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THE TRANSFORMATIONS OF ARYLOXYSULFONIUM CATIONS—II*

ORIGIN OF *PARA*-SUBSTITUTED PRODUCTS AND BENZOXATHIANS

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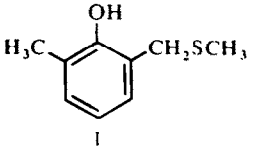
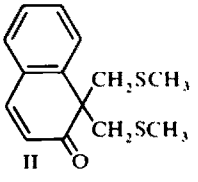
Abstract—2,6-Dimethylphenol is converted to its *p*-thiomethoxymethyl derivative on reaction with N,N'-dicyclohexylcarbodiimide and dimethyl sulfoxide in a moderately acidic medium. Similar treatment of *ortho*-unsubstituted phenols affords small amounts of products containing the 5,6-benzo-1,3-oxathian ring system in addition to the normal products described in the preceding paper.[1] Studies designed to elucidate the mechanisms of these transformations are described along with a second oxathian ring synthesis.

IN THE preceding paper[1] we outlined the reactions of phenols with dicyclohexylcarbodiimide (DCC) and dimethyl sulfoxide (DMSO) in the presence of acidic catalysts such as phosphoric acid or pyridinium trifluoroacetate. The main products from simple alkyl phenols involved substitution of one or both available *ortho*-hydrogens by thiomethoxymethyl groups (for example I from *o*-cresol). No *para*-substituted isomers were detected unless both *ortho*-positions were already occupied by alkyl groups. When the drive toward aromaticity was less urgent as in the naphthols, products of type I were joined by the bis-*o*-thiomethoxymethylated dienones (such as II from β-naphthol) and with the more acidic phenols by O-thiomethoxymethyl compounds (for example III from *o*-nitrophenol).



I



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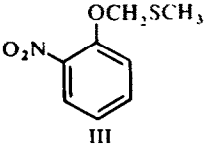
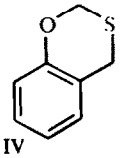


III

In addition small amounts of substances containing the 5,6-benzo-1,3-oxathian ring system also were often isolated; e.g., the parent heterocycle (IV) from phenol itself and the benz-fused analogues (V and VI) from α and β-naphthol, respectively.



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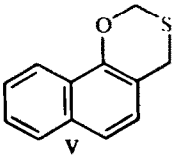
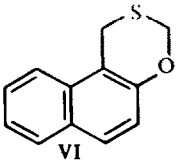


V



VI

* For Part I see preceding paper.[1]

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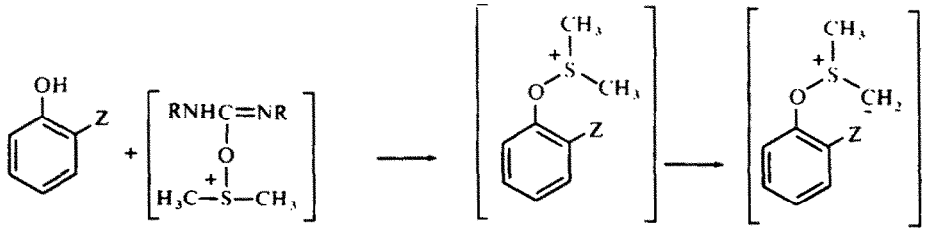
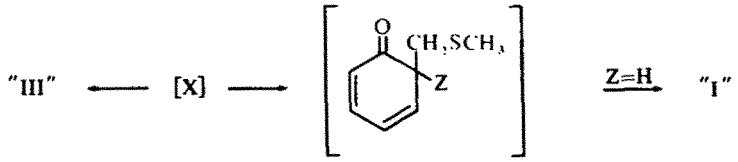
‡ Abstracted from the Ph.D. Thesis of J.P.M.[2] Additional data including reproductions of spectra may be found in this reference.

The pathway we proposed[1,3] for the formation of products in the structure classes I–III requires initial attack by the phenol (VII) at sulfur in a preformed DCC—DMSO—H^+ isourea adduct (VIII) to yield the aryloxysulfonium cation (IX) which then loses a proton to generate the sulfur stabilized ylid (X). This species can undergo a Pummerer type shift to give "III" or a Sommelet like rearrangement to the dienone (XI). Enolization of XI (Z=H) would yield phenols of class I and recyclization of these through the



VII VIII IX X

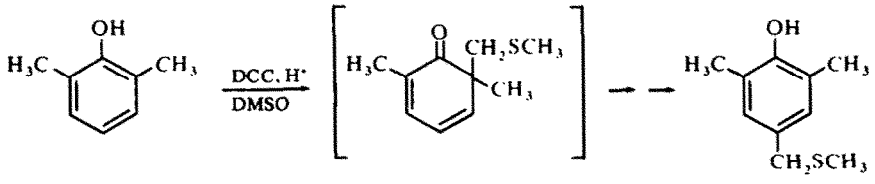


XI

mechanism to the same *ortho*-position would give the doubly thiomethoxy-methylated dienones of class II≡XI ($Z=CH_2SCH_3$). Further modifications of this mechanism will be required to explain the formation of small amounts of benzoxathians also found in these reactions as well as the isolation of *para*-substituted products from 2,6-dialkylphenols and our studies in these areas are the subject of this publication.

Mechanism of para-*substitution*

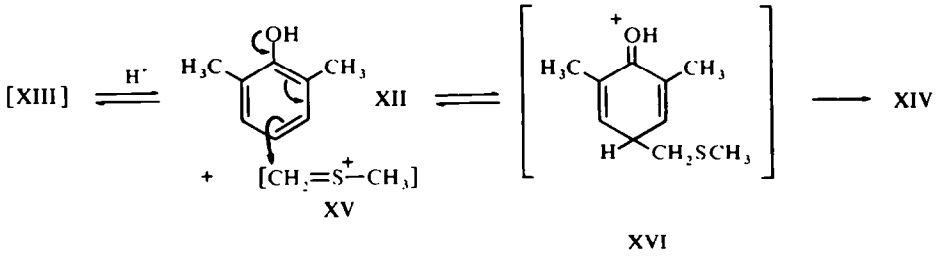
2,6-Dimethylphenol (XII) is converted to 4-thiomethoxymethyl-2,6-dimethylphenol (XIV) on treatment with DCC and DMSO in the presence of an orthophosphoric acid catalyst.



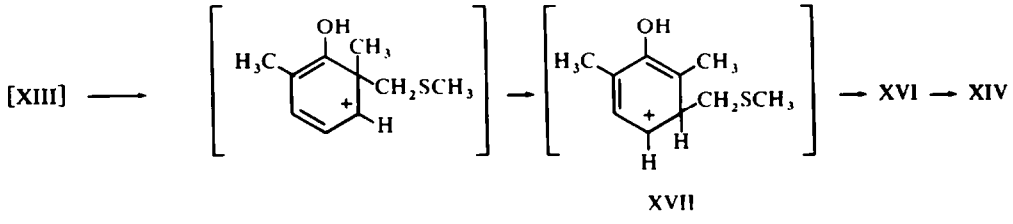
XII XIII XIV

In analogy to the simple *o*-thiomethoxymethylation process (and the formation of class I and class II products) a most attractive and precedented intermediate in this transformation would be the dienone (XIII) which could be generated without deviating from our general reaction pathway (note identity of XIII with XI[Z=Me]). In a

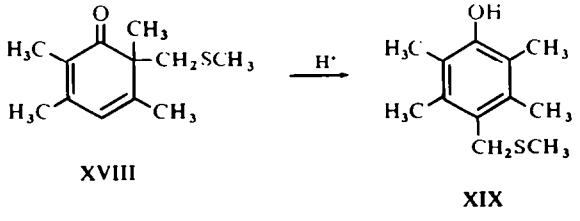
preliminary communication[3] we suggested that this intermediate yielded XIV by fragmentation to methylmethylene sulfonium cation (XV) and starting phenol (XII) followed by recombination of these species by a classical electrophilic substitution mechanism with the phenol acting in its normal role as a *para* director. Note that the



formation of XIV from XIII cannot proceed in a series of 1,2-shifts usually postulated in an ordinary dienone-phenol rearrangement[4] since this would require the isolation of at least some *meta* product by proton abstraction from the halfway intermediate (XVII).



In a preliminary communication*, Burdon and Moffatt[5] did not suggest a mechanism for *para*-substitution, but did report that mild acid treatment of the dienone (XVIII) gave the *p*-product (XIX).† However, they were unable to detect any alkylation of large excesses of anisole, N,N-dimethylaniline, or furan added as traps during the *p*-alkylation of XII and therefore reasoned that *p*-alkylation was an intramolecular process.[5] a

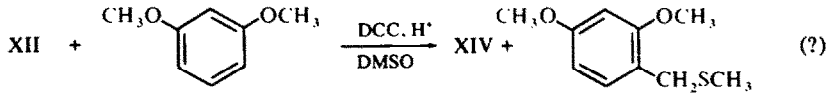


* For history of this project and relationship between research groups see preceding paper.[1]

† They have since performed a similar conversion of XIII (isolated from XII+DCC—DMSO—H⁺ by a modified reaction and isolation procedure) to XIV.[6]

conclusion inconsistent with our postulated fragmentation-recombination pathway.* We did not believe this last experiment constituted an insurmountable objection to our proposed mechanism for two reasons. First, the phenol should be a much better substrate for electrophilic attack by methylmethylenesulfonium cation (XII) than the traps the authors introduced. Second, the formation of the phenol and XV together in the fragmentation of XIII would give the phenol a spatial advantage for further reaction with XV. This should be enhanced by the attractive interaction between the electron rich phenol and the cation which would keep these two species in close proximity for a longer period and diminish the rate at which they would drift apart in the reaction medium. A successful trapping experiment would, however, be required to justify this rationalization and decide the point at issue.

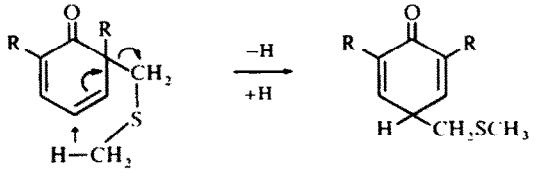
In our first attempt to trap the postulated methylmethylenesulfonium cation, we treated 2,6-dimethylphenol (XII) with DCC, DMSO, and H_3PO_4 in the presence of an excess of 1,3-dimethoxybenzene (XX) in anticipation that some thiomethoxymethylated ether (XXI) would be obtained in addition to the normal *p*-substituted phenol (XIV).



XX XXI

Dimethoxybenzene was chosen as the trapping agent because of its high activation toward electrophilic substitution, and because we had already shown that DCC, DMSO, and acid do not react with this substrate.[1] Also the expected trapping product (XXI) was prepared by a different method (*vide infra*) to insure our ability to find it in trace yield. However the yield of XIV did not decrease and XXI was not detected. Again this negative result is inconclusive and can be rationalized either in terms of an intramolecular process or as indicating that XX is not a competitive enough trap.

* This result led Burdon and Moffatt at the same time to consider an internal Claisen-like (?) pathway (i→ii) for the *ortho→para* migration. They have since described experiments designed to test this



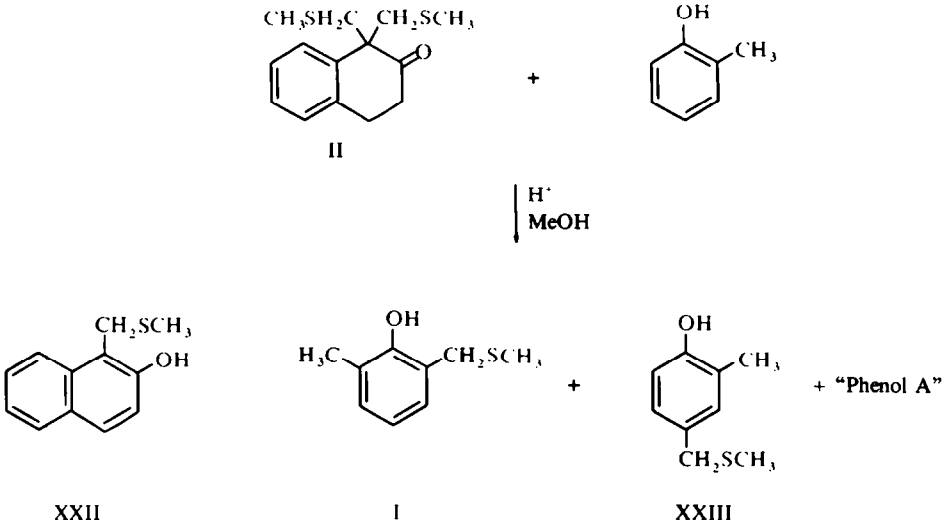
i ii

mechanism[6] and their most recently reported opinion is that it is "generally unlikely" though "definitive proof of (its) rejection" is not yet available.[6] In this context note that the deprotonation of dimethyl sulfide requires 0·45 N KNH_2/ NH_3 ($t_{\frac{1}{2}}$ = 40 min at 0°)[7] while the rearrangement of XVIII to XIX occurs readily in acidic medium.

The authors have also carried out additional trapping experiments and the *para*-rearrangement mechanism they favour[6] is now general accord with our own views though with some minor differences of nuance.

A more reactive trap is another phenol. However, in order to carry out a cross-over reaction with such a species, it is necessary that the experiment designed utilize not the 2,6-disubstituted phenol itself but one of the intermediates derived from this precursor in the course of the reaction. Since the only isolable compound fulfilling this requirement was the thiomethoxymethyl dienone (XI) we performed the following reaction.

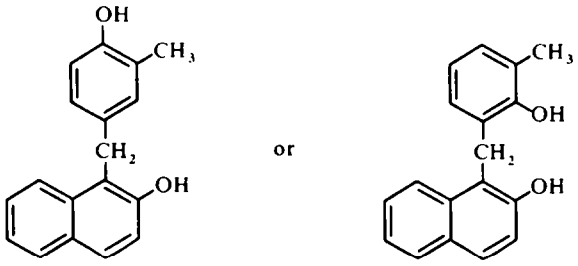
1,1-Di-thiomethoxymethyl-3,4-dehydro-2-tetralone[1] (II) and a twofold excess of *o* cresol were refluxed overnight in a methanolic acid solution. The reaction mixture was then worked-up in the usual manner and the phenolic products isolated. Five different phenols were identified in the product mixture including *o*-cresol itself, traces of 1-thiomethoxymethyl-2-naphthol (XXII) (identical to a known sample[1]), the product expected from the elimination of a methylmethylenesulfonium cation from the starting dienone, and new "Phenol A" (65%) whose structure and origin will be discussed later.



In addition, the two significant cross products, 2-methyl-6-thiomethoxymethylphenol (I) and 2-methyl-4-thiomethoxymethylphenol (XXIII), were obtained though only in very low yields (2% and 1·5%, respectively).

The isolation of even small amounts of *o*-cresol cross products was enough to satisfy our requirement and to demonstrate conclusively the intermediacy of the methylmethylenesulfonium cation (XV) and the fragmentation-recombination mechanism for the *para*-rearrangement. However, a higher percentage of crossover products would be desirable and our conviction that the solvent, MeOH, was limiting the yields of these compounds by trapping XV led us to repeat the experiment in ethylene chloride, when the same four phenolic products plus leftover *o*-cresol were isolated, but in the following amounts: "Phenol A" 80%, *o'*-thiomethoxymethyl-*o*-cresol 7%, *p*-thiomethoxymethyl-*o*-cresol 16% and 1-thiomethoxymethyl-2-naphthol 20%. As predicted higher yields of crossover products were observed, but under these conditions XV must still be involved in other side reactions. One of these is quenching by methyl mercaptan liberated in the process generating Phenol A as evidenced by the isolation of dithiomethoxymethane (found in 25% yield but much of this volatile compound was lost in the work-up).

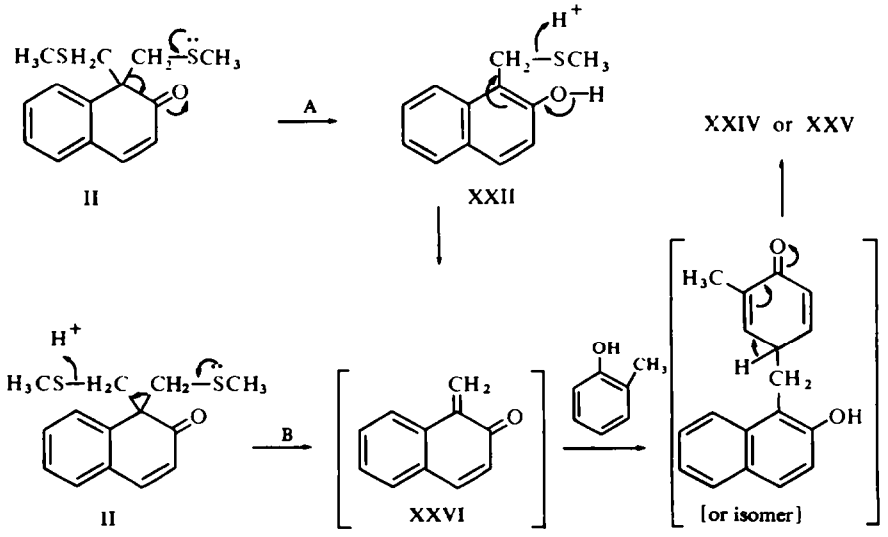
The bonus in our crossover experiment was the formation in high yield of the new compound, "Phenol A", which is believed to be either 1-(3′-methyl-4′-hydroxybenzyl)-2-naphthol XXIV or its isomer, 1-(3′-methyl-2′-hydroxybenzyl)-2-naphthol XXV from the following evidence. Its IR spectrum showed strong OH absorption (KBr), its UV spectrum exhibited the usual shift in λ_{max} upon addition of base (335 mμ to 355 mμ) and



XXIV XXV

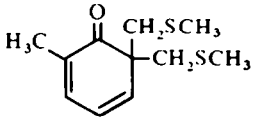
its NMR (CD_3CN) spectrum was also consistent with either structure XXIV or XXV: complex multiplet 1·8–3·2 τ (11, aromatic and phenolic hydrogens), sharp singlet 5·48 τ (2, CH_2) and sharp singlet 7·73 τ (3, Me). The base peak in its mass spectrum corresponded to a parent minus *o*-cresyl fragment, and the parent peak was almost as strong; *m/e* 264 (95%). On treatment with Ac_2O and Py., "Phenol A" yielded a crystalline diacetate whose IR has no OH absorption but did show a very intense carbonyl peak at 5·68μ (CCl_4); its NMR (CCl_4) contained a multiplet 2·2–3·2 τ (9, aromatic hydrogens), a singlet 5·77 τ (2, CH_2), a singlet 7·94 τ (6, acetyl) and a singlet 8·01 τ (3, Me). Phenol A was resistant to hydrogenation over Pd thus also eliminating an alternate benzyl ether structure.

We suggest that the diphenol is formed by electrophilic substitution at either the *ortho* or *para* position of *o*-cresol by the postulated *o*-quinonoid intermediate (XXVI). This

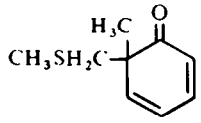


species could be generated by an acid-catalyzed Michael-like elimination of one of the initial reaction products, the 1-thiomethoxymethyl-2-naphthol (XXII) (path A), or *via* a direct elimination pathway from the dienone (II) (path B). A mixture of XXII and *o*-cresol in acid does yield the diphenol as anticipated. The unsaturated ketone (XXVI) would also have been expected to react with MeOH when this was the reaction solvent and with the phenolic OH of *o*-cresol. These reactions should, however, be reversible whereas the C-alkylation postulated above involves a final irreversible aromatization step. Some synthetic applications of the process exemplified by the sequence, XXII→[XXVI]→products, will be described in a future paper in this series.

The success of our crossover experiment encouraged us to attempt to modify the direct standard reaction of *o*-cresol with DCC—DMSO—H^+, which normally yields *o'*-thiomethoxymethyl-*o*-cresol (I) as the only phenolic product,[1] in such a way as to induce the formation of some *p*-thiomethoxymethyl-*o*-cresol (XXIII). We suspected that the main reason that *para* product had not previously been found by ourselves or Burdon and Moffatt, even though the methylmethylenesulfonium cation should have been generated by fragmentation of the expected dienone intermediates (XXVII and XXVIII)*, was because of the presence of a better trap than *o*-cresol in the reaction



XXVII



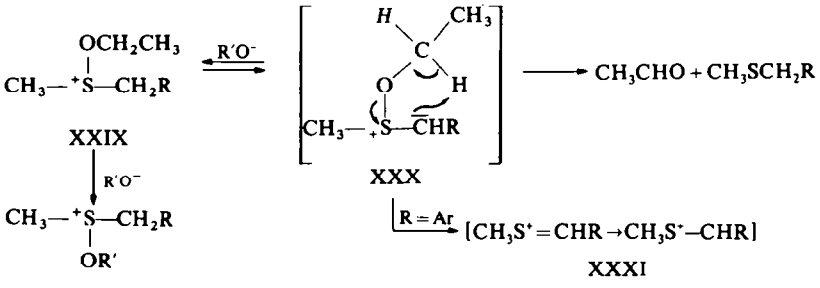
XXVIII

medium. The best traps for the methylmethylenesulfonium cation (XV) should be anions which can also act as nucleophiles. The phosphate and trifluoroacetate anions from the large quantities (0·2–0·5 eq) of acidic catalysts, H_3PO_4 or pyridinium trifluoracetate, required to initiate the reaction were therefore tentatively accused of being the culprits which blocked the route from XV to *p*-substituted-*o*-cresol (XXIII). It would be possible to decrease the concentration ratio of these anions to *o*-cresol by using much less catalyst but the consequence would not only be a reduced reaction rate but also a greatly diminished yield because of the side reaction with DCC which uses up the catalyst.[1] Since it sequesters the anion this side reaction could, however, be used to our advantage if we repeated our standard reaction of *o*-cresol with DMSO and DCC with one variation. The normal amount of pyridinium trifluoroacetate catalyst would be used, but in order to keep acidity and available trifluoroacetate anion concentration down without decreasing yields too much it would not be added at once at the start but slowly as the DCU precipitated and as it was used up in the side reaction. When performed as described, 2% of *p*-substituted phenol (XXIII) was isolated in accord with our rationale along with 41% of I (*vs.* 59% I and no XXIII [<0·5%] from the unmodified synthesis[1]).

* Because XXVII would be derived from a secondary reaction while XXVIII is the product of thiomethoxymethyl migration to the more hindered *ortho*-position, both species should be generated in low yield *vs.* the dienone which affords the normal product (I). It is therefore impossible to isolate much *para*-substituted phenol (XXIII), but since both XXVII and XXVIII should be produced in significant concentration, a small amount of XXIII should be obtainable.

During early attempts to find another route to aryloxysulfonium cations (IX) in addition to our phenol + DCC—DMSO—H^+ procedure, we discovered that the dimethylethoxysulfonium salt (XXIX, R = H) can serve as an alternate though very inefficient source of the methylmethylenesulfonium cation (XV). The reaction of XV with *o*-cresol when generated by this new procedure confirms the site of reaction findings of the key crossover experiment described previously.

Johnson *et al.*[8] have published an elaborate study of the reactions of alkoxysulfonium salts such as XXIX with alkoxides. They found that these compounds not only underwent rapid alkoxy interchange with inversion but also decomposed to the oxidized alkoxy derivatives. When R was aryl a second fragmentation of XXX to the cation

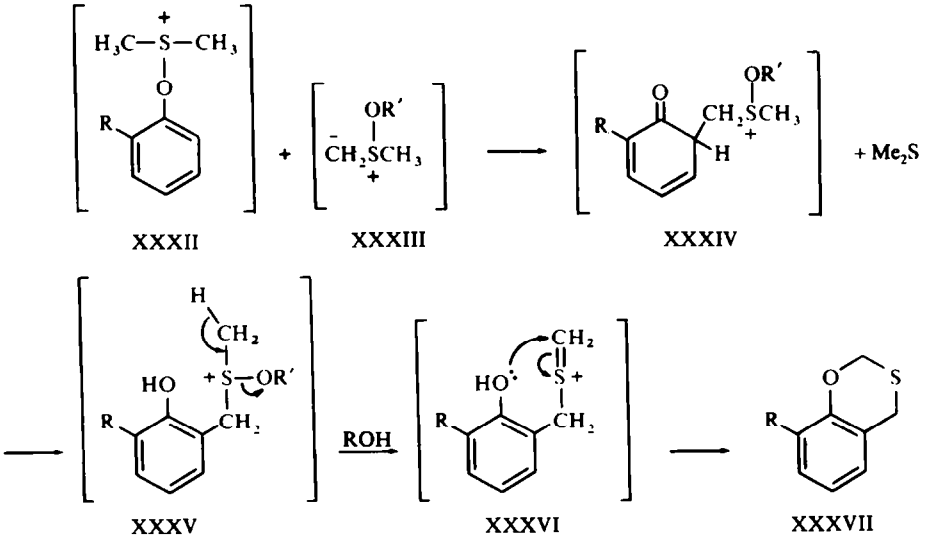


(XXXI) also became a significant reaction. In our hands no reaction occurred on treatment of *o*-cresol with an excess of XXIX (R = H) in CH_2Cl_2 and when sodium *o*-cresolate was used as substrate the exclusive process was Johnson's base-induced generation of MeCHO and Me_2S. However, when the reaction with *o*-cresol was carried out in the presence of Et_3N, very low yields of *o* and *p*-thiomethoxymethyl-*o*-cresols were obtained (2% and 4%) in addition to MeCHO and Me_2S. As noted in the preceding paragraph these products, particularly the *para*-isomer are best explained by a pathway involving electrophilic substitution of *o*-cresol by the thiomethoxymethyl cation (XV = XXXI[R = H]. The absence of these substitution products with the stronger base, *o*-cresolate, probably indicates the presence of an alternative quenching process for XV in this system rather than some obstacle to its formation. Further support for the intermediacy of XXXI[R = H] in the Et_3N reaction was provided by the conversion of *m*-dimethoxybenzene to the 4-thiomethoxymethyl substituted derivative (XXI, 12%) under similar conditions.

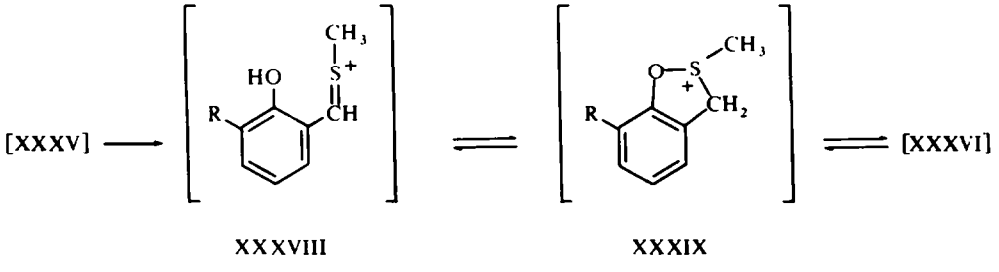
Additional chemistry of the thiomethoxymethyl cation and its derivatives will be described in future papers.[9]

Mechanism of 5,6-benzo-1,3-oxathian formation

In our preliminary communication[3] we proposed that the small amounts of benzoxathian products isolated from treatment of *o*-unsubstituted phenols with DCC—DMSO are produced by the reaction of an aryloxysulfonium cation (XXXII) (the key intermediate in the generation of *o*-thiomethoxymethyl phenols[1]) with the oxysulfonium ylid (XXXIII). This ylid, whether derived by deprotonation of another aryloxysulfonium cation molecule (XXXII) or by hydrogen abstraction from an early reaction intermediate, the DCC—DMSO—H^+ adduct (VIII),[1] was postulated to attack the available *o*-position of XXXII liberating a molecule of Me_2S and generating XXXIV. After



enolization of XXXIV, elimination of the elements R′OH from the resulting cation (XXXV) would afford XXXVI which could then cyclize to the product (XXXVII). Although benzylic hydrogens are more acidic than Me protons in simple benzyl methyl sulfonium salts,[10] ionization and elimination at the former position in XXXV to yield the S-stabilized cation (XXXVI) would not be an insurmountable mechanistic obstacle. Deprotonation at the benzylic position could be reversible and might not be followed by expulsion of $^-$OR′ while the loss of the Me H and OR′ could be favored as a concerted process. If XXXVIII were generated, cyclization of this species to XXXIX could create an alternate source of XXXVI as would a direct tautomeric equilibrium between XXXVIII and XXXVI(XXXVIII $\overset{:B}{\rightleftharpoons}$ XXXVI). Note that in the Hauser rearrangement of the benzyldimethylsulfonium cation, a more rapid benzylic C–H ionization does

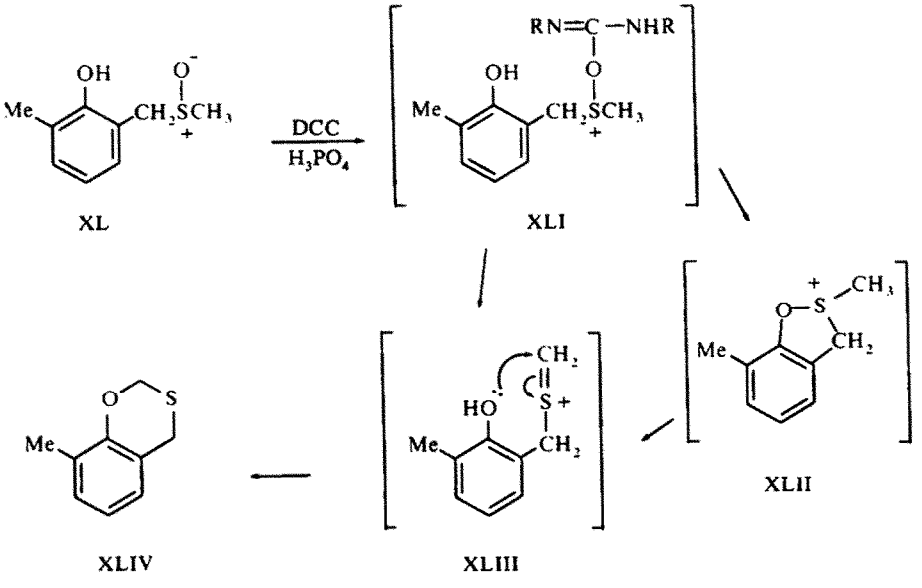


not preclude Me proton abstraction as the product determining step.[11] Note also from other work[1, 12] that the sp^3 hydrogens of XXXV, XXXVI, XXXVIII, and XXXIX would be predicted to be very acidic and easily lost under the reaction conditions. In their description of benzoxathian formation, Burdon and Moffatt[13] reproduced our mechanism in Scheme A without proposing an alternative.

This mechanism suggests a more convenient synthesis of benzoxathians utilizing a different approach to the oxysulfonium phenol intermediate (XXXV). This species with

R′ = DCCH should also be available from the reaction of an *o*-hydroxybenzyl methyl sulfoxide with DCC and acid. To test this hypothesis 2-methyl-6-thiomethoxymethylphenol (I) was oxidized to the corresponding sulfoxide (XL) with 30% H_2O_2 in HOAc and XL then treated with DCC and H_3PO_4 in C_6H_6. A 20% yield of

SCHEME B

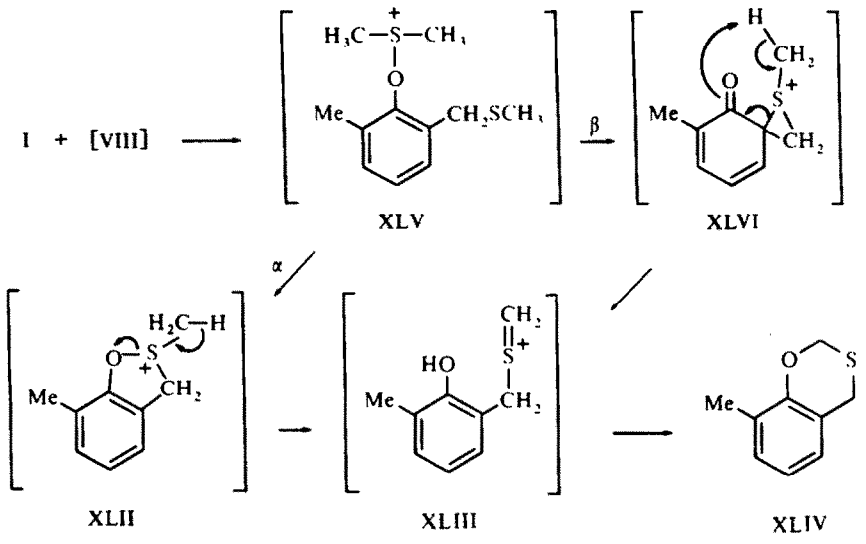


8-methylbenzo-1,3-oxathian (XLIV) was isolated. The reaction mechanism as it applies to this system is depicted in Scheme B. The route [XLI]→[XLII]→XLIV would be another example of the displacement at S discussed earlier followed by a Pummerer rearrangement. In the sequence [XLI]→[XLIII]→XLIV the presently accepted Pummerer intermediate cation[14] is generated directly and then quenched intramolecularly.

Although our ability to achieve this second oxathian synthesis was nicely in accord with Scheme A, we were later able to definitively exclude this process for the formation of XLIV in the *o*-cresol plus DCC—DMSO reaction by showing that the main reaction product, *o*′-thiomethoxymethyl-*o*-cresol (I), was converted to 6-methylbenzoxathian (XLIV) under the experimental conditions. When carried out in DMSO-d_6, the reaction (I→XLIV) produced completely undeuterated benzoxathian thus positively identifying the thiomethoxymethyl moiety of I as the source of both methylene groups of the benzoxathian and excluding pathways in which I reverted to *o*-cresol which was subsequently transformed to XLIV.

The mechanism consistent with this new data which we favour for the generation of benzoxathians in the phenol plus DCC—DMSO experiments is outlined in Scheme C. In the sequence postulated the initially formed thiomethoxymethylphenol (I) attacks the preformed DCC—DMSO—H^+ adduct (VIII) to give the aryloxysulfonium cation (XLV). This is then transformed by one of two possible routes to the cation (XLIII) which finally cyclizes to the benzoxathian (XLIV). Note that the same final step was

SCHEME C



proposed for the alternate benzoxathian synthesis (Scheme B) and supporting data referenced at that time. Evidence for the production of the aryloxysulfonium cation (XLV) has also been presented earlier in this and the preceding paper.[1] The most interesting part of Scheme C is the conversion of XLV to XLIII. One of the two pathways pictured (α) begins with a nucleophilic displacement on oxygen, a very unusual but not unprecedented process especially with non first-row nucleophiles,[15] and follows this with a Pummerer rearrangement. In the other route (β) dimethyl sulfide is eliminated by nucleophilic *ortho* attack, a standard process in other reactions of XLV (*vide supra*), but in this case the result is the generation of the resonance interrupting, strained episulfonium cation (XLVI). This is then converted to XLIII by a more rapid than ancitipated heteroatom analogue of a Woodward-Hoffmann 1,5-sigmatropic hydrogen shift or some related acid catalyzed sequence. The variants, α and β, are difficult to experimentally differentiate in this system but lead to synthetically useful predictions in other areas.

EXPERIMENTAL

The apparatus used for recording spectra and melting points was the same as that described in the preceding paper.[1] The source and purity of the reactants and PLC materials and procedures have also been previously reported.[1]

Reaction of 2,6-*dimethylphenol with* DCC—DMSO. A soln of 6·1 g (0·05 mol) of 2,6-dimethylphenol and 34 ml (0·5 mol) DMSO was placed in a 300 ml 3-neck flask fitted with a mechanical stirrer and drying tube. The flask was cooled in an ice bath and 20·6 g (0·1 mol) DCC dissolved in 35 ml of C_6H_6 added with vig. stirring followed by 1·0 g (0·01 mol) anhyd. H_3PO_4. After a few min DCU began to precipitate from the yellow soln. The ice bath was removed after 30 min and stirring was continued for 4 hr. To hydrolyze unreacted DCC, a mixture of 100 ml water, 100 ml ether and excess oxalic acid was added slowly to the stirred mixture. Vigorous gas evolution occurred causing much foaming. The DCU was filtered and washed with ether. The ether layer was washed 3 × 75 ml H_2O and 1 × 50 ml sat $NaHCO_3$. The phenols were extracted from the ether with 3 × 50 ml 10% NaOH, the alkaline extract cooled in ice bath and slowly acidified to Congo Red with conc HCl. The phenolic products were then reextracted with 2 × 75 ml ether.

dried over Na_2SO_4, and evaporated to yield an oil (5·4 g). Starting material was removed by sublimation (60–70° at 1 mm). The residual oil solidified after standing a few days; after recrystallization from n-heptane, 3·6 g (40%), m.p. 42–43° of 2,6-dimethyl-4-thiomethoxymethylphenol was obtained; NMR(τ) CCl_4: 2·92(s), 3·29(s), 6·60(s), 7·86(s), 8·13(s); ratio: 1:2:2:6:3; IR(μ) CCl_4: 2·80(sharp); MS: mol. wt. 182 (25%), P-SMe (100%). Found: C, 65·66; H, 7·75. $C_{10}H_{14}OS$ requires: C, 65·88; H, 7·74%).

The product was desulfurized with Raney nickel to 2,4,6-trimethylphenol.

Reaction of 2,6-*dimethylphenol with* DCC—DMSO *in the presence of* 1,3-*dimethoxybenzene.* In a 1 l flask were placed 12·2 g (0·1 mol) 2,6-dimethylphenol, 61·8 g (0·3 mol) DCC, and 41·4 g (0·3 mol) 1,3-dimethoxybenxene with 150 ml DMSO and 200 ml C_6H_6. Anhyd. H_3PO_4 (5·0 g, 0·05 mol) was added and the mix stirred overnight. Isolation of the phenolic products was as above. The phenolic mixture (10·1 g) was starting material and 2,6-dimethyl-4-thiomethoxymethylphenol, yields as before. TLC of the concentrated neutral fraction indicated the presence of only dimethoxybenzene. Most was removed by vacuum distillation (80° at 1 mm) and the residue again examined with TLC. 1,3-Dimethoxybenzene was still the only detectable species and no spot at the R_f of the 4-thiomethoxymethyl derivative (*vide infra*) was found.

Reaction of 1,1-*di-thiomethoxymethyl*-3,4-*dehydro*-2-*tetralone with* o-*cresol; cross-over experiment A.* A methanol soln (50 ml) containing 5·28 g (0·02 mol) 1,1-di-thiomethoxymethyl-3,4-dehydro-2-tetralone[1] and 4·32g (0·04 mol) *o*-cresol was placed in a 100 ml flask fitted with reflux condenser. A 1N methanolic HCl soln (20 ml) was added with stirring and refluxed for 14 hr. MeOH was removed *in vacuo* yielding a tan sticky solid which was dissolved in 100 ml H_2O and 200 ml EtOAc. The EtOAc phase was extracted with 2 × 100 ml 10% NaOH soln, dried over Na_2SO_4, and evaporated *in vacuo* to yellow oil (0·2 g); NMR: no aromatic protons.

The alkaline extracts were acidified and extracted with 2 × 100 ml EtOAc. Evaporation of solvent yielded 3 g of white solid which crystallized from the residual red oil. Recrystallization from MeOH–H_2O afforded 2·8 g (65%, m.p. 148–150°) of either 1-(3′-methyl-4′-hydroxybenzyl)-2-naphthol or 1-(3′-methyl-2′-hydroxybenzyl)-2-naphthol; NMR(τ) CD_3CN: 1·8–3·2(m), 5·48(s), 7·73(s); ratio: 11:2:3; IR(μ) KBr: 2·98(strong); UV(mμ) $\lambda_{max}(\varepsilon)$ MeOH: 335 (2400), 327 (2200); + NaOH: 355 (2400), 343 (2300); MS: mol. wt. 264 (95%), P-*o*-cresyl = 157 (100%). (Found: C, 81·57; H, 6·11. $C_{18}H_{16}O_2$ requires: C, 81·79; H, 6·10%).

The diphenol was resistant to hydrogenation over Pd. It formed a diacetate with Ac_2O and py; m.p. 85–87° (recrystallized from n-hexane); NMR(τ) CCl_4: 2·2–3·2(m), 5·77(s), 7·94(s), 8·01(s); ratio: 9:2:6:3; IR(μ) CCl_4: 5·68 μ; UV(mμ) $\lambda_{max}(\varepsilon)$ MeOH: 288 (8700), 279 (8300). (Found: C, 75·54; H, 5·62. $C_{22}H_{20}O_4$ requires: C, 75·83; H, 5·79%).

The other phenolic products contained in the red oil were separated on three 40 × 20 cm PLC plates developed in 1:1 C_6H_6: $CHCl_3$. The thin fast-moving band yielded 40 mg (2%) of 2-thiomethoxymethyl-6-methylphenol.[1] The slower broad band contained *o*-cresol and 4-thiomethoxymethyl-2-methylphenol. This mixture (0·15 g) was rechromatographed on a 40 cm plate with 4:1 C_6H_6: $CHCl_3$. The slower band yielded 30 mg (1·5% yield) of 2-methyl-4-thiomethoxymethylphenol (identical to an authentic sample, *vide infra*).

Cross-over experiment B. A soln of 5·0 g (0·019 mol) 1,1-di-thiomethoxymethyl-3,4-dehydro-2-tetralone[1] and 4·3 g (0·04 mol) *o*-cresol in 8 ml $ClCH_2CH_2Cl$ was treated with 1 ml TFA. The mixture was refluxed until no starting dienone remained (3 hr, followed by TLC). After workup of the phenolic fraction 3·1 g of the diphenol and 4·5 g of oil were obtained. 20% of this oil was chromatographed on a 20 × 40 cm plate developed in C_6H_6. Five phenols were isolated (total yields): 0·22 g (7%) 2-methyl-6-thiomethoxymethylphenol, 1·2 g (30%) *o*-cresol, 0·5 g (16%) 2-methyl-4-thiomethoxymethylphenol, 0·8 g (20%) 1-thiomethoxymethyl-2-naphthol[1], and 1·0 g (total of 4·1 g, 80%) diphenol.

The base-washed neutral fraction was concentrated to 0·72 g of yellow oil whose NMR indicated 80% was $CH_2(SMe)_2$ (25% of starting material); NMR(τ) CCl_4: 7·95(s), 6·46(s); ratio: 6:2. The NMR peaks increased in intensity on addition of authentic material and no new peaks appeared.

Reaction of 1-*thiomethoxymethyl*-2-*naphthol with* o-*cresol.* A soln of 0·6 g (2·9 mmol) 1-thiomethoxymethyl-2-naphthol[1] and 0·95 g (8·8 mmol) *o*-cresol in 15 ml CH_2ClCH_2Cl was treated with 0·1 ml TFA and the mixture refluxed overnight. The solvent was removed *in vacuo* and the residue dissolved in EtOAc. The diphenol, 0·35 g (50%, m.p. 148–150°), was isolated after precipitation with n-hexane.

Dimethylethoxysulfonium fluoroborate. A soln of 57 g (0·3 mol) $Et_3O^+BF_4^-$ in 120 ml CH_2Cl_2 was reacted with DMSO (23 ml, 0·33 mol) giving a nearly quantitative yield of product (m.p. 39–42°, very hygroscopic). Purification could be accomplished by dissolving the salt in the minimum amount of CH_2Cl_2 and reprecipitating it with anhyd. ether. The salt could be stored for about 2 weeks under anhyd.

ether in the refrigerator; NMR(τ) CD_3CN: 5·63(q), 6·77(s), 8·62(t); ratio: 2:6::3; CD_3OD: 5·87(q), 6·98(s), 8·86(t); ratio: 2:6:3.

Reaction of o-cresol with dimethylethoxysulfonium fluoroborate. Freshly prepared dimethylethoxysulfonium floroborate (17·6 g, 0·09 mol) was dissolved in CH_2Cl_2 (50 ml). *o*-Cresol (2·16 g, 0·02 mol) was added with stirring, then a 10 ml CH_2Cl_2 soln containing 2·8 ml (0·02 mol) Et_3N was slowly dripped into the flask (exothermic), stirring for 6 hr. The mixture was washed with 3 × 50 ml H_2O, 1 × 30 ml dil HCl, 1 × 50 ml H_2O, and finally 2 × 25 m. 1N NaOH soln. The pre-cooled alkaline extracts were acidified with conc HCl and extracted with 2 × 100 ml of ether. Evaporation of ether yielded 0·8 g of yellow oil distributed between two 20 × 20 cm PLC plates developed in C_6H_6. The fastest moving phenol (R_f=0·45, C_6H_6) was 2-thiomethoxymethyl-6-methylphenol[1] (60 mg, 2% yield). From the second band (R_f=0·3), 0·4 g of *o*-cresol was obtained. The slowest band (R_f=0·15) was isolated as an oil and shown to be 2-methyl-4-thiomethoxymethylphenol (120 mg, 4% yield); by Raney Ni desulfurization to 2,4-dimethylphenol and by the following data: NMR(τ) CCl_4: 2·93–3·45(m), 4·06(s), 6·46(s), 7·83(s), 8·10(s); ratio: 3:1:2:3:3; IR(μ) CCl_4: 2·83 (sharp), 3·0 (broad). (Found: C, 64·12; H, 7·20. $C_9H_{12}OS$ requires: C, 64·24; H, 7·19%).

Reaction of 1,3-dimethoxybenzene with dimethylethoxysulfonium fluoroborate. A soln of 21·4 g (0·114 mol) dimethylethoxysulfonium BF_4^- and 4·0 g (0·029 mol) 1,3-dimethoxybenzene in 50 ml CH_2Cl_2 was reacted with 16 ml (0·114 mol) Et_3N. After 4 hr the mixture was washed with 3 × 50 ml 5% HCl, and 1 × 50 ml H_2O. The organic layer was dried over Na_2SO_4 and concentrated *in vacuo* yielding 3 g of yellow oil which was chromatographed on a 1 meter plate with 1:1 C_6H_6: cyclohexane. The band containing the starting material (R_f=0·6) was followed closely by a band containing 0·6 g (12%) 2,4-dimethoxythiomethoxymethylbenzene; final isolation by microdistillation: bath temp 140° at 0·4 mm; NMR(τ) CCl_4: 2·76–3·78(m), 6·28(s), 6·32(s), 6·46(s), 8·09(s); ratio: 3:3:3:2:3; MS: mol. wt. 198 (20%), P-SCH_3 (100%), P-77 (42%). (Found: C, 61·00; H, 7·00. $C_{10}H_{14}O_2S$ requires: C, 60·56; H, 7·13%).

Reaction of o-cresol with DCC—DMSO: *modified procedure.* The reaction reported in the preceding paper[1] was repeated (double scale) as described except that the pyridinium trifluoroacetate was not added at once, but slowly over several min. Two effects of this change were directly noticeable. First, the exothermic reaction was mitigated and the temp. stayed close to 0° and, second, DCU slowly precipitated out during the addition. The crude phenolic fraction which contained *o*-cresol and its *o'* and *p*-thiomethoxymethyl derivatives could be separated directly by PLC as described in an earlier experiment or by initial small scale distillation followed by PLC of the distillate fractions (each fraction on a different PLC plate but all plates developed simultaneously in the same tank). The latter procedure was more convenient because the distillation sequence was *o*-cresol (A) lower b.p. than *o'*-substituted derivative (B) below the *p*-substituted derivative (C) while the R_f's were in the order B>A>C. The important *p*-substituted product was concentrated in the highest boiling fraction along with the compound whose R_f was most different; isolated yields: *o'*-thiomethoxymethyl-*o*-cresol 13·7 g (41%), *p*-thiomethoxymethyl-*o*-cresol 0·72 g (2%).

Reaction of 2-hydroxy-3-methylbenzyl methyl sulfoxide with DCC. The title sulfoxide was prepared by treating 1·7 g (0·01 mol) 2-methyl-6-thiomethoxymethylphenol[1] with 1 ml 30% H_2O_2 in 13 ml HOAc at 0° until TLC indicated all starting material was gone and replaced by a slower moving spot (30 min). All volatile materials were removed at high vacuum at room temp. to give an oil; NMR(τ) $CDCl_3$: aryl 2·84–3·42(m), CH_2 5·73 and 6·18 (AB quartet, J = 14 cps), CH_3 7·61, CH_3 7·77; ratio: 3:1:1:3:3. The crude sulfoxide (1·5 g, 0·08 mol) was combined with DCC (5·1 g, 0·025 mol) in 30 ml C_6H_6 and 0·4 g (0·04 mol) anhyd. H_3PO_4 added. The mixture was stirred overnight at room temp. Anhyd. ether was added to ppt. all DCU, which was filtered, washed with ether and discarded. The C_6H_6-ether filtrate was washed with 1 × 50 ml H_2O and 1 × 30 ml 5% NaOH soln, dried over Na_2SO_4 and evaporated to yield 0·6 g of oil, chromatographed on a 40 × 20 cm plate in C_6H_6. Several very thin bands were observed along with a much larger and faster moving band (R_f=0·73) gave 0·27 g (20%) 8-methyl-1,3-benzoxathian, pale yellow oil; NMR(τ) CCl_4: 2·97–3·37(m), 4·82(s), 6·23(s), 7·85(s); ratio: 3:2:2:3. (Found: C, 64·98; H, 6·25. $C_9H_{10}OS$ requires: C, 65·02; H, 6·07%).

Reaction of 2-methyl-6-thiomethoxymethylphenol with DCC *and* DMSO *or* DMSO-d_6. A mixture of 0·76 g (4·5 mmol) of the title phenol, 2·06 g (10 mmol) DCC, 5 ml DMSO, 10 ml C_6H_6, and 0·3 g (3 mmol) of 100% H_3PO_4 was reacted and worked up by the standard procedure. The neutral fraction, yellow oil (0·74 g), was divided between two 20 × 20 cm plates, developed in C_6H_6. The fastest moving band yielded 0·054 g (7%) of 8-methylbenzo-1,3-oxathian.

The reaction was repeated (same scale) with DMSO-d_6 (99·5% minimum isotopic purity) replacing the

DMSO. After chromatography 0·085 g (10%) of completely undeuterated 8-methylbenzo-1,3-oxathian (NMR and MS analysis) was isolated.

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