into a calibrated flask, and the optical densities of the solutions at λ_{max} were determined; the concentrations of the compounds were determined from the calibration graph.

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SYNTHESIS AND STEREOCHEMISTRY OF 3,4-DISUBSTITUTED SULFOLANES

N. N. Novitskaya, B. V. Flekhter,
and G. A. Tolstikov

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The stereochemistry of the reactions of 4-hydroxy-2-sulfolene, 4-hydroxy-3-chlorosulfolane, and 3,4-epoxysulfolane with nucleophilic reagents was studied. The optimum conditions for the preparation of sulfolanes with oxygen-containing substituents were worked out.

Little study has been devoted to the reactions of 4-hydroxy-2-sulfolene (I), 4-hydroxy-3-chlorosulfolane (II), and 3,4-epoxysulfolane (III) with nucleophilic reagents. A notable exception to this is an earlier study [1] in which it was shown that treatment of sulfolene I with sodium methoxide leads to a complex mixture of substances, the major portion of which remained unidentified.

We have previously developed methods for the preparation of cis- and trans-3,4-dihydroxysulfolanes (IV, V) by oxidation of 3-sulfolene [3]. In a continuation of our research on the synthesis of monomers from sulfolene (for example, see [4, 5]) we investigated the hydration and methanolysis of I-III.

The synthesis of 4-hydroxy-2-sulfolene (I) served as the subject of our special experiments, since we were unable to find convenient methods in the literature. We established that chlorohydrin II can be obtained in almost quantitative yield by hypochlorination of 3-sulfolene in aqueous solution. The dehydrochlorination of the chlorohydrin to give sulfolene I proceeds best (90% yield) in aqueous dioxane in the presence of an equivalent amount of KOH. The use of barium carbonate or pyridine gives I in 80 and 60% yields, respectively. The hydration of sulfolene I and the hydrolysis of chlorohydrin II in aqueous solution in the presence of KOH give mixtures of cis- and trans-diols in 65-95% yields, depending on the temperature (60-100°C) and reaction time (4-30 h). The ratio of IV to V ranges from 1:3 to 1:2. Thus the yields of diols are completely satisfactory under the described conditions. It should be noted that hydration is complicated by the formation of dimer VI, the yield of which may reach 80%. The tendency of sulfolene I to undergo dimerization is particularly high in solutions with concentrations above 0.04 M.

In the course of a study of the possibility of the use of dimer VI in the synthesis of diols we observed that it decomposes rapidly in aqueous alkaline solutions. The reaction has a distinct temperature barrier. Thus the dimer remains unchanged at 90° for 20 h, whereas after 1 h at 100°C it is converted to a mixture of

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Institute of Chemistry, Bashkir Branch of the Academy of Sciences of the USSR, Ufa 450054. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 8, pp. 1051-1055, August, 1977. Original article submitted April 22, 1976.

TABLE 1. Compositions of the Isomeric Mixtures Obtained by Heating the Individual cis- and trans-Diols in Aqueous Alkaline Solutions

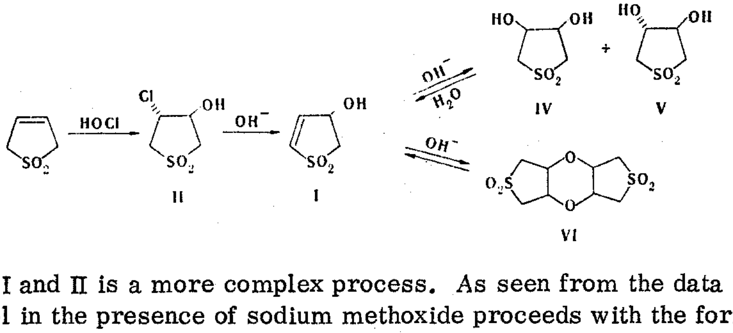
Temp., °C	Time, h	trans-Diol V, V : IV ratio	cis-Diol IV, V : IV ratio
100	3	67 : 33	49 : 51
	8	65 : 35	56 : 44
	20	63 : 37	57 : 43
	30	63 : 37	60 : 40
60	3	92 : 8	5 : 95
	8	89 : 14	7 : 93
	20	86 : 14	12 : 88
	30	85 : 15	27 : 73

TABLE 2. Products of the Reaction of Sulfolene I with Methanol

Temp., °C	Time, h	Comp. of mixture, %			
		VII	VIII	IX	X
20	48	44	51	2	3
	72	37	53	4	6
	128	34	53	5	8
40	6,5	38	57	2	3
	14	35	56	3	6
	28	31	54	6	9
65	2,5	43	54	1	2
	8	38	57	2	3
	16	36	54	4	6
	24	32	53	7	8

diols with a IV to V ratio of 33 : 67. This ratio corresponds to the equilibrium composition of the mixture of diols determined exclusively by temperature conditions. In fact, at 100°C we obtained a mixture with a similar composition (35 : 65) in experiments on the hydration of sulfolene I and the hydrolysis of chlorohydrin II with an aqueous dioxane solution of potassium hydroxide. We also established that under these conditions the individual diols are converted to a mixture of isomers with approximately the same composition (Table 1). Equilibrium mixtures of the diols with lower percentages of the IV isomer correspond to a temperature of 60°C.

Thus the results of the latter experiments enable us to propose the hydrolysis of chlorohydrin II as a convenient method for the preparation of a mixture of 3,4-dihydroxysulfolanes in which the trans isomer predominates. It is not difficult to see that the conversion of II and VI to diols proceeds through a step involving the formation of sulfolene I, which is subsequently hydrated. The stereospecificity of the addition of water is determined by the temperature conditions.



The methanolysis of I and II is a more complex process. As seen from the data in Table 2, the reaction of sulfolene I with methanol in the presence of sodium methoxide proceeds with the formation of a mixture of cis,trans-3-hydroxy-4-methoxy- (VII, VIII) and cis,trans-3,4-dimethoxysulfolanes (IX, X), the ratio of which depends on the temperature and reaction time.

As expected, a mixture of the same four compounds (VII–X) is formed when chlorohydrin II is treated with excess methanol. A mixture of methoxysulfolanes VII and VIII in a ratio of 40 : 60 is formed in up to 90% yield in the reaction with an equimolar amount of CH_3OH in dioxane at 40°C for 4 h.

In the course of an analysis of the isomer mixtures we found it necessary to obtain and identify the indi-

TABLE 3. Spectral Characteristics of 3,4-Disubstituted Sulfolanes

Compound	Characteristic frequencies, ν, cm^{-1}		Chemical shifts, δ, ppm		
	SO_2	OH (OAc)	2-H, 5-H	3-H, 4-H	CH_3
4-Hydroxy-2-sulfolene (I)*	1090, 1140, 1290, 1310	3300—3500	3,02 q 3,63 q	5,10 q	—
trans-3-Hydroxy-4-chlorosulfolane (II)	1110, 1123, 1300	3450	3,25— —4,15 m	4,80 m	—
cis-3,4-Dihydroxysulfolanediol (IV)	1085, 1115, 1135, 1272, 1295, 1310	3410	3,46 q 3,51 q	4,64 m	—
trans-3,4-Dihydroxysulfolanediol (V)	1115, 1145, 1275, 1310	3450	3,30 q 3,62 q	4,62 m	—
cis-3,4-Diacetoxysulfolane	1080, 1125, 1150, 1290, 1300, 1310	(1750)	3,46 q 3,51 q	5,6 m	2,11 s
trans-3,4-Diacetoxysulfolane	1126, 1155, 1303, 1312	(1760)	3,30 q 3,62 q	5,38 m	2,14 s
cis-3-Hydroxy-4-methoxysulfolane (VII)		3440			3,38 s
Trans-3-Hydroxy-4-methoxysulfolane (VIII)	1125, 1140, 1295, 1310	3470	2,94— —3,65 m	4,11 m 4,54 m	3,43 s
cis-3,4-Dimethoxysulfolane (IX)	1085, 1110, 1142, 1295, 1315	—	3,22— —3,30 m	4,11 m	3,38 s
trans-3,4-Dimethoxysulfolane (X)	1095, 1140, 1235, 1305	—	3,27— —3,55 m	4,18 m	3,43 s

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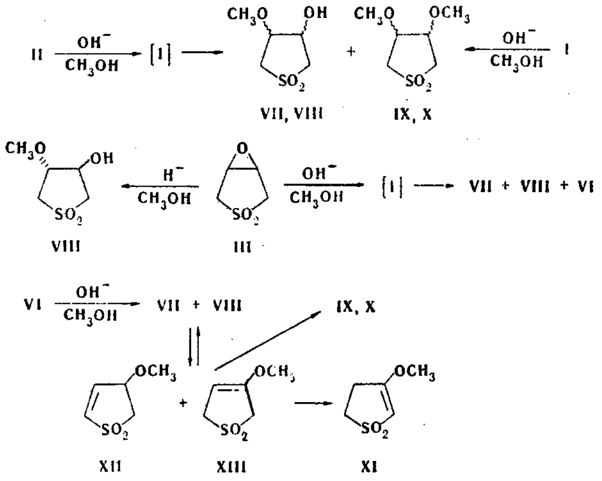
* The vinyl protons appear at 6.79 ppm (s).

vidual isomers. trans-3-Hydroxy-4-methoxysulfolane (VIII) was obtained from epoxysulfolane III and methanol in the presence of traces of sulfuric acid. It is apparent that the constants presented in [6] for the trans isomer pertain to a mixture of the isomers. Dimer VI is a third reaction product. The isomeric dimethoxysulfolanes were obtained by methylation of the corresponding diols with dimethyl sulfate. The individuality of VIII-X was confirmed by the spectral data. As seen from Table 3, the differences in the spectra are large enough to ensure sufficiently distinct qualitative identification of the isomers and their accurate quantitative determination.

Dimer VI undergoes methanolysis at 110°C in the presence of CH_3ONa to give a mixture of two dimethoxy derivatives IX and X and the previously described [1, 7] 3-methoxy-2-sulfolene (XI).

It may be assumed that the dimethoxy derivative is formed from VII and VIII through a step involving methoxysulfolenes XII and XIII, which are converted to isomer XI under severe conditions. Isomerization of this type has been noted in [8] for similar alkylthiosulfolenes.

On the basis of the above discussion one can conceive of the following scheme for the transformations:



EXPERIMENTAL

The IR spectra of thin layers of Nujol suspensions of the compounds were recorded with a UR-20 spectrometer. The PMR spectra were obtained with a Tesla BS 487B spectrometer (80 MHz) with hexamethyldisiloxane as the internal standard. The course of the reactions was followed by thin-layer chromatography on activity III Al_2O_3 with elution with a benzene–ethanol system (9 : 1). The mixtures of isomeric diols were analyzed from the areas of the signals of the acetyl protons in the PMR spectra after acetylation with acetyl chloride at room temperature. It was established by preliminary experiments that the individual diols are not isomerized under the acetylation conditions. The mixtures of methoxy derivatives were analyzed from their PMR spectra.

trans-4-Hydroxy-3-chlorosulfolane (II). Chlorine was bubbled at a rate of 700-750 ml/min for 5 h through a solution of 200 g (1.7 moles) of 3-sulfolene in 1.8 liters of water, after which the mixture was cooled, and the precipitate was removed by filtration to give 260 g (90%) of chlorohydrin II with mp 167-168° (from dichloroethane) and R_f 0.25. Found: C 28.0; H 4.3; Cl 20.6; S 18.7%. $C_4H_7ClO_3S$. Calculated: C 28.2; H 4.1; Cl 20.8; S 18.8%.

4-Hydroxy-2-sulfolene (I). A) A total of 52.2 ml of a 1.02 N aqueous KOH solution was added dropwise at 70° to a solution of 9.4 g (0.055 mole) of chlorohydrin II in 60 ml of aqueous dioxane (1 : 1) at such a rate that the medium remained constantly weakly alkaline. The reaction was monitored from the color of the indicator [a mixture of a 0.1% solution of methylene red and a 0.2% solution of methylene blue (1 : 1); transition pH 7], which was added to the reaction mixture. After all of the KOH solution had been added, the solution was heated at 70°C for 2-3 h. The mixture was then evaporated to dryness in vacuo, and the residue was extracted with acetone. The combined extracts were dried with magnesium sulfate and filtered, and the filtrate was vacuum evaporated to give 6.7 g (91%) of sulfolene I with n_D^{20} 1.5238 and R_f 0.31. Found: C 36.1; H 4.6; S 23.8%. $C_4H_6O_3S$. The acetate had mp 114-115° (from methanol) and R_f 0.75. IR spectrum: 1740 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 2.11 ppm (s, CH_3). Found: C 40.3; H 4.5; S 17.9%. $C_6H_8O_4S$. Calculated: C 40.5; H 4.5; S 18.0%.

B) A suspension of 100 g (0.6 mole) of chlorohydrin II and 70 g (0.35 mole) of $BaCO_3$ in 1 liter of water was heated with stirring to 100°C for 5-6 h, after which it was cooled, and the precipitate was removed by filtration and washed on the filter with acetone. The filtrate was worked up as in experiment A to give 70 g (85%) of sulfolene I with bp 174-175° (1 mm) and n_D^{20} 1.5242.

Hydration of Hydroxysulfolene I. A solution of 4.2 g (0.03 mole) of sulfolene I and 0.17 g (0.003 mole) of KOH in 750 ml of water was heated at 60°C for 10 h, after which the solution was cooled and neutralized, and the water was vacuum evaporated to dryness. The residue was dissolved in hot acetone, and the salt was removed by filtration. The acetone was evaporated from the filtrate to give 3.9 g (82%) of a mixture of IV and V (25 : 75). Found: C 31.4; H 5.4; S 20.9%. $C_4H_8O_4S$. Calculated: C 31.6; H 5.3; S 21.1%.

Hydration at 100°C gave a mixture of isomers IV and V (35 : 65) in 66% yield.

Hydrolysis of Chlorohydrin II. A) Water (500 ml) was added gradually to a solution of 5.1 g (0.03 mole) of chlorohydrin II in 250 ml of dioxane, after which a saturated solution of 1.68 g (0.03 mole) of KOH was added with stirring, and stirring was continued for another 30 min. A saturated aqueous solution of 0.17 g (0.003 mole) of KOH was added, and the mixture was stirred at 50-60°C for 30 h. The mixture was then worked up as in method A to give 4.3 g (95%) of a mixture of IV and V (25 : 75).

B) A total of 180 ml of a 10% aqueous KOH solution was added with stirring at 60° in the course of 10-15 min to a solution of 51.3 g (0.3 mole) of chlorohydrin II in 1500 ml of water, after which the mixture was heated at 100° for 1-1.5 h. It was then cooled, neutralized, and worked up by the usual method to give 29.4 g (65%) of a mixture of IV and V (35 : 65).

Hydrolysis of Dimer VI. A suspension of 1 g (3.7 mmole) of dimer VI and 0.03 g (0.7 mmole) of KOH in 20 ml of water was heated at 100° for 15 min, after which it was worked up in the usual manner to give a mixture of IV and V (33 : 67) in 65% yield.

General Method for the Isomerization of 3,4-Dihydroxysulfolanes. A solution of 5 g (0.033 mole) of dihydroxy derivative V and 0.17 g (0.003 mole) of KOH in 700 ml of water was heated at 60°C, and 160-ml samples of the mixture were removed after 3, 8, 20, and 30 h and worked up in the usual manner. The mixtures of IV and V were acetylated and analyzed by PMR spectroscopy.

A similar experiment was carried out at 100°C.

The isomerization of cis-3,4-dihydroxysulfolane (IV) was carried out under the same conditions.

cis- and trans-4-Hydroxy-3-methoxysulfolanes (VII and VIII). A) A 0.59-g (0.011 mole) sample of CH_3ONa was added gradually to a solution of 1.7 g (0.01 mole) of chlorohydrin II and 0.44 ml (0.011 mole) of

CH_3OH in 100 ml of dioxane, and the mixture was stirred at 40° for 4 h. It was then worked up in the usual manner to give 1.4 g (82%) of a mixture of VII and VIII (40 : 60) with R_f 0.33. Found: C 35.8; H 5.9; S 18.8%. $C_5H_{10}O_4S$. Calculated: C 36.2; H 6.0; S 19.2%.

B) A solution of 3.4 g (0.025 mole) of epoxysulfolane III and 0.2 g (0.0035 mole) of CH_3ONa in 70 ml of absolute methanol was stirred at room temperature for 14 h, after which precipitated dimer VI [0.3 g (7%)] was removed by filtration, and the filtrate was worked up in the usual manner to give 3.6 g (86%) of a mixture of VII and VIII (46 : 54).

trans-3-Hydroxy-4-methoxysulfolane (VIII). A mixture of 4.8 g (0.035 mole) of epoxy compound III, 75 ml of absolute methanol, and 0.2 ml of concentrated H_2SO_4 was heated in an autoclave at 160-170° for 5 h, after which it was cooled, neutralized, and filtered. The filtrate was evaporated, and the residue was fractionated to give 3.8 g (60%) of VIII with bp 186° (0.5 mm) and mp 75-75.5° (from ethanol). Found: C 36.8; H 6.2; S 18.8%. $C_5H_{10}O_4S$. Calculated: C 36.2; H 6.0; S 19.2%. The acetate had mp 71-72° (from ethanol). IR spectrum: 1747 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 2.14 (s, 3H, OAc) and 3.43 ppm (s, 3H, OCH_3). Found: C 40.2; H 5.8; S 15.5%. $C_7H_{12}O_5S$. Calculated: C 40.3; H 5.8; S 15.4%.

Reaction of Dimer VI with Methanol. A mixture of 1 g (0.08 mole) of dimer VI, 70 ml of methanol, and 0.8 g (0.014 mole) of CH_3ONa was heated in an autoclave at 110-120° for 5 h, after which it was worked up in the usual manner to give 0.8 g (60%) of a mixture of IX, X, and XI (11 : 19 : 70), from which 3-methoxy-2-sulfolene (XI), with mp 128-129°C (from ethanol) and R_f 0.56, was isolated by preparative TLC. IR spectrum: 1110, 1140, 1280, and 1350 (SO_2); 1616 and 1630 cm^{-1} (C=C). PMR spectrum (C_5D_5N): 2.55-2.70 (m, 2H, CH_2), 3.26-3.46 (m, 2H, H_2CSO_2), 3.42 (s, 3H, CH_3), and 6.07 ppm (s, 1H, HC=C). Found: C 41.0; H 5.5%. $C_5H_8O_3S$. Calculated: C 40.6; H 5.4%. The residue was a mixture of IX and X (37 : 63) with mp 53-54° (from CCl_4) and R_f 0.68. Found: C 40.1; H 6.8%. $C_6H_{12}O_4S$. Calculated: C 40.0; H 6.8%.

General Method for the Acetylation of the Hydroxysulfolanes. A solution of the sulfolanol or a mixture of the sulfolanols in a fivefold excess of acetyl chloride was stirred until HCl evolution ceased (2.5 h), after which the mixture was allowed to stand overnight. The degree of acetylation was followed by TLC. The mixture was vacuum evaporated to dryness, and the residue was analyzed for the absence of OH groups by means of its IR spectrum. The composition of the mixtures was analyzed from the PMR spectrum. Where necessary, the acetates were crystallized from ethanol; the products were obtained in ~95% yields.

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