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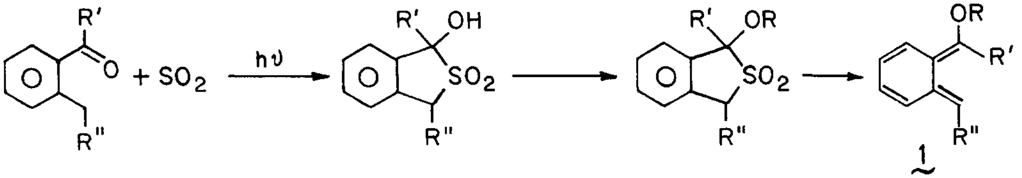
PHOTOCHEMICAL SYNTHESIS OF α-OXYGENATED BENZOTHIOPHENEDIOXIDES

James L. Charlton[1],* and Tony Durst*
Ottawa-Carleton Institute for Graduate Studies
and Research in Chemistry
Department of Chemistry
Department of Chemistry, University of Ottawa
Ottawa, Canada K1N 9B4

Summary: The photochemical synthesis of 1-hydroxy[b]benzo-1,3-dihydrothiophene-2,2-dioxides from orthomethylbenzaldehyde and its analogs is described. Some of the chemistry of these α-oxygenated sulfones, including exchange of the 1-hydroxy group with various alkoxy groups and the thermal reversion of these oxygenated derivatives to trappable 1-alkoxy-substituted o-quinodimethanes has been investigated.

The use of o-quinodimethanes 1 in organic synthesis is well established and has been reviewed by several authors (1). In conjunction with our current work on intramolecular Diels-Alder reactions of 1-quinodimethanes (2), we required a general route to the 1-alkoxy-o-quinodimethanes 1. Although such dienol ethers have been reported (3), their synthesis by reported procedures is tedious and/or lacking in generality. Based on the reports that photochemically generated o-quinodimethanes can be trapped reversibly by SO_2 (4) we have investigated the reaction scheme shown below.



Compounds 2-5 (Table)(5) were photolysed in benzene solution (0.6%), using an Hanovia 450 watt medium pressure mercury lamp and a 1 mm pyrex filter, after the solution had been purged with nitrogen and partially saturated with sulfur dioxide. The lamp was housed in a quartz water jacket and immersed in the benzene solution which was maintained at 20°C. Solutions were irradiated until the starting material appeared to be at least 75% consumed as judged by thin layer chromatography. No attempt was made to optimize yields. The sulfone 6 from o-methylbenzaldehyde 2 was isolated by crystallization from methylene chloride-hexane after removal of the benzene in vacuo at room temperature. The products from o-benzylbenzaldehyde 3 and o-methylbenzophenone 5 were obained by evaporating the benzene solution, dissolving the residue in methylene chloride, extracting with 5% aqueous bicarbonate, acidifying the aqueous fraction and extracting the product into methylene chloride. In the case of o-methylacetophenone 4, the

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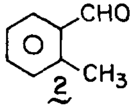
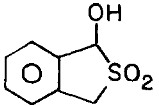
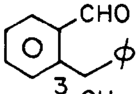
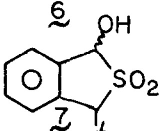
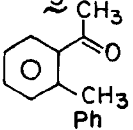
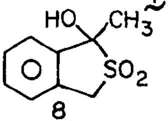
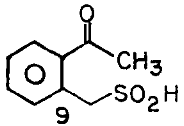
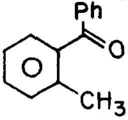
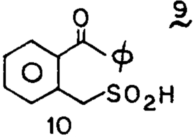
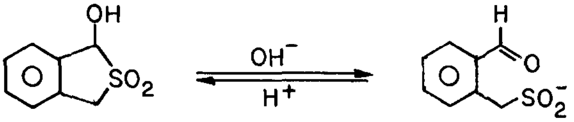
[1] Visiting Professor, 1983-84, Department of Chemistry, University of Manitoba, Winnipeg, CANADA R3T 2N2.

product crystallized from the irradiated benzene solution and could be recovered by filtration. The yields of products are given in Table 1.

TABLE

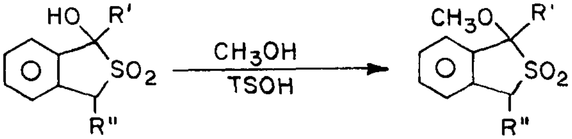
Compound	Irradiation time (hr.)	Yield	Product(s)
 2	4	56%	 6
 3	2.5	41%	 7
	3	64%	 8 +  9
	4	25%	 10

In all cases there appeared to be a ready equilibrium between the sulfone and the sulfinate forms of the product which could readily be demonstrated by recording a nuclear magnetic resonance (NMR) spectrum of the adduct in D_2O at pH 10.



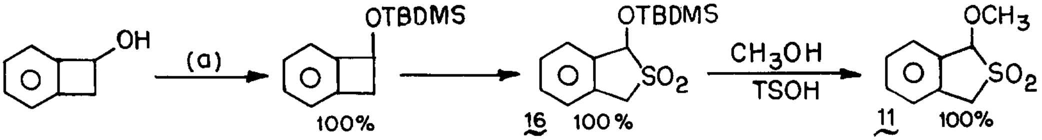
In organic solvents 6 and 7 appear to be exclusively in the sulfone form and 7 appears to be a mixture of isomers (cis and trans) as shown by the appearance of two sets of signals for the benzylic protons in the NMR consistent with an equilibrium mixture of approximately 90% 8 and 10% 9 which could not be separated by recrystallization. Based on spectral data, product 10 appears to be completely in the sulfinic acid form.

Product 6, 7 and 8 - 9 all react with excess acidic methanol to give the methoxy compounds 11 (92%), 12 (46%) and 13 (55%).



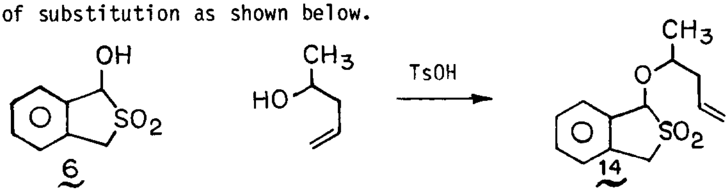
11 = R'=R"=H
12 = R'=H,R"=ϕ
13 = R'=CH_3,R"=H

All of the methoxy compounds are thermally unstable but can be recrystallized (11, toluene/hexane, -78°C; 12, benzene/cyclohexane; 13, methanol, -78°C). While 7 appears to be a mixture of isomers, its methoxy derivative 12 is produced as a single isomer. The structure of 11 was confirmed by the alternate synthesis shown below.

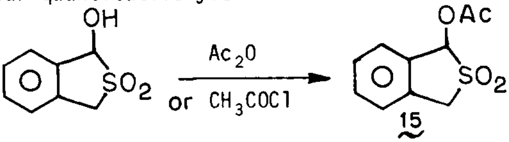


(a) tBDMS, imidazole, DMF (b) toluene, SO_2 (c) CH_3OH, p-toluenesulfonic acid.

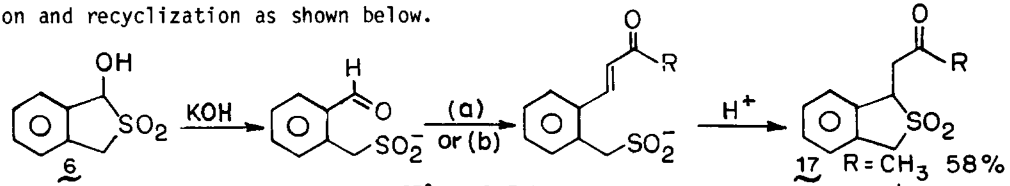
Reaction of 6 with one equivalent of an alcohol in benzene/p-toluenesulfonic acid also gave a good yield of substitution as shown below.



Compound 6 can also be reacted with acetic anhydride or acetyl chloride at room temperature to form the acetate 15 in near quantitative yield.



The fact that 6 forms the sulfinate-aldehyde in base led us to attempt an aldol condensation and recyclization as shown below.

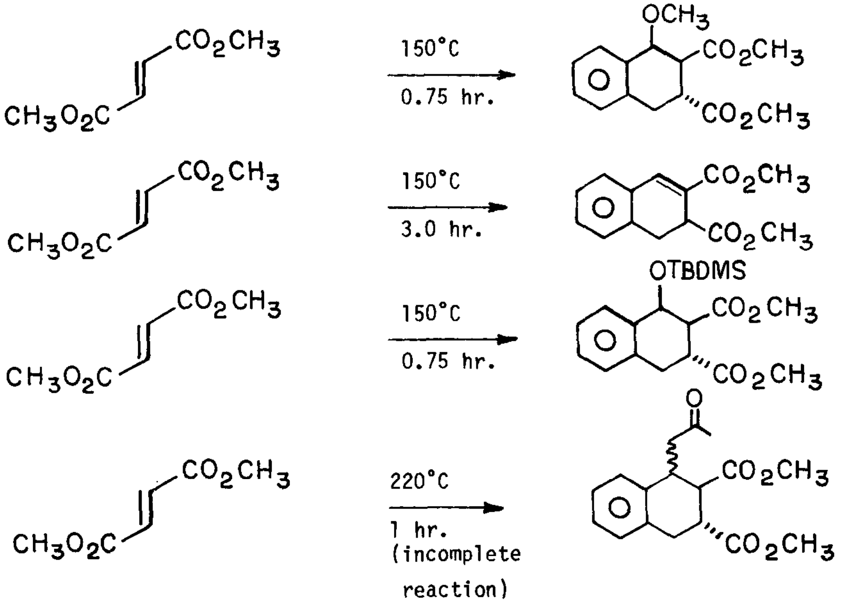


(a) 5% KOH/Methanol, excess acetone, 55° C, 1.5 hr.

(b) 10% KOH/Ethanol, acetophenone, 1 equ., reflux, 2.75 hr.

To test for reversion to quinodimethanes by extrusion of SO_2, compounds 11, 15, 16 and 17 were all thermolysed with excess dimethyl fumarate in hexachlorobutadiene as solvent. The cycloaddition products were isolated by chromatography (silica gel) and the spectral data (NMR, IR) are consistent with the structures given. The yields are typically >50%.

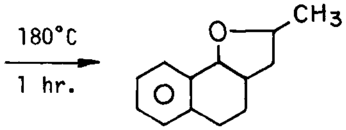
11 +, 15 +, 16 +, 17 +



mixture of isomers

Compound 14 was pyrolysed in hexachlorobutadiene alone.

14 +



mixture of isomers

We have demonstrated the trapping of photochemically generated quinodimethanes by sulfur dioxide and the subsequent conversion of the resulting sulfones to a variety of α-alkoxy, acyloxy and alkylbenzothiophenedioxides. These in turn can be thermolysed to form a range of substituted quinodimethanes which were successfully trapped with dimethyl fumarate.

Acknowledgements

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References

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6. All new compounds were characerized by ir, nmr, ms and in most instances, elemental analysis.

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