PROJECT ADMINISTRATION DATA SHEET

Project No. G-33-NO3

Project Director: Dr. Edward Burgess

Sponsor: NEU/PHS/NIH-National Institute of General Medical Sciences

Type Agreement: Grant No. 5-ROI-GM-12677-12

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Title: The Chemistry of New Functional Groups

ADMINISTRATIVE DATA

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RESTRICTIONS

See Attached N/A Supplemental Information Sheet for Additional Requirements.

Travel: Foreign travel must have prior approval — Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category.

Equipment: Title vests with N/A — none proposed

COMMENTS:

Year 12 - Prior Project No. was G-33-NO3/Burgess
Project Title: The Chemistry of New Functional Groups in Enzymes
Project No: G-33-N04
Project Director: Edward M. Burgess
Sponsor: HHS/PHS/NIH - National Institute of General Medical Sciences

Effective Termination Date: 5/31/83 (12th year)
Clearance of Accounting Charges: 5/31/83
Grant/Contract Closeout Actions Remaining:

- [ ] Final Invoice and Closing Documents
- [ ] Final Fiscal Report
- [ ] Financial Status Report (ROE)
- [ ] Final Report of Inventions
- [X] Govt. Property Inventory & Related Certificate
- [ ] Classified Material Certificate
- [ ] Other

Project is follow-on to G-33-N03

Assigned to: Chemistry (School/Laboratory)

COPIES TO:
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Research Property Management Accounting
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Wittig Reactions of Thione Methylides. The Synthesis of 13-cis Retenoic Acid

We have optimized the conditions for reaction of the ylide, 1, (generated in situ) with ketones. In model studies, using DBU as the base and acetonitrile solvent the stereochemistry of the quasi-Wittig is predominately cis (cis/trans, 3:1).

Extension of this reaction to 13-cis retenoic ester, 2, gave the stereoisomeric products in a cis/trans ratio of 2:1. LiBu₄ was added in an attempt to increase the amount of cis-product as had been previously observed in the reaction of 1 with aldehydes. Since the reaction of 1 with ketones is much slower than with aldehydes the added salt resulted in demethylation.
2. **New Wittig Reagents**

We have made considerable progress in studies of the Wittig Chemistry of the two new classes of 1,3-dipoles, Phosphine S-methylides and Phosphine Semethylides:

\[
\begin{align*}
R_3P-S-\overset{\ddot{\varepsilon}}{\text{CH}}R' \\
R_3P-\overset{\ddot{\varepsilon}}{\text{Se}}-\overset{\ddot{\varepsilon}}{\text{CH}}R'
\end{align*}
\]

The requisite precursor salts were obtained via reaction of the phosphine sulfide or selenide with iodacetic ester in the presence of aqueous sodium fluoroborate. Deprotonation of these salts with sodium methoxide, sodium hydroxide or DBU gave the transient ylides, 14 or 15, which react readily with aldehydes to give the corresponding substituted α,β-unsaturated ester in 70-80% yield.

Studies on the reaction of the title ylides with aldehydes found the stereochemistry of the acrylate ester product to be a function of the method of generating the ylide (below).

\[
\begin{align*}
\text{[\{(CH_3)_2N\}_3P-X^- + \text{BrCH}_2\text{CO}_2\text{CH}_3} \\
\text{R= NMe}_2 \\
\text{R' = CO}_2\text{Et}
\end{align*}
\]

\[
\begin{align*}
\text{[\{(CH_3)_2N\}_3P-X^- + \text{BrCH}_2\text{CO}_2\text{CH}_3} \\
\text{R= NMe}_2 \\
\text{R' = CO}_2\text{Et}
\end{align*}
\]

\[
\begin{align*}
\text{X=Se} & \\
\text{X=S}
\end{align*}
\]

\[
\begin{align*}
\text{[(CH}_3\text{)}_2\text{N\}_3\text{P-XCH}_2\text{CO}_2\text{CH}_3} & \text{ Br}^- \\
\text{R= NMe}_2 \\
\text{R' = CO}_2\text{Et}
\end{align*}
\]

A. DBU, CH$_3$CN  
B. DBU, CH$_3$CN, LiI  
C. NaOH, H$_2$O, CH$_2$Cl$_2$, Et$_3$BuN Cl$^-$  
D. NaOEt, EtOH
Thus, a stereospecific formation of either isomer may be selected using as variables the central atom of the ylides or its method of preparation. Interestingly, ylides generated with ketone stabilizing substituents (rather than ester) undergo the following internal rearrangement and fragmentation faster than reaction with an external aldehyde. We can offer no explanation for this.

In another study, we attempted the isolation of a phosphine sulfide methylide, however, after a few hours in solution this ylide underwent rearrangement to

Finally, in an attempt to generate an isolable hypervalent species:
we subjected tri-dimethylaminophosphine sulfide to bromination. The product isolated and characterized by x-ray crystallography is shown below.

\[ \text{[CH}_3\text{]}_2\text{N} \text{PO} - \text{S}^- \xrightarrow{\text{Br}_2} \text{P} - \text{S}^- \]

3. Oxidative Chemistry of Disulfides

The reaction of 1,3-dimethylimidazolthione (1) with 0.5 equivalent of bromine at 0°C in methylene chloride solution gives the disulfide, 2(\text{X=Br}), mp 240-241°C (dec.) as published in J. Amer. Chem. Soc. 99, 2376 (1977).

By suitable anionic exchange procedures various salts (\text{X=Cl}^-, \text{BF}_4^-, \text{OSO}_2\text{CF}_3^-) are available and the triflate salts have good solubility in acetonitrile and are suitable for aprotic solvent reactions. All salts are water soluble. When any one of these salts is dissolved in water the pH drops to 2. Evaporation of the water gives back quantitatively 2. Addition of base (sodium hydroxide, sodium carbonate, sodium bicarbonate) to the aqueous solutions of 2 gives dioxygen and 1. No intermediate could be detected by NMR analysis in D$_2$O. By polarography the onset of a detectable oxygen wave occurred at pH = 4.5 and the reaction is very fast at pH 6.0. Using a single cell consisting of two Pt-electrodes and an aqueous solution of a neutral electrolyte (such as NaCl) the potential across the electrodes was adjusted just below the threshold for visible gas formation at either electrode. Addition of 2 to this cell at this potential led to immediate formation of gasses at both electrodes. No quantitative measurement has been made of the efficiency (O$_2$ production vs. time vs. potential) in this cell with and without 2, but the above qualitative observation suggests that 1 may function as a catalysis for the electrolysis of water at advantageous cell voltages. It has been demonstrated that 1 is oxidized to 2 at a working anode in aqueous solution containing HCl at pH 1-2.
The exact mechanism of this reaction is unknown but the following observation suggest a few key intermediates. As a model the first step in the reductive hydrolysis of 2 may be in agreement with pH observation in water. The ability of a imidazolium substituent to stabilize hypervalent bonding at sulfur is discussed in the enclosed preprint. Action of base on 3 may give 4 which disproportionates to oxygen and I.

\[
\ce{2 + H2O &<=> N+\text{[N-H\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots]}^- + H^+ + \text{H}_2\text{O}} \\
\ce{N+\text{[N-H\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots]}^- + H^+ + \text{H}_2\text{O &<=> N+\text{[N-H\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots]}^- + \frac{1}{2} O_2 + \frac{1}{2} \text{H}_2}\text{O}}
\]

Simple sulfoxides, \(\text{R}_2\text{SO}_2\), are known to undergo disproportionation to sulfides, \(\text{R}_2\text{S}\), and sulfones, \(\text{R}_2\text{SO}_2\), at elevated temperatures and in the case of 4 this may be a facile reaction leading to 5. If this is the case then 5 must also rapidly give oxygen and I. In order to gain some support for this mechanistic model the action of various oxidizing agents on 1 to hopefully give 4 or 5 was investigated. In all cases examined (below) the oxidizing agent was catalytically converted to oxygen at fast rates even at low temperatures.

\[
\ce{1 \left\{ \begin{array}{c} \text{O}_2 \\ \text{H}_2\text{O} \\ \text{RCO}_2\text{H} \end{array} \right\} + \frac{1}{2} \text{O}_2 + \text{H}_2\text{O} + \text{RCO}_2\text{H}}
\]

However, if the oxidation of 1 was carried out at low pH with a percarboxylic acid the result was 2.

\[
\ce{1 + \text{RCO}_2\text{H} + \text{HCl \rightarrow 2 (x=\text{Cl}^-) + RC\text{O}_2\text{H}}}
\]

Even more esoteric methods of obtaining 4 led to a similar observation.

\[
\ce{\text{Na}^+ \text{OSi(CH}_3)_3 \text{Br}^- + \text{CH}_2\text{O} \rightarrow \text{Na}^+ \text{OSi(CH}_3)_3 \text{Br}^- + \text{CH}_2\text{O}}
\]

In other attempts to obtain 5 the reaction of lithio-derivative 6 with sulfur dioxide led to the formation of 1.

\[
\ce{\text{BuLi \rightarrow \text{Li}^+ \rightarrow \text{Li}^+ + \text{SO}_2 \rightarrow 1}}
\]
Details of this observation are discussed in the enclosed preprint.

We may conclude that 5 rapidly gives 1 and oxygen and that 4 may also give 1 and oxygen possibly via its transformation to 5. All of these reactions appear to proceed at rapid rates even at low temperatures and thus represent a reaction sequence with no large energy of activation single steps.

This class of reaction is not limited to 5. Oxidation of tris(dimethylamino) phosphine sulfide, 13, with NOBF4 gives a disulfide which also oxidizes water.

\[
\begin{align*}
\text{[\(\text{CH}_3\text{N}\)]}\_3\text{P}\_\text{s}{}^-\text{s}{}^-\text{P[\(\text{CH}_3\text{N}\)]}_3 & 2\text{X}^- \xrightarrow{\text{H}_2\text{O}} \text{[\(\text{CH}_3\text{N}\)]}_3\text{P}\_\text{s}{}^-\text{s}{}^- + \text{O}_2 \\
\text{[\(\text{CH}_3\text{N}\)]}_3\text{P}\_\text{s}{}^-\text{s}{}^- + \text{X}^- & \xrightarrow{-\text{H}_2\text{X}} \text{[\(\text{CH}_3\text{N}\)]}_3\text{P}\_\text{s}{}^-\text{s}{}^- + \text{O}_2 
\end{align*}
\]
Publications:

1. None in Print

2. The enclosed preprints are submitted to the J. Amer. Chem. Soc. (The Conversion of Thiourea Dioxides to Dioxygen) and the J. Org. Chem. (Substituent stabilized Thione S-Inides).

3. We contemplate a publication on the phosphine S- and Se- methylides as well as one on the retenoic acid study.
The Conversion of Thiourea Dioxide to Dioxygen

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Received

Abstract: Dimethylimidazole thione 2-H-dioxide has prepared thiourea
dioxide and 2-thionobis(2-thionobis(2-thionoimidazol) salt and found to dissolve in
hydrogen and the corresponding thione. H₂N-Bis(2-thionoimidazole) thione reacted to
the related thiourea and amide upon heating in acetonitrile solution.
Dimethylaminoiminomethane reacts with sulfur dioxide to produce bis
amidino sulfooxo sulfides. These reactions are discussed in terms of an
intermediate singlet sulfuroxane which fragments to thiourea dioxide via a
intersystem crossing process.

From both a biological and chemical viewpoint this general type of reaction of 1,2- and 1,3-diynes containing one or more carbon elements has received considerable recent attention. Prominent among these reaction intermediates are persulfites, 1, which result from the addition of an electrophilic reagent on sulfides or hydrogen peroxide or fluoro derivatives on sulfoxides. It has been shown that 1 (R = alkyl) has the ability to transfer an oxygen atom to sulfides to give sulfooxides and more radicals convert sulfides to sulfones. If 1 is derived from the sulfinyl sulfite its electrophilicity is sufficient to effect oxidation of alkenes in the absence of oxidizable reagents. 1 is ultimately converted into the sulfone, 3, possibly via the photocyclization product, the hydrogen thiodiazirane 2. From studies of the solvent effects on efficiency, an oxygen atom transfer the primary species present seems to be 1. However, when 1 (R = Ph) is generated via the sulfoxane route in the presence of a triplet energy acceptor such as 9,10-dibromanthracene, chemiluminescence or the latter is observed. This suggests that 3 is derived from 2 in a triplet state. Clearly, the reaction surface connecting 1 and 3 is most unique and deserves further study.

Employing rather Edisonian reasoning we were convinced of the possibility that the reaction above could be reversed exothermically. i.e., 3 → 2 → 0₂. If 3, by proper substitution, would have less thermodynamic stability than 2, such a reversal might be realized. With the knowledge that an electron acceptor substituent with an energetically low-lying unoccupied molecular orbital (LUMO) of the π-type attached to sulfur stabilizes a tricoordinate hypervalent sulfuroxane bonding array, a possible forward reaction might be the sequence 4 → 5 → 6. In this communication we wish to describe our observations on this strategy using an imidazolium or a dimethylamino group to properly adjust the carbonium ion substituent LUMO energy.
It has been reported that bisaminoethylcyclopropane and dimaminoethylcycloalkene salts may be lithiated by n-butyl lithium or the corresponding n-butyl lithium by n-butyl lithium at low temperatures to give substituted acyclic lithiumcarbenium ions which readily undergo SE reactions with water.

Following these observations, in order to prepare \( 4a \), we treated an anhydrous diethyl ether suspension of \( N,N' \)-dimethylamidobromide under an argon atmosphere with an excess of n-butyl lithium \((1.6 \text{ M in hexane})\) to give \( 7a \). After 6 hours at 30°C sulfur dioxide was introduced and upon standing for 24 hours unreacted starting material, lithium bromide, and \( 4a \) was isolated (quantitative yield based on a 55% conversion). No trace of the urea, \( 8a \) could be detected and if \( 4a \) was an intermediate it was converted only to \( 6a \) (no effort was made to establish that \( 6a \) was a product).

Mono-, di-, and trialkylthiourea S,S-dioxides have recently been prepared \(^{11}\) and the unsubstituted thiourea S,S-dioxide, \( 4c \), is a well known industrial reducing agent in aqueous solution. Curiously, no reports have appeared on the thermal decomposition of these dioxides in acryl.\(^{12}\) Only that solid \( N,N' \)-di(sec-butyl)thiourea S,S-dioxide decomposes to sulfur dioxide and the corresponding formamidine at \( 150^\circ C \) or that \( 4c \) gives the analogous products in refluxing acetic acid. \(^{13}\)

We find that \( 4c \) decomposes to thiourea, urea (2:3 ratio), and dioxides in refluxing anhydrous acetonitrile with a 98% conversion after 0.7 hours. For an nmr kinetic analysis, \( 6d \) (mp, 85-89° (dec.)) \(^{11} \) was prepared by the hydrogen peroxide oxidation of \( N,N' \)-di(n-butyl)thiourea according to standard published procedures. \(^{11} \) This derivative in acetonitrile provides the thiourea and formamidine (1:2.8 ratio) in a first order reaction with a composite \( k_{1}=1.0 \times 10^{-5} \text{ (r=0.9972) at 45}^\circ C.\)

\[
\begin{align*}
R^1_\text{S-O} & \rightarrow R^2_\text{S-O} & \rightarrow R^3_\text{S-O} \\
4 & 5 & 6
\end{align*}
\]

\[
\begin{align*}
R^1_\text{Li} & \rightarrow R^2_\text{Li} & \rightarrow R^3_\text{Li} \\
7 & 8
\end{align*}
\]

\[
\begin{align*}
a, R^1 = \bigg\{ \bigg\} \\
b, \text{Me}_2N^- \\
c, \text{NH}_2^- \\
d, \text{n-BuNH}^-
\end{align*}
\]
SCF-MO calculations reveal that the lowest energy mode of decomposition of 4c is dissociation into the singlet carbene and sulfur dioxide complex (with bond length of 2.05 Å) lying only 2–3 kcal/mol above the bound dioxides. This result accounts for the equilibrium of 7a and sulfur dioxide with 4c leading to isolation of a considerable amount of starting imidazolium salt after 20 hours. The foraminidines isolated in the decomposition of 4d may be ascribed to tautomerization and loss of sulfur dioxide from this complex. More interestingly, this reaction is also theoretically characterized at the molecular orbital level at a higher activation energy by the linear departure (mirror symmetry about an xy-plane) of a singlet dioxygen fragment from singlet 5. Along this fragmentation reaction coordinate an occupied-unoccupied orbital crossing occurs if a rotation about the dihedral oxygen py- and pi-orbitals is assumed. This provides the orbital rotation to product correspondence (the stationary thione fragment acting as an orbital symmetry reference) shown in Figure 1(c). At this crossing point the orbital rotation creates orbital angular momentum along the z-axis which is favorable for a large spin-orbit coupling matrix element between the excited and singlet state. Intersystem crossing to the triplet reacting complex can occur to give exothermically the lower energy triplet dioxygen. This is an unique example, unlike most forbidden pericyclic reactions, in which the triplet surface remains energetically below the singlet beyond the crossing point (Figure 2).
Figure 2. The Surfaces for Pericyclic Reactions. \( \phi \) is the lowest singlet state (ground state) and \( \psi \) the lowest triplet state. The solid line represents the path with two crossing points associated with most forbidden pericyclic reactions. The dotted line is characteristic of reactions producing a stable ground state triplet product such as diiodobenzene. If both states have the same symmetry, internucleation crossing may occur in the shaded region.

If internucleation crossing occurs before the rate determining step transition state the production of the triplet product might be enhanced by an external heavy atom effect. Unfortunately, we could find no change in product ratio for decomposition of 6d in the presence of mono- or di-iodobenzene. This suggests that the crossing point does not meet the above criterion or that the internal orbital motion produces a torque leading to a coupling matrix element which is much greater than any external heavy atom can provide.

Finally, another substituent with an energetically low-lying unoccupied orbital of the \( \pi^* \)-type which would stabilize a tricoordinate sulfurate bonding system is the phosphonium group. We explored the possibility of the reaction 9 \( \rightarrow \) 10 \( \rightarrow \) 11 \( \rightarrow \) 12.

\[
R_3P \rightarrow SO_2 \rightarrow R_3P = S^O \rightarrow R_3P = P^S \rightarrow O_2
\]

\[
10 \rightarrow \text{S} = P \rightarrow \text{P} = O \rightarrow 50
\]

\[
12 \rightarrow \text{S} = \text{SO}_2
\]
The treatment of 9\textsuperscript{17} (neat) with an excess of sulfur dioxide at \(-78\degree\) C for 72 h gave a 72\% yield of the phosphine oxide (13) and sulfide (12) in a ratio of 3:1.\textsuperscript{18} A 1:1 mixture of 12 and 13 could be accounted for by the reaction below\textsuperscript{19} without the intervention of 11 and its subsequent fragmentation. However, when this reaction was carried out under the same conditions in the presence of an equimolar amount of tribromomethane, the yield was unchanged but the ratio of 13 to 12 was 0:7. It is amusing to speculate that in this case an external heavy atom catalyst was responsible for an increased inter-system crossing efficiency in the fragmentation of an intermediate such as 11.

Acknowledgement

We wish to thank the NSH and NIH for generous financial support and Dr. Charles Litto and Kent Barenfield for their interest and suggestions.

References

(3) E.S. Foote, M.L. Ringer, and C. Gu, ibid., 103, 5245 (1981) and references therein.
(10) At no time did the reaction mixture become homogeneous. Neither N,N'-dimethylimidazolium perchlorate in methylene chloride solution or the triflate salt in THF solution give any detectable amounts of 6a in this reaction. Traces of 6a were found in the reaction of the triflate as a suspension in diethyl ether. The origin of this solvent effect is unknown.
Identified by mass spectroscopy.

A satisfactory elemental analysis was obtained.


MINDO/3 with geometry-energy optimization.

An excellent discussion of favorable orbital orientation for intramolecular crossing may be found in L. Salem and L. Howland, Angew. Chem. Int. Ed. 11, 92 (1972).

Kindly provided by Dr. Kent Borenfeld.

The balance of the reaction mixture was single unidentified 3a-containing product.

A similar mechanism accounts for the formation of only in the decomposition of 4c.
Substituent Stabilized Thione S-Imides. The Effect

of π-donor Substituents on Reactivity

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Since the first successful synthesis of isolable thione S-imides, ¹, (best represented by canonical structures ² and ³) stabilized by a combination of π-acceptor substituents ¹ or a combination of π-acceptor (R') and donor (R) groups ² interest in this new sulfur functional group has continued. Studies upon the three dimensional structural features ³, possible geometrical isomerism ⁴, photochemistry ⁴, electrophilic reactions ⁵, cycloadditions ¹ and synthetic utility ⁶ have been reported.

We undertook the synthesis of ² and ³ in order to study some fundamental reactions of thione S-imides stabilized by various π-donor substituents but with a common π-acceptor group. Both ylides (², m.p. 133-4° dec; ³, m.p. 185-190° dec.) were conveniently (91-94% yield)
prepared by the reaction of Chloramine-T trihydrate with the appropriate thiourea in methanol solution at 0-27°. Analogous reactions of dimethylthioformamide and 9-xanthione at -30° to -50° gave only sulfur and the corresponding N-tosylimine.

If the stabilizing substituents are inefficient in charge delocalization in either \( \chi \) or \( \lambda \) the ylide structure no longer lies below the valence isomeric thiaziridine, \( \theta \), in potential energy and undergoes facile [1,3]-electrocyclization to give \( \lambda \) which subsequently undergoes rapid loss of sulfur and formation of an imine, \( \xi \).

\[
\begin{align*}
\chi & \quad \text{Thione S-imide} \\
\lambda & \quad \text{Thione S-imide}
\end{align*}
\]

The difference in the thermal chemistry of \( \chi \) and \( \lambda \) reflects this. Thione S-imide, \( \chi \), having a \( \Pi \)-donor substituent which delocalized positive change over a fewer number of atoms, readily (in refluxing THF or at 120° in the solid state) gives \( \text{N-tosyl-N',N''-dimethylguanidine} \) and sulfur while \( \lambda \) with greater change delocalization is stable up to 145° (refluxing o-xylene). Both \( \chi \) and \( \lambda \) have unrestricted rotation about the C-S and C-N bonds in solution at room temperature as indicated by the nmr chemical equivalence of the N-methyl groups. Thus, the electrocyclization barrier is free of rotational constraints and determined primarily by the charge interaction between the termini of the 1,3-dipole.

A striking reversal of this reactivity difference is demonstrated in the hydrolysis of \( \chi \) and \( \lambda \). The dimethylimidazolium substituted ylide reacts very rapidly (\( t_{1/2} < 5 \text{ min} \)) with \( \text{H}_2\text{O}/\text{MeOH} \) at 25° to quantitatively afford \( \text{N,N'-dimethylimidazolthione} \) (\( \delta \)) and tosylamide while \( \chi \) is unaffected by 20% HCl in \( \text{MeOH}/\text{H}_2\text{O} \).
at 25°. It should be noted that in the observed reaction the sulfur moiety has been reduced to the thione level and the expected hydrolysis product, a thione S-oxide (\( \mathcal{Z} \)), was not present. Attempts to prepare \( \mathcal{Z} \) by other routes proved fruitless but interesting. Thioamides have been oxidized to the corresponding stable S-oxides by a variety of peroxy-compounds\(^7\). Treatment of \( \mathcal{Z} \) with a 10-fold excess of MCPBA in CH\(_2\)Cl\(_2\) at 25° resulted in a vigorous evaluation of O\(_2\) and rapid formation of m-chlorobenzoic acid while \( \mathcal{Z} \) was recovered unchanged. Similar results occurred with aqueous H\(_2\)O\(_2\). We must conclude that \( \mathcal{Z} \) undergoes a facile decomposition to dioxygen and \( \mathcal{Z} \) and thus the overall hydrolysis reaction of \( \mathcal{Z} \) may be represented by the sequence:

\[
\begin{align*}
\text{H} & \text{C} \\
\text{76NH}_2 \\
\text{2} & \rightarrow \\
\text{N} & \text{S} \\
\text{O}_2 & \\
\text{1} & \rightarrow \\
\text{N} & \text{S} \\
\text{O}_2 & \\
\text{Z} & \\
\end{align*}
\]

The difference in reactivity between \( \mathcal{Z} \) and \( \mathcal{Z} \) and the mechanism for the conversion of \( \mathcal{Z} \) to \( \mathcal{Z} \) may be explained in terms of an intermediate, \( \mathcal{Z} \), whose tricoordinate central hypervalent sulfur atom enjoys considerable stabilization.
by the equatorial \( \Pi \)-donor substituted carbocation. If the rate of hydrolysis depends upon the transition state (product-like) leading to the hypervalent intermediate, then the stability of this intermediate and the reaction rate is a function of energetic placement of the equatorial \( \Pi \)-substituent. The lowest 3-center bonding orbital (\( \sigma \)) of the coaxial hypervalent orbital array has the proper symmetry to interact with the empty substituent orbital (\( p \)) and the magnitude of this interaction is inversely dependent upon the energy difference, \( E_\sigma - E_p \) (Fig. I). The more delocalized imidazolium cation lying lower in energy is therefore more effective in stabilizing (lower energy) the hypervalent \( \sigma \)-bond, thus \( \lambda \) is more reactive than \( \zeta \).

\[ \text{Diagram for a hypervalent } \sigma \text{-bond and equitorial substituent } p \text{-orbital interaction.} \]

The effect of the \( \Pi \)-donor substituent on the chemistry of ylides \( \lambda \) and \( \zeta \) may be demonstrated in another unusual reaction. As observed in the case of thione methyldides, treatment of \( \lambda \) with tetramethylthiourea in MeCl\(_2\) solution at 30° rapidly and irreversibly affords \( \zeta \) and \( \xi \). This substituent transfer
reaction proceeds in a direction to give the ylide with the less effective Π-donor substituent. Again, if hypervalent intermediates are involved; those with imidazolium substitution at the hypervalent sulfur atom are more stable than those with the amidinium substituent. The latter, if formed, should irreversibly undergo loss of an axial ligand. A mechanism for this exchange reaction may be:

\[
\begin{align*}
R_1 & \xrightarrow{+} \text{S}\text{NR} + R_2 \xrightarrow{=} \text{S} & R_1 & \xrightarrow{+} \text{S} \xrightarrow{=} \text{NE} \\
R_2 & \xrightarrow{+} \text{S}\text{NR} + R_1 \xrightarrow{=} \text{S} & R_2 & \xrightarrow{+} \text{S} \xrightarrow{=} \text{NE}
\end{align*}
\]

\[\text{R}_1 = \text{Me}_2\text{N}^-; \quad \text{R}_2 = \text{Me}_2\text{N}^-\]

In conclusion, substituent stabilized thione S-imides demonstrate reactions which critically depend upon the ability of the Π-donor substituent to stabilize hypervalent bonding at the attached sulfur center.
**Experimental Section**

Osmotic molecular weights were determined on a Mechrolab vapor pressure osmometer (model 301A) at 37°C and mass spectra were obtained on a Hitachi Perkin-Elmer RMU-7L high resolution mass spectrometer with an 80 electron volt source. Proton nuclear magnetic resonance spectra were recorded on a Varian Associates model T-60A spectrometer and chemical shifts were reported versus an internal tetramethysilane (TMS) standard and the abbreviations s, d, t, q, and m refer to singlet, doublet, triplet, quartet, and multiplet, respectively. Carbon-13 nuclear magnetic resonance spectra were obtained on a JEOL model PFT-100 Fourier transform nmr spectrometer and the chemical shifts are reported versus a tetramethylsilane standard in the same manner as proton nmr. Infrared spectra were obtained on a Perkin-Elmer model 457 recording spectrophotometer using either 0.1 mm sodium chloride cells or a potassium bromide wafer. Ultraviolet spectra were recorded on a Beckman DB-GT spectrophotometer using one centimeter balanced quartz cells. Elemental analyses were performed by Atlantic Microlab, Inc., Atlanta, Georgia. Solids were identified by mixture melting point with authentic samples.

1,3-Dimethylimidazole-2-thione S,N-Toluenesulfonimide (3). 1,3-Dimethylimidazole-2-thione \(^9\) (12.8 g, 0.1 mole) was added in a single portion to a solution of 28.2 g (0.1 mole) of Chloramine-T trihydrate in 200 ml anhydrous methanol at 27°C. The mixture was stirred for two hours and then diluted with 75 ml anhydrous methylene chloride. The reaction mixture was then filtered through celite to remove the precipitated sodium chloride. The filtrate was cooled to -78°C and the crystalline product which separated was collected by filtration. The crude material was recrystallized from anhydrous methanol to give 28.0 g (94%) of the thione S-imide as colorless plates: mp 185-190°C (dec.); ir (KBr) 3090 (C-H), 1260 and 900 cm\(^{-1}\); Proton nmr (DMSO-\(d_6\)) \(\delta\) 7.53 (s, 2H), \(\delta\) 7.28 (q, 4H), \(\delta\) 3.75 (s, 6H),
and δ 2.25 (s, 3H); Carbon-13 nmr (DMSO-d_6) δ 147.1 (s), δ 122.92 (s), δ 35.49 (s), and δ 20.75 (s); osmotic molecular weight (CHCl_3) 299.0.

Anal. Cal. for C_{12}H_{15}N_{3}O_{2}S_{2}: C, 48.48; H, 5.00; N, 14.14; S, 21.55. Found: C, 48.25; H, 5.14; N, 14.09; S, 21.38.

This S-imide was recovered unchanged after 15 minutes reflux in o-xylene. 1,1,3,3-Tetramethyl-thiourea S-p-Toulenesulfonimide (2). 1,1,3,3-Tetramethyl-thiourea (10.0 g 0.075 mole) in 50 ml of absolute methanol was added dropwise over a period of one hour to 21.3 g (0.075 mole) of chloramine-T trihydrate; dissolved in 100 ml of methanol maintained at 0°. When the addition was complete, the reaction mixture was stirred at 0° for an additional hour, and then the precipitated sodium chloride (2.98 g) was removed by filtration. The filtrate was concentrated with a rotary evaporator under reduced pressure to a viscous oil. The oil was dissolved in 150 ml of methylene chloride and the remaining sodium chloride (total yield: 4.29 g (98%)) was removed by filtration. The methylene chloride was removed from the filtrate with a rotary evaporator under reduced pressure to afford a clear colorless oil. While the resulting oil was rapidly stirred, 100 ml of anhydrous THF was added which caused 20.6 g (91%) of 1,1,3,3-tetramethyl-thiourea S-p-toulenesulfonimide to separate as a colorless powder: mp 113-134° (dec); uv max (CHCl_3) 243 nm (shoulder, ε24,900), 272 nm (shoulder ε13,600) and 300 nm (shoulder, ε9840) ir (CHCl_3,1580 (N=S=C), 1395 and 1165 cm^{-1} (SO_2-N); Proton nmr (CDCl_3) δ 7.74 (d, 2H, J = 8 Hz, aromatic CH), 7.21 (d, 2H, J = 8 Hz, aromatic CH), 3.12 (s, 12H, [(CH_3)_2N]_2) and 2.37 (s, 3H, p-CH_3); mass spectrum, m/e (rel intensity): 269 (0.6), 155 (100), 146 (6.8), 132 (10); cryoscopic molecular weight (tert-butyl alcohol) Calculated: 301. Found: 288.
Anal. Calc. for C_{12}H_{19}N_{3}O_{2}S_{2}: C, 47.81; H, 6.35; N, 13.94; S, 21.28. Found: C, 47.57; H, 6.54; N, 13.76; S, 21.04.

Although it decomposes within a few days at room temperature, it can be stored for extended periods of time if maintained at temperatures below zero degrees.

Dimethylthioformamide. Dimethylthioformamide {\textsuperscript{10}} (5.0 g, 0.056 mole) was added dropwise over a period of 30 minutes to 15.8 g (0.056 mole) of chloramine-T trihydrate in 40 ml of absolute methanol maintained at -30 {\degree}C. As each drop was added, a precipitate of sodium chloride formed, followed immediately by an amorphous yellow precipitate of elemental sulfur. Similar results were encountered when the temperature was lowered to -50 {\degree}C. When the addition was complete, the reaction mixture was cooled to -78 {\degree}C and 75 ml of anhydrous ether was added to cause precipitation of all products. The reaction mixture was filtered and the collected precipitate was titurated with 75 ml of anhydrous THF. The insoluble inorganic substances were removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure to give a colorless powder. Infrared analysis of the powder revealed the presence of p-toluenesulfonamide and a second component having a strong absorption at 1630 cm\textsuperscript{-1}. Fractional recrystallization with anhydrous THF separated the two compounds which were identified as p-toluenesulfonamide and N-dimethylaminomethylene-p-toluenesulfonimide (6.27 g): mp 134-135 {\degree}C (lit. mp 133-135 {\degree}C).

9-Xanthione. 9-Xanthione {\textsuperscript{12}} (1.59 g, 0.0075 mole) in 35 ml of methylene chloride was added dropwise to 2.11 g (0.0075 mole) of chloramine-T trihydrate. The addition was done at various temperatures. At -30 {\degree}C a red intermediate formed immediately; however, it dissipated over a period of 30 seconds. At -50 {\degree}C the red intermediate formed at a slower rate, but it also dissipated within 30 seconds. At -78 {\degree}C there was no reaction. When the addition was complete,
the precipitated sodium chloride was removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure to afford a light yellow powder. Fractional recrystallization from 95% ethanol gave 0.026 g of N-xanthylidene-p-toluenesulfonamide mp 173-175° (lit. 13 mp 167-168°); 0.659 g of 9-xanthione and 0.571 g of p-toluenesulfonimide.

**Thermal Decomposition of \( \mathcal{Z} \).** Compound \( \mathcal{Z} \) (0.20 g, 0.0007 mole) was placed into a small tube and slowly heated in an oil bath. When the bath temperature reached ca. 115° the sample began to darken. Melting occurred over a range from 126-134°. The sample melted to a dark red melt which then faded to a light yellow. When the bath temperature had reached 140°, the sample tube was removed and allowed to cool. The resulting mass was dissolved in hot anhydrous THF and filtered from an amorphous yellow solid which was identified as elemental sulfur. The filtrate, upon cooling, deposited 0.099 g (56%) of colorless needles which were subsequently identified as N-[bis(dimethyl)amino] methylene-p-toluenesulfonimide mp 140-143° (lit. 14 mp 143-145°).

These same products were isolated when \( \mathcal{Z} \) was suspended in refluxing THF for 24 hours.

**Hydrolysis of \( \mathcal{Z} \).** Thione S-imide \( \mathcal{Z} \) (0.42 g, .0014 mole) was added to 15 ml of anhydrous methanol at 25° to afford a colorless solution. Upon addition of 3 ml of water an exothermic reaction occurred and the solution became intensely yellow and remained so for 5 minutes at which time the color faded. Evaporation of the solvent under reduced pressure gave 0.42 g of a 1:1 mixture of p-toluenesulfonimide and 1,3-dimethylimidazole-2-thione as established by nmr spectroscopy and thin layer chromatography (alumina, EtOAc/Et₂O 1:9). No other products could be detected.
Attempted Oxidation of 1,3-dimethylimidazole-2-thione. (a) To a solution of 1,3-dimethylimidazole-2-thione (1.28 g, .01 mole) in 50 ml methylene chloride at 25° was added m-chloroperbenzonic acid (17.3 g, .1 mole) in small portions. After each addition a very exothermic reaction with gas evolution occurred. The solvent was evaporated under reduced pressure and the remaining solid washed with cold aqueous sodium bicarbonate. The resultant solid appeared to be the starting thione by nmr analysis. A small sample was recrystallized from hot water and proved to be 1,3-dimethylimidazole-2-thione by mixture melting point comparison. (b) 1,3-Dimethylimidazole-2-thione (2.56 g, .02 mole) was dissolved in 200 ml water and cooled to 5° to which addition of 4 ml 30% aqueous hydrogen peroxide (1.2 g, .035 mole) led to virorous gas evolution. Under reduced pressure the volume of the resultant solution was reduced to 50 ml, cooled to 5° and the crystalline precipitate which formed (2.5 g) was identified as starting thione.

Reaction of 3 with tetramethylthiourea. To a solution of 3 (.297 g, .001 mole) in a minimum amount of CDCl₃ was added tetramethylthiourea (.132 g, .001 mole) in one portion. The reaction at 25° was followed by nmr spectroscopy and after 24 hours indicated the complete conversion of 3 to 2 and 1,3-dimethylimidazole-2-thione, without the formation of any other products. Evaporation of the solvent and crystallization of the residual solid from anhydrous methanol gave .12 g of 2.

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References and Notes


(12) A. Schonberg, O. Schutz and S. Nickel, ibid., 91, 1375 (1928).

(13) A. Schonberg and E. Singer, ibid., 101, 3445 (1928).