | C | H | S | |
| IIIa | 149,5—151 | 1665 | 1132, 1296 | 70,1 | 4,6 | 10,4 | $C_{19}H_{16}O_3S$ | 70,4 | 4,9 | 9,9 | 69 |
| IIIb | 144—145 | 1651 | 1134, 1298 | 68,6 | 4,1 | 10,8 | $C_{17}H_{12}O_3S$ | 68,9 | 4,0 | 10,8 | 64 |
| IIIc | 115—117 | 1650 | 1140, 1300 | 66,2 | 5,6 | 10,7 | $C_{16}H_{16}O_3S$ | 66,7 | 5,6 | 11,1 | 63 |
| IIId | 132—135 | 1660 | 1150, 1300 | 61,1 | 6,4 | 11,3 | $C_{13}H_{16}O_3S$ | 61,5 | 6,4 | 11,7 | 65 |

TABLE 3. $^{13}C$ NMR Spectra of Thiopyrones IIa-d and Thiopyrone Sulfones IIIa-d

| Compound | Chemical shift, δ, ppm | | | | | | |
|---|---|---|---|---|---|---|---|
| | $C_{2,6}$ | $C_{3,5}$ | $C_4$ | $C^{CH_3}$ | $C^{Ph}$ | $C_{7,8,9,10}$ | $C_{11,12,13,14}$ |
| IIa | 146,6 | 135,8 | 180,5 | 14,7 | 133,1; 128,6; 128,2; 121,1 | | |
| IIb | 146,4 | 133,1 | 180,0 | | 133,0; 128,5; 128,4; 128,0 | | |
| IIc | 145,8; 145,9 | 133,6; 133,2 | 180,4 | 14,6 | 133,6; 128,7; 128,4; 128,3 | 29,8; 24,4; 21,9; 21,6 | |
| IId | 145,0 | 133,4 | 180,2 | | | 30,0; 24,3; 22,0; 21,9 | 30,0; 24,3; 22,0; 21,9 |
| IIIa | 149,3 | 136,5 | 180,7 | 14,2 | 130,0; 129,9; 128,6; 127,4 | | |
| IIIb | 147,1 | 134,4 | 180,2 | | 129,9; 129,8; 128,3; 127,0 | | |
| IIIc | 148,9; 148,8 | 136,8; 136,2 | 179,1 | 14,1 | 129,9; 129,8; 128,5; 127,1 | 22,9; 20,4; 20,2; 20,0 | |
| IIId | 148,8 | 136,6 | 183,9 | | | 23,0; 20,6; 20,4; 19,9 | 23,0; 20,6; 20,4; 19,9 |


A B

The formation of thiopyrones was also indicated by the lack of signals for the allyl protons in the PMR spectra (Table 1) in contrast to the starting thiopyrones. The presence of a carbonyl carbon was indicated by $^{13}C$ NMR spectroscopy for all the thiopyrones obtained in the vicinity of 180 ppm (Table 2), although, in light of the above-mentioned conjugation of the carbonyl group, it does not display activity in nucleophilic reactions as in the case of ordinary ketones. In particular, the thiopyrones obtained do not react with hydrazine, 2,4-nitrophenylhydrazine and organomagnesium compounds.

For further verification of the structure and in order to study the chemical properties of the thiopyrones synthesized, we investigated their oxidation to the corresponding sulfones using hydrogen peroxide in glacial acetic acid. Sulfones IIIa-d were obtained in yields from 63 to 69% and their structures were confirmed by elemental analysis and IR and $^{13}C$ NMR spectroscopy (Tables 2 and 3).

Since structure B is impossible in the sulfones due to the lack of free electron pairs on the sulfur atom, the carbonyl group acquires "normal" character, as indicated by the appearance of an IR band for the stretching vibrations of a C=O group conjugated with a double bond at 1650-1665 $cm^{-1}$. These results and the possibility of forming the corresponding 2,4-dinitrophenylhydrazones IVa-d, whose structures were confirmed by elemental analysis and IR spectroscopy (Table 4), from the sulfones obtained indicate the presence of the carbonyl carbon at $C_{(4)}$, i.e., the formation of thiopyrone structure upon the oxidation of the corresponding 4H-thiopyrans.

The lack of side-products and the high yields of thiopyrones upon the oxidation of compounds with 4H-thiopyran structure by potassium permanganate indicate the smooth course of this reaction under these conditions. The thiapyrilium salts and their condensed analogs corresponding to the thiopyrans studied either are not oxidized at all by potassium permanganate under the same conditions (the 5,6,7,8-tetrahydrothiochromylium and symm-octahydro-

TABLE 4. Characteristics of the 2,4-Dinitrophenylhydrazones of Sulfones IVa-d

| Comp. | mp, °C (from methanol) | Found, % |  |  |  | Chemical formula | Calculated, % |  |  |  | IR spectrum, cm$^{-1}$ |  | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
|  |  | C | H | S | N |  | C | H | S | N | S=O | C=N |  |
| IVa | 230—232 | 58,9 | 4,2 | 6,4 | 10,6 | $C_{25}H_{20}N_4O_6S$ | 59,5 | 4,0 | 6,3 | 11,1 | 1350, 1090 | 1580 | 53 |
| IVb | 151—153 | 57,5 | 3,2 | 6,2 | 12,0 | $C_{23}H_{16}N_4O_6S$ | 58,0 | 3,4 | 6,7 | 11,8 | 1311, 1124 | 1583 | 37 |
| IVc | 109—112 | 56,9 | 4,9 | 7,4 | 11,3 | $C_{22}H_{20}N_4O_6S$ | 56,4 | 4,3 | 6,8 | 12,0 | 1342, 1097 | 1573 | 40 |
| IVc | 113—115 | 52,9 | 5,0 | 7,8 | 12,4 | $C_{19}H_{20}N_4O_6S$ | 52,8 | 4,6 | 7,4 | 13,0 | 1350, 1120 | 1600 | 49 |

thioxanthylium salts) or undergo oxidation over a much longer period with the formation of three or four unidentified by-products. In addition the 5,6,7,8-tetrahydrochromylium and symm-octahydrothioxanthylium salts are incapable of conversion to the corresponding thiopyrones IIc and IId not only with $KMnO_4$ but also using activated manganese dioxide in chloroform or acetonitrile as the oxidizing agent [5]. This finding indicates that the oxidation of these thiopyrans does not proceed through salt formation.

The oxidation of 4H-thiopyrans and their condensed analogs by potassium permanganate in acetone opens new possibilities by the synthesis of thiopyrones, hydrothiochromones and hydrothioxanthones. Different oxidation pathways are possible depending on the reagents used and the thiopyran structure.

## EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrometer in vaseline mull and in hexachlorobutadiene. The PMR and $^{13}C$ NMR spectra were taken on a Varian FT-80A spectrometer in $CCl_4$ and $CDCl_3$ with HMDS as the internal standard. The reaction was monitored by thin-layer chromatography on Silufol plates using 1:1 benzene—ether as the eluent and iodine vapor as the developer.

Oxidation of Thiopyrans Ia-d by Potassium Permanganate (general method). A sample of 1-2 mmoles sulfide Ia-d, 15-30 ml acetone and 6-12 mmoles potassium permanganate were added to a three-necked flask equipped with a reflux condenser and mechanical stirrer. The mixture was stirred for 0.5-1 h at 20-60°C and the $MnO_2$ precipitate was filtered off on a Büchner funnel. The solvent was removed in vacuum to yield crystalline IIa-d.

Oxidation of Thiopyrones IIa-d by Hydrogen Peroxide (general method). A sample of 0.7-2.8 ml 30% hydrogen peroxide was added to 0.84-1 mmole thiopyrones IIa-d and 2.2-4 ml glacial acetic acid and heated on a water bath for 0.5-1 h. The mixture was left at 20°C for 24 h and then diluted with 30-50 ml water. The crystalline precipitate was separated, washed with water and dried to yield thiopyrone sulfones IIIa-d.

Preparation of 2,4-Dinitrophenylhydrazones of IVa-d (general method). A sample of 2-4 mmoles 2,4-dinitrophenylhydrazine was added to 2-4 mmoles sulfones IIIa-d in 30-60 ml ethanol and then several drops of concentrated hydrochloric acid were added. The mixture was heated on a water bath with stirring until the starting sulfone disappeared as monitored by thin-layer chromatography. The mixture was then diluted with 150-300 ml water and the crystalline precipitate of 2,4-dinitrophenylhydrazones IVa-d was separated, washed with water, dried and recrystallized from methanol.

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