THE CHEMISTRY OF SULFENIMIDES

by

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Dedicated

to

My Parents

" Thanx " 
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INTRODUCTION AND BACKGROUND

Sulfenic acids (1), in which sulfur exists in its

\[ R-S-OH \]

lowest oxidation state, are highly unstable compounds and only a few have been isolated. The derivatives of sulfenic acid (2) however, are generally isolable and usually stable.

\[ R-S-Y \]

When \( Y \) is \(-\text{NH}_2\), \(-\text{NHR}\), or \(-\text{NR}_2\), the resulting class of compounds is termed sulfenamides. These compounds have been found to be of especial value to the rubber industry as accelerators in the vulcanization of rubber and, as a result, their preparation and chemistry have received much attention. More recently, Zervas has proposed the sulfenamide linkage be used in protecting the free amino group in peptide synthesis.

The first reported preparation of a sulfenamide was by Zincke who combined 2-nitrobenzene sulfonyl halide (3) and dimethyl amine (4) to obtain 2-nitrobenzenesulfenodimethylamide (5).
Starting with the appropriate thiol sulfonate, sulfenamides containing other functional groups can be prepared, whereas in Zincke's method certain functional groups (especially double bonds) are precluded since they react with the sulfenyl halide.

Most sulfenamides are crystalline substances with sharp melting points; they tend to be more soluble in solvents such as benzene or chloroform than in more polar solvents. Many are highly colored but the sulfenamide grouping itself is not chromophoric. In many of their chemical reactions sulfenamides tend to exhibit amine-like character. Like amines they are easily acetylated and benzoylated and react readily with aldehydes and ketones in a manner reminiscent of Schiff bases.

\[
\begin{align*}
\text{S-NH}_2 + \text{C}=\text{O} & \rightarrow \text{S-N}=\text{C} \text{H} \\
\text{NO}_2 & \text{NO}_2
\end{align*}
\]

Although sulfenamides are probably weakly basic, the amine-like property of salt formation on treatment with mineral acids is overshadowed by the stability of the sulfur-nitrogen linkage. In either aqueous or ethereal solutions, sulfenamides are readily hydrolyzed by acid. In non-aqueous solutions the end products are the amine salt and the sulfenyl halide or corresponding disulfide if the sulfenyl halide is not very stable.
the other hand, the sulfenamide bond seems to be quite stable in alkaline solutions. In aqueous basic solutions of permanganate or hydrogen peroxide, the sulfenamide is readily oxidized to the sulfonamide (8).  

\[ R-S-NR_2 \]

In 1951 a particular kind of sulfenamide was devised wherein the amine moiety was replaced by phthalimide. The resulting compound was patented by Kittleson and is known as Phaltan (9), a fungicide.

\[ \text{Phaltan} \]

From this specific type of sulfenamide a general class of compounds known as sulfenimides* has been derived. These N-(alkyl or aryl thio)imides (10) are important as insecticides and fungicides and, again, are effective accelerators in vulcanizing rubber.

\[ R-S-N(\text{Ar}) \]

* A conflict in terminology exists for these compounds. Kharasch, in his 1946 review of sulfenyl compounds, called compounds of the structure...
The preparation of the N-(alkyl/aryl thio)imides can follow one of two procedures. The first method, developed by Büchel and Conte, involves refluxing a solution of the N-bromoimide and disulfide under nitrogen for a short period of time. The N-bromo derivatives of succinimide, phthalimide, glutarimide and hydantoin were reacted with a variety of aromatic disulfides, benzyl disulfide, and one aliphatic disulfide, dodecyl, to give the corresponding N-(aryl or alkyl thio)imides (11-14) in 80 to 95% yields.

\[ \text{RS-NH-SR, "sulfenimides". The use of "sulfenimide" to refer to the combination structure resulting from an imide and a sulfenyl moiety (10) appears to have been first coined by Büchel and Conte in 1967. Kerwood has continued to use the term, sulfenimide, to refer to compounds of the general structure R-S-N=O. The most obvious solution to this dichotomy in nomenclature is to avoid use of the word "sulfenimide" altogether. Kharasch's compound might logically be called bis(alkyl or aryl thio)amine; the other "sulfenimide" would then be N-(alkyl or aryl thio)imide.} \]
Kerwood and Behforouz, using phthalimide, sulfenyl halide, and a tertiary amine as an hydrogen chloride scavenger (recall the main method of synthesizing sulfenamides), extended the Büchel series by preparing a wide variety of N-(alkylthio)phthalimides (15). They also reacted several other imides such as 2-benzimidazolinone 2-imidazolidone and tetrahydrophthalimide with sulfenyl halides obtaining the corresponding N-(substituted thio) imides (16 - 18).

The strengths and weaknesses of this preparative method are dependent on the sulfenyl halide: its ease of preparation, stability and reactivity.

The sulfenyl halides (19) are important synthetic
intermediates; consequently they have enjoyed a long and intensive
study of their chemistry. Chlorine is the most frequently used
halide since the sulfenyl chlorides are usually stable and isolable.
Only a very few sulfenyl bromides and even fewer iodides are known.
The most common preparation involves the chlorinolysis of the disulfide
or thiol at low temperatures (-50° to 0°) under anhydrous conditions.
Usually, as chlorine is allowed to gently bubble into the disulfide
solution, a yellowish solid forms which, when chlorine addition is
complete, disappears after agitation of the reaction mixture. The
following sequence of reactions has been determined to take place:9

\[
\begin{align*}
[1a] \quad 2 \text{R-SH} + \text{Cl}_2 & \rightarrow \text{R-S-S-R} + 2 \text{HCl} + \\
[1b] \quad \text{RS-SR} + \text{Cl}_2 & \rightarrow 2 \text{R-S-Cl} \\
[2] \quad \text{R-S-Cl} + \text{Cl}_2 & \rightarrow \text{R-S-Cl}_3 \\
[3] \quad \text{R-S-Cl}_3 + \text{RS-SR} & \rightarrow 3 \text{R-S-Cl}
\end{align*}
\]

A low temperature is necessary to prevent substitution of the α proton
by chlorine as the organosulfur trichloride (20) decomposes, [2], giving,
instead of the desired sulfenyl halide, an α-chlorinated sulfenyl halide
(21).10

\[
\begin{align*}
\text{R-CH}_2\text{-S-Cl}_3 & \rightarrow \text{R-CH-S-Cl} + \text{HCl} + \\
\text{Cl}
\end{align*}
\]
Sometimes, however, low temperature chlorinolysis does not lead to the expected sulfur - sulfur bond cleavage but to a carbon-sulfur scission instead. For example, benzyl disulfide, when treated with chlorine at $-40^\circ$, has been reported to give only benzyl chloride, but at $0^\circ$ a quantitative yield of the desired benzyl sulfenyl chloride is obtained, \(^{11}\) (determined by nmr analysis; isolation attempts led to decomposition). Similarly, t-butyl disulfide is chlorinated in boiling pentane ($30^\circ$ to $40^\circ$) to yield the desired t-butyl sulfenyl chloride; \(^{12}\) at lower temperatures carbon - sulfur bond cleavage predominates. The solvents used must be anhydrous and aprotic for moisture will readily oxidize the sulfenyl chloride to sulfonyl chloride, and active hydrogen will react with the sulfenyl chloride as soon as it is formed. Excess chlorine must be avoided for the tetrahalogen derivatives formed will yield thiolsulfonic esters on hydrolysis. Chlorinating agents other than gaseous chlorine, such as sulfuryl chloride (22), \(^{22}\) N-chlorosuccinimide (23), and N-chlorophthalimide (24) have also been used successfully to prepare sulfenyl chlorides.

\[
\begin{align*}
\text{SO}_2\text{Cl}_2 & \quad \text{N-Cl} \\
\text{22} & \quad \text{23} \\
\text{24}
\end{align*}
\]

All of the sulfenyl halides discussed are highly colored compounds; most are distillable oils possessing repulsive odors. The
aliphatic sulfenyl halides are the least stable and should be used immediately; but, if stored at dry ice temperature and under nitrogen, they can be kept for up to two weeks without appreciable decomposition. The aromatic sulfenyl halides are more stable to moisture and heat, but caution should still be exercised with respect to their decomposition. Nitro-substituted benzene sulfenyl halides are quite stable; 2,4-dinitrobenzene sulfenyl chloride is a high melting solid not easily affected by moisture.

Because the sulfenyl halides are so highly reactive, the R moiety can contain no unsaturation, and no active hydrogen. However, this seems to be the only limitation to the method of Kerwood and Behforouz for the preparation N-(alkylthio)imides.

Other than investigating new modes of synthesis, little has been reported on the chemistry of these N-(alkyl or aryl thio)phthalimides. Kerwood and Behforouz have reported a brief investigation into the stability of N-(cyclohexylthio)phthalimide (25) to acids and to bases. They found that weak bases such as triethylamine cause only slight decomposition, but that strong bases, such as aqueous potassium hydroxide, effect rapid hydrolysis even at room temperature. The products of alkaline
hydrolysis included potassium phthalate (26) (83%), cyclohexyl disulfide (27) (69%), potassium cyclohexylsulfinate (28) (17.5%), potassium cyclohexylsulfonate (29) (5%), cyclohexyl sulfide (32) (11%), ethyl phthalate (33) (3.6%), and a trace of ammonia.

![Structural formulas](image)

Acidic hydrolysis of N-(cyclohexylthio)phthalimide (25) is reported to be much slower than alkaline hydrolysis requiring up to eight hours of refluxing in acidic (concentrated hydrogen chloride) ethanol. From acidic decomposition the products obtained were phthalimide (30) (92%), cyclohexyl disulfide (27) (36%), dicyclohexyl thiolsulfonate (31) (36%), and a trace of ammonia.

![Structural formulas](image)
No attempt was made to rationalize the formation of the compounds formed on alkaline hydrolysis, but a scheme was proposed to explain the products obtained from attack by acid. Initial attack by hydrogen chloride occurs at the sulfur - nitrogen bond producing sulfenyl chloride and free imide. The other products of the reaction are then derived from reactions of the sulfenyl chloride as follows:

\[
\text{S-NO} + \text{HCl} \rightarrow \text{S-Cl} + \text{N-H}
\]
* This proposal for the presence of cyclohexyl sulfide in the hydrolysis mixture does not seem likely since it is known that the reaction of thiols with thiolsulfonates gives disulfides.\textsuperscript{29}
The combination of the properties of an imide and of bivalent sulfur in N-(alkyl/aryl thio)phthalimide compounds can give rise to unique and interesting chemistry.

Of specific interest in our laboratory was the reaction of phosphines with sulfenyl systems (34). Phosphines (35),

\[ R-S-Z-R \]  

and phosphites (36) are known to react with a variety of compounds that possess easily polarizable bonds and are thus susceptible to nucleophilic attack. Although nucleophilic reactions of triaryl or trialkyl phosphines occur smoothly, those of trialkyl phosphites are complicated by the possibility of Arbuzov rearrangement where the displaced chloride ion reattacks the alkoxy carbon giving a phosphine oxide (37) and a new alkyl chloride.

\[
\text{(EtO)}_3\text{P} + \text{R-Cl} \rightarrow \text{(EtO)}_2\text{P} + \text{Cl}^- + \text{CH}_3\text{CH}_2\text{Cl} + \text{CH}_2\text{CH}_2\text{Cl}
\]  

\[ 37 \]
It has been found by Harpp and Gleason\textsuperscript{15} that disulfides usually unaffected by triphenyl or trialkyl phosphines are desulfurized smoothly by tris(diethylamino) phosphine (38).

\[
\left( \left( \text{CH}_3\text{CH}_2 \right)_2\text{N} \right)_3\text{P}
\]

Although aminophosphines are structurally similar to phosphites, the possibility of an Arbuzov rearrangement occurring would be unlikely not only because the carbon - nitrogen bond is stronger than a carbon - sulfur bond (72 kcal. vs. 65 kcal.), but also because the resulting phosphine imide (from an Arbuzov rearrangement) would most likely be less stable than an oxygen or a sulfur analog:

\[
\begin{align*}
\text{R-CH}_2\text{-S-P-NR}_2 \quad \text{R'-CH}_2\text{R} \\
\downarrow \quad \quad \quad \quad \quad \quad \quad \quad \\
\text{S=P(NR}_2^2 + \text{RCH}_2\text{-S-R}
\end{align*}
\]

The driving force for the reaction is attributed to the conversion of a trigonal trivalent phosphorous atom using p\textsuperscript{3} bonding to a more stable tetrahedral phosphorous atom with sp\textsuperscript{3} bonding.\textsuperscript{16} Systems other than disulfides (\(Z = \text{-S}\)) have been investigated and preliminary results show that trisulfides (\(Z = \text{-SS}\))\textsuperscript{17} and thiolsulfonates (\(Z = \text{-SO}_2\))\textsuperscript{18} are also
desulfurized by aminophosphines.

In order to extend the scope of system (34) beyond $Z = S$, $N$-(alkyl/aryl thio)phthalimides (15, 12) ($Z = N$) were treated with tris(dimethylamino) phosphine (39).

If phosphorous were to initially attack sulfur, the stable phthalimide ion (the anion in salt 40) would be displaced, and subsequent attack of it on the carbon adjacent to the sulfur would effect elimination of tris(dimethylamino) phosphine sulfide (41). In contrast, initial attack by phosphorous on the nitrogen atom is less likely since displacement of mercaptide ion (a poor leaving group compared to the phthalimide ion).
anion) would be predicted, and because no stable products appear possible.

The N-alkylphthalimide (42) produced by desulfurization is the key intermediate in the Gabriel synthesis of primary amines. Thus, in general, one could convert a disulfide or thiol to a primary amine via the desulfurization of N-(alkyl thio)phthalimides with tris(dimethylamino) phosphine thus providing a versatile entry to this important class of compounds.

Until Gabriel's discovery in 1887, the best method available for the preparation of primary amines, albeit highly contaminated with secondary, tertiary, and quaternary amines, was by the alkylation of ammonia, devised by Hofmann in 1850. Gabriel, working in Hofmann's laboratory, recognized the significance of two experiments: 1) that N-alkylphthalimides could be prepared from methyl and ethyl iodides with potassium phthalimide, and 2) that N-alkylphthalimides can be readily hydrolyzed. He combined these ideas to produce his well-known synthesis of primary amines. The method was still basically the alkylation of ammonia, but the formation of other classes of amines was precluded by there being only one available hydrogen for alkylation instead of three. In its original form the reaction involved heating the alkyl halide and potassium phthalimide either neat or in a high boiling, non-polar solvent.
The insolubility of the potassium phthalimide greatly slowed the reaction and, consequently, prolonged heating (two to twenty-four hours) and high temperatures (100° to 150°) were required to effect condensation. These conditions, however, often resulted in lowered yields and intractable mixtures. In spite of these limitations, this method of preparing N-alkylphthalimides was the one commonly used until 1950 when Sheehan and Bolhofer introduced the expedient of using dimethylformamide as the solvent. In this highly polar solvent, potassium phthalimide is appreciably soluble; a mild, exothermic reaction is reported to begin spontaneously at room temperature and the reaction is essentially complete in ten minutes with respect to the more reactive halides. Substances of high purity in reasonable yield were obtained by this modification.

The importance of Gabriel's synthesis lies not only in the preparation of pure primary amines, but also in the toleration of the reaction conditions for a wide range of other functional groups which may be included in the molecule. In addition, the stability of the phthalimide moiety allows modification of functional groups before hydrolysis to the free amine. One significant limitation, however, is the failure of secondary alkyl halides to react successfully to yield the secondary N-alkylphthalimides. A few secondary halides have been utilized such as isopropyl bromide, 2-bromobutane, and bromocyclohexane, but yields of the corresponding N-alkylphthalimides are low and attendant side reactions predominate. Alkyl halides containing an ester function on the halogenated carbon atom give rise to α-amino
acids; this principle is the basis of the Sörensen amino acid synthesis in which the key intermediate compound is diethyl phthalimidomalonate.\textsuperscript{26}

Decomposition of the N-alkylphthalimides to amines can be accomplished in one of three ways:

1. **Acidic hydrolysis** — refluxing for several hours in concentrated or 20\% acid affords the amine salt (43)

\[
\text{N-R} \overset{\text{HCl}}{\rightarrow} \text{HCl} + \text{RNH}_3^+ \text{Cl}^-
\]

2. **Two stage hydrolysis** — alkaline conditions are initially employed yielding phthalamic acid (44) which is then decomposed by acid to the amine salt (43)

i) 
\[
\text{N-R} \overset{\text{aq OH}^-}{\rightarrow} \text{NH}R
\]

ii) 
\[
\text{RNH}_3^+ \text{Cl}^- + \text{HOH} \overset{\text{H}^+}{\rightarrow} \text{RNH}_3^+ \text{Cl}^-
\]
3. Hydrazinolysis — the mildest and most commonly used method today. By this technique the N-alkylphthalimide is dissolved in warm ethanol; hydrazine hydrate (equimolar) is added whereupon a flocculent, white precipitate forms (45) which is decomposed by acid to the amine salt (43) and phthalhydrazide (46). 25

\[
\text{N-R + NH}_{2}\text{NH}_2\cdot\text{H}_2\text{O} \rightarrow \text{RNH}_3\text{Cl} + \text{HCl} + \text{N-H}
\]

\[
\text{N-H} + \text{RNH}_3\text{Cl}
\]

The intent of the following research was to study several aspects of N-(alkyl/aryl thio)phthalimide chemistry. Of particular interest, _vide supra_, was the reaction of the N-(alkyl/arylthio)phthalimides with tris(dimethylamino) phosphine. If, as predicted, the product of the reaction was N-alkylphthalimide, then a synthesis of primary amines would be in hand. Of especial interest was the desulfurization of secondary N-(alkylthio)phthalimides, for if sulfur extrusion proceeded smoothly, a good route to secondary N-alkylphthalimides (virtually unattainable via the Gabriel synthesis) would be available.
Another interesting possibility was the reaction of thiols with the N-(alkyl/aryl thio)phthalimides to yield unsymmetrical disulfides (47). * 30

\[ \text{R'-SH} + \text{RS-SR'} \rightarrow \text{RS-SR'} + \text{R'-SH} \]

The nucleophilic displacement of the phthalimide moiety by a mercaptan was briefly mentioned both by Kerwood and Behforouz and by Zervas. Kerwood and Behforouz, in one step of their assay procedure to determine the purity of their "sulfenimides", reacted 2-mercaptobenzothiazole (48) with the N-(substituted thio)phthalimides obtaining the unsymmetrical disulfide (47). 8

* Except for the amino acid cystine, the disulfides found in nature are unsymmetrical. A few examples are the pancreatic hormone, insulin, which contains three disulfide linkages; oxytocin, a hormone produced by the anterior pituitary during childbirth; and lipoic acid, a co-enzyme. While there are a number of preparations in the literature 28 for unsymmetrical disulfides, no one technique suffices for all synthetic situations.
In his paper proposing the use of the sulfenamide linkage as an N-protective group in peptide synthesis, Zervas noted that if the peptide were acid sensitive, the sulfenamide group could be removed by treatment with benzene thiol.\textsuperscript{4,27} In neither case, however, did the groups pursue the synthetic possibilities inherent in their reactions.

A third aspect of N-(substituted thio)phthalimide chemistry studied was their fragmentation patterns in the mass spectrometer. No information was available in this area, and further insights into the chemistry of this unusual grouping were desired.
EXPERIMENTAL SECTION
The gas-liquid chromatographic analyses were carried out on a F&M Scientific 5750 Research Chromatograph (Hewlett-Packard) equipped with a Honeywell recorder. A 6' x 1/8" stainless steel column, 10% diethylene glycol succinate on Chromasorb W/AW-MCDS, (LAC column), was used for all analyses.

Infrared spectra were obtained with either a Perkin-Elmer Model 337 Grating Infrared Spectrometer or a Model 137 Infracord; absorptions are reported in reciprocal centimeters, and calibrated against the 1601.4 cm\(^{-1}\) band of polystyrene. Potassium bromide discs of the sample were used.

The mass spectra were produced with an AEI-MS-902 mass spectrometer equipped with a direct insertion probe.

Varian Associates A60 and T60 nmr spectrometers were used for all nmr spectra. Absorptions are reported in \(\tau\), units, relative to an internal TMS standard. The following abbreviations have been used: singlet - s; doublet - d; triplet - t; quartet - q; multiplet - m; broad - br. The \(^{31}\)P nmr spectrum was obtained from a Varian Associates DP-60 spectrometer at an oscillator frequency of 19.3 MHz.

All melting points were done on a Gallenkamp melting point apparatus and are uncorrected.

Elemental analyses were performed by C. Dasselle, Organic Microanalyses, Montreal, Quebec.

Tris(dimethylamino)phosphine was obtained from Aldrich, \(^{20}\)D 1.4644.
EXPERIMENTAL

Preparation of Sulfenyl Chlorides*

A. By Chlorinolysis.

Chlorine gas (Matheson, Coleman, and Bell, high purity grade) was condensed in a tared round bottom flask immersed in a dry-ice - acetone bath \((-78°)\) until the desired amount was obtained (the reaction was usually carried out in a 1:1 molar ratio). On warming to room temperature, the liquid chlorine gradually vaporized and was bubbled into a solution of the disulfide dissolved in a dry, aprotic solvent (usually \(\text{CCl}_4\)). As the sulfenyl chloride was formed, the reaction solution colored (yellow, orange or red). In a few cases\(^{31}\) the intermediate organosulfur trichloride precipitated subsequently disappearing as the reaction progressed. When feasible and desirable, the sulfenyl chloride was isolated by distillation. Otherwise, completeness of reaction and purity of product were ascertained by nmr spectra. By this method the following sulfenyl chlorides were prepared.

1. Ethyl sulfenyl chloride\(^{32}\) (50)

The disulfide solution was cooled in a dry ice - acetone bath before addition of the chlorine. Care was taken that the precipitating

* The sulfenyl chlorides prepared are summarized in Table 1.
organosulfur trichloride intermediate did not clog the gas inlet. Avoidance of heat was advisable, hence distillation was carried out at controlled water pressure with the receiving flask immersed in a dry ice-acetone bath. The product was a malodorous orange liquid; bp 26-27°/52 mm. (lit. 32 39°/58 mm. 6-8°/13 mm); nmr (neat): 8.58 (3H, t); 6.86 (2H, q).

2. Isopropyl sulphenyl chloride

This substance was prepared under the same conditions used for ethyl sulphenyl chloride (50). No precipitate was noted. An nmr spectrum of the crude reaction mixture showed a substantial impurity (> 10%); vacuum (water pressure) distillation was attempted but no stable boiling point was obtained (lit. 33 36°/45 mm.). The malodorous orange liquid collected was pure sulphenyl chloride as determined by an nmr spectrum (66% yield); nmr (CCl₄): 8.60 (6H, d); 6.63 (1H, heptet).

3. Benzyl sulphenyl chloride

The slurry of benzyl disulfide in CCl₄ was cooled to 0° in an ice-water bath; on addition of chlorine the reaction mixture became homogeneous and orange in color. Disappearance of the disulfide benzylic peak at 6.48 τ and appearance of the sulphenyl benzylic peak at 5.75 τ confirmed total conversion of the disulfide into the sulphenyl chloride. The product decomposed on distillation, hence the reaction mixture was used without further purification; nmr (CCl₄): 5.76 (2H, s); 2.75 (5H, s).
4. **t-Butyl sulfonyl chloride**\(^1\) (53)

The disulfide was dissolved in pentane; the reaction flask was equipped with a water condenser, for as the chlorine reacted with the disulfide, the heat of the reaction caused the pentane to reflux. No attempt was made to cool the reaction since carbon - sulfur bond scission might tend to predominate.\(^2\) The reaction mixture was used immediately without purification; the yield was assumed\(^2\) to be 85%.

5. **Cyclohexyl sulfonyl chloride**\(^3\) (54)

The mercaptan solution (CCl\(_4\)) was cooled to 0° in an ice-water bath; an outlet for the HCl gas produced during the reaction was provided by a CaCl\(_2\) drying tube. After about half the chlorine had been added the reaction solution became yellow-orange in color. The reaction solution was used without purification; conversion was assumed to be complete (repetition of literature\(^8\) preparation).

6. **Carbomethoxy sulfonyl chloride** (55)

The disulfide\(^3\) solution (CCl\(_4\)) was cooled to 0° in an ice-water bath; the chlorine was bubbled directly into the solution; the reaction solution became light orange in color; an nmr spectrum affirmed complete reaction; nmr (CCl\(_4\)): 6.18 (3H, s); 6.08 (2H, s).

7. **2-Pyridyl sulfonyl chloride** (56)

The disulfide solution (CCl\(_4\), pale yellow in color) was cooled in an ice-water bath to 0°. On addition of chlorine, the reaction
solution became deep yellow in color and a white, flocculent precipitate formed. The reaction mixture was used without further purification.
(See Figure 1).

Di-2-pyridyldisulfide was prepared by slowly adding a methanolic solution (100 ml.) of pyridine-2-thiol (10 g., 0.09 mole) and triethyl-amine (9.1 g., 0.09 mole) to a solution of iodine (12.7 g., 0.05 mole) in methanol (200 ml.). The reaction mixture was then poured into water (800 ml.), decolorized with sodium thiosulfate, and cooled whence a flocculent precipitate formed; recrystallization from CCl₄ gave 2-pyridyl disulfide (7.1 g., 72%), pale yellow needles, mp. 58-59°C; lit. 36 mp. 54-55°C, nmr (CCl₄): 2.94 (q); 2.3~ (m); 1.55 (d).

1,2-Dithiane was prepared with slight modification of the method of Gleason 38.

1,2-Dithiane 37 was synthesized by slowly adding a methanolic solution (50 ml.) of tetramethylene dithiol (20 g., 0.16 mole) and triethylamine (34 g., 0.34 mole) to a cooled (0°C) solution of iodine (42.8 g., 0.17 mole) in methanol (400 ml.). When addition was complete, the insoluble material was removed by gravity filtration. The resulting clear filtrate was diluted with an equal volume of benzene, washed with thiosulfate solution until colorless, washed once with water, dried (MgSO₄) and concentrated in vacuo (minimal heat, since heat tends to induce polymerization).
The residual yellow liquid solidified on cooling (14 g.); by sublimation (water bath, 50°, 30 mm Hg) white crystals were obtained (9.4 g., mp. 34-35°, lit. 37 30.8-31.5°).

B. By Sulfuryl Chloride

To a stirred solution of the disulfide (one mole) and triethyl amine (one ml.) in a dry solvent (preferably CCl₄) was added redistilled sulfuryl chloride (one mole). Within minutes the reaction mixture became deeply colored; protected from moisture, the reaction solution was stirred for one hour before use. Isolation of the sulfenyl chloride was not attempted. By this method the following sulfenyl chlorides were prepared.

1. Benzothiazole-2-sulfenyl chloride (58)

To a stirred suspension of 2,2'-dithiobis(benzothiazole), (Baker, mp 170-174°), and triethylamine (redistilled) in CH₂Cl₂ (reaction did not proceed in non-polar CCl₄) was added redistilled sulfuryl chloride. White fumes were given off and the yellow suspension rapidly turned to a clear, red solution. Conversion was assumed complete and the reaction mixture used without further purification.

2. n-Butyl sulfenyl chloride (59)

Initially the disulfide solution (CCl₄) was cooled to -70° (dry ice - acetone bath); after addition of the sulfuryl chloride, the
reaction solution (now orange in color) was allowed to gradually warm to room temperature and was immediately used (lit.\(^{33}\) bp 30-31°/11 mm.). An nmr spectrum indicated pure product; nmr(CCl\(_4\)): downfield shift of 24 cps of triplet (2H) with respect to that of disulfide.

3. Carbomethoxy sulfonyl chloride (55)

The disulfide\(^{35}\) solution (CCl\(_4\)) was cooled to 0° by an ice-water bath, then the sulfonyl chloride was added. Analysis by nmr indicated a 30% excess of sulfonyl chloride was required. The material was used without further purification.

C. By N-Chlorosuccinimide\(^{34}\)

To a vigorously stirred slurry of NCS* (one mole) in dry benzene or carbon tetrachloride was gradually added the thiol (one mole); when addition was complete, the colored reaction mixture was stirred at room temperature overnight. The succinimide was removed by filtration and the filtrate evaporated to dryness, refiltering as necessary. The residual oil was distilled under vacuum. By this method were prepared the following sulfonyl chlorides:

1. p-Toluene sulfonyl chloride\(^{42}\) (60)

The reaction solvent used was benzene. As the p-toluenethiol was added, the reaction mixture became quite warm hence an ice-water bath was used to control the temperature. The residual red oil obtained after

* N-chlorosuccinimide
workup was distilled to give a 62% yield of 60, a deep red liquid, bp 51-53°/0.1 mm, 56-57°/0.15 mm, (lit.42 77.5-78.5°/2.5 mm.).

2. Benzene sulfenyl chloride42 (61)

This reaction was carried out under nitrogen in CCl₄; no increase in the temperature of the reaction mixture was noted; the residual red oil obtained after work-up was distilled to give an 80% yield of 61, bp 69-70°/7 mm., (lit.42 73-75°/9 mm.), a pungent smelling red-orange liquid; nmr(CCl₄): 2.60 (m).
Preparation of Sulfenimides

A. By Reaction of Sulfenyl Chlorides with Potassium Phthalimide.

Essentially following the method of Kerwood and Behforouz, the sulfenyl chloride solution (one mole) was slowly added, under nitrogen, to a stirred slurry of potassium phthalimide (one mole) in DMF* or CCl₄. After addition was complete, the reaction mixture was stirred at room temperature, the time varying from 0.5 to 18 hours. When DMF was used as the solvent, the product was obtained by dilution of the reaction mixture with water. The flocculent precipitate which formed was filtered, dried in vacuo over P₂O₅, and recrystallized from hexane or chloroform-hexane. When CCl₄ was the solvent, the reaction mixture was poured into a separatory funnel containing ice water; the organic layer was removed, washed with water, dried (MgSO₄), and concentrated in vacuo to about 100 ml.; n-hexane was then added (five to six times the volume of the organic layer) whence white crystals formed.

The sulfenimides prepared or whose preparations were attempted are summarized in Table 2.

B. By Reaction of Thiolsulfonate and Phthalimide

1. Preparation of benzyl tolyl thiolsulfonate

Potassium p-tolyl thiolsulfonate (0.1 mole) and benzyl bromide (0.1 mole) were refluxed in 95% ethanol for five hours, then stirred over-

* dimethylformamide
Gravity filtration of the hot reaction mixture afforded a clear, colorless filtrate which was evaporated in vacuo to a yellow oil containing a small amount of white solid. This residue was taken up in CHCl₃, the solid removed by gravity filtration, and the CHCl₃ filtrate concentrated in vacuo to a yellowish oil. This oil was dissolved in boiling 95% ethanol and allowed to cool slowly to room temperature, then placed in an ice bath whence rapid crystallization afforded 24.8 g. (89%) of 63, mp 56-57.5° (lit. 43 60°).

2. Attempted preparation of N-(benzylthio)phthalimide⁸ (62)

Following the method of Dunbar and Rogers⁵, phthalimide (11.5 mmole) and benzyl tolyl thiosulfonate (63) (5.75 mmole) were refluxed in 95% ethanol for two days (use of potassium phthalimide led to elimination and polymerization). Work-up of the ethanolic reaction mixture afforded phthalimide (88% recovery) and original thiosulfonate (63) (80% recovery).

Reaction of Tris(dimethylamino)phosphine (38) with Sulfenimides*:⁴⁹

To a stirred solution or suspension of the sulfenimide in benzene (sodium dried, spectrograde) was rapidly added, under nitrogen, an equimolar quantity of aminophosphate (38), also in benzene solution. Completeness of reaction was followed by gas-liquid chromatography (hereafter referred to as glc). The yields were ascertained by quantitative nmr analysis

* These reactions are summarized in Table 3.
using a Varian T-60 spectrometer. The method consisted of comparing the initial and final area integral ratios of an internal standard (toluene or dioxane) and of the methyl groups of phosphine or phosphine sulfide. Area integration of each peak was repeated six to seven times to assure reproducibility and accuracy.

Hence,

\[
\frac{\text{area internal std.}}{\text{area } \left(\text{CH}_3\text{N}\right)_3\text{P}} = \frac{X_{\text{initial}}}{X_{\text{final}}}
\]

\[
\frac{\text{area internal std.}}{\text{area } \left(\text{CH}_3\text{N}\right)_3\text{P=SO}} = \frac{X_{\text{final}}}{X_{\text{initial}}}
\]

\[
\% \text{ yield} = \frac{X_{\text{final}}}{X_{\text{initial}}} \cdot 10^2
\]

The probable % error was calculated as follows:

\[
\frac{\text{no. H of } \left(\text{CH}_3\text{N}\right)_3\text{P}}{\text{no. H of std.}} \cdot \frac{\text{no. moles of } \left(\text{CH}_3\text{N}\right)_3\text{P}}{\text{no. moles of std.}} = Y \text{ or } X_i \text{ as determined on a weight basis}
\]

Let \( \Delta X_i \) = the difference between \( X_i \) and \( Y \) (absolute value)

Then % error = \( \frac{\Delta X_i}{Y} \cdot 10^2 \)

Isolation techniques varied with the products and their properties.

Difficulty was encountered in removing the highly polar phosphine sulfide
while maintaining the high yield of product as indicated by nmr analysis. Using these general procedures the following reactions were carried out:

A. **Desulfurization to N-Alklyphthalimides** (see Table 3)

1. **N-Ethylphthalimide** (75)

N-(Ethylthio)phthalimide (64) was rapidly desulfurized at room temperature to N-ethylphthalimide (75). Toluene was used as the internal standard in the nmr analysis. Calibration of the tolyl group with respect to either the methyl or methylene groups of the sulfenimide (64) and product (75) led to non-reproducibility in the integration, and a minute change in area (e.g. one square) effected a 10-15% difference in yield; consequently, the tolyl group was standardized with the methyl groups of phosphine (38) and phosphine sulfide (41). After removal of the benzene in vacuo, the resulting yellow oil was diluted with petroleum ether 30/60° and chilled whence white crystals formed, mp 70-72°. (lit. 44 79°). In an attempt to increase the yield, purification by column chromatography was attempted. An ethereal slurry of alumina was saturated with hydrogen chloride gas for 24 hours. This "acidic" alumina was then used to prepare the column. Elution with acidic 10:1 hexane-ethyl acetate (HCl gas was bubbled into the solution until it was acidic to pH paper) gave 75% of N-ethylphthalimide (75), mp 76-77°. It is highly possible that the strong acidic media partially hydrolyzed the N-ethylphthalimide on the column; nmr (CDCl₃); 8.73 (3H, t); 6.25 (2H, q); 2.19 (4H, d).
2. N-n-Butylphthalimide\textsuperscript{45} (76)

The internal standard used was toluene. Isolation by repeated crystallization from hexane led to a 46% yield of silvery-white needles, mp 30-33°. (lit.\textsuperscript{45} 34-35°).

3. N-Benzylphthalimide\textsuperscript{44} (77)

Dioxane was used as the internal standard; both the starting sulfinimide (62) and resulting product (77) were only partially soluble in benzene. After addition of the phosphine, the slurry became warm and turned to a yellow solution; on cooling a white precipitate settled out. After approximately one and one-half hours, the benzene was removed and hexane was added to the yellow, semi-solid residue. The hexane slurry was heated to boiling, cooled and the resulting crystals filtered. A second crop was obtained from the mother liquor by cooling it in dry ice. The two crops were combined and recrystallized from hexane to give white needles, mp 112-113°. (lit.\textsuperscript{44} 116°): 87%. A third recrystallization from CHCl\textsubscript{3}-hexane gave crystals melting 115-117°; nmr(CDCl\textsubscript{3}): 5.13 (2H, s); 2.63, 2.20 (9H, m) (benzene): 5.40 (2H, s).

4. N-Isopropylphthalimide\textsuperscript{46} (78)

The internal standard was dioxane; it was compared not to the phosphine but to the isopropyl methyl groups. Analysis was performed on the Varian A-60 spectrometer; isolation was by column chromatography following the procedure used for N-ethylphthalimide (75). White needles were obtained in 77% yield; mp 83-84°; (lit.\textsuperscript{46} 86°); nmr (CDCl\textsubscript{3}): 8.48 (6H, d); 5.39 (1H, m); 2.14 (4H, m).
B. Phosphonium Salt Formation

1. Reaction of Tris(dimethylamino)phosphine (38) and N-(Phenylthio)phthalimide (70)

After phosphine addition was complete, the reaction was stirred overnight. Removal of the benzene in vacuo (minimal heat) gave an orange oil. Analysis by $^{31}$P nmr spectroscopy gave a major peak at -59.1 ppm from $\text{H}_3\text{PO}_4$ indicative of phosphonium salt formation $^{18}$.

2. Reaction of Tris(dimethylamino)phosphine and N-(p-Tolyl thio)phthalimide (69)

After stirring for two hours from the time of addition of phosphine, the benzene was removed from the reaction mixture leaving an orange oil. The nmr spectrum (CDCl$_3$) showed a doublet for the tolyl group ($J=2$ cps) which would be expected for $^{31}$P - $^1$H coupling.$^{47}$

C. Desulfurization and Elimination

1. Reaction of Tris(dimethylamino)phosphine with N-(t-Butyl thio)phthalimide (68)

Approximately five minutes after addition of the phosphine, the clear reaction solution became milky white; the reaction was allowed to stir for 1 to 1.5 hours. Filtration gave white, fluffy crystals of phthalimide (86) mp 237-239° (lit 240°). The yellow filtrate was concentrated in vacuo to a yellow oil whose nmr spectrum showed it
to be phosphine sulfide (41). Attempts to isolate isobutylene by formation of the adduct with either bromine or 2,4-dinitrobenzene sulfenyl chloride, or by trapping the evolved gas in a cold finger and identifying it by mass spectrometry were unsuccessful. Thus, to identify and demonstrate the identity of isobutylene, the reaction was carried out in an nmr tube. After addition of the phosphine, two new peaks appeared (benzene solution: $\tau$ 8.40, 5.30). These peaks were successfully compared with the absorptions resulting from a benzene solution of isobutylene (Matheson, CP grade), (8.43, 5.28, both singlets).

2. **Reaction of Tris(dimethylamino)phosphine and N-(Cyclohexylthio)phthalimide (67)**

When phosphine (38) was added to the sulfenimide solution, the reaction solution immediately became yellow in color; no evolution of heat was noted. After 2-3 hours of stirring at 40-50°, a white solid formed; an nmr spectrum of the yellow supernate showed absorptions corresponding to cyclohexene protons (benzene: $\tau$ 8.27 (two broad peaks); 4.31 (one peak)). To this supernate was added pure cyclohexene (Matheson, chromatoquality); [ nmr (benzene): 8.23 (6H, two broad peaks); 4.30 (1H, s) ]; the peaks attributed to be cyclohexene increased in area. The white solid was filtered and identified as phthalimide, mp 237-238.5° (75% yield)
3. Reaction of Tris(dimethylamino)phosphine with

N-(Carbomethoxythio)phthalimide (71)

Addition of phosphine (38) caused the reaction to immediately color yellow, but no evolution of heat was noted. After two hours an nmr analysis was performed on the yellow supernate using toluene as the internal standard. The white solid formed was removed by filtration and identified as phthalimide (86) by infrared, mass spectra, and mp 234-235°. Analysis by glc (LAC column) of the reaction mixture after 0.25 hr. and 24 hours after phosphine addition showed, in both cases, a trace of phosphine (38), phosphine sulfide (41), and phthalimide (86). This latter assignment is uncertain since sulfenimide (71) has an identical retention time. In addition, three large peaks, corresponding to low boiling fractions left were unidentified.

D. Reaction of Tris(dimethylamino)phosphine with

N-(Benzothiazole-2-thio)phthalimide (72)

Although the purity of the starting sulfenimide (72) was in question, (see Table 2), a yellow slurry of 72 was treated with phosphine. The reaction quickly colored orange-red with a red oil precipitating; the reaction mixture was heated to reflux for approximately two hours whence solution occurred with the reaction becoming dark green in color. On cooling, a small amount of precipitate was noticed; when exposed to air, the reaction solution became dark blue in color. No further work was attempted.
Preparation of Tris(diethylamino)benzylthiophosphonium fluoroborate

Benzyl bromide (0.01 mole) in 10 ml. CH₂Cl₂ (spectrograde) was added, under nitrogen, to a cooled (-78°), stirred solution of tris(diethylamino)phosphine sulfide (0.01 mole) and silver fluoroborate (0.01 mole) in dry CH₂Cl₂. After addition was complete, the reaction mixture was gradually warmed to room temperature and stirred overnight. After filtration from the silver bromide formed, the CH₂Cl₂ solution was concentrated in vacuo at 30°. The pale yellow residue was washed ten times with 20 ml. each of hexane; redissolved in CH₂Cl₂, and filtered through Celite by gravity; the oil was reprecipitated by addition of hexane to the CH₂Cl₂ filtrate, and again washed with hexane, filtered, reprecipitated, washed with hexane, and dried under vacuum (water pressure) overnight. An nmr spectrum was carried out to ascertain the purity; (benzylic doublet 5.66). A 61.4% yield of a very hygroscopic, viscous, pale yellow oil was obtained (see Figure 6).

Reaction of Tris(diethylamino)benzylthiophosphonium fluoroborate with Potassium Phthalimide

To a stirred solution of the phosphonium fluoroborate (1.95 mmole) in benzene (sodium dried, spectrograde) under nitrogen was added potassium phthalimide (1.95 mmole). The resulting slurry was stirred at room temperature for 0.5 hr. and then refluxed for 0.5 hr. whence reaction occurred as evidenced by appearance of a deep yellow color.
The solvent was removed and an nmr spectrum carried out in CH$_2$Cl$_2$ on the residue. Disappearance of the benzyl doublet of 79 (τ 5.66) and appearance of a benzylic peak at τ 5.16 indicated formation of N-benzylphthalimide (77) (nmr spectrum of authentic sample: benzylic protons (CDCl$_3$) 5.10; the benzylic protons of sulfenimide 62 appear at 5.86 (CDCl$_3$)). Attempts to isolate the product failed. Very small quantities were used; in addition, the high polarity and solvent power of the phosphine sulfide produced rendered separations very difficult.

**Reaction of N-(Phenylthio)phthalimide (70) and Benzyl Thiol (104)**

The sulfenimide (70) (0.004 mole) and benzyl thiol (0.004 mole) were dissolved in 25 ml. of benzene and refluxed. The extent of reaction was followed by thin layer chromatography (tlc) (silica gel; benzene); after 20 hours the reaction appeared complete. The benzene was removed in vacuo (minimal heat) and the residue dissolved in CCl$_4$. The white flocculent solid was removed by filtration to give an 81% yield of phthalimide (86), mp 237-239°. The filtrate was examined by glc (LAC column, isothermal, 220°); benzyl phenyl disulfide 48 (80) was identified in greater than 90% yield.

**Reaction of N-(Benzylthio)phthalimide (62) and Thiophenol (105)**

The procedure was the same as that used in the preceding reaction. Phthalimide (86), mp 235-235°, was isolated in quantitative yield. Analysis
by glc (LAC column, isothermal, 220°), however, showed the unsymmetrical disulfide (80) greatly contaminated with the symmetrical phenyl and benzyl disulfides.

**Reaction of Tris(dimethylamino)phosphine with 4-(Benzythio) morpholine.**

**A. Preparation of 4-(Benzythio)morpholine (81)**

Following the procedure of Dunbar and Rogers\(^5\), benzyl tolyl thiosulfonate (62) (0.054 mole) and morpholine (0.12 mole, Fisher, purified) were dissolved in anhydrous ether (200 ml) and stirred at room temperature for 24 hours. The white precipitate which had formed (thiolsulfinate salt) was filtered and the clear, colorless filtrate concentrated in vacuo to afford a white solid. This was dissolved in CHCl\(_3\)-CCl\(_4\) (1:1), washed several times with water, dried (MgSO\(_4\)), filtered, and evaporated to yield slightly impure white crystals mp 58-70°. Recrystallization from hot hexane gave silvery-white plates, mp 71.5-74° (lit.\(^5\) 74-76°); nmr (CCl\(_4\)): 6.15 (4H, m); 6.48 (4H, m); 6.13 (2H, s); 2.71 (5H, s).

**B. Reaction of 4-(Benzythio)phthalimide (81) with Tris(dimethylamino)phosphine.**

To a stirred solution of the sulfenamide (81) (1.4 mmole) in benzene, (sodium dried, spectrograde), under nitrogen, was rapidly added the phosphine. After stirring overnight at room temperature, the clear,
colorless reaction solution was refluxed for two days, at which point it became pale yellow in color. After two more days at reflux the sample was analyzed by glc. Compounds identified by glc included unreacted phosphine (38), unreacted sulfenamide (81), morpholine (82), phosphine sulfide (41), and phosphine oxide (83) approximately in the ratio 3:3.5:2:5:1 as well as five smaller, unidentified peaks.

Hydrazinolysis of N-Alkylphthalimides

Following the procedure of Ing and Manske\textsuperscript{25}, N-benzylphthalimide (77) (2.5 g., 0.01 mole) was converted to benzyl amine (84) 1.10 g.; 97% yield by nmr analysis. The hydrochloride salt melted 247-250° (lit.\textsuperscript{44} 255°). N-Isopropylphthalimide (78) (1.76 g., 0.009 mole), was hydrazinolized to isopropyl amine (85), bp. 34° (lit.\textsuperscript{44} 35°) in 34% yield.

Mass Spectra of Sulfenimides

All of the N-(alkyl/aryl thio)phthalimides were subjected to fragmentation in the mass spectrometer and their fragmentation patterns studied. The results are summarized in Table 4.
RESULTS AND DISCUSSION
RESULTS AND DISCUSSION

An assortment of N-(alkyl/aryl thio)phthalimides (12) was prepared from potassium phthalimide and the corresponding sulfenyl chloride (19) in order to study their chemistry. A variety of the sulfenimides, when treated with tris(dimethylamino) phosphine (38), underwent rapid, exothermic desulfurization.

N-(Ethylthio)- (64), N-(butylthio)- (65), and N-(benzylthio) - (62) phthalimides underwent facile desulfurization by tris(dimethylamino) phosphine (38) to afford the corresponding N-substituted phthalimide in quantitative yields (nmr analysis).
The clear, colorless solution or slurry of sulfenimide rapidly colored yellow on addition of phosphine (38); the reaction solution often warmed after the phosphine addition. Isolated yields of the N-substituted phthalimides were 10 - 15% greater than those obtained by reacting potassium phthalimide and an alkyl halide in the standard Gabriel synthesis.

\[
\text{Phthalimide}^{-K^+} + R-X + \text{Phthalimide}^{-R} + K^+X^- 
\]

Especially attractive was the result obtained from the desulfurization of N-(isopropylthio)phthalimide (66). In this instance, a 95% yield of N-isopropylphthalimide (78) was indicated by an nmr spectrum, and 77% was isolated by column chromatography. Attempts by Gabriel\textsuperscript{23} or by Muller and Rieck\textsuperscript{45} to prepare 78 from isopropyl bromide and potassium phthalimide involved high temperatures (190°) and/or long hours (up to twenty), and resulted in disappointingly low yields (40%).
Several other secondary alkyl bromides have been used, but again if the reactions were successful, the yields were low.$^{22}$ In contrast, the desulfurization reaction proceeded instantaneously and at room temperature. Although more sulfoximides (12) in which R is secondary should be studied before generalizing, it appears that, via desulfurization of N-(secondary alkylthio)phthalimides by tris(dimethylamino)phosphine (38), the scope of the Gabriel reaction has been indirectly expanded to include secondary carbon systems.

\[
\begin{array}{c}
\text{O} \\
\text{N-S-R} \\
\text{O}
\end{array}
\]

12

The major difficulty encountered in the desulfurization reactions was the separation of the N-alkylphthalimide from tris(dimethylamino)phosphine sulfide (41). The high polarity of the phosphine sulfide caused the crude reaction mixture to be soluble in solvents from low to high polarity. Because most literature references report recrystallization of N-alkyl-phthalimides from ethanol, and because the phosphine sulfide was soluble in hexane, the crude reaction mixture was dissolved in boiling hexane and quickly cooled in an ice-salt water bath to afford crystals of the N-alkylphthalimide, which were contaminated with phosphine sulfide to an extent varying from ten to thirty percent (nmr analysis). Thus, since crystallization proved less than ideal in most cases (N-benzylphthalimide (77) was the exception), another method
of separation, thin layer chromatography, was tried. However, although alumina and silica gel plates and a variety of solvent systems were tried, the two products did not separate. Even in the solvent system hexane-ethyl acetate, 10:1, (which has been found to readily separate phosphine sulfide from disulfides and sulfides), the two compounds moved together. When this solvent mixture was made acidic by bubbling gaseous hydrogen chloride into it, the result was the retention of phosphine sulfide at the origin while the N-alkylphthalimide moved almost with the solvent front. In order to transfer this separation system to column chromatography, the alumina used had to be saturated with gaseous hydrogen chloride. (Woelm acidic alumina was employed but it gave no separation); however, such stringent conditions caused partial hydrolysis of the N-alkylphthalimide and the maximum yield of pure product obtained was only 77% (compared to the quantitative yield indicated by nmr analysis).

Two other methods of purification might be attempted. Ion exchange chromatography, using a strong-acid cation exchanger resin, might effect absorption of the phosphine sulfide on the resin, while the N-alkylphthalimide would be unaffected. However, partial hydrolysis of the N-alkylphthalimide by the strong-acid cation resin, which would be required because of the weak basicity of the phosphine sulfide, might be predicted. Probably the most promising method would be preparative gas-liquid chromatography, for on a LAC column, phosphine sulfide and N-alkylphthalimides were well separated, the former having the shorter retention time.
N-(t-Butylthio)- (68), and N-(cyclohexylthio)- (67), phthalimides were found to undergo desulfurization, but isobutylene and cyclohexene along with substantial amounts of phthalimide (86) were formed. The corresponding N-t-butyl- and N-cyclohexyl phthalimides were not detected. The two aromatic sulenimides, N-(phenylthio)- (70), and N-(p-tolyl thio)- (69), phthalimides, did not undergo desulfurization, but instead, formed the phosphonium salts 87, and 88, respectively. A signal at -59.1 ppm ($^{31}$P nmr) from
H$_3$PO$_4$ for 87\textsuperscript{51} and the appearance of a doublet ($J = 2$ cps) for the aromatic methyl group in 88\textsuperscript{47} by $^1$H nmr verify the existence of such salts.

The preceding results are readily explained by considering the following mechanism:
If R were hindered (i.e. cyclohexyl or t-butyl), elimination rather than substitution on the R group would occur at the phosphonium salt stage (89) resulting in phthalimide (86), the corresponding alkene (91) (90), and tris(dimethylamino) phosphine sulfide (41):

\[
\begin{align*}
\text{Phthalimide (86)} & \quad \text{Corresponding Alkene (91)} & \quad \text{Tris(dimethylamino) Phosphine Sulfide (41)}
\end{align*}
\]
It is also known that cycloalkyl halides undergo $S_N^2$ reactions slowly with $E_2$ reactions predominating. If, however, $R$ were aromatic the phosphonium salt would be isolated since desulfurization would require an unlikely nucleophilic displacement on an unactivated aromatic ring.

Evidence for the phosphonium salt intermediate (89) proposed in the general reaction mechanism was obtained by treating the authentic phosphonium salt, tris(diethylamino) benzylthio phosphonium fluoroborate (79), with potassium phthalimide under the same conditions (nitrogen atmosphere, sodium-dried benzene) as those used for the sulphenimide-aminophosphine reactions. Potassium phthalimide, on addition to a solution of 79, should attack the benzylic carbon eliminating phosphine sulfide and producing N-benzylphthalimide (77) (path i). The reverse reaction (path ii) should also be possible, where the phthalimide anion would attack the sulfur atom yielding benzylsulphenimide (62), and phosphine.

\[
\begin{align*}
\text{77} & \quad (\text{Et}_2\text{N})_3\text{P}=\text{S} \\
\text{62} & \quad + \quad (\text{Et}_2\text{N})_3\text{P} : \quad + \quad \text{KBF}_4 \\
& \quad + \quad (\text{Et}_2\text{N})_3\text{P-BF}_3 \quad + \quad \text{KF}
\end{align*}
\]
Reaction of the phosphine with sulfenimide 62 could then lead to 77; but, it has been shown that phosphine reacts preferentially with potassium fluoroborate producing a black precipitate (92). In addition to the lack of evidence of a black precipitate, the nmr spectrum of the reaction mixture gave no singlet at 5.86 \( \tau \) indicative of sulfenimide 62 (nor was the doublet of the fluoroborate salt, 79, present) but did, however, show a singlet at 5.16 \( \tau \) which compares with an authentic sample of 77 at 5.10 \( \tau \). It was, therefore, assumed that reaction was predominantly via path i.

N-(Carbomethoxythio)- (71), and N-(benzothiazole - 2-thio)- (72) phthalimides underwent anomalous reactions when treated with the aminophosphine.

![Chemical structures](image)

It was hoped that sulfenimide 71 would desulfurize to give N-carbomethoxyphthalimide (93) so that subsequent hydrolysis would afford the amino acid, glycine (94). Although carbomethoxydisulfide and trisulfide on treatment
with aminophosphine desulfurize instantaneously to yield the corresponding sulfide $^{18}$ and disulfide $^{55}$, respectively, the sulfinimide $^{71}$ did not undergo the expected desulfurization to the N-substituted phthalimide $^{93}$. Instead, phthalimide (86) was isolated in 90% yield and phosphine sulfide (41) was formed in 96% yield (nmr analysis); gas-liquid chromatographic analysis showed a small amount of phosphine (38), phosphine sulfide, phthalimide (or sulfinimide; both had the same retention time), and an unidentified, low boiling peak. Two possible schemes, resulting in the same products, can be proposed.
\[(\text{CH}_3)_2\text{N}\]_3^P: \rightarrow \begin{array}{c}
\text{CH-CO}_2\text{CH}_3 \\
\text{CH-CO}_2\text{CH}_3
\end{array} \rightarrow \\
\begin{array}{c}
\text{CHCO}_2\text{CH}_3 \\
\text{CHCO}_2\text{CH}_3
\end{array} \rightarrow 41 + 96
Precedence for ylid 95 was found in the existence of ylid 99:56

![Chemical structure](image)

The reaction of episulfides, e.g. 98, with tertiary phosphines has been reported to lead to the phosphine sulfide and corresponding olefin.57,61a However, the products proposed, 96 and 98, did not satisfy the property of being low boiling compounds having a retention time less than that of benzene. At present, the problem is still unresolved.

The reaction of N-(benzothiazole - 2 - thio) phthalimide (72) with tris(dimethylamino)phosphine was equally as intriguing and confusing as the reaction of N-(carbomethoxythio)phthalimide and phosphine. Analysis of the reaction mixture by glc indicates that phosphine oxide (100) is formed.

![Chemical structure](image)

green solution $\rightarrow^O_2$ blue solution, $(CH_3)_2N)_3P=N=NCH_3$* reflux

* May possibly be the phosphonium salt 89, $R = N\begin{array}{c}S\end{array}$
Phosphine oxide (100) has been shown to be the result of the reaction of phosphite and phthalic anhydride (101).

\[ \text{Phosphite} \rightarrow \text{Phosphine oxide} \]

Why attack at oxygen in sulfenimide 72 should have been preferred is not well understood, especially in light of the fact that the 2-position in the benzothiazole moiety is highly reactive toward nucleophilic attack. 61b

Much more work is required (including absolute assurance of the purity of the starting sulfenimides 72) before this problem can be unravelled. Because of the high reactivity of sulfenyl chlorides, the types of sulfenimides that could be employed were somewhat limited. For
example, unsaturation or active hydrogen atoms react readily with sulfenyl chlorides and therefore must be excluded from the R moiety of the sulfenyl chloride. In an effort to expand the class of sulfenimides to include multifunctional groups within R, an attempt to adapt the method of Dunbar and Rogers (the reaction of thiosulfonate and amine to yield a sulfenamide (7) to the synthesis of sulfenimides (12) was made. The thiol sulfonate (6) derived from the corresponding alkyl halide and potassium p-tolylthiolsulfonate, when heated with phthalimide would hopefully yield the desired sulfenimide. In this manner, R groups unaccessible via disulfides or thiols (which are required for the

\[
\begin{align*}
\text{R-S-Cl} \\
19 \\
20 \\
21
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C-S-S-K}^+ + \text{R-X} & \rightarrow \text{H}_3\text{C-S-PH}_{\text{SR}} + \text{N}^\text{5-R} \\
6 & \rightarrow
\end{align*}
\]

\[
\begin{align*}
\text{R} = \text{CH}_2\text{CH} = \text{CH}_2 & \quad (102) \\
= \text{CH}_2\text{CH}_2\text{OCH} = \text{CH}_2 & \quad (103)
\end{align*}
\]
sulfenyl chloride preparation), were possible and it was hoped that sulfenimides such as [102 and 103 could thus be obtained. As a trial experiment, the preparation of benzyl sulfenimide (62) from benzyl p-tolyliolsulfonate (63) and phthalimide was attempted. After two days at reflux in 95% ethanol, 80% of the starting thiosulfonate (63) and 88% of phthalimide were recovered. This method of preparation

\[
\begin{align*}
\text{63} & \quad + \quad \text{86} \\
\text{62}
\end{align*}
\]

thus did not appear applicable to the synthesis of sulfenimides.

An attempt directed towards the desulfurization of a sulfenamide (7) to an amine (higher in substitution) was tried.

\[
\begin{align*}
\text{7} & \quad \xrightarrow{?} \quad \text{41}
\end{align*}
\]
If this reaction were successful, then a potentially useful synthesis of secondary and tertiary unsymmetrical amines would be possible.

\[
\begin{align*}
R'NH_2 & \rightarrow RR'NH \rightarrow R-N-R'' \\
R_2NH & \rightarrow R_2N-R'
\end{align*}
\]

N-(Benzylthio)morpholine (81) and tris(dimethylamino) phosphine were combined, dissolved in benzene, and refluxed. After four days, the reaction mixture became yellow, indicating that a reaction had occurred. Analysis of the reaction mixture by nmr and by glc indicated a mixture of products had formed which included morpholine (82), phosphine sulfide (41), phosphine oxide (100), unreacted sulfenamide (81), a trace of unreacted phosphine (38), and several, smaller, unidentified peaks.
The most interesting products were morpholine (82) and phosphine sulfide (41). It is difficult to explain the formation of morpholine 82, and only speculation is possible until a more detailed investigation is made. The problem is as yet unresolved.

The initial step of the desulfurization reaction of sulfen-imides essentially involves an $S_N^2$ reaction with the phthalimide anion serving as an excellent leaving group, and the phosphine as the nucleophile. Retaining the good leaving group, phthalimide, but changing the nucleophile to a thiol led to the production of unsymmetrical disulfides.

\[
\begin{align*}
N-(\text{Phenylthio})\text{phthalimide (70)} \quad \text{and benzyl mercaptan (104)} \quad \text{afforded a} \\
greater than 90\% \text{ yield of benzyl phenyl disulfide (80)} \quad \text{(glc analysis);} \\
\text{but, under similar reaction conditions, } N-(\text{benzylthio})\text{phthalimide (62)} \\
\text{and phenyl mercaptan (105) yielded a mixture, in approximately equal} \\
\text{amounts, of unsymmetrical disulfide } 80, \text{ phenyl disulfide (106), and} \\
\text{benzyl disulfide (107). The results were rationalized by considering} \\
\text{the } pK_a\text{'s of the weak acids involved, the thiols and phthalimide.}
\end{align*}
\]
If the thiol has a pKₐ greater than the pKₐ of phthalimide, (8.3), nucleophilic substitution on the sulfenimide should proceed smoothly to give the unsymmetrical disulfide. If, on the other hand, the pKₐ of the thiol is less than 8.3, the products should be a mixture of symmetrical and unsymmetrical disulfides. Benzyl mercaptan (104) and thiophenol (105) have pKₐ values of 9.43 and 6.52 (or 7.78), respectively, and thus the following equilibria are expected.
The small amount of phenyl mercaptide (109) would cause disulfide interchange and its probable presence in the reaction between sulfenimide and phenyl mercaptan (105) would give the mixture of products obtained.

If the sulfenimide were prepared from N-chlorophthalimide and disulfide (Büchel and Conte's method), and then reacted with a mercaptan, it would be possible to thus proceed from a symmetrical to an unsymmetrical disulfide in good yield.
Although the fragmentation patterns in the mass spectrometer of phthalimide and a few N-alkyl/arylphthalimides have been reported, there has been no report of the fragmentation patterns of N-(substituted thio)phthalimides. Consequently, a general study of the mass spectra of the sulfenimides was undertaken. Presented here is a brief description of the possible fragmentations that could have given rise to the major peaks found for the sulfenimides after bombardment in the mass spectrometer. The inferences and conclusions culled from the spectra could be refined and elaborated by more detailed studies including isotope labeling, exact mass measurements, and calculation of metastable peaks.

There were five mass peaks commonly found in all the sulfenimides studied; the few exceptions have been noted in context with the peak concerned. These common mass peaks were 148, 147, 130, 104, and 76, and may be accounted for by the following sequences:

1/ $\text{N-S} \rightarrow \text{NR-S} \rightarrow \text{NR-S+H}\overset{\cdot}{\text{C}}\overset{\cdot}{\text{H}}$  
   a, m/e 148

2/ $\text{N-S} \rightarrow \text{NR-S} \rightarrow \text{NR-S+H}\overset{\cdot}{\text{C}}\overset{\cdot}{\text{H}}$  
   b, m/e 147

$\text{NR-C} \rightarrow \text{NR-C-CN} \rightarrow \text{NR-C-CN}$  
   c, m/e 130

$\text{NR-C-CN} \rightarrow \text{NR-C-CN-CO}$  
   d, m/e 104

$\text{NR-C-CN-CO} \rightarrow \text{NR-C-CN-CO}$  
   e, m/e 76
Peak a, m/e 148, is not found to any significant extent (greater than 10%) in N-(phenylthio)- (70), N-(p-tolythio)- (69), and N-(benzothiazole-2-thio)- (72), phthalimides. Peak c, m/e 130, is present in N-(benzythio)- (62) and N-(benzothiazole-2-thio)phthalimides to an extent of only 3%; it was not found at all in phthalimide.

In all cases the parent peak was visible, varying from less than 1% (e.g. N-(n-butythio)- (65) and N-(carbomethoxythio)- (71) phthalimides) to 100% (N-(phenylthio)-, N-(p-tolylthio)phthalimides).

N-(Ethylthio)phthalimide (64) has as its base peak m/e 148, (a), which most likely arises from fragmentation as shown in sequence (1). The major peaks are c, m/e 130, 46%; d, m/e 104, 25%; e, m/e 76, 30%; and f, m/e 60, 37%.

The other primary alkyl sulfinimide, N-(n-butythio)phthalimide (65) has g, m/e 88, as its base peak, while a is present in 48%. Other major peaks include c, 32%; d, 29%; e, 41%; f’, 41%; and h, m/e 55, 43%.
N-(Benzylthio)phthalimide, an arylalkyl sulfinamide with a primary carbon linkage to the sulfinyl sulfur, gives tropylmion, i, m/e 91, as its base peak. In addition to the common peaks a, 7%; b, 6%; c, 3%; d, 24%; and e, 22%, there were two other mass peaks, j, m/e 65, 22%; and k, m/e 122, 52%, which probably arise as follows:

* Analogous to the McLafferty Rearrangement⁶⁴
The last primary alkyl sulfenimide studied was \( N\)-(carbomethoxythio)phthalimide \(71\). The base peak, m/e 76, could have arisen from two possible fragments, \( m \) and \( \epsilon \), but an exact mass measurement of 76.0313 ± 0.0003 eliminated \( m \).

\[
\begin{align*}
\text{\( m \), m/e 76; exact mass 75.9983} \\
\end{align*}
\]
The secondary, tertiary, and cycloalkyl sulfenimides, N-(isopropylthio)- (66), N-(t-butylthio)- (68), and N-(cyclohexylthio)- (67) phthalimides, all show a base peak, m/e 179, which most likely comes about from the fragmentation necessary to yield the corresponding olefin.
Isopropylsulfenimide (66) gave, in addition to the usual mass peaks of a, 75%; b, 24%; c, 25%; d, 53%; and e, 66%, peaks p, m/e 189, 30%; q, m/e 43, 38%; r, m/e 41, 54%; and s, m/e 74, 61%

The base peak, o, dominates the spectrum of N-(t-buty1thio) phthalimide (65). The universal peaks, a through e, are present in less than 20%. In contrast, because of the availability of fragments from cyclo-
hexane, \( \text{N}(\text{cyclohexylthio}) \text{phthalimide (67)} \) has many strong peaks in addition to \( a, 18\%; b, 33\%; c, 20\%; d, 70\%; \) and \( e, 87\% \).

The base peak and the parent molecular ion are the same in the two aromatic sulenimides. \( \text{N}(\text{Phenylthio})\text{phthalimide} \) on electron impact produced the common peaks \( b \) through \( e \) in 15\%, 28\%, 37\%, and 53\% respectively and also \( w, \text{m/e 109}, 45\% \), as follows:

\[
\begin{align*}
&\text{N}(\text{cyclohexylthio})\text{phthalimide (67)} \\
&\text{N}(\text{Phenylthio})\text{phthalimide}
\end{align*}
\]
N-(p-Tolylthio)phthalimide follows similarly with the common peaks a little stronger; b, 44%; c, 26%; d, 58%; and e, 78%. The tropylium ion was also noted in 24% relative intensity.

The heteroaromatic sulfenimide, N-(benzothiazole-2-thio)phthalimide (72) gave a mass spectrum similar to that of phthalimide with m/e 147 as the base peak, not its molecular ion m/e 312 (7%) as might have been predicted on the basis of the patterns of the previous two aromatic sulfenimides. As doubt existed about the purity of this compound, no final conclusions can or should be made about the identity of such fragments.

In summary, the chemistry of an hitherto uninvestigated and interesting class of sulfur compounds, N-(substituted thio) phthalimides, has been studied. It has been found that a variety of these compounds underwent desulfurization by tris(dimethylamino) phosphine to afford the corresponding N-substituted phthalimides in good yield. In addition, the reaction of a sulfenimide and thiol may provide another route to the
synthesis of unsymmetrical disulfides. Two anomalous but intriguing reactions, involving the reaction of aminophosphine with N-(carbomethoxy-thio)-, and N-(benzothiazole-2-thio)phthalimides, have been discovered. and should provide useful further studies.
### Table 1 - Preparation of Sulfenyl Chlorides

<table>
<thead>
<tr>
<th>Sulfenyl Chloride</th>
<th>Method of Preparation</th>
<th>Yield</th>
<th>bp</th>
<th>Ref.</th>
<th>Purity Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>R-S-Cl (19)</td>
<td>R =</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH₃CH₂⁻</td>
<td>50</td>
<td>A</td>
<td>66.5</td>
<td>26-7°C</td>
<td>32 nmr; n²D 1.484 (lit.² D 1.499)</td>
</tr>
<tr>
<td>(CH₃)₂CH⁻</td>
<td>51</td>
<td>A</td>
<td>66</td>
<td></td>
<td>33 nmr</td>
</tr>
<tr>
<td>CH₃(CH₂)₂CH₂⁻</td>
<td>59</td>
<td>B</td>
<td>100</td>
<td>c</td>
<td>33 nmr</td>
</tr>
<tr>
<td>(CH₃)₃C⁻</td>
<td>53</td>
<td>A</td>
<td>85ᵃ</td>
<td>b,c</td>
<td>12⁻</td>
</tr>
<tr>
<td>C₆H₅CH⁻</td>
<td>52</td>
<td>A</td>
<td>100</td>
<td>b,c</td>
<td>34 nmr</td>
</tr>
<tr>
<td>C₆H₆⁻</td>
<td>61</td>
<td>C</td>
<td>80</td>
<td>69⁻-70°C/7mm.</td>
<td>42 nmr; bp</td>
</tr>
<tr>
<td>H₃C-C₆H₅⁻</td>
<td>60</td>
<td>C</td>
<td>62</td>
<td>56⁻-57°C/0.15mm.</td>
<td>42 nmr; bp</td>
</tr>
<tr>
<td>CH₂OC-CH₂₀</td>
<td>54</td>
<td>A</td>
<td>100ᵃ</td>
<td>c</td>
<td>8⁻</td>
</tr>
<tr>
<td>-CH₂(CH₂)₂CH₂⁻</td>
<td>55</td>
<td>A,B</td>
<td>100,100</td>
<td>c</td>
<td>e nmr</td>
</tr>
<tr>
<td>Cl₂</td>
<td>56</td>
<td>A</td>
<td>100ᵃ</td>
<td>c</td>
<td>e nmr?</td>
</tr>
</tbody>
</table>

ᵃ assumed, on basis of literature reference ¹²
ᵇ decomposed on distillation
ᶜ not isolated
ᵈ attempts to isolate led to rapid decomposition to starting disulfide
ᵉ unreported
TABLE 2
PREPARATION OF N-(ALKYL/ARYL THIO)PHthalIMides

<table>
<thead>
<tr>
<th>Sulfenimide</th>
<th>Reaction</th>
<th>Solvent</th>
<th>mp</th>
<th>Yielda</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Chemical Structure" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R =</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH₃CH₂⁻</td>
<td>64</td>
<td>DMF</td>
<td>116-117°</td>
<td>65.4</td>
<td>8</td>
</tr>
<tr>
<td>CH₃(CH₂)₂CH⁻</td>
<td>65</td>
<td>CCl₄</td>
<td>66-67°</td>
<td>57</td>
<td>8</td>
</tr>
<tr>
<td><img src="image2" alt="Chemical Structure" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H</td>
<td>67</td>
<td>CCl₄</td>
<td>108-110°</td>
<td>73</td>
<td>8</td>
</tr>
<tr>
<td><img src="image3" alt="Chemical Structure" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(CH₃)₂CH⁻</td>
<td>66</td>
<td>DMF</td>
<td>65.5-68°</td>
<td>57.6</td>
<td>8</td>
</tr>
<tr>
<td><img src="image4" alt="Chemical Structure" /></td>
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<td></td>
</tr>
<tr>
<td><img src="image5" alt="Chemical Structure" /></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image6" alt="Chemical Structure" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image7" alt="Chemical Structure" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image8" alt="Chemical Structure" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image9" alt="Chemical Structure" /></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><img src="image10" alt="Chemical Structure" /></td>
<td></td>
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<td></td>
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<tr>
<td><img src="image11" alt="Chemical Structure" /></td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a. Although previous workers used DMF, CCl₄ may be the better reaction solvent; DMF's solvation power would make isolation of the product difficult and decrease yields.

b. Lit.⁸ reported mp 16°; recrystallization three times gave mp 167.5-168°; nmr spectra are identical.

c. Literature procedure followed exactly; used phthalimide and triethyl amine, not potassium phthalimide.

d. Lit.⁸ 93-94°; recrystallization from n-hexane gave mp 109.5-11°; calc.: C: 64.4; H: 5.79; N: 5.36; found: C: 63.0; H: 5.41; N: 5.16.
TABLE 2 - continued -

<table>
<thead>
<tr>
<th>Sulfenimide</th>
<th>No.</th>
<th>Solvent</th>
<th>mp</th>
<th>Yield</th>
<th>Ref.</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH&lt;sub&gt;3&lt;/sub&gt;O-CH&lt;sub&gt;2&lt;/sub&gt;-</td>
<td>71</td>
<td>CCl&lt;sub&gt;4&lt;/sub&gt;</td>
<td>9124-126°/190°</td>
<td>56</td>
<td>f</td>
</tr>
<tr>
<td><img src="image" alt="Sulfenimide Structure" /></td>
<td>72</td>
<td>CCl&lt;sub&gt;4&lt;/sub&gt;</td>
<td>h150-152°; 180-182°</td>
<td>85</td>
<td>f</td>
</tr>
<tr>
<td>-CH&lt;sub&gt;2&lt;/sub&gt;(CH&lt;sub&gt;2&lt;/sub&gt;)CH&lt;sub&gt;2&lt;/sub&gt;-</td>
<td>74</td>
<td>DMF;CCl&lt;sub&gt;4&lt;/sub&gt;</td>
<td>unsuccessful</td>
<td>f</td>
<td></td>
</tr>
<tr>
<td><img src="image" alt="Sulfenimide Structure" /></td>
<td>73</td>
<td>DMF;CCl&lt;sub&gt;4&lt;/sub&gt;</td>
<td>unsuccessful</td>
<td>f</td>
<td></td>
</tr>
</tbody>
</table>

<sup>e</sup> Attempts to prepare these compounds in DMF resulted only in dark oils and phthalimide and, in the case of 72, starting disulfide.

<sup>f</sup> Not reported.
TABLE 2 - continued -

<table>
<thead>
<tr>
<th>R</th>
<th>No.</th>
<th>Crystals</th>
<th>nmr</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂⁻</td>
<td>64</td>
<td>long, fluffy white crystals, n-hexane</td>
<td>CDCl₃: 8.72 (3H, t); 7.02 (2H, q); 2.05 (4H, m).</td>
</tr>
<tr>
<td>CH₃(CH₂)₂CH₂⁻</td>
<td>65</td>
<td>fine, silvery-white plates, CCl₄-hexane</td>
<td>CDCl₃: 9.02 (3H, m); 8.45 (4H, m); 7.13 (2H, t); 2.10 (4H, m).</td>
</tr>
<tr>
<td>CH₃⁻</td>
<td>62</td>
<td>fluffy, white crystals, CHCl₃-hexane</td>
<td>CDCl₃: 5.84 (2H, s); 2.70 (5H, s); 2.14 (4H, m).</td>
</tr>
<tr>
<td>(CH₃)₂CH⁻</td>
<td>66</td>
<td>silvery, white plates, CHCl₃-PE 30/60.</td>
<td>DMSO-d₅: 8.78 (6H, d); 8.60 (1H, d).</td>
</tr>
<tr>
<td>(CH₃)₃C</td>
<td>68</td>
<td>silvery, white plates</td>
<td>Benzene: 8.68 (9H, s); CDCl₃: 8.60; 2.12 (4H, m).</td>
</tr>
<tr>
<td>H₂C═CH</td>
<td>67</td>
<td>fine, white plates, CHCl₃-hexane</td>
<td>CDCl₃: 8.37 (10H, two broad peaks); 8.45 (1H, one broad peak); 2.08 (4H, d).</td>
</tr>
<tr>
<td>H₃C═CH</td>
<td>69</td>
<td>pale, yellow, granular</td>
<td>DMSO-d₅: 7.63 (3H, s); 2.58 (4H, d).</td>
</tr>
<tr>
<td>H₃C═CH</td>
<td>70</td>
<td>pale, yellow, granular</td>
<td>CDCl₃: 2.50, 2.17 (two sets of multiplets).</td>
</tr>
<tr>
<td>CH₃O-C-CH₂⁻</td>
<td>71</td>
<td>silvery, white, needles, CCl₄</td>
<td>DMSO-d₅: 6.50 (3H, s); 6.40 (2H, s); 2.93 (4H, s).</td>
</tr>
<tr>
<td></td>
<td>72</td>
<td>powder</td>
<td>CDCl₃: 2.64, 2.03 (two sets of multiplets).</td>
</tr>
</tbody>
</table>

g Spectral data include nmr, ir, ms; analysis: calc: C-52.6; H-3.59; N-5.58; found: C-51.3; H- .69; N-5.79.

h First preparation yielded a violet solid, mp. 180-184°; ir showed it not to be phthalimide nor starting disulfide. The second preparation yielded a pale, yellow, powdery solid, mp. 150-152°, which by ir was identical to the first prep. compound. The two crops were combined and recrystallization attempted using CCl₄, the melting points increased, then decreased; in addition, the melting was somewhat unusual in that the solid "shrank" without liquefaction. Calc.: C-58.1; H-2.58; N-8.97; S-20.5; found: C-59.2; H-3.04; N-8.09; S-18.08. The mass spectrum showed a peak at the appropriate molecular weight, 312 (7%).

i Attempts to prepare these compounds in either DMF (polar) or CCl₄ (non-polar) were unsuccessful. Attempts at 73 led only to recovery of starting disulfide and phthalimide; only phthalimide was identified in attempts to prepare the bisulfenimide, 74.
TABLE 3 - DESULFURIZATION REACTIONS OF N-(ALKYL/ARYLTHIO)PHTHALIMIDES

<table>
<thead>
<tr>
<th>Sulfoximide</th>
<th>No.</th>
<th>N-substituted phthalimide</th>
<th>nmr</th>
<th>isolation</th>
<th>% [(CH₃)₂N]P=S</th>
<th>Phthalimide</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHT-SCH₂CH₃</td>
<td>64</td>
<td>100</td>
<td>75</td>
<td>± 6</td>
<td>73</td>
<td>64</td>
</tr>
<tr>
<td>PHT-S(CH₃)₃</td>
<td>65</td>
<td>100</td>
<td>46</td>
<td>± 4</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>PHT-SCH₂CH₂</td>
<td>62</td>
<td>93</td>
<td>87</td>
<td>± 1</td>
<td>87</td>
<td>62</td>
</tr>
<tr>
<td>PHT-SCH(CH₃)₂</td>
<td>66</td>
<td>95</td>
<td>77</td>
<td>± 8</td>
<td>77</td>
<td>66</td>
</tr>
<tr>
<td>PHT-S-</td>
<td>67</td>
<td></td>
<td>75</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHT-SC(CH₃)₃</td>
<td>68</td>
<td>100</td>
<td>86</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHT-S-</td>
<td>70</td>
<td>c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHT-S-</td>
<td>69</td>
<td>c</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHT-SCH₂COCH₃</td>
<td>71</td>
<td>96 ± 4</td>
<td>90</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PHT-S-</td>
<td>72</td>
<td></td>
<td>44</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

a column chromatography
b crystallization
c phosphonium salt formed
d unreacted phosphine indicated by glc
e [(CH₃)₂N]₃P nmr (neat): 7.55 d; (benzene): 7.52 d.
[(CH₃)₂N]₃P=S nmr (CCl₄): 7.35 d; (benzene): 7.53 d.
## TABLE 4 - MASS SPECTRA OF N-ALKYL/ARYL THIOPHTHALIMIDES

<table>
<thead>
<tr>
<th>Sulfenimide</th>
<th>No.</th>
<th>Base Peak</th>
<th>Major Peaks</th>
<th>Parent Peak</th>
</tr>
</thead>
<tbody>
<tr>
<td>PHT-H</td>
<td>86</td>
<td>147</td>
<td>104, 76, 50</td>
<td>147</td>
</tr>
<tr>
<td>PHT-S-CH₂CH₃</td>
<td>64</td>
<td>148</td>
<td>130, 60, 76, 104, 147, 50, 207</td>
<td>207</td>
</tr>
<tr>
<td>PHT-S-(CH₃)₃CH₃</td>
<td>65</td>
<td>88</td>
<td>148, 55, 60, 76, 41, 130, 104, 50, 179, 147</td>
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</tr>
<tr>
<td>PHT-S-CH₂CH=CH₂</td>
<td>62</td>
<td>91</td>
<td>122, 104, 76, 65, 45, 50, 39, 148, 147</td>
<td>269</td>
</tr>
<tr>
<td>PHT-S-CH(CH₃)₂</td>
<td>66</td>
<td>179</td>
<td>148, 76, 74, 41, 104, 43, 50, 39, 189, 151, 130, 221</td>
<td>221</td>
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<tr>
<td>PHT-S-CH₃</td>
<td>67</td>
<td>179</td>
<td>76, 114, 104, 50, 67, 81, 147, 151, 130, 228, 261</td>
<td>261</td>
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<tr>
<td>PHT-S-C(CH₃)₃</td>
<td>68</td>
<td>179</td>
<td>41, 76, 104, 50, 235, 147, 130, 148</td>
<td>235</td>
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<tr>
<td>PHT-S-CCH₃</td>
<td>70</td>
<td>255</td>
<td>76, 109, 104, 50, 130, 147</td>
<td>255</td>
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<tr>
<td>PHT-S-CH₂CH₃-C-OCH₃</td>
<td>69</td>
<td>269</td>
<td>76, 104, 123, 147, 50, 45, 130, 91</td>
<td>269</td>
</tr>
<tr>
<td>PHT-S-CCH₂-C-OCH₃</td>
<td>71</td>
<td>76</td>
<td>104, 147, 50, 103, 148, 130</td>
<td>251</td>
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<tr>
<td>PHT-S-N=S</td>
<td>72</td>
<td>147</td>
<td>76, 104, 50, 267, 312</td>
<td>312</td>
</tr>
</tbody>
</table>
FIGURE 1

NMR Spectra of 2-Pyridyl disulfide (I) and 2-Pyridyl sulfenyl chloride (II)

offset 200 cps
FIGURE 2

NMR Spectra of Benzothiazole-2-disulfide (I) and N-(Benzothiazole-2-thio)phthalimide (II)
FIGURE 3

IR Spectra of Phthalimide, Benzothiazole-2-disulfide, and N-(Benzothiazole-2-thio)phthalimide

[Graph showing IR spectra for each compound]
FIGURE 4
Spectral Data for N-(Carbomethoxythio)-phthalimide
FIGURE 5

NMR Spectra of Carbomethoxydisulfide and Carbomethoxy sulfenyl chloride

\[
\text{(CH}_3\text{O-CH}_2\text{-S)}_2
\]

\[
\text{CH}_3\text{O-CH}_2\text{-Scl}
\]
FIGURE 6

Spectral Data for Tris(diethylamino)-benzylthio-phosphonium Tetrafluoroborate, (79)

$\text{(Et}_2\text{N)}_3\text{P-S-CH}_2\text{-C}_6\text{H}_5-\text{BF}_4$
Mass Spectra of the Sulfenimides

PHT-S-CH₂CH₃

PHT-S-(CH₂)₃CH₃

PHT-S-CH₂-C₆H₅
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and Roberts, P.W., J.Org.Chem. 26, 1152 (1961);
Field, L., Harle, H., Owen, T.C., and Feiretti, A., J.Org.Chem. 29, 1632, (1964);


30. Note added in proof: Since preparation of this manuscript, a communication on this work has been published:


31. Ethyl sulfenyl chloride and tetramethylene disulfenyl chloride; see Introduction.


34. Emde, H., German patent 804572; Chem.Abstr. 46, 5291, (1952).

35. Courtesy of D.Ash, McGill University; bp. 106-107°; nmr (CCl₄):

6.35 (2H, s); 6.22 (3H, s).


40. U.S. Patent 2,257,974; Chem. Abstr. 36, 930, (1942); 37, 2746, (1943). Compound was reported as a solid, mp. 132-135°, with decomposition; from the disulfide and chlorine.

41. Prepared by P. Mathiaparanam, McGill University. Addition to 1, 3, 2-dioxaphospholene gave 93% of the desired adduct; thus conversion and purity of the sulfenyl chloride, 58, were assumed to be quantitative.


49. Note added in proof: Since preparation of this manuscript a communication on this work has been published, Harpp, D.N. and Orwig, B.A., Tetrahedron Letters, 1970, 2691.

50. Gleason, J. and Ash, D., McGill University, unpublished results.


54. Gleason, J., McGill University, private communication.

55. Ash, D., McGill University, unpublished results.


63. Ibid, p. 20.