

Stereochemistry of spirosulfuranes and their oxides: Static and dynamic aspects*

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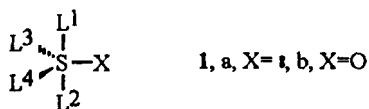
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Abstract: Efficient synthetic approaches to optically active spirosulfuranes and their oxides (including the first asymmetric synthesis) are described. The mechanism of their thermal and chemically induced racemization is discussed in the light of the experimental results obtained. The synthesis of the spirosulfurane precursors in the reaction of orthometallated cumyl (perfluorocumyl) alkoxides with prochiral sulfinyl derivatives is also briefly reported.

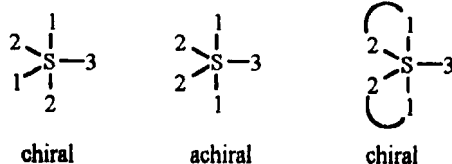
INTRODUCTION

Sulfuranes and their oxides having the general structure **1** constitute the most common group of high-coordinated sulfur derivatives (1,2).



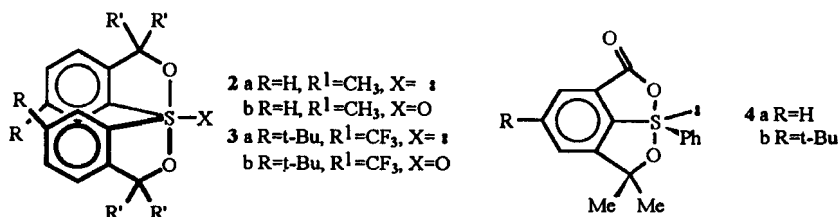
Although SCl_4 (3) and some other stable perhalogenated (4) sulfuranes have been known for more than 100 years, considerable interest has focused on their chemistry since Musher (5) indicated a possibility of synthesis and Martin and Arhart (6) and Kapovits and Kalman (7) described the preparation of the first stable spirosulfuranes. During the last two decades a number of the isolated sulfuranes and their oxides have increased very rapidly. Simultaneously they have been proposed as intermediates in various reactions of organosulfur compounds (1,2,8,9). Very often the involvement of sulfurane intermediates has been suggested to explain the mechanism of nucleophilic substitution at the sulfinyl sulfur atom (10), especially for the reactions in which retention of configuration is observed (11). These explanations are generally based on an assumption that a pseudorotation mechanism (12) interconverting one sulfurane structure into another requires passing through a very unstable sulfurane with an apical lone electron pair. In this context the synthesis of optically active sulfuranes (13) and their oxides is interesting not only as a synthetic goal, but also from the theoretical point of view. It is connected with the fact that an access to optically active structures would make the determination of their optical stability possible thus allowing to have a new insight into the problem of pseudorotation in hypervalent organosulfur derivatives having a trigonal bipyramidal geometry with the lone electron pair occupying an equatorial site.

Considering stereochemical aspects in the chemistry of sulfuranes and their oxides it should be noted that these compounds become chiral only when they contain at least three different ligands. However, due to the topological properties of such molecules the spiro systems containing two pairs of equivalent substituents (unlike the acyclic analogs) are chiral.



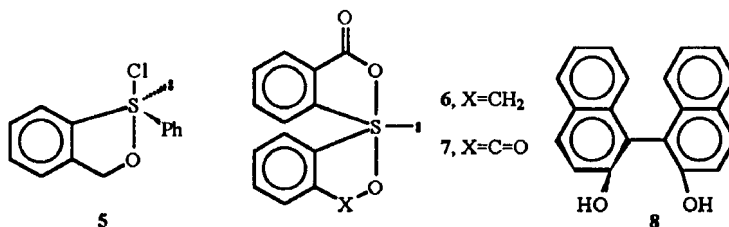
* Dedicated to Professor S. Oae on the occasion of his 75th birthday

Taking into account this fact we have decided to check if it would be possible to prepare optically active spiro-sulfuranes **2a**, **3a** and **4** containing bidentate and tridentate ligands, respectively, by asymmetric synthesis and kinetic resolution procedures and optically active spiro-sulfurane oxides **2b** and **3b** via selective oxidation of the parent sulfuranes **2a** and **3a**. Having in hands the optically active species we would be able to undertake studies on their thermal and chemically induced racemization. The outcome of these studies is reported here.



SYNTHESIS OF OPTICALLY ACTIVE SULFURANES AND THEIR OXIDES

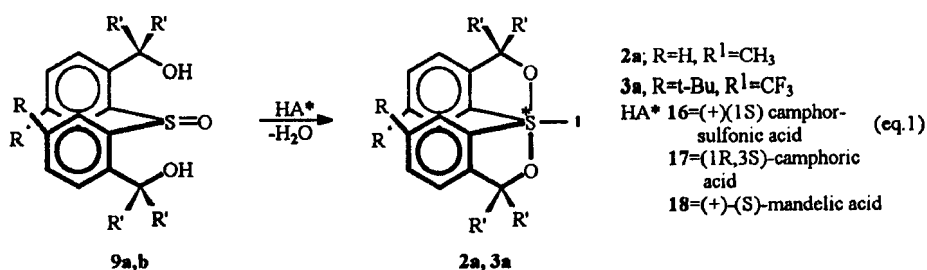
The first optically active sulfurane, the (+) enantiomer of the monocyclic chlorosulfurane **5** was reported in 1977 (13). More recently, a few other sulfuranes have been prepared as optically active species, among them spiro-sulfuranes **6** and **7** (14,15).



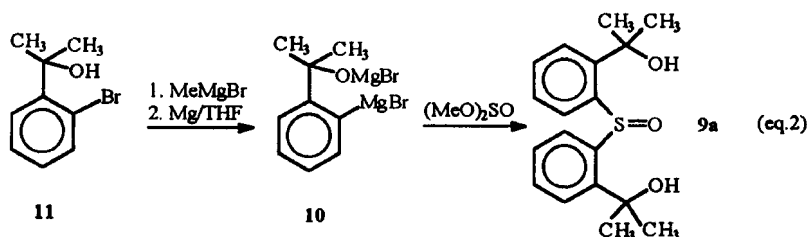
Our first efforts to prepare optically active sulfuranes **2a**, **3a** and **4** were based on resolution of racemic mixtures with enantiomers of 2,2'-dihydroxy-1,1'-binaphthol **8** which was earlier recognised as an effective reagent for optical resolution (16) and as a chiral solvating agent (17). We have found that racemic **8** forms also crystalline complexes with spiro-sulfuranes **2a** and **4a,b** with a 1:1 stoichiometry containing usually one molecule of a solvent used. Moreover, we have observed a very effective optical resolution of racemic sulfurane **4a** with (+)-(R)-**8** (18).

Thus, when the racemic sulfurane **4a** and optically active **8**, mixed in a 2:1 ratio were dissolved in CH₂Cl₂ a 1:1 complex of (+)-(R)-**8** and (+)-**4a** was instantaneously formed. Partial decomposition of this complex by washing with 10% KOH gave the optically active spiro-sulfurane **4a** having $[\alpha]_D^{20} = +18.1 \pm 0.3$ (0.4, CHCl₃). The opposite enantiomer which was not bonded was also isolated and exhibited $[\alpha]_{589} = -17.8$ (CHCl₃). The optical purity of this sample was found to be 100% (from the ¹H-NMR spectrum recorded in the presence of (-)-(R)-2,2,2-trifluoro-1-(9-anthranil) ethanol (19) as a chiral solvating agent).

The second approach used by us for the preparation of optically active spiro-sulfuranes **2a** and **3a** was based on asymmetric dehydration of the prochiral sulfoxide diols **9**. It is quite reasonable to expect that this reaction may be utilized in the synthesis of optically active sulfuranes, provided that it will be carried out under asymmetric conditions.

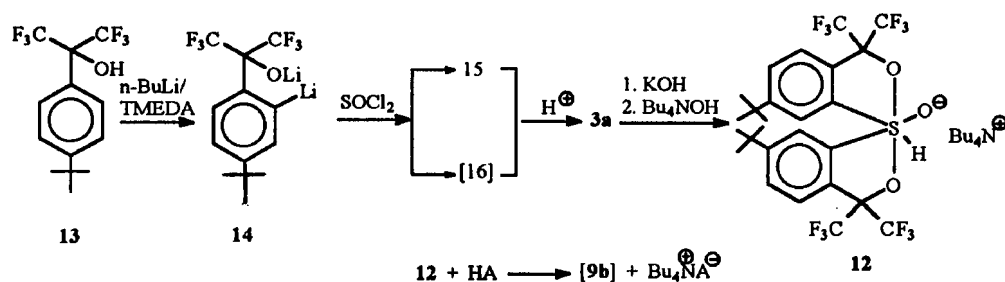


Prochiral sulfoxide diol **9a** was isolated in 76% yield in the reaction of the Grignard reagent **10**, prepared from *o*-bromocumyl alcohol **11**, and dimethyl sulfite (eq.2).

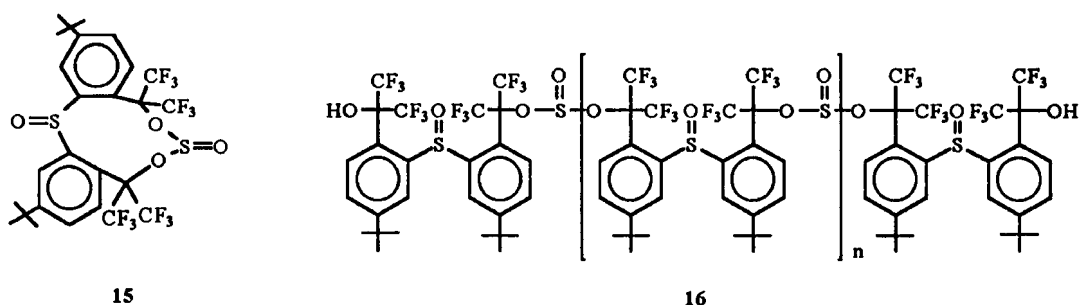


The sulfoxide diol **9b** derived from perfluorocumyl alcohol **13** cannot be isolated due to instantaneous cyclization to the spirosulfurane **3a** (20). Therefore, it was generated in situ from the persulfurane **12** which was prepared starting from perfluorocumyl alcohol **13** as shown in Scheme 1.

Scheme 1

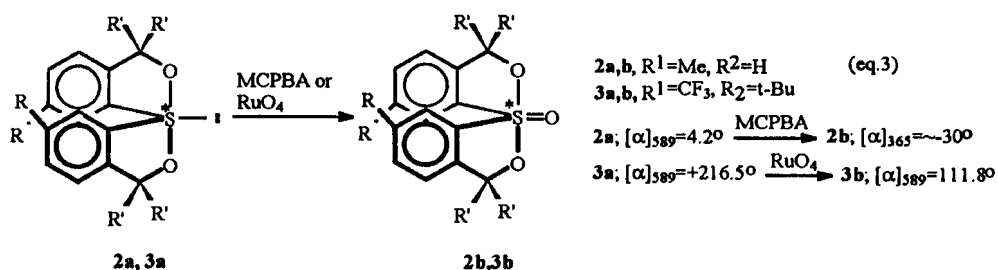


It is interesting to note that in the reaction of SOCl_2 with the dilithioderivative **14** cyclic and acyclic sulfites **15** and **16** were formed as precursors of the sulfurane **3a**. The cyclic sulfite **15** was isolated and fully characterized and the intermediary formation of the linear polysulfite **16** was supported by the spectral data.



Having in hands the sulfoxide diol **9a** and persulfurane **12** we have carried out their dehydration in the presence of optically active acids and found that (see eq.1) the corresponding optically active spirosulfuranes **2a** and **3a** were formed in good chemical yields (>80%) but with low enantiomeric excess (below 5%) (21a,b). Fortunately, we were able to increase substantially the optical purities of the isolated samples of **2a** by partial dissolving in petroleum ether and **3a** by recrystallization from the same solvent. Thus a sample of **2a** with $[\alpha]_{\text{D}}^{-1.1}$ (C_6H_6 ; e.e.=2.9%) upon four partial dissolving steps left the solid undissolved sample with $[\alpha]_{\text{D}}^{-4.7}$ (C_6H_6 ; e.e.=14.3%) On the other hand, five recrystallizations of the sample of **3a** with $[\alpha]_{589}^{+12.5}$ (C_6H_6) from petroleum ether afforded the solid sample with $[\alpha]_{589}^{+216.5}$. We believe that the latter value corresponds to 100% e.e. because it was not changing after additional recrystallization. It should be noted that the optically active spirosulfurane **2a** having much higher optical purity could be isolated, though in very low chemical yield, by changing the isolation procedure. The optical purity of such a sample with $[\alpha]_{589}^{-28.1}$ (C_6H_6) was found to be 74.9%.

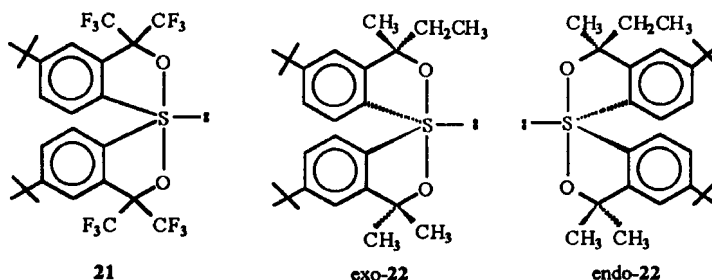
Because there have been no reports on the isolation of optically active sulfurane oxides we have decided to obtain them by stereoselective oxidation of the parent chiral sulfuranes discussed above (21c,d) (eq.3).



The optically active oxide **2b** was prepared via oxidation of **2a** with meta-chloroperbenzoic acid (MCPBA). All attempts to obtain it via oxidation with ozone (22), were unsuccessful. Synthesis of the optically active oxide **3b** was based on the stereoselective conversion of the chiral sulfurane **3a** using ruthenium tetraoxide according to the procedure reported earlier (23).

RACEMIZATION OF SULFURANES AND THEIR OXIDES

The racemization of the optically active chlorosulfurane **5** was found to be rapid at room temperature ($\Delta G^*=25$ kcal/mol at 23°C) (13). From high temperature ¹⁹F-NMR of spiro-sulfurane **21** a lower limit for ΔG^* of 25kcal/mol at 200°C was set for its racemization (24). The configurational stability of **22** was determined by measuring the rate of isomerization of exo-**22** to endo-**22**. From this rate a lower limit for $\Delta G^*=30$ kcal/mol at 84°C was determined (25). Till now there has been no report on the racemization of the corresponding sulfurane oxides.



We have found that the thermal racemization of the spiro-sulfuranes **2a** and **3a** and the oxide **3b** can be conveniently followed by polarimetry in the temperature range of 80-150°C (Table 1). On the other hand, at these temperatures the sulfurane **4a** maintains its optical activity and the sulfurane oxide **2b** racemizes very rapidly at room temperature ($k=2.4 \cdot 10^{-4} \text{ sec}^{-1}$).

TABLE 1. Kinetic data on the racemization of sulfuranes **2a** and **3a** and oxide **3b** in anisole.

2a		3a		3b	
temp. [°C]	k·10 ³ sec ⁻¹	temp. [°C]	k·10 ³ sec ⁻¹	temp. [°C]	k·10 ³ sec ⁻¹
80	1.00	130.2	0.766	90	3.06
90	3.06	140.2	2.20	100	8.38
104	14.03	151.8	7.85	110	22.35
151.8	1110.0			130.2	135.0
ΔH [*] =28.4 kcal/mol ΔS [*] =-1.5 eu		ΔH [*] =35.6 kcal/mol ΔS [*] =5.6 eu		ΔH [*] =26 kcal/mol ΔS [*] =6 eu	

The solvent effect on the rate of the racemization of the sulfuranes **3a** was examined and the results are collected in Table 2.

TABLE 2. The racemization of spiro-sulfurane **3a** in different solvents

Solvent	$k \cdot 10^5 \text{sec}^{-1}$			E_a [kcal/mol]	ΔH^* [kcal/mol]	ΔS^* [eu]
	130.2°C	140.2°C	151.8°C			
anisole	0.76	2.20±0.07	7.85±0.02	36.4	35.6	5.6
tetrachloro ethylene	1.006	2.97±0.04	9.68±0.29	35.5	34.7	4.0
pyridine/ H ₂ O ^A	3.73	8.51±0.18	20.90±0.2	27.1	26.3	-14.2
CH ₃ COOH/ (CH ₃ CO) ₂ O ^B	0.92	2.63±0.04	8.22±0.04	34.4	33.6	1.1

Apparently the racemization is insensitive to the nature of a solvent as it can be expected for an unimolecular process. Only in a mixture of pyridine with water almost a 4 fold increase of the rate was observed while the entropy of activation was simultaneously lowered. This relationship indicates that in this solvent mixture an associative mechanism can operate. In the light of this observation it was interesting to check how the rate of racemization would change in the system containing organic acid and water. The relevant data collected in Tables 3 and 4 clearly indicate huge acceleration of this process for the sulfurane **3a** in trifluoroacetic acid containing water. In this context it is interesting to note that the sulfurane oxide **3b** keeps its optical activity in this solvent.

TABLE 3. The racemization of **3a** in carboxylic acid, containing water, as a solventCH₃COOH

T [°C]	$k \cdot 10^5 \text{sek}^{-1}$	
90	0.80	$E_a=20.3$ kcal/mol
110	3.67	$\Delta H^*=19.5$ kcal/mol
130	13.17	$\Delta S^*=-28.4$ e.u.

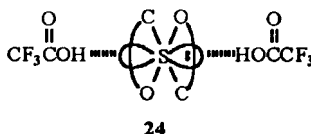
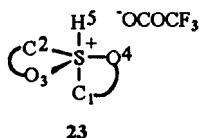
CF₃COOH

T [°C]	$k \cdot 10^5 \text{sek}^{-1}$	
24.8	1.28	$E_a=15.4$ kcal/mol
54.9	14.00	$\Delta H^*=14.6$ kcal/mol $\Delta S^*=-31.2$ e.u.

TABLE 4. The racemization of **3a** in toluene in the presence of CF₃COOH/(CH₃CO)₂O at 130.2°C

[CF ₃ COOH]·10 ² mol/l	$k \cdot 10^5 \text{sek}^{-1}$
0.00	0.77
0.71	2.77
1.42	4.99
1.93	7.67
2.60	10.84
3.63	16.64
5.13	28.64

There are six mechanisms which could account for the racemization of spiro-sulfuranes **2a** and **3a**: a) hydrolysis to the symmetrical diol, which could recombine to form racemic sulfurane, b) heterolytic oxygen-sulfur bond cleavage to yield a sulfonium salt which, before recombination, could racemize via pyramidal inversion, c) Berry pseudorotation processes involving intermediate structures with geometries near TBP with an apical electron pair, d) an inversion through a planar transition state (cuneal inversion), e) the acid catalyzed Berry pseudorotation with the transition state **23**, f) the acid-catalyzed cuneal inversion via the transition state **24**.



The first mechanism is undoubtedly responsible for very fast racemization of the sulfurane **3a** in the carboxylic acid/water system. The second possibility can be neglected because the racemization of **2a** constitutes a very clean process and any by-products, which should result from the intermediate sulfonium salt, are not detected. The Berry pseudorotation sequence is not a very attractive pathway for the racemization of the sulfuranes **2a** and **3a** in water-free solvents because such a mechanism must involve two structures with an apical lone electron pair. Such structures, due to the presence of a formal two-center four-electron bond, is very unlikely to be formed. Therefore, in these cases an alternative mechanism with the square planar transition state operates. On the other hand, the Berry pseudorotation is responsible for the trifluoroacetic acid catalyzed racemization of the sulfuranes **3a** in toluene and the noncatalyzed thermal racemization of its oxide **3b** in anisole.

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