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S-Oxides of 2-Arylsubstituted 4,4-Diphenyl-1,3-oxathiolan-5-ones

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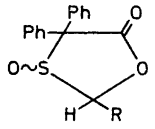
By oxidation of the corresponding 2-aryl-4,4-diphenyl-1,3-oxathiolan-5-ones with either peroxysebacic acid or hydrogen peroxide, twentythree 2-aryl-4,4-diphenyl-1,3-oxathiolan-5-one-3-oxides were prepared. The relative configuration of the two diastereomeric pairs is proposed on the basis of their NMR spectra. From these spectra the type of anisotropy of the $>\overset{+}{S}-\overline{O}$ group is discussed. In addition some new oxathiolanones are described.

Only one example of an oxathiolanone *S*-oxide of the type I

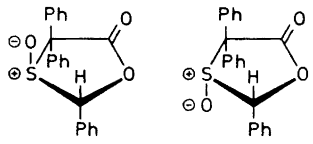


R = Aryl

I

has been described in the literature. Bistrzycki and Brenken [1] prepared 2,4,4-triphenyl-1,3-oxathiolan-5-one-3-oxide by oxidation of the corresponding oxathiolanone with chromium(VI) oxide in glacial acetic acid. The yield, however, was low and the compound was difficult to purify. We have prepared a series of 2-aryl-4,4-diphenyl-1,3-oxathiolan-5-one-3-oxides in nearly quantitative yield by oxidation of the corresponding oxathiolanones with either peroxysebacic acid in boiling benzene or hydrogen peroxide in glacial acetic acid at room temperature.

It was previously observed by Bistrzycki and Brenken [1] that the compound prepared by them showed a rather unsharp melting point. From the NMR spectrum of 2,4,4-triphenyl-1,3-oxathiolan-5-one-3-oxide (see below) it can be clearly seen that the compound isolated is a mixture of two isomers to which we will assign the structures II and III

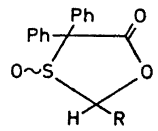


II (*E*-form) III (*Z*-form)

Each of these two diastereomeric compounds must exist in two optically active forms.

With an extension of the rules given by Blackwood *et al.*[2,3] for description of *cis-trans* isomerism about a double bond * we can say that II has an *E* configuration and III has a *Z* configuration.

We have prepared the following compounds IVa—x



IV

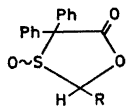
IV	R	IV	R
a	Pentadeuteriophenyl	m	2-Methylphenyl
b	2,6-Dichlorophenyl	n	3- »
c	2-Bromophenyl	o	4- »
d	3- »	p	2-Methoxyphenyl
e	4- »	q	3- »
f	2-Chlorophenyl	r	4- »
g	3- »	s	4-Methylsulfonylphenyl
h	4- »	t	2-Ethoxyphenyl
i	2-Nitrophenyl	u	2,4,6-Trimethylphenyl
j	3- »	v	4-*tert*-Butylphenyl
k	4- »	x	2-Pentyloxyphenyl
l	Phenyl		

It is normally possible to obtain the *S*-oxides free of oxathiolanones and in quantitative yield by oxidation with peroxysebacic acid in refluxing benzene, but in the cases where R is alkylphenyl (IVm,n,o,u,v) it was not possible to obtain the oxidation product free of oxathiolanone without using an extremely large excess of peroxysebacic acid.** It was not possible to use a higher-boiling solvent because the oxathiolanones decompose at higher temperature with the formation of olefins.[5] In these cases, however, it was pos-

* We are considering the bond between C-2 and S as a double bond and use the sequence rules of Cahn, Ingold and Prelog [4] without considering the other ring atoms. We can then use the descriptors *Z* and *E* in the same manner as Blackwood *et al.*[2,3]

** The same was found in the cases where R was strictly aliphatic but these compounds will not be discussed in this paper.

Table 1. 2-Aryl-4,4-diphenyl-1,3-oxathiolan-5-one-3-oxides.



R	Formula	Chemical shifts of H-2 in τ units	Amounts of isomers %	Analyses (C, H, S)
Pentadeuteriophenyl	$C_{21}H_{11}D_5O_3S$	4.00 4.11	72 28	Found: 71.10; — 9.00 Calc.: 71.39; — 9.06
2,6-Dichlorophenyl	$C_{21}H_{14}O_3Cl_2S$	3.75	100	Found: 60.75; 3.27; 7.80 Calc.: 60.45; 3.38; 7.68
2-Bromophenyl	$C_{21}H_{15}BrO_3S$	3.68 3.83	33 67	Found: 58.90; 3.64; 7.74 Calc.: 59.05; 3.54; 7.50
3-Bromophenyl	$C_{21}H_{15}BrO_3S$	4.00 4.13	55 45	Found: 59.20; 3.69; 7.30 Calc.: 59.05; 3.54; 7.50
4-Bromophenyl	$C_{21}H_{15}BrO_3S$	4.02 4.15	79 11	Found: 58.92; 3.62; 7.67 Calc.: 59.05; 3.54; 7.50
2-Chlorophenyl	$C_{21}H_{15}ClO_3S$	3.47 3.65	44 56	Found: 65.80; 4.01; 8.38 Calc.: 65.90; 3.95; 8.38
3-Chlorophenyl	$C_{21}H_{15}ClO_3S$	3.98 4.13	64 36	Found: 65.80; 4.08; 8.42 Calc.: 65.90; 3.95; 8.38
4-Chlorophenyl	$C_{21}H_{15}ClO_3S$	4.03 4.15	75 25	Found: 65.90; 4.06; 8.56 Calc.: 65.90; 3.95; 8.38
2-Nitrophenyl	$C_{21}H_{15}NO_5S$	3.23	100	Found: 64.25; 4.02; 8.09 Calc.: 64.12; 3.84; 8.13
3-Nitrophenyl	$C_{21}H_{15}NO_5S$	3.81 3.97	55 45	Found: 63.95; 3.96; 8.16 Calc.: 64.12; 3.84; 8.13
4-Nitrophenyl	$C_{21}H_{15}NO_5S$	3.73 3.87	40 60	Found: 64.40; 3.96; 8.08 Calc.: 64.12; 3.84; 8.13
Phenyl	$C_{21}H_{16}O_3S$	3.98 4.10	72 28	Found: 72.50; 4.80; 9.12 Calc.: 72.37; 4.64; 9.21
2-Methylphenyl	$C_{22}H_{18}O_3S$	3.83	55[a] 45	Found: 72.80; 5.06; 8.82 Calc.: 72.92; 5.01; 8.83
3-Methylphenyl	$C_{22}H_{18}O_3S$	4.05 4.15	63 37	Found: 73.16; 5.11; 8.92 Calc.: 72.92; 5.01; 8.83
4-Methylphenyl	$C_{22}H_{18}O_3S$	4.10 4.13	68 22	Found: 72.82; 5.11; 8.81 Calc.: 72.92; 5.01; 8.83
2-Methoxyphenyl	$C_{22}H_{18}O_4S$	3.68	100	Found: 69.50; 4.76; 8.23 Calc.: 69.83; 4.80; 8.46

Table 1. Continued.

3-Methoxyphenyl	$C_{22}H_{18}O_4S$	4.00 4.15	78 22	Found: 69.68; 4.90; 8.39 Calc.: 69.83; 4.80; 8.46
4-Methoxyphenyl	$C_{22}H_{18}O_4S$	4.05 4.13	50 50	Found: 69.55; 4.82; 8.41 Calc.: 69.83; 4.80; 8.46
4-Methylsulfonyl-phenyl	$C_{22}H_{18}O_5S_2$	3.90 4.02	58 42	Found: 61.70; 4.40; 14.97 Calc.: 61.97; 4.26; 15.00
2-Ethoxyphenyl	$C_{23}H_{20}O_4S$	3.67	100	Found: 70.60; 5.23; 8.37 Calc.: 70.40; 5.23; 8.16
2,4,6-Trimethyl-phenyl	$C_{24}H_{22}O_3S$	4.08	100	Found: 74.01; 5.71; 8.10 Calc.: 73.83; 5.68; 8.19
4-*tert*-Butylphenyl	$C_{25}H_{24}O_3S$	4.00 4.13	67 33	Found: 74.20; 6.06; 8.09 Calc.: 74.24; 5.98; 8.09
2-Pentyloxyphenyl	$C_{26}H_{26}O_3S$	3.68	100	Found: 71.70; 6.07; 7.36 Calc.: 71.87; 6.03; 7.37

NMR spectra are recorded in chloroform-*d* at 40°C.

[a] As the signals due to the two forms coincidentally appear as one singlet at 40°C (see text) the yields of the isomers are based upon the integral values of the signals due to the methyl group.

sible to obtain complete oxidation by using hydrogen peroxide in acetic acid at room temperature.

Compound IVs was prepared by oxidation of 2-(4-mercaptomethylphenyl)-4,4-diphenyl-1,3-oxathiolan-5-one with hydrogen peroxide; attempts to utilize peroxysebacic acid for this oxidation resulted in formation of an oil. The fact that two signals due to H-2 are found in the NMR spectrum of compound IVs shows that it is the exocyclic sulfur that is oxidised to a sulfone, because the asymmetry of the endocyclic sulfur responsible for the existence of the two isomers II and III would have disappeared, if this sulfur atom had been so oxidised. Compound IVs showed absorption in the infrared spectrum at 1150 cm^{-1} and 1320 cm^{-1} characteristic of sulfones,[6] and an additional band at 1050 cm^{-1} characteristic of sulfoxides.[6] All of the other *S*-oxides prepared only show absorption in the 1050 cm^{-1} region.

It was not possible in any case to oxidise the sulfur atom in the ring to the oxidation state of sulfone, either with peroxysebacic acid or with hydrogen peroxide in glacial acetic acid at 90°C.

The relative amounts formed of the isomers II and III were almost the same whether peroxysebacic acid or hydrogen peroxide was used as the oxidising agent. We have not as yet been able to separate the two diastereomeric isomers by crystallisation. It is possible to separate the isomers by thin-layer chromatography on alumina with benzene-cyclohexane (1:1), but attempts to separate them by preparative layer chromatography were unsuccessful. Extensive decomposition and formation of the corresponding aldehyde took place. By column chromatography it was not possible to obtain any separation.

NUCLEAR MAGNETIC RESONANCE SPECTRA

The general feature of the NMR spectra is a multiplet corresponding to the aromatic protons in the region 2.0 τ—3.5 τ and one or two singlets in the region 3.5 τ—4.5 τ corresponding to H-2. The NMR spectrum of IVm is shown in Fig. 1 as a typical example.

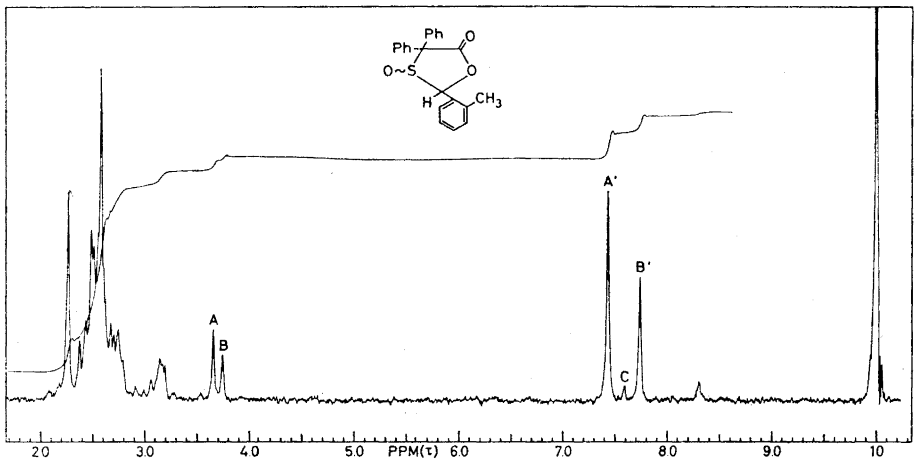


Fig. 1. 60 Mc/s NMR spectrum of IVm in chloroform-*d* with TMS as internal standard at 0°C. A and A′ are the signals from H-2 and the methyl group, respectively, in the *Z* form. B and B′ are signals from the same groups in the *E* form. C is the signal from the methyl group in the parent oxathiolanone.

When two singlets are present in the region 3.5 τ—4.5 τ the integrated spectrum shows that these signals correspond to one proton; this is also the case when only one singlet is present. The signal due to H-2 in the oxathiolanone *S*-oxides is always found at higher field than the signal from H-2 in the parent oxathiolanones (*cf.* Tables 1 and 4 and Ref. 5). When the spectrum shows two singlets due to H-2, the singlet at lower field is usually slightly broader than the singlet at higher field. When the temperature is increased both singlets move towards higher field and collapse, but reappear as two singlets when the temperature is increased further over the coalescence temperature; at this elevated temperature the broad signal is now found at higher field than the sharp signal. This effect is observed in both polar and non-polar solvents, but the coalescence temperature varies with the polarity of the solvent. If only one singlet due to H-2 is found at 40°C the chemical shift shows very little temperature dependence in non-polar solvents. By coincidence the signals due to H-2 in IVm appear as a singlet at 40°C, but appear as two singlets at both higher and lower temperature.

Table 2. Chemical shift of H-2 in 2,4,4-triphenyl-1,3-oxathiolan-5-one-3-oxide in $CDBr_3$ and $(CD_3)_2SO$ at various temperatures.

Solvent \ Temp. °C	40	50	60	70	80	90	100	110	120	130	140
$CDBr_3$	3.88	3.91	3.93	3.95	3.98	4.00	4.03,b	4.03,s	4.03,s	4.03,b	4.07
	4.00	4.01	4.01	4.01	4.03	4.03					4.03
$(CD_3)_2SO$	3.38	3.40	3.48,b	3.51,s	3.55	3.58	3.60	3.67			
	3.43	3.45			3.53	3.55	3.55	3.56			

Chemical shifts are in τ units.
b=broad, s=sharp.

The position of the signals due to H-2 is dependent on the polarity of the solvent; the signals are found at highest field in the least polar solvent (*cf.* Table 3). However, the position of these signals did not change as the substrate concentration was varied from 1 % to 20 % in chloroform-*d*.

Table 3. Chemical shift of H-2 in 2,4,4-triphenyl-1,3-oxathiolan-5-one-3-oxide in different solvents at 40°C.

CCl_4	CS_2	C_6D_6	$CDCl_3$	$CDBr_3$	CD_3NO_2	CD_3CN	$(CD_3)_2SO$	CF_3COOH
4.25	4.28	4.32	4.02	3.88	3.78	3.78	3.38	3.88
4.32	4.38	4.38	4.10	4.00	3.88	3.87	3.43	4.00

Chemical shifts are in τ units.

Due to the complexity of the aromatic part of the spectra we did not analyse this region in detail, but one general feature will be mentioned. In the spectra of all of the oxathiolanone *S*-oxides a signal is found at approximately 0.1 ppm lower field than the signals from the other aromatic protons. This signal always corresponds to two protons and is not found in the corresponding oxathiolanone. It must be due to protons in the 4-phenyl groups, because it is also found in the spectrum of IVa.

When alkyl or alkoxy substituents are present in the 2-phenyl group, the signal due to the alkyl groups always appears as two signals as seen in Fig. 1. In IVm,n, and o the signals from the methyl group are found at 7.50 τ and 7.78 τ; 7.62 τ and 7.80 τ; 7.62 τ and 7.70 τ, respectively.

The above experimental data are in agreement with the hypothesis that the oxidation products of the oxathiolanones consist of the two isomers II and III. In the *Z* form (III) the interaction between the sulfoxide oxygen and the *ortho* protons of the 2-phenyl group is greater than it is in the *E* form (II) and thus the rotation of the phenyl group is more hindered in the *Z* form, so that it "will spend more of its time" in a conformation where H-2 lies in the plane of the phenyl ring, than it will in a conformation where H-2 is over the plane of the phenyl ring. This phenomenon causes a broader signal due to H-2 in the *Z* form because of the longer relaxation time. One should expect to find the signal due to H-2 in the *E* form at higher field because the action of the field induced by the phenyl group is averaged out to a smaller value by the free rotation of the phenyl group in this form. The population of all conformations in the *E* form is in average the same. When the temperature is increased the phenyl group in the *Z* form will rotate more freely and the *Z* form will be more similiar to the *E* form, and thus the signal due to H-2 will move towards higher field.

When R in IV is phenyl or *meta* or *para* substituted phenyl, the *Z* isomer is formed in higher yield than the *E* isomer (*cf.* Table 1); this would not be expected if the reaction was controlled by steric factors only. It must therefore be concluded that inductive factors also play a role in determining the stereochemistry of the new asymmetric center formed in the oxidation reaction. If bulky substituents are present in one or both *ortho* positions of the 2-phenyl group the isomer predominantly, or exclusively, formed is the *E* isomer. These data are in agreement with the correlation between the NMR spectra and the configuration given above.

The dependence of the chemical shift of the signals due to H-2 on the polarity of the solvent is probably not caused by the sulfoxide existing as a dimer,[7] because the chemical shifts do not depend on the concentration. From consideration of molecular models it can be seen that it would be rather difficult for these sulfoxides to dimerise, because of the steric effect of the three phenyl groups. The effect observed must, therefore, be due to association of the sulfoxides with the smaller solvent molecules. In trifluoroacetic acid solution we are probably observing the protonated form of the sulfoxide as proposed by Watson.[8]

The nature of the anisotropy caused by the $>\overset{+}{S}-\overline{O}$ group has been discussed by other authors. It has been claimed by Edmundson [9] that the anisotropy should be of the same type as that found for the carbonyl group, whereas Buck *et al.*[10] presume that the anisotropy should be of the acetylenic type. To us, the problem seems more complex for our compounds, than either of these treatments imply, and we have not been able to bring our experimental data into complete harmony with either of the above theories.

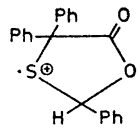
The correlation between the configuration and the NMR signals due to H-2 given above, is in accordance with the assumption of an acetylene-like anisotropy for the sulfoxide group. If we are considering Fig. 1 the positions of the signals due to the methyl group (A′ and B′) are not in accordance with an acetylene-like anisotropy. Inspection of the integrals shown in the figure indicates that the signals A and A′ must be due to the same isomer, the *Z* isomer, and B and B′ must be due to the *E* isomer. As the methyl group in

the *Z* configuration would be in the cone at the end of the sulfoxide group, and in the *E* configuration above the sulfoxide group, the location of the signals found is that which would be expected, if the anisotropy was of the same sort as that found for the carbonyl group.

THE REACTION OF OXATHIOLANONE *S*-OXIDES WITH CONCENTRATED SULFURIC ACID

It has previously been described by Pedersen [11] that 2,4,4-triphenyl-1,3-oxathiolan-5-one, upon dissolution in concentrated sulfuric acid and subsequent dilution with water, yielded 1,3-diphenylisobenzothiophen. The *S*-oxide of this compound, *i.e.* IVl, gave, as did the parent oxathiolanone, a deep red solution in concentrated sulfuric acid. An opaque yellow solution was obtained upon dilution with water. Extraction of the yellow aqueous solution with chloroform caused the chloroform to take on a faint yellow colour. By the lack of fluorescence of the solution in ultraviolet light it can be concluded, that the colour is not caused by 1,3-diphenylisobenzothiophene. We were not able to isolate anything well defined from the water solution.

It was not possible to detect any paramagnetic species by examining the ESR spectrum of sulfuric acid solutions of oxathiolanones,[11] but weak ESR signals could be observed in sulfuric acid solutions of the corresponding *S*-oxides. In the case of IVl a doublet was found, which is in accordance with the existence of the cation radical V.



V

As it was not possible to obtain well-resolved spectra of the other *S*-oxides, we were not able to analyse them further. The existence of such radicals as V is in agreement with the investigation of phenoxathiin-5-oxide by Shine and Small.[12]

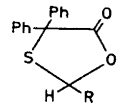
EXPERIMENTAL

NMR spectra were recorded on a Varian A-60A spectrometer. The spectra were obtained from approximately 5 % solutions in chloroform-*d* at 40°C with TMS as internal standard, unless specified otherwise.

Oxathiolanones (*cf.* Table 4). These compounds were prepared from aldehydes and thiobenzilic acid as described previously.[5]

Oxathiolanone S-oxides (*cf.* Table 1). As examples of the two oxidation methods used, we present the following procedures.

Table 4. 2-Substituted 4,4-diphenyl-1,3-oxathiolan-5-ones.



R	Formula	Yield %	M.P. °C	Chemical shift of H-2 in τ units	Analyses (C, H, S)
tert-Butyl	$C_{19}H_{20}O_2S$	81	69 – 70	4.15	Found: 73.25; 6.36; 10.46 Calc.: 73.06; 6.45; 10.25
2-(5-Methyl-thienyl)	$C_{20}H_{16}O_2S_2$	30	74 – 75.5	3.70	Found: 68.00; 4.63; 18.25 Calc.: 68.18; 4.58; 18.17
4-Thiocyanatophenyl	$C_{22}H_{15}NO_2S_2$	69	136 – 137	3.81	Found: 67.81; 3.88; 16.37 Calc.: 67.86; 3.88; 16.43
4-Carboxyphenyl	$C_{22}H_{16}O_4S$	89	208 – 209	3.58	Found: 70.00; 4.36; 8.62 Calc.: 70.21; 4.29; 8.50
4-Mercaptomethyl-phenyl	$C_{22}H_{18}O_2S_2$	89	100 – 101	3.88	Found: 69.65; 4.73; 16.94 Calc.: 69.83; 4.80; 16.90
2-Ethoxyphenyl	$C_{23}H_{20}O_3S$	74	105 – 106	3.35	Found: 73.52; 5.46; 8.70 Calc.: 73.39; 5.36; 8.50
2,5-Dimethoxy-phenyl	$C_{23}H_{20}O_4S$	90	120 – 121	3.60	Found: 70.23; 5.17; 8.03 Calc.: 70.40; 5.14; 8.15
2,4,6-Trimethyl-phenyl	$C_{24}H_{22}O_2S$	68	152 – 153	3.50	Found: 76.95; 5.87; 8.58 Calc.: 76.98; 5.92; 8.55
4-*tert*-Butylphenyl	$C_{24}H_{24}O_2S$	66	138 – 139	3.85	Found: 76.94; 6.32; 8.29 Calc.: 76.57; 6.43; 8.50
2-Pentyloxyphenyl	$C_{26}H_{26}O_3S$	77	91 – 92	3.38	Found: 74.75; 6.33; 7.56 Calc.: 74.62; 6.29; 7.65

NMR spectra are recorded in chloroform-*d* at 40°C.

2,4,4-Triphenyl-1,3-oxathiolan-5-one-3-oxide. Method A. 2,4,4-Triphenyl-1,3-oxathiolan-5-one (640 mg, 2 mmol) was refluxed for 3 h in 30 ml of benzene with 4 g (6 mequiv.) of peroxysebacic acid urea inclusion compound (Schuchardt). After cooling the urea and sebacic acid were removed by filtration and washed with 50 ml of benzene. The combined filtrate and washings were evaporated *in vacuo* at 30°C. The residue, a colourless oil, crystallised upon trituration with methanol. The compound was recrystallised from propanol. Yield 600 mg. It was found that when all the chemicals used were absolutely dry no oxidation took place. When a drop of water was added the reaction started.

Method B. 2,4,4-Triphenyl-1,3-oxathiolan-5-one (1.4 g) was dissolved in 30 ml of glacial acetic acid and 1 ml of 30 % aqueous hydrogen peroxide was added. The solution

was kept at room temperature for 48 h and then was poured into 150 ml of water. The resulting solid was removed by filtration and washed with water. The compound was recrystallised from propanol. Yield 1.4 g.

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