

Studies of Isobenzothiophenes

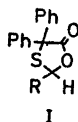
II. Formation of Thiiranes and Unsaturated Compounds by Pyrolysis of 2-Substituted 4,4-Diphenyl-1,3-oxathiolan-5-ones

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Pyrolysis of 2-substituted 4,4-diphenyl-1,3-oxathiolan-5-ones did not give rise to isobenzothiophenes, but to olefins; thus it was found that pyrolysis of 2-aryl-4,4-diphenyl-1,3-oxathiolan-5-ones and 2-(2-arylvinyl)-4,4-diphenyl-1,3-oxathiolan-5-ones resulted in the formation of 1,1,2-triarylethylenes and 1,1,4-triaryl-1,3-butadienes, respectively. Furthermore, it was shown in all cases that substituted thiiranes were intermediates. The NMR spectra of several 2-substituted 4,4-diphenyl-1,3-oxathiolan-5-ones were recorded and the position of the 2-proton in the spectra is given.

Earlier, it was shown that isobenzothiophenes are formed on treatment of various 2-aryl-4,4-diphenyl-1,3-oxathiolan-5-ones with concentrated sulfuric acid and subsequent dilution with water.^{1,2} The yields, however, were never more than 30 %. By PLC (Preparative Layer Chromatography), it could be shown that elementary sulfur corresponding to the missing 70 % of the material was formed during the reaction. Therefore, it was desirable to find a less drastic method of synthesis. Pyrolysis of different oxathiolanones with alumina as a catalyst was tried, but in no case were any isobenzothiophenes found.



Instead, pyrolysis of I (R = phenyl) gave rise to 1,1,2-triphenylethylene, elementary sulfur and a dark coloured oil, shown by TLC (Thin Layer Chromatography) not to contain isobenzothiophenes. The oil was not further investigated. When the oxathiolanone was pyrolysed without catalyst at

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



R	Formula	Yield %	M.p. °C	Analyses (C,H,S)
C ₆ D ₅	C ₂₁ H ₁₁ D ₅ O ₃ S	85	97.0—98.0	Found: 74.50; — 9.24 Calc.: 74.79; — 9.49
2,4-Cl ₂ C ₆ H ₃	C ₂₁ H ₁₄ Cl ₂ O ₃ S	60	105.0—106.0	Found: 63.05; 3.61; 8.19 Calc.: 62.85; 3.52; 7.99
2,6-Cl ₂ C ₆ H ₃	C ₂₁ H ₁₄ Cl ₂ O ₃ S	75	186.0—187.5	Found: 62.85; 3.45; 7.93 Calc.: 62.85; 3.52; 7.99
2-Br-C ₆ H ₄	C ₂₁ H ₁₅ BrO ₃ S	92	129.0—130.0	Found: 61.28; 3.57; 7.52 Calc.: 61.60; 3.68; 7.78
3-Br-C ₆ H ₄	C ₂₁ H ₁₅ BrO ₃ S	85	98.5—100.0	Found: 61.65; 3.96; 7.70 Calc.: 61.60; 3.68; 7.78
C ₆ H ₅ CO	C ₂₂ H ₁₆ O ₃ S	70	112.0—113.0	Found: 73.05; 4.37; 8.78 Calc.: 73.32; 4.48; 8.88
3-CH ₂ C ₆ H ₄	C ₂₂ H ₁₈ O ₃ S	82	88.0—89.0	Found: 75.95; 5.05; 9.05 Calc.: 76.25; 5.23; 9.24
2-CH ₃ OC ₆ H ₄	C ₂₂ H ₁₈ O ₃ S	89	99.0—100.0	Found: 73.00; 4.93; 8.81 Calc.: 72.92; 5.01; 8.84
3-CH ₃ OC ₆ H ₄	C ₂₂ H ₁₈ O ₃ S	84	103.0—104.0	Found: 72.80; 4.98; 8.92 Calc.: 72.92; 5.01; 8.84
C ₆ H ₅ (CH ₃)CH	C ₂₃ H ₂₀ O ₃ S	52	85.0—86.5	Found: 76.75; 5.37; 8.94 Calc.: 76.65; 5.59; 8.88
4-C ₂ H ₅ C ₆ H ₄	C ₂₃ H ₂₀ O ₃ S	82	89.5—90.5	Found: 76.45; 5.45; 8.91 Calc.: 76.65; 5.59; 8.88
4-C ₆ H ₅ CH ₂ OC ₆ H ₄	C ₂₇ H ₂₀ O ₃ S	79	100.0—101.0	Found: 76.35; 4.81; 7.76 Calc.: 76.40; 4.81; 7.52

150°C, the same olefin and sulfur were found and only very small amounts of by-products were formed.

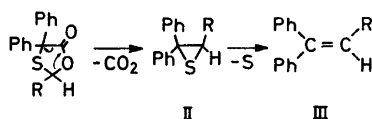
Since tetraphenylethylene and 1,2-diphenylethylene never were formed as products of pyrolysis, it seemed reasonable to suspect the existence of an intermediate in which carbon atoms 2 and 4 are directly linked. In order to check this hypothesis, the reaction was followed by means of TLC. Only two spots were present in the first minutes of reaction, one at the starting point and one with R_F 0.29; after half an hour, four spots were found, one at the starting point and the others with R_F values of 0.29, 0.47, and 0.88. The spot with R_F 0.29 attained its maximum intensity after 2 h and then started to

diminish. When the pyrolysis was stopped after 20 h, only the spots with R_F 0.47 and 0.88 were still present.

In order to identify the spots found with TLC, the reaction was stopped at different stages and the compounds present were separated by means of PLC. In this way, it was found that the spot at the starting point corresponded to the starting material, that with R_F 0.29 to 2,2,3-triphenylthiirane, that with R_F 0.47 to 1,1,2-triphenylethylene, and that with R_F 0.88 to elementary sulfur.

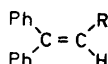
It is well known that aryl-substituted thiiranes such as tetrakis-(4-methoxyphenyl)thiirane are thermally unstable and lose sulfur with the formation of, in this example tetrakis-(4-methoxyphenyl) ethylene.³ Triaryl-substituted thiiranes have not, so far as is known, been described. The 2,2,3-triphenylthiirane in heptane solution showed UV absorption bands at 225 $m\mu$ and 235 $m\mu$ (shoulder), but after the solution was refluxed for 2 h the UV spectrum changed to that of triphenylethylene, showing absorption at 233 and 320 $m\mu$. The 2,2,3-triphenylthiirane was characterized by its elementary analysis and NMR spectrum. The 60 Mc/s NMR spectrum showed a multiplet at 2.5 τ –3.1 τ , corresponding to 15 protons, and a singlet at 5.36 τ , corresponding to one proton. In 1,2-diphenylthiirane, the signal from the α -protons is found at 5.04 τ .⁴ The thiirane was different in this respect from the oxathiolanone, where the signal from the lone proton was found at 3.87 τ (cf. Table 3), and the ethylene, where it was found at 3.01 τ .

When the maximum concentration of thiirane was reached after approximately 2 h, the amount present was small. From the pyrolysis of 2 g of oxathiolanone, only 40 mg of thiirane could be isolated. It was not found possible to increase the amount of thiirane by altering the temperature of the pyrolysis or by using a solvent. An attempt was therefore made to find a more stable thiirane by changing the substituent in the 2-position of the oxathiolanone. In this way it was found possible to alter the rate of decomposition of the oxathiolanone, but the maximum amount of thiirane present was not altered, *i.e.* the substituent has the same effect on the decomposition of the thiirane as on the decomposition of the oxathiolanone. These findings fit with the reaction scheme shown.



The reaction could be followed visually by the evolution of carbon dioxide. It was found that the reaction took place only if R was aryl or 2-arylvinyl. If R was aliphatic (methyl), acyl (benzoyl), or aralkyl (α -methylbenzyl), or the 2-carbon atom was a spiro atom as in 4,4-diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-cyclopentane, no reaction of this sort took place. At higher temperatures the oxathiolanones with such substituents decomposed to give complex mixtures, containing up to ten components, which were not further characterized.

Table 2. 2-Substituted 1,1-diphenylethylenes.



R	Formula	Yield %	M.p. °C	Analyses (C,H,N or halogen)
C ₆ D ₅	C ₂₀ H ₁₁ D ₅	69	69.0—70.0	Found: 91.75; Calc.: 91.96;
2-BrC ₆ H ₄	C ₂₀ H ₁₅ Br	56	61.5—62.5	Found: 71.70; 4.52; 23.56 Calc.: 71.66; 4.51; 23.84
3-BrC ₆ H ₄	C ₂₀ H ₁₅ Br	59	oil	Found: 71.90; 4.65; 23.90 Calc.: 71.66; 4.51; 23.84
4-BrC ₆ H ₄	C ₂₀ H ₁₅ Br	47	78.0—79.5 (lit. ⁹ 77)	
3-ClC ₆ H ₄	C ₂₀ H ₁₅ Cl	57	oil	Found: 82.47; 5.23; 11.96 Calc.: 82.60; 5.21; 12.18
4-ClC ₆ H ₄	C ₂₀ H ₁₅ Cl	84	76.0—76.5 (lit. ⁹ 76—77)	
2-NO ₂ C ₆ H ₄	C ₂₀ H ₁₅ NO ₂	55	131.0—132.0 (lit. ¹⁰ 133)	
3-NO ₂ C ₆ H ₄	C ₂₀ H ₁₅ NO ₂	72	77.0—78.0 (lit. ¹⁰ 75)	
4-NO ₂ C ₆ H ₄	C ₂₀ H ₁₅ NO ₂	60	153.0—154.0 (lit. ¹⁰ 150)	
C ₆ H ₅	C ₂₀ H ₁₆	78	70.5—71.5 (lit. ¹¹ 72)	
2-OCH ₃ C ₆ H ₄	C ₂₁ H ₁₈ O	49	80.5—82.0	Found: 88.25; 6.28 Calc.: 88.08; 6.34
3-OCH ₃ C ₆ H ₄	C ₂₁ H ₁₈ O	55	oil	Found: 87.85; 6.14 Calc.: 88.08; 6.34
4-OCH ₃ C ₆ H ₄	C ₂₁ H ₁₈ O	73	81.0—82.0 (lit. ¹² 81—82)	
C ₆ H ₅ CH=CH	C ₂₂ H ₁₈	85	101.0—102.0 (lit. ¹³ 101—102.0)	
4-(CH ₃) ₂ CHC ₆ H ₄	C ₂₃ H ₂₂	57	63.0—64.0	Found: 92.85; 7.49 Calc.: 92.57; 7.43
4-C ₆ H ₅ CH ₂ OC ₆ H ₄	C ₂₇ H ₂₂ O	59	105.0—106.0	Found: 89.40; 6.09 Calc.: 89.47; 6.12

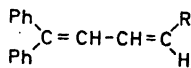
Electron-donating substituents on the 2-phenyl group such as methoxy groups in *ortho* and *para* positions, increased the rate of decomposition, whereas a *m*-methoxy group was without effect. Electron-withdrawing substituents decreased the rate of decomposition. These findings are in agreement

with the ability of a methoxy group to reduce the positive charge on carbon number two in the oxathiolanone and of the nitro group to augment it. These effects work in the same direction in the oxathiolanone and in the thiirane, which explains why a greater amount of thiirane was not found in the pyrolysis of an oxathiolanone that decomposed rapidly.

The gas from the pyrolysis was examined by mass spectrometry. Its mass spectrum showed two main peaks, M_{28} and M_{44} . The ratio M_{28}/M_{44} was found to be the same as in the mass spectrum of carbon dioxide, *i.e.* the gas was pure carbon dioxide, no carbon monoxide being formed.

If R in I was aromatic, triarylethylenes were formed. These compounds have been of great interest because of their oestrogenic⁵ and antigonadotropic⁶ activity. Some of the compounds we have synthesized in this way have previously been prepared by various methods.⁷⁻¹³ The method described by us should be suitable for synthesis of any ethylene of this type, provided that the aldehyde for synthesizing the oxathiolanone is available.

If R in I is 2-arylvinyl, the product of pyrolysis is a trisubstituted 1,3-butadiene IV.

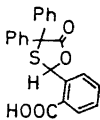


IV

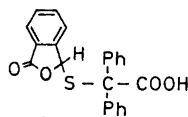
From the pyrolysis of I (R = $-\text{CH}=\text{CH}-\text{Ph}$), IV (R = Ph) was isolated. For further characterization of this compound, preparation of the Diels-Alder adduct with maleic anhydride was attempted, but it was not possible to isolate any adduct. However, from consideration of a model it can be seen that the compound has no possibility of assuming the planar cisoid configuration, which is prerequisite for the Diels-Alder reaction.

Only in the case I (R = Ph) was the product of pyrolysis examined with the aid of PLC. In the other cases, the reaction was followed by TLC, and the results found by TLC were always as described for R = Ph (*vide supra*). In all cases, the final product of the reaction was isolated.

Bistrzycki *et al.*¹² condensed *o*-phthalaldehydic acid with thiobenzilic acid and isolated a compound for which they suggested the constitutions V or VI.



V



VI

The NMR spectra of all the oxathiolanones investigated showed an intense signal at 2.76 τ . This was the main signal in the spectrum of 2-pentadeuterio-phenyl-4,4-diphenyl-1,3-oxathiolan-5-one and so must represent the phenyl groups in the 4-position. This peak was not found in the spectrum of the compound that is either V or VI. The signal from the single proton was found

Table 3. Chemical shifts of the C-2 proton in 2-substituted 4,4-diphenyl-1,3-oxathiolan-5-ones.



R	Chemical shifts	R	Chemical shifts
CH ₃	4.70,q	C ₆ H ₅	3.87,s
C ₂ H ₅	4.86,t	4-OHC ₆ H ₄	3.93,s
C ₆ D ₅	3.86,s	3-CH ₃ C ₆ H ₄	3.89,s
2,4-Cl ₂ C ₆ H ₃	3.50,s	4-CH ₃ C ₆ H ₄	3.90,s
2,6-Cl ₂ C ₆ H ₃	3.11,s	C ₆ H ₅ CO	3.58,s
2-BrC ₆ H ₄	3.48,s	2-OCH ₃ C ₆ H ₄	3.41,s
3-BrC ₆ H ₄	3.95,s	3-OCH ₃ C ₆ H ₄	3.89,s
4-BrC ₆ H ₄	3.91,s	4-OCH ₃ C ₆ H ₄	3.94,s
3-ClC ₆ H ₄	3.91,s	4-C ₂ H ₅ C ₆ H ₄	3.88,s
4-ClC ₆ H ₄	3.92,s	4-(CH ₃) ₂ CHC ₆ H ₄	3.90,s
2-NO ₂ C ₆ H ₄	3.04,s	4-C ₆ H ₅ CH ₂ OC ₆ H ₄	3.93,s
3-NO ₂ C ₆ H ₄	3.74,s		
4-NO ₂ C ₆ H ₄	3.75,s		

Chemical shifts are in τ units, s = singlet, t = triplet, q = quartet.

at 3.71 τ , farther upfield than for any of the known oxathiolanones with R = *ortho*-substituted aryl. The spectrum further showed a singlet corresponding to one proton at 0.02 τ . This should be the signal from the carboxylic proton for it disappeared by addition of D₂O. Structure V is therefore not reconcilable with the observed spectrum. That V was not the right structure was further confirmed by the fact that it was impossible to isolate an olefin from the pyrolysis of the compound.

We have recorded the NMR spectra of several oxathiolanones. The spectra all consisted of a multiplet corresponding to the aromatic protons and a singlet corresponding to the 2-proton. The chemical shift of this proton varied with the substituent R (*cf.* Table 3). These chemical shifts did not show correlation with the Hammett sigma-values.

EXPERIMENTAL

NMR spectra were obtained on a Varian A-60A spectrometer from approx. 10 % solutions in CDCl₃ with TMS as internal standard.

Thin layer chromatography (TLC). The chromatograms were run on 8 × 10 cm plates coated with 0.25 mm of alumina (HF₂₅₄, Merck). The plates were developed with light petroleum (b.p. 60–90°C) and the spots were visualized with UV light. *R_F* values were calculated as average of several chromatograms.

Preparative layer chromatography (PLC). The method described by Halpaap¹⁵ was employed. The plates were 20 × 100 cm. The thickness of the layer (alumina PF₂₅₄, Merck) was 2 mm. The plates were developed 4–6 times with light petroleum (b.p. 60–90°C) and the compounds located with UV light.

Oxathiolanones (*cf.* Table 1). These were prepared from aldehydes and thiobenzilic acid as described in the literature.^{2,14,16}

4,4-Diphenyl-1,3-oxathiolan-5-one-2-spiro-1'-cyclopentane. Prepared from cyclopentanone and thiobenzilic acid after the method described by de Vivar.¹⁶ Yield 87%. M.p. 87.5–88.5°C, recrystallized from methanol. (Found: C 73.30; H 5.98; S 10.12. Calc. for C₁₉H₁₅O₂S: C 73.53; H 5.85; S 10.31).

2,2,3-Triphenylthiirane. 1,4,4-Triphenyl-1,3-oxathiolan-5-one (2 g) was pyrolysed in a bath at 130°C for 2 h. The product was dissolved in 10 ml of CHCl₃ and the solution applied to a plate for PLC and separated as described above. The zone corresponding to the thiirane was extracted in the cold with 500 ml of CHCl₃ in a chromatographic column. The solution was evaporated at room temperature *in vacuo* to leave a crystalline compound. Crystallisation from pentane raised the m.p. from 81°C to 87–88°C. Yield 40 mg. (Found: C 83.20; H 5.49; S 11.14. Calc. for C₂₀H₁₆S: C 83.31; H 5.59; S 11.11).

Substituted ethylenes and substituted butadienes. 1 g of oxathiolanone was heated in a bath at 150°C for 20 h, after which time the evolution of carbon dioxide had ceased. The melt was dissolved in 10 ml of ethyl acetate and filtered to remove sulfur. The solution was added to 6 g of neutral alumina and the mixture evaporated to dryness. The alumina was placed at the top of a chromatographic column packed with 35 g of neutral alumina in light petroleum (b.p. 60–90°C). The column was eluted with light petroleum (b.p. 60–90°C) to give first sulfur and next the ethylene. If more polar substituents such as methoxy or nitro groups were present, it was necessary to change the solvent to a mixture of ethyl acetate and light petroleum (1:1) after the sulfur was out. The solution was evaporated and the compound recrystallized from methanol or ethanol. The compounds with a *meta*-substituted phenyl group were very difficult to get crystalline, and some were isolated as oils purified by repeated chromatography. For the compounds prepared in this way, *cf.* Table 2.

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