THE SYNTHESIS OF SOME THIIRANES, DITHIIRANES, RELATED AMINO-MERCAPTANS AND THEIR THIOACETATES

Thesis for the Degree of M. S.
MICHIGAN STATE UNIVERSITY
Bart Jacob Bremmer
1962

THE SYNTHESIS OF SOME
THIIRANES, DITHIIRANES, RELATED AMINO-MERCAPTANS
AND THEIR THIOACETATES

By

Bart Jacob Bremmer

A THESIS

Submitted to the College of Science and Arts
of Michigan State University of Agriculture and
Applied Science in partial fulfillment of
the requirements for the degree of

MASTER OF SCIENCE

Department of Chemistry

1962

DEDICATION

To my wife Anita and our children Jackie and Randy,
for their loss of my leisure time.

ACKNOWLEDGMENT

Sincere appreciation for the aid and guidance
given by
Professor Robert D. Schuetz
during the course of this investigation is
expressed by the author.

He also is indebted to the management of
The Dow Chemical Company
who by their encouragement of the Graduate Extension Program at Midland and by their generous
financial support during the residence period
at Michigan State University, made possible the
completion of this study.

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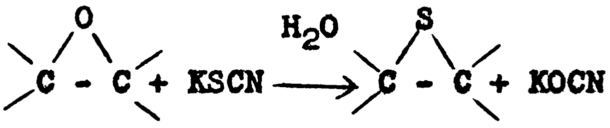
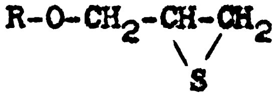
ABSTRACT

An objective of this investigation was to synthesize previously undescribed thiiranes and more specifically to develop synthetic methods for the preparation of dithiiranes.

The starting materials used were the corresponding epoxides and diepoxides. The method used for the synthesis of the majority of the thiiranes was similar to the procedure of Snyder, Stewart and Ziegler (1) modified in several cases. In this method, aqueous potassium thiocyanate is allowed to react with the corresponding epoxide to obtain the desired thiirane.



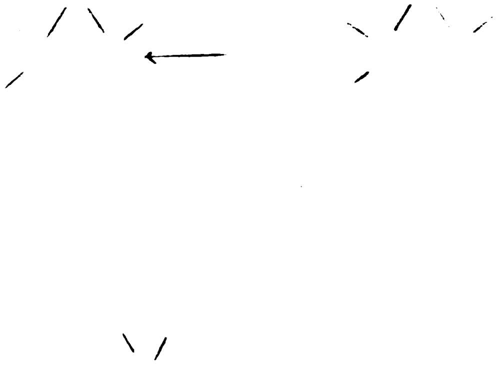
The thiiranes synthesized by this procedure were,



$$\mathrm{R{-}O{-}CH_2{-}\underbrace{CH{-}CH_2}_{S}}$$

where R = allyl and p-tert butylphenyl.

The dithiiranes were obtained from epoxys frequently used in the resin industry, namely diglycidyl ether of bisphenol A, resorcinol diglycidyl ether and hydroquinone diglycidyl ether.



Their sulfur analogs appeared to be crystalline solids, which could be purified by crystallization from ethanol.

An additional episulfide, 1-methyl-1,2-epithio-4-isopropenylcyclohexane was prepared from the corresponding epoxide using the procedure of Bordwell and Anderson (2).

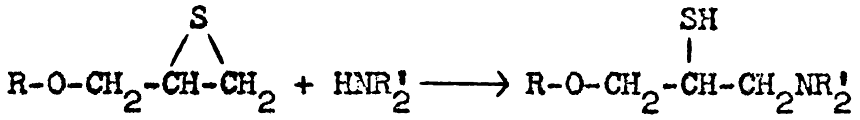
Infrared spectra of the thiiranes and dithiiranes synthesized in this investigation were made, as well as of the epoxides from which they were prepared.

A further objective of this study was to prepare amino-mercaptans from the thiiranes mentioned above. It was anticipated that such compounds would possess antiradiation properties as drugs. Doherty, Burnett and Shapira (3) have reported that several compounds with the general structure,

$$HS(CH_2)_nNRR$$

have shown promising antiradiation properties.

The product resulting from the interaction of thiiranes and secondary amines correspond closely to simple derivatives of this general structure where $n = 2$:



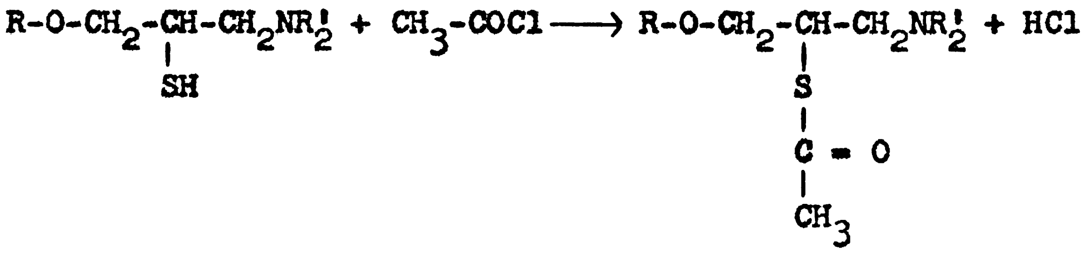
$$R\text{-}O\text{-}CH_2\text{-}\overset{\overset{S}{/\ \backslash}}{CH\text{-}CH_2} + HNR'_2 \longrightarrow R\text{-}O\text{-}CH_2\text{-}\overset{\overset{SH}{|}}{CH}\text{-}CH_2NR'_2$$

R = allyl, phenyl

HNR'_2 = morpholine, piperidine and diethylamine.

The reactions were conducted in the presence of a nonionizing solvent such as benzene or ethyl ether using a molar excess of amine over the thiirane. In most cases, the product was isolated as the hydrochloric acid salt.

Finally, the thioacetates of the amino-mercaptans described were prepared using a modification of the procedure of Clinton, Salvador and Laskowski (4) in which acetylchloride is allowed to react with the amino-thiol in benzene as a solvent followed by neutralization of the hydrochloric acid salt.



$$R\text{-}O\text{-}CH_2\text{-}\underset{\underset{SH}{|}}{CH}\text{-}CH_2NR'_2 + CH_3\text{-}COCl \longrightarrow R\text{-}O\text{-}CH_2\text{-}\underset{\substack{|\\ S\\ |\\ C=O\\ |\\ CH_3}}{CH}\text{-}CH_2NR'_2 + HCl$$

R = allyl, phenyl

$-NR'_2$ = morpholino and piperidino

Where R = allyl, the compounds were isolated as the amine and as the amine hydrochloride. Where R = phenyl, the compounds could not be distilled and were obtained only as their hydrochloric acid salts.

Compounds of this type resemble the structure of acetyl choline, a drug having important physiological properties. These related sulfur compounds may therefore have properties resembling those of acetylcholine.

References

(1) H. R. Snyder, J. M. Stewart and J. B. Ziegler, J. Am. Chem. Soc., 69, 2672 (1947).

(2) F. G. Bordwell and H. M. Anderson, J. Am. Chem. Soc., 75, 4959 (1953).

(3) D. G. Doherty, W. T. Burnett, Jr., and R. Shapira, Radiation Research, 7, 13 (1957).

(4) R. O. Clinton, U. J. Salvador; S. C. Laskowski, J. Am. Chem. Soc., 76, 5152 (1953).

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INTRODUCTION

The sulfur analogs of the alcohols (mercaptans), ethers (thioethers), esters (thioesters) and furans (thiophenes) have received considerable attention and a wide variety of uses for some of them have been found. Such is not the case with the sulfur analogs of the oxiranes or epoxides which are referred to as thiiranes or episulfides.

The epoxides have found extensive applications as intermediates in the synthesis of alcohols, glycols and polyglycols. Since the commercial introduction of epichlorohydrin by the Shell Chemical Company, shortly after the Second World War, the production of epoxy resins has reached a substantial volume, predicted to reach 85-95 million pounds by 1966 (13).

Several commercial processes for epoxidation of olefinic compounds have further advanced epoxy resin technology and production (14,15). The success of the epoxies is not shared by the closely related episulfides. While a higher than one oxirane functionality is of vital importance in epoxy resins, no thiirane with more than one thiirane group per molecule had been reported at the initiation of this study. The instability of many of the episulfides, difficulties in the experimental procedures available for their synthesis, and, more important, the lack of any extensive utility are

some of the reasons why this group of compounds has received limited attention.

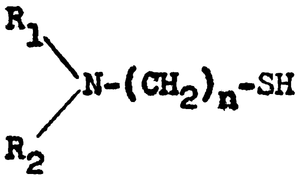
Some uses for episulfides and their derivatives have been reported, however. Alkenesulfides have found some industrial use in the modification of wool fibers (16,17) or to introduce sulfur into synthetic or polymeric materials where it is desirable to improve such properties as affinity for dyestuffs, resistance to water and organic solvents (18).

Some reaction products of ethylenesulfide with primary and secondary amines (19) and mercaptans (20) are useful starting materials for the industrial preparation of dyes, textile aids, medicaments and vulcanization accelerators. A Stanford Research Institute report (21) points out that episulfides permit easy access to potential anticancer agents. A unique sugar episulfide was developed by this same Institute and was used in an attempt to synthesize potential antiradiation drugs (59,60).

More recently it has been found that certain thiiranes and some of their derivatives have antituberculosis activity (22,23,24,25,26). In one of these reports, (25) Acred and Brown, state that "Since the majority of episulphides are very active in vivo, it would appear that the episulphide structure is a necessary moiety for antitubercular activity." The report also mentions that "The compounds with an episulphide

ring must, however, be comparatively simple in order to be active." Some of the compounds that have been synthesized during the course of this investigation may therefore very well possess antitubercular properties.

The primary aim of this work, however, was to synthesize some amino-mercaptans which may find utility as antiradiation drugs. It has been shown (27,28,29) that one class of compounds which shows antiradiation properties has the general structure



where n should be smaller than 3. Compounds with n = 2 and those with branching in the alkyl moiety can be prepared by the reaction of thiiranes with secondary amines, several of which were prepared in the course of this investigation.

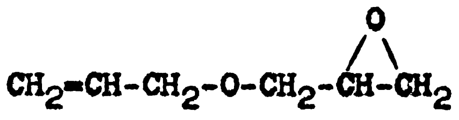
The reaction products of dithiiranes with secondary amines could result in more active antiradiation drugs, since they would contain the desired groupings at both ends of the molecules.

Although none of these compounds have been prepared as yet, the successful synthesis of several dithiiranes, described in this study, opens up this possibility. Finally, the thioacetates of the amino-mercaptans, as

described above, were prepared. These compounds are structurally related to acetylcholine, a substance with a very powerful physiological activity, being many times more active than choline itself. By analogy, it was anticipated that the thioacetates would be more active as antiradiation drugs, or would have certain physiological properties similar to acetylcholine, such as a depressant of blood pressure, or as an agent causing muscle contraction.

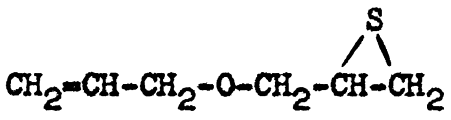
The terminology associated with the cyclic three membered sulfides parallels the nomenclature for the cyclic three membered ethers. The names thiirane, episulfide, alkenesulfide or epithio of the sulfur compounds, correspond to oxirane, epoxide, alkeneoxide and epoxy of the cyclic ethers. A few alicyclic sulfides are described as thiacycloalkanes.

The nomenclature used for cyclic sulfides by Chemical Abstracts, in most cases, amounts to replacing the term epoxy in the corresponding cyclic ether by the term epithio. For example, the compound



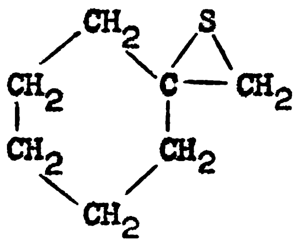
$$CH_2{=}CH{-}CH_2{-}O{-}CH_2{-}\overset{\diagup\,O\,\diagdown}{CH{-}CH_2}$$

is named allyl 2,3-epoxypropyl ether, while the corresponding



$CH_2=CH-CH_2-O-CH_2-CH-CH_2$

is referred to as allyl 2,3-epithiopropyl ether. Exceptions to this rule are found in certain bicyclic compounds where one ring has the episulfide structure. In such case, the term thiabicyclo or thiaspiro- is used. For instance,



is referred to as 1-thiaspiro[2.5]octane.

In the present study, the nomenclature employed is that of Chemical Abstracts when dealing with new or less familiar compounds. This includes all of the cyclic sulfides, their derivatives and certain of the cyclic ethers. A few of the epoxides, however, are better known by names not in use by Chemical Abstracts. Such names will be used occasionally, where it adds to the clarity of the text. For example, the Chemical Abstracts name m-bis(2,3-epoxypropoxy)benzene is replaced by the more familiar resorcinol diglycidylether.

HISTORICAL

The Preparation of Thiiranes

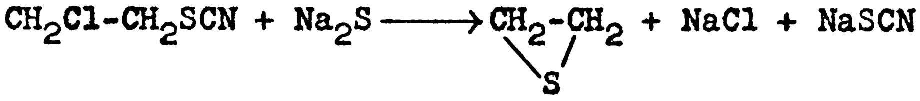
An excellent review of the literature covering the synthesis of episulfides was prepared by Jacobs (2) in 1959. Since then, little has been published in this field, with the exception of the work by Doyle and his co-workers (23). These investigators, in a search for antituberculous drugs, synthesized some new thiiranes using the method of Harding, Owen and Miles (30,31), consisting of the alkaline hydrolysis of acetylated, propylated and butyrated hydroxythiols. The method was successful in the case of the acetates and moderately successful with the propionates.

Adams and co-workers (24) made several substituted propylenesulfides from the corresponding oxides and thiourea.

Although Jacobs has reported the history of the thiiranes in detail (2), some of the highlights deserve attention here to provide proper origination to the work reported here. The parent thiirane, ethylenesulfide was made relatively late in the development of the thiiranes. In 1920, Delepine (32,33) allowed an aqueous solution of sodium sulfide to react with ethylene chlorothiocyanate (made from symmetrical

dichloroethylene and potassium thiocyanate) to obtain ethylenesulfide in low yield.

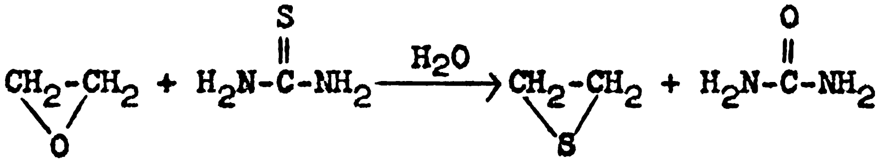
$$CH_2Cl\text{-}CH_2Cl + KSCN \longrightarrow CH_2Cl\text{-}CH_2SCN$$



Later Delepine and Eschenbrenner (34) found that the yield of ethylenesulfide is considerably improved when using ethylene dithiocyanate as the starting material.

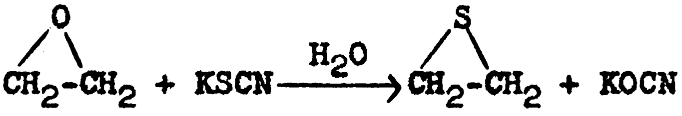
This method has since been utilized by Mousseron (35) to prepare 1-thiaspiro[2.5]octane, 1,1-$\overline{C_6H_{10}\text{-}CH_2S}$.

Dachlauer and Jackel (36) have introduced the use of aqueous thiourea to synthesize alkenesulfides from the corresponding epoxides.



This method was later extended by Culvenor, Davies and Pausacker (9) and more recently improved by Bordwell and Anderson (10). The latter investigators showed that in the formation of propylenesulfide from propyleneoxide a considerable reduction in the amount of polymeric materials resulted by increasing the acidity of the reaction mixture. The yield of propylenesulfide was increased by 20%, for example, by adding 2.5 mole per cent of acid (hydrochloric, sulfuric, acetic, perchloric, benzoic, p-toluenesulfonic) to the aqueous solution of thiourea. An equimolar quantity of acid yielded a 50% increase of the episulfide. A β-hydroxythiouronium salt is formed when an equivalent amount of an acid is used in the reaction between an alkeneoxide and thiourea. This salt may be made to yield the alkenesulfides on alkaline hydrolysis.

Dachlauer and Jackel (37) also described the use of potassium thiocyanate in an aqueous solution at room temperature to transform epoxides into episulfides.



This general procedure has been extended by Snyder, Stewart and Ziegler (1) and also by Price and Kirk (38). The reaction is general and remains one of the most convenient laboratory procedures for the synthesis of cyclic sulfides. This process or modifications thereof was used in the majority of the reactions in which thiiranes were synthesized during the present investigation.

Infrared Spectra of Thiiranes

The initial work on the infrared spectrum of ethylenesulfide was that of Thompson and Dupre (39). Guthrie, Scott and Waddington (40) observed, however, that certain of the bonds reported by Thompson and Dupre (39) were due to traces of polymerized sulfide and/or other impurities. At about the same time, Thompson and Cave (41) reinvestigated the infrared spectrum confirming the observations of Guthrie and co-workers (40).

Recently, Moore and Porter (42) reported the principal bands observed in the infrared spectrum of 1,2-epithio-octane.

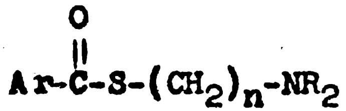
Amino-Mercaptans - Derivatives of Thiiranes

Ring cleavage of thiiranes by primary and secondary amines have been described by Reppe and Nicolai (43). They conducted the cleavage reaction at 100-200°C. in the presence of a substance capable of lowering the pH of the reaction, such as phenol. Snyder, Stewart and Ziegler (1) carried out the reaction of several alkenesulfides with a variety of primary and secondary amines at or near 100°C. for reaction periods of 10 to 20 hours in the absence of a solvent or catalyst. They observed no beneficial effect when either phenol or aluminum chloride was added. Only "normal" ring fission was observed by Snyder and his associates. In all instances,

more or less of the initially formed aminothiol reacted further to form polymeric material. The use of excess amine depressed this polymer formation reaction. Braz (44) demonstrated that the severe reaction conditions previously employed (43) were not necessary and frequently were undesirable, since they favor side reactions. He also observed that when freshly prepared ethylenesulfide was added to a solution of the amine in an ionizing solvent, and this was set aside at room temperature for a few hours, almost complete conversion of the sulfide to polymeric material occurred. On the other hand, when a nonionizing solvent was employed, such as ethyl ether or benzene, polymerization of the sulfide was almost completely suppressed and the amount of aminothiol substantially increased. This procedure was used by Schmolka and Spoerri (45) and more recently by Jacobs and Schuetz (61), who observed similar results as those reported by Braz (44), namely, utilization of a nonionizing solvent and molar excess of amine tend to increase the yield of the amino-mercaptan. The reaction of diethyl amine and alkyl 2,3-epithiopropyl ethers was reported (61) to be erratic. Instead of isolating the amino-mercaptan, the final distillation resulted in the recovery of the starting materials in almost quantitative amounts. Jacobs and Schuetz suggested that these amino-mercaptans readily split out diethyl amine.

Aminothioesters

Clinton, Salvador and Laskowski (4,46 and previous references cited) of the Sterling-Winthrop Research Institute have synthesized a considerable number of aminothioesters. These compounds were reported to possess activity as local anesthetics. Their general structure can be represented as



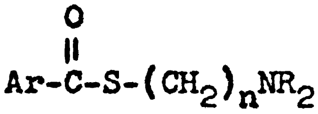
$$Ar-\overset{\overset{O}{\|}}{C}-S-(CH_2)_n-NR_2$$

where Ar is an aromatic or substituted aromatic nucleus and n is 2, 3 or 4. Similar work was reported by Karjala and Mc Elvain (47) and Lischer and Jordan (48) who prepared a series of 3-dialkylaminopropyl 4-aminothiolbenzoate hydrochlorides via 3-chloropropyl 4-nitrothiolbenzoate. Hansen and Fosdick (49) prepared the thio analog of novacaine or procaine which is called thiocaine using a substituted thiolbenzoate as an intermediate. The thiocaine,

$$p-NH_2C_6H_4COSCH_2CH_2N(C_2H_5)_2$$

was found to have more anesthetic efficiency, but was more toxic than the related novacaine (50). In all cases mentioned, the sulfur in these aminothioesters

was introduced by means of a thiol acid (47,48,49) or from a dialkylaminoalkanethiol, $HS(CH_2)_nNR_2$ (4). In none of the cases reported were there any substituents on the polymethylene chain of the general formula

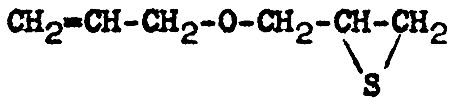


$$Ar{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}S{-}(CH_2)_nNR_2$$

Such a structural change could be obtained (with n = 2) by the reaction of dialkyl amine with thiiranes, (other than ethylenesulfide) followed by the reaction of the product with an acid chloride.

EXPERIMENTAL

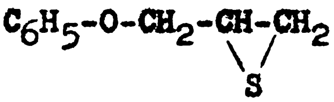
Preparation of Allyl 2,3-Epithiopropyl Ether



The thiirane was prepared from the corresponding oxirane and aqueous potassium thiocyanate, utilizing the procedure of Snyder, Stewart and Ziegler (1).

In a 500 ml. three-necked flask fitted with a sealed stirrer, dropping funnel and reflux condenser, were placed 97 g. (1.0 mole) of potassium thiocyanate and 100 ml. of water. To this vigorously stirred solution was added dropwise 114 g. (1.0 mole) of allyl glycidyl ether (used as obtained from the Shell Chemical Co.) during an hour and three quarters. The turbid solution was stirred for an additional three hours and set aside overnight. The two-phase system was separated and the organic phase was treated as described above with a fresh aqueous solution of potassium thiocyanate (50 g. of the salt in 100 ml. of water) for six hours. The two-phase system was again separated and the aqueous layer was combined with the first aqueous phase and extracted with three 25 ml. portions of ether. The combined ether extracts and organic phase were dried over anhydrous sodium sulfate and the ether removed. The crude product was distilled under vacuum through a 23 x 1.8 cm. column packed with 1/8 inch glass helices. The major fraction distilled at 46-48°C. (4 mm.); n_D^{25} 1.4913. A yield of 63.5% was obtained. Elemental analysis for $C_6H_{10}OS$ gave the following results. Calculated: C, 55.35; H, 7.74; S, 24.62. Found: C, 55.53; H, 7.82; S, 24.58.

Preparation of 2,3-Epithiopropyl Phenyl Ether



$C_6H_5\text{-}O\text{-}CH_2\text{-}\underset{\diagdown S \diagup}{CH\text{-}CH_2}$

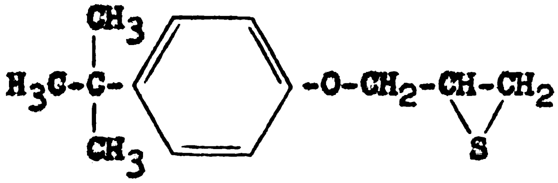
A 150 g. (1.0 mole) quantity of phenyl glycidyl ether (used as obtained from the Shell Chemical Co.) was added in a single portion to a solution prepared from 242 g. (2.5 moles) of potassium thiocyanate dissolved in 200 ml. of water and 150 ml. of ethanol and contained in a 1-L. three-necked flask equipped with a mechanical stirrer, reflux condenser and thermometer. After the reaction mixture was set aside overnight, an additional 150 g. (1.0 mole) of phenyl glycidyl ether was added to the reaction mixture and it was stirred vigorously for thirty-six hours. The supernatant layer and the aqueous phase were decanted from the precipitated potassium cyanate into a 1-L. separatory funnel. The potassium cyanate was rinsed

with two 50 ml. portions of ether, and these were transferred to the separatory funnel and used to extract the 2,3-epithiopropyl phenyl ether. The ether extract was washed twice with 100 ml. portions of saturated sodium chloride solution and dried over anhydrous sodium sulfate. The ether was removed in vacuo and the liquid product distilled under reduced pressure through a 50 cm. Vigreux column. The main fraction distilled at 106°C. (0.9-1.1 mm.); n_D^{25} 1.5738. The yield of the product was 57.3%. Physical constants reported by Jacobs (2) for 2,3-epithiopropyl phenyl ether: b.p. 106°C. (1 mm.); n_D^{25} 1.5735.

Distillation of p-Tert Butylphenyl Glycidyl Ether

p-tert Butylphenyl glycidyl ether obtained from The Dow Chemical Company as a special sample was distilled under reduced pressure through a 50 cm. Vigreux column. The main portion distilled between 98-100°C. (0.2 mm.); n_D^{25} 1.5129. Epoxy equivalent weight calculated: 206; Found: 208.5. Slagh and Alquist (5) describe this material as a colorless mobile liquid boiling at 145-152°C. at 0.2 inch pressure.

Preparation of p-Tert Butylphenyl 2,3-Epithiopropyl Ether



The experimental procedure employed in the synthesis of this material was the same as that used to prepare 2,3-epithiopropyl phenyl ether with the exception that a volume of acetone, equal to the volume of water used, was added to the initial charge of reactants to insure a homogenous reaction mixture. After two separate distillations of the crude product, there was obtained, in small yield*, a colorless liquid, which distilled at 119°C. (0.25 mm.); n_D^{25} 1.5443. Elemental analysis for $C_{13}H_{18}OS$. Calculated: C, 69.68; H, 7.94; S, 14.22. Found: C, 70.22; H, 8.16; S, 14.42.

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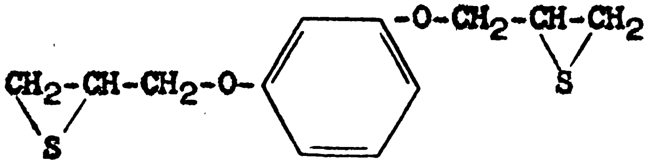
*The yields of some of the reactions are not indicated. These are the reactions that required many crystallizations or repeated distillations for purification. These yields are therefore low. Since these reactions were only run once or twice, good conditions were not found and considerably higher yields can be expected in subsequent trials. The yields as obtained are therefore close to meaningless.

Distillation of Crude Resorcinol Diglycidyl Ether

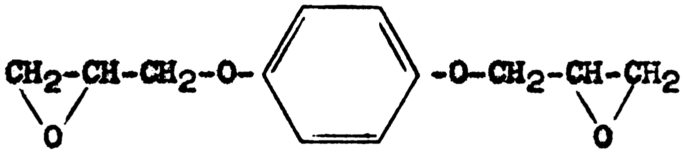
Resorcinol diglycidyl ether, supplied by the Koppers Chemical Company under the trade name Kopoxite 159, was distilled in vacuo through a 20 cm. Vigreux column. The main fraction distilled at 177-188°C. (1.4 mm.) (the wide boiling range is due to a mixture of diastereoisomers); n_D^{25} 1.5389; n_D^{20} 1.5408. Epoxy equivalent weight calculated: 111.1; Found: 114. Physical constants reported by Werner and Farenhorst (3) for resorcinol diglycidyl ether: b.p. 210-220°C. (12 mm.); n_D^{20} 1.5408.

Preparation of m-Bis(2,3-Epithiopropoxy)Benzene



A 500 ml. flask equipped with a stirrer, thermometer and reflux condenser was charged with 121 g. of potassium thiocyanate (1.25 moles), 100 ml. of water, 75 ml. of ethanol and 57 g. (0.5 equivalent) of resorcinol diglycidyl ether and the mixture was set aside overnight. The initially clear reaction mixture became turbid in about one hour and the following day a white solid had precipitated from the solution. The mixture was then stirred for twelve hours and the precipitate was removed by filtration and extracted with 300 ml. of benzene. The benzene extraction was repeated a second time with 100 ml. of benzene. The benzene extracts were combined and dried over anhydrous sodium sulfate. The major portion of the benzene was removed by evaporation in vacuo causing a white precipitate to form. The latter was recovered by filtration and weighed 15.4 g. after drying. From the mother liquor an additional 39.5 g. of the white solid was obtained by evaporation of the benzene. Part of the initial crystalline material was recrystallized four times from absolute ethanol to obtain a white crystalline material which melted at 111.5-113.5°C. Elemental analysis for $C_{12}H_{14}O_2S_2$ gave the following results. Calculated: C, 56.66; H, 5.55; S, 25.21. Found: C, 56.48; H, 5.42; S, 25.07.

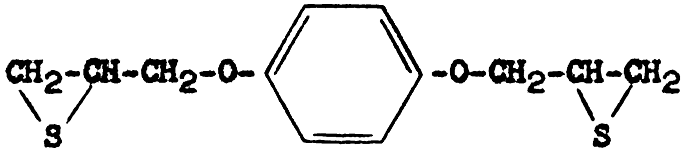
Preparation of Hydroquinone Diglycidyl Ether



A two liter flask was equipped with a stirrer, thermometer, water separator, condenser and nitrogen gas inlet tube. In the flask were placed 165 g. (1.5 moles) of hydroquinone and 1387.5 g. (15 moles) of epichlorohydrin. The stirred mixture was heated to 104°C. and 249.6 g. (3.12 moles) of 50% NaOH solution was added to it. The reaction temperature was maintained at 104°C. by steam distilling water and epichlorohydrin from the reaction mixture. The epichlorohydrin was separated from the steam distillate and returned to the reaction vessel. The addition of the sodium hydroxide required two hours and forty minutes. When all the base had been added, the excess epichlorohydrin was removed by distillation to a pot temperature of 150°C. (30 mm.) and replaced by an equal volume of toluene. The insoluble salt formed during the reaction was removed by filtration and the toluene was removed under reduced pressure. The crude product was distilled under vacuum through a 20 cm. Vigreux column. The major portion boiled at 174-184°C. (0.5 mm.) (the wide boiling point range is due to diastereoisomers).

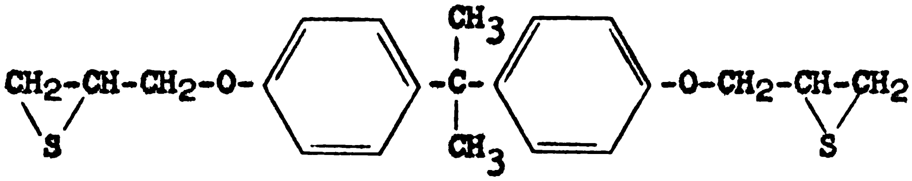
A 56.4% yield was obtained. Epoxy equivalent weight calculated: 111.1; Found: 113.5; m.p. 90-101°C. Physical constants reported by Werner and Fahrenhorst (3) for hydroquinone diglycidyl ether: b.p. approximately 155°C. (0.03 mm.); m.p. one isomer 89.5-90.5°C.; other isomer 118-119°C.

Preparation of p-Bis(2,3-Epithiopropoxy)Benzene



A 500 ml. three-necked flask equipped with a sealed stirrer, thermometer and reflux condenser was charged with 25.5 g. (0.26 mole) of potassium thiocyanate, 20 ml. of water and a warm solution of 15 g. (0.13 equivalent) of hydroquinone diglycidyl ether dissolved in 75 ml. of acetone. The reaction mixture was heated to 50°C. and kept at this temperature for 30 minutes and was then set aside overnight. The following day the crystalline solid which had formed was recovered by filtration and extracted with 150 ml. of carbon tetrachloride. The carbon tetrachloride extract was dried over anhydrous sodium sulfate and the solvent was removed in vacuo. The crude product thus obtained was recrystallized six times from ethanol to obtain a white crystalline material; m.p. 134.5-136.5°C. Elemental analysis for $C_{12}H_{14}O_2S_2$. Calculated: C, 56.66; H, 5.55; S, 25.21. Found: C, 56.65; H, 5.80; S, 25.12.

Preparation of 2,2-Bis[p-(2,3-Epithiopropoxy)Phenyl] Propane



In a 500 ml. three-necked flask fitted with a sealed stirrer, reflux condenser and thermometer, were placed 121 g. (1.25 moles) of potassium thiocyanate, 75 ml. of water, 130 ml. of acetone and 88 g. (0.5 equivalent) of distilled diglycidyl ether of bisphenol A (obtained from The Dow Chemical Company as DER 332 LC). The reaction mixture was stirred vigorously for three and a half hours during which a mass of white crystalline material formed in the initially clear solution. The reaction mixture was heated to 60°C. for three hours and an aliquot was taken from which the crystals were recovered by filtration, washed with water and recrystallized from ethanol. The melting point of this material was 88-91°C. This procedure was again repeated after an additional reaction period of four

hours at 60°C. The melting point of the product here was 91-93°C. Following a third reaction period of four hours at 60°C., all the crystalline material formed during the reaction was filtered out, washed with water and recrystallized from ethanol to obtain a 35% yield of a white crystalline material melting at 93-95°C. Elemental analysis for $C_{21}H_{24}O_2S_2$ gave the following results. Calculated: C, 67.71; H, 6.49; S, 17.21. Found: C, 67.70; H, 6.45; S, 17.38.

Preparation of 3-Chloro-1,2-Propanediol

(Glycerine α-monochlorohydrin)

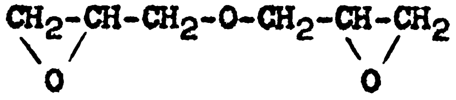
$CH_2Cl-CH_2OH-CH_2OH$

In a one liter three-necked flask equipped with a sealed stirrer, thermometer and reflux condenser were placed 277.5 g. (3 moles) of commercial epichlorohydrin, 540 g. (30 moles) of water and 0.55 g. of concentrated sulfuric acid. The stirred reaction mixture was kept at a temperature of 75-85°C. for three hours, cooled to room temperature and neutralized (pH of 7) with 25% aqueous sodium hydroxide. Excess water was then removed from the reaction mixture and the crude product was distilled under reduced pressure through a 50 cm. Vigreux column. The main portion distilled between

98 and 99°C. (3.4 mm.). A yield of 79.5% was obtained; n_D^{25} 1.4790; $n_D^{17.5}$ 1.4813. Physical constants reported by Boesekens and Hermans (6) for glycerine α-monochlorohydrin; b.p. 116°C. (11 mm.); $n_D^{17.5}$ 1.4820.

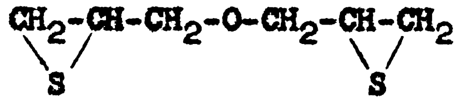
Preparation of Bis(2,3-Epoxypropyl)Ether

(Diglycidyl Ether)



The procedure followed was that described by Dudley (7). A two liter three-necked flask equipped with a stirrer, thermometer, condenser and dropping funnel was charged with 223 g. (2.2 moles) of 3-chloro-1,2-propanediol and 5.1 g. concentrated sulfuric acid. The mixture was heated to 95°C. and 185 g. (2.0 moles) of epichlorohydrin added during two and one half hours. After adding the epichlorohydrin, the reaction mixture was kept at 95° for three hours, cooled and set aside overnight. Benzene, 176 g., was then added and the solution was chilled to below 0° in an ice-salt bath. Next, a solution containing 193 g. (4.83 moles) of sodium hydroxide dissolved in 285 g. of water was added during an hour and three quarters, while holding the reaction temperature below 5°C. Following neutralization, the mixture was stirred for a half hour and filtered to remove the sodium chloride. The benzene layer was separated and the aqueous layer extracted with 188 g. of benzene. The benzene extracts were combined with the initial layer and after removing the benzene by distillation under reduced pressure, a 55% yield of the crude bis(2,3-epoxypropyl)ether was obtained. Vacuum redistillation of the ether through a 50 cm. Vigreux column gave an 18% yield of the pure product, boiling at 96-97°C. (9 mm.); n_D^{25} 1.4458. Epoxy equivalent weight calculated: 65; Found: 65.9. The boiling point for bis(2,3-epoxypropyl)ether is reported by Dudley (7) as 96-97°C. (9 mm.). Its refractive index at 25°C., as reported by Roach and Wittcoff (8), is 1.4455.

Attempted Preparation of Bis(2,3-Epithiopropyl)Ether

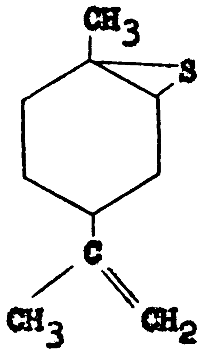


A 500 ml. three-necked flask equipped with a stirrer, thermometer, dropping funnel and a condenser was charged with 61 g. (0.63 mole) of potassium thiocyanate and 50 ml. of water. A 33 g. quantity (0.5 equivalent) of bis(2,3-epoxypropyl)ether was added dropwise during 50 minutes. The exothermic reaction

was kept below 32°C. by external cooling. Following the addition of the epoxy ether, the reaction mixture was stirred for an hour and fifty minutes, 60 ml. of benzene was added and the mixture was stirred an additional forty-five minutes. The benzene layer was separated from the aqueous layer and the latter extracted three times with 25 ml. portions of ether. The ether extracts and benzene layer were combined, washed three times with 50 ml. portions of distilled water and dried over anhydrous sodium sulfate. The ether and benzene were removed in vacuo. The product was distilled under reduced pressure through a short path distilling apparatus. One fraction distilled at 82-83°C. (0.25 mm.); n_D^{25} 1.5498. Elemental analysis of this material for $C_6H_{10}OS_2$ gave the following results. Calculated: C, 44.41; H, 6.21; S, 39.52. Found: C, 44.89; H, 6.37; S, 37.39. The second fraction distilled at 83-85°C. (0.2 mm.); n_D^{25} 1.5508. Elemental analysis, Found: C, 45.17; H, 6.39; S, 40.30.

Preparation of 1-Methyl-1,2-Epithio-4-Isopropenylcyclohexane

(Limonene Monoepisulfide)



The product was prepared from the corresponding oxide, limonene monoxide, obtained from the Food Machinery and Chemical Corporation. Several experimental procedures were examined. The epoxide was used as received and had the following physical properties: epoxy equivalent weight calculated: 152; Found: 159.9; n_D^{25} 1.4651; n_D^{20} 1.4672. Literature values n_D^{20} 1.4697 (11).

<u>The modified procedure of Snyder, Stewart and Ziegler (1):</u>

In a 500 ml. three-necked flask equipped with a stirrer, thermometer and condenser was placed 135 g. (1.4 moles) of potassium thiocyanate, 100 ml. of water, 75 ml. of ethanol and 80 g. (0.5 equivalent) of 1-methyl-1,2-epoxy-4-isopropenylcyclohexane (limonene monoxide). The heterogenous two-layer reaction was stirred vigorously for 16 hours. An aliquot of the organic phase of the reaction mixture was taken and, on removal of the solvent only, starting material was obtained. The reaction was then refluxed for fifteen hours, cooled, transferred to a separatory funnel and the water layer removed. The salt which had formed during the reaction was rinsed twice with 50 ml. portions of ether. The ether extracts were combined with the organic layer, which was washed twice with 50 ml. portions of a saturated sodium chloride solution and dried over anhydrous sodium sulfate. The solvents were removed in vacuo, and the product distilled in vacuum through a 50 cm. Vigreux column. A yield of 37.9 g. consisting mainly of starting material was obtained. A second attempt to prepare this thiirane using this method by replacing the ethanol with acetone gave similar results.

The method of Culvenor, Davies and Pausacker (9):

Into the apparatus described above, with the aid of a dropping funnel, was placed 42 g. (0.55 mole) of thiourea and 140 ml. of methyl alcohol. The stirred mixture was cooled to 1-2°C. and held there while 80 g. (0.5 equivalent) of 1-methyl-1,2-epoxy-4-isopropenylcyclohexane was added dropwise to it, during an hour. The reaction mixture was allowed to warm to room temperature, stirred an additional four hours, then poured into 300 ml. of water and extracted with three 75 ml. portions of n-pentane. The combined extracts

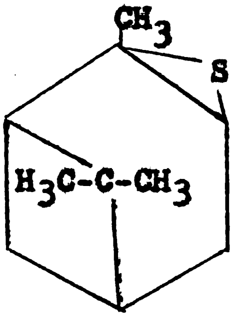
were dried over anhydrous sodium sulfate and the n-pentane was removed in vacuo. Epoxide was recovered in a 95.5% yield.

The method of Bordwell and Anderson (10):

In the same apparatus were placed 175 ml. of water, 13.5 ml. (0.5 equivalent) of sulfuric acid and 38 g. (0.5 mole) of thiourea. The contents were cooled to 0°C. and held between 0-5°C. while 80 g. (0.5 equivalent) of 1-methyl-1,2-epoxy-4-isopropenylcyclohexane was added dropwise during two hours. The reaction flask was kept immersed in the ice-bath for an additional twenty minutes. External cooling was removed and the reaction mixture was allowed to warm to room temperature in three hours. An aqueous sodium carbonate solution (53 g., 0.5 mole in 250 ml. of water) was added to the acidic reaction mixture during a half hour. Two layers formed, the upper organic was a resin-like white material. This was separated from the aqueous layer and extracted with four 50 ml. portions of n-pentane. Only a small part of this material was soluble in n-pentane. The hydrocarbon extract was dried over anhydrous sodium sulfate and the n-pentane removed in vacuo. The crude material was distilled under reduced pressure through a short path distilling apparatus. The 1-methyl-1,2-epithio-4-isopropenylcyclohexane distilled at 63-65°C. (3 mm.); n_D^{25} 1.5152 and was obtained in a 9.6% yield. Elemental analysis for $C_{10}H_{16}S$ gave the following results. Calculated: C, 71.36; H, 9.58; S, 19.05. Found: C, 71.38; H, 9.39; S, 19.06.

Attempted Preparation of 2,3-Epithiopinene

(α-Pinene Episulfide)

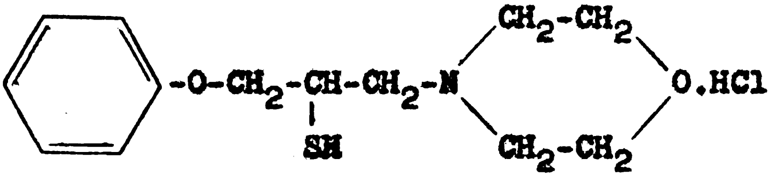


The synthesis of this optically active thiirane was attempted starting with α-pinene oxide (Food Machinery and Chemical Corporation). The epoxide was used as received and had a n_D^{25} of 1.4672; n_D^{20} 1.4692. Literature values n_D^{20} 1.4697 (12). The usual methods for the determination of epoxy equivalent are not applicable to α-pinene oxide (12).

Three procedures were tried in the attempt to make this thiirane. The procedure of Snyder, Stewart and Ziegler (1) as well as that of Culvenor, Davies and Pausacker (9) resulted in the recovery of the epoxide starting material. The method of Bordwell and Anderson (10) as described under the preparation of

1-methyl-1,2-epithio-4-isopropenylcyclohexane gave mostly polymeric material.

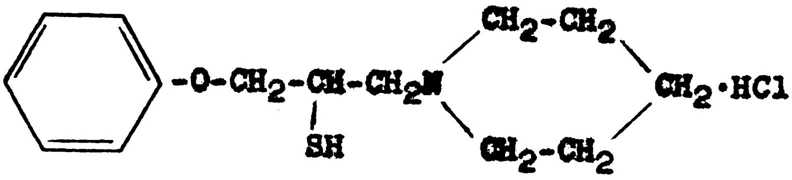
Preparation of α-Phenoxymethyl-4-Morpholineëthanethiol Hydrochloride



A 125 ml. filter flask was charged with 8.7 g. (0.1 mole) of morpholine and 7.5 ml. of benzene. The amine solution was cooled to 0°C. and a prechilled solution of 8.3 g. (0.05 mole) of 2,3-epithiopropyl phenyl ether dissolved in 7.5 ml. of benzene was added portionwise during a ten minute period. The reaction mixture was held at 0°C. for an additional hour and then warmed to room temperature. Subsequently, the filter flask was equipped with a condenser and its side arm closed off. The reaction mixture was then heated for one hour at its reflux temperature. The excess morpholine and benzene were removed in vacuo. The residue was dissolved in about 25 ml. of dry ether and dry hydrogen chloride gas was bubbled into the solution. The white precipitate which formed was recrystallized three times from a mixture (1:1) of isopropyl alcohol and methanol. The α-phenoxymethyl-4-

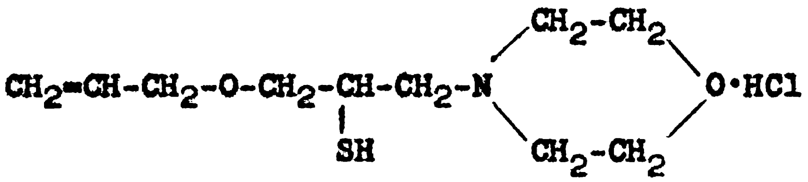
morpholineëthanethiol hydrochloride, melting at 166-168°C., was obtained in a 55.5% yield. Elemental analysis for $C_{13}H_{19}NO_2S \cdot HCl$ gave the following results. Calculated: C, 53.87; H, 6.96; S, 11.06; N, 4.83; Cl, 12.23. Found: C, 53.91; H, 6.89; S, 11.04; N, 4.72; Cl, 12.26.

Preparation of α-Phenoxymethyl-1-Piperidineëthanethiol Hydrochloride



This compound was prepared from piperidine and 2,3-epithiopropyl phenyl ether utilizing the procedure previously described for the synthesis of α-phenoxymethyl-4-morpholineëthanethiol hydrochloride. The α-phenoxymethyl-1-piperidineëthanethiol hydrochloride was obtained after three recrystallizations from isopropyl alcohol in a 35.0% yield and melted at 122.5-124.5°C. Elemental analysis for $C_{14}H_{21}NOS \cdot HCl$ gave the following results. Calculated: C, 58.41; H, 7.70; S, 11.14; N, 4.86; Cl, 12.32. Found: C, 58.56; H, 7.51; S, 11.34; N, 4.79; Cl, 12.62.

Preparation of α-(Allyloxy)Methyl-4-Morpholineëthanethiol Hydrochloride

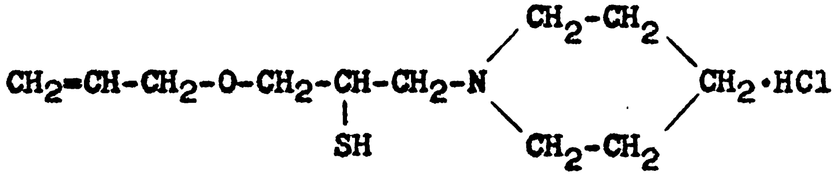


A 125 ml. filter flask was charged with 8.7 g. (0.1 mole) of morpholine and 7.5 ml. of anhydrous ether. The solution was cooled to 0°C. and a prechilled solution of 6.5 g. (0.05 mole) of allyl 2,3-epithiopropyl ether dissolved in 7.5 ml. of anhydrous ether was added portionwise during ten minutes. The reaction mixture was held at 0°C. for an additional hour and then warmed to room temperature. The filter flask was then equipped with a condenser and its side arm closed off. The reaction mixture was heated for an hour at its reflux temperature. The excess morpholine and ether were removed in vacuo and the residue was dissolved in about 25 ml. of anhydrous ether. Dry hydrogen chloride was passed into the ether solution, precipitating a white solid. This was recrystallized four times from a mixture (1:1) of isopropyl alcohol and ether. The pure hydroscopic compound was obtained in a 55.2% yield and melted at 79.8-81.8°C.

Elemental analysis for $C_{10}H_{19}NO_2S \cdot HCl$ gave the following results. Calculated: C, 47.31; H, 7.94;

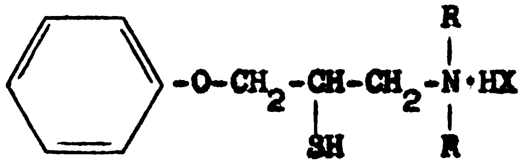
S, 12.63; N, 5.54; Cl, 13.97: Found: C, 47.04; H, 7.90; S, 12.48; N, 5.22; Cl, 13.68.

Attempted Preparation of α-(Allyloxy)Methyl-1-Piperidineëthanethiol Hydrochloride



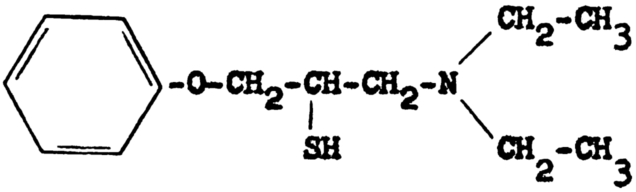
Piperidine and allyl 2,3-epithiopropyl ether were allowed to interact in the manner described for the preparation of α-(allyloxy)methyl-4-morpholineëthanethiol hydrochloride. The α-(allyloxy)methyl-1-piperidineëthanethiol hydrochloride could not be obtained in the pure form due to its very hydroscopic nature.

Attempted Preparation of 1-Dialkylamino-3-Phenoxy-2-Propanethiol Salts



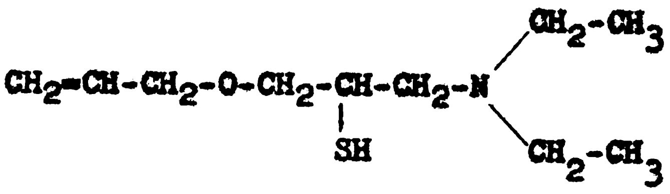
Diethylamine and 2,3-epithiopropyl phenyl ether were allowed to interact as previously described under the preparation of α-(allyloxy)methyl-4-morpholineëthanethiol. The salts of the following acids were prepared: hydrochloride acid, p-toluene sulfonic acid, naphthalene sulfonic acid, sulfuric acid, picric acid, phosphoric acid.. However, none of these salts could be obtained in a good crystalline form, making further purification impossible. Similar results were obtained with the salts of the reaction product obtained by the interaction of di-n-butylamine and 2,3-epithiopropyl phenyl ether.

Preparation of 1-Diethylamino-3-Phenoxy-2-Propanethiol



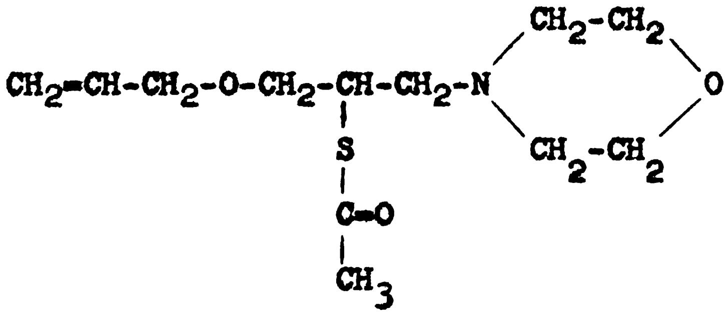
Jacobs and Schuetz (61) have shown that compounds of this type will readily decompose to the materials from which they are easily prepared, namely, the dialkylamine and thiirane. Because the salts of the acids most likely to be crystalline compounds turned out to be oil-like materials, making their further purification impossible, it was decided to prepare the 1-diethylamino-3-phenoxy-2-propanethiol from very pure starting materials and thus obtain the pure compound. Carefully purified 2,3-epithiopropyl phenyl ether was allowed to react with freshly redistilled diethylamine in the manner described under the preparation of α-(allyloxy)methyl-4-morpholineëthanethiol. The product was obtained in a quantitative yield, n_D^{25} 1.5280. Titration with 0.1-N H_2SO_4 indicated an amine equivalent weight of 244.3. Calculated 239.5. Elemental analysis for $C_{13}H_{21}NOS$, Calculated: C, 65.20; H, 8.84; N, 5.88; S, 13.39. Found: C, 65.17; H, 8.71; N, 5.56; S, 13.26.

Attempted Preparation of 1-Allyloxy-3-Diethylamino-2-Propanethiol



Freshly redistilled diethylamine was allowed to react with very pure allyl-2,3-epithiopropyl ether following the experimental procedure described under the preparation of 1-diethylamino-3-phenoxy-2-propanethiol. The yield, in this case, was only 90.6% of the theoretical yield, n_D^{25} 1.4780. Titration with 0.1-N H_2SO_4 indicated an amine equivalent weight of 215.0. Calculated 203.5. Elemental analysis for $C_{10}H_{21}NOS$. Calculated: C, 59.04; H, 10.41; N, 6.93; S, 15.76. Found: C, 59.13; H, 10.91; N, 5.96; S, 16.92.

Preparation of S-(1-Allyloxymethyl-2-Morpholinoethyl) Thioacetate

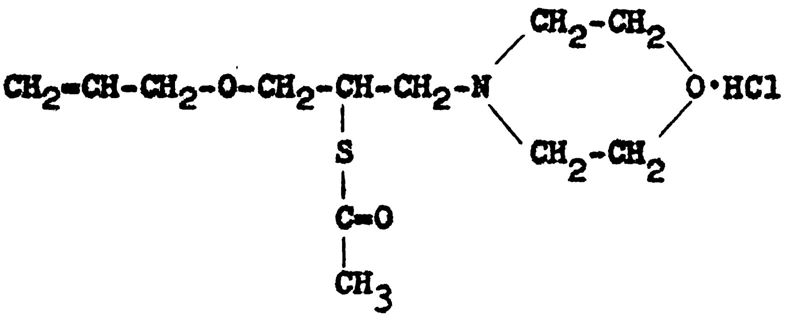


In a 500 ml. three-necked flask equipped with a stirrer, reflux condenser and dropping funnel was placed 133.8 g. (1.54 moles) of morpholine dissolved in 100 ml. of benzene. The solution was cooled to 0°C. A prechilled mixture of 100 g. (0.77 mole) of allyl 2,3-epithiopropyl ether dissolved in 90 ml. of benzene was added during 10 minutes. The reaction mixture was kept at 0°C. for an additional hour and then warmed to room temperature, followed by heating at its reflux temperature for an hour. The benzene and excess morpholine were removed in vacuo. The intermediate crude α-phenoxymethyl-4-morpholineëthanethiol was obtained in 90.2% yield.

The corresponding thioacetate was synthesized following a slightly modified procedure described by Clinton, Salvador and Laskowski (4). A solution of 31.0 g. (0.383 mole) of acetyl chloride dissolved in 125 ml. of benzene was placed in a 500 ml. three-necked

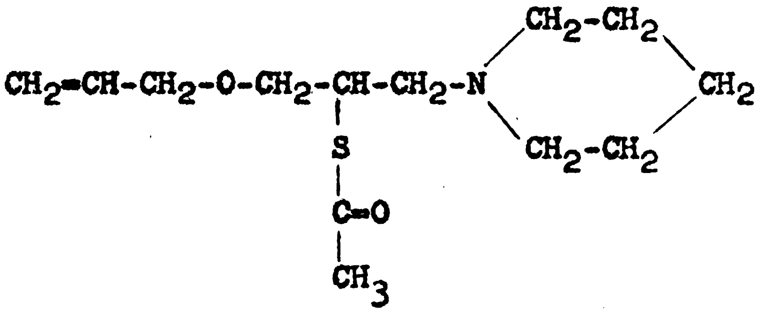
flask equipped with a stirrer, condenser and dropping funnel. To the stirred acetyl chloride solution, kept at 50°, was slowly added 49.9 g. (0.23 mole) of α-phenoxymethyl-4-morpholineëthanethiol dissolved in 100 ml. of benzene. After the addition of the mercaptan, the reaction mixture was stirred for 10 minutes, cooled and 140 ml. of water added. The aqueous layer was made strongly alkaline by the addition of powdered potassium carbonate. The benzene layer was separated, washed with water, then with a sodium bicarbonate solution, again with water, dried over anhydrous sodium sulfate, and the benzene removed in vacuum. The crude product was distilled under diminished pressure through a 50 cm. Vigreux column. The major fraction distilled at 136-137°C. (2 mm.); n_D^{25} 1.4967. A yield of 42.3% based on allyl 2,3-epithiopropyl ether was obtained. Titration with 0.1-N HCl indicated an amine equivalent weight of 257.7. Calculated 259.5. Elemental analysis for $C_{12}H_{21}NO_3S$. Calculated: C, 55.55; H, 8.16; N, 5.43; S, 12.36. Found: C, 55.63; H, 8.24; N, 5.14; S, 12,36.

Preparation of S-(1-Allyloxymethyl-2-Morpholinoethyl) Thioacetate Hydrochloride



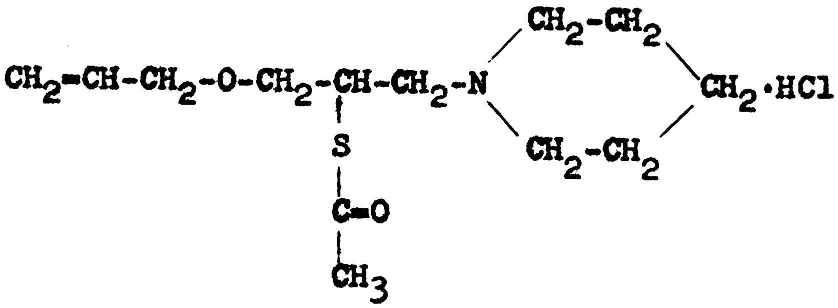
A 6 g. quantity of S-(1-allyloxymethyl-2-morpholinoethyl)thioacetate was dissolved in 25 ml. of anhydrous ether and dry hydrogen chloride was passed into the solution. The resulting precipitate was recrystallized four times from isopropyl alcohol. The compound was obtained in a 66.2% yield and melted at 142.5-144.5°C. Elemental analysis for $C_{12}H_{21}NO_3S \cdot HCl$. Calculated: C, 48.71; H, 7.49; N, 4.76; S, 10.84; Cl, 11.98. Found: C, 48.94; H, 7.52; N, 4.65; S, 10.56; Cl, 11.90.

Preparation of S-(1-Allyloxymethyl-2-Piperidinoethyl) Thioacetate



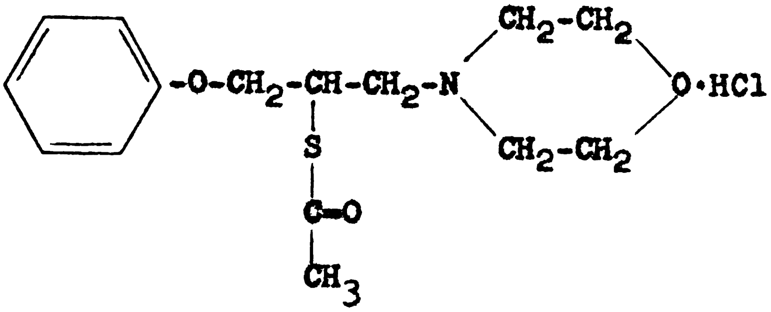
This compound was synthesized in an identical manner to S-(1-allyloxymethyl-2-morpholinoethyl)thioacetate using piperidine instead of morpholine. The compound was obtained in a 48.6% yield based on allyl 2,3-epithiopropyl ether. The major fraction distilled at 125-127°C. (2 mm.); n_D^{25} 1.4932. Titration with 0.1-N HCl indicated an amine equivalent weight of 261.5. Calculated 257.5. Elemental analysis for $C_{13}H_{23}NO_2S$. Calculated: C, 60.64; H, 9.00; N, 5.47; S, 12.45. Found: C, 60.77; H, 8.98; N, 5.54; S, 12.62.

Preparation of S-(1-Allyloxymethyl-2-Piperidinoethyl) Thioacetate Hydrochloride



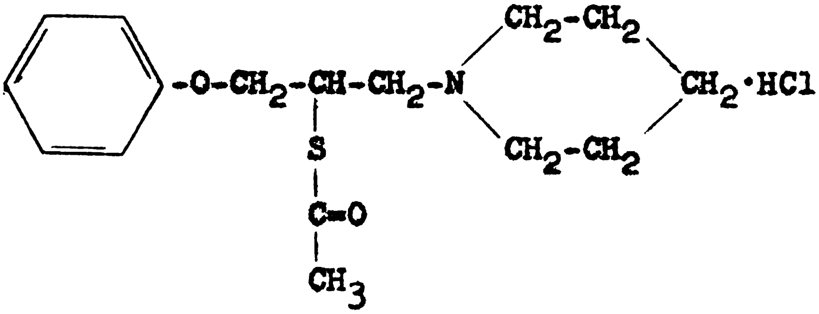
A 3 g. quantity of S-(1-allyloxymethyl-2-piperidinoethyl)thioacetate was dissolved in 12 ml. of anhydrous ether and the solution was treated with dry hydrogen chloride. The resulting amine salt was recrystallized three times from a mixture (3:1) of ether and isopropyl alcohol. The material, obtained in a 58.8% yield, melted at 90-92°C. Elemental analysis for $C_{13}H_{23}NO_2S \cdot HCl$. Calculated: C, 53.12; H, 8.23; N, 4.79; S, 10.91; Cl, 12.06. Found: C, 53.04; H, 8.08; N, 4.66; S, 10.80; Cl, 12.13.

Preparation of S-(2-Morpholino-1-Phenoxymethylethyl) Thioacetate Hydrochloride



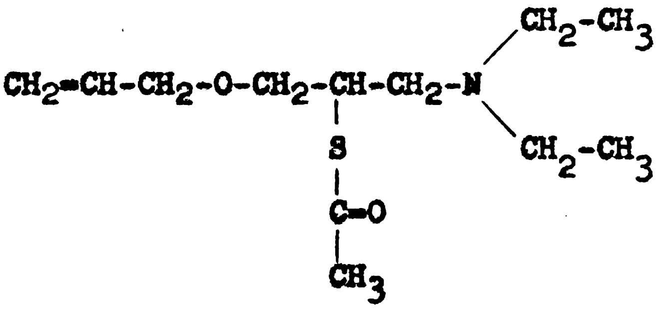
The S-(2-morpholino-1-phenoxymethylethyl)thioacetate was prepared from 2,3-epithiopropyl phenyl ether, morpholine and acetyl chloride following the experimental procedure for the synthesis of S-(1-allyloxymethyl-2-morpholinoethyl)thioacetate. The compound could not be purified by vacuum distillation as it decomposed when heated in vacuum. Its hydrochloride salt was prepared by passing dry hydrogen chloride gas into an ethereal solution of the compound and recrystallizing the resulting salt three times from a solvent mixture (1:1) of methyl alcohol and isopropyl alcohol. A yield of 35.1%, based on 2,3-epithiopropyl phenyl ether, was obtained. The pure product melted at 183-185°C. Elemental analysis for $C_{15}H_{21}NO_3S \cdot HCl$. Calculated: C, 54.27; H, 6.68; N, 4.24; S, 9.66; Cl, 10.68. Found: C, 54.91; H, 6.74; N, 3.89; S, 9.76; Cl, 10.87.

Preparation of S-(2-Phenoxy-1-Piperidinomethylethyl) Thioacetate Hydrochloride



This thioester was prepared in the same manner described for the preparation of S-(2-morpholino-1-phenoxymethylethyl)thioacetate hydrochloride using piperidine instead of morpholine. After three recrystallizations from isopropyl alcohol, the material was obtained in a 29.9% yield, based on 2,3-epithiopropyl phenyl ether. It melted at 134-136°C. Elemental analysis for $C_{16}H_{23}NO_2S{\cdot}HCl$. Calculated: C, 58.42; H, 7.35; N, 4.28; S, 9.75; Cl, 10.47. Found: C, 58.21; H, 7.40; N, 4.11; S, 9.52; Cl, 10.38.

Attempted preparation of S-[(2-Allyloxy-1-Diethylaminomethyl)ethyl]Thioacetate



This compound was prepared in a manner described under synthesis of S-(1-allyloxymethyl-2-morpholinoethyl)thioacetate, using diethylamine, allyl 2,3-epithiopropyl ether and acetyl chloride as the starting materials. The product was purified by distillation under reduced pressure through a 7" x 1/2" column packed with a glass spiral. The main portion distilled between 101-101.5°C. (2 mm.); n_D^{25} 1.4753. A yield of 62.1% was obtained. Titration with 0.1-N HCl indicated an amine equivalent weight of 242.7. Calculated 245.4. Elemental analysis for $C_{12}H_{23}NO_2S$. Calculated: C, 58.74; H, 9.45; N, 5.71; S, 13.07. Found: C, 57.76; H, 9.01; N, 5.29; S, 12.34. Apparently some slight decomposition took place either during or after the distillation.

Infrared Spectra

The infrared spectra of all the mono- and diepisulfides synthesized and the mono- and diepoxides from which they were prepared were determined.

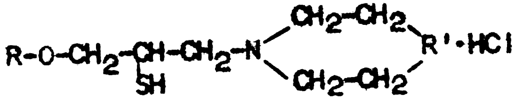
A Perkin-Elmer Infrared Spectrophotometer was used. A nujol mull between salt plates was prepared when the sample was a crystalline compound. A film between salt plates was used when the sample was a liquid. An additional spectrum (number 15) showing the absorbtion of nujol alone is included for use of comparison of epoxides and episulfides where one is a liquid and the other crystalline.

TABLE 1: PROPERTIES AND ANALYSIS[a] OF MONOEPISULFIDES AND DIEPISULFIDES

Compound	Formula	M.P.	B.P.	Mm.	n_D^{25}	Carbon, %		Hydrogen, %		Sulfur, %	
						Calcd.	Found	Calcd.	Found	Calcd.	Found
Allyl 2,3-epithiopropyl ether	$C_6H_{10}OS$	-----	46-48	4	1.4913	55.35	55.53	7.74	7.82	24.62	24.58
p-tert Butylphenyl 2,3-epithiopropyl ether	$C_{13}H_{18}OS$	-----	119	25	1.5443	69.68	70.22	7.94	8.16	14.22	14.42
m-Bis(2,3-epithiopropoxy)benzene	$C_{12}H_{14}O_2S_2$	111.5-113.5[b]	---	--	--	56.66	56.48	5.55	5.42	25.21	25.07
p-Bis(2,3-epithiopropoxy)benzene	$C_{12}H_{14}O_2S_2$	134.5-136.5[b]	---	--	--	56.66	56.65	5.55	5.80	25.21	25.12
2,2-Bis[p-(2,3-epithiopropoxy)phenyl]propane	$C_{21}H_{24}O_2S_2$	93-95[b]	---	--	--	67.71	67.70	6.49	6.45	17.21	17.38
1-Methyl-1,2-epithio-4-isopropenylcyclohexane	$C_{10}H_{16}S$	-----	63-65	3	1.5152	71.36	71.36	9.58	9.39	19.05	19.06

[a] Microanalysis by Microtech Labs., Skoky, Illinois. [b] Recrystallized from ethanol.

TABLE II: PROPERTIES AND ANALYSIS[a] OF AMINE THIOL HYDROCHLORIDES



R	R'	Formula	M.P.	Carbon, %		Hydrogen, %		Sulfur, %		Nitrogen, %		Chlorine, %	
				Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
C_6H_5	CH_2	$C_{14}H_{21}NOS \cdot HCl$	122.5-124.5[b]	58.41	58.56	7.70	7.51	11.14	11.34	4.86	4.79	12.32	12.62
C_6H_5	0	$C_{13}H_{19}NO_2S \cdot HCl$	166-168[c]	53.87	53.91	6.96	6.89	11.06	11.04	4.83	4.72	12.23	12.26
$CH_2{=}CH{-}CH_2$	0	$C_{10}H_{19}NO_2S \cdot HCl$	79.8-81.8[d]	47.31	47.04	7.94	7.90	12.63	12.48	5.54	5.22	13.97	13.68

TABLE II A: PROPERTIES AND ANALYSIS[a] OF 1-DIETHYLAMINO-3-PHENOXY-2-PROPANETHIOL

Formula	n_D^{25}	Carbon, %		Hydrogen, %		Sulfur, %		Nitrogen, %	
		Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
$C_{13}H_{21}NOS$	1.5280	65.20	65.17	8.84	8.71	13.39	13.26	5.88	5.56

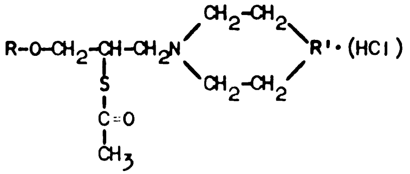
[a] Microanalysis by Microtech. Labs., Skokie, Illinois.

[b] Recrystallized from isopropyl alcohol.

[c] Recrystallized from isopropyl alcohol-methanol mixture.

[d] Recrystallized from isopropyl alcohol-ether mixture.

TABLE III: PROPERTIES AND ANALYSIS[a] OF AMINE THIOACETATES AND AMINE THIOACETATE HYDROCHLORIDES



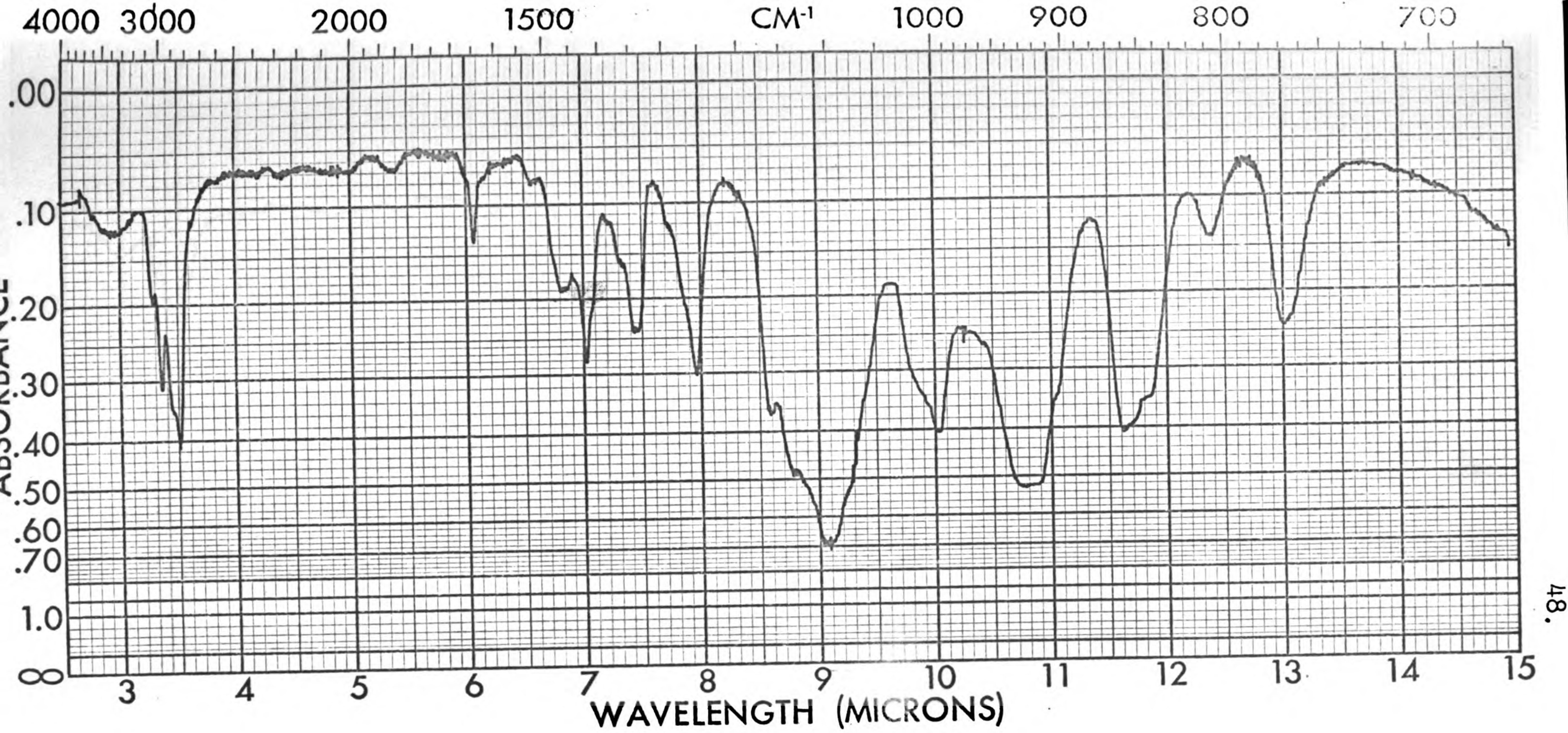
R	R'	Formula	M.P.	B.P.	Mm.	n_D^{25}	Carbon, %		Hydrogen, %		Sulfur, %		Nitrogen, %		Chlorine, %	
							Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found	Calcd.	Found
$CH_2=CH-CH_2$	O	$C_{12}H_{21}NO_3S$	---	136-137	2	1.4967	55.55	55.63	8.16	8.24	12.36	12.36	5.43	5.14	---	---
$CH_2=CH-CH_2$	O	$C_{12}H_{21}NO_3S \cdot HCl$	142.5-144.5[b]	---	--	---	48.71	48.94	7.49	7.52	10.84	10.56	4.76	4.65	11.98	11.90
$CH_2=CH-CH_2$	CH_2	$C_{13}H_{23}NO_2S$	---	125-127	2	1.4932	60.64	60.77	9.00	8.98	12.45	12.62	5.47	5.54	---	---
$CH_2=CH-CH_2$	CH_2	$C_{13}H_{23}NO_2S \cdot HCl$	90-92[c]	---	--	---	53.12	53.04	8.23	8.08	10.91	10.80	4.79	4.66	12.06	12.13
C_6H_5	O	$C_{15}H_{21}NO_3S \cdot HCl$	183-185[d]	---	--	---	54.27	54.91	6.68	6.74	9.66	9.76	4.24	3.89	10.68	10.87
C_6H_5	CH_2	$C_{16}H_{23}NO_2S \cdot HCl$	134-136[b]	---	--	---	58.42	58.21	7.35	7.40	9.75	9.52	4.28	4.11	10.47	10.38

[a] Microanalysis by Microtech. Labs., Skoky, Illinois.

[b] Recrystallized from isopropyl alcohol.

[c] Recrystallized from ether-isopropyl alcohol mixture.

[d] Recrystallized from methanol-isopropyl alcohol mixture.



SAMPLE:
Allyl glycidyl ether

PHASE: Film

SAMPLE PREPARATION:

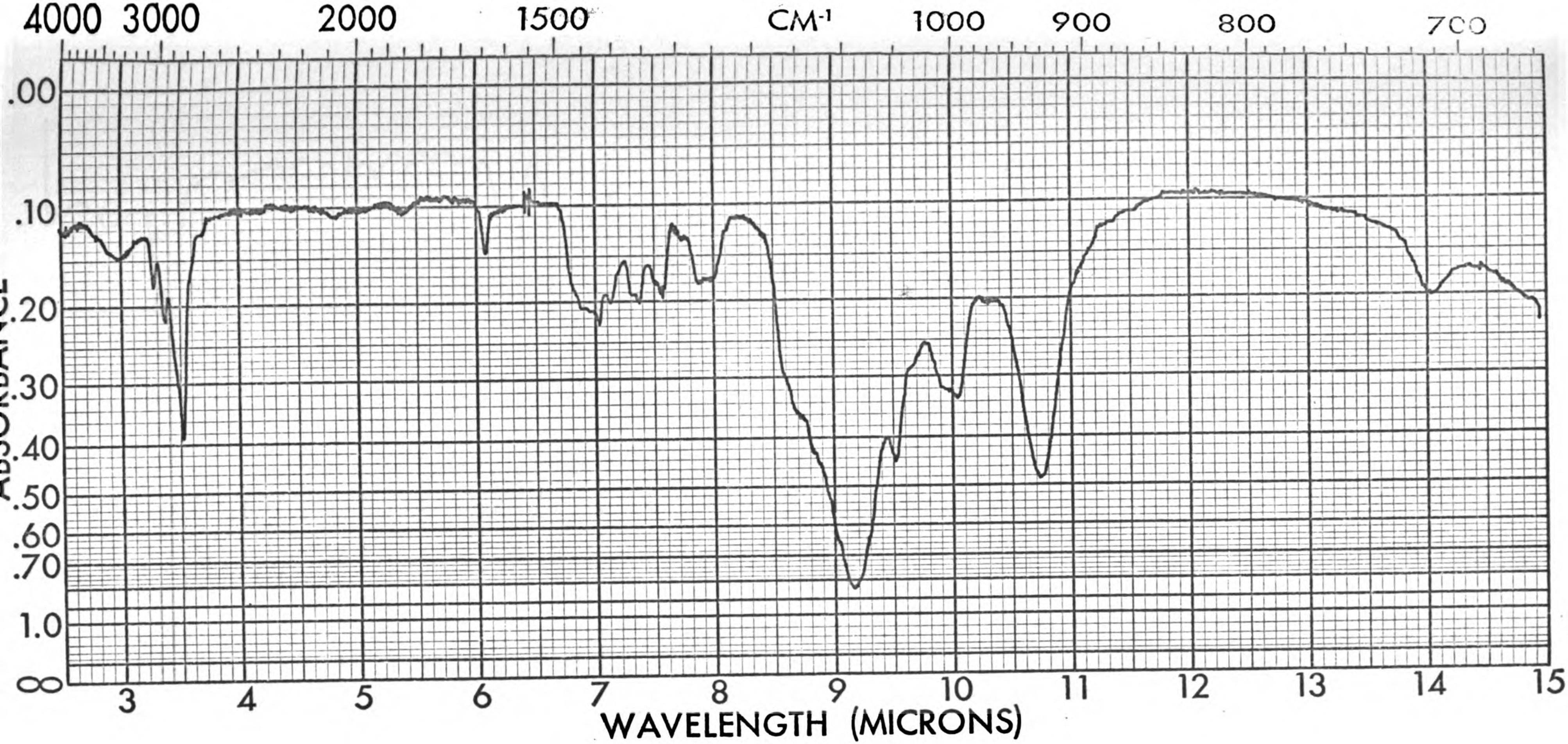
SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 1

SPL. REF.

DATE 7-22-61

OPER. B. J. Bremmer



SAMPLE: Allyl 2,3-epithiopropyl ether	PHASE: Film SAMPLE PREPARATION:	SOLVENT			SPECTRUM # 2
		CELL			SPL. REF.
		WEIGHT			DATE 7-22-61
		VOLUME			OPER. B. J. Bremmer
		CONC.			

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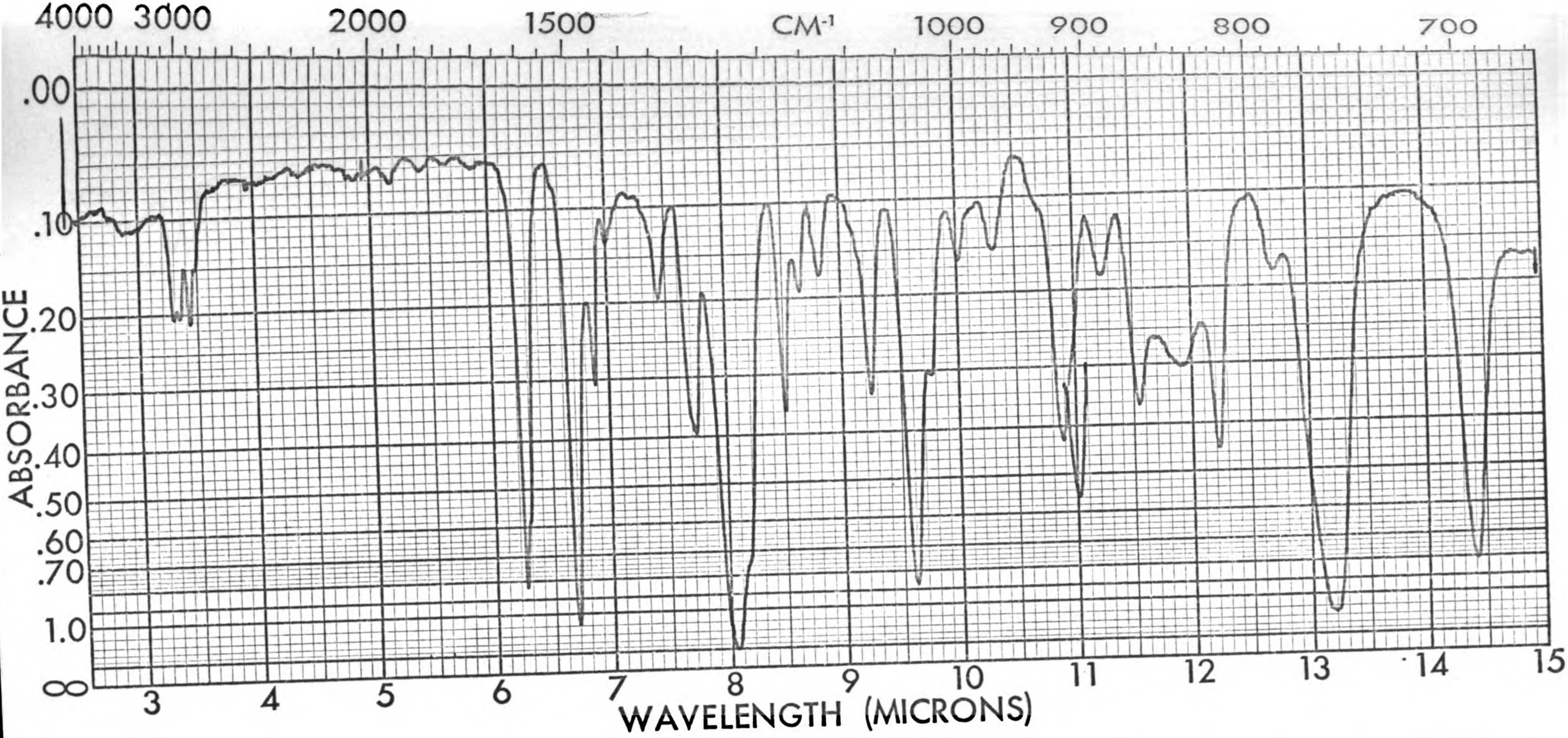
CHART NO. 34776



SAMPLE:

Phenyl glycidyl ether

PHASE: Film

SAMPLE PREPARATION:

SOLVENT

CELL

WEIGHT

VOLUME

CONC.

SPECTRUM # 3

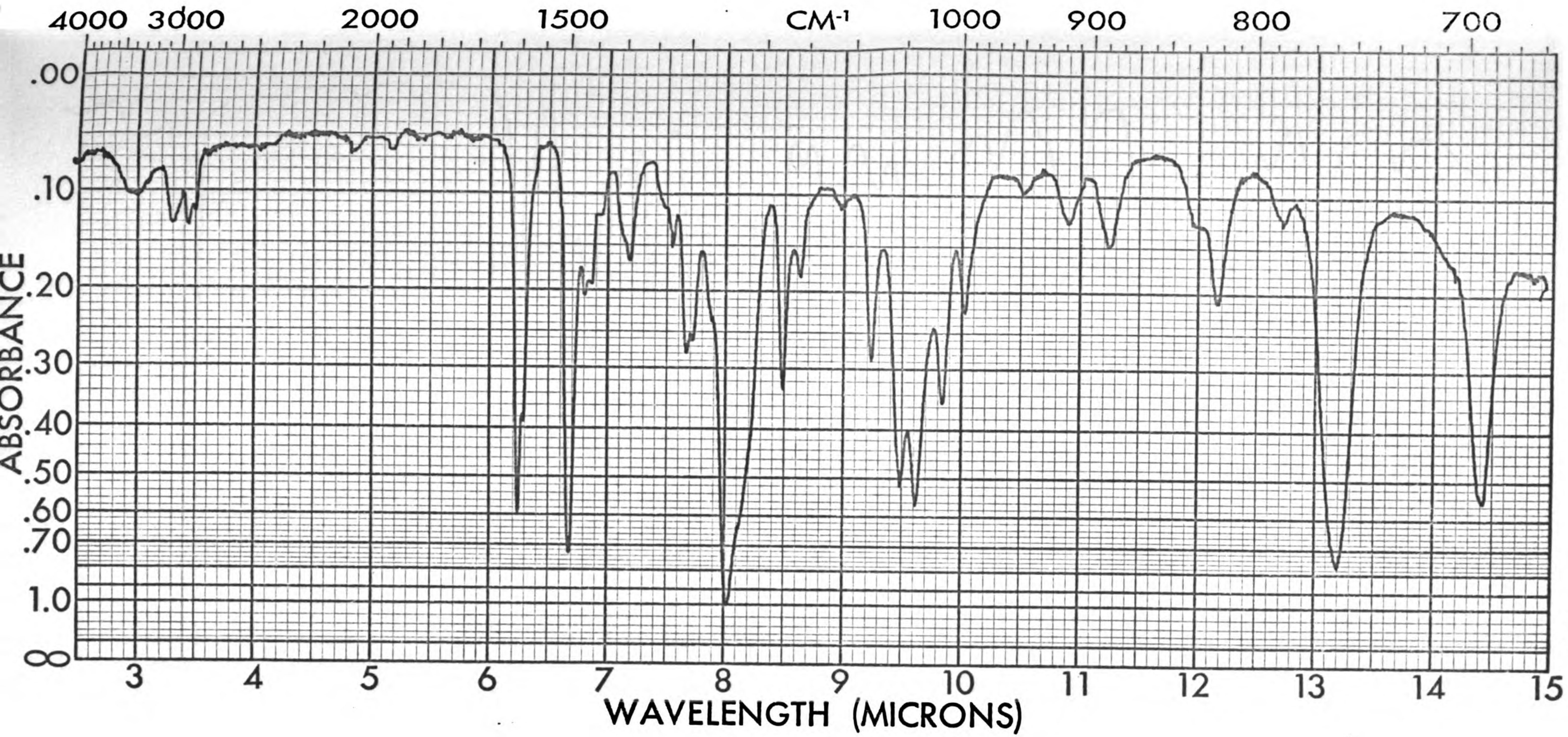
SPL. REF.

DATE 10-1-60

OPER. B. J. Bremmer

CHART NO. 34776

DOW CHEMICAL COMPANY SPECTROSCOPY LABORATORY MIDLAND, MICHIGAN



SAMPLE:

2,3-Epithiopropyl
phenyl ether

PHASE: Film

SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 4

SPL. REF.

DATE 7-22-61

OPER. B. J. Bremmer

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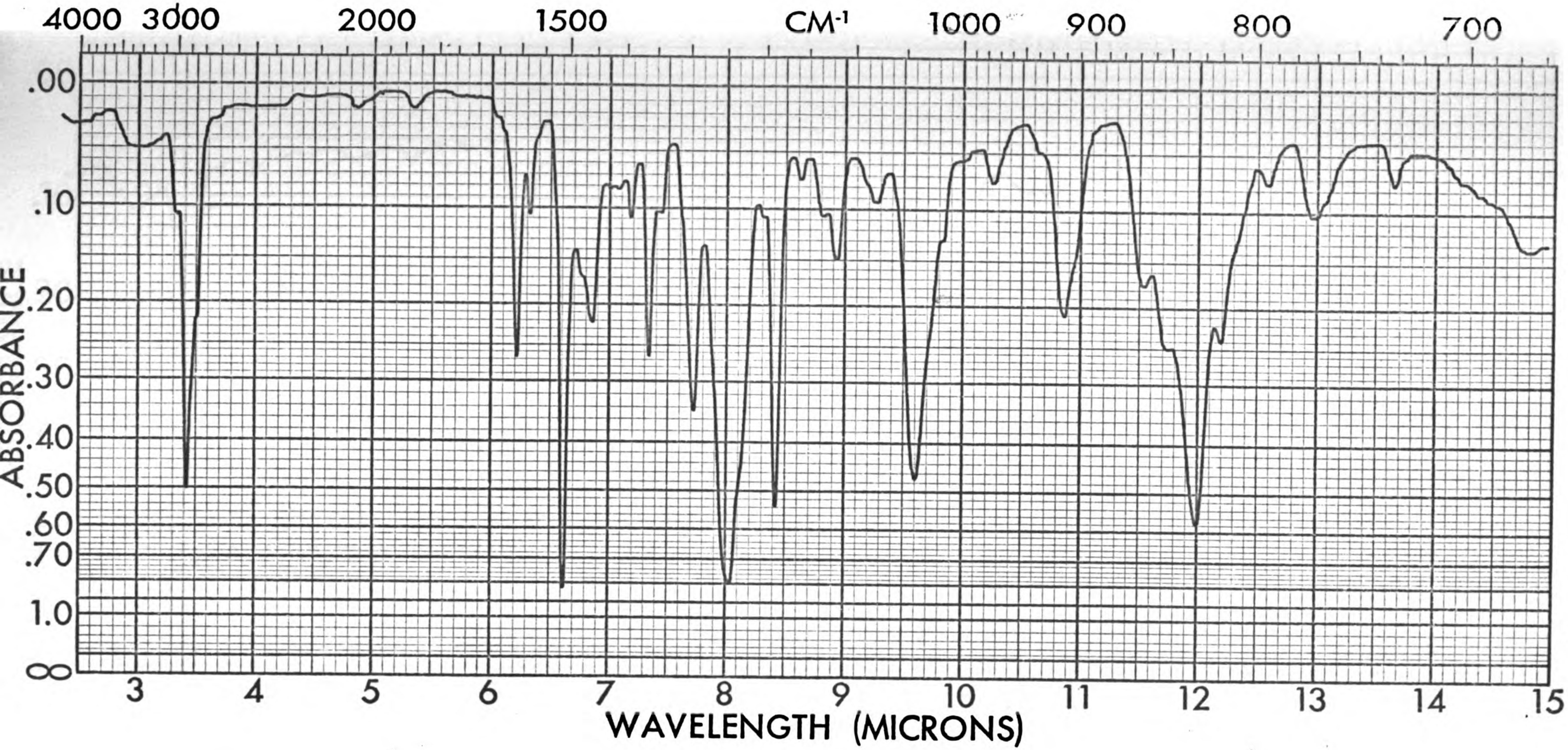

SAMPLE:

p-tert Butylphenyl
glycidyl ether

PHASE: Film

SAMPLE PREPARATION:

SOLVENT

CELL

WEIGHT

VOLUME

CONC.

SPECTRUM # 5

SPL. REF.

DATE 7-18-61

OPER. B. J. Bremmer

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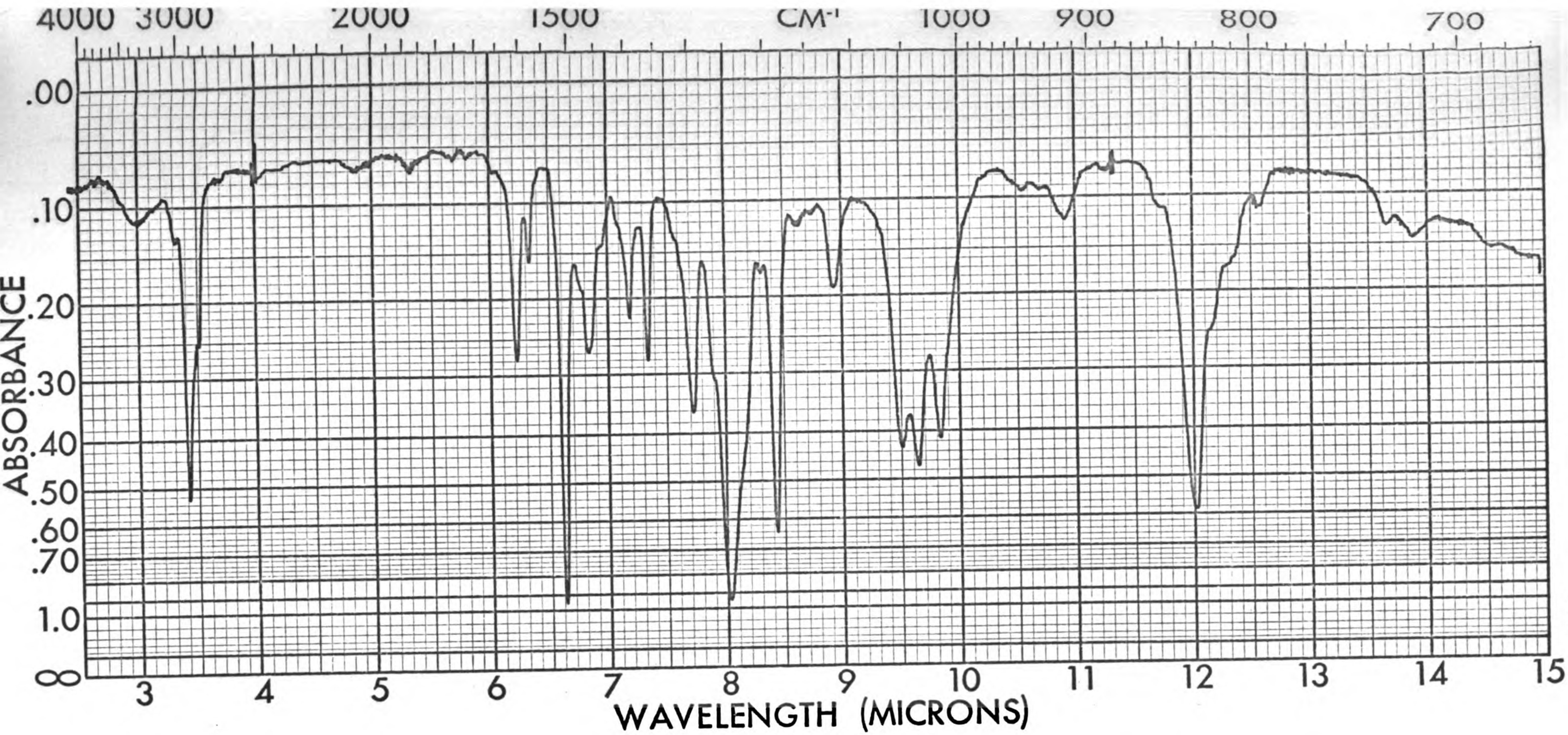
CHART NO. 34776



SAMPLE:

p-tert Butylphenyl
2,3-epithiopropyl ether

PHASE: Film

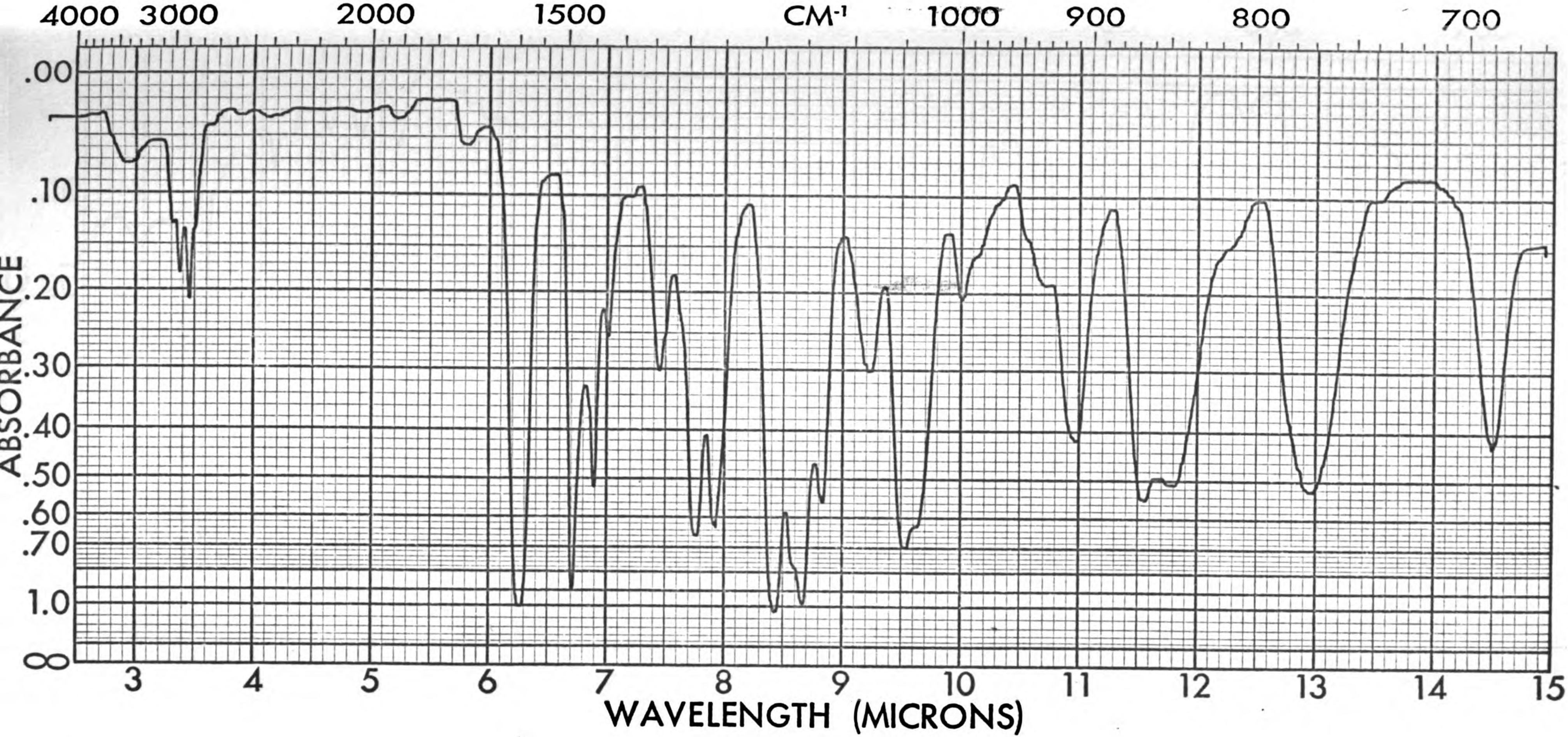
SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 6
SPL. REF.
DATE 7-22-61
OPER. B. J. Bremmer

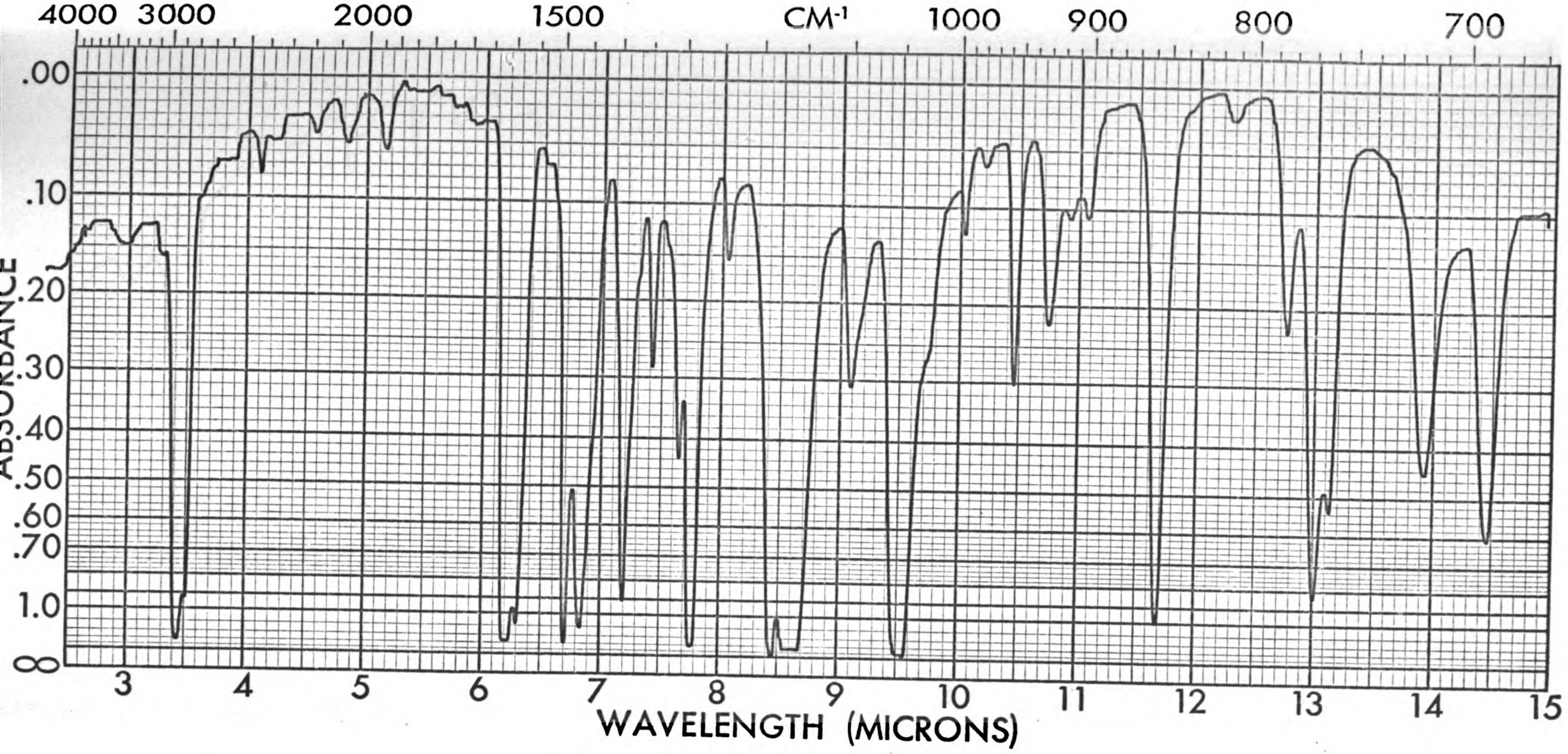
DOW CHEMICAL COMPANY   SPECTROSCOPY LABORATORY   MIDLAND, MICHIGAN

CHART NO. 34776



SAMPLE: Resorcinol diglycidyl ether	**PHASE:** Film **SAMPLE PREPARATION:**	**SOLVENT**			**SPECTRUM #** 7 **SPL. REF.** **DATE** 7-18-61 **OPER.** B. J. Bremmer
		CELL			
		WEIGHT			
		VOLUME			
		CONC.			

DOW CHEMICAL COMPANY SPECTROSCOPY LABORATORY MIDLAND, MICHIGAN CHART NO. 34776



SAMPLE: m-Bis(2,3-epithiopropoxy)benzene	**PHASE:** Nujol mull **SAMPLE PREPARATION:**	**SOLVENT**			**SPECTRUM #** 8 **SPL. REF.** **DATE** 7-18-61 **OPER.** B. J. Bremmer
		CELL			
		WEIGHT			
		VOLUME			
		CONC.			

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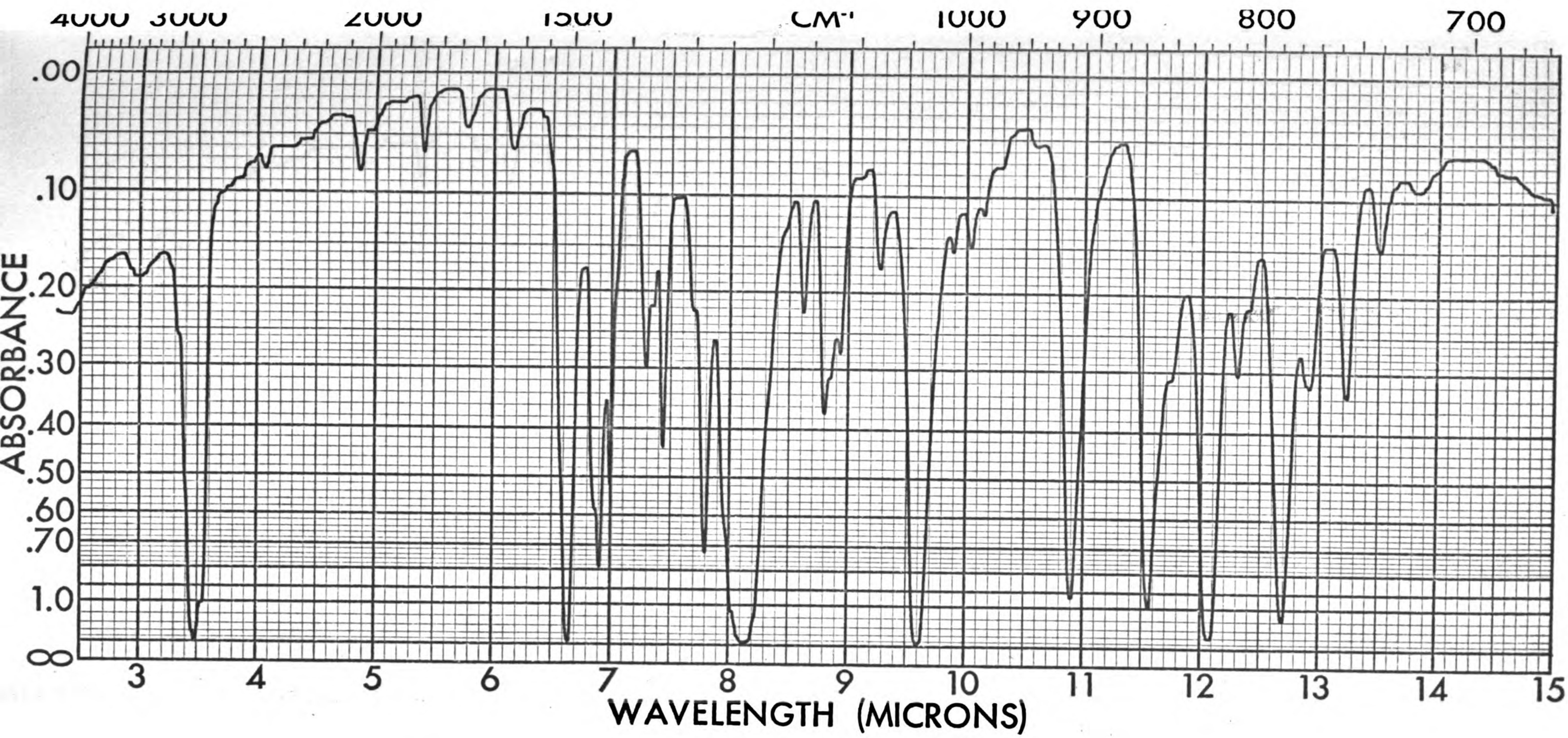
CHART NO. 34776



SAMPLE:
Hydroquinone diglycidyl ether

PHASE: Nujol mull

SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 9
SPL. REF.
DATE 7-18-61
OPER. B. J. Bremmer

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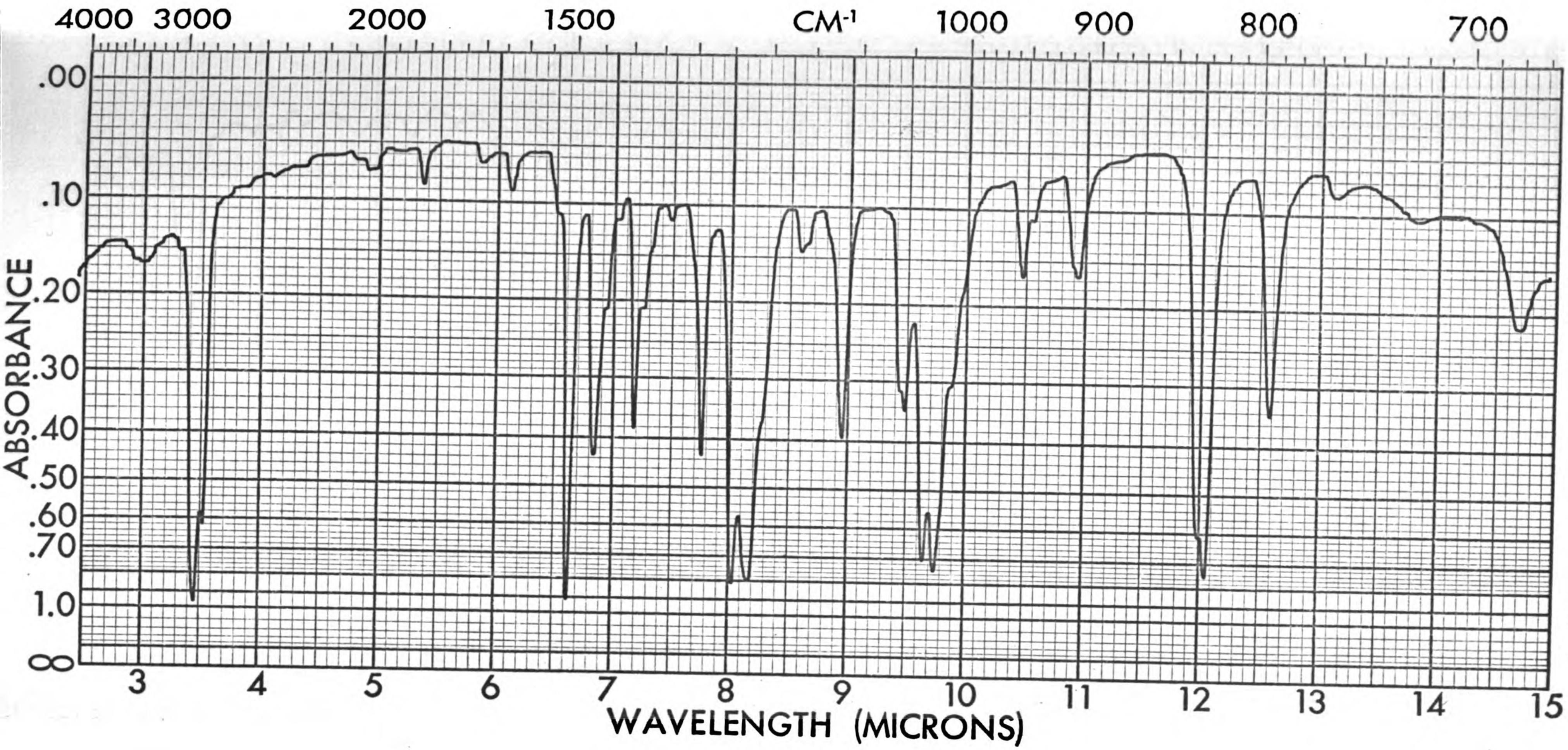
CHART NO. 34776



SAMPLE:

p-Bis(2,3-epithio-
propoxy)benzene

PHASE: Nujol mull

SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 10

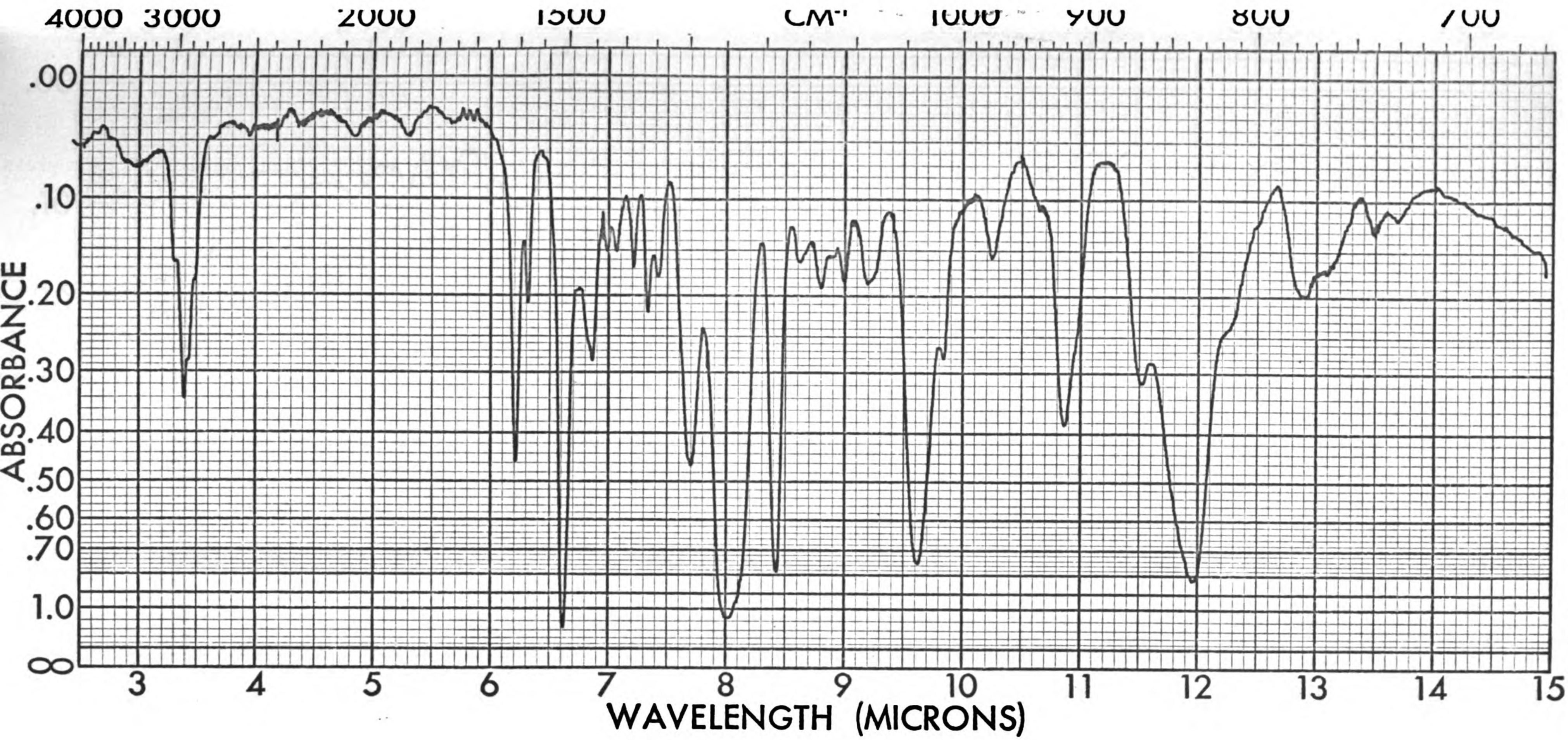
SPL. REF.

DATE 7-18-61

OPER. B. J. Bremmer

DOW CHEMICAL COMPANY SPECTROSCOPY LABORATORY MIDLAND, MICHIGAN

CHART NO. 34776



SAMPLE:

Bisphenol A diglycidyl ether

PHASE: Film

SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

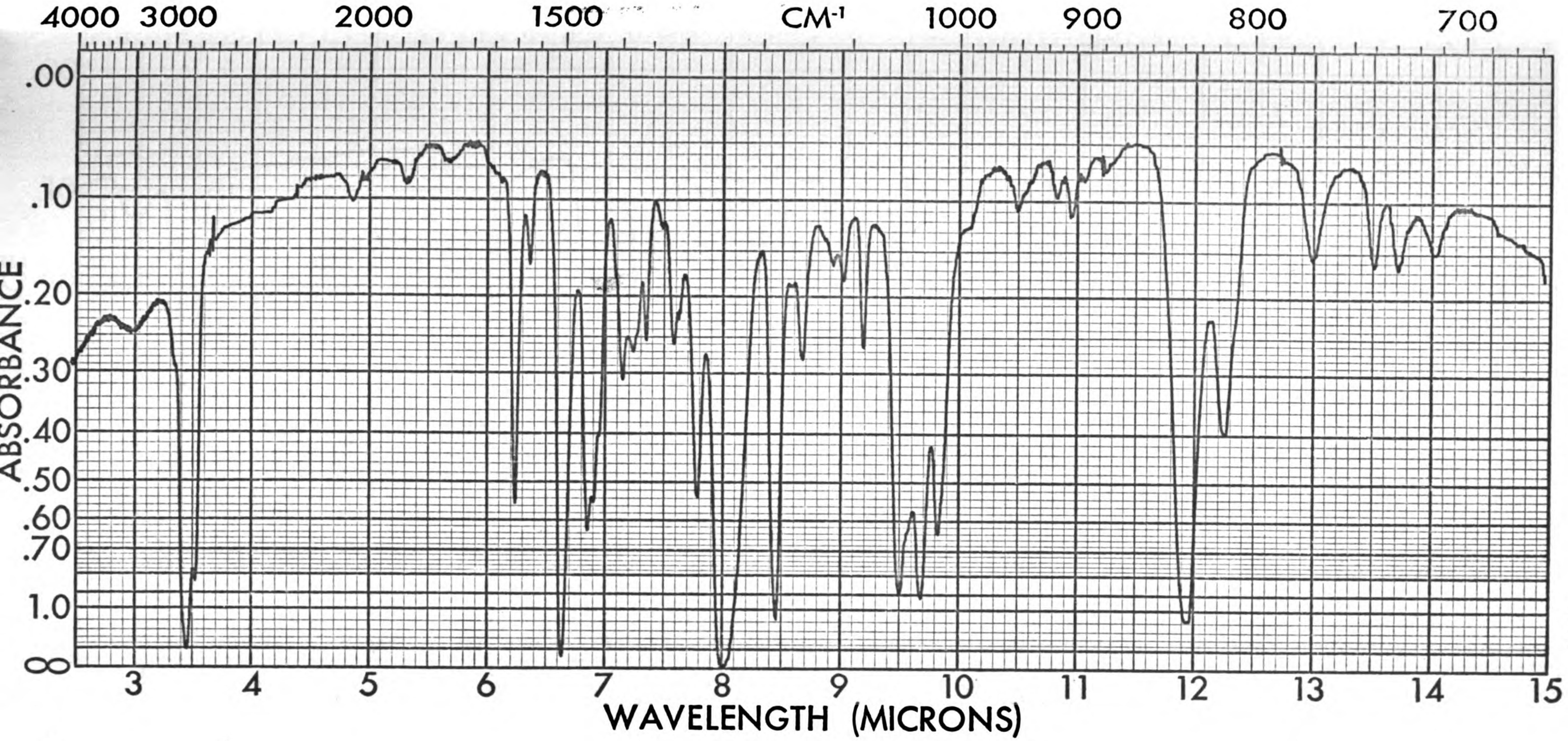
SPECTRUM # 11

SPL. REF.

DATE 7-22-61

OPER. B. J. Bremmer

DOW CHEMICAL COMPANY SPECTROSCOPY LABOR/TORY MIDLAND, MICHIGAN CHART NO. 34776



SAMPLE: 2,2-Bis⎡p-(2,3-epithiopropoxy)phenyl⎤propane

PHASE: Nujol mull

SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 12

SPL. REF.

DATE 7-22-61

OPER. B. J. Bremmer

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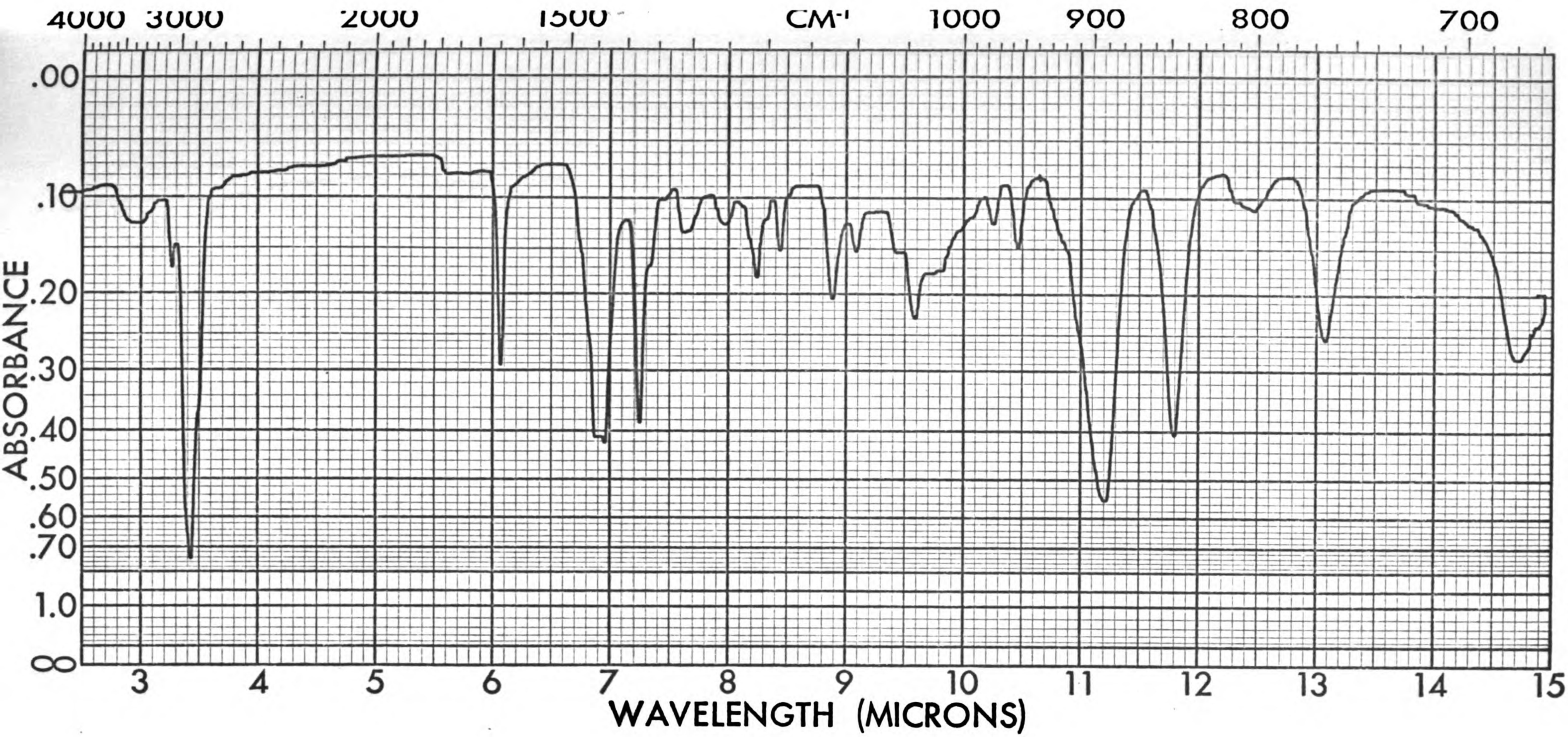


SAMPLE:
Limonene monoxide

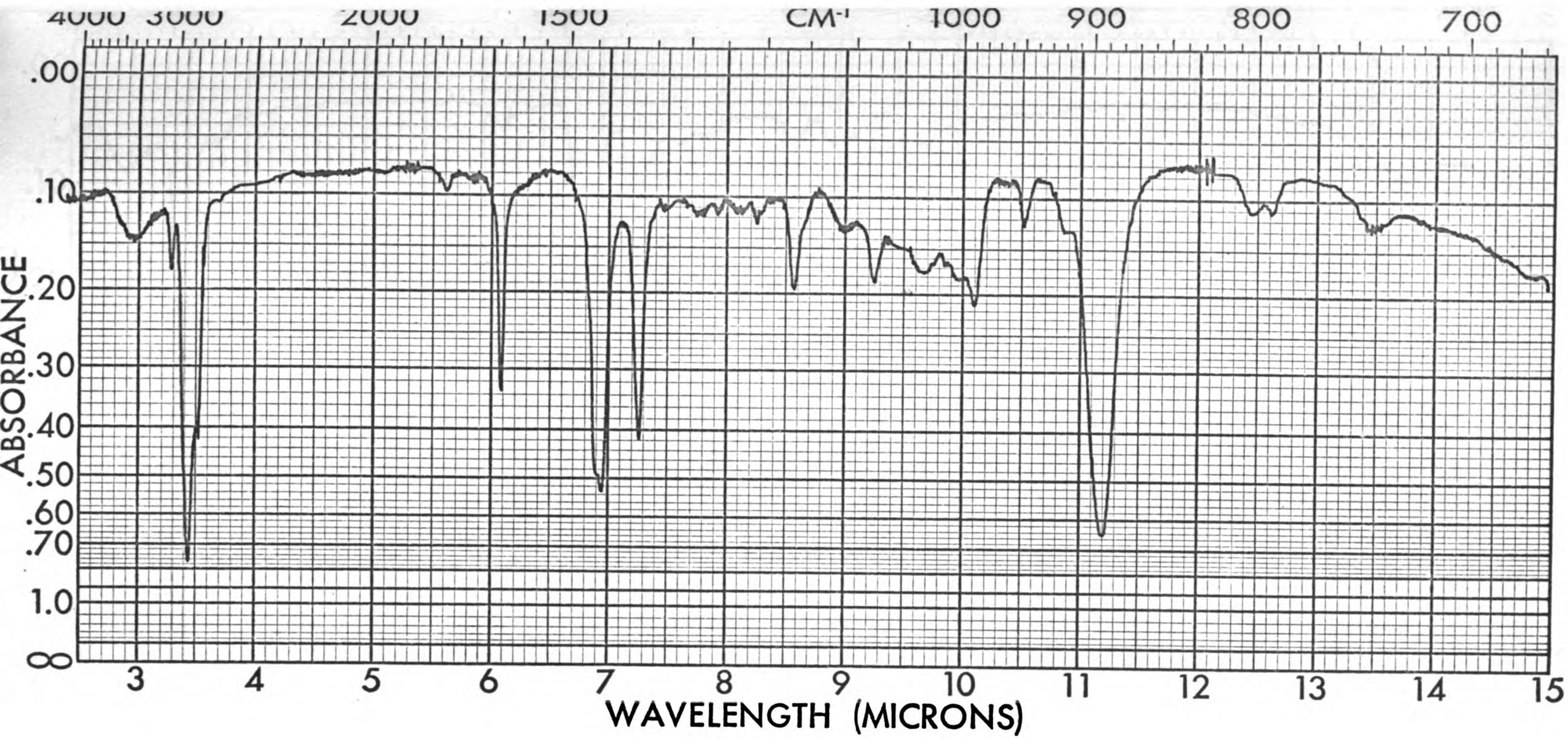
PHASE: Film

SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 13
SPL. REF.
DATE 7-18-61
OPER. B. J. Bremmer

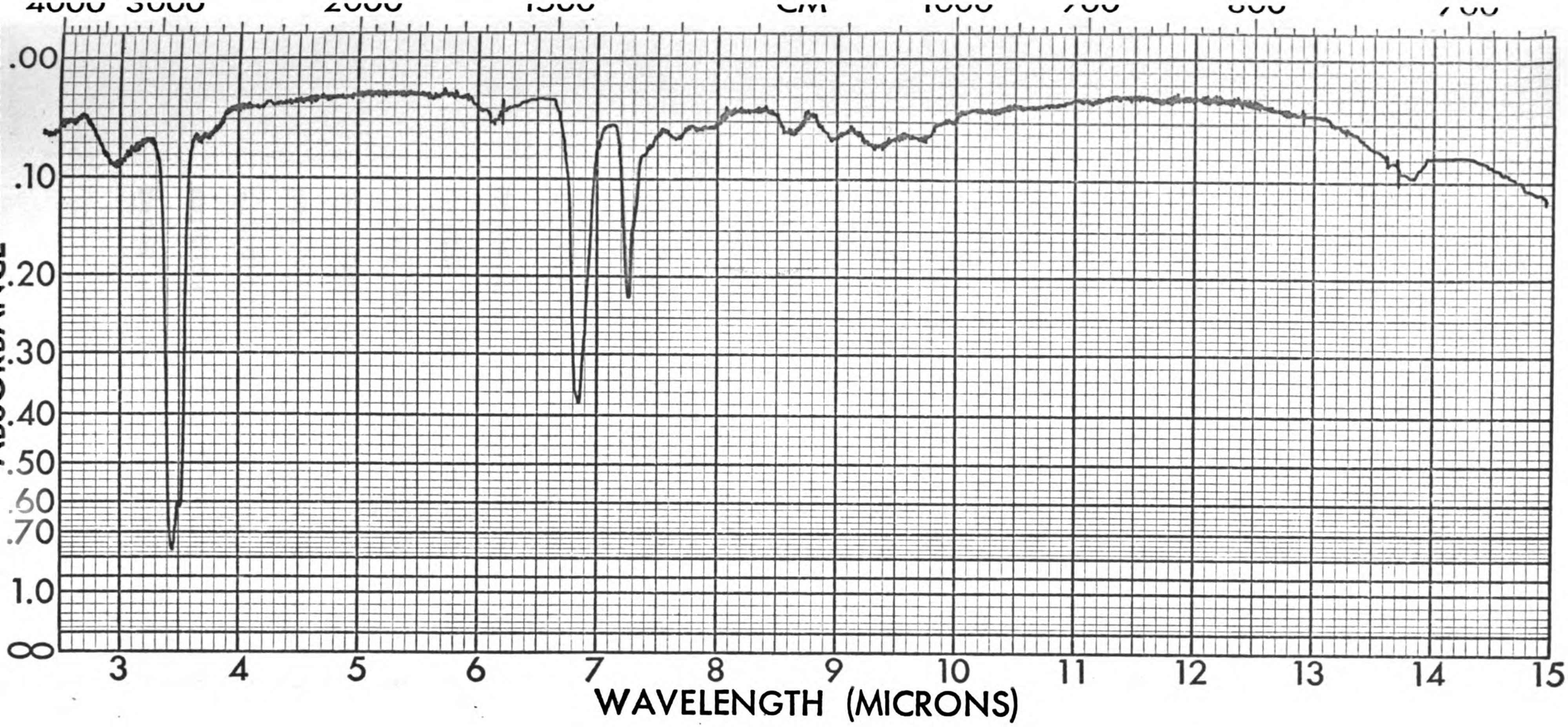
DOW CHEMICAL COMPANY SPECTROSCOPY LABORATORY MIDLAND, MICHIGAN CHART NO. 34776



SAMPLE: 1-Methyl-1,2-epithio-4-isopropenylcyclohexane	**PHASE:** Film **SAMPLE PREPARATION:**	**SOLVENT**		**SPECTRUM #** 14
		CELL		**SPL. REF.**
		WEIGHT		**DATE** 7-22-61
		VOLUME		**OPER.** B. J. Bremmer
		CONC.		

DOW CHEMICAL COMPANY SPECTROSCOPY LABORATORY MIDLAND, MICHIGAN

CHART NO. 34776



SAMPLE: Nujol

PHASE: Film

SAMPLE PREPARATION:

SOLVENT		
CELL		
WEIGHT		
VOLUME		
CONC.		

SPECTRUM # 15

SPL. REF.

DATE 7-23-61

OPER. B. J. Bremmer

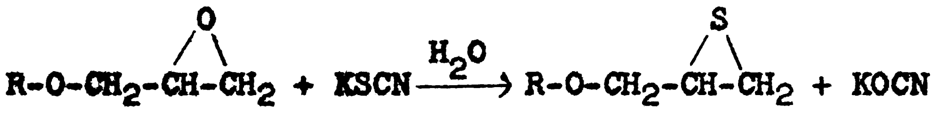
DOW CHEMICAL COMPANY SPECTROSCOPY LABORATORY MIDLAND, MICHIGAN

CHART NO. 34776

DISCUSSION

Thiiranes and Dithiiranes

The synthesis of episulfides from their corresponding epoxides by their reaction with aqueous potassium thiocyanate at room temperature or lower, as initially reported by Dachlauer and Jackel (37) and later extended by Snyder, Stewart and Ziegler (1), is quite successful for simple molecules. Schuetz and Jacobs (62) experienced no experimental difficulties in obtaining a series of thiiranes derived from simple glycidyl ethers and aqueous potassium thiocyanate,



$R = CH_3, C_2H_5, i\text{-}C_3H_7, n\text{-}C_3H_7, n\text{-}C_4H_9, \text{ and } C_6H_5$

In the present work dealing with more complex molecules, and especially with the higher molecular weight diepoxides as the starting material, it was found that little reaction, if any, took place under the same conditions. This is probably due to the low solubility of the epoxide in the aqueous potassium thiocyanate solution at room temperature. Jacobs' synthesis of 2,3-epithiopropyl phenyl ether in which water was used as the only solvent could not be

duplicated. An attempt to conduct this reaction at higher temperatures (40-50°C.) resulted in a very low percent conversion to the thiirane. Dioxane was reported (51) to be a suitable solvent to use with water in the synthesis of styrene sulfide. The reaction temperature used in this case was 60°C. Attempts to make the dithiiranes from resorcinol diglycidyl ether, and the diglycidyl ether of bisphenol A, using a 50% aqueous dioxane solution of potassium thiocyanate at room temperature resulted in very low conversion to the corresponding thiiranes. When higher reaction temperatures were applied (60°C.), polymerization and/or decomposition of the presumably formed dithiiranes took place. The use of an aqueous ethanol solution in the preparation of cyclohexene sulfide has been reported by E. E. Van Tamelen (52) who carried out the reaction at room temperature for an extended period of time. When this solvent combination was used, the preparation of 2,3-epithiopropyl phenyl ether was accomplished without difficulties. On the other hand, allyl 2,3-epithiopropyl ether was obtained in good yield using only water as the solvent. Apparently, the solubility or miscibility of its corresponding epoxide in aqueous potassium thiocyanate was sufficient to make the reaction proceed at a reasonable rate.

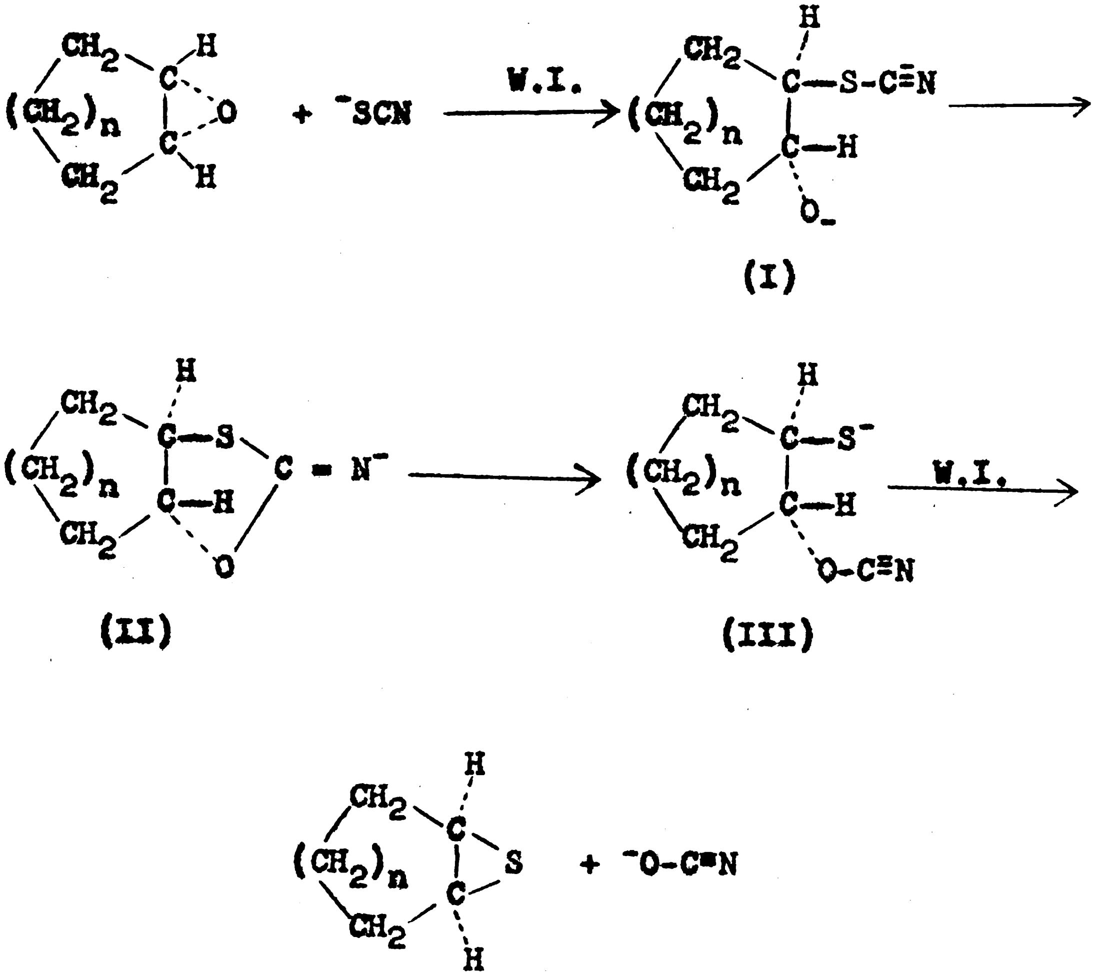
In the preparation of p-tert butylphenyl glycidyl ether, the solubility of the starting epoxide in a water-ethanol mixture was not sufficient to obtain the proper conditions for reaction to occur at a measurable rate. Therefore, a volume of acetone equal to the volume of water used was added with the ethanol. Under these conditions the reaction took place, but the yield was low. Better yields would be expected when acetone and some water are used as the solvent system, and the reaction is conducted at slightly elevated temperatures. Since p-tert butylphenyl 2,3-epithiopropyl ether can be prepared and distilled, the lower alkylphenyl 2,3-epithiopropyl ethers could become available as well.

The first dithiirane obtained in this study was made from resorcinol diglycidyl ether. In some preliminary work, attempts had been made to isolate some of the m-bis(2,3-epithiopropoxy)benzene by distillation from the partially polymerized product. The latter material was obtained from the reaction, at elevated temperatures, of the corresponding epoxide, with potassium thiocyanate in dioxane and water as the solvent mixture. In no case was this distillation successful. Fortunately, this dithiirane, as well as several others, turned out to be crystalline solids which could be purified by recrystallization from ethanol without much trouble. In the preparation of m-bis(2,3-epithiopropoxy)benzene, an ethanol-water mixture was used as the solvent mixture with a rather

large excess of potassium thiocyanate. This procedure was employed as it was intended to add a second portion of the resorcinol diglycidyl ether after the reaction had been allowed to stand overnight. However, such a large quantity of a white precipitate was formed in the initially clear reaction mixture that it was thought advisable to recover the dithiirane formed, rather than add additional quantities of the diepoxide. However, it is probable that the large excess of potassium thiocyanate contributes to a higher conversion of the epoxide to the thiirane. Further, the extraction of the product with benzene could be eliminated. The crystalline product could be recovered by filtration, washed with water, dried and recrystallized from ethanol. This procedure was later followed in the synthesis of 2,2-bis[p-(2,3-epithiopropoxy) phenyl]propane.

The solubility of hydroquinone diglycidyl ether in an ethanol-water mixture was found to be very low. Acetone appeared to be a better solvent, but at room temperature the diepoxide crystallized rather readily from an acetone-water mixture. The reaction was therefore run at an elevated temperature for a short period of time. The product obtained melted at 134.5-136.5°C. This, however, was only one isomer out of the possible two that could be formed. The Dutch chemists, Werner

and Farenhorst (3,53), reported that two isomers are formed in the reaction of excess epichlorohydrin and hydroquinone. Hydroquinone diglycidyl ether has two asymmetric carbon atoms and occurs in two diastereoisomeric forms, a racemate and a meso form. Werner and Farenhorst (3,53) were able to separate the diastereoisomers, which were present in approximately equal quantities, by fractional crystallization. The lower melting isomer (m.p. 89.5-90.5°C.) dissolved much more readily in various solvents than the higher melting one (m.p. 118-119°C.). By analogy, it would be expected that p-bis(2,3-epithiopropoxy)benzene would also exist in two isomeric forms. Since the starting material, in this work, was a mixture of the isomers of hydroquinone diglycidyl ether, a mixture of the isomers of the corresponding dithiirane was obtained, together with some of the unreacted and half reacted diepoxide (both isomers). This made the separation of all the product isomers extremely difficult. The only product that could be isolated must therefore be the high melting isomer of p-bis(2,3-epithiopropoxy)benzene (m.p. 134.5-136.5°C.). It would be of interest to repeat this dithiirane synthesis with both the low melting and high melting hydroquinone diglycidyl ether as individual starting material. It would be expected that the low melting diepoxide would give the low melting dithiirane and the high melting hydroquinone diglycidyl ether, the high melting p-bis(2,3-epithiopropoxy)benzene. This result is predictable because of the stereospecific nature of the reaction. Van Tamelen (54) has presented evidence supporting a mechanism for such a stereospecific reaction illustrated in the alicyclic series.



(I)

(II)

(III)

The mechanism implies two Walden inversions. The ring opening of cyclohexene oxide (n = 2) has been shown to proceed, in all cases studied, with exclusive Walden inversion in acid, neutral or basic media. Thus, the ring opening of this oxide leads to the anion of trans-2-hydroxycyclohexyl thiocyanate. Migration of the cyano group from sulfur to oxygen via the cyclic intermediate (II), which Price and Kirk (55) later proved was present by isolating its N-(p-nitrobenzoyl) derivative, results in the formation of the anion of trans-2-mercaptocyclohexyl cyanate, which is favorably oriented for a trans ring-closure to yield the cyclic sulfide and cyanate ion.

Furthermore, Price and Kirk (55) observed that the reaction of potassium thiocyanate with D(+)-2,3-epoxybutane produced the L(-)-2,3-epithiobutane, substantiating the mechanism proposed.

Because of the stereospecificity in the reaction of epoxides with thiocyanate ions, the meso form of hydroquinone diglycidyl ether would become a meso form in the p-bis(2,3-epithiopropoxy)benzene and the racemate of the diglycidyl ether would become a racemic mixture. Werner and Farenhorst (3,53) were unable to completely separate the isomers of resorcinol diglycidyl ether nor the isomers of the diglycidyl ether of bisphenol A. If complete conversion of these compounds to the

corresponding dithiiranes were accomplished, their complete isomer separation may be possible with the sulfur compounds.

Considerable difficulty was encountered in the preparation of 2,2-bis[p-(2,3-epithiopropoxy)phenyl] propane with sufficiently high purity to obtain a satisfactory elemental analysis. When the reaction was conducted at temperatures below 60°C. for an extended period of time (11 hours), a crystalline material was obtained melting below 92°C., which was low in sulfur content. Repeated recrystallizations from ethanol, methanol, tetrahydrofuran and benzene and mixtures of these failed to improve the purity of this material. It was not until the reaction was forced to very near completion that a pure compound could be obtained after a single recrystallization from ethanol.

Two attempts were made to prepare bis-(2,3-epithiopropyl)ether from the corresponding diglycidyl ether. The latter was synthesized in low yield following the method described by Dudley (7). In the initial synthetic attempt, the diglycidyl ether used as the starting material was somewhat high in hydrolyzable chlorine content (0.45%) and rather high in epoxy equivalent weight (70.7, theory is 65). Some gel formation occurred in the early stages of the

reaction conducted to synthesize the dithiirane. Attempted purification of the crude dithiirane under reduced pressure resulted in its polymerization. A second synthesis attempt with purer diglycidyl ether (0.23% hydrolyzable chlorine; epoxy equivalent weight 65.9) resulted in no gel formation during the reaction and the resulting dithiirane could be distilled. What was later observed in the preparation of other episulfides was again substantiated here, namely, that pure starting materials are necessary for the reaction to proceed smoothly. With starting materials of high purity, the reaction of diepoxides with potassium thiocyanate may be conducted for longer periods of time and at higher reaction temperatures without detrimental effects and increased yields. When diglycidyl ether of high purity is employed, the bis(2,3-epithiopropyl) ether can be obtained pure, since the last attempt to obtain this material came very close to synthesizing it in a pure form.

Considerable experimental work was conducted in an effort to synthesize two related thiiranes, 1-methyl-1,2-epithio-4-isopropenylcyclohexane (limonene monoepisulfide) and 2,6,6-trimethyl-2,3-epithiobicyclo/‾3.1.1_/heptane (α-pinene episulfide). The method of Snyder, Stewart and Ziegler (1) was tried using a variety of solvent combinations and in all

cases two layers formed in the reaction mixture. The conversion of the epoxide to its sulfur analog was low. With elevated reaction temperatures, the product polymerized readily, while part of the starting material was recovered.

The use of the method of Culvenor, Davies and Pausacker (9) resulted in only the recovery of starting material. The procedure of Bordwell and Anderson (10) yielded the 1-methyl-1,2-epithio-4-isopropenylcyclohexane in low yield. The same procedure, however, gave a polymeric material in the attempted preparation of 2,6,6-trimethyl-2,3-epithiobicyclo[3.1.1]heptane (α-pinene episulfide).

Infrared Spectra of Oxiranes and Thiiranes

While it was not the main objective of this investigation to assign all the frequencies of the infrared spectra of the thiiranes synthesized, it was thought to be of value to compare their infrared spectra with those of the corresponding epoxies. It was found that certain consistent differences exist in the infrared spectra of the two classes of compounds.

After studying the infrared spectra of twenty-six epoxy compounds, Patterson (56) proposed that the epoxy bands are present in the 11.0 and 12.0 micron region. The bands vary from 10.52 (950 cm.$^{-1}$) to

11.58 microns (863 cm.$^{-1}$) in the 11 micron region, and from 11.57 (864 cm.$^{-1}$) to 12.72 microns (786 cm.$^{-1}$) in the 12 micron region. Two compounds reported by Patterson were also used in this investigation, namely, allyl glycidyl ether and phenyl glycidyl ether, and the absorbtion spectra determined in this work are in good agreement with that previously reported. Absorbtion in what Patterson refers to as the 12 micron region were found in all the infrared spectra of the oxirane compounds examined in the present study. With several compounds, a double absorbtion was noticed in this general area. In all cases, these bands were absent in the corresponding thiirane compounds (Table IV) with the exception of an absorbtion at 11.69 microns (855 cm.$^{-1}$) in m-bis(2,3-epithiopropoxy)benzene which is due to a meta substituent on the aromatic nucleus. Although the double absorbtion in the epoxy compounds is not too distinct in all cases, it is highly probable that there are two bands due to the epoxy group in the 12 micron region, instead of a single one as initially reported by Patterson. It is quite apparent that these absorbtions disappear when the oxirane oxygen is replaced by a sulfur atom. (Table IV, first two columns).

In the 11 micron region, the epoxy compounds investigated had a band between 10.86 (921 cm.$^{-1}$) and

10.94 microns (914 cm.$^{-1}$), with the exception of limonene monoxide. The intensity of this absorbtion due to the epoxy ring diminished greatly or almost disappeared when going to the corresponding thiiranes. (Table IV, second two columns). Why the absorbtion does not disappear entirely in the sulfur compounds is not clear.

It was further observed that a weak absorbtion between 8.80 (1138 cm.$^{-1}$) and 8.88 microns (1128 cm.$^{-1}$) is present in all epoxy compounds reported here. This absorbtion is very weak in allyl glycidyl ether and p-tert butylphenyl glycidyl ether, but very well definite in the spectra of the other epoxy compound. This band has not been reported in the literature as an absorbtion due to the epoxy ring, at least not in compounds of some complexity. An absorbtion in this vicinity at 8.60 microns (1165 cm.$^{-1}$) has been reported, however, for ethylene oxide (58). The thiiranes obtained from the epoxides synthesized during the course of this study do not show absorbtion between 8.80 and 8.88 microns. (Table IV, fifth and sixth columns). The band at 8.60 microns present in ethylene oxide does not appear to be present in ethylene sulfide either (40).

A band characteristic of the epoxide ring at about 8 microns was reported by Patterson (56) and earlier by Field, Cole and Woodford (57). This

absorbtion was present in all the oxirane compounds examined in this work, although it was very weak in the case of limonene monoxide. The corresponding thiiranes all have absorbtions in the same region, although less intense in the case of allyl 2,3-epithiopropyl ether. In the cases of m- and p-bis(2,3-epithiopropoxy)benzene an additional absorbtion seems to be present at 8.05 microns (1241 cm.$^{-1}$) and 8.02 microns (1248 cm.$^{-1}$) which was not present in the corresponding epoxy compounds. The entire region around 8 microns is too complicated, however, to base any definitive conclusions on the limited data available.

A strong absorbtion at 13.2 microns, reported by Patterson (56) in epoxy ethers, was not present in the hydrocarbon ethers. He reported a similar band in the epoxy esters, in 1,4-pentadiene dioxide and one just detectable in butadiene monoxide. It also appears in epichlorohydrin, propene oxide and octene-1-oxide. Although the band is relatively much weaker than the bands in the 11 and 12 micron region, the possibility that this is due to the oxirane ring cannot be ignored according to Patterson. Such bands were found in the same region in some of the epoxy compounds studied. They are most pronounced in the allyl glycidyl ether at 13.01 microns (769 cm.$^{-1}$), p-tert butylphenyl glycidyl ether at 12.98 microns (771 cm.$^{-1}$), hydro-

quinone diglycidyl ether at 13.21 microns (757 $cm.^{-1}$) and limonene monoxide at 13.19 microns (758 $cm.^{-1}$). In all these cases, this absorbtion is not present in the sulfur analog, which supports the possibility that the absorbtion around 13 microns is caused by the oxirane group. Moreover, changes also occur in the 12 micron region in going from the epoxide to the corresponding thiirane in the case of resorcinol diglycidyl ether and the diglycidyl ether of bisphenol A. These changes are, however, of such nature that the interpretation is very difficult.

In a search for a band specific to the thiirane group, it was found than an absorbtion at about 9.5 microns (1054 $cm.^{-1}$) is very probably due to the thiirane group. This at least seems to be the case in the thiiranes derived from glycidyl ethers. In all these compounds, an absorbtion was observed at about 9.5 microns, which is not present in the epoxy compounds. The only apparent exception is the resorcinol diglycidyl ether sulfur analog. Here a strong absorbtion was found at 9.5 microns in both the oxirane and thiirane compounds. Table IV, the last two columns, summarizes these data in more detail.

Finally, some of the thiirane compounds have an absorbtion at about 10.4-10.5 microns which is not present in the epoxies. This band is especially strong in m-bis(2,3-epithiopropoxy)benzene, but was also quite easily observed in several of the other episulfides.

In summary, it can be said that the epoxy absorbtions in the 11 and 12 micron region as reported by Patterson (56) diminish greatly or disappear, respectively, when the oxirane is converted to the corresponding thiirane. The region at 8 microns is too complicated for interpretation at this time with the limited number of corresponding epoxy and sulfur analogs available for comparison. An absorbtion in the 13 micron region appears to be present in several oxirane compounds, which disappears when the corresponding thiirane is prepared from them. An absorbtion specific for the thiirane compounds, derived from glycidyl ethers, seems to be present at about 9.5 microns and another one, which is less pronounced and not as general in the 10.4-10.5 micron region.

TABLE IV: SOME INFRARED ABSORBTION BANDS OF OXIRANES AND THIIRANES

Compound	Absorbtion at about 11.5-12.0 microns		Absorbtion at about 10.85-10.95 microns		Absorbtion at about 8.8-8.9 microns		Absorbtion at about 9.49-9.51 microns	
	Wave length microns	Wave number $cm.^{-1}$	Wave length microns	Wave number $cm.^{-1}$	Wave length microns	Wave number $cm.^{-1}$	Wave length microns	Wave number $cm.^{-1}$
Allyl glycidyl ether	11.62 11.82[a]	860 846[a]	10.86[a]	921[a]	8.80	1138	No abs.	No abs.
Allyl 2,3-epithiopropyl ether	No abs.	No abs.	No abs.	No abs.	No abs.	No abs.	9.51	1050
Phenyl glycidyl ether	11.55 11.95[a]	965 837[a]	10.90[a]	917[a]	8.81	1135	No abs.	No abs.
2,3-Epithiopropyl phenyl ether	No abs.	No abs.	10.90[c]	917[c]	No abs.	No abs.	9.49	1059
p-tert Butylphenyl glycidyl ether	11.55 11.75	965 850	10.87	920	8.81	1135	No abs.	No abs.
p-tert Butylphenyl 2,3-epithiopropyl ether	No abs.	No abs.	10.90[c]	917[c]	No abs.	No abs.	9.50	1054
Resorcinol diglycidyl ether	11.55 11.80	965 848	10.98	912	8.83	1131	9.50	1054
m-Bis(2,3-epithiopropoxy)benzene	11.69[b]	855[b]	10.92[c]	916[c]	No abs.	No abs.	9.50	1054
Hydroquinone diglycidyl ether	11.56 11.75	964 850	10.90	917	8.80	1138	No abs.	No abs.
p-Bis(2,3-epithiopropoxy) benzene	No abs.	No abs.	10.92[c]	916[c]	No abs.	No abs.	9.50	1054
Bisphenol A diglycidyl ether	11.53	868	10.88	919	8.80	1138	No abs.	No abs.
2,2-Bis/_p-(2,3-epithiopropoxy)phenyl_/propane	No abs.	No abs.	10.94[c]	914[c]	No abs.	No abs.	9.50	1054
Limonene monoxide	11.80	848	No abs.	No abs.	8.88	1128	No abs.	No abs.
1-Methyl-1,2-epithio-4-isopropenylcyclohexane	No abs.	No abs.	No abs.	No abs.	No abs.	No abs.	No abs.	No abs.

[a] Reported by W. A. Patterson (56).

[b] Due to meta substitution on benzene ring.

[c] Intensity of absorbtion substantially less than in corresponding oxirane compound.

Aminothiols - Derivatives of Thiiranes

The reaction between thiiranes and secondary amines is rather straightforward as long as certain conditions are observed. These conditions have been reported by Jacobs and Schuetz (61) and earlier by Braz (44). A nonionizing solvent should be employed and a molar excess of the amine should be present during the reaction.

Difficulties encountered, however, were the decomposition of several of the aminothiols during purification by distillation, the hydroscopic character of many of their hydrochlorides, and the failure to obtain crystalline salts of many of the aminothiols.

In general, crystalline hydrochloride salts could be formed from the aminothiols based on piperidine and morpholine, although in one case, α-(allyloxy)methyl-1-piperidineëthanethiol hydrochloride, the compound was too hydroscopic to obtain it in the pure form.

Secondary amines which do not have ring structures as do morpholine and piperidine appear to react with the thiiranes without difficulty. However, as noticed by Jacobs and Schuetz (61), the aminothiols which are formed decompose in the final distillation into the starting materials which are recovered. In this study, an attempt was made to isolate the salts of various

acids of 1-diethylamino-3-phenoxy-2-propanethiol and of 1-di-n-butylamine-3-phenoxy-2-propanethiol. The acids used were hydrochloric acid, p-toluene sulfonic acid, naphthalene sulfonic acid, sulfuric acid, picric acid and phosphoric acid. In no case could a crystalline compound be obtained which made further purification impossible. Due to these difficulties, the amount of aminothiols synthesized was limited. It therefore was decided to prepare a few amino-mercaptans from diethylamine and two of the thiiranes, starting with very pure reactants so that a pure product would be obtained without crystallization or distillation. This approach was indeed successful in the case of 1-diethylamino-3-phenoxy-2-propanethiol, but did not result in a pure compound when diethylamine was allowed to react with allyl 2,3-epithiopropyl ether.

Finally, it should be reported that by analogy to the findings of Snyder, Stewart and Ziegler (1) the aminothiols are assumed to consist largely, if not solely, of the secondary mercaptan structure as shown in Tables II and II A.

Aminothioacetates

These compounds were prepared by the reaction of the aminothiols, discussed in the previous section of this thesis, and acetyl chloride (4). The aminothio-

acetates are less hydroscopic and more stable than their corresponding aminothiols. For instance, it was possible to purify by crystallization the S-(1-allyloxymethyl-2-piperidinoethyl)thioacetate hydrochloride, which could not be done with the corresponding aminomercaptan. Further, the S-(1-allyloxymethyl-2-morpholinoethyl)thioacetate and the similar piperidino compound could be purified by distillation. This again was not possible with the corresponding aminothiols. Even the related diethylaminothioacetate could be distilled, without readily splitting out diethylamine, as was the case with the aminothiol from which this compound was prepared. Some decomposition must, however, have occurred in the distillation of S-[(2-allyloxy-1-diethylaminomethyl)ethyl]thioacetate, since the compound was not obtained in good purity. A purer product might be obtainable with a more efficient column under higher vacuum. Unfortunately, the salts of this compound did not form a crystalline material, and further purification was not possible.

Purification by distillation of the S-(2-phenoxy-1-piperidinomethylethyl)thioacetate and the corresponding morpholino compound was not possible due to rather extensive decomposition. Their hydrochloride salts, however, were crystalline solids which could be purified readily. Further details on the amino-

thioacetates synthesized during this investigation are summarized in Table IV.

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