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TOWARD THE SYNTHESIS OF ILLUDIN-S. III. THE
THERMAL DECOMPOSITION OF SULFONES AND
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I. The Reactivity of The Anion Derived from 2-Propenyl-1,3-Dithiane

II. Studies Directed Toward The Synthesis of Illudin-S

III. The Thermal Decomposition of Sulfones and Sulfoxides

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

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degree of

DOCTOR OF PHILOSOPHY

BY

HOWARD LEWIS TUGGLE

Norman, Oklahoma

1974

I. THE REACTIVITY OF THE ANION DERIVED FROM 2-PROPENYL-
1,3-DITHIANE

II. STUDIES DIRECTED TOWARD THE SYNTHESIS OF ILLUDIN-S

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APPROVED BY

DISSERTATION COMMITTEE

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Janie and Johnnita

ACKNOWLEDGEMENTS

AN INVESTIGATION OF THE REACTIVITY OF THE ANION DERIVED

FROM 2-PROPENYL-1,3-DITHIANE

History and Background

The observations by Arens,[1] Ohno[2] and Truce[3] that strong bases
converted mercaptals to their corresponding anions (see scheme 1) added a
new dimension to carbanion chemistry. The stability of these carbanions
is attributed to the overlap between the vacant d-orbitals of the sulfur
atoms and the adjacent carbanion and the inductive effect of the sulfur
atoms of the mercaptal groups.

Subsequent alkylation and acylation of these anions followed
by hydrolysis or desulfurization of the products provided new synthetic
routes to a wide variety of functional groups. However, the yields of
the products were low due to a competing reaction between the anion and
the solvent, dimethylformamide. Furthermore, the synthetic utility of

$$R-CH_2-\overset{O}{\overset{\|}{C}}-R' \xleftarrow[\substack{2.\ R'-\overset{O}{\overset{\|}{C}}-Cl \\ 3.\ Ra-Ni}]{1.\ base} R-\overset{\overset{Et-S\ \ S-Et}{\diagdown\diagup}}{\underset{H}{C}} \xrightarrow[\substack{2.\ MeI \\ 3.\ HgCl_2}]{1.\ base} R-\overset{O}{\overset{\|}{C}}-CH_3$$
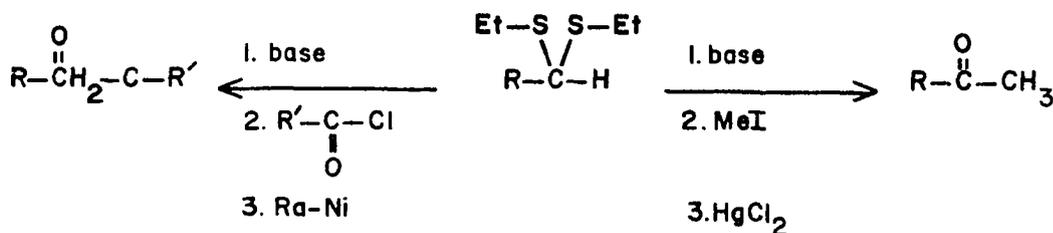
Scheme 1

anions derived from mercaptals is also limited by their failure to react with secondary halides and carbonyl compounds.

The synthetic utility of thiocarbanions suggested by the work of Arens and coworkers and Truce was greatly expanded by Corey and Seebach[4] who investigated the reactivity of anions derived from 1,3-dithiane 1 and substituted 1,3-dithianes 3.
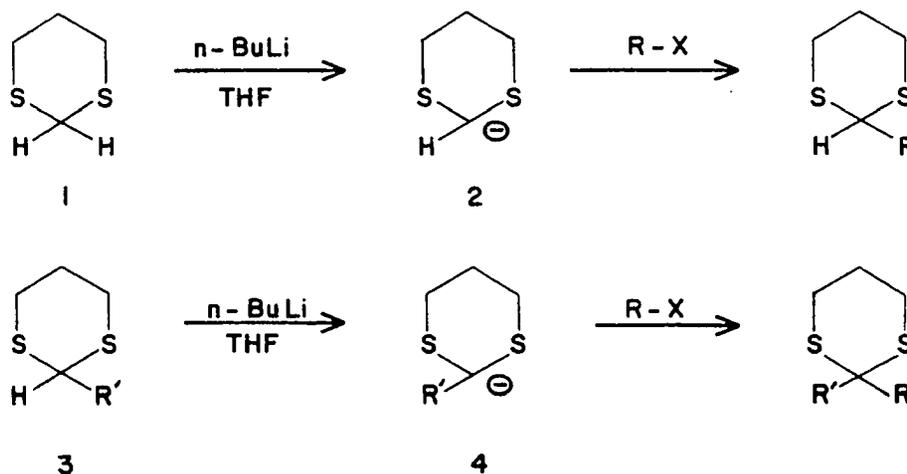
Scheme 2

Their remarkable ease of preparation, relative stability, and exceptional reactivity established anions of type 2 and 4 as extremely useful intermediates in organic synthesis.

Anions of types 2 and 4 with R = primary, secondary, or t-alkyl, allyl, benzyl and aryl have been generated. They undergo alkylation with primary and secondary halides and dihalides (see scheme 2) to give excellent yields (70-90%) of purified products. The anions 2 and 4 react with epoxides (see scheme 3) to form mercaptals of β-hydroxy ketones or aldehydes, e.g. 5, in good yields; reaction with aldehydes and ketones yield mercaptals of α-hydroxy aldehydes and ketones, e.g. 6.
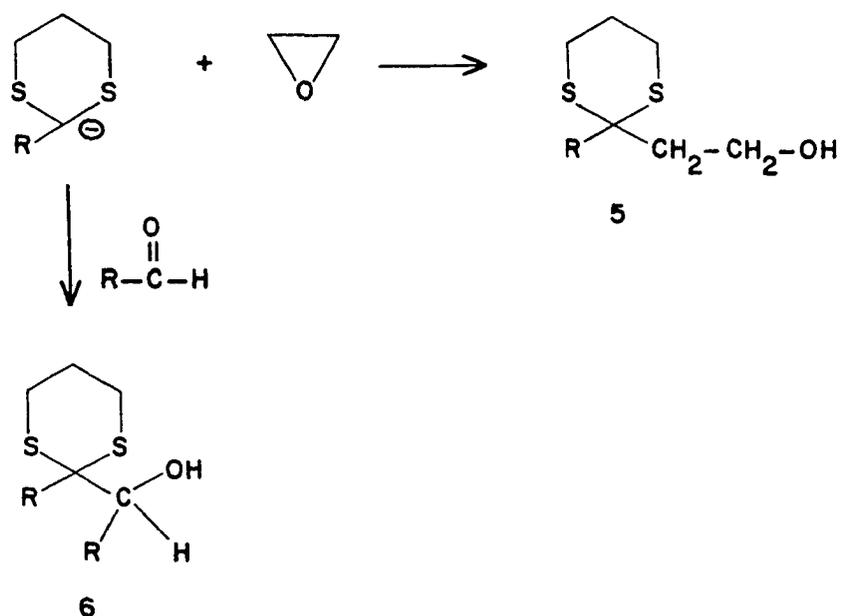
Scheme 3

Imines, nitriles and carbon dioxide react with the anions to form products which can be subsequently hydrolyzed to the corresponding amino ketones or aldehydes, diketones or keto aldehydes and α-keto acids.

In general, acid chlorides and esters proved to be unsatisfactory as acylating agents; benzoyl chloride and methyl benzoate reacted with 2 to form the di-addition product. Even in the presence of a
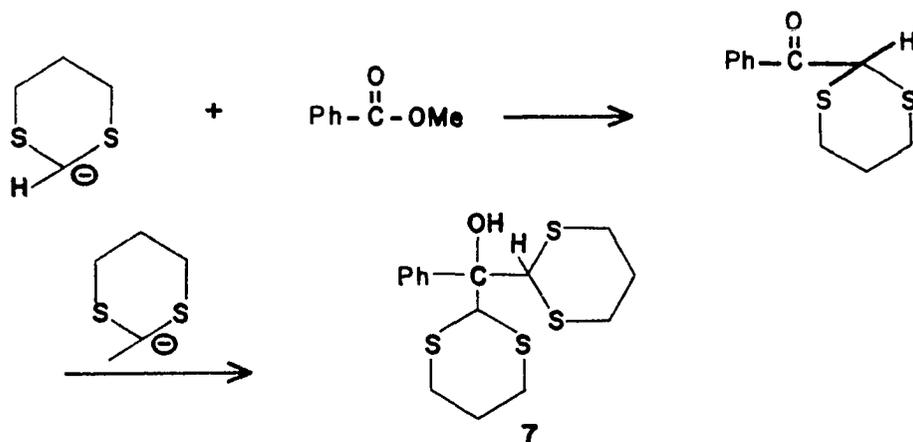
tenfold excess of methyl benzoate, the ketone formed from the initial

reaction of 2 with the ester reacted further with 2 to form 7.

In addition to Corey and coworkers, Carlson and Helquist[6] have

investigated the reactivity of carbanions which are stabilized by sulfur

in its various oxidation states. These workers oxidized 1,3-dithiane

(1) to 1,3-dithiane monoxide (8) by treatment with 1 equivalent of

sodium metaperiodate. Treatment with n-butyllithium rapidly converted

8 to the anion 9.
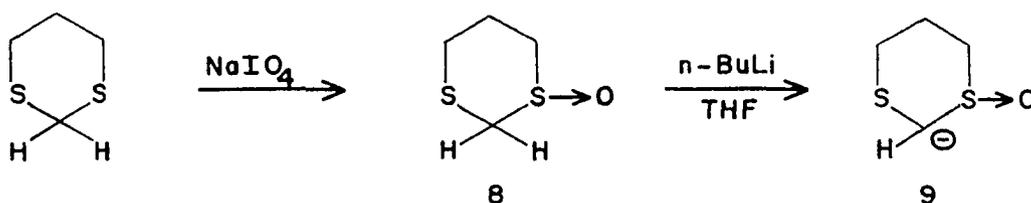
The anion 9 exhibited behavior which is characteristic of both

anion 2 and the anion of dimethyl sulfoxide as evidenced by its rapid

reactions (see scheme 4) with benzophenone to form 10 and with ethyl
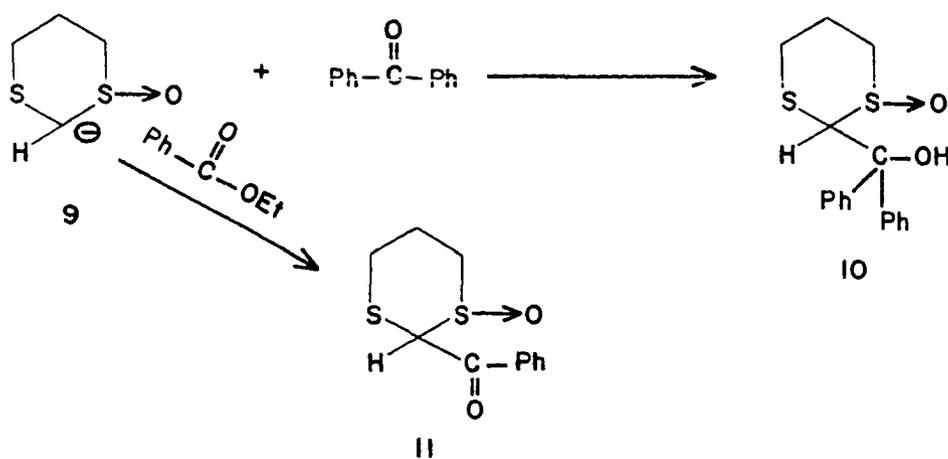
Scheme 4

benzoate to form the β-ketosulfoxide 11. The reaction of 9 with ethyl

benzoate to form 11 is in sharp contrast to the reaction of 2 with ethyl

benzoate which resulted in the formation of the di-addition product 7.

Anions derived from mercaptoles, 1,3-dithianes, and 1,3-dithiane

monoxide do not undergo conjugate addition to α,β-unsaturated carbonyl

systems. Both 9 and 2 react with α,β-unsaturated carbonyl systems[5,6]

(Michael acceptors) in a 1,2-manner; anions derived from mercaptoles

do not react in any manner with α,β-unsaturated carbonyl compounds.

Otherwise, the chemical behavior of anions derived from mercaptoles,

1,3-dithianes and 1,3-dithiane monoxide is identical to the chemical

behavior of other carbanions.

INTRODUCTION

Anions derived from the dithianes of α,β-unsaturated aldehydes present an interesting problem in that reaction can occur at either of two sites, α or γ to the geminal sulfur atoms. Since the chemical behavior of this type of anion has not been reported in the literature and since one of the reactions in a proposed synthesis (see section II of this thesis) of the natural product illudin-S entailed the reaction of such an ambident nucleophile, an investigation of the behavior of such allylic anions with alkylating and acylating reagents was undertaken. The results of this investigation will be presented in this section.

The dithiane $\underline{12}$ used in the preliminary investigation was pre-

pared by reacting crotonaldehyde with 1,3-propanedithiol in the presence

of a catalytic amount of boron trifluoride-etherate.

$$\underset{\underset{CH_3}{}}{\overset{\overset{H}{|}\ \overset{H}{|}\ \overset{O}{\|}}{C=C-C-H}} \quad + \quad H-S-(CH_2)_3-S-H \quad \xrightarrow[\ CHCl_3\ ]{BF_3-\text{etherate}}$$

$$\underset{\underline{12}}{\overset{\overset{H}{|}\ \overset{H}{|}\ \overset{S\ S}{\diagup\ \diagdown}}{CH_3-C=C-C-H}}$$
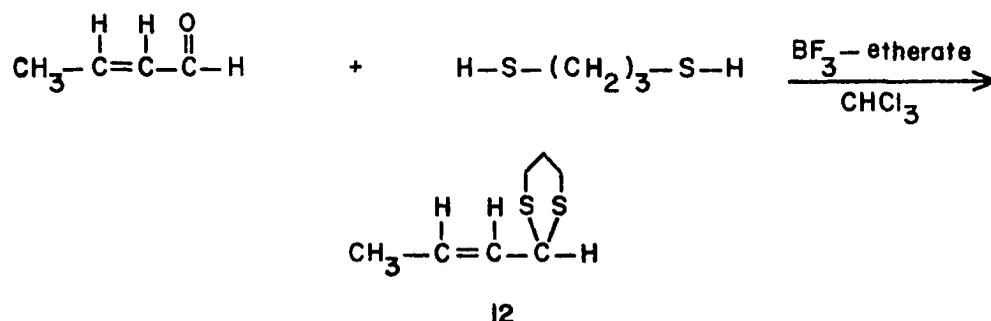
The nmr spectrum of $\underline{12}$ exhibits a signal at 5.0–6.2 ppm due to the two

olefinic protons. This signal appears as a complex multiplet. The

signal for the proton on carbon bearing the geminal sulfur atom appears

as a doublet (J = 6 Hz) at 4.62 ppm. The signals for the six methylene

protons of the six membered ring appear as multiplets at 2.5–3.0 and

1.8–2.3 ppm. The signal for the vinyl methyl appears as a doublet

(J = 5 Hz) at 1.70 ppm.

A solution of $\underline{12}$ in tetrahydrofuran was treated with 1 equi-

valent of n-butyllithium, and the resulting anion was subsequently

reacted with an excess of ethyl iodide. A single organic product $\underline{13}$

was obtained in 80% yields.

The mass spectrum of 13 exhibits a parent ion at m/e 188 and

a base peak at m/e 85. An examination of the nmr spectrum of 13 re-

vealed that the absorptions in the olefinic region correspond to two

protons. In contrast, if the alkylation had occurred at the position

γ to the geminal sulfur atoms, the resulting product 14 would exhibit

only one olefinic proton absorption in its nmr spectrum rather than two

as in 13. The evidence obtained from a comparison of the nmr spectra

of 12 and 13 indicated that the alkylation of the anion of 12 with ethyl

iodide had occurred exclusively at the position α to both sulfur atoms

and thus 13 has the structure indicated.

$$
12 \xrightarrow[\text{2) EtI}]{\text{1) n}-\text{BuLi, THF}}
\begin{array}{c}
\underset{\text{H}}{|}\ \underset{\text{H}}{|}\ \underset{\text{S}}{\diagup}\underset{\text{S}}{\diagdown} \\
CH_3-C=C-C-Et \\
\end{array}
$$

13

$$
\begin{array}{c}
\underset{\text{H}}{|}\ \underset{\text{H}}{|}\ \underset{\text{S}}{\diagup}\underset{\text{S}}{\diagdown} \\
CH_3-C-C=C \\
|\\
Et
\end{array}
$$

14
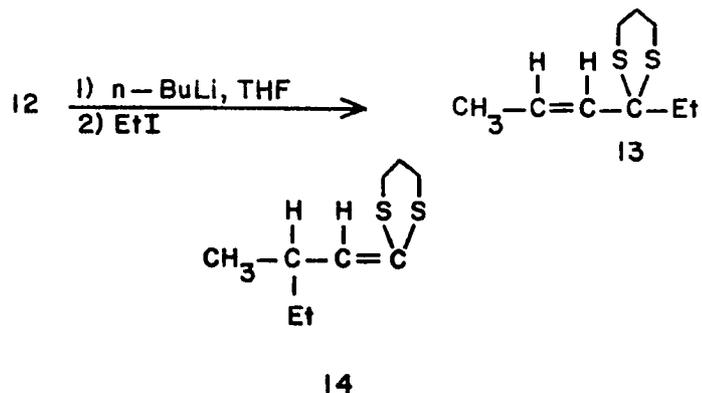
Additional evidence which further confirmed the structure of

13 was obtained from its transformation products. Raney nickel in

refluxing ethanol converted 13 to hexane; when a solution of 13 and

methyl iodide in aqueous acetone[7] was refluxed for twenty-four hours,

ethyl propenyl ketone 15 (identified as its 2,4-dinitrophenylhydrazone)

was obtained in 75-80% yields.

$$
13 \xrightarrow[\text{H}_2\text{O}]{\text{MeI, CH}_3-\overset{\text{O}}{\overset{\|}{\text{C}}}-\text{CH}_3}
CH_3-CH=CH-\overset{\text{O}}{\overset{\|}{C}}-Et
$$

15
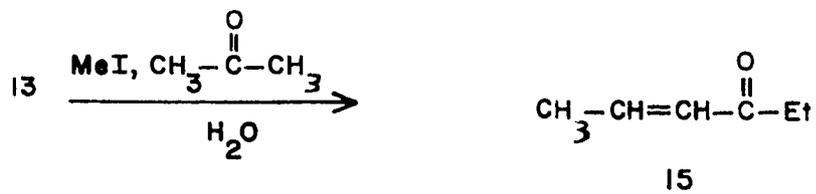
Several attempts to hydrolyze 13 (see Table 1) to 15 employing mercury

salts were unsuccessful. Invariably, the treatment of 13 with mercuric

chloride and mercuric oxide in tetrahydrofuran or acetonitrile resulted

in the formation of a solid product which was not identified. Corey

and coworkers[8] have observed that unsaturated dithianes cannot be suc-

cessfully hydrolyzed to the corresponding unsaturated aldehydes and

ketones with mercury salts due to concomitant reaction of the double

bond. Thus a plausible explanation for the failure of mercury salts to

convert 13 to 15 has been presented. However, when a solution of 13

in methanol was treated with mercuric chloride and mercuric oxide, a

small quantity of a product (less than 1% yield) was obtained. This

product was not fully characterized, but its nmr and ir spectra indi-

cated that it was probably 5-methoxy-2-hexanone which could have re-

sulted from the conjugate addition of methoxide ion to 15.

When the anion of 12 was treated with 1 equivalent of benzal-

dehyde, a mixture of the diastereoisomeric forms of 16 was obtained.
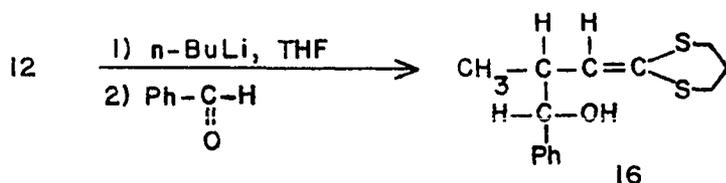
The mass spectrum of 16 exhibits peaks at m/e 266 (M^+) and 108 (base

peak). The ir spectrum shows absorptions at 3450 cm^{-1} (OH) and 1692

cm^{-1} (C=C). The nmr spectrum of product 16 showed the following im-

portant features: two broad singlets at 7.4 and 7.2 ppm (aromatic

protons), a pair of doublets at 5.25 (J = 5 Hz) and 4.5 ppm (J = 8 Hz),

TABLE 1

Some Procedures for Hydrolyzing Dithioketals

to Carbonyl Compounds

Protection Group	Moles of Reagent Per Mole of Thioketal	Aqueous Solvents (%) Experimental Conditions	Yield % of Carbonyl Product	Ref.
dithiane	NBS (6-9) $AgNO_3$ (4-4.5)	MeCN (80) or $(CH_3)_2CO$ (96) RT 10 min	75-80	8
dithiane	NCS (4.0)[a] $AgNO_3$ (4-4.5)	MeCN (80) or $(CH_3)_2CO$ (96) RT 10 min	71-100	8
dithiane	Hgo or $CdCo_3$ and Hg Cl_2 (2-3)	$(CH_3)_2CO$ (95) MeCN (90-95) Reflux	70-80	5
dithiane	BF_3-etherate HgO	THF, (15%) ACOH	30-80%	11
dithiane and dithiolane	MeI (excess)[b]	$(CH_3)_2CO$ reflux several hours	Not Reported	7
dithiolane	Chloramine-T (4)	C_2H_5OH (80)	86%	10

Methods a and b are suitable for unsaturated dithianes.

olefinic proton, and a pair of doublets at .9 (J = 5 Hz) and .6 ppm (J = 8 Hz), terminal methyl.

The evidence provided by its nmr spectrum unequivocally established 16 as a mixture of diastereoisomers. The signals for the aromatic protons, the olefinic protons and the methyl groups are clearly distinguishable for each isomer; furthermore, the ratio of the intensities of each pair of these signals is approximately (3:2). Further justification for this structural assignment was provided by the structure of the product 17 which resulted from the treatment of a solution of 16 in tetrahydrofuran with dilute hydrochloric acid. The ir spectrum of 16 exhibited a strong absorption at 1778 cm^{-1} (γ-lactone carbonyl). The mass spectrum of 17 exhibited a molecular ion at m/e 176; the nmr spectrum of 17 showed the following important features: a 5 proton multiplet at 7.1-7.9 due to the aromatic protons; signals for the benzylic proton, doublets at 5.62 (J = 5 Hz) and 4.95 ppm (J = 7 Hz) respectively; and signals for the methyl group, doublets at 1.25 (J = 7 Hz), and .7 ppm (J = 5 Hz). The signals for the remaining protons appear as a multiplet at 2.0-3.2 ppm. Thus, β-methyl-γ-phenyl-γ-butyrolactone 17 is a mixture of diastereoisomers just as its precursor, 16.

16   HCl, THF   →

17
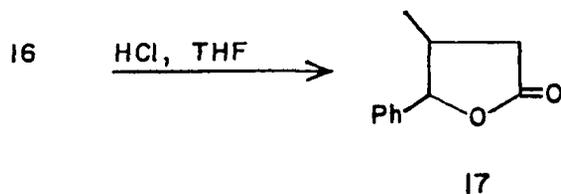
When the anion of 12 was treated with 1 equivalent of ethyl

benzoate, a compound formulated as 18 was the only product isolated

from the reaction mixture. Presumably, the anion of 12 reacted ini-

tially with ethyl benzoate to form the ketone 19 which then reacted

with an additional mole of the anion of 12 to form the di-addition

product 20. This is consistent with the observation of Corey and co-

workers who reacted the anion of 1,3-dithiane with a tenfold excess

of ethyl acetate and obtained the di-addition product; inverse addition

produced the same results.
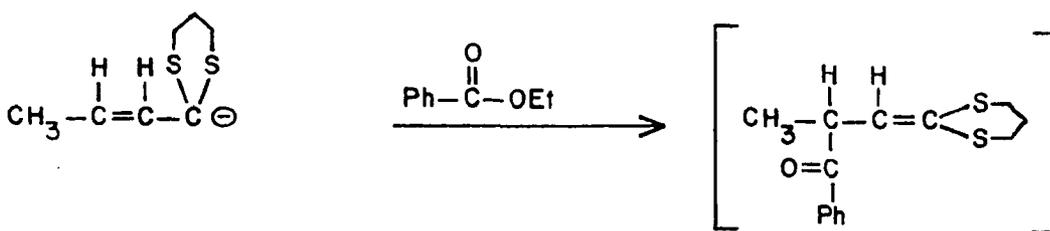
18
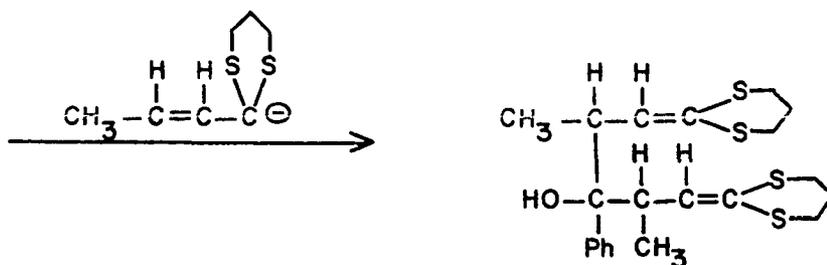
19

SUMMARY

Anions derived from the dithianes of α,β-unsaturated aldehydes alkylate at the position α to both sulfur atoms, acylate at the position γ to both sulfur atoms and undergo addition to carbonyl compounds (aldehydes and ketones) at the position γ to both sulfur atoms. Hydrolysis of the products resulting from the alkylation of these anions provides a new route to the synthesis of α,β-unsaturated ketones.

During this study considerable effort was devoted to the hydrolysis of the dithiane 13 to the corresponding α,β-unsaturated ketone. Procedures utilized in attempts to effect these conversions along with other procedures reported in the literature are summarized in Table 1.

13

EXPERIMENTAL

All metling points and boiling points are uncorrected. All solvents were redistilled prior to use. Anhydrous solvents were prepared by distillation from calcium hydride. Column chromatography supports were silicAR CC-7 (Mallinckrodt, 100/200 mesh) and silica Gel H (Merck AG, Darmstadt). Thin layer chromatography was performed on 5 x 20 cm glass plates coated with silica gel H (Merck AG, Darmstadt). The developed plates were exposed to iodine vapor for visualization of the chromatogram.

Gas chromatographic analyses were performed on a Varian Aerograph Model 1220-1 or Aerograph Model 1740-1 gas chromatograph. The infrared spectra were taken on a Beckman IR-8 spectrometer as potassium bromide pellets or in solutions of carbon tetrachloride or chloroform. Ultraviolet spectra (uv) were taken in 95% ethanol solutions with a Hitachi Perkin-Elmer, model 124 spectrometer. Nuclear magnetic resonance spectra (nmr) were taken on Varian A-60 or T-60 spectrometers using tetramethylsilane (TMS) as an internal reference. Samples were run in varying concentrations of carbon tetrachloride and deuteriochloroform. Chemical shifts are reported in δ-units (parts per million from TMS) and are followed by the multiplicity of the signal, the number of protons, the corresponding coupling constant and the assignment. The multiplicities are denoted by the symbols: s, singlet; d, doublet; dd, double doublet; t, triplet; and m, multiplet.

The mass spectra were taken on a Hitachi Perkin-Elmer RMU-7 spectrometer using perfluorokerosene as an internal reference. Major peaks and molecular ions are reported followed by percentage of the base peak.

Combustion analyses were carried out by Bernhardt Laboratories in Mülheim, West Germany.

2-propenyl-1,3-dithiane (12)

A solution of 80 g (1.14 mol) of crotonaldehyde and 108 g (1 mol) of 1,3-propanedithiol in 500 ml of chloroform was placed in a 1 l three-necked flask which was equipped with a magnetic stirring bar and an addition funnel. The flask was immersed in an ice-water bath at 0° and 15 ml of boron trifluoride-etherate was added slowly to the contents of the flask. The reaction mixture was stirred for 12 hr during which time the temperature of the bath was allowed to rise to room temperature. The chloroform solution was first washed with a 10% solution of sodium bicarbonate and then with a saturated solution of sodium bisulfite. The chloroform solution was then dried over anhydrous sodium sulfate and evaporated to yield 156.8 g (96%) of the crude dithiane. Distillation of 78 g of crude product yielded 60.4 g (80%) of 2-propenyl-1,3-dithiane as a colorless liquid, bp 77-78° (1 mm). An analytical sample was obtained by collecting a middle fraction from the distillate, bp 77-78° (1 mm); n_D^{25} 1.5771; ir (thin film) 1658 cm^{-1} (carbon-carbon double bond); 1419 cm^{-1} (carbon-sulfur stretch); nmr (CDCl$_3$) δ 5.3-6.3 (m, 3, olefinic protons), 4.65 (proton on C-2 of the dithiane ring), 2.70-2.95 (m, 4, methylene protons on carbons 4 and 6 in the dithiane ring), 1.8-2.2 (m, 2, remaining methylene protons of the dithiane ring), 1.7 (d, 3,

J = 5 Hz, vinyl methyl); mass spectrum 163 (1), 162 (19), 161 (7),

160 (69), 119 (23), 105 (12), 103 (15), 95 (16), 87 (15), 86 (47), 85

(100), 74 (25), 73 (23), 71 (11), 58 (10), 55 (13), 53 (18), 47 (16),

46 (25), 45 (68), and 41 (33).

$\underline{\text{Anal}}$. Calcd. for $C_7H_{12}S_2$: C, 52.50; H, 7.50; S, 40.00. Found:

C, 52.40; H, 7.63; S, 40.11.

2-Ethyl-2-propenyl-1,3-dithiane (13)

A solution of 24 g (.15 mol) of 2-propenyl-1,3-dithiane in 200

ml of dry tetrahydrofuran was placed in a 500 ml three-necked flask

which was equipped with a mechanical stirrer, a septum cap and a nitrogen

inlet. The flask was immersed in a dry ice-acetone bath at -60-70° and

the solution was stirred under a nitrogen atmosphere (which was maintained

throughout the experiment) while .15 mol of n-butyllithium in hexane was

added to the contents of the flask. Stirring was continued for 4 hr

at -50-60° and then 42.6 g (.30 mol) of ethyl iodide was added to the

reaction mixture. Stirring was continued for 18 hr at 0-5°, and then

the reaction mixture was acidified to a pH of 4 with 10% hydrochloric

acid and extracted twice with 150 ml portions of chloroform. The chloro-

form solution was washed with a saturated solution of sodium bisulfite,

dried over anhydrous sodium sulfate and evaporated to yield 24 g (85%)

of crude product. Distillation of the crude product yielded 20.85 g

(74%) of 2-ethyl-2-propenyl-1,3-dithiane as a colorless liquid, bp 96-98°

(1 mm). An analytical sample was obtained by collecting a middle fraction

from the distillate, bp 96-98° (1 mm), n_D^{25} 1.5570; ir (thin film) 1650

cm^{-1} (carbon-carbon double bond), 1435 cm^{-1} (carbon-sulfur stretch);

nmr (CDCl$_3$) δ 5.17-6.2 (m, 2, olefinic protons), 2.3-3.1 (m, 4, methylene

protons on carbons 4 and 6 of the dithiane ring), 1.6–2.3 (complex multiplet, 7, contains discernible d at 1.8 corresponding to a vinyl methyl group; remaining signals due to methylene of ethyl group and C-5 protons of dithiane ring); .90 (t, 3, J = 6 Hz, terminal methyl); mass spectrum 189 (7), 188 (60), 164 (11), 159 (45), 135 (21), 115 (10), 114 (36), 113 (35), 107 (22), 106 (10), 99 (17), 87 (10), 86 (12), 85 (100), 84 (15), 81 (21), 73 (31), 47 (20), 45 (35), and 41 (45).

<u>Anal.</u> Calcd. for $C_9H_{15}S_2$: C, 57.45; H, 8.51. Found: C, 57.24; H, 8.32.

1-(1,3-propylenedithio)-3-methyl-4-hydroxy-4-phenyl-1-butene (<u>16</u>)

A solution of 12 g (.075 mol) of 2-propenyl-1,3-dithiane in 100 ml of dry tetrahydrofuran was placed in a 500 ml three-necked flask which was equipped with a mechanical stirrer, a septum cap and a nitrogen inlet. The flask was immersed in a dry ice-acetone bath at -70° and the solution was stirred under a nitrogen atmosphere which was maintained throughout the experiment while a solution of .075 mol of n-butyllithium in hexane was added by means of a syringe to the contents of the flask. The reaction mixture was stirred for 4 hr at -70° and 8 g (.075 mol) of benzaldehyde was added to the contents of the flask. Stirring was continued for 5 min at -70°, then the reaction mixture was acidified with 10% hydrochloric acid and extracted twice with two 100 ml portions of chloroform. The chloroform solution was washed several times with a saturated solution of sodium bisulfite and dried over anhydrous sodium sulfate. Evaporation of the solvent yielded 12.6 g (78.8%) of a diastereoisomeric mixture of 1-(1,3-propylenedithio)-3-methyl-4-hydroxy-4-phenyl-1-butene as an oily solid. Three recrystallizations from 95%

ethanol yielded an analytical sample, mp 74-77°; ir (KBr) 3440 cm^{-1}

(hydroxyl), 1692 cm^{-1} (carbon-carbon double bond), 1415 cm^{-1} (carbon-

sulfur stretch); nmr (CDCl$_3$) δ 7.1-7.5 (m, total 5, aromatic protons),

5.3 and 4.6 (doublets, total 1, J = 6 Hz, and J = 8 Hz, olefinic protons),

3.2-3.7 (m, 2, allylic proton and the benzylic proton), 1.8-3.0 (m, 7,

protons of the dithiane ring and hydroxylic proton), 1.05 and .90 (dou-

blets, total of 3, J = 6 Hz, and J = 7 Hz, methyl); mass spectrum 267

(2), 266 (8), 133 (11), 120 (33), 119 (20), 110 (12), 108 (100), 93 (16),

47 (11), 43 (27), and 41 (10).

<u>Anal</u>. Calcd. for C$_{14}$H$_{18}$S$_2$O: C, 62.95; H, 6.76; O, 6.01. Found:

C, 62.95; H, 6.66; O, 5.87.

The Reaction of the Anion of 2-propenyl-1,3-dithiane (<u>12</u>)
with Ethyl Benzoate

A solution of 2 g (12.5 mmol) of 2-propenyl-1,3-dithiane in 100

ml of dry tetrahydrofuran was placed in a 500 ml three-necked flask which

was equipped with a mechanical stirrer, a gas inlet and a septum cap.

The flask was immersed in a dry ice-acetone bath at -30°, and the reac-

tion was placed under a nitrogen atmosphere which was maintained through-

out the experiment. A solution of 12.5 mmol of n-butyllithium in hexane

was added by means of a syringe to the contents of the flask. The reaction

mixture was stirred at -30° for 4 hr and 6.75 g (45 mmol) of ethyl ben-

zoate was added to the contents of the flask. Stirring was continued

for 18 hr at 0-5°, and then the reaction mixture was acidified to a pH

of 4 with a 10% hydrochloric acid and extracted twice with 100 ml portions

of chloroform. The chloroform solution was dried over anhydrous sodium

sulfate and evaporated to yield 8.54 g of a mixture of ethyl benzoate and

the di-addition product 20. The mixture was shaken with 25 ml of ethyl

acetate and white crystals separated from the solution. The crystals

were collected by suction filtration and air dried to yield 3.71 g (70%)

of the di-addition compound 20, mp 138-139°. Two recrystallizations

from hexane-methylene chloride yielded an analytical sample, mp 142-143°;

ir (KBr) 3505 cm^{-1} (hydroxyl), 1405 cm^{-1} (carbon-sulfur stretch); nmr

(CDCl$_3$) δ 7.0-7.75 (m, 5, aromatic protons), 6.3 (d, 1, J = 10 Hz, ole-

finic proton), 5.8-5.9 (m, 1, olefinic proton), 3.1-3.7 (m, 2, allylic

protons), 1.4-3 (m, 12, all of the methylene protons of the dithiane

ring), 1.90, 0.60 (doublets, total of 3, J = 5 Hz, J = 6 Hz, methyls);

mass spectrum 424 (3), 266 (12), 265 (16), 264 (100), 161 (10), 160

(11), 159 (60), 132 (10), 129 (13), 115 (14), 106 (15), 105 (25), 104

(20), 86 (10), 85 (25), 84 (10), 77 (15), 73 (13), 57 (44), 56 (28),

49 (17), 44 (15), 43 (25), 42 (16) and 41 (50).

<u>Anal</u>. Calcd. for C$_{21}$H$_{28}$S$_4$O: C, 59.43; H, 6.60; S, 30.19.

Found: C, 59.29; H, 6.64; S, 30.23.

β-Methyl-γ-phenylbutyrolactone (17)

A solution of 250 mg (.94 mmol) of 16 and 5 ml of 10% hydrochloric

acid in 25 ml of tetrahydrofuran was heated at 50° for 2 hr, cooled to

room temperature and extracted with 100 ml of chloroform. The chloro-

form solution was dried over anhydrous sodium sulfate and evaporated

to yield .205 g of an oil which was a mixture of 1,3-propanedithiol and

β-methyl-γ-phenylbutyrolactone (17). The oil was dissolved in 25 ml of

95% ethanol, 1 g of potassium hydroxide was added, and the reaction

mixture was refluxed for 12 hr and then evaporated to dryness. The

solid residue was washed several times with ether and air dried. The

residue was then treated with 5 ml of concentrated hydrochloric acid and extracted twice with 50 ml portions of ether. The ether solution was dried over anhydrous sodium sulfate and evaporated to yield 99.2 mg (60%) of β-methyl-γ-phenylbutyrolactone as a colorless oil; ir (thin film) 1785 cm^{-1}(lactone carbonyl); nmr (CDCl$_3$) δ 7.2-7.9 (m, 5, aromatic protons), 5.60, 4.90 (both doublets, total 1, J = 5 Hz, J = 8 Hz, benzylic proton on carbon bearing oxygen), 2.1-3.0 (m, remaining ring protons), 1.25, .70 (both doublets, total 3, J = 5 Hz, J = 8 Hz, methyl); mass spectrum 177 (5), 176 (45), 117 (13), 116 (5), 115 (10), 107 (100), 106 (24), 105 (99), 91 (14), 79 (15), 78 (10), 77 (36), 70 (14), 69 (11), 65 (6), 50 (18), and 40 (31).

<u>Anal</u>. Calcd. for C$_{11}$H$_{12}$O$_2$: C, 75.00; H, 6.82. Found: C, 73.50; H, 6.89.

Ethyl Propenyl ketone (<u>15</u>)

A mixture of 1 g (5.3 mmol) of 2-ethyl-2-propenyl-1,3-dithiane (<u>13</u>), 5 ml of methyl iodide, 1 ml of water and 50 ml of acetone was refluxed for 24 hr and then distilled at atmospheric pressure until most of the acetone was removed. The mixture was cooled to room temperature, 3 ml of water was added and the mixture was distilled through a short path distillation column. A fraction consisting of a mixture of the ketone <u>15</u> and water was collected, bp 98-101°. The mixture was poured into 25 ml of ether and the ether layer was collected and dried over anhydrous sodium sulfate. Evaporation of the ether and subsequent distillation yielded .360 g (69%) of dry ethyl propenyl ketone, bp 81-82° (12 mm); 2,4-dinitrophenylhydrazone, mp 168-169°, n_D^{25} 1.4380 [Lit.[9] bp 76.2° (8.5 mm); 2,4-dinitrophenyhydrozone, mp 170°].

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II. STUDIES DIRECTED TOWARD THE SYNTHESIS OF ILLUDIN-S

History and Background

The fungal metabolites illudin-S (1) and illudin-M (2) were
first isolated from jack-o'-lantern mushrooms in 1950 by Anchel and
coworkers.[1] Somewhat later, but before the structure of 1 and 2 had
been published, Japanese investigators[2,3] isolated a substance which
they named lampterol from the poisonous mushroom, Lampteromyces japoni-
cus, which grows on rotten beech trees in Japan. It was later found
that lampterol is identical to illudin-S, and since the latter name
was the first reported in the literature, it has been retained as the
family name for a group of closely related compounds.

The illudins are of considerable interest because of their
antitumor activity, antibacterial activity and their possession of a
unique non-isoprenoid structure. Anchel and McMorris[3] assigned struc-
tures 1 and 2 except for absolutely stereochemistry; the structure which
they assigned to 1 was corroborated by an independent investigation[4]
carried out in Japan.

1   2

22
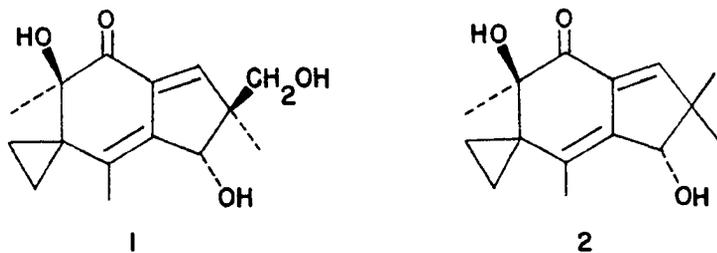
Matsumoto and coworkers[5,6] have accomplished the total synthesis

of $\underline{1}$ and $\underline{2}$. In preparation for their total synthesis of $\underline{1}$ and $\underline{2}$, they

conducted several preliminary investigations into the synthesis of key

intermediates which possess the structural features of the illudins

and the necessary functionality required for conversion to the illudins.

The first such compound to be prepared[7] was $\underline{9}$. The series of

reactions leading to the synthesis of $\underline{9}$ is outlined in Scheme 1. The

β-ketosulfoxide $\underline{3}$ required for the synthesis of $\underline{9}$ was prepared (see

scheme 1) from methylsulfinyl carbanion and the ethylene ketal of 1-

acetyl-1-carboethoxycyclopropane by the method of Corey and Chaykovsky.[8]

The Michael addition of $\underline{3}$ to $\underline{4}$ in ethanol catalyzed by sodium

ethoxide afforded $\underline{5}$ as the only product in 60% yields. Amalgamated alu-

minum foil in dioxane–water at room temperature converted $\underline{5}$ to $\underline{6}$ which was

transformed to the triketone $\underline{7}$ by p-toluenesulfonic acid in aqueous

acetone. Potassium t-butoxide in t-butyl alcohol transformed $\underline{7}$ to the

diketone $\underline{8}$. Methyl magnesium iodide (1 equivalent) reacted selectively

with the non-conjugated carbonyl group of $\underline{8}$ to form $\underline{9}$.

After synthesizing compound $\underline{9}$, Matsumoto and coworkers[9] pro-

ceeded by a similar series of reactions to synthesize the more highly

functionalized illudin precursor $\underline{16}$. The sequence of reactions leading

to the synthesis of $\underline{16}$ is depicted in scheme 2. The series of reactions

employed in the synthesis of $\underline{10}$, the other intermediate required for

the synthesis of $\underline{15}$, is also shown in scheme 2.

Treatment of $\underline{A}$ with iodine in methanol yielded an epimeric pair

of tetrahydrofuranones $\underline{17}$. Sodium borohydride reduction of $\underline{17}$ yielded

$\underline{18}$ (an isomeric mixture of tetrahydrofuranols) which was converted to $\underline{19}$

Scheme 1

by treatment with acetic anhydride in pyridine. Dilute hydrochloric

acid converted 19 to the ketoaldehyde 20 which in turn was cyclized to

10 by sodium hydride in refluxing benzene.

The Michael addition of 3 to 10 in ethanol catalyzed by sodium

ethoxide yielded 11 as the only product. In the presence of acetic
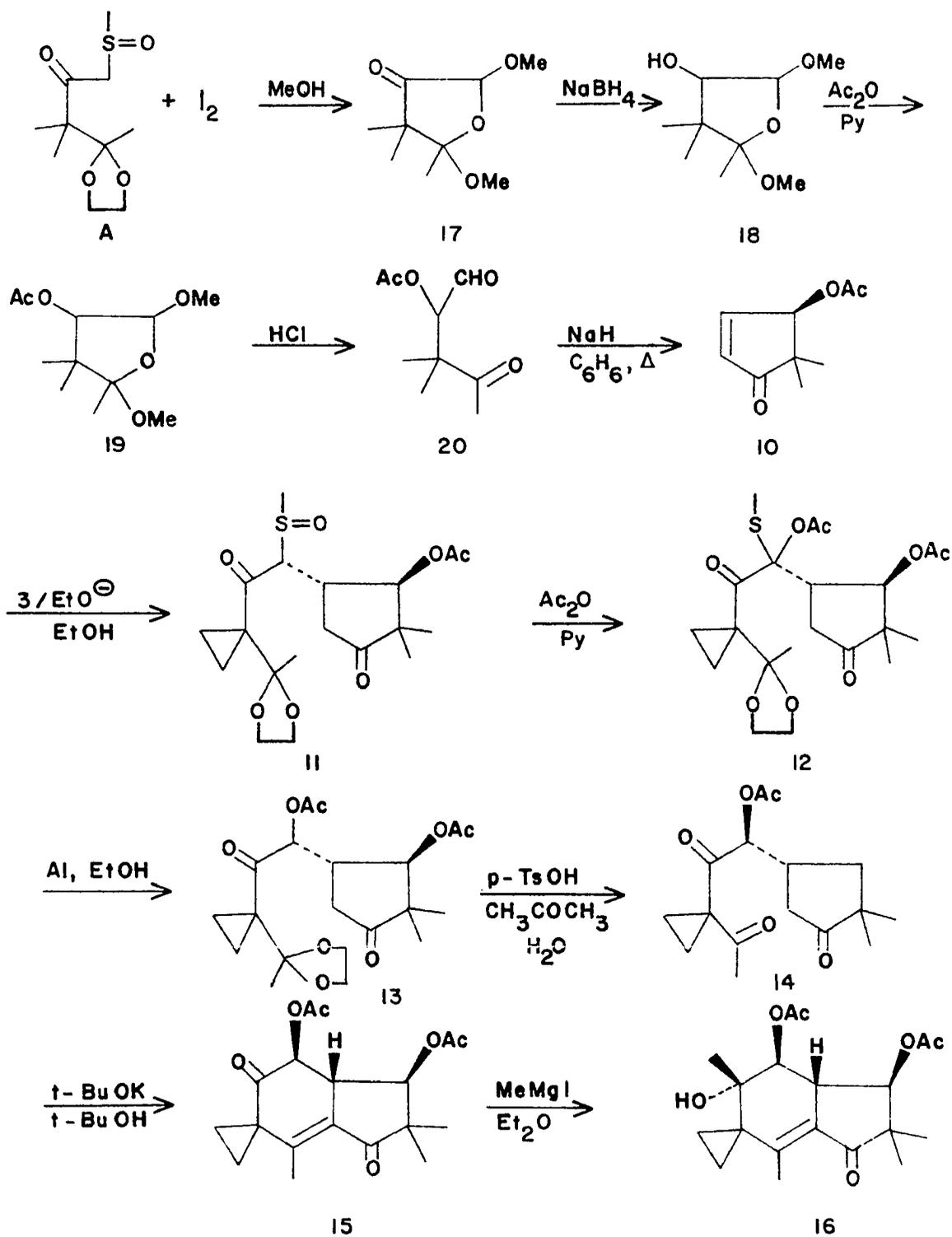
Scheme 2

anhydride and pyridine 11 underwent the Pummerer[10] rearrangement to

form 12. Treatment of 12 with amalgamated aluminum in ethanol afforded

13 which was subsequently transformed to the triketone 14 by aqueous

acetone containing a trace of p-toluenesulfonic acid.

Potassium-t-butoxide in t-butyl alcohol transformed 14 to the

enone 15. Matsumoto and coworkers[9] based their stereochemical assign-

ment in 15 on the following evidence: J_{AX} = 9 Hz, therefore, H_A and
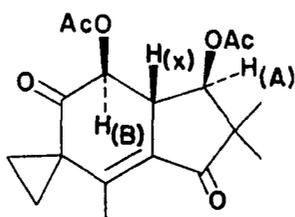
15

H_X are trans to each and axial to the cyclopentanone ring.[14] Since

J_{BX} = 12 Hz, it was similarly concluded[14] that H_B and H_X are also trans

to each other and axial to the cyclohexanone ring. Thus, it was con-

cluded that 15 has the stereochemistry shown in scheme 2. Compound 15

was converted to 16 by methylmagnesium iodide which reacted selectively

with the six-membered carbonyl group in a highly stereoselective manner.

The sequence of reactions leading to the synthesis of the ex-

ploratory compound 16 provided the key intermediate 12 which ultimately

lead to the synthesis of illudin-M (2).[5] When 12 was heated in ethanol

(see scheme 3), it rearranged to 21. Treatment of 21 with potassium-

t-butoxide in t-butyl alcohol afforded 22 which was then converted to

the acetate 23. Methyl magnesium iodide also reacted selectively with

the six-membered ring carbonyl group of <u>23</u> in a highly stereoselective

manner to form <u>24</u>. Reduction of <u>24</u> with sodium borohydride in tetra-

hydrofuran yielded the diol <u>25</u> as the only product. Treatment of <u>25</u>
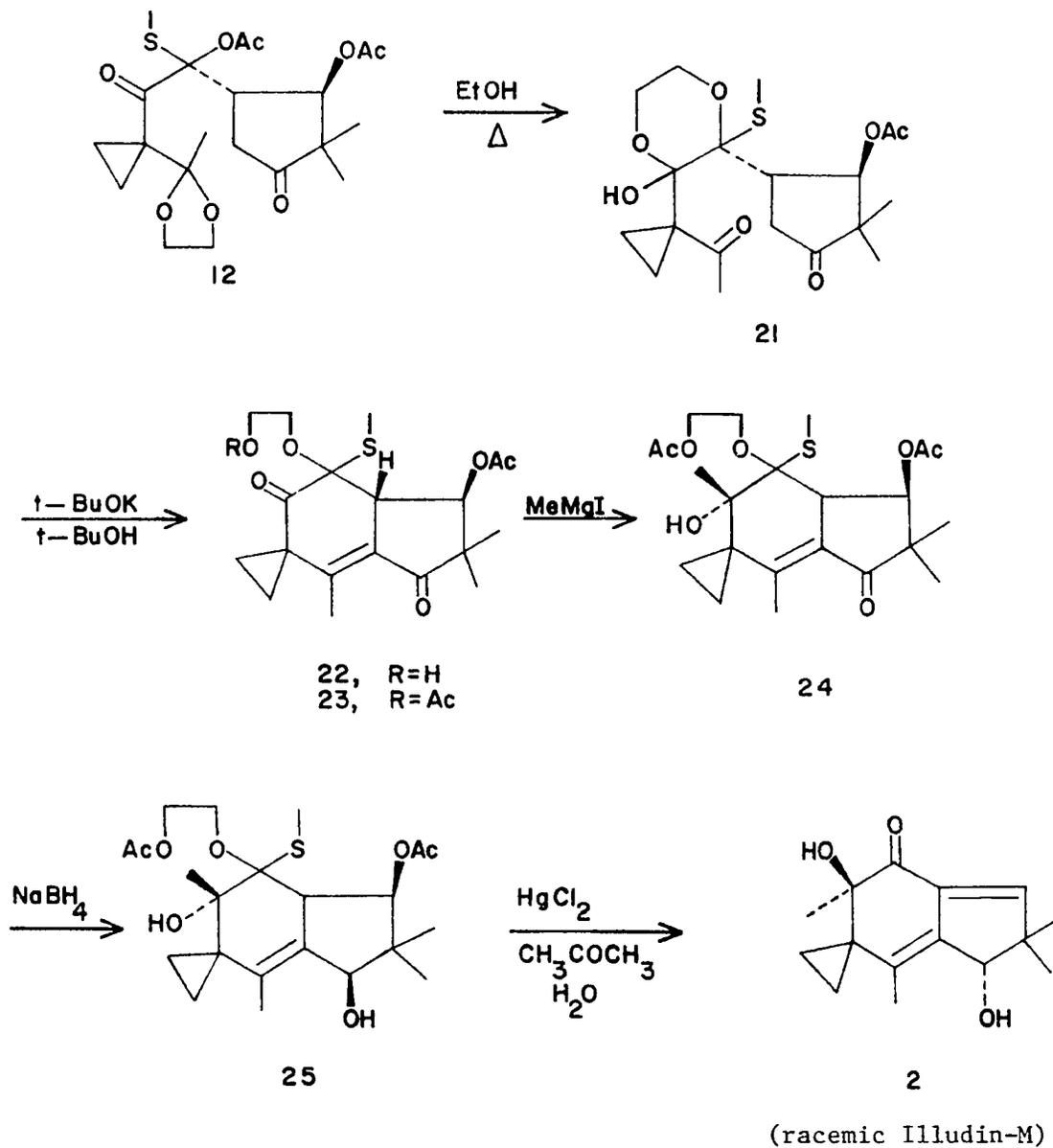
(racemic Illudin-M)

Scheme 3

with mercuric chloride in aqueous acetone afforded racemic illudin-M (2).

The chemical and physical properties of the synthetic illudin-M (2) were

identical in all respects to the natural occurring substance.

Proceeding by a similar sequence of reactions (see scheme 4),

Matsumoto and coworkers[6] synthesized illudin-S (1). The treatment of 3

with potassium t-butoxide in t-butyl alcohol followed by the addition of

26 afforded the Michael adduct 27 in 70% yields. When 27 was treated with

methoxyacetic anhydride, the Pummerer[10] rearrangement occurred to form 28

in quantitative yields. In the presence of ethanol, 28 was transformed

to 29; potassium t-butoxide in t-butyl alcohol converted 29 to the α,β-

unsaturated ketone 30. The treatment of 30 with acetic anhydride in pyri-

dine resulted in the acetylation of the hydroxyl group to form 31.

Methyl magnesium iodide (one equivalent) reacted selectively

with the six-membered ring carbonyl group of 31 to form 32; this reac-

tion was also highly stereoselective. Sodium borohydride in tetrahydro-

furan transformed 32 to 33 which in turn was converted to 34 by mercuric

chloride in aqueous acetone. Compound 34 was hydrolyzed to illudin-S

(1) by treatment with aqueous sodium carbonate. The physical and chemical

properties of the synthetic illudin-S (1) were found to be identical

in all respects to the natural occurring substance.

Illudin S has been assigned[13] the absolute configuration implied

in formula 1, based on an application of the dibenzoate chirality rule to

a phenolic degradation product. It has been theorized that the biogenesis of

1 and 2 from farnesyl phosphate[3,11,12] occurs in the manner indicated in

scheme 5. According to that biosynthetic hypothesis, humelene serves as

a precursor of the unique non-isoprenoid structure of the illudins.

Investigators are conducting experiments in an effort to determine the

biosynthetic sequence leading to the illudins.

Scheme 4

Mevalonic Acid $\longrightarrow$
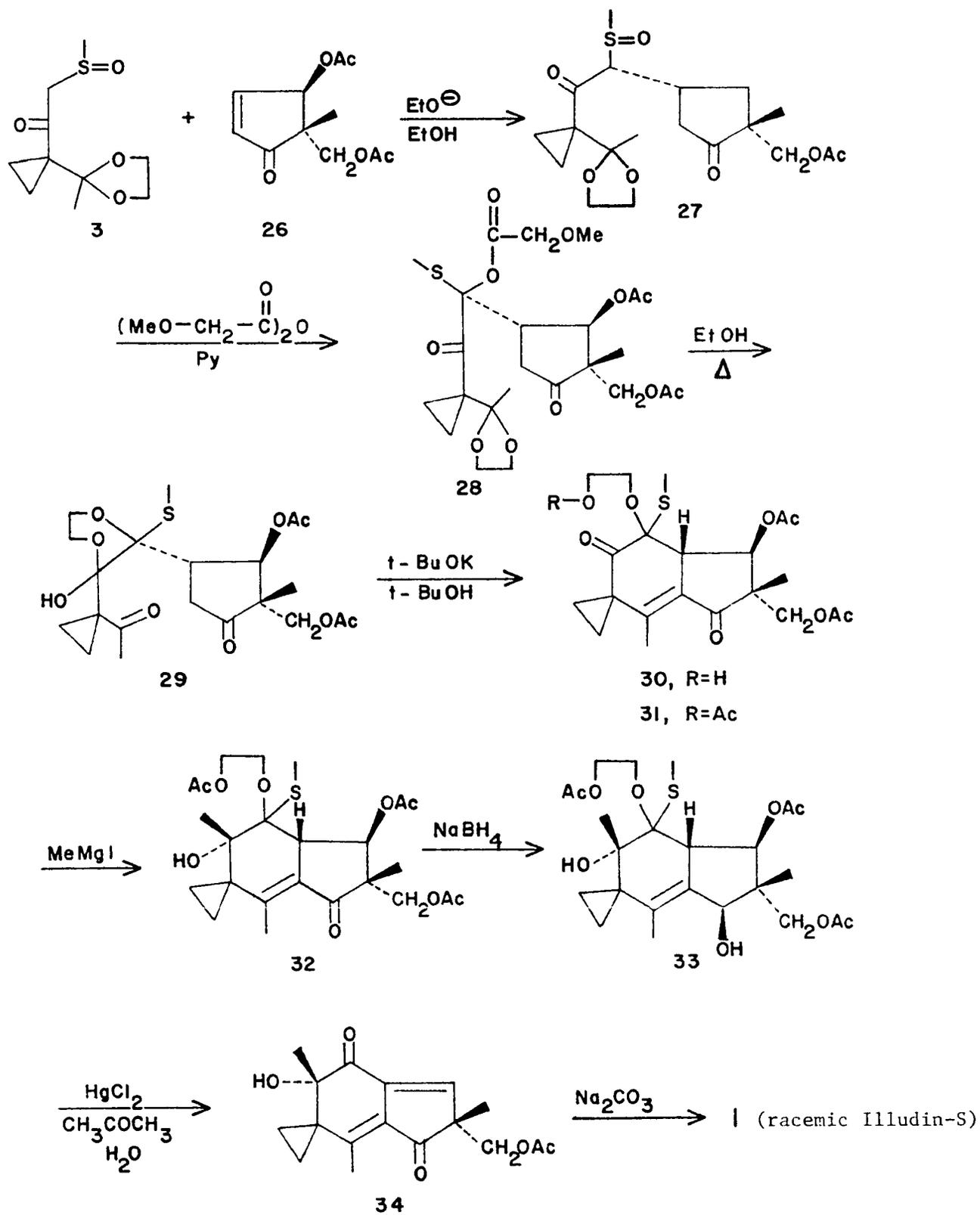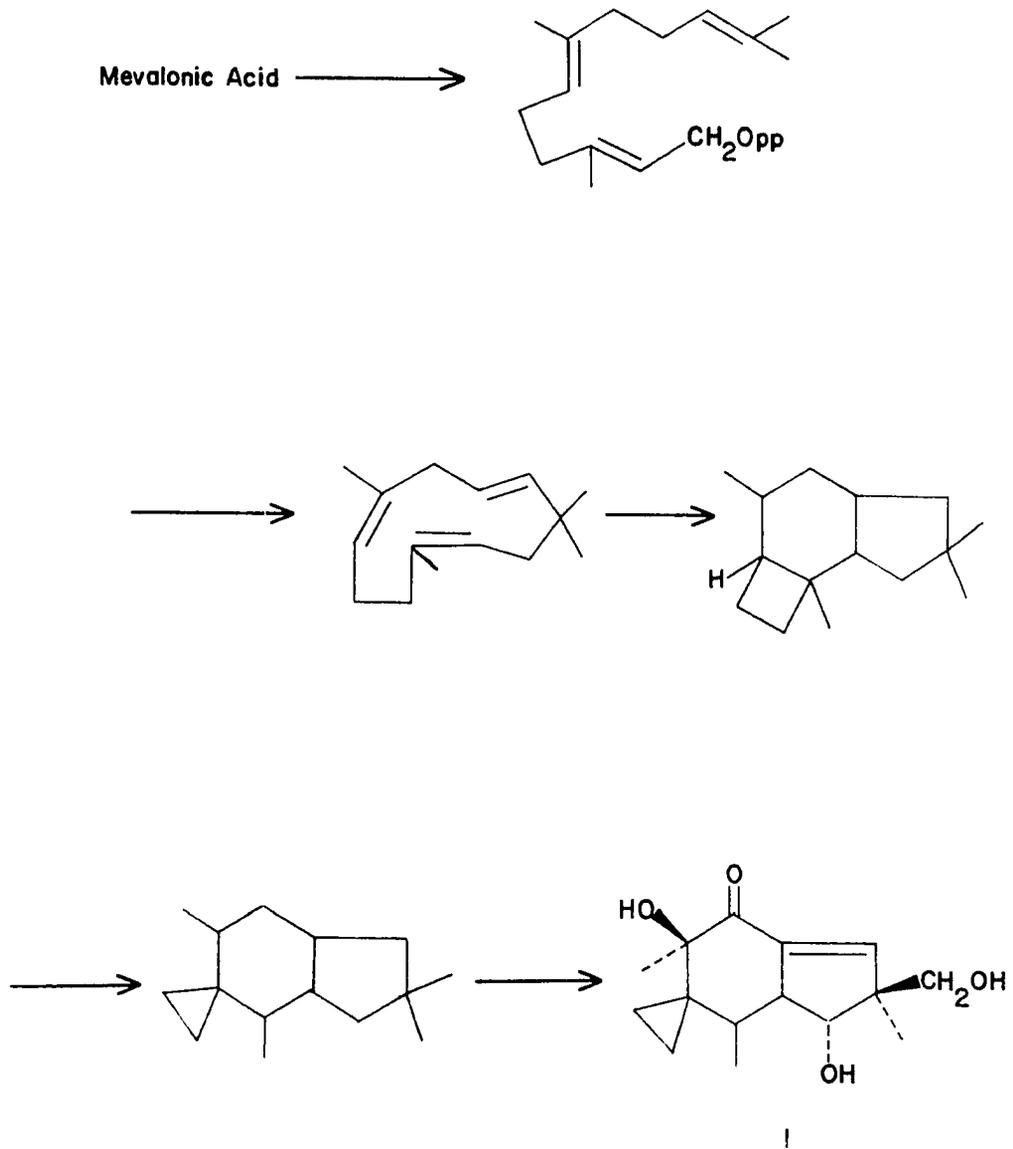
Scheme 5

INTRODUCTION

The objective of this study was to develop a sequence of reactions which would ultimately lead to the synthesis of the natural product illudin-S (1). The general approach to the synthesis of 1 is depicted in scheme 6 in which the principal reaction leading to the illudin skeleton involves the combination of the dithiane 40 with 1,1-diacetylcyclopropane (41). Several alternate approaches to the synthesis of the key intermediates 39 and 40 will be discussed in this section.

A preliminary report on the synthesis of 2[5] appeared about the time this work was initiated. An examination of the sequence of reactions employed by Matsumoto and coworkers in the synthesis of 2 revealed that the plan for synthesizing 1 and 2 laid out for evaluation in this thesis was different from that of the Japanese workers, and if successful would result in a shorter synthesis of 1 and 2. In view of the fact that the synthesis of 2 had been reported, it was decided to explore methods for synthesizing 1.

Scheme 6

Compound 41 was prepared by the method of Ichakawa and coworkers.[15]

$$CH_2{=}CH_2 \quad \begin{array}{l} \text{I. } Hg(OAc)_2, \text{ AcOH} \\ \hline \text{2. } CH_3{-}COCH_2{-}COCH_3, \text{ NaOH} \\ \text{3. KOH} \end{array} \longrightarrow$$

41
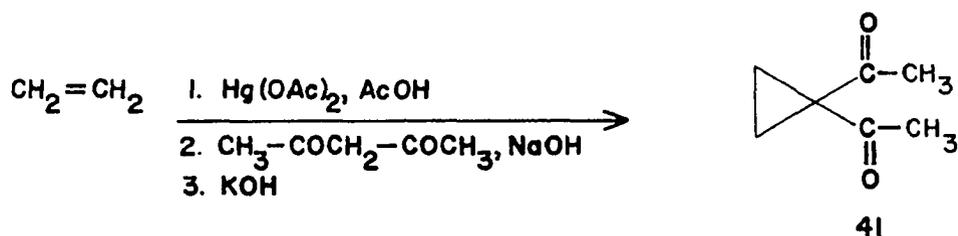
2-methyl-2-carbomethoxycyclopentanone (35) was prepared by a slight modification of the procedure of Meyer and coworkers.[17]

$$MeO{-}\overset{O}{\overset{\|}{C}}{-}(CH_2)_4{-}\overset{O}{\overset{\|}{C}}{-}OMe \quad \begin{array}{l} \text{I. NaH (xylene)} \\ \hline \text{2. MeI} \\ \text{3. H}^+ \end{array} \longrightarrow$$

35
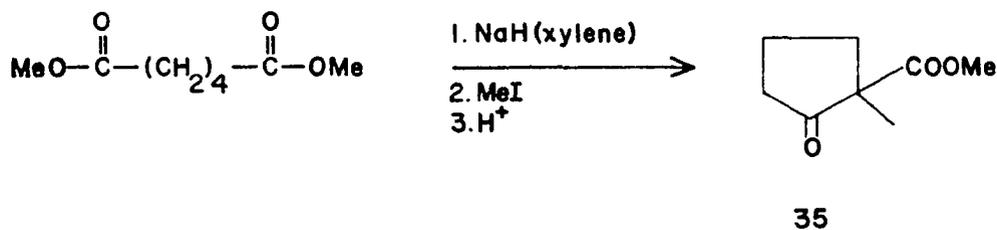
During the early stages of this reaction, the originally fluid suspension of sodium hydride in xylene turned to a thick mush as a result of the insolubility of the enolate of the β-keto ester obtained as a result of step 1. Consequently, the reaction mixture was difficult to stir by ordinary methods and as a result poor yields of the final product 35 were obtained. However, the yield of 35 was improved considerably

33

by rapid stirring and keeping the reaction mixture fluid by continuously adding solvent at intervals throughout the initial stage of the reaction (enolate formation).

Treatment of 35 with an excess of bromine in methylene chloride afforded 36 in 95% yield (80%) purified. The next step in the reaction sequence called for the dehydrobromination of 36 to 2-bromo-4-methyl-4-carbomethyoxycyclopentene-3-one (37). However, the possibility of the direct conversion of 36 to 38 by the action of alcoholic potassium cyanide was recognized. This conversion could take place by an initial dehydrobromination of 36 to 37 which in turn could undergo a conjugate addition of cyanide ion followed by a second dehydrobromination to give 38. When a solution of 36 in methanol was actually treated with a suspension of potassium cyanide in methanol, a dark tar was obtained. Analysis of the tar by nmr and ir spectroscopy indicated that no olefinic or nitrile groups were present in the product.

After attempts to convert 36 directly to 38 proved to be unsuccessful, attention was directed to accomplishing this conversion in a stepwise sequence, the first of which consisted of the dehydrobromination of 36. Lithium carbonate in dimethylformamide,[18] diazobicyclo [4.3.0] nonene (DBN),[19] and collidine[20] have been used to successfully convert α-haloketones to the corresponding α,β-unsaturated ketones. When a solution of 36 in benzene was treated with diazobicyclo [4.3.0]nonene, a dark tar resulted. Chromatography of the tar on silica gel yielded a small quantity of 37, the desired product. Other dehydrohalogenation procedures employed in attempts to improve the yield of 37, including lithium carbonate in acetone and collidine in acetone, were also unsuccessful. In general, tars and unaltered 36 were recovered.

The dehydrobromination of <u>36</u> (see scheme 7) was ultimately

accomplished by treatment with sodium bicarbonate in dimethylformamide,

whereupon <u>37</u> was obtained in 80% yields. Treatment of a solution of

<u>37</u> in acetonitrile and acetic acid with potassium cyanide afforded <u>38</u>

in 66-70% yields without isolation of any intermediates.
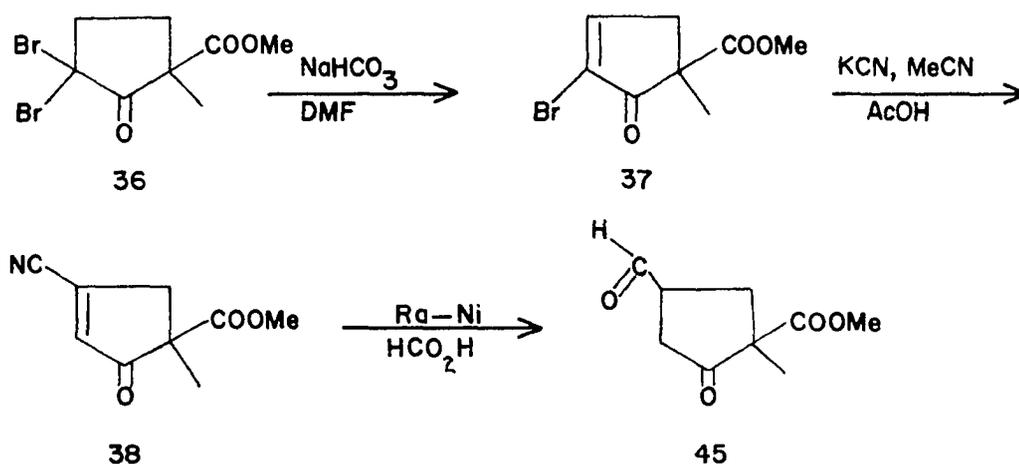
Scheme 7

The next two steps in the reaction sequence called for the con-

version of <u>38</u> to the α,β-unsaturated aldehyde <u>39</u>. and the conversion

of <u>39</u> to the dithiane <u>40</u> (see scheme 6). Table summarizes some reported

methods for converting nitriles to aldehydes. In our

initial approach to the problem of converting the nitrile <u>38</u> to the

α,β-unsaturated aldehyde <u>39</u>, various modifications of the procedures of

TABLE 2

A Survey of Literature Procedures for Reducing

Nitriles to Aldehydes

Reducing Agent	Solvent	Conditions	% Yield of Aldehyde	Ref.
DiBAH	Et_2O, $MeCl_2$ or	RT. or reflux	70-80	24
LiAl(OEt)$_3$ H	Et_2O, T.H.F.	0°	80-90	22
Raney Nickel and $NaH_2PO_3 \cdot H_2O$	NCOOH, or ACOH,H_2O pyridine	R.T.	70-90	21
Raney nickel	formic acid 45-50%	80	80-90	21
HCl, SnCl$_2$	Et_2O	0°	50-90	23
Hydrazine and Raney nickel	H_2O	R.T.	75-80	33

Statsun and Backberg[21] were employed. It was assumed that the nitrile

group in 38 would resemble that of benzonitrile in terms of chemical

reactivity and, therefore, if benzonitrile could be successfully reduced

to benzaldehyde by these procedures, the nitrile 38 could be success-

fully reduced to the aldehyde 39 under similar conditions. Indeed, when

benzonitrile was treated with Raney nickel in formic acid, benzaldehyde

was obtained in 80% yields. However, when the nitrile 38 was subjected

to the same reaction conditions employed in the reduction of benzonitrile,

unaltered 39 was recovered from the reaction mixture.

After several attempts to convert 38 to 39 using the procedures

of Statsun and Backberg proved unsuccessful, the reaction conditions

were reviewed to determine which factors could be varied in order to

bring about the reduction of 38 to 39. The variables considered were

the amount of Raney nickel used per gram of nitrile, the volume of formic

acid, used per gram of nitrile, the amount of water in the formic acid, the

reaction time, the reaction temperature, and the activity of the Raney nickel

catalyst. Each cf these factors was varied one at a time, but none of the reduc-

tion attempts converted 38 to the desired aldehyde 39. However, when

a solution of 38 in 75% formic acid was treated with Raney nickel cata-

lyst (1 to 1.5 grams of catalyst per gram of nitrile) at 75-80° for

1-1.5 hours, the saturated aldehyde 45 (see scheme 2) was obtained in

50-60% yields. Thus it was concluded that 38 could not be reduced to 39

by the Raney nickel procedures. It was further concluded that the a-

mount of Raney nickel per gram of nitrile, the reaction time and the

reaction temperature were critical to the reduction of 38 to the saturated

aldehyde 45. (See table 3 for more details.)

38

TABLE 3

Results of Attempts to Reduce The Nitrile 38

to the Aldehyde 39

Moles of 38	Reducing Agent and No. of Moles	Solvent + Conditions	Product + % Yield
.0042	Li(OEt)$_3$-Al-H (.0042)	Et$_2$O, 0°	38 (45)
.004	Li(OEt)$_3$-Al-H (.004)	Et$_2$O, R.T. 1 hr	38 (80)
.011	Li(OEt)$_3$-Al-II (.001)	THF R.T. 42 hr Reflux 2 hr	38 (90)
.007	DIBAH (.007) R.T. 3 hr	Benzene R.T. 3 hr	38 (80)

Raney Nickel Procedures

Grams of 38	Grams of Catalyst	Aqueous Solvent	Conditions	% Yield of Product
2	3	50% formic acid	60°, 2 hr	(52) saturated aldehyde 45
2	3	44% formic acid	100°, 7 min	(52) sat. ald. 45
2	2	45% formic acid, 1,2 dichloroethane	30-60° 3 hr	(60) of 45
2	6	44% formic acid	Reflux 5 min	(48) of 45
1	.5	50% formic acid	50-60° 15 min	(80) of 38
1	1.5	50% formic acid	50-60° 15 min	(55) of 45

After attempts to reduce 38 to 39 with various modifications of
the Raney nickel procedures proved unsuccessful, some other procedures
for the conversion of nitriles to aldehydes were explored. A search
of the literature revealed that the methods of Brown,[22] Stephens,[23]
Meyer[25,26] and procedures employing diisobutylaluminum hydride[24] have
been used to convert nitriles to aldehydes.

The first of these procedures to be explored was the method
employing lithium triethoxyaluminum hydride which was developed by
Brown.[22] In an effort to develop the technique for applying this poten-
tially useful reaction to the problem of reducing 38 to 30, it was de-
cided that an attempt should be made to duplicate the results obtained
by Brown and coworkers in one of their experiments. Accordingly, benzo-
nitrile was treated with lithium triethoxyaluminum hydride, and benzal-
dehyde was obtained in 80% yields. Brown and coworkers reported a 90%
yield.

Since the attempt to duplicate the experimental results of
Brown and coworkers[22] proved successful, the nitrile 39 and lithium tri-
ethoxyaluminum hydride (1:1 molar ratio) were reacted under the same
experimental conditions employed in the reduction of benzonitrile.
However, only unaltered 38 was recovered from the reaction mixture.
Similar results were obtained when a solution of 38 and triethoxyaluminum
hydride (1:1 molar ratio) in tetrahydrofuran was refluxed for about four
hours. Next, compound 38 was treated with a tenfold excess of lithium
triethoxyaluminum hydride, and the reaction mixture worked up with deu-
terium oxide. The ir spectrum of the resulting product exhibited strong
absorptions at 3450 cm^{-1} (hydroxyl), 2215 cm^{-1} (nitrile) and 1645 cm^{-1}

(carbon-carbon double bond) and lacked the carbonyl absorptions due to

the ester and ketone functions of 38. The nmr spectrum of the product

indicated that the acidic methylene protons of 38 did not exchange with

deuterium.

38
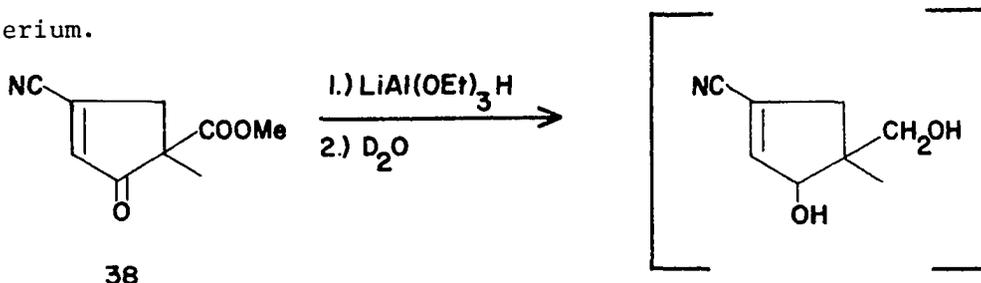
It had been postulated that the inertness of the nitrile function in

38 toward reducing agents might be due to abstraction of the ring

methylene protons by the reducing agents to give an enolate that would

not react further. However, the evidence presented above does not sup-

port this hypothesis.

The failure of these established reduction procedures to effect

the conversion of 38 to 39 indicated that a stronger reducing agent

should be employed. Accordingly, a solution of 38 and diisobutylaluminum

hydride (1:1 molar ratio) in benzene was refluxed for four hours; un-

altered 38 was recovered from the reaction mixture. When a solution

of 38 and lithium aluminum hydride (4:1 molar ratio) in ether was

stirred at -70° for one hour, the ester function of 38 was partially

reduced. The ir spectrum of the product mixture exhibited absorptions

at 3500 cm^{-1} (OH), 1745 cm^{-1} (ester) and 1710 cm^{-1} (ketone). Further

analysis of the mixture by thin layer chromatography (tlc) and nmr

spectroscopy indicated that the mixture consisted mostly of 38 and that

no aldehyde was formed.

Next, the method of Stephens[23] was utilized in an attempt to

reduce 38 to 39. It is reported that the Stephens method fails to

convert α,β-unsaturated nitriles to the corresponding aldehydes. Never-

theless, a mixture of 38 and stannic chloride in absolute ether was

treated with dry hydrogen chloride gas; however, only unaltered 38 was

recovered from the reaction mixture.

Finally, the procedure developed by Meyers and coworkers[26] was

employed in an attempt to convert 38 to 39 (see scheme 8). Based on
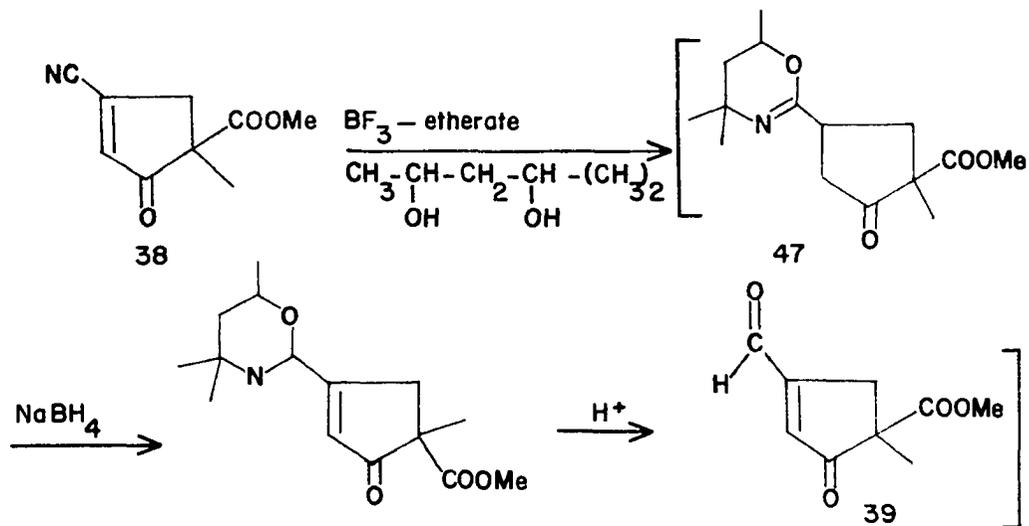
Scheme 8

the examples reported by Meyers and collaborators, it was anticipated

that boron trifluoride-etherate catalyzed reaction of 38 with 2-methyl-

2,4-pentanediol would result in the formation of the 1,3-oxazine 47.

However, when a solution of 38, 2-methyl-2,4-pentanediol and boron

trifluoride etherate in ether was maintained at 0° for 48 hours, no

appreciable reaction occurred.

In view of the failures encountered in attempts to convert 38

to 39 and the fact that 38 could be successfully reduced to the saturated

aldehyde 45 (see scheme 2), some methods for dehydrogenating 45 to give

39 were considered. Literature reports indicated that dichlorodicyano-

quinone and selenium dioxide[32] would convert some saturated steriodal

ketones to the corresponding α,β-unsaturated ketones. When a solution

of 45 and dichlorodicyanoquinone in benzene was refluxed for about two

hr, a dark colored tarry product was obtained. Analysis of the reaction

mixture by tlc and nmr spectroscopy indicated the presence of a com-

plex mixture of products which exhibited no aldehyde or olefinic pro-

tons. Hence it was concluded that decarbonylation of the aldehyde 45

had taken place during the dehydrogenation attempts. Similar results

were obtained when selenium dioxide was reacted with 45

Since all attempts to convert 38 to the corresponding aldehyde

39 failed, the physical data on compound 38 was re-examined. This

examination revealed that the structure assigned to 38 was fully con-

sistent with all spectra and analytical data except that the ir spectra

of 38 exhibits very weak absorption in the region of 2210 cm^{-1}. A

search of the literature revealed that, in general, α,β-unsaturated

nitriles substituted in the β-position with a carbonyl group show vir-

tually no absorption in the region 2210 cm^{-1}.[27,28]
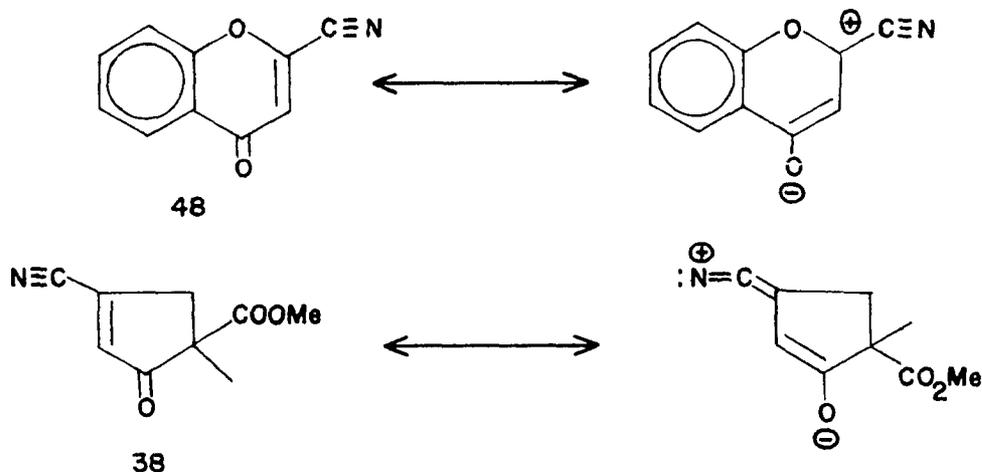
In order to account for this abnormality it was proposed that electrons

are displaced toward the more electronegative carbonyl group in the

manner indicated for compounds 38 and 48. If the dipolar form of 38 contributes significantly to its overall electronic structure, this might explain why this compound fails to undergo reduction to the corresponding aldehyde.

In view of the fact that cyanide ion adds readily to 37 to form 38 (see scheme 2), it was believed that some other nucleophiles would undergo the Michael reaction with 37 to form precursors to 39 and 40 (see scheme 1). Accordingly the anion of nitromethane[20,30] was prepared by treating nitromethane with potassium t-butoxide in t-butyl alcohol; however, no appreciable reaction occurred when 37 was added to the anion. Attempts to catalyze the addition of nitromethane to 37 with potassium fluoride[31] in absolute ethanol were also unsuccessful. Several attempts to add the anions of 1,3-dithiane and 1,3-dithiane monoxide to 39 were also futile. As a result of these failures, the approaches to the synthesis of 39 and 40 involving the Michael reaction were abandoned and attention was again turned to compound 38.

Treatment of 38 with p-toluenesulfonic acid and ethylene glycol in refluxing benzene (see scheme 9) resulted in the ketalization of the carbonyl group of 38 to form 49 in high yields. The mass spectrum of 49 showed a molecular ion at m/e 223. In sharp contrast to compound 38, the ir spectrum of 49 showed a pronounced absorption at 2210 cm^{-1} due to the cyano group. The nmr spectrum of 49 showed the following important features: a one proton triplet at 6.1 ppm (J = 1.0 Hz), olefinic proton, and a four proton multiplet at 3.95-4.25 ppm, protons on carbons bearing oxygens. The reaction of 49 with Raney nickel and sodium hypophosphite in acetic acid, water and pyridine (1:1:2) afforded
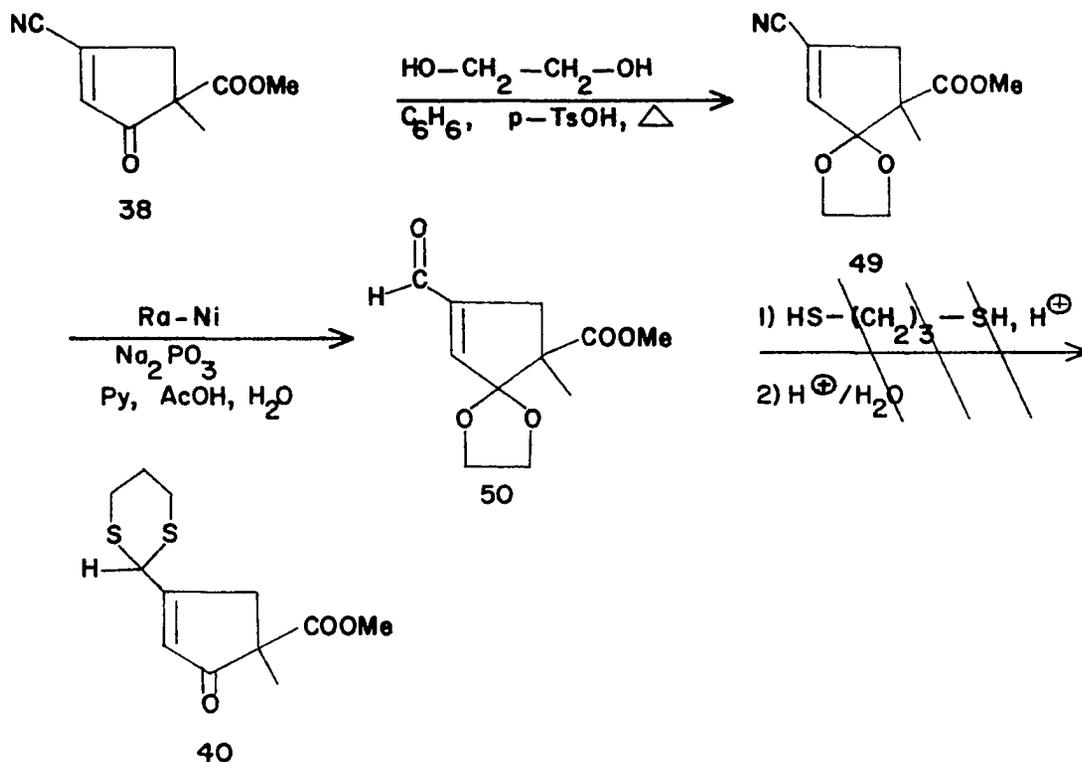
Scheme 9

the aldehyde 50 in 60% yields. The mass spectrum of 50 exhibited a

molecular ion at m/e 226. The ir spectrum showed significant absorp-

tions at 1740 cm^{-1} (ester carbonyl) and 1685 cm^{-1} (aldehyde carbonyl).

The uv spectrum showed λ_{max}^{EtOH} 218 mμ (ε, 18,000). The nmr spectrum of

50 showed the following important features: a sharp singlet at 9.5

ppm, aldehyde proton; a triplet at 6.4 ppm (J = .5 Hz) olefinic proton,

and a four proton multiplet at 3.90-4.25 ppm, protons on carbon atoms

bearing oxygens.

The next step in the reaction sequence called for the reaction

of 50 with 1,3-propanedithiol (see scheme 4) followed by hydrolysis of

ketal moiety to form the ketothioacetal 40. When this reaction was

attempted using boron trifluoride-etherate as the catalyst, a mixture

of products inseparable by alumina or thin layer chromatography

was isolated. This mixture exhibited practically no olefinic proton absorption in its nmr spectrum. Presumably, the 1,3-propanedithiol reacted with the carbon-carbon double bond of 50 as well as the aldehyde function under the reaction conditions (chloroform, 0°). Inverse addition (the addition of a solution of 1,3-propanedithiol and the acid catalyst) to the aldehyde produced the same results. The use of weaker acid catalysts such as p-toluenesulfonic acid, zinc chloride, and stannic chloride, as well as varying the reaction temperature from 0° to -70° were to no avail. Other attempts to circumvent the problem posed by the facile addition of 1,3-propanedithiol to carbon-carbon double bond of 50 were also futile; these attempts included hydrolysis of the ketal function and bromination of the double bond. In view of these insurmountable difficulties combined with the time and effort devoted to the project, the attempt to synthesize 1 was abandoned.

SUMMARY

Attempts to synthesize illudin-S (1) resulted in the preparation of the compounds depicted in scheme 10.
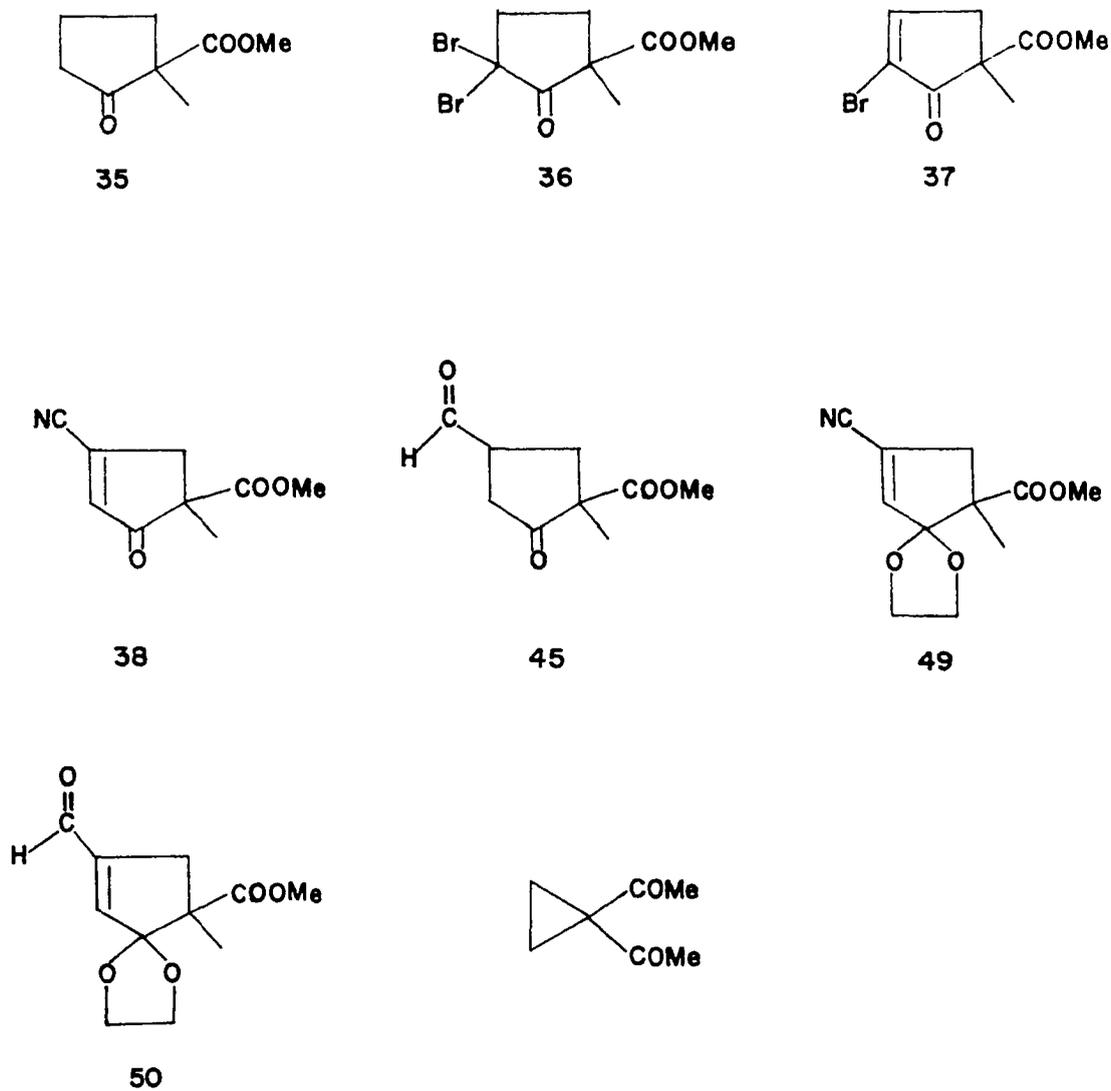
Scheme 10

EXPERIMENTAL

All melting points and boiling points are uncorrected. All solvents were redistilled prior to use. Anhydrous solvents were prepared by distillation from calcium hydride. Column chromatography supports were silicAR CC-7 (Mallinckrodt, 100/200 mesh) and silica gel H (Merck AG, Darmstadt). Thin layer chromatography was performed on 5 x 20 cm glass plates coated with silica gel H (Merck AG, Darmstadt). The developed plates were exposed to iodine vapor for visualization of the chromatogram.

Gas chromatographic analyses were performed on a Varian Aerograph Model 1220-1 or Aerograph Model 1240-1 gas chromatograph. The infrared spectra were taken on a Beckman IR-8 as potassium bromide pellets or in solutions of carbon tetrachloride or chloroform. Ultraviolet spectra (uv) were taken in 95% ethanol solutions with the Hitachi Perkin-Elmer, Model 124, spectrometer.

Nuclear magnetic resonance spectra (nmr) were taken on a Varian A-60 or T-60 spectrometers using tetramethylsilane (TMS) as an internal reference. Samples were run in varying concentrations of carbon tetrachloride and deuterochloroform. Chemical shifts are reported in δ-units (parts per million from TMS), and are followed by the multiplicity of the signal, the number of protons, the corresponding coupling constant and the assignment. The multiplicities are denoted by the symbols: s, singlet; d, doublet; dd, double doublet; t, triplet; and m, multiplet.

The mass spectra were taken on a Hitachi Perkin-Elmer RMU-7E

spectrometer using perfluorokerosene as an internal reference. Major

peaks and molecular ions are reported followed by percentage of the base peak.

Combustion analyses were carried out by Bernhardt Laboratories

in Mülheim, West Germany, and Mr. E. Meier, Chemistry Department, Stan-

ford University, Palo Alto, California.

2-Methyl-2-Carbomethoxycyclopentanone (35)

The procedure of Meyer and coworkers[17] was used.

To a 5-1 three-necked flask which was equipped with a mechanical

stirrer, a Vigrueaux column carrying a distillation head, and an addition

funnel were added 24 g (1 mol) of sodium hydride as a 57% dispersion in

mineral oil and 2 1 of dry xylene. Under a nitrogen atmosphere (which

was maintained throughout the reaction) 174 g (1 mol) of dimethyl adipate

was added and the reaction mixture was stirred and the methanol xylene

azeotrope was slowly distilled. After about 2 hr a thick mush formed and

an additional 100-1500 ml of xylene was added to the reaction mixture.

The reaction mixture was stirred rapidly and the distillation was continued

until the temperature of the distillate reached 120°. The reaction mix-

ture was cooled to room temperature, 213 g (1.5 mol) of methyl iodide was

added to the reaction mixture and stirring was continued for 16 hr. An

additional 71 g (.5 mol) of methyl iodide was added to the reaction mixture,

stirring was continued for 24 hr and the mixture was distilled in order to re-

move the excess methyl iodide. The mixture was cooled to room temperature,

500 ml of 10% hydrochloric acid was added to the mixture and the layers were

separated. The aqueous layer was extracted once with 500 ml of 1:1 ether-

benzene, the combined organic layers were washed with a saturated solution of

sodium bisulfite and dried over anhydrous sodium sulfate. Removal of the solvents by distillation yielded 145.2 g of a mixture of the crude keto ester and mineral oil. Distillation of the mixture on a spinning band column yielded 114.5 g (78%) of 2-methyl-2-carbomethoxycyclopentanone ($\underline{35}$) as a colorless liquid, bp 92-94° (6 mm), n_D^{25} 1.4532 [Lit[16] bp 105-106° (15 mm)]; ir (CCl_4) 1760 cm^{-1} (ketone carbonyl), 1740 cm^{-1} (ester carbonyl); nmr ($CDCl_3$) δ 3.68 (s, 3, ester methyl), 1.85-2.6 (m, 6, methylene protons), 1.23 (s, 3, quatenary methyl).

5,5-Dibromo-2-methyl-2-carbomethoxycyclopentanone ($\underline{36}$)

A solution of 104 g (0.66 mol) of 2-methyl-2-carbomethoxycyclopentanone ($\underline{35}$) in 350 ml of dichloromethane was placed in a one liter three-necked flask which was equipped with a magnetic stirring bar, an addition funnel, and a condenser. The contents of the flask were stirred and 224 g (1.4 mol) of bromine in 50 ml of dichloromethane was added dropwise to the flask over a 30 min period. Hydrogen bromide was evolved immediately, and stirring was continued for an additional 12 hr. The methylene chloride solution was first washed with a 10% sodium bicarbonate solution to remove the hydrogen bromide, and then with a saturated solution of sodium bisulfite to remove the excess bromine. The methylene chloride solution was then dried over anhydrous sodium sulfate and evaporated to yield 190 g (91%) of the dibromide as a yellow oil. Distillation of 10 g of the crude product yielded 8.2 g (75%) of 2-methyl-2-carbomethoxy-5,5-dibromocyclopentanone ($\underline{36}$) as a colorless liquid, bp 98-100° (2 mm). An analytical sample was obtained by collecting a middle fraction from the distillate, bp 98-100° (2 mm), n_D^{25} 1.5198; ir (CCl_4) 1768 cm^{-1} (ketone carbonyl), 1735 cm^{-1} (ester carbonyl);

nmr (CCl$_4$) δ 3.73 (s, 3, ester methyl), 1.85-3.2 (m, 6, methylene protons), 1.58 (s, 3, quatenary methyl); mass spectrum 316 (13), 315 (3), 314 (20), 312 (13), 286 (28), 185 (19), 175 (34), 173 (29), 165 (21), 127 (39), 95 (23), 69 (100), 66 (25), 65 (24), 59 (25), 41 (70).

Anal. Calcd for C$_8$H$_{10}$Br$_2$O$_3$:   C, 30.57; H, 3.19; O, 15.29. Found: C, 30.78; H, 3.34; O, 15.45.

2-Bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37)

A mixture of 21 g (.25 mol) of sodium bicarbonate and 62.8 g (.20 mol) of 2-methyl-2-carbomethoxy-5,5-dibromocyclopentanone (36) and 125 ml of dimethylformamide was placed in a 500 ml three necked flask which was equipped with a magnetic stirring bar and a condenser. The flask was immersed in an oil bath, the temperature of the bath was raised to 80°, and the reaction mixture was stirred and heated for 4 hours with the temperature of the bath being maintained at 80-85°. Then the reaction mixture was allowed to cool to room temperature and poured into 500 ml of benzene. The benzene solution was filtered in order to remove the insoluble inorganic residue, and washed several times with water to remove the dimethylformamide. The benzene solution was dried over anhydrous sodium sulfate and the solvent was evaporated to yield 38.5 g (83.3%) of crude product as a dark brown oil. Distillation of the crude product yielded 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37) as a colorless oil (31.5 g, 70%), bp 132-134° (1 mm). The oil crystallized on cooling to form a white solid, mp 48-49°. An analytical sample was obtained by collecting a middle fraction from the distillate, bp 132-134° (1 mm), mp 48-49°. Recrystallization from hexane-methylene chloride did not change the melting point;   ir (CCl$_4$)

1745 cm^{-1} (ester carbonyl), 1725 cm^{-1} (ketone carbonyl), 1585 cm^{-1}

(carbon-carbon double bond); uv (λ_{max}^{EtOH}) 243 mμ (ε 6,857); nmr (CCl$_4$)

δ 7.86 (t, 1, J = 2 Hz, olefinic proton), 3.68 (s, 3, ester methyl),

3.30 (dd, 1, J = 2 Hz, J = 18 Hz, methylene proton), 2.60 (dd, 1, J

= 2 Hz, J = 18 Hz, methylene proton), 1.40 (s, 3, quatenary methyl);

mass spectrum, 235 (2), 234 (24), 233 (3), 232 (22), 175 (15), 174 (12),

173 (14), 172 (10), 121 (100), 66 (21), 65 (32), 59 (13), 53 (11),

41 (15).

<u>Anal</u>. Calcd. for C$_8$H$_9$BrO$_3$: C, 41.20; H, 3.85; Br, 34.33.

Found: C, 41.37; H, 3.90; Br, 34.41.

4-Methyl-1-cyano-4-carbomethoxy-2-cyclopenten-3-one (38)

Into a 500 ml three-necked flask which was equipped with an

addition funel, a magnetic stirring bar and a gas inlet were placed

26 g (.4 mol) of potassium cyanide and 125 ml of acetonitrile. The

gas inlet was connected to a trap containing a saturated solution of

sodium hydroxide.   A solution of 31 g (.13 mol) of 2-bromo-5-methyl-

5-carbomethoxy-2-cyclopenten-1-one (37) in 100 ml of acetic acid was

added dropwise to the mixture over a 30 min period. The reaction mixture

was stirred at room temperature until all of the starting compound had

reacted as indicated by nmr and thin layer chromatographic analysis

(about 5 days). The reaction mixture was then poured into 300 ml of

benzene and washed several times with a 10% solution of sodium bicar-

bonate in order to remove the acetic acid. The benzene solution was

then dried over anhydrous sodium sulfate and evaporated to yield 20 g

(86%) of a yellow oil. Distillation yielded 16.4 g (70%) of 4-methyl-

1-   -4-carbomethoxy-2-cyclopenten-3-one (38) as a light yellow oil

bp 120-122° (1 mm), mp 38-39°. Recrystallization from 1:1 hexane-methyl-

ene chloride did not change the melting point. An analytical sample

was obtained by collecting a middle fraction from the distillate, bp

120-122° (1 mm), mp 38-39°; ir (CCl_4) 1755 cm^{-1} (ketone carbonyl), 1725

cm^{-1} (ester carbonyl); 1595 cm^{-1} (carbon-carbon double bond); uv (λ_{max}^{EtOH})

250 mμ (ε 22,000); nmr (CCl_4) δ 6.75 (t, 1, J = 1.5 Hz, olefinic pro-

ton), 3.72 (s, 3, ester methyl), 3.45 (dd, 1, J = 1.5 Hz, J = 18 Hz,

methylene proton), 2.75 (dd, 1, J = 1.5 Hz, J = 18 Hz, methylene proton),

1.45 (s, 3, quatenary methyl); mass spectrum, 180 (6), 179 (42), 168

(35), 164 (60), 148 (29), 147 (65), 316 (29), 121 (21), 120 (100),

119 (57), 109 (28), 108 (55), 93 (23), 92 (58), 91 (37), 81 (26), 69

(20), 66 (36), 65 (76), 59 (44), 55 (20), 51 (20), 43 (41), 41 (53).

Anal. Calcd. for $C_9H_9NO_3$: C, 60.34; H, 5.03; N, 7.82; O, 26.81.
Found: C, 60.26; H, 5.16; N, 7.73; O, 26.67.

Methyl 1-methyl-4-cyano-2-ethylenedioxy-3-cyclopenten-1-carboxylate (49)

In a 500 ml one-necked flask which was equipped with a Dean

Stark phase separator (carrying a reflux condenser) and a magnetic stir-

ring bar were placed 6 g (.033 mol) 4-methyl-1-cyano-4-carbomethoxy-

1-cyclopenten-3-one (38), 10 g (.16 mol) of ethylene glycol, 50 mg of

p-toluenesulfonic acid and 60 ml of dry benzene. A sufficient quantity

of dry benzene was placed in the phase separator in order to maintain

a constant volume of benzene within the flask during the reaction and

the reactiom mixture was stirred and refluxed with the continuous re-

moval of water for a period of about 60 hr. The benzene solution was

washed once with 50 ml of a 10% solution of sodium bicarbonate and

dried over anhydrous sodium sulfate. The benzene was removed on the

rotary evaporator to yield 6.38 g (92%) of the cyano ketal as a yellow

solid, mp 56-58°. Recrystallization from 1:1 benzene-hexane yielded

6.2 g (88%) of methyl 1-methyl-4-cyano-2-ethylenedioxy-3-cyclopenten-1-

carboxylate (49) as a white crystalline solid, mp 59-60°. Two recrystal-

lizations from benzene-hexane yielded an analytical sample, mp 60-61°;

ir (KBr) 2218 cm^{-1} (nitrile stretch), 1745 cm^{-1} (ester carbonyl), 1632

cm^{-1} (carbon-carbon double bond stretch), 1075 cm^{-1} (carbon-oxygen

stretch); uv (λ_{max}^{EtOH}) 215 mμ (ε 680); nmr (CDCl$_3$) δ 6.10 (t, 1, J = 1.5

Hz, olefinic proton), 3.95-4.20 (m, 4, methylene protons on carbons bear-

ing oxygens), 3.70 (s, 3, ester methyl), 3.45 (dd, 1, 1.5 Hz, J = 18

Hz, one of the methylene protons of the five membered ring), 2.35 (dd,

1, J = 1.5 Hz, J = 18 Hz, remaining methylene proton of the five mem-

bered ring), 1.35 (s, 3, quatenary methyl); mass spectrum 224 (5),

223 (29), 208 (84), 192 (93), 191 (20), 166 (54), 164 (70), 165 (100),

151 (33), 137 (20), 136 (62), 135 (20), 134 (24), 124 (30), 121 (25),

120 (45), 119 (33), 107 (30), 123 (60), 103 (20), 93 (46), 92 (32),

91 (55), 90 (23), 86 (24), 80 (37), 79 (76), 78 (27), 77 (65), 76 (21),

69 (22), 66 (38), 65 (39), 64 (44), 63 (36), 59 (54), 53 (25), 52 (50),

51 (66), 50 (54), 40 (39).

$\underline{Anal}$. Calcd. for C$_{11}$H$_{13}$NO$_4$: C, 59.20; H, 5.83; N, 6.78.

Found: C, 59.05; H, 5.85; N, 6.41.

3-Ethylenedioxy-4-methyl-4-carbomethoxycyclopenten-1-carboxaldehyde (50)

The procedure followed was that of Staskun and Backberg.[21]

A suspension of 10 g of Raney nickel catalyst (1:1 nickel-aluminum)

and 200 ml of 2N sodium hydroxide were stirred at room temperature for

40 minutes in a 2-1 flask. The base was decanted and the activated catalyst

was washed three times with water. Then a solution of 10 g (.045 mol)

of methyl 1-methyl-4-cyano-2-ethylenedioxy-3-cyclopenten-1-carboxylate

(49) in 100 ml of methanol, 400 ml of a 2:1:1 mixture of pyridine-acetic

acid-water and 40 g (.30 mol) of sodium hypophosphite was added to the

flask and the reaction mixture was stirred at room temperature in a

nitrogen atmosphere for 12 hr. The reaction mixture was filtered with

suction and the filtrate was poured into 600 ml of chloroform. The

chloroform solution was washed first with a 10% solution of hydrochloric

acid in order to remove the pyridine, and then a 10% solution of sodium

bicarbonate to remove the acetic acid. The chloroform solution was then

dried over anhydrous sodium sulfate and evaporated on the rotary evapora-

tor to yield 6.8 g (68%) of the crude aldehyde 50 as a dark yellow solid,

mp 65-66°. Recrystallization from hexane-methylene chloride (1:1)

yielded 5.2 g (52%) of 3-ethylenedioxy-4-methyl-4-carbomethoxycyclopenten-

1-carboxaldehyde (50) as a white solid, mp 68-69°. Two recrystalliza-

tions from benzene-hexane yielded an analytical sample, mp 69-70°; ir

($CHCl_3$) 2820 and 2715 (formyl carbon-hydrogen stretch), 1735 (ester

carbonyl), 1685 (aldehyde carbonyl), and 1625 cm^{-1} (carbon-carbon double

bond); uv (λ_{max}^{EtOH}) 215 mμ (ε 18,000); nmr ($CDCl_3$) δ 9.5 (s, 1, aldehyde

proton), 6.4 (t, J = 1.5 Hz, 1, olefinic proton), 4.2-3.8 (m, 4, methy-

lene protons on carbon atoms bonded to oxygens), 3.6 (s, 3, ester methyl),

3.3 (dd, 1, J = 1.5 Hz, J = 18 Hz, methylene proton of five membered

ring), 2.3 (dd, 1, J = 1.5 Hz, J = 18 Hz, methylene proton of five mem-

bered ring), 1.35 (s, 3, quatenary methyl); mass spectrum 227 (3), 226

(16), 182 (30), 150 (25), 125 (16), 123 (19), 122 (26), 101 (43), 95

(32), 84 (30), 69 (55), 59 (35), 58 (28), 56 (14), 55 (20), 45 (20),

43 (41), 42 (15), and 41 (100).

<u>Anal</u>. Calcd. for $C_{11}H_{14}O_5$: C, 58.41; H, 6.19. Found: C, 57.71; H, 5.88.

1,3 Dithiane

In a one liter three-necked flask which was equipped with a reflux condenser, an addition funnel, and a magnetic stirring bar were placed 300 ml of chloroform and 10 ml of boron trifluoride etherate. The chloroform was refluxed gently, and 57 g (.75 mol) of freshly distilled dimethoxymethane and 54 g (.50 mol) of 1,3-propanedithiol were added slowly through the addition funnel. When the addition was completed, the heating was ceased and the reaction mixture was stirred for 12 hours at room temperature. The chloroform solution was washed twice with 50 ml of a 10% solution of sodium hydroxide, dried over anhydrous sodium sulfate and evaporated on the rotary evaporator to yield 48.3 g (80%) of 1,3-dithiane as a crystalline white solid, mp 48-49° [lit.[33] mp 54°].

1,3-Dithiane Monoxide

The procedure used was that of Carlson and Helquist.[34] A solution of 4 g (.033 mol) of 1,3-dithiane in 250 ml of methanol was placed in a 500 ml three-necked flask which was equipped with an addition funnel and a mechanical stirrer. The flask was immersed in an ice-water bath at 10°, the solution was stirred and a solution of 7.36 g (.034 mol) of sodium metaperiodate in 70 ml of water was added to the reaction mixture over a 30 min period. Stirring and cooling were continued for 30 min, and then the mixture was filtered to remove the sodium iodate. The filtrate was evaporated to near dryness on the rotary

evaporator and extracted with chloroform. The chloroform solution was

dried over anhydrous sodium sulfate and evaporated to yield 3.98 g (90%)

of crude 1,3-dithiane monoxide, mp 80-82°. Two recrystallizations from

cyclohexane-chloroform 1:1 yielded 3.42 g (83%) of 1,3-dithiane monoxide

as a white solid, mp 87-88° [Lit. mp 87°].

4-Methyl-3-oxo-4-carbomethoxycyclopentane-1-carboxaldehyde (45)

The procedure followed was a slight modification of the proce-

dure of Staskun and Backberg.[21] A suspension of 6 g of Raney nickel

alloy and 120 ml of 2N sodium hydroxide was stirred for 40 min at room

temperature. The base was decanted and the activated catalyst was washed

three times with water. Then 15 ml of water was added to the activated

catalyst and the mixture was heated to 80° and a solution of 2 g (11 mmol)

of methyl 1-methyl-4-cyano-3-ethylenedioxy-3-cyclopenten-1-carboxylate

(38) in 17 ml of 88% formic acid was added to the mixture. The heating was con-

tinued at 80° for 5 min and the hot reaction mixture was then poured

into 50 ml of water and extracted with 100 ml of chloroform. The chloro-

form solution was washed several times with a 10% solution of sodium

bicarbonate and dried over anhydrous sodium sulfate. Evaporation of the

solvent yielded .950 g (49%) of a mixture of the diastereomeric forms

of 45 as a dark yellow oil. Bulb to

bulb distillation of the oil yielded .732 g (37%) of the aldehyde as a color-

less oil, bp 110-112° (.2 mm). An analytical sample was prepared by

preparative gas chromatography (JXR 3%, 1.5% gas chrom. Q 8' x 3/8");

ir (CCl_4) 2705 cm^{-1} (formyl C-H), 1755 cm^{-1} (ester carbonyl), 1740-1720

cm^{-1} (ketone and aldehyde carbonyls); nmr ($CDCl_3$) δ 9.8 (bs, 1, aldehyde

proton), 3.8, 3.68 (singlets, total of 3 H, ester methyl), 1.75-3.4

(m, 5, methylene protons), 1.4, 1.35 (singlets, total of 3 H,

quaternary methyl); mass spectrum 184 (7), 153 (28), 127 (16), 125 (20),

124 (17), 122 (16), 121 (38), 110 (18), 100 (98), 96 (21), 95 (17),

94 (50), 93 (28), 84 (19), 83 (80), 82 (17), 81 (16), 80 (16), 77 (35),

76 (15), 73 (16), 68 (77), 67 (15), 66 (80), 65 (15), 59 (17), 58 (20),

55 (26), 54 (44), 45 (87), 44 (100), 43 (48), 42 (71), 41 (20) and

40 (90).

   <u>Anal</u>. Calcd. for $C_9H_{12}O_4$:   C, 58.66; H, 6.52.   Found: C, 58.17;

H, 6.47.

   <u>The attempted reaction of the anion of 1,3-dithiane</u> with <u>2-bromo-</u>

<u>5-methyl-5- carbomethoxy -2-cyclopenten-1-one</u> (<u>37</u>). The apparatus was

flame dried in a nitrogen atmosphere which was maintained throughout the

experiment. A solution of 2.27 g (.021) of 1,3-dithiane in 100 ml of

dry, freshly distilled tetrahydrofuran was placed in 250 ml three necked

flask which was equipped with a septum cap, a mechanical stirrer and

nitrogen inlet. The flask was flushed with nitrogen, immersed in a

dry ice-acetone bath at -30° and 13.1 ml of a 1.6 molar solution

of n-butyllithium in hexane was slowly added by means of a syringe to

the flask. The reaction mixture was stirred for 3 hr at -30°, and a solu-

tion of 5 g (.021 mol) of 2-bromo-5-methyl-5-carbomethoxy-2-cyclopen-

ten-1-one (<u>37</u>) in 25 ml of dry tetrahydrofuran was added slowly to the

reaction mixture. Stirring was continued for 48 hr at 0-10°, the reac-

tion mixture was poured into 100 ml of water and acidified to a pH of 4

with 2N hydrochloric acid. The reaction mixture was extracted twice

with 100 ml portions of chloroform. The chloroform solution was dried

over anhydrous sodium sulfate and removed on the rotary evaporator to yield 5.83 g of product mixture. Analysis of the mixture by tlc and nmr spectroscopy indicated that no appreciable reaction occurred.

The attempted Michael Addition of the anion of 1,3-dithiane monoxide with 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37). The procedure of Carlson and Helquist[34] was used to prepare the anion of 1,3-dithiane monoxide. A nitrogen atmosphere was maintained throughout the experiment. A 250 ml three-necked flask containing a solution of 2.94 g (.216 mol) of 1,3-dithiane monoxide in 100 ml of tetrahydrofuran was immersed in a calcium chloride-ice water bath at -10° and 13.1 ml of a 1.6 molar solution of n-butyllithium was added to the flask over a 5 min period. The reaction mixture was stirred at -10° for 30 min and a solution of 5 g (.216 mol) of 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37) in 50 ml of tetrahydrofuran was added to the anion. Stirring was continued for 1 hr at 0° and 24 hr at room temperature. The reaction mixture was then acidified with 1N hydrochloric acid and extracted with 100 ml of chloroform. The chloroform solution was dried over anhydrous sodium sulfate and evaporated to yield a mixture of a polymeric substance and 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37).

The attempted Stephen Reduction of 4-methyl-1-cyano-4-carbomethoxy-1-cyclopenten-3-one (38). The procedure of Stephens[23] was used.

Preparation of the stannous chloride reducing agent. To a beaker containing 30 ml of acetic anhydride, 22.6 g (.1 mol) of stannous chloride dihydrate was slowly added. The anhydrous salt separated from

the solution immediately. The salt was collected by suction filtration and air dried under vacuum. Yield of anhydrous stannous chloride was 18.5 g (97%).

In a dry 250 ml three-necked flask which was equipped with calcium chloride tubes and a gas inlet was placed a suspension of 1.5 g (8 mmol) stannous chloride in 50 ml of absolute ether. The suspension was saturated with dry hydrogen chloride gas until a homogeneous mixture was attained. Then a solution of 1 g (5.6 mmol) of 4-methyl-1-cyano-4-carbomethoxy-1-cyclopenten-3-one in 10 ml of absolute ether was added to the reaction mixture. The reaction mixture was stirred at room temperature and after about 10 minutes a yellow oil separated from the solution. Stirring was continued for an additional 4 hr at room temperature, and the ether was decanted. The oil was collected, refluxed with 100 ml of water for 2 hr and poured into 100 ml of ether. The ether solution was dried over anhydrous sodium sulfate and removed on the rotary evaporator to yield .895 g of unaltered 38.

The reaction of 4-methyl-3-oxo-4-carbomethoxycyclopentane-1-carbox-aldehyde (45) with selenious acid. The procedure of Schafer[32] was used.

A solution of 200 mg (1.12 mmol) of 45

and 200 mg of selenious acid in 10 ml of benzene was refluxed in a nitrogen atmosphere for 24 hr. Evaporation of the solvent left .358 g of a dark residue which was filtered through a column containing 20 g of activity 6 neutral alumina. Analysis of the product by thin layer chromatography and nmr spectroscopy indicated a complex mixture of products which exhibited no olefinic or aldehyde protons.

Similar results were obtained when dichlorodicyanoquinone was substituted for selenious acid in the above procedure.

The reaction of sodium cyanide with (36). A suspension of 1 g (17 mmol) of sodium cyanide and .7 g (2.2 mmol) of 5,5-dibromo-2-methyl-2-carbomethoxycyclopentanone (36) in 50 ml of methanol was refluxed in a nitrogen atmosphere for 18 hr and cooled to room temperature. The reaction mixture was concentrated on the rotary evaporator and dissolved in 100 ml of methylene chloride. The methylene chloride solution was washed several times with water and dried over anhydrous sodium sulfate. Evaporation of the methylene chloride yielded a dark tar which exhibited no olefinic or nitrile absorption when analyzed by nmr and ir spectroscopy.

The reaction of 5,5-dibromo-2-methyl-2-carbomethoxycyclopentanone (36) with 1,5-diazobicyclo[4.3.0]-5-nonene (DBN). The procedure of Oidiger[19] was used.

A solution of 8 g (.025 mol) of 5,5-dibromo-2-methyl-2-carbomethoxycyclopentanone (36) and 3.1 g (.025 mol) of DBN in 100 ml of dichloromethane was stirred in a nitrogen atmosphere at 0° for 1.5 hr. The dichloromethane solution was washed several times with a 10% solution of hydrochloric acid and dried over anhydrous sodium sulfate. Evaporation of the solvent yielded 5.2 g of a dark yellow oil. Analysis by thin layer chromatography indicated the presence of two products. The oil was chromatographed on 280 g of 100-200 mesh silic acid (50 x 4-1/2 cm column). A solution of 6.2 g of the oil was eluted with benzene and 75 ml fractions were collected. Fractions 14 + 15 were combined; evaporation of the solvent yielded .620 g of the unreacted amine. After fraction 16, the solvent was changed to 95% benzene-5%

ethyl acetate. Fractions 25 and 26 yielded 2.78 g (47%) of 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37) as a yellow solid, mp 48-49°.

The attempted reaction of the anion of nitromethane with 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37). The nitromethane was dried over anhydrous sodium sulfate and distilled from calcium hydride. The apparatus was flame-dried in a nitrogen atmosphere which was maintained throughout the experiment.

In a 250 ml three-necked flask which was equipped with a gas inlet and an addition funnel was placed a mixture of 1.3 g (.02 mol) of nitromethane, 1.16 g (.02 mol) of sodium methoxide and 50 ml of absolute methanol. The flask was immersed in an ice-water bath at 0-5°, flushed with nitrogen, and the reaction mixture was stirred for 1 hr at 0-5°. A solution of 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37) in 25 ml of absolute methanol was then added to the reaction mixture and stirring was continued for 12 hr at 0-10° at which time an aliquot was removed from the flask and analyzed by thin layer chromatography and nmr spectroscopy. No appreciable reaction occurred under these conditions. Similar results were obtained when the reaction was run at room temperature or refluxed.

When the above procedure was repeated using potassium-t-butoxide in t-butanol instead of sodium methoxide in methanol, only starting materials were recovered.

The attempted Michael addition of the anion of nitromethane to 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one (37) using potassium fluoride as the catalyst. A mixture of 1.8 g (.03 mol) of nitromethane, 2.33 g (.01 mol) of 2-bromo-5-methyl-5-carbomethoxy-2-cyclopenten-1-one

(37) and .1 g potassium fluoride in 50 ml of absolute ethanol was refluxed
for 8 hr. The ethanol solution was poured into 100 ml of water and ex-
tracted twice with 100 ml portions of ether. The ether solution was
dried over anhydrous sodium sulfate and evaporated to yield 2.25 g of
the unaltered 37.

The attempted reaction of 2-methyl-2,4-pentanediol with (38).
A 125 ml Erlenmeyer flask containing a solution of 1.2 g (.01 mol) of
2-methyl-2,4-pentanediol, 1 g (.006 mol) of 4-methyl-1-cyano-4-carbo-
methoxy-1-cyclopenten-3-one (38), and .1 ml boron trifluoride-etherate
in 25 ml of absolute ether was stored in a refrigerator for 48 hr.
Analysis of the mixture by tlc indicated that no reaction had occurred.

The reaction of 1,3-propanedithiol with 3-ethylenedioxy-4-methyl-
4-carbomethoxycyclopenten-1-carboxaldehyde (50). A solution of 2.8 g
(12 mmol) of 3-ethylenedioxy-4-methyl-4-carbomethoxycyclopenten-1-carbox-
aldehyde (50) in 15 ml of chloroform was placed in a 100 ml three-necked
flask. The flask was placed in an ice-water bath at 0°, flushed with
nitrogen and a solution of 1.23 g (12 mmol) of 1,3-propanedithiol and
.1 ml of boron trifluoride-etherate in 15 ml of chloroform was added
to the flask over a 10 min period. The reaction mixture was stirred
for 12 hr at 0° in a nitrogen atmosphere and poured into 100 ml of
chloroform. The chloroform solution was washed with a 10% solution of
sodium carbonate and dried over anhydrous sodium sulfate. Evaporation
of the solvent yielded 2.92 g of an oil whose nmr spectrum exhibited no
olefinic proton absorptions. The above procedure was repeated using
zinc chloride, stannic chloride, and p-toluenesulfonic acid as cata-
lysts. Similar results were obtained in each case.

1,1-Diacetylcyclopropane (41)

The procedure of Ichakawa and coworkers[15] was used.

A suspension of 64 g (.2 mol) of mercuric acetate and 60 g (1 mol) of glacial acetic acid was treated with ethylene until the mixture became homogeneous. The reaction mixture was then treated successively with 10 ml of a 10% solution of sodium hydroxide, 40 g (.4 mol) of acetylacetone and 15 g of 70% perchloric acid. After standing overnight, the mixture was treated with a 10% solution of sodium chloride and white crystals separated from the solution. The crystals were collected, air dried and recrystallized from 95% ethanol to give 52 g (75%) of 3,3-diacetylpropylmercuric chloride, mp 132-133° [Lit[15] 131-132°].

A suspension of 50 g (.14 mol) of the mercury salt and 70 ml of 10% potassium hydroxide was allowed to stand at room temperature for 2 hr. The reaction mixture was filtered and the filtrate was extracted with ether. The ether solution was dried over anhydrous sodium sulfate and evaporated to yield 4.5 g of crude product. Distillation yielded 3.8 g of 1,1-diacetylcyclopropane, bp 52-53°, (2 mm) n_D^{25} 1.4524 [Lit[15] bp 74-74.5° (8 mm)].

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III. The Thermal Decomposition of Sulfones and Sulfoxides

History and Background

The pyrolysis of sulfones (see scheme 1) has been used extensively in theoretical and synthetic organic chemistry. Leonard[1] pyrolyzed sulfones of type 1 at low pressures and temperatures of 600-700° and obtained good yields of symmetrical diarylethanes.

$$R-Ph-CH_2-SO_2-CH_2-Ph-R \xrightarrow{\triangle} R-Ph-CH_2-CH_2-Ph-R + SO_2$$

1

$$R=CH_3 ; OCH_3$$

$$Ph-SO_2-Ph \xrightarrow{\triangle} C_6H_6 + SO_2$$

2

$$Ph-SO-Ph \xrightarrow{\triangle} C_6H_6 + SO_2$$

3

$$Ph-SO_2-CH_2-CH=CH_2 \xrightarrow{\triangle} Ph-CH_2-CH=CH_2 + SO_2$$

4

5

6

7
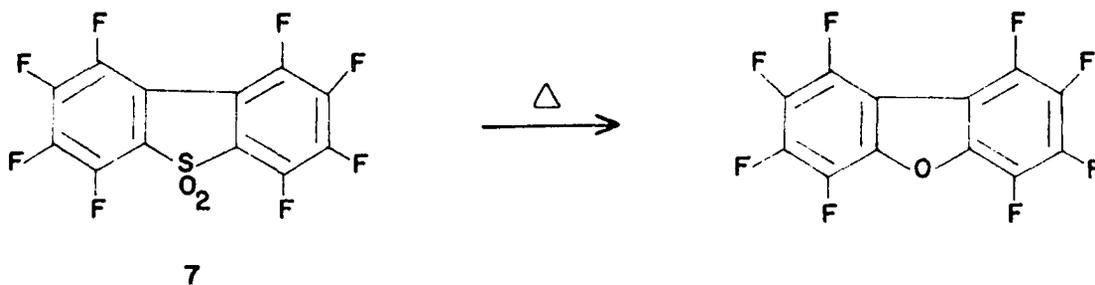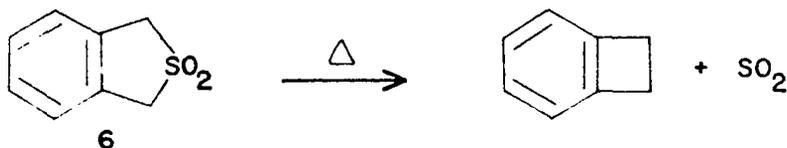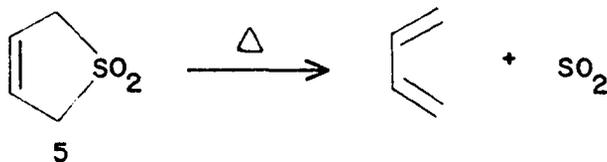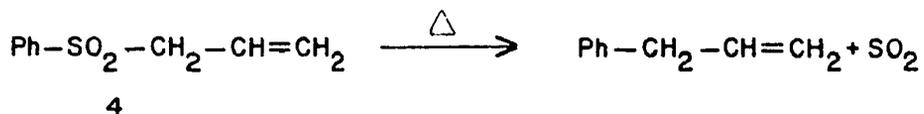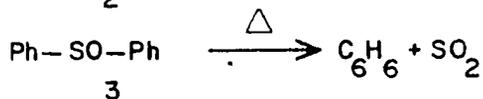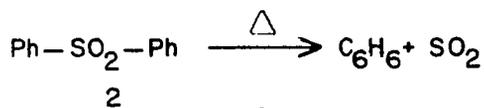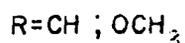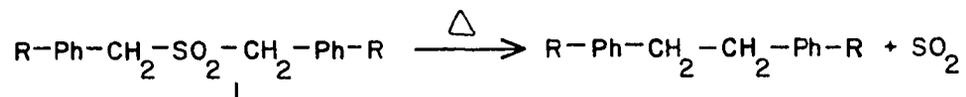
Scheme 1

Scheme 2
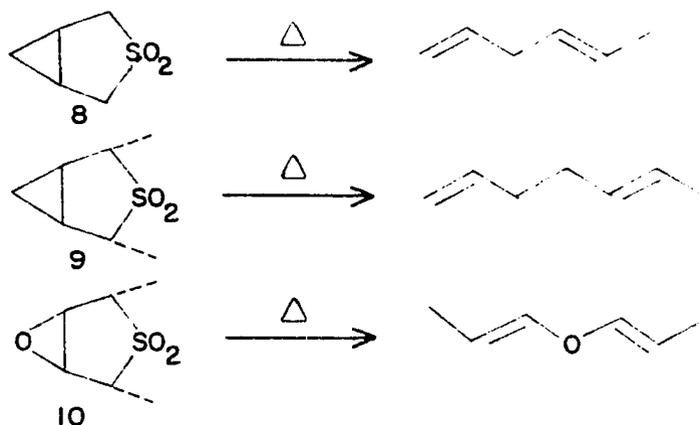
Levy and Ambrose[2] studied the kinetics of the decomposition of

sulfone 2 and the sulfoxide 3. Lacombe and Stewart[3] observed that the

allylic sulfone 4 lost sulfur dioxide and formed an olefin when heated at

300-400°. Cava and Deanna[4] obtained good yields of benzocyclobutene from

the vapor phase pyrolysis of 6. The thermal decomposition of 6 has analogy

to the well known thermal decomposition of 5.[12] Chambers and Cunningham[8]

observed that the mass spectrum of 7 exhibited a peak at (M^+) - 48. This

indicated that 7 could possibly eliminate sulfur monoxide when pyrolyzed.

When 7 was pyrolyzed, the ether that was formed corresponded to the loss

of sulfur monoxide.

Mock[5] investigated the thermal decomposition of sulfones of the

type depicted in scheme 2. These reactions were found to be stereospecific

in some cases and stereoselective in others and they provided a new route

to the synthesis of alkenes, polyalkenes and divinyl ethers. Furthermore,

Mock found these reactions were useful in elucidating the concepts of

orbital symmetry.

INTRODUCTION

Kissick[6] prepared 1,1,3,3-tetraoxo-2,2-diphenyl-1,3-dithiolane and pyrolyzed it at 240°. Sulfur dioxide was evolved, and a mixture of the starting disulfone and another product were recovered from the reaction mixture. Somewhat later the other product was identified as benzophenone.

The objective of this investigation was to determine the scope and limitations of the reaction suggested by the work of Kissick, identify all of the reaction products and propose reasonable mechanistic pathways for their formation. Several sulfones and sulfoxides were pyrolyzed, and the results will be presented in this section.

RESULTS AND DISCUSSION

The sulfones and sulfoxides utilized in this study were prepared

from compounds 11-18. The reactions employed in the preparation of

compounds 11-18 are depicted in scheme 3. The dithiolanes 11-15 and the

dithiane 16 were routinely prepared from the appropriate ketone (alde-

hyde in the case of 12) and 1,2-ethanedithiol (1,3-propanedithiol in

the case of 16). The oxathiolane 17 was prepared from benzophenone and

2-mercaptoethanol by the method of Marshall and Stevenson.[9] The mercap-

tole 18 was prepared from benzophenone and ethanethiol by the method of

Wolfrom and Karabinos.[10]

The cyclic disulfones 19-23 were prepared by oxidation of the cor-

responding dithiolanes (dithiane in the case of 23) with an excess of pera-

cetic acid. In order to ensure complete oxidation of the dithiolane

11 and the dithiane 16 to the corresponding disulfones, it was necessary

to carry out these oxidations in dilute solutions (ca. 1 g of the di-

thiolane per 25 ml of solvent). Under these conditions the reaction

mixture remained homogeneous and 11 and 16 were completely oxidized to

the corresponding disulfones. In contrast, when the oxidation of 11

was carried out in more concentrated solutions, a crystalline substance

separated from the hot solution before the oxidation was complete. This

substance was a mixture of the desired disulfone 19 and small quantity

of an impurity (presumably the trioxide).

$$Ph-\overset{\overset{\displaystyle O}{\|}}{C}-Ph + H-S-CH_2-CH_2-SH \xrightarrow[\text{p-TsOH}]{C_6H_6} Ph-\overset{\overset{\displaystyle S\quad S}{\diagup\quad\diagdown}}{C}-Ph$$

11

$$Ph-\overset{\overset{\displaystyle O}{\|}}{C}-H + H-S-CH_2-CH_2-SH \xrightarrow[\text{p-TsOH}]{C_6H_6} Ph-\overset{\overset{\displaystyle S\quad S}{\diagup\quad\diagdown}}{C}-H$$

12

$$Ph-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3 + HS-CH_2-CH_2-SH \xrightarrow[\text{p-TsOH}]{C_6H_6} Ph-\overset{\overset{\displaystyle S\quad S}{\diagup\quad\diagdown}}{C}-CH_3$$

13

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-(CH_2)_5-CH_3 + H-S-CH_2-CH_2-SH \longrightarrow CH_3-\overset{\overset{\displaystyle S\quad S}{\diagup\quad\diagdown}}{C}-(CH_2)_5-CH_3$$

14

$$\overset{\displaystyle +}{\bigcirc}=O + H-S-CH_2-CH_2-SH \xrightarrow[\text{p-TsOH}]{C_6H_6} \overset{\displaystyle +}{\bigcirc}\overset{S}{\underset{S}{\diagup}}$$

15

$$Ph-\overset{\overset{\displaystyle O}{\|}}{C}-Ph + HS-(CH_2)_3-SH \xrightarrow[\text{p-TsOH}]{C_6H_6} Ph-\overset{\overset{\displaystyle S\quad S}{\diagup\quad\diagdown}}{C}-Ph$$

16

$$Ph-\overset{\overset{\displaystyle O}{\|}}{C}-Ph + HO-CH_2-CH_2-SH \xrightarrow[\text{p-TsOH}]{Ph-CH_3} Ph-\overset{\overset{\displaystyle O\quad S}{\diagup\quad\diagdown}}{C}-Ph$$

17

$$Ph-\overset{\overset{\displaystyle O}{\|}}{C}-Ph + H-S-CH_2-CH_3 \xrightarrow[\text{Na}_2SO_4]{ZnCl_2} \overset{\displaystyle Et-S\quad S-Et}{Ph-\overset{\displaystyle |}{C}-Ph}$$

18

Scheme 3

11 $\xrightarrow[\Delta]{H_2O_2, \ AcOH}$

structure 19

12 $\xrightarrow[\Delta]{H_2O_2, \ AcOH}$

structure 20 (bracketed, labeled)

13 $\xrightarrow[\Delta]{H_2O_2, \ AcOH}$

structure 20

14 $\xrightarrow[\Delta]{H_2O_2, \ AcOH}$

structure 21

15 $\xrightarrow[\Delta]{H_2O_2, \ AcOH}$

structure 22

16 $\xrightarrow[\Delta]{H_2O_2, \ AcOH}$

structure 23

17 $\xrightarrow[Et_2O]{}$ (m-Cl-C$_6$H$_4$-CO$_3$H)

structure 24

18 $\xrightarrow[Et_2O]{}$ (m-Cl-C$_6$H$_4$-CO$_3$H)

structure 25

Scheme 4

Attempts to oxidize the dithiolane 12 to the corresponding di-
sulfone by this procedure produced disappointing results. When 12 was
heated with excess peracetic acid, an exothermic reaction occurred, and
a crystalline substance immediately separated from the solution. The ir
spectrum of this substance exhibited strong absorptions at 1310 and 1130
cm^{-1} (sulfone) and 1030 cm^{-1} (sulfoxide). The evidence obtained from the
ir spectrum and tlc analysis indicated that the crystalline substance was
a mixture of the trioxide (see scheme 4) and a small quantity of benzoic
acid. When the mixture was treated with a dilute solution of sodium
bicarbonate, the trioxide was hydrolyzed to benzaldehyde. Similar results
were obtained when 12 was treated with excess m-chloroperbenzoic acid.
The disulfone 25 was prepared by the oxidation of the mercaptole 18
with m-chloroperbenzoic acid. The unstable sulfone 24 was prepared by
the oxidation of the oxathiolane 17 with excess m-chloroperbenzoic acid.
On standing at room temperature for about 48 hours, the sulfone 24 spon-
taneously decomposed to give benzophenone. However, a freshly prepared
sample gave satisfactory spectral data.

The sulfoxides 26 and 27 utilized in this investigation were pre-
pared by the oxidation of 11 and 17 with hydrogen peroxide in dioxane.
Hydrogen peroxide in acetone hydrolyzed 17 to benzophenone. However, a
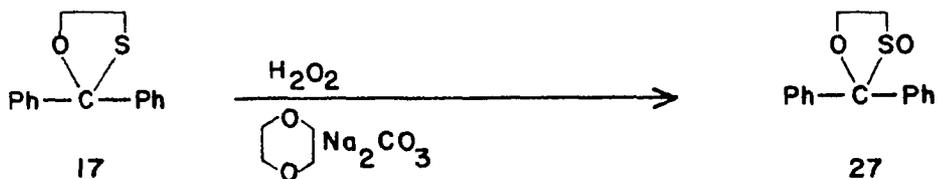
solution of hydrogen peroxide in dioxane buffered with a 10% solution of
sodium carbonate convered 17 to the sulfoxide 27.
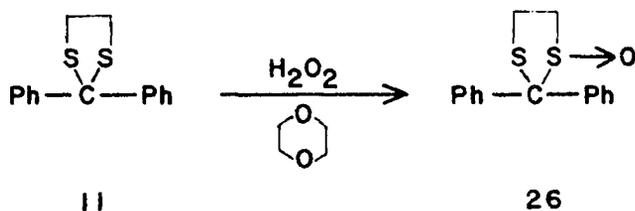
Several attempts were made to oxidize 11 to the disulfoxide, but dis-

appointing results were obtained. Invariably, product mixtures were ob-

tained when 11 was heated with 2 equivalents or more of hydrogen peroxide.

Analysis of the mixtures by ir and mass spectroscopy indicated the presence

of both the monosulfoxide and the disulfoxide. Attempts to oxidize the

monosulfoxide (which was present in the mixture) to the disulfoxide resulted

in the formation of a product whose ir spectrum exhibited both sulfone and

sulfoxide absorptions. This product was presumably the trioxide. Theo-

retically, the disulfoxide or the isomeric monosulfone could result from

the treatment of a dithiolane with 2 equivalents of an oxidizing agent.

However, ir spectroscopy can easily distinguish between these two pos-

sibilities for the ir spectra of sulfones exhibit two strong absorptions

at 1300-1330 cm^{-1} and 1010-1030 cm^{-1}, whereas the ir spectra of sulfoxides

exhibit a single absorption at 1010-1030 cm^{-1}.

The primary objective of this study was to determine the scope of

the reaction suggested by the work of Kissick,   all of the reaction

products and propose reasonable mechanistic pathways for their formation.

In an effort to accomplish this objective, 1,1,3,3-tetraoxo-2,2-diphenyl-

1,3-dithiolane (19) was pyrolyzed under the following conditions: at 225°

and atmospheric pressure, at 225° and 2 mm of pressure, and at 225° and

atmospheric pressure in the presence of a trace of benzoyl peroxide. In

each instance the thermal decomposition of 19 yielded benzophenone, sulfur,

ethylene and sulfur dioxide. Under the first set of experimental conditions the product yields were as follows: benzophenone (.006 mol), sulfur (.0025 mol), ethylene (.0058 mol) and sulfur dioxide (.007 mol). Taking the yield of benzophenone as unity, this corresponds to a molar ratio of (1: .4: .96:1.16). Only the yields of benzophenone and sulfur were determined when $\underline{19}$ was pyrolyzed under the last two sets of conditions. The reaction products were identified by comparison of their spectral or physical pro-

$$\underset{\textbf{19}}{\underset{Ph-C-Ph}{\overset{O_2S\diagup SO_2}{\diagdown\diagup}}} \xrightarrow{\triangle} \underset{Ph-C-Ph}{\overset{O}{\overset{\|}{}}} + CH_2 = CH_2 + SO_2 + S$$
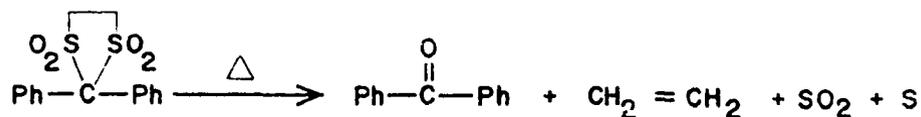
perties with those of authentic samples or with published data. In the cases of ethylene and sulfur dioxide, the ir spectra were compared with published ir spectra of authentic samples. Ethylene was also converted to ethylene dibromide which in turn was identified by comparing its nmr spectrum and refractive index with those of distilled samples. Benzophenone was identified by direct comparison to an authentic sample with respect to melting point, nmr and ir spectra. Sulfur was identified by its melting point.

The evidence obtained from studies of the thermal decomposition of $\underline{19}$ indicated that radical chains probably were not involved in the decomposition pathway since benzoyl peroxide, a powerful radical chain initiator, had no effect on the reaction. The results also established that the carbonyl oxygen atom of benzophenone came from the sulfone group since benzophenone was obtained when $\underline{19}$ was pyrolyzed in an evacuated system (no other source of oxygen was present in the system). This fact and the formation of all the observed products can be rationalized by the

intramolecular free radical pathway depicted in scheme 5.

The stoichoimetry of the pathway depicted in scheme 5 requires that sulfur monoxide[8] be formed as a product from the thermal decomposition of 19. However, the instability[7] of sulfur monoxide renders its detection impossible; at all temperatures sulfur monoxide undergoes rapid disproportionation to give sulfur dioxide. Thus, the recovery of sulfur from the thermal decomposition of 19 combined with the fact that sulfur dioxide
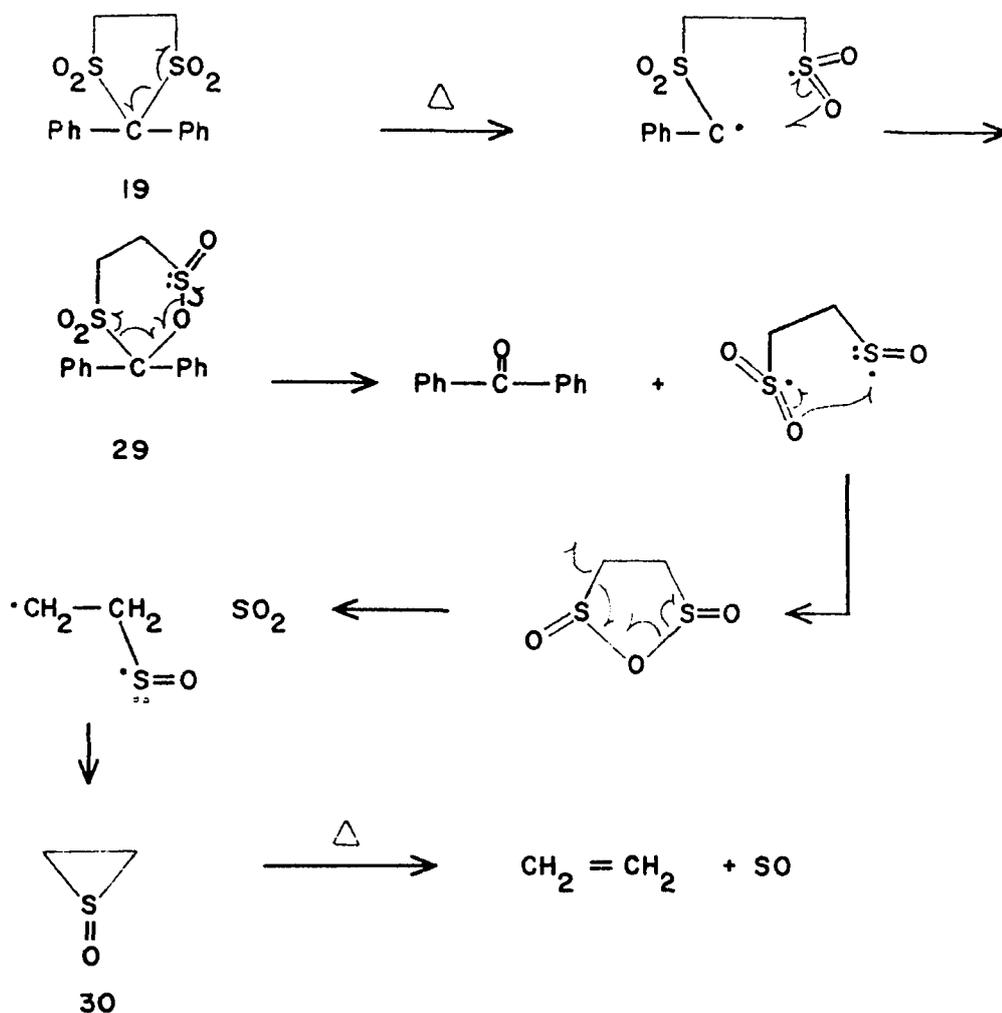
Scheme 5

was formed in larger quantities than ethylene gives credence to the con-
jecture that sulfur monoxide was formed from the decomposition of 19.

Therefore, the mechanism depicted in scheme 5 is fully consistent with

the observed facts. The failure of benzoyl peroxide to facilitate the

decomposition of 19 does not rule out an intramolecular free radical path-

way such as the one outlined in scheme 5, but indicates homolytic cleavage

of the disulfone is facile and does not require an external initiator.

Another reasonable mechanism for the thermal decomposition of 19

is depicted in scheme 6. This proposed mechanism entails a heterolytic

fission of the carbon sulfur bond of 19 to give the carbonium ion 28 which
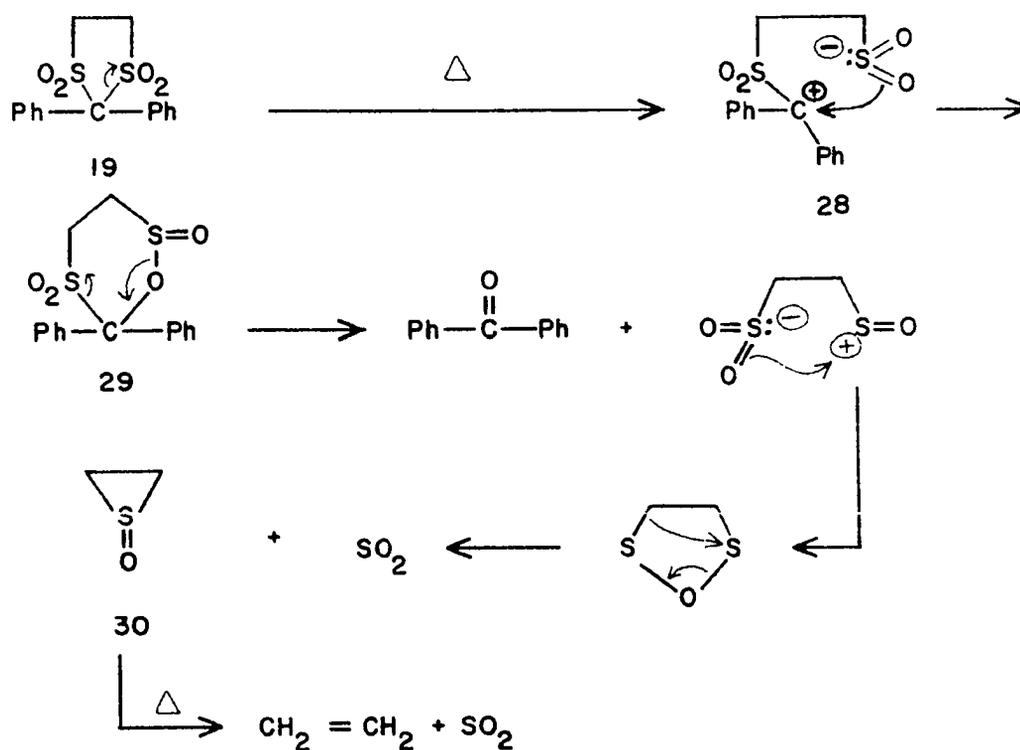
Scheme 6

in turn cyclizes to the six-membered ring intermediate 29. The mechanistic

pathways outlined in schemes 5 and 6 propose that 29 is the intermediate

which gives rise to benzophenone and that the episulfoxide 30 gives rise

to ethylene and sulfur monoxide. Thus, the products resulting from the

thermal decomposition of 19 can reasonably be imagined to arise from a

free radical pathway, a carbonium ion pathway or by competing pathways

involving both carbonium ions and free radicals.

The results of the thermal decomposition of compounds 19-27 are out-

lined in scheme 7 and Table 4. All of the products resulting from the

$$Ph-\overset{O_2S\diagdown SO_2}{\underset{19}{C}}-Ph \quad \overset{\Delta}{\longrightarrow} \quad Ph-\overset{O}{\underset{}{C}}-Ph \; + \; CH_2=CH_2 \; + \; SO_2 \; + \; S$$

$$Ph-\overset{O_2S\diagdown SO_2}{\underset{20}{C}}-CH_3 \quad \overset{\Delta}{\longrightarrow} \quad Ph-\overset{O}{\underset{}{C}}-CH_3 \; + \; CH_2=CH_2 \; + \; SO_2 \; + \; S$$

$$CH_3-\overset{O_2S\diagdown SO_2}{\underset{21}{C}}-(CH_2)_5-CH_3 \quad \overset{\Delta}{\longrightarrow} \quad \text{No Reaction}$$

$$\overset{SO_2}{\underset{22}{\diagup}}\quad \overset{\Delta}{\longrightarrow} \quad \text{No Reaction}$$

$$Ph-\overset{O_2S\diagdown SO_2}{\underset{23}{C}}-Ph \quad \overset{\Delta}{\longrightarrow} \quad Ph-\overset{O}{\underset{}{C}}-Ph \; + \; \left[\overset{\triangle}{\underset{?}{}} \right] \; +SO_2 \; +S$$

$$Ph-\overset{O\diagdown SO_2}{\underset{24}{C}}-Ph \quad \overset{\Delta}{\longrightarrow} \quad Ph-\overset{O}{\underset{}{C}}-Ph + CH_2=CH_2 + SO_2$$

$$Ph-\overset{EtSO_2\diagdown SO_2Et}{\underset{25}{C}}-Ph \quad \overset{\Delta}{\longrightarrow} \quad Ph-\overset{O}{\underset{}{C}}-Ph \; + \; ?$$

$$Ph-\overset{S\diagdown S=O}{\underset{26}{C}}-Ph \quad \overset{\Delta}{\longrightarrow} \quad Ph-\overset{O}{\underset{}{C}}-Ph \; + CH_2=CH_2 \; + \; S$$

$$Ph-\overset{O\diagdown S=O}{\underset{27}{C}}-Ph \quad \overset{\Delta}{\longrightarrow} \quad Ph-\overset{O}{\underset{}{C}}-Ph$$
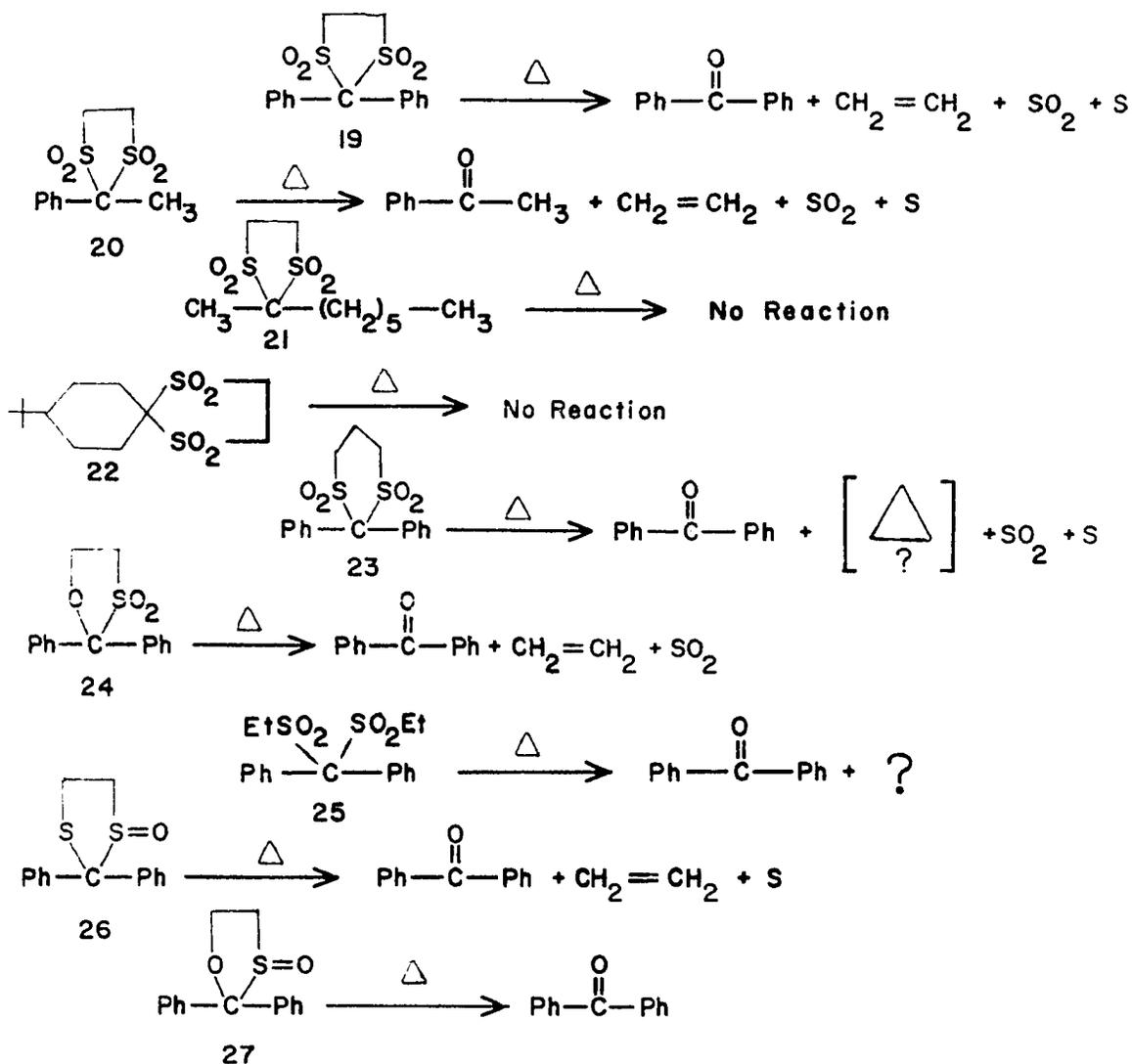
Scheme 7

TABLE 4

The Results of the Thermal Decomposition

of Sulfoxides and Sulfones

Compound	Experimental Conditions	% Yield of Products
19	225° (2 mm)	benzophenone 65% sulfur 60% ethylene, sulfur dioxide
19	225° (atm. pres.)* peroxides present	benzophenone 62%, sulfur 58% ethylene and sulfur dioxide (yields no det.)
19	225° (atm. pres.)*	sulfur 60%, benzophenone 65% ethylene 60%, SO$_2$ 66%
20	250-260° (2 mm)	Acetophenone 33%
21	200° (2 mm)	90% of 21 recovered
21	300° (2 mm)	89% of 21 recovered
22	400° (2 mm)	85% of 22 was recovered
22	500° (atm. pres.)*	88% of 22 was recovered
23	300° (atm. pres.)*	benzophenone (76.5%), sulfur 58% sulfur dioxide 55%
23	300° (2 mm)	benzophenone 70%, sulfur 62%
24	140° (2 mm)	benzophenone 65%
25	200° (5 mm)	benzophenone 70%
27	120-130° (2 mm)	benzophenone 78%
26	130-140° (atm. pres.)*	benzophenone 74%, sulfur 28% ethylene 64% no sulfur dioxide was detected.

*Pyrolyzed under a sweep of nitrogen gas.

decomposition of 19 and 26 were identified. Sulfur dioxide, sulfur, benzophenone

and a product tentatively identified as cyclopropane resulted from the pyrolysis

of 23. In all other instances only the ketone was fully characterized.

The aliphatic disulfones 21 and 22 were found to be thermally stable at

temperatures 100-200° above their melting points ($68°$ and 252°). This may

be attributable to the destabilizing effect that the sulfone group would

have on the intermediate (radical or carbonium ion) that would result from

the cleavage of the carbon sulfur bond. Compound 20 decomposed slowly at

temperatures 120° above its melting point (131-133°).

In sharp contrast to the thermal behavior of 20, 21 and 22, com-

pounds 24 and 27 (freshly prepared samples) decompose smoothly and com-

pletely at their melting points. On standing at room temperature for

about 48 hours both 24 and 27 spontaneously decomposed into benzophenone.

A concerted pathway (see scheme 8) is very favorable for the thermal

decomposition of 24 and 27.
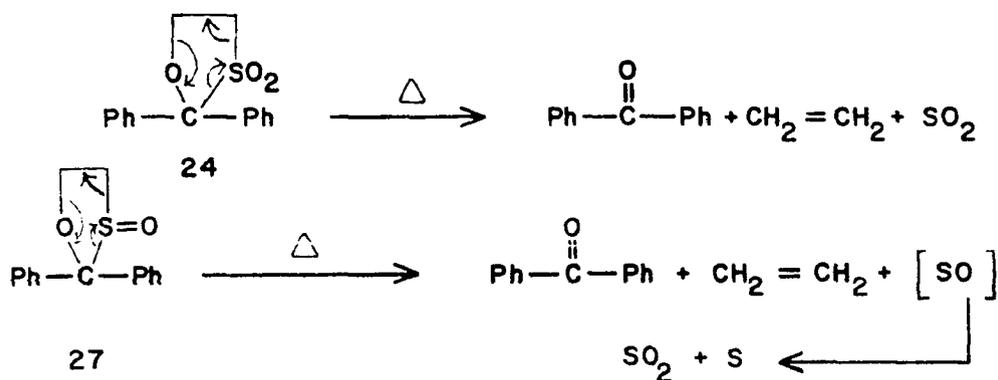
Scheme 8

Compound 23, 25 and 26 decomposed smoothly and completely at

temperatures 10-20° above their melting points. The decomposition of 26

can proceed by a radical pathway similar to the one depicted in scheme 5

or the carbonium ion pathway similar to the one depicted in scheme 6.

A possible pathway for the decomposition of the non-cyclic sulfone

25 is depicted in scheme 9. However, benzophenone was the only reaction

product identified from the pyrolysis of 25, and, therefore, any discus-

sion regarding the mechanism of the decomposition of 25 in the absence of

a complete identification of all of the reaction products is pure con-

jecture. The decomposition of 23 can proceed by the radical pathway

depicted in scheme 10; however, the evidence for the formation of cyclo-

propane from the thermal decomposition of 23 is not yet convincing.
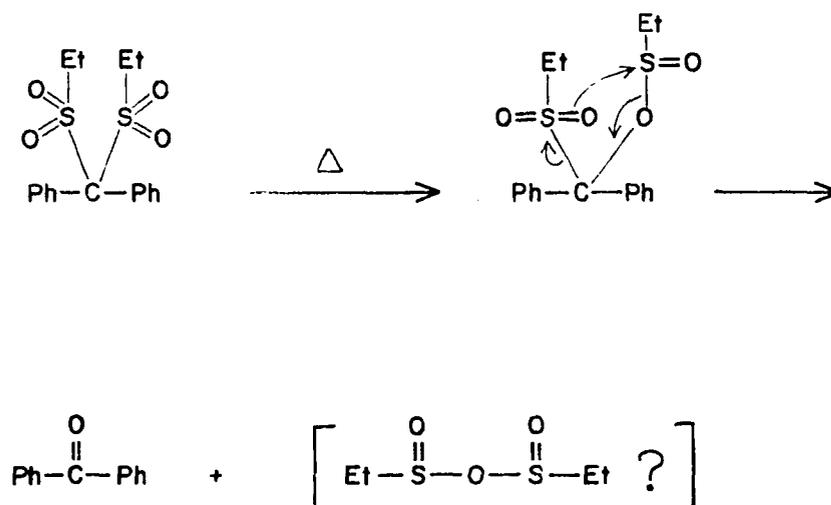
Scheme 9
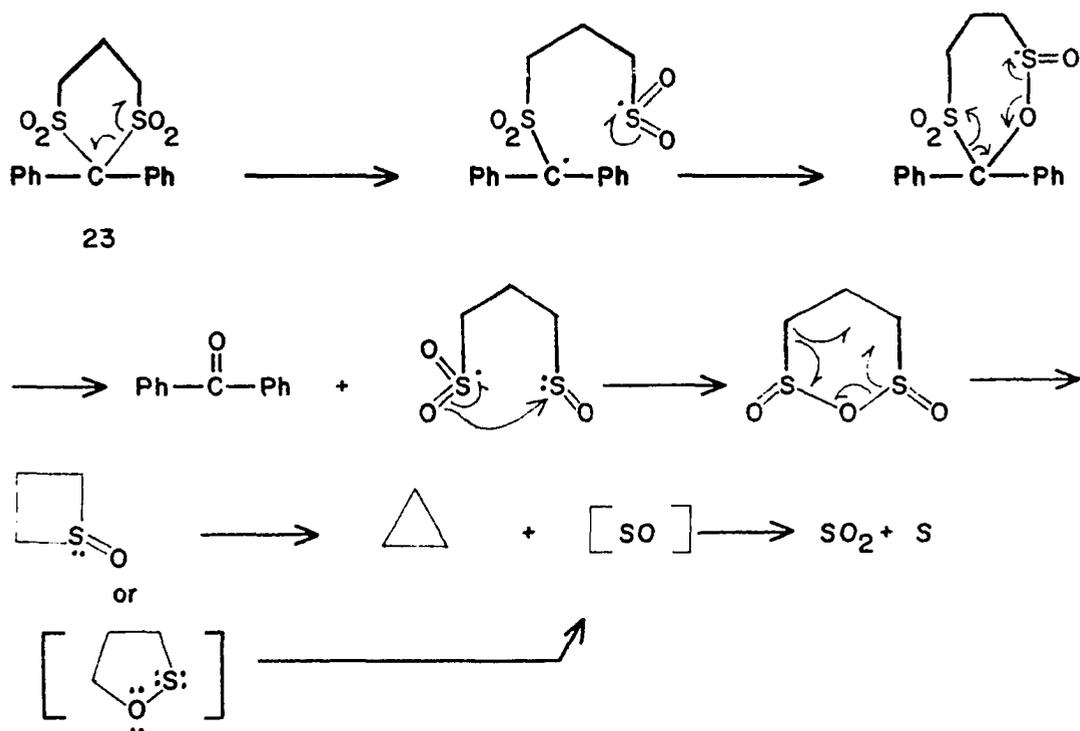
Scheme 10

Three general pathways are proposed for the thermal decomposition of the sulfones and sulfoxides utilized in this investigation. The illustrative free radical pathway depiced in schme 5, the carbonium ion pathway depicted in scheme 6 and the concerted pathway depicted in scheme 8 are consistent with all of the observed facts. Additional experiments which would allow one to distinguish between these three mechanisms have not yet been carried out

SUMMARY

The results of this investigation indicate that disulfones de-

rived from the dithiolanes of aliphatic ketones are themally stable, and

that disulfones derived from mixed dithiolanes (one alkyl group and one

aromatic ring bonded to carbonyl carbon atom of the original ketone) de-

compose very slowly at temperatures far above their melting points. In

contrast, sulfones and sulfoxides derived from the dithiolanes, dithianes,

mercaptoles and oxathiolanes of aromatic ketones undergo facile decom-

position at their melting points and temperatures 10-20° above their melt-

ing points. This evidence suggests that the initial step in the decom-

position pathway involves homolytic fission (see scheme 5) or heterolytic

fission (see scheme 6) of the carbon sulfur bond to generate either a free

radical or a carbonium ion on the carbon atom bearing the aromatic rings.

All new compounds used in this investigation gave satisfactory

spectral data. The data taken on known compounds is consistent with the

data reported in the literature.

EXPERIMENTAL

All melting points and boiling points are uncorrected. All solvents were redistilled prior to use. Anhydrous solvents were prepared by distillation from calcium hydride. Column chromatography supports were silicAR CC-7 (Mallinckrodt, 100/200 mesh) and silica gel H (Merck AG, Darmstadt). Thin layer chromatography was performed on 5 x 20 cm glass plates coated with silica gel H (Merck AG, Darmstadt). The developed plates were exposed to iodine vapor for visualization of the chromatogram.

Gas chromatographic analyses were performed on a Varian Aerograph Model 1220-1 or Aerograph Model 1740-1 gas chromatograph. The infrared spectra were taken on a Beckman IR-8 spectrometer as potassium bromide pellets or in solutions of carbon tetrachloride or chloroform. Ultraviolet spectra (uv) were taken in 95% ethanol solutions with a Hitachi Perkin-Elmer, Model 124 spectrometer.

Nuclear magnetic resonance spectra (nmr) were taken on the Varian XL-100, or T-60 spectrometers using tetramethylsilane (TMS) as an internal reference. Samples were run in varying concentrations of carbon tetrachloride and deuteriochloroform. Chemical shifts are reported in δ-units (parts per million from TMS) are followed by the multiplicity of the signal, the number of protons, the corresponding coupling constant and the assignment. The multiplicities are denoted by the symbols:

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s, singlet; d, doublet; dd, double doublet; t, triplet; and m, multiplet.

The mass spectra were taken on a Hitachi Perkin-Elmer RMU-7E spectrometer using perfluorokerosene as an internal reference. Major peaks and molecular ions are reported followed by percentage of the base peak.

Combustion analyses were carried out by Bernhardt Laboratories in Mülheim, West Germany, and Mr. E. Meier, Chemistry Department, Stanford University, Palo Alto, California

2,2-Diphenyl-1,3-dithiolane (11)

A solution of 9.4 g (.10 mol) of 1,2-ethanedithiol, 18.2 g (.10 mol) of benzophenone and .1 g of p-toluenesulfonic acid in 200 ml of benzene was refluxed for 12 hr and cooled to room temperature. The benzene solution was washed once with 25 ml of a 10% solution of sodium bicarbonate and dried over anhydrous sodium sulfate. Removal of the benzene on a rotary evaporator and a vacuum pump yielded 25.1 g (97%) of the dithiolane as an oily solid, mp 97-99°. Recrystallization from 95% ethanol yielded 23.8 g (90%) of 2,2-diphenyl-1,3-dithiolane as a white crystalline solid, mp 101-102.5°. [lit mp[14] 102°]; ir (CCl$_4$) 1440 cm^{-1} (carbon-sulfur stretch); nmr (CDCl$_3$) δ 7.1-7.75 (m, 10, aromatic protons), 3.40 (s, 4, methylene protons).

1,1,3,3-Tetraoxo-2,2-diphenyl-1,3-dithiolane (19)

In a 250 ml flask was placed a mixture of 2.58 g (10 mmol) of 2,2-diphenyl-1,3-dithiolane, 10 ml of 30% hydrogen peroxide and 50 ml of acetic acid. The reaction mixture was heated on a steam bath for 12 hr and cooled to room temperature. Upon cooling, white crystals

separated from the solution. The crystals were collected by suction

filtration, washed with benzene and air dried to yield 3.15 g (98%) of

1,1,3,3-tetraoxo-2,2-diphenyl-1,3-dithiolane as a white crystalline solid,

mp 217-210°. Two recrystallizations from benzene yielded an analytical

sample, mp 222-222.5°; ir (KBr) 1332 cm^{-1} (sulfone stretch), 1123 cm^{-1}

(sulfone stretch); nmr (CF_3COOH) δ 7.35-7.75 (m, 10, aromatic protons),

4.30 (s, 4, methylene protons); mass spectrum 258 (70), 192 (12), 166

(100), 121 (20), 92 (10), 77 (75), 64 (60), 49 (12) and 43 (15).

Anal. Calcd. for $C_{15}H_{14}S_2O_4$: C, 55.90; H, 4.35; S, 19.87.

Found: C, 55.81; H, 4.44; S, 19.87.

2,2-Diphenyl-1,3-dithiane (16)

In a 500 ml flask was placed 9.1 g (.05 mol) of benzophenone,

5.4 g (.05 mol) of 1,3-propanedithiol, .5 g of p-toluenesulfonic acid

and 300 ml of benzene. The reaction mixture was refluxed for 12 hr and

cooled to room temperature. The benzene solution was washed with a

10% solution of sodium bicarbonate and dried over anhydrous sodium sul-

fate. Removal of the benzene on a rotary evaporator and a vacuum pump

yielded 13.5 g (99%) of the dithiane as a white solid, mp 97-98°. Two

recrystallizations from 95% ethanol yielded 12.4 g (91%) of 2,2-diphenyl-

1,3-dithiane as a white crystalline solid, mp 109-110°. [Lit.[15] mp 110°];

ir (CCl_4) 1440 cm^{-1} (carbon-sulfur stretch); nmr (CCl_4) δ 7.15-7.75 (m,

10, aromatic protons), 2.70 (t, 4, J = 6 Hz, methylene protons on carbon

atoms bearing sulfurs), 1.8-2.1 (m, 2, remaining methylene protons).

1,1,3,3-Tetraoxo-2,2-diphenyl-1,3-dithiane (23)

In a 500 ml flask was placed a mixture of 2.72 g (.01 mol) of

2,2-diphenyl-1,3-dithiane, 10 ml of 30% hydrogen peroxide and 100 ml of

glacial acetic acid. The flask was heated on a steam bath, and after about 45 min, white crystals separated from the hot solution. The flask was stored in a refrigerator for 2 hr, and the crystals were collected by suction filtration and air dried to yield 3.11 g (92.8%) of the sulfone, mp 251-252°. Two recrystallizations from benzene yielded an analytical sample, mp 254-254.5°; ir (KBr) 1335 cm^{-1} (sulfone stretch), 1130 cm^{-1} (sulfone stretch); nmr (CF$_3$COOH) δ 7.35-7.90 (m, 10, aromatic protons), 3.70 (t, 4, J = 6 Hz, methylene protons on carbon atoms bearing sulfone), 2.65-2.95 (m, 2, remaining methylene protons); mass spectrum 336 (2), 209 (16), 208 (72), 207 (10), 183 (40), 182 (85), 179 (36), 167 (35), 166 (100), 165 (69), 130 (20), 105 (58), 91 (27), 90 (30), 64 (12), and 41 (19).

<u>Anal</u>. Calcd. for C$_{16}$H$_{16}$S$_2$O$_4$: C, 57.14; H, 4.76; S, 19.05. Found: C, 57.18; H, 4.79; S, 19.20.

2-(4-t-Butylspirocyclohexyl)-1,3-dithiolane (<u>15</u>)

A solution of 2.35 g (.025 mol) of 1,2-ethanedithiol, 3.85 g (.025 mol) of 4-t-butycyclohexanone, and .1 g of toluenesulfonic acid in 100 ml of benzene was refluxed for 12 hr and cooled to room temperature. The benzene solution was washed with 25 ml of a 10% solution of sodium bicarbonate and dried over anhydrous sodium sulfate. The benzene was removed on a rotary evaporator and a vacuum pump to yield 5.64 g (98%) of the dithiolane as white flakes, mp 64-65°. Two recrystallizations from 95% ethanol yielded an analytical sample, mp 65-65.5°; ir (KBr) 1460 cm^{-1} (carbon-sulfur stretch); nmr (CCl$_4$) δ 3.25 (bs, 4, methylene protons of the dithiolane ring), 2.3-1.2 (m, 9, protons of the cyclohexane ring), .9 (s, 9, protons of the t-butyl group); mass spectrum

232 (4), 231 (7), 230 (100), 133 (13), 132 (39), 131 (55), 87 (16), 81

(39), 79 (13), 62 (14), 58 (34), 56 (10), 44 (41), and 42 (26).

Anal. Calcd. for $C_{12}H_{22}S_2$:   C, 62.61; H, 9.56.   Found: C, 62.70;

H, 9.44.

1,1,3,3-Tetraoxo-2-(4-t-butylspirocyclohexyl)-1,3-dithiolane (22)

A solution of 2.3 g (.01 mol) 2-(4-t-butylspirocyclohexyl)-1,3-

dithiolane and 8 ml of 30% hydrogen peroxide in 50 ml of glacial acetic

acid was heated on a steam bath for 12 hr and cooled to room temperature.

White crystals (flakes) separated from the solution upon cooling. The

crystals were collected by suction filtration, washed several times with

benzene and air dried to yield 2.85 g (94%) of the sulfone as white

flakes, mp 251-252°. Recrystallization from chloroform did not change

the melting point; ir (KBr) 1298 cm^{-1} (sulfone stretch), 1122 cm^{-1} (sul-

fone stretch); nmr (CF_3COOH) δ 3.92 (s, 4, methylene protons of the

dithiolane ring), 1.0 - 2.7 (m, 9, methylene protons of the cyclohexane

ring), .95 (s, 9, protons of the t-butyl group); mass spectrum 294 (1),

234 (62), 202 (41), 141 (22), 139 (25), 139 (49), 119 (35), 97 (31),

96 (30), 95 (37), 93 (20), 91 (24), 78 (44), 77 (55), 79 (60), 75 (48),

67 (30), 65 (40), 64 (9), 56 (43), 55 (100), 54 (85), 53 (46), 51 (38),

and 41 (38).

Anal. Calcd. for $C_{12}H_{22}S_2O_4$:   C, 48.97; H, 7.48; S, 21.76.

Found: C, 49.04; H, 7.62; S, 21.96.

2-Phenyl-2-methyl-1,3-dithiolane (13)

A solution of 7.3 g (.05 mol) of acetophenone, 9.42 g (.05 mol)

of 1,2-ethanedithiol and .5 g of p-toluensulfonic acid in 250 ml of

benzene was refluxed for 12 hr and cooled to room temperature. The

benzene solution was washed with 50 ml of a 10% solution of sodium bi-carbonate and dried over anhydrous sodium sulfate. Removal of the benzene on a rotary evaporator and a vacuum pump yielded 10.4 g (99%) of the crude dithiolane as a clear liquid. Distillation yielded 9.7 g (83%) of 2-methyl-2-phenyl-1,3-dithiolane as a colorless liquid, bp 134-135.5° (3.5 mm): n_D^{25} 1.6158. [Lit[16] bp 131° (3 mm) n_D^{25} 1.6162.]

1,1,3,3-Tetraoxo-2-methyl-2-phenyl-1,3-dithiolane (20)

In a 250 ml flask was placed 4.2 g (.02 mol) of 2-methyl-2-phenyl-1,3-dithiolane, 15 ml of 30% hydrogen peroxide, and 60 ml of glacial acetic acid. The reaction mixture was stirred at 70-80° for 12 hr, cooled to room temperature, and poured into 500 ml of chloroform. The chloroform solution was washed several times with a 10% solution of sodium bicarbonate and dried over anhydrous sodium sulfate. Evaporation of the chloroform on a rotary evaporator and a vacuum pump yielded 5.11 g (98%) of the sulfone as a white powder, mp 128-130°. Recrystallization from hexane-dichloromethane (1:1) yielded 4.8 g (92%) of 2-methyl-2-phenyl-1,3-dithiolane as a white crystalline solid, mp 132-133°. Three recrystallizations from hexane-dichloromethane (1:1) yielded an analytical sample, mp 132-132.5°; ir (KBr) 1315 cm^{-1} (sulfone stretch), 1122 cm^{-1} (sulfone stretch); nmr (CDCl$_3$) δ 7.82-7.25 (m, 5, aromatic protons), 3.7 (s, 4, methylene protons), 2.15 (s, 3, methyl); mass spectrum 264 (4), 167 (44), 115 (17), 103 (33), 102 (100), 101 (48), 76 (39), 75 (33), 64 (2), 49 (14), and 41 (20).

Anal. Calcd. for $C_{10}H_{12}S_2O_4$: C, 46.15; H, 4.62; S, 24.62. Found: C, 46.11; H, 4.62; S, 24.47.

2-Methyl-2-hexyl-1,3-dithiolane (14)

A solution of 6.4 g (.05 mol) of 2-octanone, 4.7 g (.05 mol)
of 1,2-ethanedithiol and .5 g of p-toluenesulfonic acid in 100 ml of ben-
zene was refluxed for 12 hr and cooled to room temperature. The ben-
zene solution was washed with 50 ml of a 10% solution of sodium bicarbonate
and dried over anhydrous sodium sulfate. Removal of the benzene on the
rotary evaporator yielded 10.05 g (99%) of 2-methyl-2-hexyl-1,3-dithiolane
as a colorless liquid. Distillation yielded 9.25 g (90%) of the dithio-
lane as a colorless liquid, bp 107-109° (2.5 mm) n_D^{25} 1.5108 [Lit.[17] bp
120° (6 mm) n_D^{25} 1.5110].

1,1,3,3-Tetraoxo-2-methyl-2-hexyl-1,3-dithiolane (21)

A solution of 5 g (.024 mol) of 2-methyl-2-n-hexyl-1,3-dithio-
lane, 15 ml of 30% hydrogen perioxide, 50 ml of glacial acetic acid
was stirred at 70-80° for 12 hr, cooled to room temperature, and poured
into 500 ml of chloroform. The chloroform solution was washed several
times with a 10% solution of sodium bicarbonate and dried over anhydrous
sodium sulfate. Removal of the chloroform on the rotary evaporator
and the vacuum pump yielded 5.79 g (90%) of crude product, mp 66-67°.
Recrystallization from hexane-dichloromethane (1:1) yielded 5.25 g (81.5%)
of 1,1,3,3-tetraoxo-2-methyl-2-hexyl-1,3-dithiolane as white flakes, mp 68-69°.
Two recrystallizations from hexane-dichloromethane gave an analytical
sample, mp 68-69°; ir (KBr) 1305 cm^{-1} (sulfone stretch), 1105 cm^{-1}
(sulfone stretch); nmr (CDCl$_3$) δ 3.6 (s, 4, methylene protons of the
five-membered ring), 2.3-1.9 (m, 2, methylene protons on carbons bearing
the sulfonyl group), 1.7 (s, 3, quatenary methyl), 1.25-1.55 (m, 8,
remaining methylene protons), .95 (t, 3, J = 3 Hz, terminal methyl);

mass spectrum 268 (2), 112 (25), 111 (10), 71 (15), 70 (44), 57 (11),

56 (100), 44 (25), 43 (11), 42 (40), and 40 (10).

Anal. Calcd. for $C_{10}H_{20}S_2O_4$: C, 44.77; H, 7.46; S, 23.87.

Found: C, 44.78; H, 7.40; S, 23.98.

2,2-Diphenyl-1,3-oxathiolane (17)

The procedure of Marshall and Stevenson[9] was used.

A solution of 29 g (0.16 mol) of benzophenone, 14 g (.18 mol)

of 2-mercaptoethanol and 1 g of p-toluenesulfonic acid in 250 ml of dry

toluene was refluxed for 3 hr and cooled to room temperature. Upon

cooling, an amorphous solid separated from the solution. The mixture

was filtered with suction, and the residue was washed with 100 ml of

ether. The combined filtrates were washed once with 50 ml of a 10%

solution of sodium bicarbonate and dried over anhydrous sodium sulfate.

Evaporation of the solvents on the rotary evaporator yielded 20.6 g of

a colorless oil. The oil was filtered through a column (48 x 4.5 cm)

containing a slurry of 200 g of activity 1 neutral alumina in benzene.

The oil was washed down the column with 300 ml of dry benzene, and one

500 ml fraction was collected. The benzene was removed on a rotary

evaporator to yield 8.5 g (22%) of the oxathiolane as a colorless oil

which crystallized on cooling in a refrigerator, mp 49–51°. Recrystal-

lization from methanol yielded 7.5 g (19%) of the oxathiolane as a white

crystalline solid, mp 52–53°. [Lit.[9] mp 52°]; ir (CCl_4) 1440 cm^{-1}

(carbon-sulfur stretch), 1052 cm^{-1} (carbon-oxygen stretch); nmr ($CDCl_3$)

δ 7.1–7.6 (m, 10, aromatic protons), 4.18 (t, 2, J = 6 Hz, protons on

carbon bearing oxygen), 3.18 (t, 2, J = 6 Hz, protons on carbon bearing

sulfur).

2,2-Diphenyl-1,3-dithiolane-1-oxide (26)

A mixture of 4.0 g (15.5 mmol) of 2,2-diphenyl-1,3-dithiolane

and 20 ml of dioxane and 10 ml of 30% hydrogen peroxide was stirred

at room temperature for 24 hr, and poured into 100 ml of water. White

crystals separated from the solution. The crystals were collected by

suction filtration and air dried to yield 4.41 g (98%) of the sulfoxide,

mp 122-124°. Two recrystallizations from hexane-methylene chloride

(1:3) yielded an analytical sample, mp 125-125.5°. Ir (KBr) 1055 cm^{-1}

(sulfoxide stretch); nmr (CDCl$_3$) δ 7.25-7.8 (m, 10, aromatic protons),

2.8-4.0 (m, 4, methylene protons); mass spectrum 274 (3) M$^+$, 258 (3), 192

(12), 181 (25), 163 (17), 124 (10), 121 (20), 105 (100), 77 (75), 64

(10), 60 (15), 59 (15), 50 (47), 49 (12), and 43 (15).

Anal. Calcd. for C$_{15}$H$_{14}$S$_2$O: C, 65.69; H, 5.11; S, 23.36.

Found: C, 65.50; H, 5.18; S, 23.60.

3,3-Dioxo-2,2-diphenyl-1,3-oxathiolane (24)

A solution of 0.50 g (2.1 mmol) 2,2-diphenyl-1,3-oxathiolane and

1.38 g (8 mmol) of m-chloroperbenzoic acid in 50 ml of absolute ether

was stirred at room temperature for 24 hr during which time a white

solid precipitated from the solution. The precipitate was collected

by suction filtration and washed with ether and air dried. The yield

of the crude sulfone was .523 g (95%), mp 132-134°.

Recrystallization from acetone-ether yielded .493 g (90%) of

3,3-dioxo-2,2-diphenyl-1,3-oxathiolane as a white crystalline solid,

mp 134-135°. Two recrystallization from acetone-ether yielded a spectral

sample, mp 136-136.5°. This compound decomposed on standing at room

temperature for 48 hr, therefore, no elemental analysis could be obtained;

ir (CHCl$_3$) 1309 cm^{-1} (sulfone stretch), 1130 cm^{-1} (sulfone stretch);

nmr (CDCl$_3$) δ 7.2–7.9 (m, 10, aromatic protons), 4.5 (t, 2, J = 7 Hz, protons on carbon bearing oxygen), 3.22 (t, 2, J = 7 Hz, protons on carbon bearing the sulfone); mass spectrum, 274 (2), 182 (100), 105 (40), 77 (75), 64 (30), 50 (47), 49 (12) and 43 (15).

2,2-Diphenyl-1,3-oxathiolane-3-oxide (27)

A mixture of .50 g (2.1 mmol) of 2,2-diphenyl-1,3-oxathiolane, 5 ml of 10% sodium carbonate, 10 ml of 30% hydrogen peroxide and 50 ml of dioxane was heated on a steam bath for 30 min and then stirred at room temperature for 4 hr. The reaction mixture was then diluted with water, and white crystals separated from the solution. The crystals were collected by suction filtration and air dried to yield .539 g (99%) of the crude sulfoxide, mp 88–90°. Recrystallization from methylene chloride-hexane yielded .486 g (90%) of 2,2-diphenyl-1,3-oxathiolane-1-oxide as a white crystalline solid, mp 93–94°. Two recrystallizations from methylene chloride-hexane yielded a spectral sample, mp 93–94°; ir (CCl$_4$) 1075 cm^{-1} (sulfoxide stretch), 1059 cm^{-1} (carbon-oxygen stretch); nmr (CDCl$_3$) δ 4.65–4.92 (m, 1, proton on carbon bearing oxygen), 4.–4.45 (m, 1, proton on carbon bearing oxygen), 2.9–3.35 (m, 2, methylene protons on carbon bearing sulfoxide); mass spectrum 258 (3), 183 (24), 182 (35), 165 (10), 106 (16), 105 (100), 92 (12), 77 (75), 76 (11), 60 (15), 51 (20), and 50 (7). This compound is unstable, therefore, no satisfactory data could be obtained.

Benzophenone diethylmercaptole (18)

The procedure of Wolfrom and Karabinos[10] was used.

A mixture of 4.448 (.055 mol) of ethanethiol, 1.5 g of freshly fused zinc chloride and 2 g of anhydrous sodium sulfate was placed in a 250 ml flask. The flask was immersed in an ice-water bath at 0°, and 9.1 g (.05 mol) of benzophenone was added to the flask and the reaction mixture was stirred at 0-5° for 24 hr. The reaction mixture was then poured into 50 cc of ice water, and the organic layer was removed and washed with 50 ml of a 10% solution of sodium hydroxide and dried over anhydrous sodium sulfate. The solvent was evaporated and the crude mercaptole 14.38 g (98%) was collected and distilled to give 13.8 g (95%) of benzophenone diethyl mercaptole as a color-less liquid, bp 182-184 (.3 mm); [Lit[10] bp 146-150° (.07 mm).]

Benzophenone diethyl mercaptole tetraoxide (25)

A solution of 5.76 g (.02 mol) of benzophenone diethyl mercap-tole and 20.6 g (.12 mol) of m-chloroperbenzoic acid in 100 ml of ether was stirred at room temperature, and after about 4 hrs a white solid separated from the solution. The solid was collected by suction fil-tration, washed with ether and air dried. The yield of crude product was 6.9 g (98%), mp 195-198°. Two recrystallizations from methylene chloride-hexane yielded an analytical sample, mp 197-197.5°; ir (KBr) 1290 cm^{-1} (sulfone stretch), 1105 cm^{-1} (sulfone stretch); nmr (CDCl$_3$) δ 7.28-8 (m, 10, aromatic protons), 3.1 (q, 4, J = 7 Hz, methylene pro-tons of ethyl groups), 1.1 (t, 6, J = 7 Hz, terminal methyls); mass spec-trum 260 (3), 259 (16), 185 (2), 84 (16), 83 (100), 166 (5), 165 (8), 164 (28), 163 (4), 162 (4), 137 (4), 115 (3), 106 (5), 105 (61) and 77 (19).

<u>Anal</u>. Calcd. for $C_{17}H_{20}S_2O_4$: C, 59.97; H, 5.68; S, 18.20.

Found: C, 57.73; H, 5.76; S, 18.31.

The Pyrolysis of Sulfones and Sulfoxides

Description of Apparatus.

The appratus consisted of a pyrex tube 33 cm X 1.5 cm which was connected to a flask for adding solids at one end and to a trap or to a series of traps at the other end. The tube was packed with sufficient glass beads and glass wool to cover a length of approximately 4-5 cm.

Pyrolysis of 1,1,3.3-tetraoxo-2,2-diphenyl-1,3-dithiolane (19)

A. Pyrolysis at atmospheric pressure under nitrogren.

The pyrolysis tube was connected to a series of three traps. The first trap (empty) was immersed in an ice-water bath at 0°, the second trap contained 25 ml of a 1% solution of sodium hydroxide and the third trap contained a solution of 2 g of bromine in 50 ml of carbon tetrachloride. The system was swept with nitrogen, the tube was heated to 225° and 3 g (9.3 mmol) of the disulfone 19 was added slowly to the tube over a 10 min period. The temperature of the tube was maintained at 225° for 5 min and the tube was cooled to room temperature. The first trap was rinsed with chloroform, and after evaporation of the chloroform 1.203 g (72%) of benzophenone, mp 48-49° was recovered. The benzophenone was further char-- acterized by comparing its ir and nmr spectra with the ir and nmr spectra of authentic samples. The yellow residue which remained in the first trap was dissolved in carbon disulfide; evaporation of the carbon disulfide yielded 80.1 mg of sulfur, mp 119-121°. The sodium bisulfite solution in

the second trap was heated at 80° for 24 hr with 5 ml of 30% hydrogen
peroxide. The solution was cooled to room temperature and treated with
excess barium hydroxide. The precipitate of barium sulfate was collected
and dried in an oven at 200°. The yield of barium sulfate was 1.6310 g
(.007 mol); the yield of sulfur dioxide (calculated on the basis of the
barium sulfate) was .413 g (70%). The carbon tetrachloride solution in
the third trap was washed with a saturated solution of sodium bisulfite,
dried over anhydrous sodium sulfate and distilled at atomspheric pressure.
The yield of ethylene dibromide was 1.102 g (5.3 mmol), n_D^{25} 1.5382
[Lit.[12] 1.5389]. The yield of ethylene (calculated on the basis of the
ehtylene dibromide obtained) was .149 g (60%).

B. Pyrolsis In the Presence of Benzoyl Peroxide.

A trace of benzoyl peroxide and 3 g (9.3 mmol) of 19 were pyro-
lyzed under the conditions described above. The results are reported in
Table 4 at the end of this section.

C. Pyrolysis of 19 at Reduced Pressure.

The pyrolysis apparatus was connected to a trap which was immersed
in liquid nitrogen and 2 g (6.3 mmol) of 19 was pyrolyzed at 225° and 2
mm of pressure. The trap was connected to a vacuum line and the mixture
was distilled into a gas ir cell at room temperature until a pressure of
4 cm was obtained. The ir spectrum of the mixture indicated the presence
of sulfur dioxide and ethylene as determined by comparison of the ir
spectra of the mixture with published ir spectra of sulfur dioxide and
ehtylene. Benzophenone and sulfur were identified as previously described.

The yields are reported in Table 4.

The Pyrolysis of 1,1,3,3-tetraoxo-2-methyl-
2-phenyl-1,3-dithiolane (20)

The pyrolysis set up was connected to a trap which was immersed in a dry ice-acetone bath and 1 g (4 mmol) of 20 was pyrolyzed at 250-260° and 2 mm of pressure. Acetophenone was recovered from the trap. See Table 4 for details.

Pyrolysis of 1,1,3,3-tetraoxo-2-methyl-2-hexyl-1,3-dithiolane (21)

To the tube was added 1 g (3.8 mmol) of 21 which was pyrolyzed at 200° and 2 mm of pressure, and in a separate experiment 1 g (3.8 mmol) of 21 was pyrolyzed at 300° and 2 mm of pressure. The results are reported in Table 4.

Pyrolysis of 1,1,3,3-tetraoxo-2-(4-t-butyl-
spirocyclohexyl)-1,3-dithiolane (22)

To the tube was added 1 g (3.5 mmol) of 22 which was pyrolyzed at 400° and 2 mm of pressure, in a separate experiment 1 g (3.5 mmol) of 22 was pyrolyzed at 500° and 2 mm of pressure. The results are reported in Table 4.

Pyrolysis of 1,1,3,3-tetraoxo-2,2-diphenyl-1,3-dithiane (23)

To the tube was added 2 g (6 mmol) of 23 which was pyrolyzed under a nitrogen sweep at 300°. Sulfur dioxide, benzophenone and sulfur were collected and identified by the methods previously described. See Table

4 for more details.

To the tube was added 1 g (3 mmol) of 23 which was pyrolyzed at 300° and 2 mm of pressure. The reaction products were collected in a trap which was immersed in a liquid nitrogen bath. The ir spectrum of the gaseous mixture (taken as previous descibed) showed the presence of sulfur dioxide and a substance whose ir spectrum resembled the ir spectrum of cyclopropane. Benzophenone and sulfur were obtained. The yields are reported in Table 4.

Pyrolysis of 2,2-diphenyl-1,3-oxathiolane-1,1-dioxide (24)

To the tube was added 2.78 g (.01 mol) of freshly prepared 24 which was pyrolyzed at 150° and 2 mm of pressure. The results are reported in Table 4.

Pyrolysis of benzophenone diethyl mercaptole tetraoxide (25)

To the tube was added 0.5 g (1.4 mmol) of 25 which was pyrolyzed at 200° and 2 mm of pressure. The results are reported in Table 4.

Pyrolysis of 2,2-diphenyl-1,3-dithiolane monoxide (26)

To the tube was added 2.5 g (9.2 mmol) of 26 which was pyrolyzed at 130-140° and 1 atm of pressure. Benzophenone, sulfur and ethylene dibromide were recovered. See Table 4 for yields.

Pyrolysis of 2,2-diphenyl-1,3-oxathiolane-monoxide (27)

To the tube was added 2 g (7.8 mmol) of 27 which was pyrolyzed at 120-130° and 2 mm. The results are reported in Table 4.

2-Phenyl-1,3-dithiolane (12)

A solution of 5.3 g (.05 mol) of benzaldehyde, 4.7 g (.05 mol) of 1,2-ethanedithiol and 2 ml of boron trifluoride-etherate in 50 ml of chloroform was stirred at room temperature for 12 hr. The chloroform solution was then washed with a 10% solution of sodium bicarbonate and dried over anhydrous sodium sulfate. Evaporation of the chloroform yielded 8.9 g (98%) of crude product. Distillation yielded 8.5 g (93%) of 2-phenyl-1,3-dithiolane as a colorless liquid, bp 134-136° (3.5 mm), n_D^{25} 1.6366 [Lit.[13] bp 109.5° (.7 mm) n_D^{25} 1.6368].

The Oxidation of 2-phenyl-1,3-dithiolane

A mixture of 2 g (.011 mol) of 12, 10 ml of 30% hydrogen peroxide and 50 ml of glacial acetic acid was stirred at room temperature and after about 5 min a white solid separated from the solution. The solid was collected by suction filtration, washed with benzene and air dried to yield 1.8 g of a product whose ir spectrum exhibited absorptions at 1310, 1120 and 1030 cm^{-1} (sulfone and sulfoxide), 1710 cm^{-1} (benzoic acid).

Attempts to oxidize 12 with m-chloroperbenzoic acid produced similar results.

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