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THIAOZONIDE FORMATION BY SINGLET OXYGEN CYCLOADDITION TO 2,5-DIMETHYLTHIOPHENE

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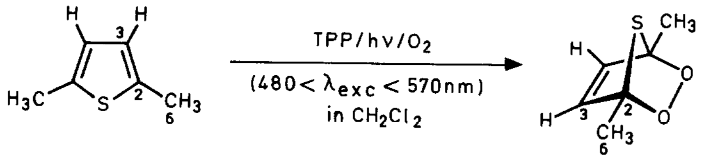
Summary: Singlet oxygen reacts with 2,5-dimethylthiophene (1) exclusively by (4+2)-cycloaddition to yield the thiaozonide 2. The structure of this product is inferred from its ^{1}H- and ^{13}C NMR spectra. Neat thiaozonide 2 decomposes violently at room temperature. In aprotic non-polar and in protic polar solvents it is slowly transformed into cis-sulfine 3c and cis-2,5-dione 4c, which rearranges to the trans-isomer 4t. A mechanism for the transformation reaction is proposed.

Unlike furan and tetraphenylfuran, thiophene and tetraphenylthiophene were found to be unreactive toward photosensitized oxygenation[1,2]. In 1970, two research groups showed that 2,5-dimethylthiophene (1) reacts with singlet oxygen to yield cis-sulfine 3c as the major product in methanol[3,4] accompanied by trans-3-hexene-2,5-dione (4t) as a minor product (about 35:1)[3]. In chloroform, the ratio of 3c:4t was found to be 2:1, and Skold and Schlessinger discussed various pathways for the formation of 3c and 4t via intermediates such as the thiaozonide 2, the oxathiirane 5, the persulfoxide 6, the sulfur ylide dioxetane 7, and the zwitterionic peroxide 8[3,5]. That thiaozonide 2 is one of perhaps several intermediates was recently shown by Adam and Eggelte[6] who prepared the saturated thiaozonide from 2 by low-temperature photooxygenation of 1 followed by immediate reduction of the product mixture with diazene.

We now wish to present evidence that the (4+2)-cycloaddition product, the thiaozonide 2, is the only primary product of the singlet oxygen reaction with 1 in chloroform, methylene chloride, and methanol (MeOH). Subsequent transformations of 2 yield 3c and 4t, probably via biradicals 9 and 10 (Scheme 1) as is inferred from comparison with rearrangements of ozonides obtained from furans[7,8] (Scheme 2).

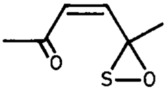
2,5-Dimethylthiophene (1) consumed one molecule of oxygen[9] if irradiated in the presence of a typical singlet oxygen photosensitizer such as rose bengale (RB) (in MeOH) and tetraphenylporphin (TPP) (in $CHCl_3$ and CH_2Cl_2) at 13°C. In order to avoid the formation of substantial amounts of resinous products, rather diluted solutions of 1 were applied, and the reactions were interrupted after about 80% of 1 had reacted. After removal of the solvent at -20°C/10^{-4} Torr, the remaining dark oil was cooled to -50°C and then dissolved in $CDCl_3$/$CFCl_3$ (about 3:1), precooled to this temperature.

The ^{1}H- and ^{13}C NMR spectra exhibited signals due to the starting material (1) as well as new signals which are compatible with structure 2 but not with any of the other structures, 5 through 8, discussed as possible intermediates.



1 **2**

^{1}H-NMR^{11}(-40°C): δ(ppm) =	2.40 (s,6H)		1.95 (s,6H)
	6.37 (s,2H)		6.18 (s,2H)
^{13}C-NMR^{11}(-50°C): δ(ppm) =	15.59 (q, C_6)		15.39 (q, C_6)
	124.91 (d, C_3)	Δ_3 = + 14.38	139.29 (d, C_3)
	138.01 (s, C_2)	Δ_2 = − 32.60	106.61 (s, C_2)



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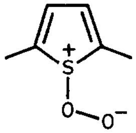

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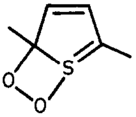

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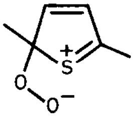

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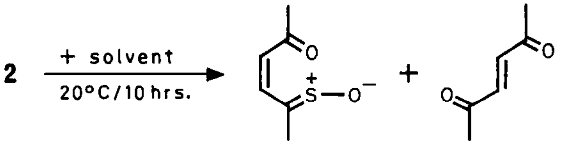
The ^{13}C NMR shift differences Δ_2 and Δ_3 (see above) correspond very well with those observed for the oxygen analogs of 1 and 2 (Δ_2 = -37.83, Δ_3 = + 17.91)[7,8,12], which is considered as further evidence that the product is 1,4-dimethyl-2,3-dioxa-7-thia-bicyclo(2.2.1) hept-5-ene (2).

Attempts to isolate 2 free of solvents failed. Removal of $CDCl_3/CFCl_3$ at -30°C/10^{-4} Torr followed by distillation of the residue at 15°C/10^{-4} Torr into a trap cooled to -78°C yielded a yellowish oil which decomposed violently at room temperature at normal pressure. No elemental analysis and molecular weight determination could thus be made.

If the yellowish oil was dissolved in CCl_4, $CHCl_3$, CH_2Cl_2, and MeOH, it was slowly transformed into the cis-sulfine 3c and the trans-dione 4t; the transformation was complete after about ten hours at room temperature[13].



3c **4t**

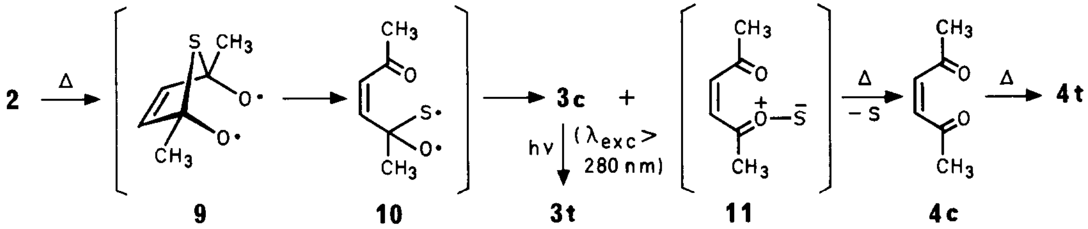
solvent	**3c** (%)	**4t** (%)
CCl_4	40	60
$CHCl_3$	55	45
CH_2Cl_2	51	49
MeOH	85	15

As expected, the same yields of 3c and 4t were obtained if 1 was subjected to photosensitized oxygenation in $CHCl_3$, CH_2Cl_2, and MeOH without isolation of thiaozonide 2[15].TPP-photosensitized oxygenation of 1 in CCl_4, however, did not yield 3c and 4t; the only product we were able to isolate so far is acetone. As yet, we have no explanation for this result; but, clearly, thiaozonide 2 is not an intermediate in this case.

If the photooxygenation in CH_2Cl_2 was interrupted after about 20% of 1 had reacted with singlet oxygen, the reaction mixture contained small amounts of cis-3-hexene-2,5-dione (4c)[16] which slowly underwent the well-known thermal isomerization[3,14] to the trans-isomer 4t indicating that 4c is the precursor of 4t in the transformation reaction of 2.

Since 3c is neither thermally nor photochemically[15] transformed into 4c, the latter originates from 2 by sulfur extrusion whereas the former is afforded from 2 by rearrangement. Concerted processes may be envisaged for both reactions. However, it appears to be more likely that the two transformations occur via common intermediates such as the biradicals 9 and 10 (Scheme 1).

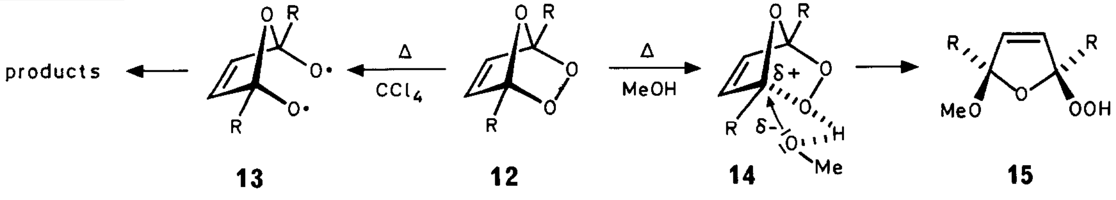
Scheme 1



The O-O bond is certainly the most labile bond of 2; it should be cleaved homolytically in in the aprotic chlorinated solvents to yield biradical 9. Rearrangement of 9 to 10 should be exothermic since a C-S-σ-bond (≈ 65 kcal/mol) is broken but a C-O-π-bond (≈ 95 kcal/mol) is formed and since one of the oxygen radical sites is substituted by a sulfur radical site. Biradical 10 may then undergo a further rearrangement to cis-sulfine 3c and to the cis-carbonyl-sulfide 11 with about equal probabilities[17]. Loss of sulfur from 11[18] yields 4c which is thermally isomerized to 4t.

We have recently discussed rearrangements of furan-endoperoxides such as 12 as occurring via biradicals (13) in aprotic non-polar solvents[8]. In MeOH, however, hydrogen bonding leads to heterolysis of the C-O bond and addition of alcohol to the developing cation under retention of configuration (Scheme 2)[20].

Scheme 2



a: R = H; b: R = CH_3

Thiaozonide 2 does not add methanol. One may conceive of a polar rearrangement of 2 to give 3c via stages similar to that of 14. However, one does not see why then a methoxy hydroperoxide similar to that of 15 should not be formed. It appears to be more likely that the homolytic cleavage of the O-O bond in 2 is much faster than in 12b and that the developing cation 14 from 12 is better stabilized than the corresponding cation from 2[22]. If 12a is reacted with MeOH, both pathways, the radical as well as the polar pathway, are pursued[8].

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9. A 25 ml irradiation unit with automatic oxygen-consumption recording system[10] was used. A 150 W Halogen-Bellaphot lamp (Osram) and a band filter transparent between 480 and 570 nm (Hoya) were applied for electronic excitation of RB and TPP (both at $5 \cdot 10^{-4}$ M). The solvents containing 1 at initial concentrations of $2 \cdot 10^{-2}$ M and the sensitizer were saturated with oxygen before irradiation. The irradiation unit, the oxygen burette and the tubing connecting the unit with the burette were kept at (13 ± 0.1)°C by cooling with water; thermostat JULBO-P.
10. a. H.Paur, Dissertation, University of München, 1982;
    b. K.Gollnick, H.Paur, A.Griesbeck, manuscript in preparation.
11. ^{1}H- and ^{13}C NMR spectra were taken on a Bruker WP-80-CW spectrometer using TMS as internal standard.
12. The oxygen analogs of 1 and 2 exhibit ^{13}C signals at 13.36 (q, C_6); 106.19 (d, C_3), and 150.17 (s, C_2) for 2,5-dimethylfuran, and at 13.48 (q, C_6); 124.12 (d, C_3) and 112.34 (s, C_2) for the endoperoxide (= ozonide).
13. 3c: ^{1}H NMR ($CDCl_3$, 20°C): δ = 2.21 (s, 3H); 2.43 (s, 3H); AB-system centered at 6.42 and 7.58 (J_{AB} = 10 cps). - Ref. 3: 2.26; 2.43; AB-system centered at 6.40 and 7.53 (J_{AB} = 10 cps). - - 4t: ^{1}H NMR: δ = 2.28 (s, 6H); 6.67 (s,2H).- Ref. 8, 14: 2.28; 6.67.
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15. If no filter was used (λ_{exc} > 280 nm), 3c was slowly isomerized to the trans-sulfine 3t : ^{1}H NMR: δ = 2.26 (s, 3H); 2.46 (s, 3H); AB-system centered at 6.28 and 7.97 (J_{AB} = 16 cps). - Ref. 3: 2.28; 2.41; AB-system centered at 6.17 and 7.83 (J_{AB} = 16 cps).
16. 4c: ^{1}H NMR: δ = 2.31 (s, 3H); 6.71 (s, 2H).
17. Whether biradical 10 rearranges directly to 3c + 11 or via the oxathiirane 5 may remain an open question.
18. According to a recent theoretical study[19], loss of sulfur from a biradical like 10 or a carbonyl sulfide like 11 should occur via an activation barrier of less than 10 kcal/mol.
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20. In contrast to our previous assumption[7], the addition of MeOH to 12b yields the cis-isomer 15 rather than the corresponding trans-isomer, as was revealed by X-ray analysis[21].
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22. The efficiency of carbenium ion stabilization by an α-oxygen vs. an α-sulfur atom appears to be very much dependent on the individual system used; see, for example, ref. 23a (for O > S) and ref. 23b (for S > O).
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