SYNTHESIS OF ALKYL AND ALKENYL FURYL SULFOXIDES AND THEIR BEHAVIOR IN THE PUMMERER REACTION

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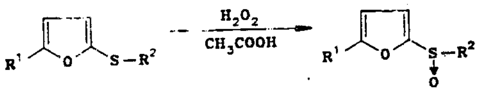
Oxidation of alkyl(alkenyl) furyl sulfides by hydrogen peroxide in glacial acetic acid affords alkyl(alkenyl) furyl sulfoxides, which react with acetic acid, acetic anhydride, and a mixture of acetic and trifluoroacetic anhydrides to give α-acyloxy-substituted and unsaturated sulfides as products, while for allyl 2-(5-methylfuryl) sulfoxide a thienofuran compound is obtained.

The Pummerer reaction is one of the common methods for inserting functional groups into organic sulfur compounds [1]. However, up to the present time the behavior of sulfoxides containing furan fragments in their structure under the conditions of this reaction has not been studied. At the same time, the conversions of compounds with this type of structure when treated with electrophilic reagents may become convenient methods for obtaining various compounds of the furan series.

Oxidation of the appropriate sulfides by hydrogen peroxide in glacial acetic acid at 0-5°C [2] was adopted in the present work for the synthesis of alkyl(alkenyl) furyl sulfoxides:



I–VI

I, IV—VI $R^1=CH_3$, II, III $R^1=H$; I $R^2=CH_3$, II, IV $R^2=C_3H_7$, III, V $R^2=CH_2CH=CH_2$, VI $R^2=CH_2C(CH_3)=CH_2$

Under these conditions alkyl(alkenyl) furyl sulfides are selectively oxidized to sulfoxides with yields of up to 98%. The heteroaromatic part of the molecule is unaffected by oxidation, whereas all previously known methods for hydroxylating furan compounds have been accompanied by ring openings of the heterocycle [3].

TABLE 1. Results of Pummerer Rearrangement of Sulfoxides IV-VI

Reagent	Solvent	T_{reac}, °C	Time, h	Degree of conversion of sulfoxide, %	Yield of reaction products, %						
					VII	VIII	XIII	XIV	IX	X	XII
Sulfoxide IV											
AcOH	o-Xylene	100	8	85	28	9	—	—	—	—	—
AcOH	o-Xylene	130	8	86	14	24	—	—	—	—	—
Ac_2O	Ac_2O	100	6	97	48	14	—	—	—	—	—
$Ac_2O+(CF_3CO)_2O$	Ac_2O	20	3	81	35	25	—	—	—	—	—
Sulfoxide VI											
AcOH	o-Xylene	110	8	89	—	—	6	39	—	—	—
Ac_2O	Ac_2O	100	7	91	—	—	23	46	—	—	—
$Ac_2O+(CF_3CO)_2O$	Ac_2O	20	2	90	—	—	32	42	—	—	—
Sulvoxide V											
AcOH	o-Xylene	100	4	81	—	—	—	—	19	14	—
Ac_2O	Ac_2O	100	7	96	—	—	—	—	18	36	—
$Ac_2O+(CF_3CO)_2O$	Ac_2O	20	2	86	—	—	—	—	5	24	36

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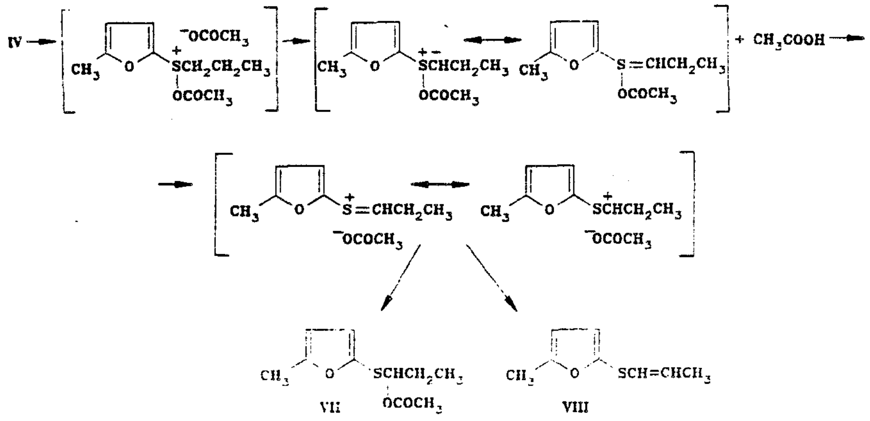
An investigation of the behavior of propyl 2-(5-methylfuryl) sulfoxide (IV) under the conditions of the Pummerer reaction showed that on treatment with acetic acid, acetic anhydride, or a mixed anhydride formed by interaction of acetic and trifluoroacetic anhydrides, its main course of conversion is formation of 1-acetoxypropyl 2-(5-methylfuryl) sulfide (VII) and 1-propenyl 2-(5-methylfuryl) sulfide (VIII) (Table 1):



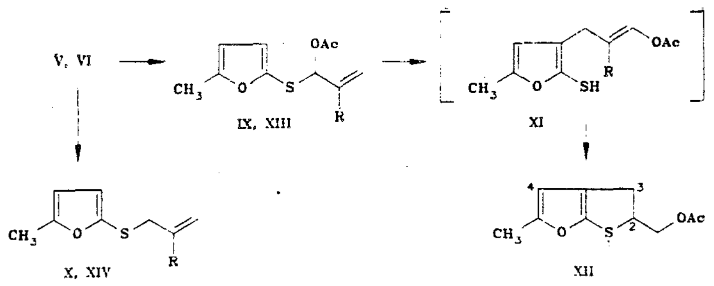
In the PMR spectrum of sulfide VIII the value of the spin-spin coupling constant in the propenyl group (J_{12} = 6 Hz) suggests that the cis configuration of 1-propenyl 2-(5-methylfuryl) sulfide is mainly formed.

The occurrence of substantial quantities of VIII in the reaction products is due to elimination of acetic acid, which can occur at one of the intermediate stages of the Pummerer reaction as well as from the molecule of sulfide VII. Positive evidence for this assumption is given by the fact that when the temperature of the experiment is increased from 100 to 130°C the yield of sulfide VIII rises from 9 to 24%.

The higher yield of sulfide VIII obtained when the reaction is carried out in a mixed anhydride compared to acetic acid and acetic anhydride is probably due in this case to the existence of two intermediate ion pairs, the second of which is more labile since CF_3COO^- is a better leaving group than CH_3COO^-.

When sulfoxides containing multiple bonds in the side-chain are considered, their pattern of behavior during the Pummerer rearrangement varies considerably (Table 1). Thus for allyl 2-(5-methylfuryl) sulfoxide (V) the main reaction products are 1-acetoxyallyl 2-(5-methylfuryl) sulfide (IX) and allyl 2-(5-methylfuryl) sulfide (X), which is in good agreement with the results from the conversion of alkylaromatic sulfoxides [4].

The most interesting result was obtained when the rearrangement of sulfoxide V was carried out in a mixture of acetic and trifluoroacetic anhydrides, where one of the main reaction products proved to be a condensed heterocycle — 2-acetoxymethyl-5-methyl-2,3-dihydrothieno[2,3-b]furan (XII):



V, IX, XI R=H; VI, XIII, XIV R=CH$_3$

The formation of thienofuran XII can be seen as the results of two reactions occurring in succession — Pummerer rearrangement to give sulfide IX and conversion of compound IX obtained by a sigmatropic [3,3]-shift to the unstable intermediate thiol XI, which in turn cyclizes to form furan XII. The PMR spectrum of this compound contains a complex multiplet in the region 3.0-4.0 ppm due to the protons of the dihydrothiophene ring and the CH_2 group directly attached to the acetoxy group. These findings are in good agreement with those in the literature, according to which the signals from the protons in the dihydrothiophene ring occur in the region 2.5-4.3 ppm [5, 6]. An intense absorption band in the region 1760-1700 cm^{-1} in compound XII indicates the presence of an ester group.

When 2-methylallyl 2-(5-methylfuryl) sulfoxide (VI) underwent rearrangement, the formation of the corresponding heterocyclic compound did not occur, and the main reaction products were 1-acetoxy-2-methylallyl 2-(5-methylfuryl) sulfide (XIII) and 2-methylallyl 2-(5-methylfuryl) sulfide (XIV). The formation of the latter, as for sulfide X, may occur either at one of the stages of the Pummerer reaction or as a result of disproportionation of initial sulfoxides V and VI.

EXPERIMENTAL

PMR spectra were recorded on a Varian T-60 spectrometer in CCl_4 with TMS as internal standard; IR spectra were recorded in KBr pellets on an IKS-22 instrument. Initial sulfides were obtained according to the method in [7] by the action of alkyl halide on the appropriate thiolate. Column chromatography and TLC were carried out on silica gel 40/100 μm and Silufol in the system hexane—CCl_4—ether (47:43:10).

Sulfoxides I-VI [8]. To a solution of 1-2 g of sulfide in 10-15 ml of glacial acetic acid cooled to 5°C and with constant agitation was slowly added dropwise 30% hydrogen peroxide at a 1:1 molar ratio to sulfide. After the reaction was complete (TLC) the mixture was dissolved in 150 ml of chloroform and the chloroform extract was washed with water and a solution of sodium bicarbonate. The chloroform was distilled off and the residue was treated by means of column chromatography.

Rearrangement of Sulfoxides. Initial sulfoxide and electrophilic reagent (acetic acid or acetic anhydride) at a molar ratio of 1:1 and solvent were mixed in a thermostatted flask fitted with a reflux condenser and thermometer in an atmosphere of argon. When the reaction was complete the solvent and residual acetic acid or acetic anhydride were distilled off. Isolation and purification of the reaction products were carried out on plates with a mobile layer of silica gel. Rearrangement in the presence of the mixed anhydride was carried out according to a modified method [9]: 0.015 mole of trifluoroacetic anhydride was dissolved in 10 ml of acetic anhydride and the mixture was agitated for 5 h at 20°C, 0.01 mole of sulfoxide was added and after several minutes 0.02 mole of pyridine was also added; the mixture was agitated over a period of 30 min to 3 h. After the reaction was complete the mixture was dissolved in ether, washed with a 10% solution of hydrochloric acid, a solution of sodium bicarbonate, and water, and the ether extract was then dried over sodium sulfate. The solvent was distilled off and the reaction mixture separated on plates with a mobile layer of silica gel.

Methyl 2-(5-Methylfuryl) Sulfoxide (I). Yield 70%, n_D^{20} 1.5318. PMR spectrum: 6.8 (1H, d, 3-H); 6.1 (1H, d, 4-H); 2.5 (3H, s, $S—CH_3$); 2.3 ppm (3H, s, 5-CH_3). IR spectrum: 1070-1050 cm^{-1} (S=O).

Propyl 2-Furyl Sulfoxide (II). Yield 98%, n_D^{20} 1.4880. PMR spectrum: 7.3 (1H, d, 5-H); 6.6 (1H, d, 3-H); 6.2 (1H, d, 4-H); 2.8 (2H, t, $S—CH_2$); 1.7 (2H, m, CH_2); 1.0 ppm (3H, t, CH_3). IR spectrum: 1070-1030 cm^{-1} (S=O).

Allyl 2-Furyl Sulfoxide (III). Yield 85%, n_D^{20} 1.5227. PMR spectrum: 7.3 (1H, d, 5-H); 6.5 (1H, d, 3-H); 6.2 (1H, d, 4-H); 5.1-5.3 (3H, m, $CH=CH_2$); 3.2 ppm (2H, d, $S—CH_2$), IR spectrum: 1050-1030 cm^{-1} (S=O).

Propyl 2-(5-Methylfuryl) Sulfoxide (IV). Yield 87%, n_D^{20} 1.5084. PMR spectrum: 6.7 (1H, d, 3-H); 6.0 (1H, d, 4-H); 2.9 (2H, t, $S—CH_2$); 2.2 (3H, s, 5-CH_3); 1.7 (2H, m, CH_2); 1.1 ppm (3H, t, CH_3). IR spectrum: 1070-1020 cm^{-1} (S=O).

Allyl 2-(5-Methylfuryl) Sulfoxide (V). Yield 98%, n_D^{20} 1.5084. PMR spectrum: 7.0 (1H, d, 3-H); 6.3 (1H, d, 4-H); 5.1-5.3 (3H, m, $CH=CH_2$); 3.7 (2H, d, $S—CH_2$); 2.3 ppm (3H, s, 5-CH_3). IR spectrum: 1060-1020 cm^{-1} (S=O).

2-Methylallyl 2-(5-Methylfuryl) Sulfoxide (VI). Yield 75%, n_D^{20} 1.5243. PMR spectrum: 7.0 (1H, d, 3-H); 6.2 (1H, d, 4-H); 4.7-5.1 (3H, d, $=CH_2$); 3.8 (2H, d, $S—CH_2$); 2.4 (3H, s, 5-CH_3); 1.8 ppm (3H, s, $CH_3C=C$). IR spectrum: 1050-1020 cm^{-1} (S=O).

1-Propenyl 2-(5-Methylfuryl) Sulfide (VIII). Yield 35%. PMR spectrum: 6.3 (1H, d, 3-H); 5.8 (1H, d, 4-H); 4.8-5.1 (2H, m, S—CH=CH); 2.3 (3H, s, 5-CH_3); 1.9 ppm (3H, d, CH_3).

1-Acetoxypropyl 2-(5-Methylfuryl) Sulfide (VII). Yield 50%, n_D^{20} 1.4751. PMR spectrum: 6.9 (1H, d, 3-H); 6.1 (1H, d, 4-H); 4.2 (1H, t, S—CH); 2.4 (3H, s, 5-CH_3); 2.1 (3H, s, $OCOCH_3$); 1.7 (2H, m, CH_2); 1.2 ppm (3H, t, CH_3). IR spectrum: 1760-1700 (C=O) and 1240-1220 cm^{-1} (C—O).

1-Acetoxyallyl 2-(5-Methylfuryl) Sulfide (IX). Yield 40%, n_D^{20} 1.4650. PMR spectrum: 6.9 (1H, d, 3-H); 6.1 (1H, d, 4-H); 5.2 (3H, m, CH=CH_2); 3.8 (1H, d, S—CH); 2.4 (3H, s, 5-CH_3); 2.1 (3H, s, $OCOCH_3$). IR spectrum: 1770-1720 (C=O), and 1250-1230 cm^{-1} (C—O).

1-Acetoxy-2-methylallyl 2-(5-Methylfuryl) Sulfide (XIII). Yield 50%, n_D^{20} 1.4823. PMR spectrum: 6.9 (1H, d, 3-H); 6.1 (1H, d, 4-H); 4.9 (3H, m, CH_2=); 3.8 (1H, s, S—CH), 2.4 (3H, s, 5-CH_3); 2.1 (3H, s, $OCOCH_3$); 1.9 ppm (3H, s, CH_3-C=C). IR spectrum: 1760-1710 (C=O), 1230-1200 cm^{-1} (C—O).

2-Acetoxymethyl-5-methyl-2,3-dihydrothieno[2,3-b]furan(XII). Yield 40%, n_D^{20} 1.4598. PMR spectrum: 6.1 (1H, s, 4-H); 3.0-4.0 (5H, m, CH_2—OAc; 3-$H_{(2)}$, 2-H); 2.3 (3H, s, 5-CH_3); 2.1 (3H, s, $OCOCH_3$). IR spectrum: 1760-1700 (C=O) and 1250-1220 cm^{-1}.

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