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Reactions of organic sulfoxides

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REACTIONS OF ORGANIC SULFOXIDES

by

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INTRODUCTION

The ready availability of dimethyl sulfoxide in recent years has led to extensive research programs concerned with the utilization of the remarkable physical and chemical properties of not only dimethyl sulfoxide but sulfoxides in general. As a dipolar aprotic solvent it has found ever increasing use particularly as medium for the generation of carbanions under relatively mild conditions. Sulfoxides are also extremely useful reagents capable of undergoing oxidation, reduction, or rearrangement, as well as carbanion formation at the alpha position. This study was undertaken in hopes of expanding the synthetic utility of the known condensation of sulfoxides with esters to give a class of compounds known as β-keto sulfoxides.

LITERATURE SURVEY

Sulfoxides can be prepared in a variety of ways; these methods have been reviewed in several places (1-3). The properties of sulfoxides, dimethyl sulfoxide in particular, as solvents and reactants have also been extensively reviewed (3-7).

The methylsulfinylcarbanion has been generated in low equilibrium concentrations by alkali metal alkoxides (8-11). This

$$CH_3SOCH_3 + \underline{t}\text{-BuOK} \rightleftharpoons CH_3SOCH_2K + \underline{t}\text{-BuOH}$$

equilibrium has been measured to be 3.3×10^{-5} at 25° in pure dimethyl sulfoxide (12). In dilute solutions this allows approximately equal concentrations of t-butoxide and methylsulfinylcarbanion. The equilibrium is rapidly established as shown by the rapid formation of adducts with carbonyl groups (13,14).

The methylsulfinylcarbanion has also been formed in an irreversible fashion by using sodium hydride, sodium amide, lithium hydride, and butyllithium as the base (8,15,16).

$$CH_3SOCH_3 + NaH \rightarrow CH_3SOCH_2Na + H_2$$

The extremely reactive species formed in this manner has been named "dimsylsodium" (17). Recently there has been a tendency to speak of the "dimsyl" anion regardless of the method of formation. This is not a particularly sound practice because of the wide range of basicity, H^-, available in different systems of base and dimethyl sulfoxide. For example, the basicity dimethyl sulfoxide-methanol-sodium methoxide has been shown to vary from 12 to 19 as the solvent goes from pure methanol to 95% dimethyl sulfoxide (18). Further reduction of the alcohol content to

0.02% raises the basicity to 27 (19). "Dimsylsodium" itself has a basicity of 31 to 33 (17).

Preparation from sodium hydride requires heating the suspension at 70-75°, but care should be taken since extensive decomposition takes place above 80° (14). Several reports of explosive decomposition have been made (20,21). These explosions occurred in reactions involving several moles of sodium hydride. However, reactions involving two moles of methylsulfinyl carbanion have been carried out routinely in these laboratories without incident.

Recently the methylsulfinyl carbanion has been prepared from sodium hydride and dimethyl sulfoxide by subjecting the suspension to ultrasonic radiation instead of heat (22). Solutions prepared in this manner are clear and exhibit very little decomposition. If mineral oil is layered on top, the solution may be frozen and stored at least two months. Aliquots may be taken by hypodermic or pipette simply by thawing the solution and then refreezing the remainder.

The methylsulfinylcarbanion forms adducts with ketones (9,13,14,23,24), aldehydes (13,16,25), olefins (23,24,26,27), alkynes (28), benzyne (13,16), epoxides (29,30), and esters (10,15,16). Certain aromatic compounds have been methylated by attack of the methylsulfinylcarbanion followed by base catalyzed elimination of methylsulfinic acid (27,31).

Beta-keto sulfoxides were not prepared until 1963, although the analogous beta-keto sulfides and beta-keto sulfones had been known for twenty years (32-34). The direct oxidation of β-keto sulfides to sulfoxides has not been accomplished. This is probably best accounted for by the difficulty of stopping the oxidation at an intermediate stage and the

tendency of the sulfoxides to undergo the Pummerer rearrangement in the generally acid oxidation media (10,35). The intermediacy of β-keto sulfoxides has been postulated in the air oxidation of mixtures of thiols and phenylacetylene, (35). Similar oxidations of olefins with thiols give rise to β-hydroxy sulfoxides (36,37).

$$PhC{\equiv}CH + RSH + O_2 \rightarrow PhC(OOH)=CHSR \rightarrow (PhCOCH_2SOR) \rightarrow PhCOCH(OH)SR$$

The first β-keto sulfoxide isolated ω-(methylsulfinyl)-p-methoxyacetophenone, was prepared by oxidation with active manganese dioxide of the β-hydroxy sulfoxide formed by addition of the methylsulfinylcarbanion to anisaldehyde (23). A more convenient preparation was found to be the alkoxide catalyzed condensation of dimethyl sulfoxide with aromatic esters (10). This reaction was later extended to aliphatic esters by using dimsylsodium (15,16). The analogous β-keto sulfones can be prepared by adding dimethyl sulfone to the reaction mixture (8).

In the course of this study a series of disulfoxides and disulfones were prepared. It was desirable to reductively desulfurize these compounds.

Generally sulfones are quite resistant to reduction. Two thiophene-1, 1-dioxides have been reduced to the sulfides by zinc in hydrochloric and acetic acid mixtures (38,39). Lithium aluminum hydride has in some cases reduced sulfones to sulfides (39) and alpha-disulfones to disulfides and mercaptans (40). Reductions with cleavage of sulfur has been accomplished in a few cases. Aryl or aryl-alkyl sulfones produce hydrocarbons and sulfinic acids when treated with sodium amalgam (41).

$$ArSO_2R + NaHg \rightarrow ArSO_2H + RH$$

Complete reduction to hydrocarbon for both alkyl and aryl sulfones may be effected by high temperatures and pressure hydrogenation using a molybdenum sulfide catalyst (42). Beta-keto sulfones have been desulfurized

$$RSO_2R \xrightarrow[375^{\circ}\ 100\ ATM\ H_2]{Mo_2S_3} 2RH$$

by aluminum amalgam (15,16).

$$RCOCH_2SO_2CH_3 + Al(Hg) \rightarrow RCOCH_3$$

A number of aryl sulfones have been reduced to hydrocarbons by Raney nickel (43).

Sulfoxides are much more readily reduced than sulfones. Sulfoxides may be reduced to sulfides by zinc in acetic acid (3,15). However, in certain activated molecules, such as β-keto sulfoxides, the C-S bond is cleaved by this reagent (44). This same cleavage can also be accomplished by using aluminum amalgam (15,16). Lithium aluminum hydride has been used to reduce sulfoxides to sulfides without cleavage of the C-S bond (39,45). However, the milder sodium borohydride in aqueous solution does not affect the sulfoxide moiety (46). Certain thianthrone sulfoxides have recently been reported to be reduced to sulfides by sodium borohydride (47). Diborane, which can be generated from sodium borohydride and boron trifluoride, reacts with dimethyl sulfoxide to yield sulfide (48,49). Although relatively few cases have been reported, sulfoxides can be reduced with cleavage of the C-S bond by Raney nickel (40). An active nickel catalyst prepared <u>in situ</u> by reaction of nickel chloride with sodium borohydride in ethanol has been used to reduce sulfoxides to hydrocarbons

(50). The fact that the catalyst is not pyrophoric and the time saved because prior preparation of the catalyst is not necessary are advantages which more than offset the slightly poorer yields.

RESULTS AND DISCUSSION

The methylsulfinylcarbanion ($CH_3SOCH_2^-$), formed in dimethyl sulfoxide solutions of strong bases, has been shown to react with esters to give good yields of β-keto sulfoxides (8,10,15,16). An analogous reaction of the methylsulfonylcarbanion ($CH_3SO_2CH_2^-$) yields the β-keto sulfones (8).

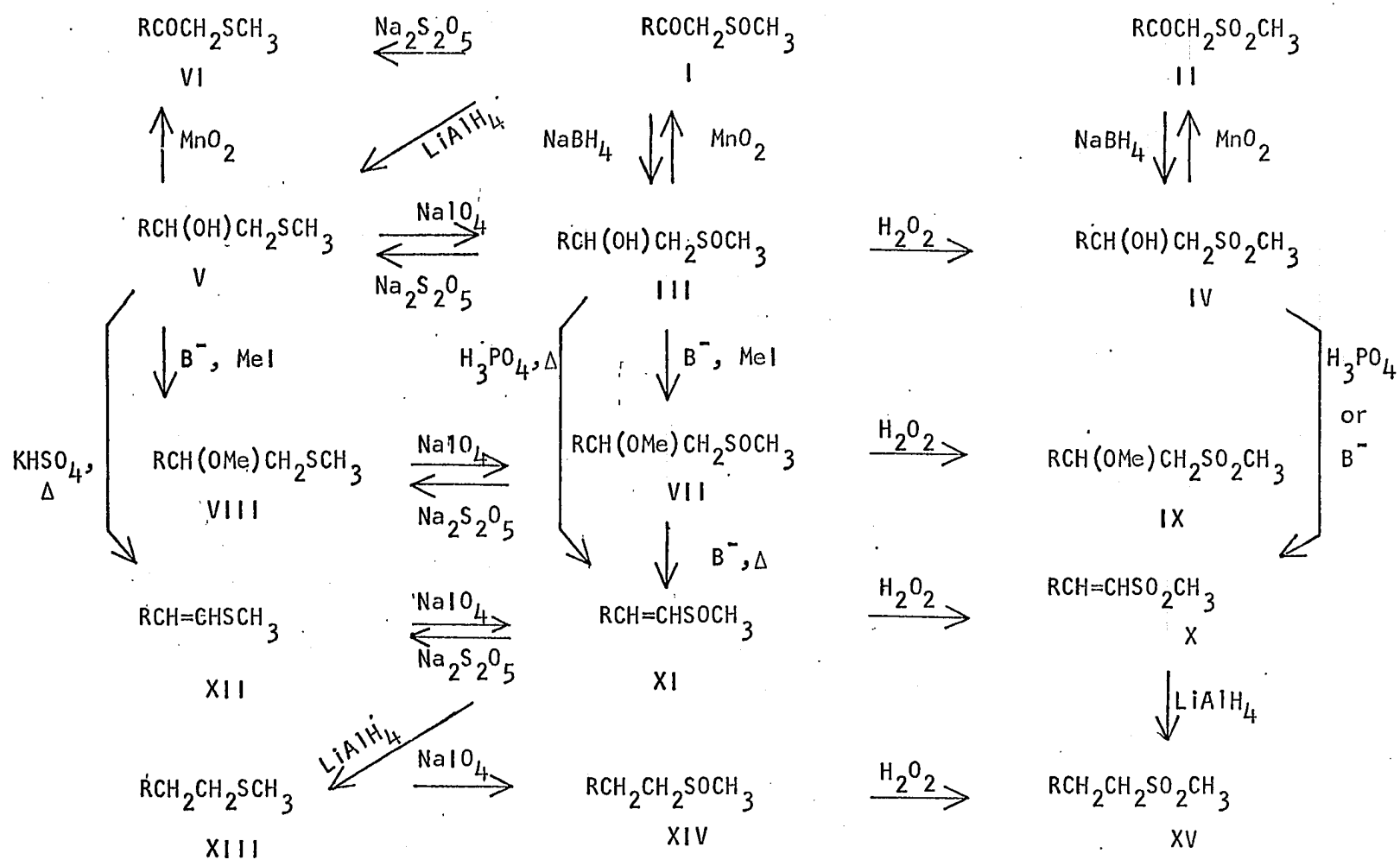
$$CH_3SOCH_2^- + RCOOR' \rightarrow [RCOCHSOCH_3]^- \rightarrow RCOCH_2SOCH_3$$

β-Keto sulfoxides can be converted to a variety of products with or without the sulfur moiety. Some of the major reactions investigated which lead to sulfur containing products are summarized in Figure 1.

β-Keto sulfoxides cannot be converted directly to β-keto sulfones since the conventional reagent (acidic hydrogen peroxide) causes β-keto sulfoxides to undergo the Pummerer rearrangement to yield α-keto hemimercaptals.

$$RCOCH_2SOCH_3 \xrightarrow{H+} RCOCH(OH)SCH_3$$

β-Hydroxy sulfoxides (IIIa, IIIb) and β-hydroxy sulfones (IVa) are readily prepared by the reduction of the β-keto sulfoxides (Ia, Ib) or β-keto sulfones (IIa) with sodium borohydride in cold aqueous methanol. The reverse reactions are readily achieved by the use of active manganese dioxide. The sulfoxide group of β-hydroxy sulfoxides is not as labile with respect to the Pummerer rearrangement as in the β-keto sulfoxide; consequently, oxidation by acidic hydrogen peroxide to β-hydroxy sulfones is possible. β-Hydroxy sulfoxides and sulfones have been prepared previously by the addition of the methylsulfinylcarbanion (13,14,25) or the methylsulfonylcarbanion (34) or the corresponding Grignard reagents



a, R = phenyl; b, R = cyclohexyl

Figure 1. Reactions of β-keto sulfoxides

(33,51) to aldehydes and ketones, and by the autoxidation of mixtures of certain olefins and mercaptans (36,37).

The selective reduction of a sulfoxide to a sulfide in the presence of other functionality had been reported for the case methionine-S-oxide (52). The reducing agent employed was aqueous sodium metabisulfite ($Na_2S_2O_5$) at room temperature for several days. Under these conditions β-keto sulfoxide (Ia) remained unchanged for up to ten days. However, increasing the temperature to approximately 90° for 24 hours produced the β-keto sulfide (VIa) in 50-55% yield. The increase in acidity as the reaction proceeds causes a competing reaction path-Pummerer rearrangement, loss of methyl mercaptan to form phenylglyoxal, and formation of the water soluble bisulfite addition product. In other sulfoxides where rearrangement is not facile excellent yields of sulfide are obtained (see experimental). When the reduction was attempted using sodium bisulfite instead of sodium metabisulfite only unreacted keto sulfoxide and the bisulfite adduct of phenylglyoxal were obtained.

Simultaneous reduction of both the ketone and the sulfoxide to give the β-hydroxy sulfide (Va, Vb) can be achieved by refluxing with lithium aluminum hydride in tetrahydrofuran. Compound Va can be oxidized to the β-hydroxy sulfoxide (IIIa) with sodium metaperiodate or to the β-hydroxy sulfone (IVa) with acidic hydrogen peroxide or to the β-keto sulfide (VIa) with active manganese dioxide. β-Keto sulfides can of course be easily prepared by the reaction of the mercaptide anion with phenacyl halides.

β-Hydroxy sulfoxides IIIa and IIIb upon treatment with sodium hydride in tetrahydrofuran react to form white solids which upon treatment with

methyl iodide yield the corresponding β-methoxy sulfoxides (VIIa, VIIb). Similar treatment of the β-hydroxy sulfide Va yields the β-methoxy sulfide (VIIIa). However, treatment of the β-hydroxy sulfone IVa with sodium hydride failed to form a salt; and treatment of the reaction mixture with either water or methyl iodide before product isolation had no effect upon the product isolated, which was ω-(methylsulfonyl)-styrene (Xa). Apparently the equilibrium between the alkoxide anion and the carbanion is such that elimination is greatly preferred for the β-hydroxy sulfone ($R = C_6H_5$).

$$RCH(O^-)CH_2SOCH_3 \rightleftharpoons [RCH(OH)CHSOCH_3]^-$$

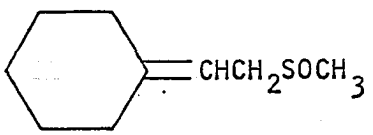
$$RCH(O^-)CH_2SO_2CH_3 \rightleftharpoons [RCH(OH)CHSO_2CH_3]^- \rightarrow RCH{=}CHSO_2CH_3 + {}^-OH$$

Treatment of the β-hydroxy sulfone, IVa, or β-hydroxy sulfoxide, IIIa, with phosphoric acid resulted in the formation of the unsaturated sulfone (Xa) and unsaturated sulfoxide (XIa) respectively. Apparently only a single isomer (trans) was formed. The olefinic hydrogens had coupling constants of $|J_{AB}| \pm 15.6$ c.p.s. in both cases. Distillation of the β-hydroxy sulfide, Va, from potassium bisulfate yielded the unsaturated sulfide (XIIa) as a mixture of trans (predominant), $|J_{AB}| \pm 15.8$ c.p.s., and cis (minor), $|J_{AB}| = 11$ c.p.s., isomers. The sodium metabisulfite reduction of the trans unsaturated sulfoxide, XIa, gave pure trans sulfide (XIIa). The unsaturated sulfide is readily oxidized to the sulfoxide (XIa) or sulfone (Xa).

Attempts to prepare a β-methoxy sulfone (IXa) by oxidation of VIIa with acidic hydrogen peroxide gave rise to mixtures of IXa and Xa which could not be separated. Evidently IXa is very sensitive to the elimination

of methanol under either acidic or basic conditions.

Treatment of VIIa with sodium hydride followed by heating in tetrahydrofuran solution gives rise to ω-methylsulfinylstyrene (XIa). Treatment of VIIb under identical conditions yielded the β,γ-unsaturated sulfoxide ω-(methylsulfinylmethyl) methylenecyclohexane (XIb').



XIb'

This result is in accord with the reports that basic solutions of unsaturated sulfoxides equilibrate to give predominantly the β,γ-isomers (53-55).

Reduction of the unsaturated sulfoxide XIa with lithium aluminum hydride gave the saturated sulfide (XIIIa) which could be oxidized to ω-(methylsulfinyl) ehtylbenzene (XIVa) or ω-(methylsulfinyl) ethylbenzene (XVa). The latter compound can also be prepared by the lithium aluminum hydride reduction of the unsaturated sulfone (Xa).

Since sulfoxides with beta hydrogens have been shown to readily undergo pyrolysis to yield olefins (56), pyrolysis of the β-hydroxy and β-methoxy sulfoxides seemed to be a very plausible route to ketones and enol-ethers respectively. Pyrolysis of IIIa and IIIb yielded acetophenone and acetylcyclohexane respectively. The same ketones can be obtained from the corresponding β-hydroxy sulfides Va and Vb by heating in the presence of a trace of dicumyl peroxide, presumably via the following reaction sequence.

$$\text{Dicumyl peroxide} \xrightarrow{\Delta} C^{\cdot}$$

$$C^{\cdot} + RCH(OH)CH_2SCH_3 \longrightarrow CH + R\dot{C}(OH)CH_2SCH_3$$

$$R\dot{C}(OH)CH_2SCH_3 \longrightarrow RC(OH)=CH_2 + CH_3S^{\cdot}$$

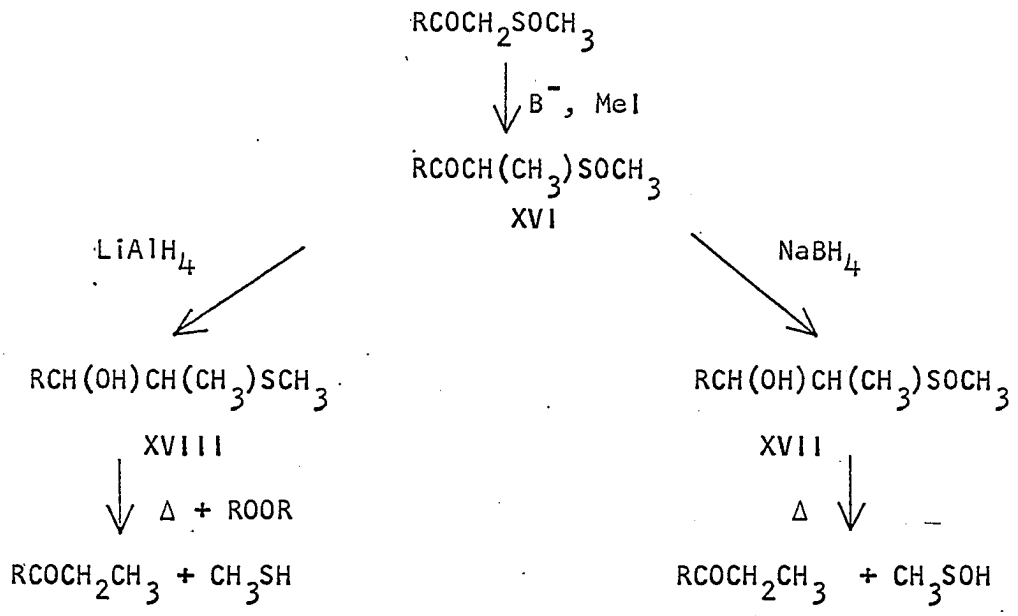
$$CH_3S^{\cdot} + RCH(OH)CH_2SCH_3 \longrightarrow CH_3SH + R\dot{C}(OH)CH_2SCH_3$$

Pyrolysis of VIIa, however, did not yield the desired enolether. The main product was acetophenone; presumably the methanesulfinic acid formed in the reaction catalizes the decomposition of any enol-ether present.

$$RCH(OMe)CH_2SOCH_3 \xrightarrow{\Delta} RC(OMe)=CH_2 + CH_3SOH \longrightarrow RCOCH_3$$

Compound VIIIa failed to react with dicumyl peroxide under the conditions employed.

The synthetic utility of β-keto sulfoxides is significantly enhanced by the fact that the methylene group alpha to both the carbonyl and the sulfoxide functions can be alkylated in high yield (46,57). Formation of propiophenone in 67% yield from XVIII has been achieved. Considerably lower yields of propiophenone (approximately 30%) have been observed in the pyrolysis of XVIIa. The conversion of XVIIb and XVIIIb to ketones has not yet been achieved by these routes.



a, R = C_6H_5, b, R = C_6H_{11}

The synthesis of enol-ethers has been accomplished by a different route. Treatment of β-methoxy sulfides with potassium t-butoxide in dimethyl sulfoxide in a nitrogen atmosphere produces mixtures of enol-ethers and unsaturated sulfides. Table I summarizes the data for a number of compounds of this type. Compounds in which $R_4 = C_6H_5$ were prepared from the reaction of thiophenol with phenacyl chloride followed by C-methylation, sodium borohydride reduction, and O-methylation. Although with one exception the final step yields are roughly comparable for both $R_4 = CH_3$, C_6H_5, the latter series is preferable because all steps in the latter series are equal or better yields, cleaner reactions, and much shorter reaction times. The one exception, 2-phenyl-2-methoxy-t-butyl methylsulfide (XXa), has proven to be very difficult to obtain in a pure state. The dimethylation of the β-ketosulfoxide is not clean. There is evidence that after monoalkylation a significant amount of O-methylation

Table 1. Preparation of enol ethers by base catalyzed elimination of β-methoxy sulfides

$$R_1CH(OMe)CR_2R_3SR_4 \xrightarrow{B^-} R_1CH(OMe)=CR_2R_3 + R_1CH=CR_2SR_4$$

β-Methoxy Sulfide				Percent Yield	
R_1	R_2	R_3	R_4	Enol-Ether	Unsaturated sulfide
C_6H_5	H	H	CH_3	56	16
"	CH_3	H	CH_3	43	Nil
"	CH_3	CH_3	CH_3	?	?
"	H	H	C_6H_5	49	15
"	CH_3	H	C_6H_5	64	Nil
"	CH_3	CH_3	C_6H_5	82	Nil

is taking place. The distillation of (XXa) has proved ineffectual. Attempted column chromatography on alumina led to complete decomposition. Therefore, the material subjected to the reaction was not completely pure. No enol-ether was detected (no analogous ketone either). The enol-ethers are extremely sensitive to acid and hydrolyze readily to their respective ketones.

β-Hydroxy sulfoxides or vinyl sulfoxides can be converted to the acetylenic sulfides. Treatment of IIIa with thionyl chloride yields a chlorostyrenyl sulfide (from nmr) which can be dehydrohalogenated with alcoholic potassium hydroxide to yield methyl phenethynyl sulfide (XXVII) in a 63% overall yield. Evidence for the proposed reaction scheme is furnished by

the observation that XIa reacts with thionyl chloride to give the methyl chlorostyrenyl sulfide in high yield.

$$\text{IIIa} + SOCl_2 \rightarrow C_6H_5CH(Cl)CH_2SOCH_3 \rightarrow C_6H_5CH{=}CHSOCH_3$$

$$\xrightarrow{SOCl_2} C_6H_5C(Cl){=}CHSCH_3 \xrightarrow[C_2H_5OH]{KOH} \underset{\text{XXVII}}{C_6H_5{\equiv}CSCH_3}$$

The intermediate methyl chlorostyreyl sulfide could not be obtained in a highly purified state. Four isomeric structures are possible (cis, trans, α-chloro, β-chloro) and in some samples four methyl singlets could be detected by n.m.r. although one singlet greatly predominated (2.41 p.p.m.). However, all samples gave only a single sharp vinyl resonance at 6.57 p.p.m. The predominant structure of the methyl chlorostyrenyl sulfide was proven as α-chloro-β-methylmercaptostyrene by the observation that β-phenyl-β-deuterioxy-α, α-dideuterioethyl methyl sulfoxide ($C_6H_5CH(OD)CD_2SOCH_3$) reacted with thionyl chloride to give a methyl chlorostyrenyl sulfide without any absorption by a vinyl proton in n.m.r.

$$C_6H_5CH(OD)CD_2SOCH_3 + SOCl_2 \rightarrow C_6H_5C(Cl){=}CDSCH_3$$

$$+ SO_2 + 2DCl + HCl$$

Treatment of β-deuterio-β-methylsulfinylstyrene with thionyl chloride yielded a methyl chlorostyrenyl sulfide with 0.2 of a vinyl hydrogen atom absorbing at 6.57 p.p.m. Apparently, the major reaction is to yield the α-chloro-β-deuterio-β-methylmercaptostyrene.

$$C_6H_5CH{=}CDSOCH_3 + SOCl_2 \rightarrow C_6H_5C(Cl){=}CDSCH_3 + SO_2 + HCl$$

However, the hydrogen chloride formed partially exchanges with the deuterium atom in β-deuterio-β-methylsulfinylstyrene. Such exchange is not experimentally observed starting from

$$C_6H_5CH{=}CDSOCH_3 + HCl \rightarrow C_6H_5CH{=}CHSOCH_3 + DCl$$

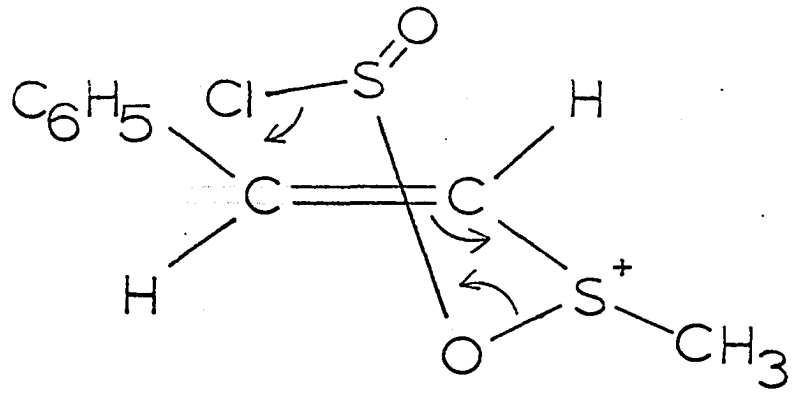
the α,α-dideuterio-β-deuterioxy sulfoxide because the reaction with thionyl chloride produces two moles of deuterium chloride to one mole of hydrogen chloride. The reaction of thionyl chloride with β-methylsulfinylstyrene gave only tars in pyridine solution.

From the above observations it is obvious that transition state A is preferred to B or C in the reaction of thionyl chloride with the unsaturated sulfoxide. The preferance of A over B or C may be due to steric effects in the non-planar transition state or due to the stability of the reaction products

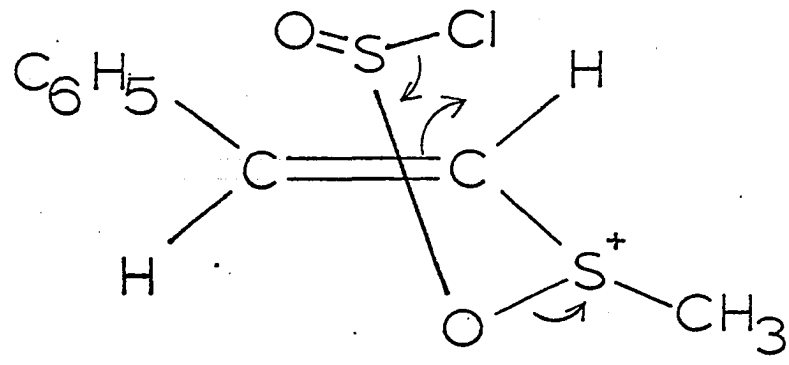
$$A \rightarrow C_6H_5CH(Cl){=}\overset{+}{S}CH_3$$

$$B \text{ or } C \rightarrow C_6H_5\overset{+}{C}HCH(Cl)SCH_3$$

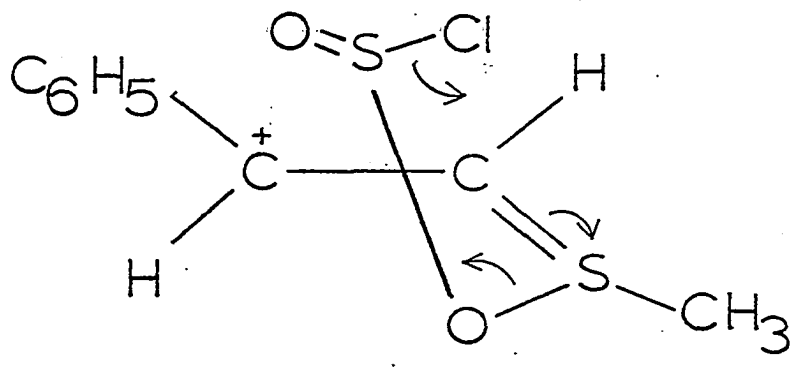
In a similar manner it seemed logical that β-methylsulfinylstyrene (XIa) would rearrange to an enol-acetate (XXXVIIIa) if transition state A^1 (transition states A^1, B^1, and C^1 are analogous to transition states A, B, and C in Figure 2, substituting an acetyl group for the chlorosulfinyl group) were preferred; if transition states B^1 or C^1 were preferred, a different enol-acetate (XXIXa) would be formed. Hydrolysis of XXVIIa would yield -methylmercapto)acetophenone (VIa). Hydrolysis of XXIXa would give the methyl thioester of phenylacetic acid (XXXa). However, the actual product found upon refluxing XIa in acetic anhydride, neutralization with sodium bicarbonate, and extraction with chloroform was acetoxymethyl β-styrl



A



B



C

Figure 2. Transition states for the reaction of thionyl chloride with ω-methylsulfinylstyrene

sulfide (XXXIa). Evidently the intermediate acetoxy sulfonium salt is not as readily attacked by the double bond as is the chlorosulfinyl sulfonium salt. In this case, therefore, a normal Pummerer rearrangement is obtained, directed to the alpha carbon bearing the most acidic hydrogen, i, e. the carbon best able to support a partial negative charge as required for the favored mechanism of the Pummerer rearrangement (58,59).

Treatment of XXXIa with mineral acid causes a disproportionation to formaldehyde and the β-styryl mercaptal of formaldehyde (XXXIIa). This reaction has previously been noted for simple hemimercaptals of formaldehyde (60). The attempted sodium borohydride reduction of XXXIa in aqueous alcohol gave no apparent reaction. Lithium aluminum hydride reduction in tetrahydrofuran gave a small amount of a multicomponent oil with an extremely sickening stench, possible due to β-styryl mercaptan or its tautomeric thioaldehyde. Attempts to isolate this mercaptan as its copper or mercury mercaptide failed.

In view of the facile alkylation of the methylene of β-keto sulfoxides, acylation also seemed to be a promising extension. Acylation would give β, β-diketo sulfoxides (XXXII) which should hydrolyze to give triketones (XXXIII) or their hydrates.

$$\underset{\text{I}}{RCOCH_2SOCH_3} \xrightarrow{B^-(R'CO)_2O} \underset{\text{XXXII}}{RCOCH(COR')SOCH_3} \xrightarrow{H^+} \underset{\text{XXXIII}}{RCOCOCOR'}$$

$$\text{I} \xrightarrow{B^-,(R'CO)_2O} \underset{\text{XXXIV}}{RCOCH(OR')SCH_3}$$

However, acylation attempts using sodium hydride and acid anhydrides

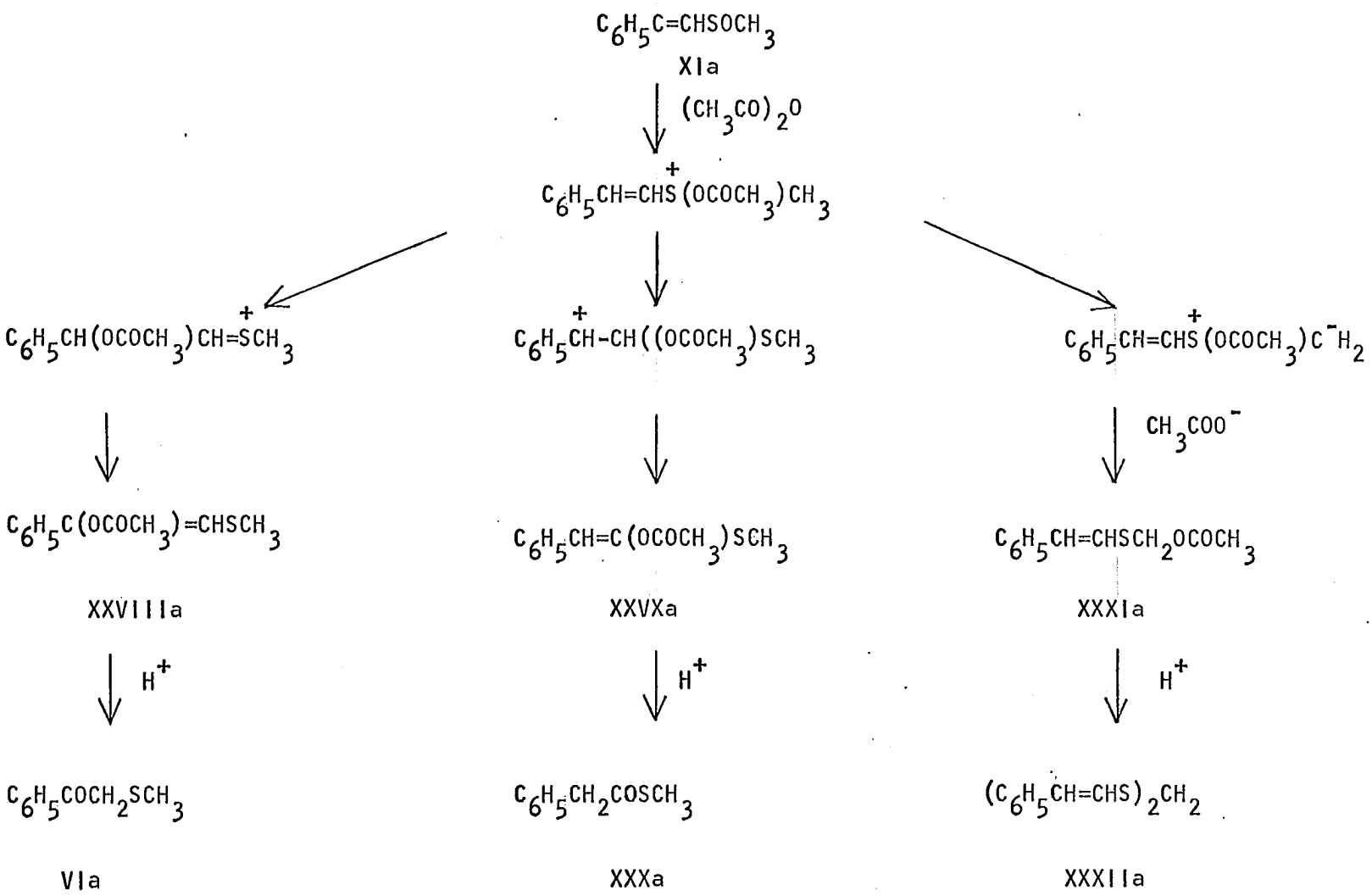


Figure 3. The possible reactions of acetic anhydride with ω-methylsulfinylstyrene.

produced only Pummerer rearrangement products - α-acyloxy sulfides (XXXIV). When the reaction was tried using previously monoalkylated β-keto sulfoxide (XVIa), only o-acylation was detected. Possibly, the additional alkyl substituent gives some added stabilization to the double bond of the enolate anion and causes the equilibrium between the carbanion and the enolate anion to shift in favor of the latter. (A similar effect is noted in dialkylation. See experimental section.) It was not possible to purify the o-acylated product due to instability with respect to distillation or chromatography. Their existence is justified only by n.m.r. and infrared spectroscopy.

Acylation of the β-keto sulfides followed by oxidation to the sulfoxides would give the desired product. When ω-(methylmercapto)acetophenone (VIa) was treated with sodium hydride and acetic anhydride it too gave exclusive o-acylation. This enol-acetate (XXVIIIa) is a stabile crystalline material. It has been shown previously that o-acylation is the rule for β-keto sulfones(61).

One other alternate route to the desired β,β-diketo sulfoxides was attempted utilizing alkylsulfinyl chlorides (RS(O)Cl) (XXXV) which are now readily available (62,63). However, treatment of the sodium salts of β-diketones in tetrahydrofuran with methylsulfinyl chloride led to products which contained no sulfoxide. The infrared spectrum, however, did indicate a sulfone group. Further analytical data proved the products to be sulfone-sulfides of the structure XLI. One may visualize alternate pathways to such a product. Both paths would involve the initial formation of the β, β-diketo sulfoxide (XXXVI). Path A assumes that the methine proton in XXXVI

is so acidic that immediately upon forming XXXVI reacts with another molecule of the β-diketone salt to form another sodium salt (XXXVII).

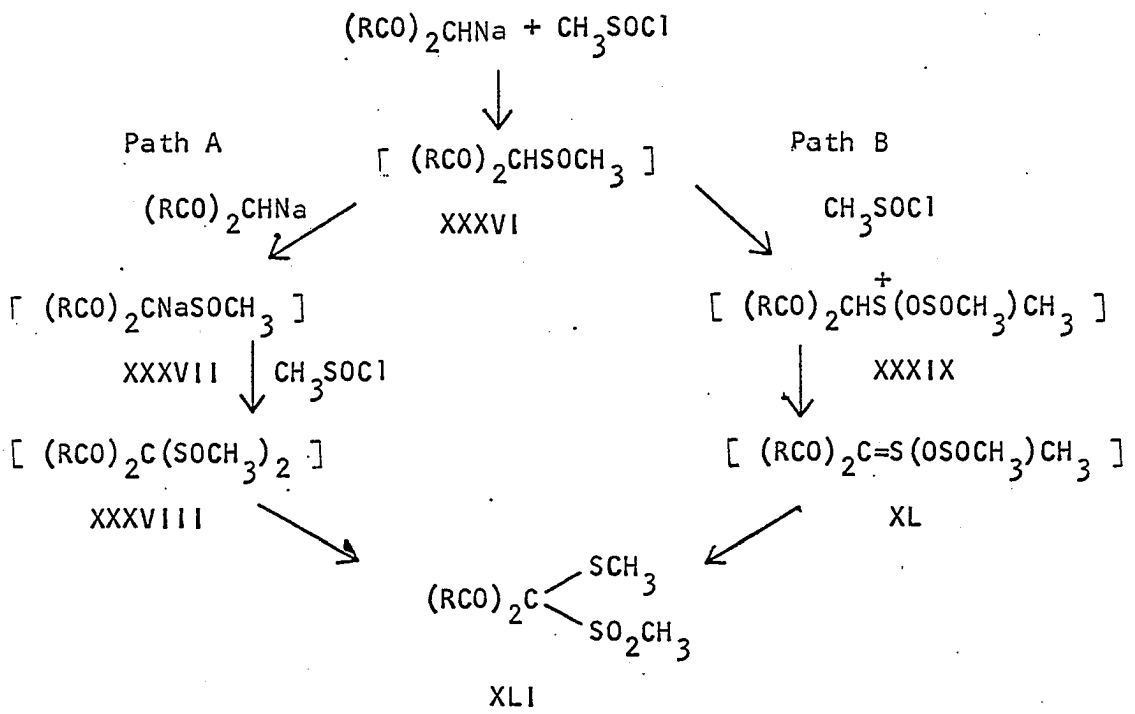
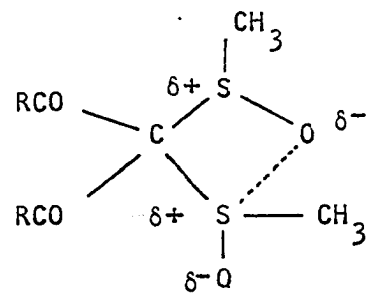


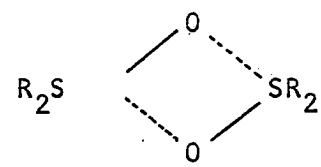
Figure 4. The possible reaction paths of methylsulfinyl chloride with the sodium salt of a β-diketone.

Intermediate XXXVII then reacts with another molecule of methylsulfinyl chloride to give a disulfoxide (XXXVIII) which undergoes an intramolecular disproportionation to the product. Such a disproportionation might be pictured as taking place through a transition state such as D.

Similar disproportionations have been postulated in 1,4-dithiadiene systems (3). Sulfoxides have also been shown to exist in solution as dimers of type E by n.m.r. techniques (64) and by vapor phase osmometry (65). Dimethyl sulfoxide itself has been shown to form association polymers in the



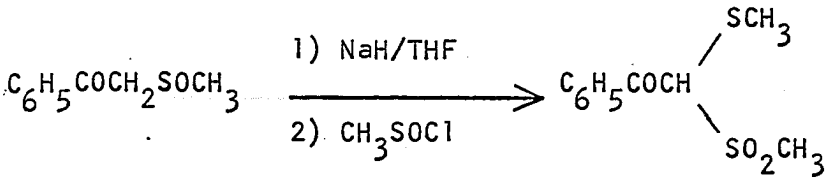
D



E

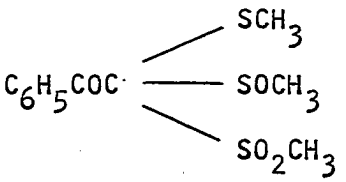
neat state (66) or in benzene solution (67). Path B requires the reaction of XXXVI with another molecule of methylsulfinyl chloride to form a sulfonium salt (XXXIX). Intermediate XXXIX loses a proton to give XL which rearranges to give the product. In agreement with experimental results, both mechanisms require that only 50% of the diketone react when equimolar amounts of reactants are used. When the diketone itself is refluxed with methylsulfinyl chloride no reaction occurs. When two equivalents of methylsulfinyl chloride to one equivalent of sodium salt was used the yield increased slightly--from 31 to 40% based on the salt. This increase is not sufficient to demand that path B is the proper one. An argument against path B can be made from the fact that acyl halides react with sulfoxides to form α-halo sulfides (68-70). Therefore, if intermediates like XXXIX and XL are involved, attack by an external nucleophile, chloride, should be favored over a cyclic intramolecular rearrangement. Evidence against path

A, however, is also available. Methylsulfonyl chloride (CH_3SO_2Cl) adds only once to salts of β-diketones to give moderate yields of the sulfone analog of XXXVI (32). Also, when the sodium salt of Ia was treated with methylsulfinyl chloride a 75% yield of benzoyl(methylmercapto)(methylsulfonyl)methane (XLIII) was obtained. A mechanism similar to path A would



Ia XLII

predict the formation of the very interesting species (XLIII) containing a sulfide, sulfoxide, and sulfone group all attached to the same carbon atom. More work in this area is necessary before a definite mechanism can be assigned.



XLIII

Other attempted acylations of β-keto sulfoxides which failed include reaction with excess ethyl benzoate in the initial condensation reaction yielding β-keto sulfoxide (10). Acylations of the β-keto sulfoxide were were attempted in ethyl acetate. Neither lithium or sodium salts of the β-keto sulfoxide underwent C-acylation. Intramolecular condensation of β-acyloxy sulfoxides (XLIV) with β-keto sulfoxides failed to yield C-acylated products.

$RC(OCOR')CH_2SOCH_3$

XLIV

An obvious extension of the condensation of dimethyl sulfoxide with esters was the condensation with diesters to produce cyclic products. Becker and Russell have shown that dimethyl sulfoxide in the presence of sodium methoxide adds to diethyl phthalate to yield the 1,3-indandione system (8,58). The reaction product isolated upon acidification with hydrochloric acid proved to be 2-chloro-2-methylmercapto-1,3-indandione (XLVI). The reaction of XLVI with hot water leads to good yields of ninhydrin hydrate (XLVII). A probable reaction sequence is shown in Figure 5. Intermediate XLV has been isolated (58).

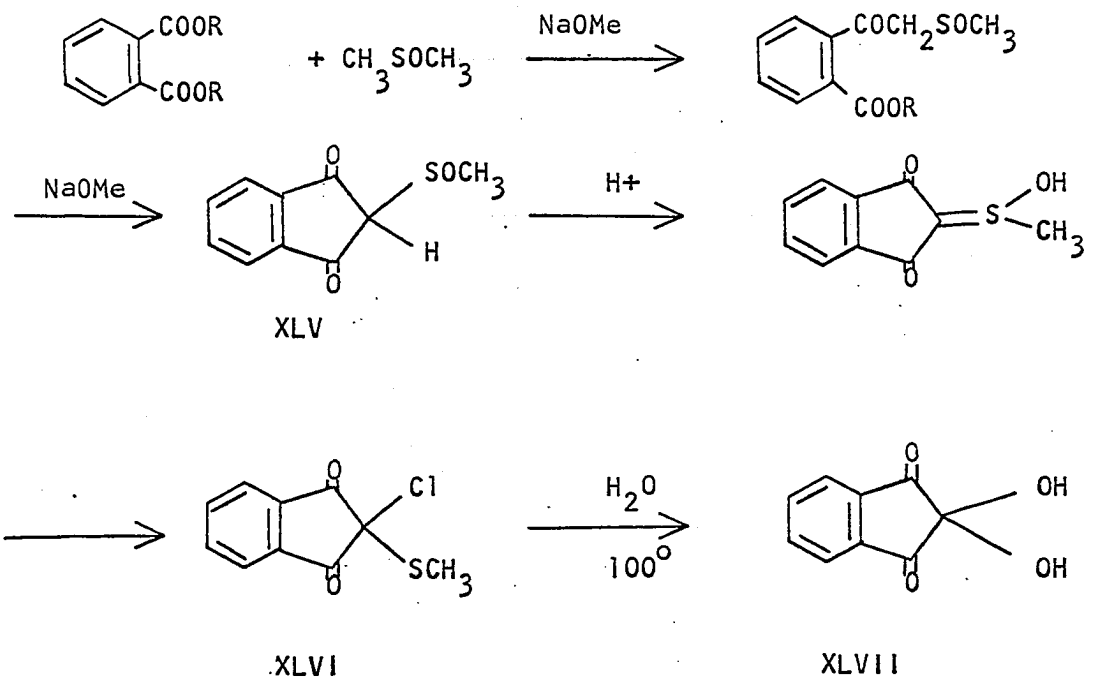
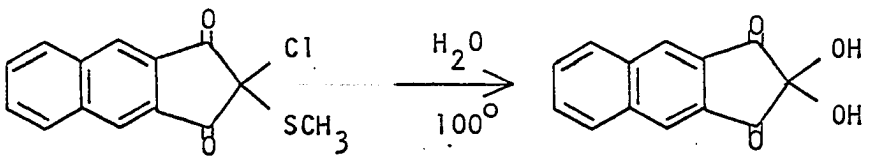


Figure 5a. Sodium methoxide catalzed reaction of dimethyl sulfoxide with diethyl phthalate.

In attempting to generalize this reaction and form a series of cyclic triketones or triketone hydrates little success has been attained. Only in the case of dimethyl 2,3-naphthalene dicarboxylate was the analogous α-

chlorothioether (XLVIII) obtained, and that only in poor yield and contaminated with large quantities of the diacid.



XLVIII XLIX

The conversion of XLVIII to XLIX can be effected but in lower yield than the conversion XLVI to XLVII. Considerable amounts of a brown, insoluble solid which does not melt below 325° are also formed. The reaction with 1,8-naphthalene dicarboxylates led only to anhydride formation. Attempts to react esters of maleic and 2,3-dimethylmaleic acids yielded only tarry residues from which no identifiable product could be obtained.

Since the more reactive carbanion from sodium hydride and dimethyl sulfoxide is capable of reacting with aliphatic esters, it was decided to explore this area. The first aliphatic diester tried was dimethyl 3,3-dimethylglutarate. The product isolated upon quenching with water, neutralization, and extraction proved to be a mixture of the diastereomers of 5,5-dimethyl-2-(methylsulfinyl)-3-(methylsulfinylmethyl)-Δ^2-cyclohexenone (LIII).

Two different routes to LIII can be envisioned, Figure 5. Of these two, path A seems the more likely since path B involves an intermediate (LI) which should lead to a triketone. It also seems more reasonable that in the presence of a large excess of relatively free carbanion both ester groups would react with different methylsulfinylcarbanions. In the case of the alkoxide catalyzed reaction of diethyl phthalate, only a low

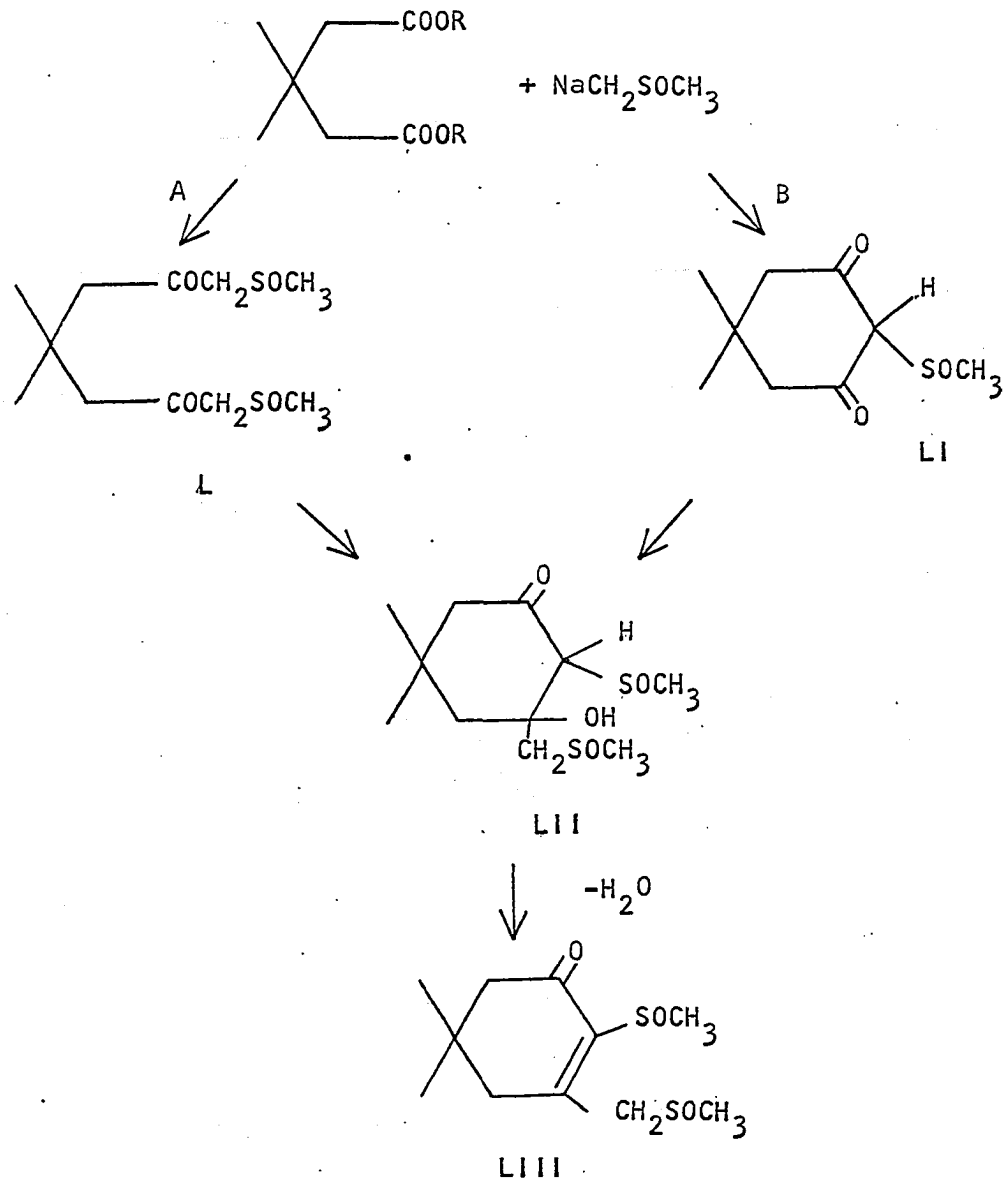
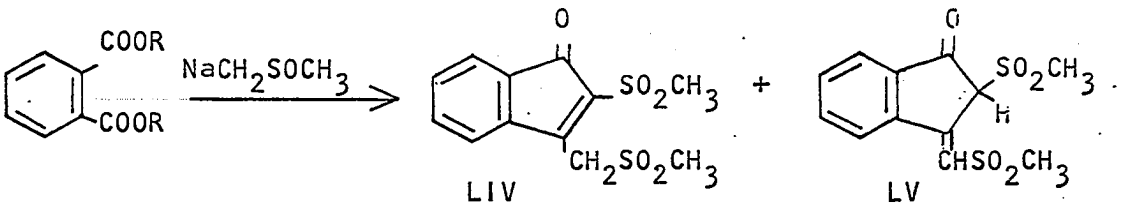


Figure 5b. Possible reaction paths for the reaction of sodium methylsulfinylmethane with dimethyl 3,3-dimethylglutarate.

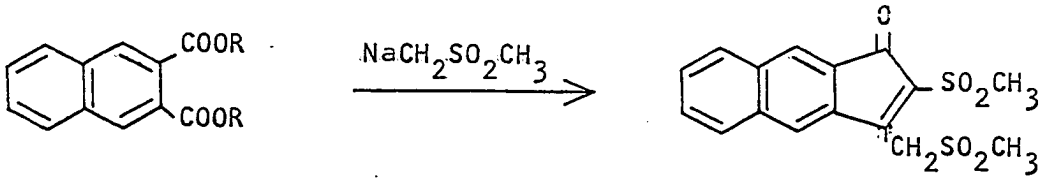
concentration of the carbanion is present. Consequently, the reaction of one ester group forms a β-keto sulfoxide which has a more acidic hydrogen atom than dimethyl sulfoxide and can successfully compete for the remaining base. Hence, only one mole of dimethyl sulfoxide is incorporated. This

fundamental difference between the two systems should demand that different products be formed in those systems which are reactive to both; i. e., aromatic esters. Indeed, when diethyl phthalate was reacted with the methylsulfonyl carbanion, prepared from sodium hydride and dimethyl sulfone in dimethyl sulfoxide solution, two products (LIV and LV) were formed. Both products had incorporated two moles of dimethyl sulfone. Compound



LIV LV

LV differed only in the direction in which water had eliminated could be converted to LIV treatment with base in dimethyl sulfoxide. The analogous reaction with the methylsulfinyl carbanion itself gave no identifiable product. The dimethyl 2,3-naphthalene dicarboxylate behaved similarly although only the product with the double bond in the ring (LVI) was found.



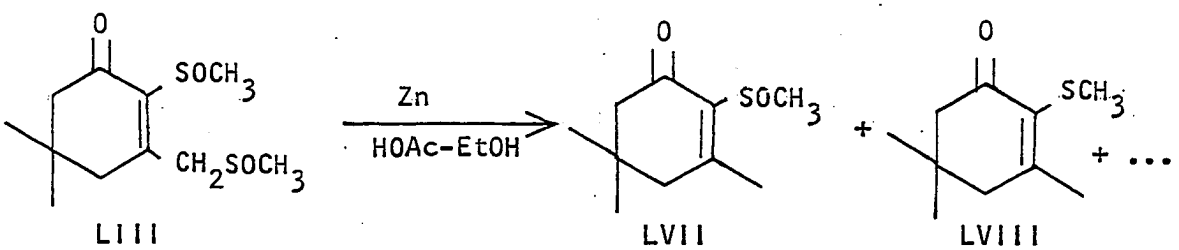
LVI

Further evidence that the concentration of the carbanion is the factor which determines the product is the fact that when the reaction is run in the inverse manner, i.e., adding the preformed carbanion dropwise to a well-stirred solution of the diester, one obtains the chlorindandione XLVI and the chloronaphthindandione XLVIII in 31 and 59% yields, respectively. Here again, however, the 1,8-naphthalene dicarboxylate and maleate systems do not give identifiable products.

Before proceeding to find other similar cyclic condensations it seemed advisable to study the chemistry of LIII itself. If compounds of this type could be reductively desulfurized, one could obtain β-methyl cyclic ketones. Ketones of this sort could be of value to electron spin resonance studies of semidione radical anions being conducted in these laboratories. Russell and Mikol have shown that β-keto sulfoxides are reduced to methyl ketones in good yield by zinc in acetic acid-absolute ethanol solution (44). When compound LIII was treated in a similar manner

$$RCOCH_2SOCH_3 \xrightarrow[HOAc\text{-}EtOH]{Zn} RCOCH_3$$

for one hour a 30% yield of 3,5,5-trimethyl-2-(methylsulfinyl)-2-cyclohexenone (LVII) was formed. Longer reaction times gave a wide variety of products, the most predominant being the analogous sulfide (LVIII).

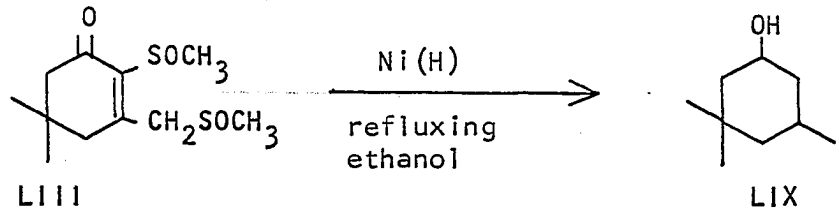


LIII LVII LVIII

Reductions with aluminum amalgam in aqueous tehalydrofuran and sodium or lithium in liquid ammonia also gave mixtures of products.

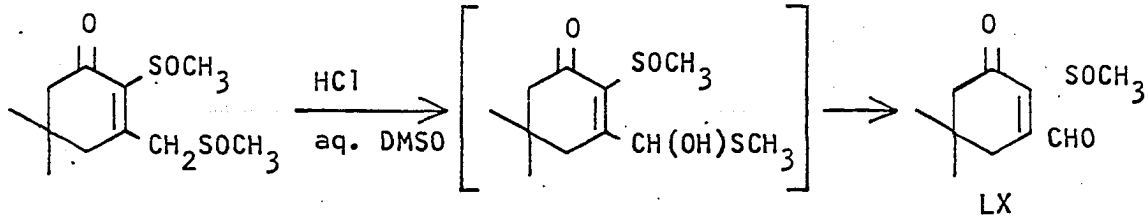
Raney nickel (W-2) proved to be an effective method of accomplishing this complete desulfurization. The drawbacks of this method are the time required to prepare the catalyst and the fact that massive amounts of Raney nickel are required since sulfur poisons the catalyst. A ratio

approximately twenty-five to one, Raney nickel to substrate, in refluxing ethanol was required. The product isolated from the reaction of LIII was a mixture of the isomers of 3,5,5-trimethylcyclohexanol (LIX).



LIII LIX

Compound LIII, when treated with hydrochloric acid in aqueous dimethyl sulfoxide, rapidly undergoes the Pummerer rearrangement at the activated position. Under these conditions the hemimercaptal formed also splits out methyl mercaptan to give an aldehyde (LX).

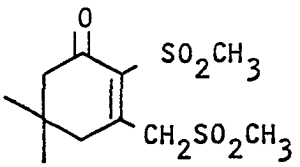


LX

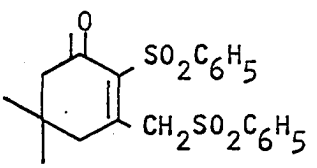
The reaction is complete in about 30 minutes. Under these same conditions ω-(methylsulfinyl)acetophenone takes 24 hours to rearrange; and, the product isolated is the hemimercaptal (10). The remaining sulfoxide group in compound LX is very labile with respect to disproportionation with the dimethyl sulfoxide in the solvent. Thus LX is always contaminated by the analogous sulfide (LXI).

This facile rearrangement is one of the major reasons for the relatively low yields (38-58%) of LIII. As formed in the basic reaction media the product exists as an enolate anion. It is necessary to neutralize the solution to convert to the ketonic form which can be extracted. Even

very careful neutralization in well mixed, iced solutions cannot prevent some loss *via* rearrangement. In order to circumvent this problem, the reaction was run with the methylsulfonylcarbanion to produce the analogous sulfone which could not undergo the Pummerer rearrangement. In this manner yields of slightly greater than 80% of compound LXII were obtained.



LXII

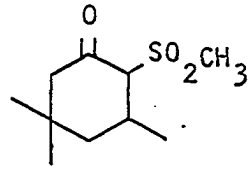


LXIII

The attempted desulfurization of LXII with Raney nickel produced only a mixture of products which still contained a sulfone group. The literature has very few examples of the desulfurization of sulfones. The one case where aliphatic sulfones have been reduced to hydrocarbons required 350°, 100 atmospheres of hydrogen pressure, and a molybdenum sulfide catalyst (42). However, it was noted that several sulfones containing an aromatic moiety in the molecule had been reduced to hydrocarbons under relatively mild conditions (43). Therefore, the condensation was carried out using methyl phenyl sulfone in the place of dimethyl sulfone. Compound LXIII was obtained in 46% yield and was readily reduced to 3,5,5-trimethylcyclohexanol (LIX) by Raney nickel in reluxing ethanol. However, the reduced yield of the condensation product (probably due to the increased steric requirement of the phenyl groups although no effort was made to maximize this yield) and the large excess of catalyst required combined with the large molecular weight reduction of the final step make

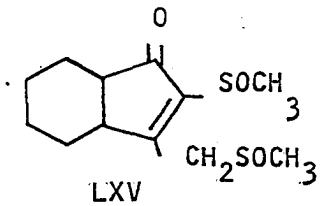
the entire route somewhat impractical.

The significantly more convenient conditions of the Papa-Schwenck reduction (The nickel-aluminum alloy is added directly to a hot solution of the sulfone in aqueous sodium hydroxide.) (71,72) allows the clean partial reduction the dimethyl sulfone adduct (LXII) to a monosulfone (LXIV) in 94% yield.

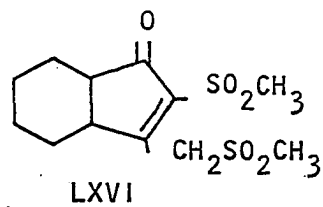


LXIV

Diethyl cyclohexane-cis-1,2-dicarboxylate reacts with the methylsulfinyl carbanion to give a 29% yield of hexahydro-2-(methylsulfinyl)-3-(methylsulfinylmethyl)-Δ^2-inden-1-one (LXV). The analogous reaction with



LXV



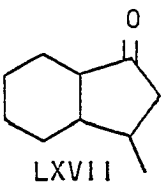
LXVI

the methylsulfonyl carbanion produced a 93% yield of hexahydro-2-(methylsulfonyl)-3-(methylsulfonylmethyl)-Δ^2-inden-1-one (LXVI).

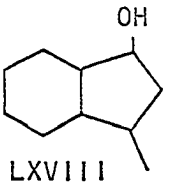
Compound LXV when treated with Raney nickel in refluxing ethanol for four hours gave a 70% yield of hexahydro-3-methyl-1-indanone (LVII). Longer reaction times introduced two isomeric alcohols (LXVIII) into the mixture. Compound LXVI gave only partial reduction to LXIX after six hours.

Attempts to effect ring closure to a bicylo-(3,3,1) system by condensation with dimethyl 1,3-cyclohexanedicarboxylate failed. The methyl-

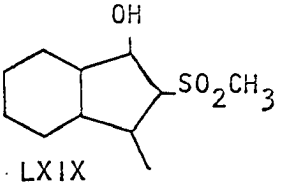
sulfinyl carbanion gave no identifiable product and the methylsulfinyl



LXVII

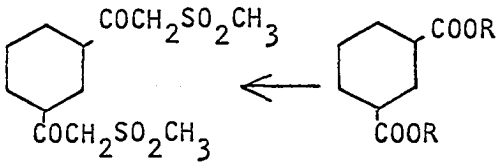


LXVIII



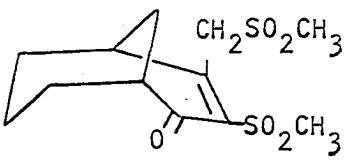
LXIX

carbanion added two moles dimethyl sulfone but did not cyclize. Reaction periods of up to ten days and temperatures up to 80° were tried. Compound LXX was treated with potassium t-butoxide in dimethyl formamide or dimethyl



LXX

+ $NaCH_2SO_2CH_3$



LXXI

sulfoxide, but only starting material was recovered.

Two products are possible in the reaction of the methylsulfonyl carbanion with dimethyl homophthalate--LXXII in which the double bond and the ketone are in direct conjugation with the aromatic ring, and LXXIII in which the double bond and the aromatic ring are in cross conjugation with the ketone (Figure 6). In both ketones, however, the situation is highly favorable for tautomerization to the corresponding naphthols (LXXIV and LXXV). Apparently, compound LXXIII is formed preferentially since its tautomer (LXXV) was the only naphthol found. The only other product found was LXXVI in which only one ester group had reacted. It was found only in those reactions which had reaction times of two hours or less. Proof of structure of LXXV was obtained by reduction with Raney nickel in ethanol to yield the known 3-methyl-5,6,7,8-tetrahydro-1-naphthol (LXXVII). The Papa-

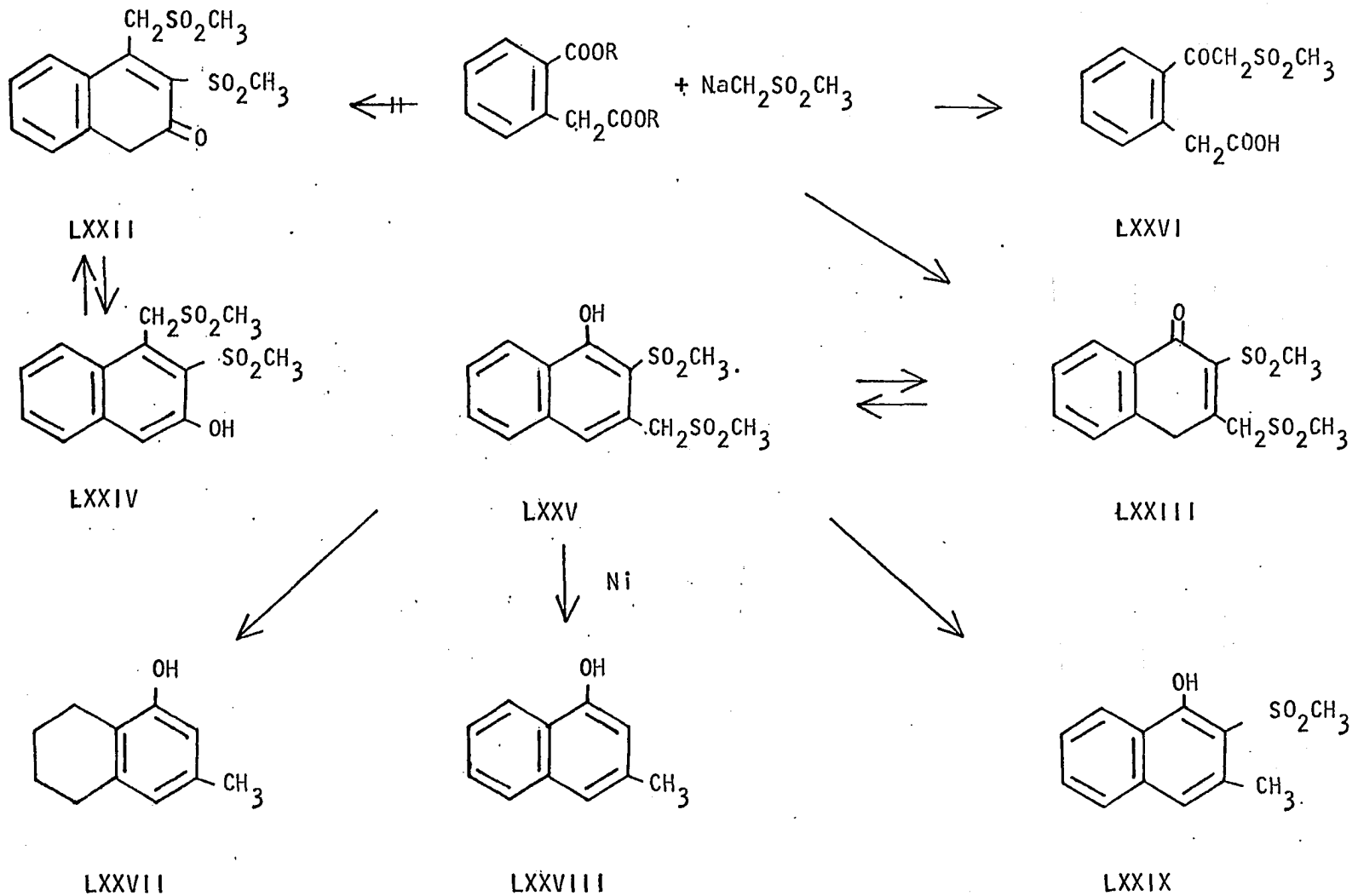


Figure 6. The reaction of methylsulfonylmethylsodium with dimethyl homophthalate.

Schwenck reduction of LXXV gave rise to two compounds--3-methyl 1-naphthol (LXXVIII) and 3-methyl-2-(methylsulfonyl)-1-naphthol (LXXIX). Either LXXVIII or LXXIX could be made to predominate by a ration of approximately 3 to 1 by varying the amount of nickel-aluminum alloy used. Neither could be obtained exclusively. With large excesses of alloy some tetralol formation was observed.

One aromatic diester gave the same product regardless of the source or concentration of the carbanion. Dimethyl diphenate (LXXX) adds two moles of the methylsulfinyl carbanion and closes to a seven membered ring but does not eliminate water (Figure 7). Since the preferred conformation of diphenates has the ester groups on opposite sides, both esters react with the methylsulfinyl carbanion before rotation about the diphenyl linkage and cross-linking to LXXXI can take place. At first glance, it would appear that elimination of water should be more facile in this case than in any of the others since very extensive conjugation appears to be possible. However, if one tries to make the molecular model of LXXXII one notes considerable strain. Heating in base and dimethyl sulfoxide does not effect the dehydration. The addition of methyl iodide to form a more favorable leaving group led to no identifiable product.

Reduction of LXXXI with zinc and acetic acid removes the activated sulfoxide group to give LXXXIII as a mixture of diastereomers.

Treatment of LXXXI with hydrochloric acid in aqueous dimethyl sulfoxide leads to an interesting rearrangement product (LXXXIV). Compound LXXXIV was too unstable to withstand the rigors of being sent microanalysis, but spectral data (including mass spectrum) indicate its existence.

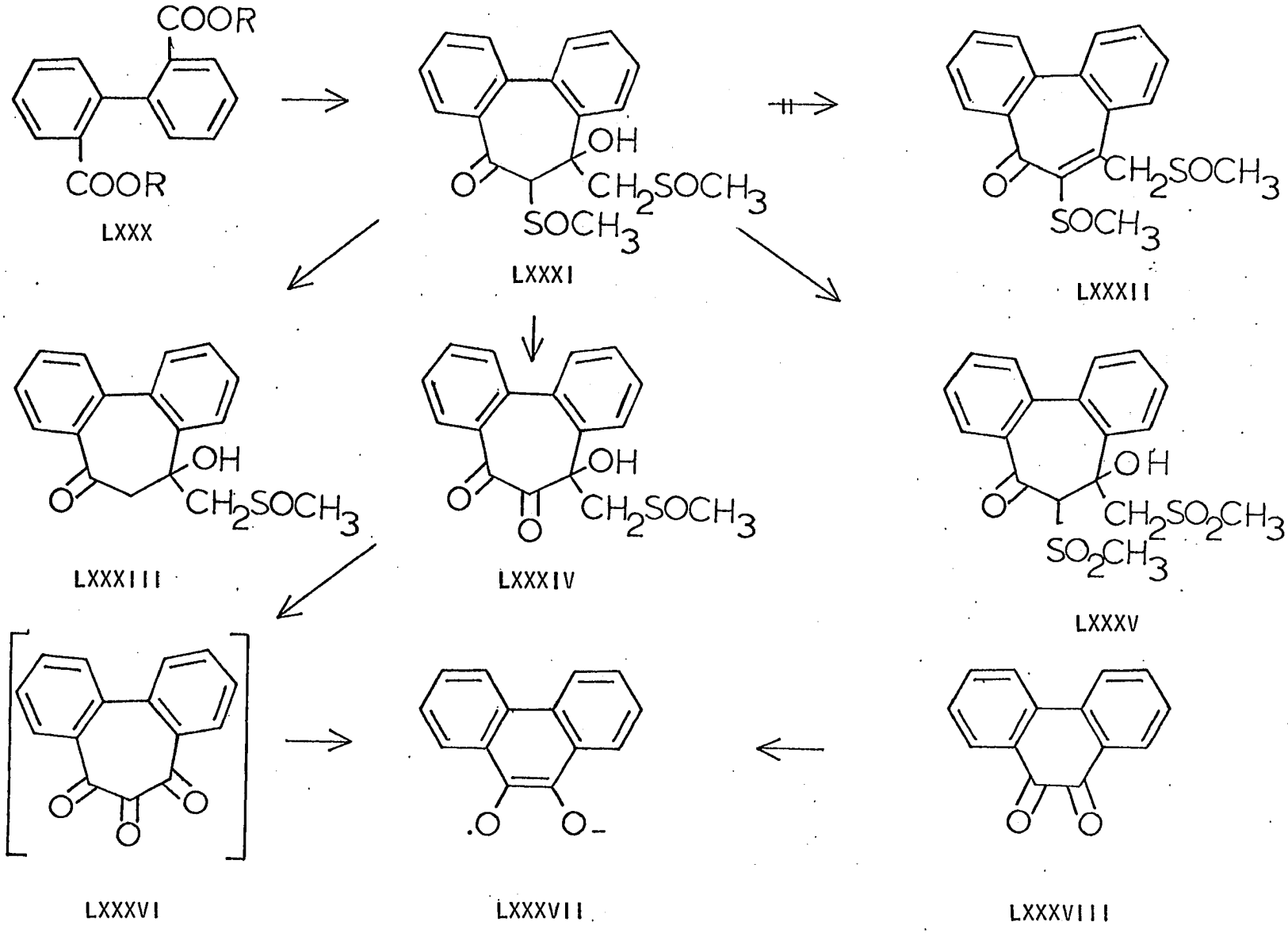


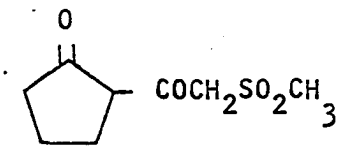
Figure 7. Products derived from diethyl diphenate

If compound LXXXIV is treated with potassium t-butoxide in dimethyl sulfoxide in an electron spin resonance cell, a strong signal indicates the presence of a radical species. The spectrum consists of a major quintet (1.68 gauss) with further splitting (approximately 0.4 gauss) given in spectrum or Figure 8. This spectrum could be explained by saying that the base removes the hydroxyl proton of LXXXIV and then a methylsulfinyl carbanion is ejected to give a triketone (LXXXVI). Since under these conditions triketones normally loses carbon monoxide to form a semidione radical anion with one less carbon atom (73), the radical observed would be 9,10-phenanthrene semiquinone (LXXXVII). The published spectrum of LXXXVII (74,75) was very similar but had been observed in aqueous solution. When 9,10-phenanthrene quinone was reduced by electron transfer from propiophenone in dimethyl sulfoxide a spectrum was obtained which was superimposable with that observed for LXXXIV.

Compound LXXXI can be oxidized in poor yield by hydrogen peroxide to the analogous sulfone (LXXXV) which can also be made by direct condensation of the methylsulfonyl carbanion with dimethyl diphenate in 92% yield.

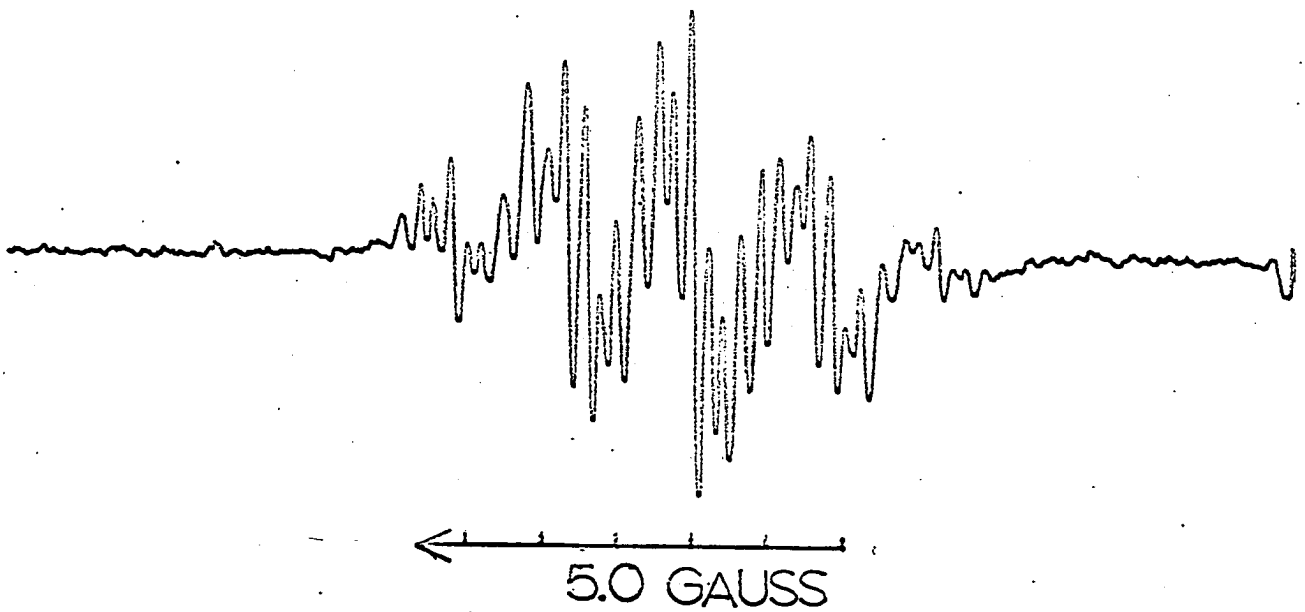
Attempts to form an aliphatic seven-membered ring from dimethyl adipate and the methylsulfonyl carbanion gave only LXXXIX, the product from initial Dieckmann condensation (76) followed by condensation of the remaining ester group.

$$(CH_2)_4(COOR)_2 + NaCH_2SO_2CH_3 \rightarrow$$

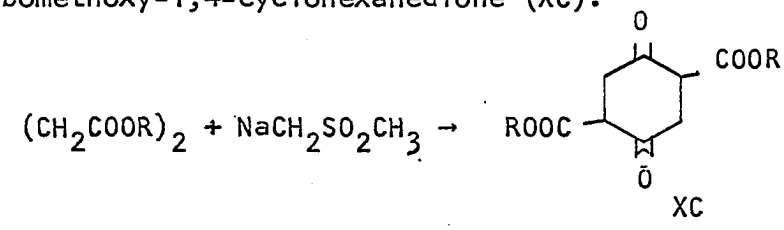


LXXXIX

Figure 8. First-derivative e.s.r. spectrum of 9, 10-phenanthrene semiquinone produced by the reaction of LXXXIV with potassium t-butoxide in dimethyl sulfoxide.

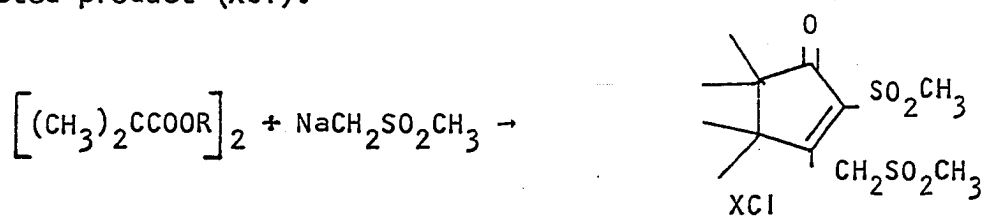

5.0 GAUSS

Dimethyl succinate prefers to condense with itself to give the dimer 2,5-dicarbomethoxy-1,4-cyclohexanedione (XC).



XC

However, dimethyl tetramethylsuccinate which cannot self-condense gives the expected product (XCI).

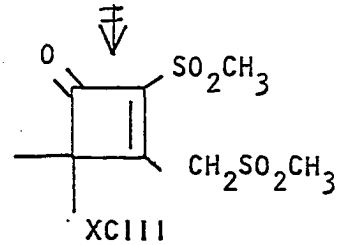


XCI

Diethyl dimethylmalonate undergoes condensation at both ester groups; but, as expected, it does not cyclize to give a cyclobutenone derivative (XCIII).

$$(CH_3)_2C(COOR)_2 + NaCH_2SO_2CH_3 \rightarrow (CH_3)_2C(COCH_2SO_2CH_3)_2$$

XCII

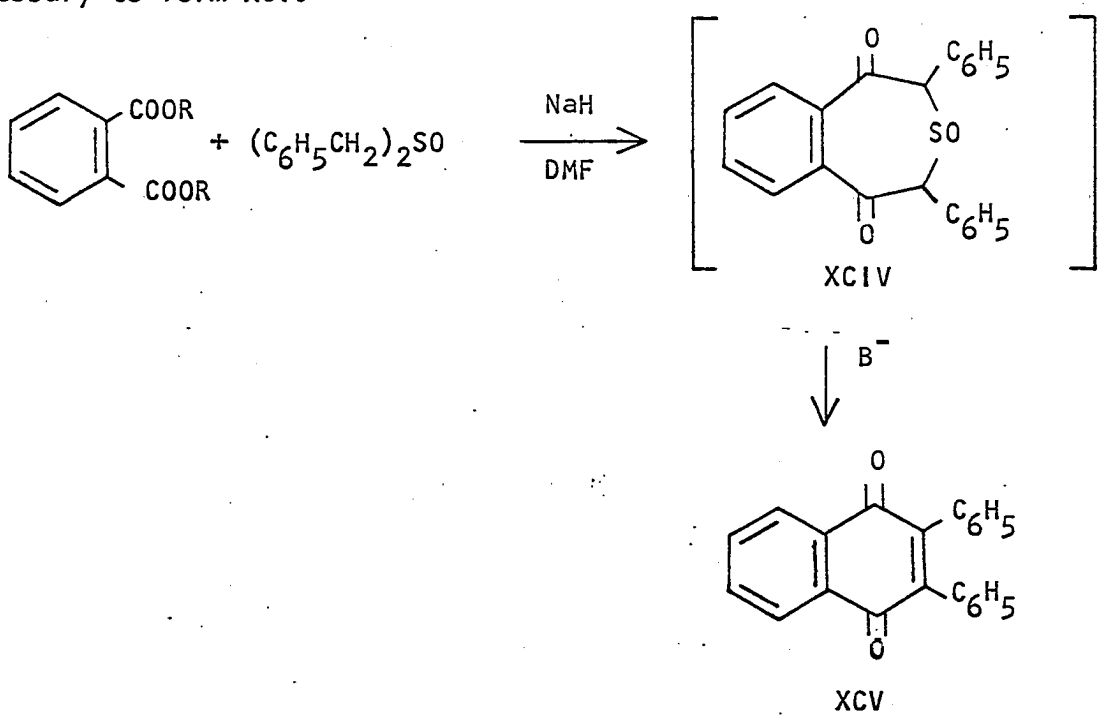


XCIII

Attempted condensations with both dimethyl oxalate and diethyl carbonate failed to give a product although on an e.p.r. scale a radical was obtained for the oxalate case which indicated that condensation had taken

place (73). In both cases a gas was evolved upon neutralization of the basic reaction media.

One other condensation is of interest. It is the one case where there is evidence for both carbon atoms alpha to the sulfoxide reacting. When diethyl phthalate was added to a slurry of sodium hydride and dibenzyl sulfoxide in dimethylformamide at 60° yields varying from 0 to 24% of 2,3-diphenyl-1,4-naphtha-quinone (XCV) were obtained. The other product which was identified was trans-stilbene, which is known to arise from heating dibenzyl sulfoxide with base in dimethylformamide (77). It seems likely XCV could arise from XCIV in a similar manner. The low, varying yields are consistent with the unfavorable competition due to the difficulty of attaining conditions suitable for the multistep reaction sequence necessary to form XCV.



EXPERIMENTAL

All melting points were determined on a Mel-Temp or Fischer-Johns melting point apparatus and are uncorrected. Microanalyses were performed by Spang Microanalytical Laboratories, Ann Arbor, Michigan, or Schwartzkopf Microanalytical Laboratories, Woodside, New York. Infrared spectra were taken on a Perkin-Elmer Model 21 double beam infrared spectrophotometer. Nuclear magnetic resonance spectra were obtained on either Varian Associates HR-60 or A-60 spectrophotometers. All chemical shifts are reported as parts per million from tetramethylsilane (δ scale).

Dimethyl sulfoxide was distilled from calcium hydride under reduced pressure and stored over Molecular Sieves in tightly sealed glass containers. Tetrahydrofuran was distilled as needed from lithium aluminum hydride. Sodium hydride was obtained as a 50-60% suspension in mineral oil from Metal Hydrides, Incorporated. The mineral oil was removed just prior to use by washing with Skellsolve A and decanting three times. All reactions involving the presence of a base in dimethyl sulfoxide were run in an atmosphere of dry prepurified nitrogen. All esters were prepared from commercially available acids by sulfuric acid catalyzed esterification with the following exceptions. Dimethyl 1,8-naphthalenedicarboxylate was prepared from the disilver salt and methyl iodide in a sealed tube (78). Dimethyl cis-1,2-cyclohexanedicarboxylate was prepared by the Diels-Alder reaction of 1,3-butadiene and maleic anhydride, esterification, and hydrogenation of the double bond with a palladium charcoal catalyst at 1 to 2 atmospheres of hydrogen pressure (79). Dimethyl tetramethylsuccinate was prepared by coupling the monomethyl ester of dimethylmalonic acid in the

presence of potassium persulfate (80). All other chemicals were commercially available and unless otherwise stated were used as received.

Experimental Detail for Products Derived from β-Keto Sulfoxides

Preparation of β-keto sulfoxides, I

ω-(Methylsulfinyl)-acetophenone, Ia, and (methylsulfinylmethyl) cyclohexyl ketone, Ib, were prepared as previously reported (10,15,16).

Preparation of β-hydroxy-β-phenethyl methyl sulfoxide, IIIa

Compound Ia (30 g.) was dissolved in 100 ml. of water and cooled in an ice bath. While stirring with a magnetic stirrer, sodium borohydride (1.70 g.) in 10 ml. of water was added slowly. After stirring for two hours the solution was thoroughly extracted with chloroform. The extracts were dried over magnesium sulfate and filtered. Evaporation of the solvent left a colorless oil which after removal of the final traces of solvent at 1 mm. crystallized in colorless needles (29.9 g., 98%) melting at 78-123. Recrystallization from ethyl acetate did not effect separation of the diastereomers. The infrared spectrum was super-imposable with an authentic sample prepared by addition of the methylsulfinyl carbanion to benzaldehyde (25).

Preparation of β-hydroxy-β-cyclohexylethyl methyl sulfoxide, IIIb

By the same procedure used to prepare IIIa, compound Ib (2.04 g.) gave IIIb (1.98 g., 97%) as a white solid. Recrystallization from isopropyl ether permitted separation into two pairs of isomers, the more soluble isomer melting at 50-52 and the more insoluble isomer melting a 94-96. The

sample for analysis was not separated into diastereomers.

Analysis — Calcd. for $C_9H_{18}O_2S$: C, 56.82; H, 9.54; S, 16,82. Found: C, 57.02; H, 9.55; S, 16.83.

Infrared — (chloroform) 2.97, 3.45, 3.52, 6.82, 7.23, 7.70, 7.9-8.6 (broad), 9.75 (broad), 10.40, 10.75, 11.23 microns.

N. M. R. — (deuterochloroform) broad absorption 1.0-2.0 (10H); multiplet 2.6-2.9 (5H); broad absorption 3.8-4.1 (2H). Shaking the sample with deuterium oxide reduced the absorption at 3.8-4.1 by one proton.

Preparation of β-hydroxy-β-phenethyl methyl sulfone, IVa

By the same procedure used to prepare IIIa, compound IIa (o.10 g.) gave IVa (7.89 g., 86%) as colorless crystals melting at 102-104°. crystallization from benzene-carbon tetrachloride mixtures raised the m.p. to 105-106°(lit. (34) m.p. 106-106.5°).

Preparation of β-hydroxy-β-phenethyl methyl sulfide, Va

According to the procedure of G. J. Mikol of the laboratories, a solution of Ia (20.0 g.) in 200 ml. of tetrahydrofuran was added dropwise lithium aluminum hydride (6.5 g.) suspended in tetrahydrofuran at a rate sufficient to maintain reflux. The mixture was refluxed for 24 hours, cooled, and diluted carefully with 100 ml. of water. The hydroxides which were formed were dissolved with hydrochloric acid. The aqueous solution was extracted with chloroform. The combined extracts were dried over magnesium sulfate and filtered. Removal of the solvent left a yellow liquid which was

distilled at 1 mm. A fraction boiling at 92-95 (13,54 g., 73%) was collected (lit. (81) b.p. 142-3 at 15 mm.).

Preparation of β-hydroxy-β-cyclohexylethyl methyl sulfide, Vb

When Ib (9.90 g.) was treated in the manner used to prepare Va, the product Vb (6.54 g., 75%) was obtained as the fraction boiling at 92° at 1 mm.

Analysis — Calcd. for $C_9H_{18}OS$: C, 62.04; H, 10.41; S, 18.37. Found: C, 61.93; H, 10.36; S, 18.29.

Infrared — (carbon tetrachloride) 2.90, 3.45, 3.52, 6.81, 9.40, 11.00, 11.24 microns.

N.M.R. — (carbon tetrachloride) broad absorption 1.0-2.0 (11H); singlet 2.09 (3H); multipet 2.4-2.7 (2H); singlet 2.81 (1H); multiplet 3.203.6 (1H). Shaking the sample with deuterium oxide removes the singlet at 2.81.

Preparation of β-methoxy-β-phenethyl methyl sulfoxide, VIIa

Compound IIIa (9.20 g.) in 100 ml. of tetrahydrofuran was added to a suspension of sodium hydride (1.10 g.) in 25 ml. of tetrahydrofuran at such a rate that refluxing did not occur. Excess methyl iodide was added. The mixture was then added carefully to 500 ml. of water. The aqueous mixture was extracted with chloroform. The extracts were dried over magnesium sulfate and filtered. Removal of the solvent left a light yellow oil which was vacuum distilled. The fraction boiling at 135-7° at 1 mm. (6.48 g., 72%) was collected.

Analysis Calcd. for $C_{10}H_{14}O_2S$: C, 60.59; H, 7.07; S, 16.14
Found: C, 60.38; H, 7.13; S, 16.07

Infrared (chloroform) 3.42, 3.54, 6.24, 6.70, 6.89, 7.12, 7.38, 7.70, 8.74, 9.10 (intense), 9.75 (broad, intense), 10.15 microns.

N.M.R. (carbon tetrachloride) 2 singlets 2.46 and 2.52 (total 3H); multiplet 2.7-3.1 (2H); 2 singlets 3.19 and 3.22 (total 3H); multiplet 4.5-4.7 (2H); broadened singlet 7.30 (5H).

Preparation of β-methoxy-β-cyclohexylethyl methyl sulfoxide, VIIb

By repetition of the procedure used to prepare VIIa, compound IIIb (5.10 g.) produced compound VIIb (3.95 g., 72%) as a mixture of diastereomers boiling at 118-139° at 0.5 mm.

Analysis Calcd. for $C_{10}H_{20}O_2S$: C, 58.80; H, 9.87; S, 15.67.
Found: C, 58.67; H, 9.76; S, 15.80.

Infrared (carbon tetrachloride) 3.45, 3.51, 6.92, 9.15, 9.55 microns.

N.M.R. (carbon tetrachloride) broad absorption 1.0-2.0 (11H); multiplet 2.5-2.9 (5H); multiplet 3.2-3.5 (4H).

Preparation of β-methoxy-β-phenethylmethyl sulfide, VIIIa

In the manner used to prepare VIIa, compound Va (20.1 g.) produced VIIIa (17.17 g., 81%) boiling at 86-91° at 2mm. The compound was identified by oxidation to the sulfoxide and comparison with an authentic sample of VIIa.

Preparation of β-methoxy-β-cyclohexylethyl methyl sulfide, VIIIb

In the manner used to prepare VIIa, compound Vb (4.90 g.) produced VIIIb (3.90 g., 65%) boiling at 49-54° at 0.10-0.15 mm.

Analysis — Calcd. for $C_{10}H_{20}OS$: C, 63.79; H, 10.71; S, 17.00. Found: C, 63.92; H, 10.54; S, 16.87

Infrared — (carbon tetrachloride) 3.47, 3.52, 6.92, 9.15 microns.

N.M.R. — (carbon tetrachloride) broad absorption 1.0-2.0 (11H); singlet 2.09 (3H); doublet 247 and 257 (2H); broad absorption 2.8-3.2 (1H); singlet 3.35 (3H).

Preparation of ω-methylsulfinylstyrene, XIa

Compound VIIa (1.98 g.) in 25 ml. of tetrahydrofuran was added to a suspension of sodium hydride (0.36 g.) in 25 ml. of tetrahydrofuran. The mixture was refluxed for one hour and then poured into water. The aqueous solution was extracted with chloroform. The extracts were dried over magnesium sulfate and filtered. Removal of the solvent left XIa (1.64 g., 100%) as a slightly yellow solid, m.p. 45-50°. Recrystallization from ether raised the m.p. to 61-2°.

Analysis — Calcd. for $C_9H_{10}OS$: C, 65.05; H, 6.07; S, 19.26. Found: C, 65.21; H, 6.14; S, 19.20.

Infrared — (chloroform) 3.38, 6.20, 6.92, 7.13, 7.75, 9.65 (broad), 10.45 (intense) microns.

N.M.R. — (carbon tetrachloride) singlet 2.60 (3H); AB quartet $\delta_A = 6.91$. $\delta_B = 7.20$, $|J_{AB}| = 15.5$ c.p.s.; multiplet 7.2-7.6 (5H).

Preparation of ω-(methylsulfinylmethyl)-methylenecyclohexane, XIb'

When compound VIIb (4.08 g.) was treated with base as in the above procedure, XIb' (3.4 g., 100%) was obtained as a pasty solid. Recrystillization from ethyl acetate gave a white solid, m.p. 38-9°. The material may also be distilled at 92-4° at 0.1 mm.

Analysis Calcd. for $C_9H_{16}OS$: C, 62.76; H, 9.36; S, 18.58
Found: C, 62.66; H, 9.29; S, 18.61.

Infrared (carbon tetrachloride) 3.41, 3.50, 6.04, 6.81, 7.03 7.11, 7.45, 7.76, 9.50 (broad, intense), 10.15, 10.46, 10.75, 11.20, 11.82 microns.

N.M.R. (carbon tetrachloride) broad absorption 1.3-2.3 (10H); singlet 2.41 (3H); doublet centered at 3.35, J = 8 c.p.s. (2H); triplet centered at 5.13, J = 8 c.p.s. (1H).

Preparation of methyl ω-styryl sulfide, XIIa

Potassium hydrogen sulfate (50 g.) was placed in a flask equipped with a pressure compensating dropping funnel and a distillation head. The temperature was raised to 230° and the pressure was reduced to 0.3 mm. After one hour Va (11.56 g.) was added dropwise. The dark brown distillate was taken up in ether, dried over magnesium sulfate, and filtered through charcoal. Removal of the solvent gave 5.23 g. of a light yellow liquid. The liquid was fractionally distilled and the fraction boiling at 110-3° at 3 mm. (3.96 g., 38%) was collected. The cis olefin is reported to boil at 100-5° at 4mm. (82).

N.M.R. (carbon tetrachloride) singlet 2.23 (3H); AB quartet δ_A= 6.18, δ_B= 6.66, J_{AB} = 15.6 c.p.s. (2H); multiplet

7.0-7.4 (5H). A low intensity quartet δ_A= 6.02, δ_B= 6.32, J_{AB} = 11.0 c.p.s. indicates the presence of a trace of the cis olefin.

Preparation of ω-methylsulfonylstyrene, Xa

Compound IVa (5.00 g.) in 100 ml. of tetrahydrofuran was added to a suspension of sodium hydride (2.56 g.) in 25 ml. of tetrahydrofuran. The mixture was refluxed for one hour and then poured into water. The aqueous solution was extracted with chloroform. The extracts were dried over magnesium sulfate and filtered. Removal of the solvent gave Xa (3.42 g., 74%) as a pasty solid. Recrystallization from aqueous ethanol raised the m.p. to 78-9°. A mixed m.p. with an authentic sample prepared by phosphoric acid catalyzed dehydration of IVa showed now depression.

N.M.R. (deuterochloroform) singlet 3.02 (3H); AB quartet δ_A= 6.99, δ_B7.66, J_{AB} = 15.5 c.p.s. (2H); multiplet 7.2-7.6 (5H).

Preparation of β-phenethyl methyl sulfide, XIIIa

When XIa (0.85 g.) was refluxed with lithium aluminum hydride in tetrahydrofuran the product obtained was XIIIa (0.6 g., 82%), b.p. 65-7° at 1 mm. Proof of structure was obtained by integrated n.m.r. spectrum and by oxidation to the known sulfone, m.p. 83-5° (lit. (83) m.p. 85-6°).

N.M.R. (carbon tetrachloride) singlet 2.00 (3H); multiplet 2.4-3.0 (4H); broadened singlet 7.15 (5H).

Preparation of β-phenethyl methyl sulfone, XVa

When compound Xa (5.00 g.) was refluxed with lithium aluminum hydride

in tetrahydrofuran the product obtained was XVa (2.80 g., 55%), m.p. after recrystallization from methanol, 86-7° (lit. (83) m.p. 85-6°).

Sodium metaperiodate oxidations

All of the sodium metaperiodate reactions were carried out essentially by the method of Leonard and Johnson (84,85).

Compound VA (500 mg.) when treated with sodium metaperiodate gave a light yellow solid. Recrystallization from ethyl acetate gave pure IIIa (410 mg., 75%). The infrared spectrum was superimposable with IIIa prepared by sodium borohydride reduction of Ia.

Compound VIIIa (5.46 g.) when oxidized by sodium metaperiodate produced VIIa (5.35 g., 90%). The infrared spectrum was superimposable with VIIa produced by methylation of IIIa.

Compound XIIa (500 mg.) when oxidized by sodium metaperiodate produced XIa (424 mg., 77%). The infrared spectrum was superimposable with XIa produced by treatment of VIIa with base. A mixed m.p. showed no depression.

Compound XIIIa (1.00 g.) when oxidized with sodium metaperiodate produced XIVa (0.79 g., 72%) as a colorless oil.

Analysis — Calcd. for $C_9H_{12}OS$: C, 64.27; H, 7.19; S, 19.03. Found: C, 64.17; H, 6.97; S, 19.19.

Infrared — (chloroform) 3.42, 6.25, 6.70, 6.80, 9.75 (broad, intense).

N.M.R. — (carbon tetrachloride) singlet 2.40 (3H); broadened singlet 2.90 (4H); singlet 7.18 (5H).

Hydrogen peroxide oxidations

In all reactions the material to be oxidized was dissolved in a minimal amount of glacial acetic acid. Excess hydrogen peroxide was added, and the reaction mixture was warmed on a steam bath for 30 minutes. The mixture was diluted with an equal volume of water and cooled. If crystallization did not occur the solution was neutralized with sodium bicarbonate and extracted with chloroform. After drying the extracts over magnesium sulfate the solvent was removed to give the product.

Compound IIIa (10.0 g.) when treated with acidic hydrogen peroxide gave IVa (9.02 g., 83%) m.p. 102-4°. The infrared spectrum was superimposable with IVa produced by sodium borohydride reduction of IIa.

Compound XIa (1.00 g.) when treated with acidic hydrogen peroxide gave Xa (0.93 g., 85%) m.p. 67-70°. Recrystallization from aqueous ethanol raised the m.p. to 77-9°. The infrared spectrum was superimposable with Xa produced by acid and base catalyzed dehydration of IVa.

Compound XIVa (501 mg.) when treated with acidic hydrogen peroxide gave XVa (492 mg., 89%). The infrared spectrum was identical with XVa produced by lithium aluminum hydride reduction of Xa.

Manganese dioxide oxidations

The use of manganese dioxide to oxidize β-hydroxy sulfoxides to β-keto sulfoxides has been reported previously (25). The same procedure was used to oxidize the analogous β-hydroxy sulfides and sulfones.

Compound Va (123 mg.) when oxidized with manganese dioxide gave VIa (99 mg., 82%). The infrared spectrum was superimposable with that of an

authentic sample prepared from ω-bromoacetophenone and methyl mercaptan.

Compound IVa (100 mg.) when oxidized with manganese dioxide gave IIa (89 mg., 88%) m.p. 97-100°. Recrystallization from a chloroform-ethanol mixture raised the m.p. to 104-6. A mixed m.p. with an authentic sample showed no depression.

Sodium metabisulfite reductions

For all reactions the reactants were dissolved in water and heated to approximately 90° while stirring for 24 hours. For every gram of sulfoxide to be reduced, ten grams of sodium metabisulfite and 25 ml. of water were used. At the end of the reaction period the mixture was cooled and extracted thoroughly with ether. The extracts were dried over magnesium sulfate and filtered. Removal of the solvent gave the corresponding sulfide, usually in a high state of purity.

Compound Ia (2.00 g.) when treated with sodium metabisulfite gave VIa (0.95 g., 52%). The infrared spectrum was identical with VIa prepared from ω-bromoacetophenone and methyl mercaptan.

Compound IIIa (4.60 g.) when treated with sodium metabisulfite gave Va (3.90 g., 93%). The infrared spectrum was identical to Va prepared by the lithium aluminum hydride reduction of Ia.

Compound VIIa (1.00 g.) when treated with sodium metabisulfite gave VIIIa (0.73 g., 80%). The infrared spectrum was identical to that of VIIIa prepared by the action base and methyl iodide on Va.

Compound XIa (1.00 g.) when treated with sodium metabisulfite gave XIIa (0.59 g., 66%). The infrared spectrum was identical to XIIa prepared by dehydration of Va with potassium bisulfate.

Compound XLIV (2.00 g.) when treated with sodium metabisulfite gave β-acetoxy-β-phenethyl methyl sulfide (1.65 g., 89%). The infrared spectrum was identical to that of the compound prepared by the reaction of Va with acetyl chloride in pyridine.

Pyrolysis reactions of β-hydroxy sulfoxides

The material to be pyrolyzed was placed in a small flask equipped with a reflux condenser. The flask was then immersed in a Wood's metal bath at 230-240° for 15 minutes. The pyrolysate was then either chromatographed on silica gel or taken up in ethanol, filtered through charcoal, and treated with 2,4-dinitrophenylhydrazine. The results are shown in Table 2.

Table 2. Pyrolysis of β-hydroxy sulfoxides

Material Pyrolyzed	Product	Yield (%)
$C_6H_5CH(OH)CH_2SOCH_3$	$C_6H_5COCH_3$	77
$C_6H_{11}CH(OH)CH_2SOCH_3$	$C_6H_{11}COCH_3$	26
$C_6H_5CH(OH)CH(CH_3)SOCH_3$	$C_6H_5COCH_2CH_3$	29
$C_6H_{11}CH(OH)CH(CH_3)SOCH_3$	$C_6H_{11}COCH_2CH_3$	trace

Reactions of dicumyl peroxide with β-Hydroxy Sulfides

The substrate was placed in a small flask equipped with a reflux condenser. Approximately 0.1 equivalent of dicumyl peroxide was added. The flask was immersed in an oil bath at 150-5° for 24 hours. The stench of methyl mercaptan immediately became noticeable. The mixture was then fractionally distilled through a Vigreux column. The results are summarized in Table 3.

Table 3. Decomposition of β-hydroxy sulfides by free radical mechanism

Substrate	mmoles Substrate	mmoles Dicup	Product[a]	mmoles (Yield %)
$C_6H_5CH(OH)CH_2SCH_3$	20.6	2.9	$C_6H_5COCH_3$[b]	19.0 (93)
$C_6H_{11}CH(OH)CH_2SCH_3$	36.4	3.5	$C_6H_{11}COCH_3$	29.8 (82)
$C_6H_5CH(OH)CH(CH_3)SCH_3$	21.5	2.9	$C_6H_5COCH_2CH_3$	14.8 (67)
$C_6H_{11}CH(OH)CH(CH_3)SCH_3$	15.8	1.8	$C_6H_{11}COCH_2CH_3$	trace

[a] Some acetophenone was found in all cases, presumably due to decomposition of dicumyl peroxide.

[b] When the reaction is carried out in a sealed tube using t-butyl peroxide the main product is the methyl mercaptal of acetophenone (86).

Preparation of ω-methyl-ω-(methylsulfinyl)-acetophenone, XVI

Using the procedure of G. J. Mikol of these laboratories, sodium hydride (0.54 g.) was slurried with 50 ml. of tetrahydrofuran. While stirring, Ia (3.64 g.) in 100 ml. of tetrahydrofuran was added dropwise.

A white solid formed immediately. Fifteen minutes after the addition was complete, excess methyl iodide was added and the mixture was allowed to stir at room temperature for 3 hours. The reaction mixture was poured into 400 ml. of water containing a few crystals of sodium thiosulfate. The aqueous solution was extracted thoroughly with chloroform. The combined extracts were dried over magnesium sulfate and filtered. Removal of the solvent gave XVIa (3.95 g., 100%) as a light yellow oil shown by n.m.r. to be an approximately equal mixture of the expected diastereomers. Upon cooling in an ice bath and triturating with ether one of the diastereomers crystallized. Filtration and washing with more ether gave a white solid, m.p. 74-5°.

Analysis — Calcd. for $C_{10}H_{12}O_2S$: C, 61.21; H, 6.17; S, 16.31. Found: C, 61.23; H, 6.19; S, 16.19.

Infrared — (chloroform) 3.26, 3.35, 6.00 (intense), 6.26, 6.32, 6.90, 7.27, 7.56, 7.71, 9.16 (broad, intense), 9.99, 10.44, 10.67 microns.

N.M.R. — (deuterochloroform) Doublet centered at 1.56, J = 7 c.p.s. (3H); singlet 2.52 (3H); quartet centered at 4.73, J = 7 c.p.s. (1H); multiplet 7.2-8.2 (5H).

Preparation of 1-(methylsulfinyl)-ethyl cyclohexyl ketone, XVIb

In a manner similar to the preparation of XIVa, Ib (7.80 g.) produced XVIb (8.40 g., 100%). Here again crystallization of one diastereomer was effected, m.p. 36-40°.

Analysis — Calcd. for $C_{10}H_{18}O_2S$: C, 59.38; H, 8.97; S, 15.82. Found: C, 59.39; H, 8.95; S, 15.84.

Infrared (carbon tetrachloride) 3.42, 3.51, 5.90 (intense), 6.80, 7.05, 7.30, 7.60, 7.75, 8.26, 8.78, 8.95, 9.40 (broad, intense), 10.25, 10.70, 11.24 microns.

N.M.R. (carbon tetrachloride) broad absorption 1.0-3.0 (17H); quartet centered at 4.08, J = 7 c.p.s. (1H).

Preparation of (1-hydroxy-1-phenyl)-2-propyl methyl sulfide, XVIIIa

Compound XVIa (18.2 g.) when treated with lithium aluminum hydride in the same manner as for the conversion of Ia to Va, produced XVIIIa (12.8 g., 69%), b.p. 105-6° at 0.5 mm. (lit. (85) b.p. 85-7° at 0.3 mm.).

Analysis Calcd. for $C_{10}H_{14}OS$: C, 65.91; H, 7.74; S, 17.56.
Found: C, 66.02; H, 7.69; S, 17.48.

Preparation of (1-cyclohexyl-1-hydroxy)-2-propyl methyl sulfide, XVIIIb

Compound XVIb (9.40 g.) when treated with lithium aluminum hydride in the same manner as for the conversion of Ia to Va, produced XVIIIb (6.27 g., 72%), b.p. 86-8° at 0.5 mm.

Analysis Calcd. for $C_{10}H_{20}OS$: C, 63.79; H, 10.71; S, 17.00
Found: C, 63.83; H, 10.64; S, 16.94.

Infrared (carbon tetrachloride) 2.78, 3.43, 3.50, 6.80, 7.20 7.35, 7.50, 7.65, 7.95, 8.95, 9.18, 10.10, 10.50, 11.25 microns.

N.M.R. (carbon tetrachloride) broad absorption 1.0-1.9 (14H); singlet 1.99 (3H); singlet 2.55 (1H); singlet 3.15 (1H). Shaking the sample with deuterium oxide removed the singlet at 2.55.

Preparation of 1-phenyl-2-(methylsulfinyl)-propanol, XVIIa

Compound XVIa (19.8 g.) when reduced with sodium borohydride as in the conversion of Ia to IIIa gave XVIIa (19.7 g., 98%) as light yellow oil which crystallized after standing for 3 weeks, m.p. 79-101° after recrystallization from ethyl acetate. (The time required for the reaction of methylated β-keto sulfoxides to go to completion is greater than 2 times the time needed for unmethylated β-keto sulfoxides due to the added steric hinderance.)

Analysis — Calcd. for $C_{10}H_{14}O_2S$: C, 60.59; H, 7.12; S, 16.15. Found: C, 60.37; H, 7.27; S, 16.29.

Infrared — (chloroform) 3.00, 3.40 (broad), 6.26, 6.71, 6.90, 7.28 7.55, 7.72, 9.85 (broad, intense), 10.60 microns.

N.M.R. — (Deuterochloroform) multiplet 0.8-1.1 (3H); multiplet 2.4-3.2 (4H); broad absorption 4.3-5.5 (2H); singlet 7.32 (5H). Shaking the sample with deuterium oxide reduces the absorption at 4.3-5.5 by 1 proton.

Preparation of 1-cyclohexyl-2-(methylsulfinyl)-propanol, XVIIb

In the same manner reduction with sodium borohydride of XVIb (3.76 g.) gave XVIIb (3.73 g., 98%).

Analysis — Calcd. for $C_{10}H_{20}O_2S$: C, 58.80; H, 9.87; S, 15.67. Found: C, 58.71; H, 9.73; S, 15.64.

Infrared — (chloroform) 2.95, 3.42, 3.50, 6.90, 9.80 (broad, intense), 10.26 microns.

N.M.R. — (Deuterochloroform) practically continuous absorption from 0.8-4.2; integration useless.

Preparation of 1-methoxy-1-phenyl-2-propyl methyl sulfide, XIXa

Compound XXVIIIa (13.6 g.) when treated with base and methyl iodide as in the conversion of Va to VIIIa, produced XIXa (7.40 g., 51%) as a mixture of diastereomers boiling at 68-71° at 0.2 mm.

Infrared (carbon tetrachloride) 3.35, 3.42, 3.54, 6.24, 6.88, 6.95, 7.27, 7.36, 8.38, 8.90, 9.17 (intense), 9.75, 10.45 microns.

N.M.R. (carbon tetrachloride) 2 doublets centered at 1.00 and 1.24, J = 7 c.p.s. (total 3H); 2 singlets 1.78 and 2.02 (total 3H); multiplet 2.5-3.0 (1H); broadened singlet 3.12 (3H); 2 doublets centered at 4.03 and 4.08, J = 7 c.p.s. (total 1H); broadened singlet 7.21 (5H).

Preparation of 2-phenyl-2-methoxy-t-butyl methyl sulfide, XXa

Compound Ia was treated 2 equivalents of sodium hydride and an excess of methyl iodide in dimethyl sulfoxide solution according to the procedure of Gassman and Richmond (57). The produce mixture was very crude. N.M.R. at this point indicated that a large part of the material had undergone o-methylation after mono-C-methylation. Column chromatography was used to separate approximately a 40% yield of ω,ω-dimethyl-ω-(methylsulfinyl)-acetophenone still as an oil which would not crystallize. This material was reduced with lithium aluminum hydride

N.M.R. (carbon tetrachloride) overlapping singlets 1.54 and 1.58 (total 6H); singlet 2.30 (3H); multiplet 7.2-7.6 (3H); multiplet 7.8-8.1 (2H).

as in the conversion of Ia to Va. The crude product obtained here was directly treated with sodium hydride and methyl iodide in tetrahydrofuran. The spectra of the crude product were in accord with impure XXa. Distillation could not effect the removal of all the impurities. Attempts to chromatograph the material led to decomposition. Consequently, only impure material obtained.

Preparation of β-methoxy-β-phenethyl phenyl sulfide, XXI

Using the method of Werner (88) and 87% yield of ω-(phenylmercapto)-acetophenone was obtained from phenacyl chloride and thiophenol. This keto sulfide (11.4 g.) in 50 ml. of methanol was reduced sodium borohydride (0.5 g.) in 50 ml. of water. After stirring at room temperature for 2 hours the reaction mixture was worked up as in the conversion of Ia to IIIa. The hydroxy sulfide was obtained as a colorless oil (11.10 g. 96%). The hydroxy sulfide (11.0 g.) was treated with sodium hydride and methyl iodide in the same manner as for the conversion of Va to VIIIa to yield XXI (11.0 g., 94%), b.p. 130-2° at 0.2 mm.

Infrared (carbon tetrachloride) 3.30, 3.35, 3.42, 3.55, 6.75, 6.88, 6.95, 7.40, 9.05, 9.16 (intense), 10.25, 10.98 microns.

N.M.R. (deuterochloroform) multiplet 2.8-3.5 with a methyl spike at 3.20 (total 5H); multiplet 4.1-4.4 (1H); multiplet 7.0-7.5 (10).

Preparation of 1-methoxy-1-phenyl-2-propyl phenyl sulfide, XXII

ω-(Phenylmercapto)-acetophenone (22.8 g.) in 50 ml. of dimethyl sulfoxide was added to a slurry of sodium hydride (2.4 g.) in 25 ml. of

dimethyl sulfoxide in a nitrogen atmosphere. When the evolution of hydrogen had ceased, methyl iodide (14.2 g.) was added. The reaction was stirred for 30 minutes, quenched with 300 ml. of water, and thoroughly extracted with chloroform. The extracts were washed with water and dried over magnesium sulfate. Removal of the solvent gave crude ω-methyl-ω-(methylmercapto)-acetophenone (23.4 g., 97%) which was reduced with sodium borohydride (97% yield) and o-methylated (95% yield) as in the preparation of XXI. An overall yield of 77% was obtained from phenacyl chloride. The mixture of diastereomers (predominantly one) boiled at 110-115° at 0.06 mm.

Infrared (carbon tetrachloride) 3.30, 3.36, 3.42, 3.54, 6.75, 6.88, 6.95, 7.27, 7.35, 8.25, 8.45, 8.63, 9.16 (intense), 9.75, 10.45 microns.

N.M.R. (carbon tetrachloride) 2 doublets centered at 1.05 and 1.22, J = 7 c.p.s. (totat 3H); multiplet 3.1-3.8 with spikes at 3.17 and 3.22 (total 4H); doublet centered at 4.10 (1H); multiplet 7.0-7.5 (10H).

Preparation of 1-methoxy-1-phenyl-2-methyl-2-propyl phenyl sulfide, XXIII

In the same fashion as in the preparation of XXII, ω-(phenylmercapto)-acetophenone was dimethylated in one step (91% yield), reduced with sodium borohydride (91% yield), and o-methylated (97% yield). The overall yield of XXIII from phenacyl chloride was 70% as white crystals, m.p. 67-71°. Recrystallization from hexane raised the m.p. to 70-71°.

Infrared (carbon tetrachloride) 3.30, 3.38, 3.42, 3.55, 6.70, 6.88, 6.95, 7.25, 7.35, 8.66, 8.96, 9.11 (intense)

9.33, 9.76, 10.54, 10.95 microns.

N.M.R. (deuterochloroform) singlet 1.05 (3H); singlet 1.22 (3H); singlet 3.21 (3H); singlet 4.08 (1H); multiplet 7.1-7.7 (10H).

Preparation of enol-ethers from β-methoxy sulfides

In all cases the β-methoxy sulfide in dimethyl sulfoxide was placed in a flask equipped with a magnetic stirrer, reflux condenser, and a nitrogen inlet and outlet. An excess of potassium t-butoxide was added and the temperature raised to 70-75°. Reaction times for phenyl sulfides were 5 hours. For the methyl sulfides times of 12 to 24 hours were required. After the desired reaction time, the mixture was cooled and poured into ice water. After extraction with ether, the extracts were washed with water and dried over magnesium sulfate. Removal of the solvent gave the crude product from which the enol-ether was distilled. The pot residue was chromatographed on silica gel to obtain unsaturated sulfides if the crude n.m.r. indicated their presence.

Compound VIIIa (9.1 g.) when treated with potassium t-butoxide (6 g.) in 25 ml. of dimethyl sulfoxide gave α-methoxy styrene XXIV (3.74 g., 56%) boiling at 50-51° at 2 mm. (lit. (89) b.p. 30-2° at 0.4 mm.) and XIIa (1.25 g., 16%) identical with that produced by sodium metabisulfite reduction of XIa. Compound XXIV was readily converted to acetophenone by a trace of acid.

Infrared (carbon tetrachloride) 3.33, 3.40, 3.52, 6.09, 6.25, 6.70, 6.80, 6.88, 7.59, 7.62, 7.77, 8.36, 8.85, 9.30, 8.54, 11.08 microns.

N.M.R. (carbon tetrachloride) singlet 3.70 (3H); 2 doublets 4.10 and 4.58, J = 3 c.p.s. (total 2H); multiplet 7.0-7.6 (5H).

Mass Spectrum molecular ion = 134.

Compound XIX (4.90 g.) when treated with potassium t-butoxide (3 g.) in 25 ml. of dimethyl sulfoxide gave α-methoxy-β-methylstyrene (XXV) (1.72 g., 43%) as a mixture of isomers boiling at 56-7° at 2 mm. (lit. (90) b.p. 96-8° at 19 mm.). No unsaturated sulfide could be detected by n.m.r. Compound XXV was readily converted to propiophenone by treatment with a trace of acid.

Infrared (carbon tetrachloride) 3.28, 3.34, 3.40, 3.53, 6.04, 6.25, 6.69, 6.81, 6.90, 7.32, 7.60, 7.68, 7.79, 7.94, 8.20, 8.35, 8.86, 9.10, 9.31, 9.54, 9.72, 9.85, 10.52, 10.91, 11.07 microns.

N.M.R. (carbon tetrachloride) 2 doublets centered at 1.67, 1.74, J = 7 c.p.s. (total 3H); 2 singlets 3.45 and 3.54 (total 3H); 2 quartets centered at 4.69 and 5.22 (total 1H); multiplet 7.0-7.5 (5H).

Mass Spectrum molecular ion = 148

Only impure XX was available and when it was treated with potassium t-butoxide in dimethyl sulfoxide no trace of α-methoxy-β,β-dimethylstyrene was detected by n.m.r.

Compound XXI (10.8 g.) when treated with potassium t-butoxide (6 g.) in 50 ml. of dimethyl sulfoxide gave α-methoxy-styrene (XXIV) (2.65 g., 49%) and β-(phenylmercapto)-styrene (1.44 g., 15%). The sulfide was identified by hydrogen peroxide oxidation to the sulfone, m.p. 73-74°

(lit. (91) m.p. 74-74.5°).

Compound XXII (3.03 g.) when treated with potassium t-butoxide (1.7 g.) in 25 ml. of dimethyl sulfoxide gave α-methoxy-β-methylstyrene (XXV) (1.18 g., 64%). No unsaturated sulfide was detected by n.m.r.

Compound XXIII (3.40 g.) when treated with potassium t-butoxide (2.5 g.) in 25 ml. of dimethyl sulfoxide gave α-methoxy-β,β-dimethylstyrene (XXVI) (1.65 g., 82%) boiling at 59-60° at 2 mm. as the only detectable product.

Infrared (carbon tetrachloride) 3.36, 3.45, 3.54, 6.02, 6.71, 6.85, 6.94, 7.26, 7.31, 7.80, 7.89, 8.40, 8.82 (intense), 9.35, 9.55, 9.76, 10.24, 10.90 microns.

N.M.R. (carbon tetrachloride) singlet 1.60 (3H); singlet 1.79 (3H); singlet 3.20 (3H); singlet 7.21 (5H).

Mass Spectrum molecular ion = 162.

Preparation of methyl phenethynyl sulfide, XXVII

Compound IIIa (46 g.) in 200 ml. of methylene chloride was added dropwise to thionyl chloride (118 g.) in 200 ml. of methylene chloride. The mixture was stirred for 10 hours. The solvent and the excess thionyl chloride were removed on a steam bath. The residue was distilled under reduced pressure, 108-114° at 0.5-1.0 mm., to give a light yellow liquid (39 g.). This was dissolved in 150 ml. of absolute ethanol and added dropwise to potassium hydroxide (29 g.) in 100 ml. of absolute ethanol. The mixture was refluxed overnight. After filtering, the solvent was removed at aspirator pressure. The product (XXVII) (23.2 g., 63%) was distilled at 85-7° at 2 mm. (lit. (92) b.p. 74° at 2mm.)

Infrared (carbon tetrachloride) 3.26, 3.42, 4.62, 6.27, 6.73, 6.94, 7.04, 7.64, 9.39, 9.76, 10.28, 11.00, 11.62 microns.

N.M.R. (carbon tetrachloride) singlet 2.38 (3H); multiplet 7.1-7.5 (5H).

Methyl phenethynyl sulfide could also be prepared by the reaction of ω-methylsulfinylstyrene (XIa) with thionyl chloride followed by alcoholic potassium hydroxide treatment. The same intermediate methyl chlorostyrenyl sulfide was produced as formed in the reaction of thionyl chloride with IIIa. The intermediate methyl chlorostyrenyl sulfide had a single olefinic hydrogen resonance at 6.57 δ in the n.m.r. and gave an infrared olefinic absorption at 6.04 microns in carbon tetrachloride.

Preparation of ω,ω-dideuterio-ω-(methylsulfinyl)-acetophenone

Compound Ia was dissolved in deuterium oxide containing a trace of potassium carbonate. After stirring for 1 hour at room temperature the solution was thoroughly extracted with chloroform, dried over magnesium sulfate, and filtered. Removal of the solvent gave a white solid, m.p. 83-84.5°.

N.M.R. (deuterochloroform) singlet 2.72 (3H); multiplet 7.3-8.1 (5H).

Preparation of β-phenyl-β-deuterioxy-α,α-dideuterioethyl methyl sulfoxide

In the same manner as the conversion of Ia to IIIa, sodium borohydride reduction of ω,ω-dideuterio-ω-(methylsulfinyl)-acetophenone in deuterium oxide gave a 97% yield of β-phenyl-β-deuterioxy-α,α-dideuterioethyl methyl sulfide as a mixture of diastereomers.

N.M.R. (deuterochloroform) overlapping singlets 2.48 and 2.56 (total 3H); broad absorption 4.8-5.3 (1H); broadened singlet 7.33 (5H).

Preparation of β-deuterio-β-methylsulfinyl)-styrene

Treatment of β-phenyl-β-deuterioxy-α,α-dideuterioethyl methyl sulfoxide (3.00 g.) with excess sodium hydride and methyl iodide in tetrahydrofuran as in the preparation of XIa produced β-deuterio-β-(methylsulfinyl)-styrene (2.08 g.), m.p. 62-3.

N.M.R. (carbon tetrachloride) singlet 2.59 (3H); broadened singlet 7.08 (1H); multiplet 7.1-7.6 (5H).

Preparation of α-chloro-β-deuterio-β-methylmercapto)-styrene

Treatment of either β-phenyl-β-deuterioxy-α,α-dideuterioethyl methyl sulfoxide of β-deuterio-β-(methylsulfinyl)-styrene with thionyl chloride produced predominantly α-chloro-β-deuterio-β-(methylmercato)-styrene. The n.m.r. showed a methyl absorption at 2.41 p.p.m. and aromatic absorption at 7.2-7.6 p.p.m. In the β-deuterio-β-(methylsulfinyl)-styrene case some exchange occurred as evidenced by olefinic absorption at 6.57 p.p.m. which integrated to less than 0.2 of a proton based on the integration of the methyl peak. The α-chloro-β-deuterio-β-(methylmercapto)-styrene produced from β-phenyl-β-deuterioxy α,α-dideuterioethyl methyl sulfoxide did not show any absorption in the olefinic region in the n.m.r.

Preparation of acetoxymethyl β-styryl sulfide, XXXIa

Compound XIa (5.00 g.) in 20 ml. of acetic anhydride was placed on a steam bath for 12 hours. The mixture was cooled and added cautiously to a

saturated solution of sodium bicarbonate. When the reaction had ceased, the mixture was extracted thoroughly with chloroform. The extracts were dried over magnesium sulfate. Removal of the solvent followed by distillation under reduced pressure gave XXXIa (4.78 g., 92%) as a colorless liquid boiling at 94-95° at 0.08 mm.

Analysis — Calcd. for $C_{11}H_{12}O_2S$: C, 63.45; H, 5.81; S, 15.37. Found: C, 63.40; H, 5.84; S, 15.38.

Infrared — (carbon tetrachloride) 3.32, 5.71 (intense), 6.27, 6.70, 6.93, 7.07, 7.32, 7.59, 7.95, 8.39 (intense), 9.84, 10.25, 10.65 microns.

N.M.R. — (carbon tetrachloride) singlet 1.98 (3H); singlet 5.22 (2H); AB quartet, $\delta_A = 6.53$, $\delta_B = 6.77$, $J_{AB} = 15.5$ c.p.s. (2H); broadened singlet 7.18 (5H).

Reaction of acetoxy β-styryl sulfide, XXXIa, with mineral acid.

Compound XXXIa (1.00 g.) in 5 ml. of water and 10 ml. of 85% phosporic acid was refluxed for 2 hours. Upon cooling, the reaction mixture was extracted with chloroform and dried over magnesium sulfate. Removal of the solvent gave the β-styryl mercaptal of formaldehyde (XXXIIa) (0.68 g.) as a brown oil. Compound XXXIIa apparently decomposed on attempted g.l.p.c. purification. It was necessary to raise the temperature too high to elute the material in a reasonable time. Column chromatography on silica gel using benzene as the eluent did not remove the color. Other attempts at hydrolysis of XXXIIa using hydrochloric acid and aqueous ethanol solvent led to the same product. However, traces of acetaldehyde were detected by n.m.r.

Attempted acylation of ω-(methylsulfinyl)-acetophenone, Ia

Compound Ia (9.10 g.) in 100 ml. of tetrahydrofuran was added dropwise to well stirred slurry of sodium hydride (1.3 g.) in 50 ml. of tetrahydrofuran. After the evolution of hydrogen had ceased, acetic anhydride (5.1 g.) was added dropwise. The reaction mixture was stirred at room temperature for 2 hours, then quenched with water, and extracted with chloroform. The extracts were washed with saturated sodium bicarbonate solution and then water. After drying over sodium sulfate, the solvent was removed to give a light yellow oil. Distillation gave ω-acetoxy-ω-(methylmercapto)-acetophenone (XXXIVa) (8.35 g., 75%) boiling at 98-100° at 0.1 mm. Identical material could be obtained by treatment of ω-hydroxy-ω-(methylmercapto)-acetophenone (Pummerer rearrangement product of Ia) with acetic anhydride in pyridine.

Infrared (carbon tetrachloride) 3.30, 3.43, 3.50, 5.70 (intense), 5.92 (intense), 6.27, 6.91, 7.00, 7.32, 7.45, 8.25 (broad, intense), 9.60, 10.45, 11.15 microns.

N.M.R. (carbon tetrachloride) singlet 1.99 (3H); singlet 2.08 (3H); singlet 6.74 (1H); multiplet 7.2-7.5 (3H); multiplet 7.8-8.1 (2H).

Attempted acylation of (methylsulfinylmethyl) cyclohexyl ketone, Ib

By the same procedure used in the attempted acylation of Ia, compound Ib (4.6 g.) when treated with sodium hydride (0.8 g.) and acetic anhydride (2.6 g.) produced XXXIVb (4.05 g., 71%), b.p. 105-9° at 0.5 mm. Identical material could be obtained by treating the Pummerer rearrangement product of Ib with acetic anhydride in pyridine.

Infrared (carbon tetrachloride) 3.42, 3.51, 5.70 (intense), 5.83 (intense), 8.80, 9.65, 10.28, 10.95 microns.

N.M.R. (carbon tetrachloride) broad absorption 1.0-3.0 with methyl singlets at 1.99 and 2.10 (total 17H); singlet 5.90 (1H).

Attempted acylation of ω-methyl-ω-(methylsulfinyl)-acetophenone, XVIa

When the same procedure used in the attempted acylation of Ia was applied to XVIa (4.90 g.) the light yellow oil (5.55 g.) obtained gave spectra indicative of a mixture of starting material and o-acylated product. The infrared showed carbonyl absorption at 5.65 microns, vinyl acetate C-O stretch at 8.33 microns, and sulfoxide absorption at 9.55. The n.m.r. showed that most of the normal aromatic absorption (2 ortho protons shifted to lower field than the meta and para protons when a carbonyl is adjacent to the ring) had collapsed to a more compact absorption envelope slightly to higher field. Attempts to separate the enol-acetate from Ia by column chromatography on silica gel apparently led to hydrolysis since only Ia was obtained upon elution.

Acylation of ω-(methylmercapto)-acetophenone, VIa

Following the same procedure used for the attempted acylation of Ia, compound VIa (4.15 g.), sodium hydride (0.6 g.), and acetic anhydride (2.55 g.) produced exclusively the o-acylated product (XXVIIIa) (4.92 g., 92%) as a viscous oil. The oil slowly crystallized upon standing. Recrystallization from ether gave colorless prisms, m.p. 55-56°.

Analysis Calcd. for $C_{11}H_{12}O_2S$: C, 63.45, H, 5.81, S, 15.37.
Found: C, 63.62; H, 5.82, S, 15.35.

Infrared (carbon tetrachloride) 3.30, 3.43, 5.66 (intense), 6.23, 6.70, 7.00, 7.32, 8.40 (intense), 9.62, 9.75, 11.20 microns.

N.M.R. (carbon tetrachloride) singlet 2.23 (3H); singlet 2.30 (3H); singlet 6.31 (1H); broadened singlet 7.26 (5H).

Preparation of 3-(methylmercapto)-3-(methylsulfonyl)-2,4-pentanedione, XLI (R = CH_3)

A solution of 2,4-pentanedione (10.0 g.) in 100 ml. of tetrahydrofuran was added dropwise with stirring to a suspension of sodium hydride (2.4 g.) in 25 ml. of tetrahydrofuran. When the evolution of hydrogen ceased, methylsulfinyl chloride (9.8 g.) was added cautiously. The reaction mixture was allowed to stir overnight at room temperature. The mixture was poured into 400 ml. of water and extracted throughly with chloroform. The extracts were dried over magnesium sulfate. Removal of the solvent gave 11.6 g. of a yellow pasty mass. Two recrystallizations from a chloroform-ether mixture gave XLI (7.0 g., 31% based on pentanedione) as colorless needles, m.p. 102.5-104°.

Analysis Calcd. for $C_7H_{12}O_4S_2$: C, 37.50; H, 5.40; S, 28.55. Found: C, 37.35; H, 5.41; S, 28.85.

Infrared (chloroform) 3.42, 5.81 (intense), 7.14, 7.38 (intense), 7.60 (intense), 8.85 (intense), 10.40, 11.4 microns.

N.M.R. (deuterochloroform) singlet 2.29 (3H); singlet 2.41 (6H); singlet 3.10 (3H).

Preparation of dibenzoyl-(methylmercapto)-(methylsulfonyl)-methane, XLI ($R = C_6H_5$)

By the same procedure described for the preparation of XLI ($R = CH_3$), dibenzoylmethane (4.48 g.) was treated with sodium hydride (0.5 g.) and methylsulfinyl chloride (2.0 g.). Fractional crystallization of the crude product mixture gave unreacted dibenzoylmethane and XLI ($R = C_6H_5$) (1.94 g., 28% based on dibenzoylmethane), m.p. 143-4°.

Analysis Calcd. for $C_{17}H_{16}O_4S_2$: C, 58.62; H, 4.63; S, 18.32.
Found: C, 58.33; H, 4.71; S, 18.14

Infrared (chloroform) 5.95 (intense), 6.02 (intense), 6.26, 6.33, 6.92, 7.54, 7.64 (intense), 8.80 (intense), 9.95, 10.37 microns.

N.M.R. (deuterochloroform) singlet 2.20 (3H); singlet 3.21 (3H); multiplet 7.2-7.6 (6H); multiplet 7.8-8.2 (4H).

Preparation of ω-(methylmercapto)-ω-(methylsulfonyl)-acetphenone, XLII

A solution of ω-(methylsulfinyl)-acetophenone (9.10 g.) in 150 ml. of tetrahydrofuran was added with stirring to a suspension of sodium hydride (1.2 g.) in 25 ml. of tetrahydrofuran. When the evolution of hydrogen had ceased, methylsulfinyl chloride (5.0 g.) was added dropwise. Stirring was continued for 1 hour after the addition was complete. The reaction mixture was poured into 300 ml. of water and extracted with chloroform. After drying over magnesium sulfate, the solvent was removed to give XLII (9.15 g., 75%) as a white solid, m.p. 100-111°. Recrystallization from a chloroform-ether mixture raised the m.p. to 115-7°.

Analysis Calcd. for $C_{10}H_{12}O_3S_2$: C, 49.18, H, 4.95; S, 26.21.

Found: C, 49.06; H, 4.91; S, 26.15.

Infrared (chloroform) 5.97 (intense), 6.26, 6.92, 7.08, 7.65 (intense), 7.85, 9.01 (intense), 10.50 microns.

N.M.R. (deuterochloroform) singlet 2.47 (3H); singlet 3.23 (3H); singlet 5.36 (1H); multiplet 7.4-7.7 (3H); multiplet 7.9-8.1 (2H).

Preparation of β-acetoxy-β-phenethyl methyl sulfoxide, XLIVa

Compound IIIa (18.4 g.) was dissolved in 100 ml. of pyridine. Twenty milliliters of acetic anhydride was added carefully. The mixture was stirred at room temperature for 24 hours and then poured into 300 ml. of water. After thorough extraction with chloroform, the extracts were washed with dilute hydrochloric acid and then water. After drying over magnesium sulfate, the solvent was removed to give XLIVa (11.4 g., 47%) melting at 107-110°. Recrystallization from ether raised the m.p. to 110-111°.

Analysis Calcd. for $C_{11}H_{14}O_3S$: C, 58.40; H, 6.24; S, 14.10.
Found: C, 58.40; H, 6.19; S, 14.30.

Infrared (chloroform) 3.42, 5.75 (intense), 6.70, 6.88, 7.13, 7.30, 7.71, 8.2 (broad, intense), 9.6 (broad, intense), 10.25, 10.50 microns.

N.M.R. (deuterochloroform) singlet 2.00 (3H); multiplet 6.0-6.3 (1H); singlet 7.36 (5H).

Experimental Detail for the Condensations of Dimethyl Sulfoxide and Dimethyl Sulfone with Dicarboxylic Esters And Further Reactions of the Condensation Products

Preparation of 2-chloro-2-(methylmercapto)-1,3-naphthindandione, XLVIII: Reaction of dimethyl 2,3-naphthalenedicarboxylate with dimethyl sulfoxide in the presence of sodium methoxide

According to the procedure of Becker and Russell (8), dimethyl 2,3-naphthalenedicarboxylate (2.44 g.) in 10 ml. of dimethyl sulfoxide was added dropwise to a suspension of sodium methoxide (2.16 g.) in 20 ml. of dimethyl sulfoxide. The mixture was stirred under nitrogen for 4 hours. The solvent was removed under reduced pressure (1 mm., bath temperature 65°). To the pasty yellow residue was added 50 ml. of ice water and 50 ml. of ether. The aqueous layer was added dropwise to a well stirred beaker of 5M hydrochloric acid (100 ml.) in an ice bath. The yellow precipitate was filtered and dried in a vacuum desiccator. This material (2.55 g.) which proved to be mostly 2,3-naphthalenedicarboxylic acid, was taken up in hot 95% ethanol. Upon slight cooling, light yellow crystals of XLVIII (337 mg., 12%) formed, m.p. 145-150°. (The solution was still slightly warm when filtered since strong cooling brought out the acid.) Recrystallization from a chloroform-hexane mixture raised the m.p. to 154-155°.

Analysis — Calcd. for $C_{14}H_9ClO_2S$: C, 60.76; H, 3.28; Cl, 12.81; S, 11.59.

Found: C, 60.91; H, 3.46; Cl, 12.70; S, 11.45.

Infrared — (chloroform) 5.71 (intense), 5.82 (intense), 6.18, 6.91,

7.15, 9.00 (broad), 11.00 microns.

N.M.R. (deuterochloroform) singlet 2.48 (3H); multiplet 7.6-7.9 (2H); multiplet 8.0-8.3 (2H); singlet 8.53 (2H).

Mass Spectrum molecular ion = 276; $M^+ + 2$ = 39% of M^+ indicating 1 chlorine atom and 1 sulfur atom.

Preparation of 2-chloro-2-(methylmercapto)-1,3-naphthindandione, XLVIII: Inverse addition of methylsulfinylcarbanion to dimethyl 2,3-naphthalenedicarboxylate.

A solution of methylsulfinylcarbanion made from sodium hydride (2.4 g.) and 50 ml. of dimethyl sulfoxide was added over a 1 hour period by a hypodermic syringe to dimethyl 2,3-naphthalenedicarboxylate (6.10 g.) in 50 ml. of dimethyl sulfoxide. Vigorous stirring is essential during the addition. As soon as the addition was complete, the mixture was poured into 100 ml. of ice water. Ether extraction was employed to remove any unreacted ester. The aqueous layer was added dropwise to 100 ml. of 6M hydrochloric acid in an ice bath. The precipitate was filtered and dried to give XLVIII (4.10 g., 59%). The infrared and n.m.r. spectra were identical with that of the material produced by the sodium methoxide catalyzed reaction.

Preparation of 1,2,3-naphthindantrione hydrate, XLIX

Compound XLVIII (1.00 g.) was added to 500 ml. of hot water in a 1 liter erlenmeyer flask and kept on a steam bath for 24 hours. The volume was reduced to approximately 100 ml. The reaction mixture was filtered while hot to remove a brown, extremely insoluble solid (upon drying this

solid weighing 240 mg. did not melt below 325°, and was very insoluble in most of the common organic solvents). Upon cooling to room temperature, the filtrate deposited XLIX (280 mg., 34%) as light yellow needles, m.p. 278-280° after turning green upon loss of water at 140-150° (lit. (93) m.p. 279-281°, loses water at 150° and turns green). Both XLVIII and XLIX give a green color reaction with amino acids in contrast to the purple color with ninhydrin.

N.M.R. (dimethyl sulfoxide) broad absorption 7.3-7.7 (2H); multiplet 7.7-8.0 (2H); multiplet 8.2-8.5 (2H); singlet 8.74 (2H). Shaking the sample with deuterium oxide causes the absorption at 7.3-7.7 to disappear.

Mass Spectrum as expected, XLIX shows no molecular ion--only $(M - 18)^{+} = 210$.

Preparation of 5,5-dimethyl-2-(methylsulfinyl)-3-(methylsulfinylmethyl)-Δ^2-cyclohexenone, LIII

A solution of dimethyl 3,3-dimethylglutarate (4.7 g.) in 50 ml. of tetrahydrofuran was added dropwise to a solution of methylsulfinylcarbanion prepared under nitrogen from sodium hydride (2.4 g.) and 50 ml. of dimethyl sulfoxide. The mixture was stirred for three hours at room temperature and then poured into 100 ml. of ice water, carefully neutralized with dilute hydrochloric acid, and thoroughly extracted with chloroform. The extracts were dried over magnesium sulfate and filtered. Removal of the solvent on a rotary evaporator yielded a yellow oil. Trituration with cold ether produced LIII (3.0 g., 46%), m.p. 68-81°. Column chromatography on silica gel produce an additional 0.8 g. for a total yield of

58%. Recrystallization from chloroform-ether solution did not effect separation of the diastereomers, m.p. 68-88°.

Analysis Calcd. for $C_{11}H_{18}O_3S_2$: C, 50.37; H, 6.92; S, 24.90. Found: C, 50.47; H, 7.00; S, 24.68.

Infrared (chloroform) 3.42, 6.01 (intense), 6.26 (intense), 6.83, 7.12, 7.30, 7.40, 7.71, 8.80, 8.98, 9.65 (broad, intense), 10.20, 10.45, 11.06 microns.

N.M.R. (deuterochloroform) singlet 1.11 (6H); singlet 2.40 (2H); singlet 2.65 (2H); 2.75 (3H); 2 singlets 2.97 and 2.99 (total 3H); multiplet 3.6-5.2 (2H).

In addition, the chromatography produced a yellow oil (0.3 g.) shown to be 5,5-dimethyl-2-(methylmercapto)-3-carboxaldehyde-2-cyclohexenone (LXI).

Infrared (carbon tetrachloride) 3.38, 3.42, 3.50, 5.93 (intense), 5.98 (intense), 6.80, 7.05, 7.21, 7.31, 8.00, 8.45, 8.74, 8.88, 9.07, 10.15, 10.45, 11.24 microns.

N.M.R. (carbon tetrachloride) singlet 1.05 (6H); 2 singlets 2.73 and 2.40 (total 7H); singlet 10.56 (1H).

Mass Spectrum molecular ion = 198; $(M+2)^+$ ion = 6% of M^+ indicating one sulfur atom.

Preparation of 2-(methylsulfonyl)-3-(methylsulfonylmethyl)-indenone, LIV

To a solution of methylsulfonylcarbanion prepared under nitrogen from dimethyl sulfone (9.4 g.), sodium hydride (2.4 g.), and 50 ml. of dimethyl sulfoxide was added diethyl phthalate (5.55 g.) in 50 ml. of tetrahydrofuran. After stirring for 3 hours at room temperature, the

mixture was poured into water and acidified with hydrochloric acid. The mixture was thoroughly extracted with chloroform. The extracts were washed with water and dried over magnesium sulfate. Removal of the solvent gave LIV (5.20 g., 70%) as a bright yellow solid m.p. 173-178°. Several recrystallizations from hot chloroform-methanol mixtures raised the m.p. to 193-5°.

Analysis Calcd. for $C_{12}H_{12}O_5S_2$: C, 48.01; H, 4.03; S, 21.32. Found: C, 47.98; H, 4.05; S, 21.38.

Infrared (Potassium bromide) 3.32, 3.43, 5.82 (intense), 6.22, 6.36, 6.88, 7.10, 7.32, 7.67 (intense), 8.45, 8.75 (intense), 9.01, 9.25, 9.70, 10.35, 10.78, 11.53, 13.15 (broad), 13.77 microns.

N.M.R. (Deuterochloroform) singlet 3.17 (3H); singlet 3.26 (3H); singlet 4.98 (2H); broadened singlet 7.56 (4H).

Mass Spectrum molecular ion = 300.

Upon standing overnight the aqueous phase deposited some white crystal (773 mg., 10%) of an isomer (LV) melting at 215-217°. This compound was considerably more insoluble than LIV.

Infrared (potassium bromide) 3.32, 3.42, 5.76 (intense), 6.11, 6.26, 6.31, 6.80, 7.03, 7.67 (intense), 7.86, 8.08 8.32, 8.48, 8.84 (intense), 9.47, 10.43, 11.79, 11.95, 12.24, 12.55, 13.01, 13.20, 13.35 microns.

N.M.R. (trifluoroacetic acid) singlet 3.48 (6H); doublet centered at 6.18, J = 1.5 c.p.s. (1H); doublet centered at 7.40, J = 1.5 c.p.s. (1H); multiplet 7.7-8.2 (4H).

Mass Spectrum molecular ion = 300.

Preparation of 2-(methylsulfonyl)-3-(methylsulfonylmethyl)-naphthindenone, LVI

Dimethyl 2,3-naphthalenedicarboxylate (2.44 g.) in 10 ml. of dimethyl sulfoxide was added dropwise to a solution of methyl-sulfonyl-carbanion prepared under nitrogen from dimethyl sulfone (3.8 g.) and sodium hydride (1 g.) in 25 ml. of dimethyl sulfoxide. After stirring for 3 hours at room temperature, the mixture was poured into water and acidified with hydrochloric acid. A yellow precipitate formed immediately. Filtration and vacuum drying produced LVI (2.94 g., 84%), m.p. 225-235°, decomposition. Recrystallization from acetic acid-ethanol raised the m.p. to 244-246°, decomposition.

Analysis — Calcd. for $C_{16}H_{14}O_5S_2$: C, 54.86; H, 4.03; S, 18.27. Found: C, 54.85; H, 4.06; S, 18.27.

Infrared — (potassium bromide) 3.33, 3.42, 5.88 (intense), 6.16, 6.24, 6.40, 6.90, 7.10, 7.65 (intense), and 8.59, 8.80 (intense), 9.46, 10.38, 11.10, 12.79 microns.

N.M.R. — (trifluoroacetic acid) 2 singlets 3.47 and 3.52 (total 6H); singlet 5.37 (2H); multiplet 7.6-8.2 (6H).

The zinc-acetic acid reduction of LIII

According to the procedure of Russell and Mikol (44), compound LIII (9.20 g.) dissolved in 300 ml. of acetic acid-ethanol solvent (60-40 by volume) was added slowly to a well stirred slurry of zinc dust (20 g.) in 300 ml. of the same mixed solvent. Stirring was continued for 1 hour. The mixture was filtered, and the solids were washed with benzene. The filtrate was neutralized with sodium bicarbonate and extracted with

benzene. The combined benzene solutions were dried over magnesium sulfate. Removal of the solvent gave 2-(methylsulfinyl)-3,5,5-trimethyl-Δ2-cyclohexenone (LVII) (2.2 g., 31%), m.p. 77-78°.

Analysis Calcd. for $C_{10}H_{16}O_2S$: C, 59.98; H, 8.05; S, 15.98. Found: C, 59.88; H, 8.19; S, 15.89.

Infrared (chloroform) 3.40, 6.00 (intense), 6.23, 6.82, 7.11, 7.20, 7.30, 7.40, 7.72, 7.90, 8.80, 8.96, 9.60, (broad, intense), 10.50, 10.75 microns.

N.M.R. (deuterochloroform) singlet 1.05 (6H); 2 singlets 2.32 and 2.38 (total 7H); singlet 2.90 (3H).

If the reaction was allowed to run for longer periods of time, a large number of products were obtained, the major one being 2-(methylmercapto)-3,5,5-trimethyl-2-cyclohexenone (LVIII), b.p. 82-84° at 0.5 mm. Compound LVIII could be oxidized to LVII.

N.M.R. (deuterochloroform) singlet 1.02 (6H); broadened singlet 2.21 (6H); broadened singlet 2.35 (4H).

The Raney nickel reduction of LIII

Compound LIII (2.00 g.) was dissolved in 200 ml. of absolute ethanol and placed in a flask containing approximately 50 g. of W-2 Raney nickel (94). The flask was equipped with an efficient stirrer and a reflux condenser. While stirring, the ethanol was heated to reflux. After 6 hours the reaction was cooled and filtered through scintered glass funnel. The residue was thoroughly washed with ethanol, taking care to always keep the filter cake covered with solvent (Raney nickel is highly pyrophoric). Removal of the ethanol produced 3,3,5-trimethylcyclo-

hexanol (LIX) (692 mg., 64%) as a colorless oil which solidified when a seed crystal from an authentic sample was added. The authentic sample was prepared by a two-step reduction (hydrogen over palladium on charcoal followed by sodium borohydride) of isophorone. The infrared spectra were superimposable.

The Pummerer rearrangement of LIII

Compound LIII (0.8 g.) was dissolved in 2 ml. of dimethyl sulfoxide, 10 ml. of water, and 2 ml. of concentrated hydrochloric acid. A yellow oil began to settle out of solution almost immediately. The reaction appeared to be complete in 30 minutes but was allowed to proceed for 2 hours. The n.m.r. showed 2 aldehyde protons at 10.56 p.p.m. and 11.00 p.p.m. in roughly equal amounts. The peak at 10.56 had been shown to arise from the aldehyde function of LXI (see preparation of LII). Although the compounds could not be isolated the peak at 11.00 p.p.m. was assumed to belong to the corresponding sulfoxide (LX).

Preparation of 5,5-dimethyl-2-(methylsulfonyl)-3-(methylsulfonyl-methyl)-Δ^2-cyclohexenone, LXII

Dimethyl 3,3-dimethylglutarate (4.70 g.) was reacted under nitrogen with the methylsulfonyl carbanion prepared from dimethyl sulfone (9.4 g.), sodium hydride (2.4 g.), and 50 ml. of dimethyl sulfoxide. When worked up by the procedure used in the preparation of LIV, LXII (5.89 g., 80%) was obtained as a white solid m.p. 150-162°. Recrystallization from chloroform raised the m.p. to 174-174.5°. Compound LXII was obtained in low yield when only one equivalent of carbanion was used. Compound LXII

(70%) was also obtained when potassium t-butoxide was used instead of sodium hydride as the base. If one equivalent of dimethyl sulfone was used with 4 equivalents of base the product was still LXII (22%). Inverse addition of the carbanion to the diester also led to LXII (31%).

Analysis — Calcd. for $C_{11}H_{18}O_5S_2$: C, 44.90; H, 6.17; S, 21.76. Found: C, 45.06; H, 6.13; S, 21.78.

Infrared — (chloroform) 3.45, 5.93 (intense), 6.25 (intense), 6.81, 7.13, 7.28, 7.37, 7.65 (intense), 8.84 (intense), 9.08, 10.17, 10.35, 10.65, 10.80, 11.60 microns.

N.M.R. — (deuterochloroform) singlet 1.09 (6H); singlet 2.45 (2H); singlet 2.79 (2H); singlet 3.08 (3H); singlet 3.27 (3H); singlet 4.88 (2H).

Preparation of 5,5-dimethyl-2-(phenylsulfonyl)-3-(phenylsulfonylmethyl)-Δ^2-cyclohexenone, LXIII

Essentially the same procedure as for the preparation of LIV was used; but, phenyl methyl sulfone (15.6 g.) was used instead of dimethyl sulfone. Dimethyl 3,3-dimethylglutarate (4.70 g.) gave LXIII (4.84 g., 46%) as white crystals, m.p. 205-207°.

Analysis — Calcd. for $C_{21}H_{22}O_5S_2$: C, 60.28; H, 5.30; S, 15.30. Found: C, 60.66; H, 5.35; S, 15.10.

Infrared — (chloroform) 3.40, 5.93 (intense), 6.29 (intense), 6.82, 6.91, 7.12, 7.20, 7.30, 7.37, 7.63 (intense), 8.74 (intense), 9.27 (intense), 10.02 microns.

N.M.R. — (deuterochloroform) singlet 1.03 (6H); singlet 2.27 (2H); singlet 2.90 (2H); singlet 5.12 (2H); multiplet

7.4-7.7 (6H); multiplet 7.9-8.2 (4H).

The reaction of Raney nickel with LXII

When compound LXII was treated with W-2 Raney nickel in refluxing ethanol for periods up to 48 hours only mixtures of compounds still containing sulfones were obtained. Adding external hydrogen pressure (up to 1000 p.s.i.) had no effect. However, when the reaction was carried out in the manner of Papa and Schwenck (71,72) a single product was obtained. Compound LXII (3.00 g.) in 100 ml. of 10% sodium hydroxide was heated to approximately 90° and treated with Raney nickel-aluminum alloy (10 g.) in small portions while stirring. Stirring and heating were continued for 1 hour after the addition was complete. The volume was maintained constant by the addition of water from time to time. The mixture was filtered while hot and washed with several volumes of hot water. (Caution! The residue is pyrophoric.) The filtrate was added to an excess of hydrochloric acid to avoid the precipitation of aluminum salts. The acidic solution was extracted with chloroform. After drying over magnesium sulfate the solvent was removed to give a white solid, 2-(methylsulfonyl)-3,5,5-trimethylcyclohexanone (LXIV) (2.09 g., 94%), m.p. 67-70°. Recrystallization from ether raised the m.p. to 71-72°.

Analysis — Calcd. for $C_{10}H_{18}O_3S$: C, 55.03; H, 8.31; S, 14.66
Found: C, 55.08; H, 8.30; S, 14.69.

Infrared — (carbon tetrachloride) 3.42, 5.86 (intense), 6.87, 7.12, 7.25, 7.33, 7.64 (intense), 8.44, 8.82 (intense), 9.10, 9.27, 9.57, 10.45, 11.38 microns.

N.M.R. (carbontetrachloride) singlet 1.02 (6H); doublet centered at 1.30, J = 6.5 c.p.s. (3H); broad absorption 1.5-1.7 (2H); broadened singlet 2.30 (2H); multiplet 2.4-2.9 (1H); singlet 2.97 (3H); doublet centered at 3.50, J = 10 c.p.s. (1H).

The reaction of Raney nickel with LXIII

Compound LXIII (500 mg.) was treated with Raney nickel (40 g.) in 200 ml. of refluxing ethanol for 12 hours. When worked up as in the reaction of LIII the product was 3,5,5-trimethylcyclohexanol (LIX) (69 mg., 47%). The infrared spectrum was identical with an authentic sample.

Preparation of hexahydro-2-(methylsulfinylmethyl)-Δ2-inden-1-one, LXV

The procedure used was the same as for the preparation of LIII. Diethyl cis-1,2-cyclohexanedicarboxylate (5.70 g.) gave LXV (2.30 g., 29%) as a white solid, m.p. 131-134°. Recrystallization from a chloroform-ether mixture raised the m.p. to 134-137°, decomposition.

Analysis Calcd. for $C_{12}H_{18}O_3S_2$: C, 52.55; H, 6.62; S, 23.34. Found: C, 52.41; H, 6.65; S, 23.47.

Infrared (chloroform) 3.43, 3.51, 5.88 (intense), 6.30, 6.37, 6.95, 7.14, 7.38, 7.76, 8.61, 8.95, 9.15, 9.55 (broad, intense), 10.50 (broad), 11.67 microns.

N.M.R. (deuterochloroform) broad absorption 1.0-3.0 with methyl singlets at 2.72 and 2.99 (total 16H); AB quartet (almost AX) $\delta_A = 3.98$, $\delta_B = 4.90$, $|J_{AB}| = 12$ c.p.s. (2H).

The reaction of Raney nickel with LXV

Compound LXV (567 mg.) was treated with Raney nickel (15 g.) in 250 ml. of refluxing ethanol for 5 hours. Work up as in the reaction of LIII gave hexahydro-3-methyl-1-indanone (LXVII) (221 mg., 70%). The 2,4-dinitrophenylhydrazone melted a 151-3° (lit. (95) m.p. 152-4°).

Infrared (carbon tetrachloride) 3.42, 3.50, 5.75 (intense), 6.91, 7.10, 7.27, 8.60, 8.87, 9.33 microns.

N.M.R. (carbon tetrachloride) broad absorption 0.8-2.6 with doublet centered at 1.02, J = 6.5 c.p.s.

If the reaction is allowed to go for longer times two alcohols (LXVIII) appear at the expense of LXVII. The 3 components can be separated by g.l.p.c. on a 6 foot 20% GEXE60 silicone gum on Chromosorb W column.

Preparation of hexahydro-2-(methylsulfonyl)-3-(methylsulfonylmethyl)-Δ^2-inden-1-one, LXVI

Using the same procedure as for the preparation of LIV, diethyl cis-1,2-cyclohexanedicarboxylate (5.70 g.) gave LXVI (6.60 g., 93%) as a pale yellow solid, m.p. 141-144°. Recrystallization from methanol raised the m.p. to 143-144°.

Analysis Calcd. for $C_{12}H_{18}O_5S_2$: C, 47.06; H, 5.63; S, 20.90. Found: C, 47.00; H, 5.71; S, 20.83.

Infrared (chloroform) 3.41, 3.48, 5.81 (intense), 10.37, 10.49, 11.09, 11.60 microns.

N.M.R. (deuterochloroform) broad absorption 1.0-3.0 (10H); singlet 3.12 (3H); singlet 3.20 (3H); AB quartet

(almost AX) $\delta_A = 4.18$, $\delta_B = 5.40$, $|J_{AB}| = 12$ c.p.s. (2H).

The reaction of Raney nickel with LXVI

Compound LXVI (2.00 g.) was treated with W-2 Raney nickel (50 g.) in 200 ml. of refluxing ethanol for 6 hours. Work up as in the reaction of LIII gave a pasty solid (550 mg.) which was put on a Florisil column and eluted with chloroform. In this way hexahydro-2-(methylsulfonyl)-3-methyl-1-indanol (LXIX) (373 mg., 25%) was obtained as a white solid, m.p. 151°.

Infrared (chloroform) 2.83, 3.44, 3.51, 6.94, 7.12, 7.75, (intense), 8.91 (intense), 9.44, 10.35, 11.06 microns.

N.M.R. (deuterochloroform) broad absorption 0.8-2.4 with a doublet rising out at 1.18, J = 6.5 c.p.s. (total 14H); broad absorption 2.6-2.8 (1H); multiplet 2.9-3.2 with singlet at 3.05 (total 4H); multiplet 3.7-4.1 (1H). Shaking with deuterium oxide causes the absorption 2.6-2.8 to disappear.

The reaction of the methylsulfonylcarbanion with dimethyl cis-1,3-cyclohexanedicarboxylate

Using the same procedure as for the preparation of LIV, dimethyl cis-1,3-cyclohexanedicarboxylate (5.0 g.) gave 1,3-cyclohexylenyl cis (methylsulfonylmethyl) ketone (LXX) (5.25 g., 65%) as a white solid m.p. 153-155°. Recrystallization from chloroform with a trace of methanol raised the m.p. to 157-158°.

Analysis Calcd. for $C_{12}H_{20}O_6S_2$: C, 44.44; H, 6.22; S, 19.74.

Found: C, 44.37; H, 5.93; S, 19.89.

Infrared (potassium bromide) 3.33, 3.41, 3.51, 5.86 (intense), 6.89, 7.10, 7.33, 7.65 (intense) 8.20, 8.65 (intense), 8.87 (intense), 9.45, 9.15, 10.33, 10.66, 11.08, 11.26, 12.44, 13.10, 13.75 microns.

N.M.R. (trifluoroacetic acid) broad absorption 1.0-3.2 (10H); singlet 3.30 (6H); singlet 4.57 (4H).

No bicyclic compound (LXXI) could be detected even when the reaction time was extended to ten days or when the reaction temperature was raised to 80°. Treatment of LXX with potassium t-butoxide in dimethylformamide had no effect. When the reaction was run with the methylsulfinylcarbanion only a trace of material was recovered by the extraction with chloroform. The infrared of this trace indicated a conjugated carbonyl at 6.01 microns as well as the non-conjugated carbonyl at 5.86 microns.

Preparation of 2-(methylsulfonyl)-3-(methylsulfonylmethyl)-1-naphthol, LXXV.

The procedure used was essentially the same as that used for the preparation of LIV; however, the reaction time was extended to 20-24 hours. Dimethyl homophthalate (10.4 g.) gave LXXV (14.90 g., 95%) as a fluffy, pinkish solid, m.p. 194-200°. Recrystallization from acetic acid raised the m.p. to 200-202°.

Analysis Calcd. for $C_{13}H_{14}O_5S_2$: C, 49.68; H, 4.49; S, 20.36.

Found: C, 50.00; H, 4.47; S, 20.58.

Infrared (potassium bromide) 2.90, 3.22, 3.31, 3.40, 6.15, 6.27, 6.34, 6.65, 7.15, 7.65 (intense), 7.78, 7.93 (intense);

8.15, 8.62, 8.76, 8.95 (intense), 9.05, 9.21, 9.91, 10.35, 10.45, 10.92, 11.08, 11.50, 12.01, 13.07 (intense), 14.08.

N.M.R. (dimethyl sulfoxide) singlet 3.02 (3H); singlet 3.52 (3H); singlet 5.25 (2H); multiplet 7.5-8.0 (4H); multiplet 8.2-8.5 (1H); very low intensity broad absorption 10.5-11.5 (1H). Running the sample in hexadeuteriodimethyl sulfoxide causes the 10.5-11.5 absorption to disappear and causes a multiplet characteristic of pentadeuteriodimethylsulfoxide to appear at 2.6.

(trifluroacetic acid) singlet 3.27 (3H); singlet 3.45 (3H); singlet 4.80 (2H); multiplet 7.5-8.0 (4H); multiplet (1H); the hydroxyl proton falls under the solvent peak.

Mass Spectrum molecular ion = 314; $(M+2)^{+}$ = 9.6% of the molecular ion intensity indicating 2 sulfur atoms.

If shorter reaction times are used the acid (LXXVI) derived from addition to the aromatic ester and hydrolysis of the aliphatic ester is obtained in addition to LXXV. Compound LXXVI usually crystallizes slowly from the aqueous layer after filtration of LXXV. The white needles melt at 176-179°.

Infrared (potassium bromide) 2.8-4.0 (broad), 5.86 (intense), 5.93 (intense), 6.25, 6.35, 6.68, 6.91, 7.02, 7.68 (intense), 8.10, 8.27, 8.53, 8.90 (intense), 10.24,

10.49, 10.70, 11.16, 11.28, 11.80, 12.25, 12.88, 13.38, 14.10, 14.85 microns.

N.M.R. (of the methyl ester) (deuterochloroform) singlet 3.12 (3H); singlet 3.68 (3H); singlet 3.95 (2H); singlet 4.57 (2H); multiplet 7.2-8.0 (4H).

Mass Spectrum molecular ion = 256.

The reaction of Raney nickel with LXXV

Compound LXXV (2.00 g.) was treated with W-2 Raney nickel (50 g.) in 200 ml. of refluxing ethanol for 6 hours. Work up according to the procedure for the reaction of LIII gave 3-methyl-5,6,7,8-tetrahydro-1-naphthol (LXXVII) (372 mg., 36%), m.p. 92-95°. Recrystallization from hexane raised the m.p. to 95-96° (lit. (95) m.p. 98.5°).

Infrared (carbon tetrachloride) 2.77, 3.42, 6.17, 6.35, 6.95, 7.46, 7.64, 7.77, 7.87, 8.16, 8.30, 8.67, 9.35, 9.63, 11.10 microns.

N.M.R. (carbon tetrachloride) broad absorption 1.5-2.0 (4H); singlet 2.11 (3H); broad absorption 2.3-2.8 (4H); singlet 5.12 (1H); 2 broadened singlets 6.19 and 6.33 (total 2H). Shaking the sample with deuterium oxide removes the peak at 5.12.

Mass Spectrum molecular ion = 162.

When the Papa-Schwenck technique was employed two different products were obtained. Compound LXXV (3.00 g.) was dissolved in 100 ml. of 10% sodium hydroxide and the temperature raised to approximately 90°. Nickel-aluminum alloy (15 g.) was added in small portions. Heating was con-

tinued for one hour after the addition was complete. The mixture was filtered while hot and washed with several volumes of hot water. The filtrate was acidified with hydrochloric acid and extracted with chloroform. After drying, the solvent was removed to give an oil (1.55 g.). Upon trituration with hexane part of the oil dissolved while the rest formed a semisolid mass. Cooling the hexane in the freezer gave 3-methyl-1-naphthol (LXXVIII), m.p. 88-89° (lit. (96) m.p. 89-89.5°).

N.M.R. (carbon tetrachloride) singlet 2.30 (3H); singlet 5.52 (1H); doublet centered at 6.45, J = 1.5 c.p.s. (1H) multiplet 7.1-7.8 (4H); multiplet 7.9-8.2 (1H). Shaking the sample with deuterium oxide removed the absorption at 5.52.

The residue from trituration with hexane was recrystallized twice from ether to LXXIX, m.p. 93.5-94°. The yields were determined from the integration of the n.m.r. of the mixture to be 28% LXXVIII and 50% LXXIX.

Analysis Calcd. for $C_{12}H_{12}O_3S$: C, 61.01; H, 5.12; S, 13.55. Found C, 60.96; H, 5.07; S, 13.50.

Infrared (carbontetrachloride) 3.13, 3.27, 6.16, 6.30, 6.37, 6.69, 6.98, 7.15 (intense), 7.62, 7.68, 7.95 (intense), 8.20, 8.63, 8.27, 9.00 (intense), 9.18, 9.80, 10.05, 10.50 (intense), 11.48, 11.90 microns.

N.M.R. (carbon tetrachloride) singlet 2.65 (3H); singlet 3.15 (3H); multiplet 7.0-7.6 (4H); multiplet 8.2-8.4 (1H); singlet 11.05 (1H). Shaking the sample with deuterium oxide removes the absorption at 11.05.

Following the same procedure but using 200 ml. of sodium hydroxide and

40 g. of nickel-aluminum alloy compounds LXXVIII and LXXIX were obtained in 47 and 18% yields respectively. A trace of LXXVII was also detected.

Preparation of 3-hydroxy-2-(methylsulfinyl)-3-(methylsulfinylmethyl)-dibenzocycloheptanone, LXXXI

Using the same procedure as in the preparation of LIII, diethyl diphenate (LXXX) (14.9 g.) gave LXXXI (14.3 g., 79%) as a light yellow solid, m.p. 150-177°. Recrystallization from ethyl acetate removed the yellow color but did not change the melting range significantly. The same product was obtained when the reaction was carried out using potassium t-butoxide according to the procedure of Russell, et al. (10). This substance was extremely insoluble in most normal solvents. It dissolved but reacted with trifluoroacetic acid. Dimethyl sulfoxide was a fair solvent; but, it obscures the resonances of the methylsulfinyl groups in the n.m.r. Hexadeuteriodimethyl sulfoxide causes not only the hydroxyl but also the methylene and methine protons to disappear. This made it impossible to get an adequate n.m.r. spectrum; however, spectra of the analogous sulfone were obtained. No trace of the tropolone derivative (LXXXII) was found.

Analysis Calcd. for $C_{18}H_{18}O_4S_2$: C, 59.66; H, 5.01; S, 17.66.
Found: C, 59.51; H, 5.13; S, 17.74.

Infrared (potassium bromide) 2.90, 3.25, 3.35, 3.44, 5.98 (intense), 6.28, 6.39, 6.77, 6.94, 7.10, 7.35, 7.75, 7.85, 7.95, 8.36, 8.89, 9.63 (intense), 9.80, 10.10, 13.23 (intense) microns.

Mass Spectrum molecular ion = 362; showed strong $(M-18)^+$ peak.

Preparation of 3-hydroxy-3-(methylsulfinylmethyl)-dibenzocycloheptanone, LXXXIII

According to the procedure of Russell and Mikol (44), compound LXXXI (8.70 g.) dissolved in 75 ml. of acetic acid-ethanol (60-40 by volume) was added slowly to a cooled slurry of zinc dust (20 g.) in 75 ml. of the same mixed solvent. Rapid stirring was employed throughout the reaction. The cooling bath was removed after the addition was complete. The reaction was allowed to come to room temperature for 3 hours. Work up as described by Russell and Mikol gave LXXXIII (5.25 g., 87%) as a mixture of diastereomers, m.p. 160-168°.

Analysis — Calcd. for $C_{17}H_{16}O_3S$: C, 67.99; H, 5.37; S, 10.66. Found: C, 68.08; H, 5.11; S, 10.62.

Infrared — (potassium bromide) 3.15 (broad), 6.00 (intense), 6.28, 6.79, 6.95, 7.06, 7.63, 7.79, 8.01, 8.18, 8.50, 8.88, 9.03, 9.35, 9.50, 9.95 (intense), 10.15, 10.55, 12.80, 13.31 (intense), 13.56 microns.

N.M.R. — (deuterochloroform) 2 singlets 2.32 and 2.35 (total 3H); singlet 3.07 (2H); multiplet 3.3-3.6 (2H); singlet 5.41 (1H); multiplet 7.3-8.1 (8H). Shaking the sample with deuterium oxide removed the singlet at 5.41.

Preparation of 3-hydroxy-3-(methylsulfinylmethyl)-dibenzo-1,2-cycloheptanedione, LXXXIV

Compound LXXXI (1.0 g.) was dissolved in 10 ml. of dimethyl sulfoxide. To this solution 3 ml. of water and 2 ml. of concentrated hydrochloric acid were added. The mixture was allowed to stand for 24 hours. The reaction

mixture was diluted with 25 ml. of water and extracted with chloroform. The extracts were washed with water and dried over magnesium sulfate. Removal of the solvent gave a yellow paste. Addition of ether containing a trace of chloroform gave LXXXIV (0.37 g., 42%) as a yellow solid which decomposed at 180-190°. Compound LXXXIV decomposes upon standing; consequently, no accurate elemental analysis could be obtained. This substance is also very insoluble. It reacts with trifluoroacetic acid; however, if one works rapidly a fair spectrum can be obtained. The spectrum after one hour is consistent with the Pummerer rearrangement product.

Infrared (potassium bromide) 3.10 (broad), 5.82 (intense), 5.93 (intense), 6.26, 6.78, 6.91, 7.03, 7.15, 7.76, 8.00, 8.19, 8.82, 9.00, 9.18, 9.80, 9.98, 10.30, 10.55, 11.20, 12.53, 12.85, 13.21, 13.37 (intense) microns.

N.M.R. (trifluoroacetic acid) trace of singlet at 2.30; singlet 2.62; AB quartet $\delta_A = 3.60$, $\delta_B = 4.02$, $J_{AB} = 14$ c.p.s.; broad absorption 7.5-8.2; the hydroxyl proton falls under the solvent peak. If one designates the aromatic region as 8 protons the AB quartet is 2 protons and the singlet at 2.62 is slightly less than 3 protons. As the reaction proceeds the singlet at 2.30 grows at the expense of the one at 2.62. In one hour the spectrum showed: singlet 2.30 (2H); singlet 3.43 (2H) (as the asymetric sulfoxide is destroyed it is consistent that the AB quartet should collapse); broad absorption 7.2-8.1 (8H).

Mass Spectrum molecular ion = 3.4.

E.S.R. (dimethyl sulfoxide) and potassium t-butoxide, no oxygen) major pentent (1.68 gauss); further split to approximate pentet (0.4 gauss); spectrum is superimpossible with spectrum from 9,10-phenantrenequinone.

Preparation of 3-hydroxy-2-(methylsulfonyl)-3-(methylsulfonylmethyl)-dibenzocycloheptanone, LXXXV

Using the same procedure as in the preparation of LIV, diethyl diphenate (7.45 g.) gave LXXXV (9.15 g., 92%), m.p. 173-177°. Recrystallization from glacial acetic acid raised the m.p. to 187-188°. Compound LXXXV could also be prepared by oxidation of LXXXI with hydrogen peroxide.

Analysis Calcd. for $C_{18}H_{18}O_6S_2$: C, 54.82; H, 4.60; S, 16.23. Found: C, 54.70, H, 4.65; S, 16.23.

Infrared (potassium bromide) 2.95, 3.33, 3.40, 5.99 (intense), 6.29, 6.40, 6.70, 6.88, 6.95, 7.10, 7.70 (intense), 7.95, 8.75, 8.86 (intense), 10.00, 10.28, 11.12, 12.38, 12.88, 13.27 (intense), 13.72 microns.

N.M.R. (trifluoroacetic acid) singlet 3.22 (6H); broad singlet 4.80 (3H); multiplet 7.2-8.0 (8H); the hydroxyl proton falls under the solvent peak.

The reaction of the methylsulfonylcarbanion with dimethyl adipate

When dimethyl adipate (4.35 g.) was treated with the methylsulfonylcarbanion as in the preparation of LIV, the major product isolated was

(methylsulfonylmethyl)2-oxocyclopentyl ketone (LXXXIX) (3.45 g., 67%) a white solid melting at 90-5°. Recrystallization from chloroform raised the m.p. to 98-100°. A dark red color was obtained with ferric chloride.

Analysis — Calcd. for $C_8H_{12}O_4S$: C, 47.06; H, 5.92; S, 15.67. Found: C, 47.17; H, 5.98; S, 15.80.

Infrared — (chloroform) 2.8-4.0 (broad), 5.98 (intense, shoulder at 5.86), 6.20 (intense), 6.85, 6.92, 7.15, 7.39, 7.60 (intense), 7.81, 8.75 (intense), 9.17, 10.40, 11.02, 11.80 microns.

N.M.R. — (deuterochloroform) multiplet 1.8-2.9 (6H); singlet 3.91 (2H); broad singlet 13.0 (1H). Shaking with deuterium oxide removed the absorption at 13.0.

A trace of the straight chain disulfone was found, m.p. 130-132°.

The reaction of the methylsulfonylcarbanion with dimethyl succinate

When dimethyl succinate (8.00 g.) was treated under nitrogen with the methylsulfonylcarbanion as in the preparation of LIV, the only product isolated was 2,5-dicarbomethoxy-1,4-cyclohexanedione (XC) (1.50 g., 33%), m.p. 154-154.5° (lit. (97) m.p. 155.5-7°). A dark purple color was obtained with ferric chloride.

Infrared — (chloroform) 2.75-4.0 (broad), 6.03 (intense), 6.17 (intense), 6.95, 7.45 (intense), 8.82, 9.35, 10.56 microns.

N.M.R. — (deuterochloroform) singlet 3.16 (4H); singlet 3.79 (6H); singlet 12.10 (2H). Shaking the sample with deuterium oxide removed the absorption at 12.10.

Preparation of 2-(methylsulfonyl)-3-(methylsulfonylmethyl)-4,4,5,5-tetramethylcyclopentenone, XCI

Diethyl tetramethylsuccinate (2.20 g.) was treated with the methylsulfonyl carbanion as in the preparation of LIV. Work up gave a semi-solid paste (1.9 g.) which appeared to be a mixture of the cyclic and non-cyclic adducts. Recrystallization once from ethyl acetate and twice from chloroform-ether mixtures gave pure XCI (1.03 g., 34%), m.p. 179.5-180°.

Analysis — Calcd. for $C_{12}H_{20}O_5S_2$: C, 46.75; H, 6.54; S, 20.76. Found: C, 46.70; H, 6.50; S, 20.70.

Infrared — (chloroform) 3.42, 5.79 (intense), 6.21, 6.87, 7.16, 7.24, 7.29, 7.63 (intense), 8.70, 8.85 (intense), 10.38 microns.

N.M.R. — (deuterochloroform) singlet 1.10 (6H); singlet 1.20 (6H); 2 singlets 3.17 and 3.21 (total 6H); singlet 4.82 (2H).

The reaction of the methylsulfonylcarbanion with diethyl dimethylmalonate

When diethyl dimethylmalonate (4.70 g.) was treated with the methylsulfonyl carbanion as in the preparation of LIV, only the non-cyclic product XCII (1.15 g., 16%) was isolated, m.p. 107-108°.

Analysis — Calcd. for $C_9H_{16}O_6S_2$: C, 38.03; H, 5.67; S, 22.52. Found: C, 38.14; H, 5.66; S, 22.45.

Infrared — (potassium bromide) 3.31, 3.39, 3.44, 5.86 (intense), 6.83, 6.94, 7.08, 7.17, 7.27, 7.35, 7.55, 7.65 (intense)

7.76, 8.23, 8.32, 8.51, 8.62, 8.88 (intense), 9.42, 10.00, 10.30, 10.78, 11.37, 12.45 microns.

N.M.R. (trifluoroacetic acid) singlet 1.57 (6H); singlet 3.01 (6H); singlet 4.62 (4H).

Preparation of 2,3-diphenyl-1,4-naphthoquinone, XCV

Dibenzyl sulfoxide (3.5 g.) and sodium hydride (1.5 g.) in 100 ml. of dimethyl formamide were placed in a water bath at 70°. Diethyl phthalate (3.4 g.) was added dropwise with stirring. After the addition was complete, the heating was continued for one hour. The mixture was stirred for two hours at room temperature. The reaction was quenched with water. The aqueous mixture was extracted with ether. The extracts were dried over magnesium sulfate. Removal of the solvent gave an oil which was chromatographed on alumina. A trace of stilbene (less than 0.1 g.) was eluted with hexane. A hexane-benzene mixture gave XCV (1.1 g., 24%), m.p. 132-138°. Recrystallization from glacial acetic acid raised the m.p. to 139.5-140.5° (lit. (98) m.p. 139-140°). Later elution fractions included unreacted starting material and indefinable tars. Attempts to repeat this reaction sometimes led to zero % yield of quinone. Wide variations as to temperature, reaction time, time of addition of ester, reactant concentration, and solvent did not produce a consistently good method.

Infrared (chloroform) 3.33, 6.02 (intense), 6.26, 6.70, 6.75, 6.92, 7.44, 7.57, 7.77 (intense), 9.01, 9.46, 9.75, 10.00 microns.

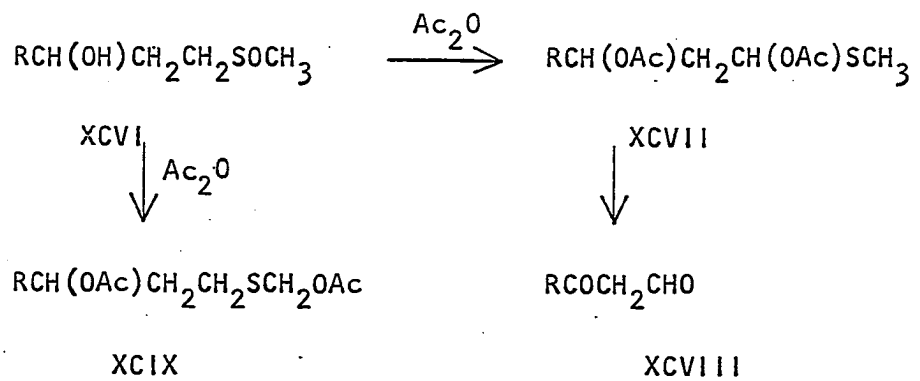
N.M.R. (deuterochloroform) multiplet 6.9-7.3 (10H); multiplet 8.0-8.3 (2H).

APPENDIX

Miscellaneous Reactions

A number of other projects were started and brought to a halt when it became evident that the initial goal could not be achieved and no worthy secondary goal could be determined. Nevertheless, in a few cases certain individual experiments were of interest and should be mentioned.

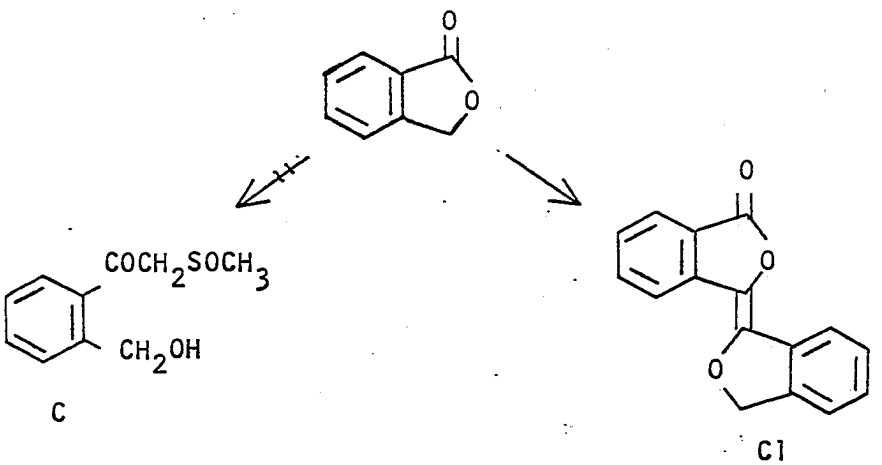
The methylsulfinylcarbanion adds to epoxides of terminal olefins such as styrene to give γ-hydroxy sulfoxides with exclusive addition to the terminal carbon atom. This result has been corroborated by the recent application of this reaction to long chain alpha-olefins to produce detergents (29,30). Our interest was in a potential β-carbonyl system which might be derived from rearrangement of the sulfoxide, oxidation of the benzylic acetate, and cleavage of the hemimercaptal. The rearrangement, however, is directed to the methyl group instead of the methylene group giving XCIX rather than XCVII. This problem could be



circumvented by using methyl phenyl sulfoxide; but, it is not nearly as readily available as dimethyl sulfoxide and is more difficult to work with since it is a solid at room temperature. When the reaction was tried with

chalcone epoxide (benzalacetophenone epoxide) a very complex product mixture was obtained. Spectra of the crude material indicated that addition to the carbonyl as well as addition to both ends of the epoxide had taken place.

Since dimethyl sulfoxide condensed so readily with esters, it seemed possible that a similar reaction might take place with lactones. Such a reaction would have the advantage of introducing an additional functionality (an hydroxyl group) with which to work. Unfortunately, when the reaction was tried with phthalide self-condensation took place to give CI instead of the desired product (C).



C CI

Electron spin resonance studies in these laboratories had indicated the formation of radical anion (CII) when the methylsulfinylcarbanion reacts with esters of lactic acid (73). It was hoped that it might be

$$CH_3CH(OH)COOR + NaCH_2SOCH_3 \rightarrow CH_3CH(OH)COCH_2SOCH_3 \rightarrow$$

$$CH_3C(O^{\cdot}) = C(O^{-})CH_3$$

CII

possible to isolate an addition product CIII from mandelic esters. The reaction with ethyl mandelate failed to give an identifiable product.

$C_6H_5CH(OH)COCH_2SOCH_3$

CIII

However, when the acetate of ethyl mandelate was reacted a low yield (13%) of 1-phenyl-1,2-propandedione was obtained. This product must result from addition followed by pyrolytic elimination of methane sulfinic acid upon distillation. Reactions with ethyl benzoylformate gave no identifiable products.

Previously it had been shown that unsaturated sulfoxides generated in situ were capable of adding carbanions in the Michael manner (25). Since the unsaturated sulfoxide, XIa, was readily available, the addition of acetophenone was carried out to give a γ-keto sulfoxide (CIV). Pyrolysis of CIV gave an olefin (CV) which rapidly isomerized to dypnone (CVI).

$$C_6H_5COCH_2CH(C_6H_5CH_2SOCH_3 \xrightarrow{\Delta} C_6H_5COCH_2C(C_6H_5) = CH_2$$

CIV

$$\downarrow \text{CV}$$

$$C_6H_5COCH = C(CH_3)C_6H_5$$

CVI

Experimental Detail for Miscellaneous Reactions

The reaction of the methylsulfinylcarbanion with styrene oxide

Styrene oxide (30 g.) was added dropwise under nitrogen to the methylsulfinylcarbanion prepared from sodium hydride (6 g.) in 125 ml. of dimethyl sulfoxide. The reaction was stirred at room temperature for 3 hours. The mixture was poured into an equal volume of water and extracted with chloroform. The extracts were dried over magnesium sulfate and filtered. Removal of the solvent gave γ-hydroxy-γ-phenyl propyl methyl sulfoxide (XCVI, R = C_6H_5) (17.2 g., 36%) as an oil which would not crystallize.

N.M.R. (Deuterochloroform) broad absorption 1.7-2.9 with singlet sticking out a 2.30 (total 7H); broad absorption 4.5-5.1 (2H); singlet 7.25 (5H). Shaking the sample with deuterium oxide removed one proton from the absorption at 4.5-5.1 and left a triplet centered at 4.70, J = 7 c.p.s.

Reaction of acetic anhydride with XCVI

Compound XCVI (R = C_6H_5) (2.00 g.) in 10 ml. of acetic anhydride was heated on a steam bath for 20 hours. The mixture was neutralized with saturated sodium bicarbonate and extracted with chloroform. The extracts were dried and filtered. Removal of the solvent gave XCIX (R = C_6H_5) (1.7 g., 62%) which was also an oil.

N.M.R. (deuterochloroform) broad absorption 1.8-2.8 with strong singlet at 1,99 (total 10H); singlet 5.03 (2H); triplet centered at 5.76, J = 7 c.p.s. (1H); singlet 7.22 (5H).

The reaction of the methylsulfinylcarbanion with phthalide

Phthalide (6.60 g.) in 25 ml. of dimethyl sulfoxide was added dropwise under nitrogen to the methylsulfinylcarbanion prepared from sodium hydride (2.4 g.) and 100 ml. of dimethyl sulfoxide. After stirring for 1 hour at room temperature the mixture was worked up according to the procedure for LIII. The crude brown solid was washed thoroughly with ether to give CI (2.7 g., 44%) as bright yellow solid, m.p. 211-215°. The material was extremely insoluble; consequently, the integral of the n.m.r. taken at very high spectrum amplitude was of little value. The spectrum did indicate, however, only one singlet at 5.65 p.p.m. in addition to the aromatic region.

Infrared (chloroform) 5.75 (intense), 5.96, 6.24, 6.86, 7.46, 7.78, 8.90, 9.08, 9.29, 9.95, 10.26, 11.17 microns.

Mass Spectrum molecular ion 250.

The reaction of the methylsulfinylcarbanion with the acetate of ethyl mandelate

Ethyl mandelate was converted to the acetate by treatment with acetic anhydride in pyridine. The distilled acetate (11.1 g.) was added dropwise to the methylsulfinyl carbanion prepared from sodium hydride (4 g.) and 100 ml. of dimethyl sulfoxide. After 2 hours the reaction was worked up as in the preparation of LIII. The crude oil was distilled at 80-100° at 0.7 mm. with a pot temperature of 150°. The yellow distillate (1.0 g.) was shown by g.l.p.c. to be greater than 90% 1-phenyl-1,2-propanedione. The infrared and n.m.r. spectra were identical with that of an authentic sample (Aldrich).

Michael addition of acetophenone to XIa

Sodium hydride (2.5 g.) was slurried in 150 ml. of tetrahydrofuran. Acetophenone (12.0 g.) was added and the reaction mixture warmed until hydrogen started to evolve. Compound XIa (17.7 g.) in 50 ml. of tetrahydrofuran was added and the temperature maintained at 55° for 30 minutes. After cooling, the mixture was poured into 100 ml. of water and extracted with chloroform. The extracts were dried over magnesium sulfate and filtered. Removal of the solvent gave CIV (26.2 g., 88%), m.p. 133-136°. Recrystallization from a methylene chloride-ether mixture raised the m.p. to 139-139.5°. The material had a light cotton-like consistency.

Analysis — Calcd. for $C_{17}H_{18}O_2S$; C, 71.31; H, 6.34; S, 11.17. Found: C, 71.43; H, 6.53; S, 11.20

Infrared — (chloroform) 3.28, 3.41, 5.95 (intense), 6.26, 6.32 6.70, 6.90, 7.12, 7.34, 7.6-8.5 (broad), 9.80 (broad), 10.18, 10.42, 10.75 microns.

N.M.R. — (deuterochloroform) singlet 2.49 (3H); multiplet 2.9-4.2 (5H); multiplet 7.2-7.6 (8H); multiplet 7.8-8.0 (2H).

Pyrolysis of CIV

Compound CIV (2.50 g.) was placed in a 10 ml. flask equipped with a short-path distillation head. The pressure was reduced 0.1 mm. The flask was immersed in an oil bath at 180°. A light yellow oil distilled at 130-2°. The oil (1.65 g., 85%) proved to be a mixture (n.m.r.) of CV and CVI. Column chromatography on either alumina or silica gel causes isomerization of CV to CVI.

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