GEORGIA INSTITUTE OF TECHNOLOGY — OFFICE OF CONTRACT ADMINISTRATION

PROJECT ADMINISTRATION DATA SHEET

[X] ORIGINAL [ ] REVISION NO. ____

Project No. G-33-N04 DATE 3-23-82

Project Director: Dr Edward Burgess School/~~Lab~~ Chemistry

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

Type Agreement: Grant No. 5-R01-GM-12677-12

Award Period: From 3-1-82 To ~~2-28-83~~ 5/31/83 (Performance) ~~5-31-83~~ 8/31/83 (Reports)

Sponsor Amount: $93,155 Contracted through:

Cost Sharing: $ 4,903 (G33-313) ~~GTRI~~/GIT

Title: The Chemistry of New Functional Groups in Enzymes

ADMINISTRATIVE DATA — OCA Contact Don Hasty

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Defense Priority Rating: N/A

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Security Classification: N/A

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RESTRICTIONS

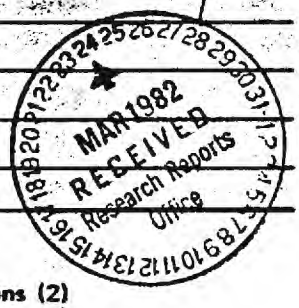
See Attached NIH Supplemental Information Sheet for Additional Requirements.

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 G33-N03/Burgess



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GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION SHEET

Date September 1, 1983

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
- [X] 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~~)

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G-33-N04

Grant 5 R01 GM 12672

The Chemistry of New Functional Groups in Enzymes

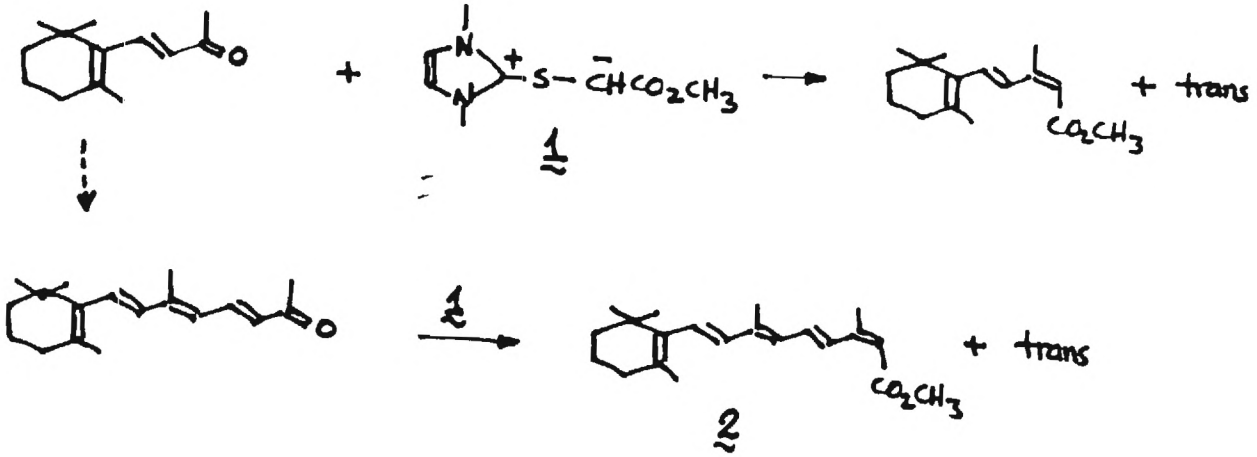
Edward M. Burgess
School of Chemistry
Georgia Institute of Technology

03/01/79 - 02/28/83

Final Progress Report

1. Wittig Reactions of Thione Methylides. The Synthesis of 13-cis Retenoic Acid

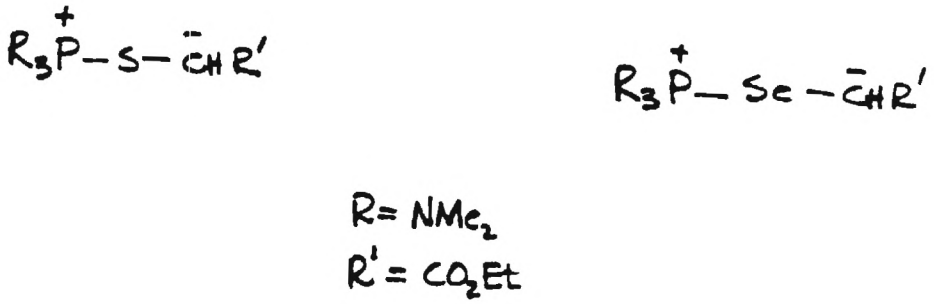
We have optimized the conditions for reaction of the ylide, 1, (generated in situ) with ketones. In model studies, usind DBU as the base and acetonitrile solvent the stereochemistry of the quasi-Wittig is predominately cis (cis/trans, 3:1)



Extension of this reaction to 13-cis retenoic ester, 2, gave the stereoisomeric products in a cis/trans ratio of 2:1. $LiBI_4$ 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.

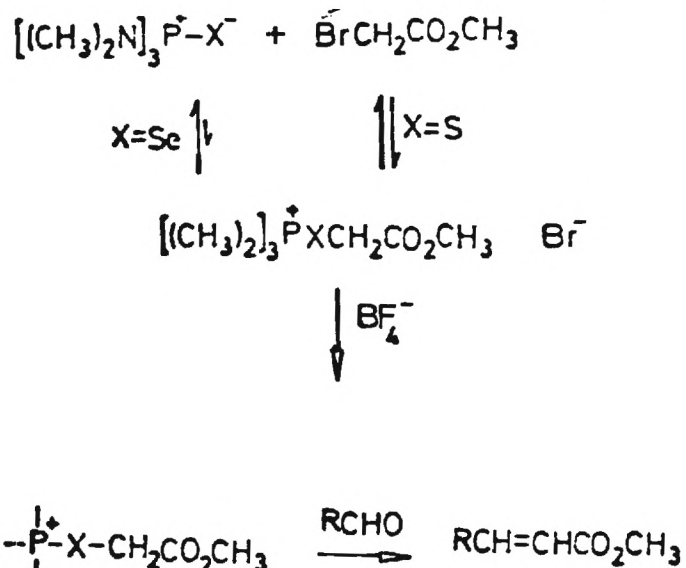
2. New Wittig Reagents

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:



The requisite precursor salts were obtained via reaction of the phosphine sulfide or selenide with iodacetic ester in teh presence of aqueous sodium fluoroborate. Deprotonation of these salts with sodium methoxide, sodium hyroxide 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).

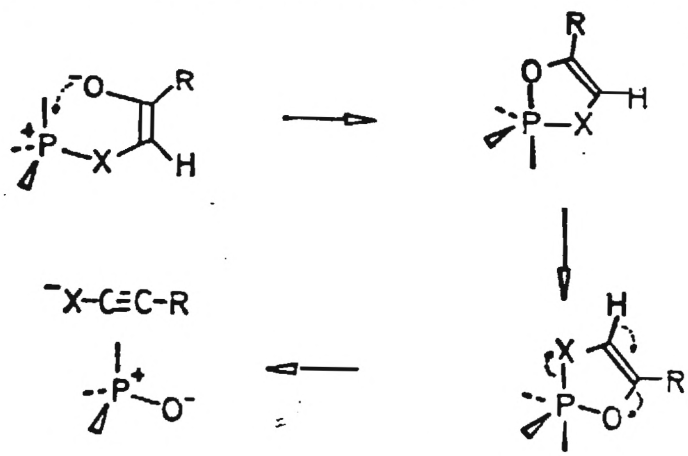


A. DBU, CH_3CN
B. DBU, CH_3CN, LiI
C. NaOH, H_2O, CH_2Cl_2, $Et_3BuN^+Cl^-$
D. NaOEt, EtOH

R=Ph

	X = S		X = Se	
	Z	E	Z	E
A	60	40	60	40
B	75	25	98	2
C	70	30	50	50
D	0	100	50	50

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.



R= Ph, CH_3

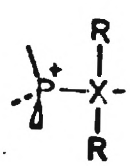
In another study, we attempted the isolation of a phosphine sulfide methylide,

$$[(CH_3)_2N]_3\overset{+}{P}S\overset{-}{C}(CO_2CH_3)_2$$

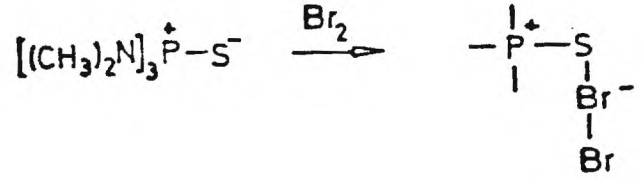
however, after a few hours in solution this ylide underwent rearrangement to

$$[(CH_3)_2N]_3\overset{+}{P}\underset{\substack{|\\ S^-}}{C}(CO_2CH_3)_2$$

Finally, in an attempt to generate an isolable hypervalent species:



we subjected tri-dimethylaminopnosphine sulfide to bromination. The product isolated and characterized by x-ray crystallography is shown below.



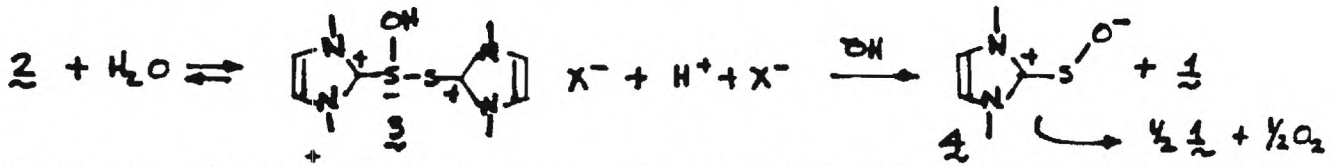
3. Oxidative Chemistry of Disulfides

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

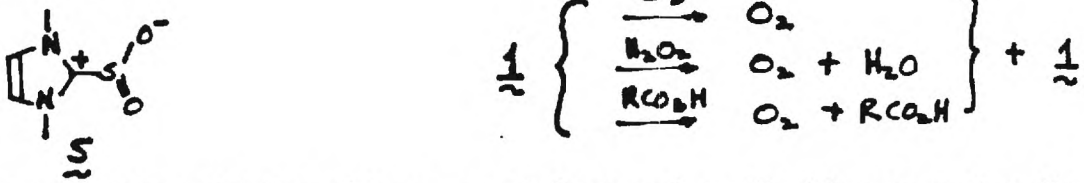
The following observations in the chemistry of 2 have not been published.

By suitable anionic exchange procedures various salts ($X=Cl^-$, BF_4^-, $OSO_2CF_3^-$) are available and the triflate salts have good solutility 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 dioxgyen and 1. No intermediate could be detected by NMR analysis in D_2O. By polarography the onset of a detectable oxygen wave occured 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 3 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 1.

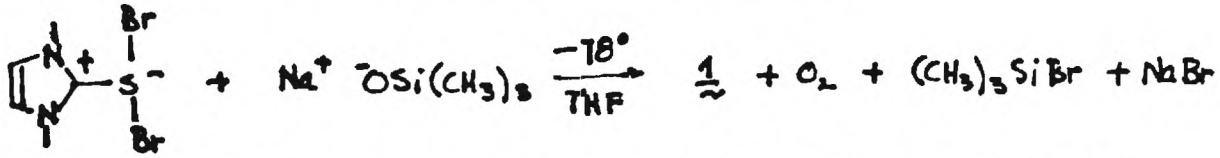


Simple sulfoxides, $R_2\overset{+}{S}-O^-$, are known to undergo disproportionation to sulfides, R_2S, and sulfones, R_2SO_2 at elevated temperatures and in the case of 4 this may be a facile reaction leading to 5. If this is the case then 5 must also rapidly give oxygen and 1, In order to gain some 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.

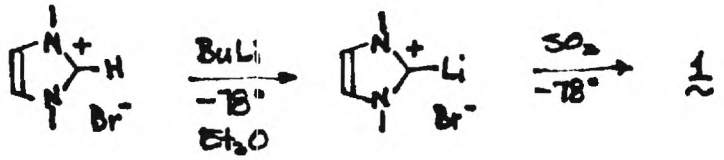


However, if the oxidation of 1 was carried out at low pH with a percarboxylic acid the result was 2.

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



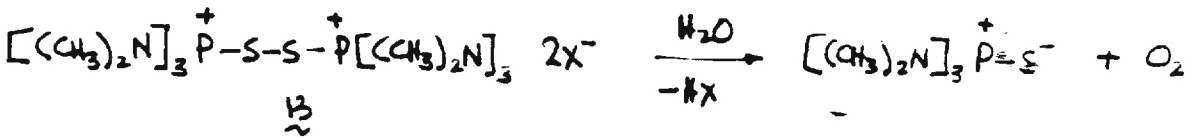
In other attempts to obtain 5 the reaction of lithio-derivative 6 with sulfur dioxide led to the formation of 1.



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 6. Oxidation of tris(dimethylamino) phosphine sulfude, 13, with $NOBF_4$ gives a disulfide which also oxidizes water.



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 Dioxides to Dioxygen

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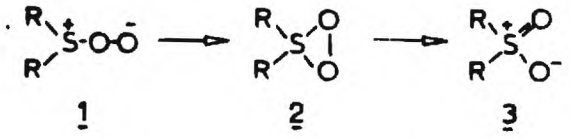
School of Chemistry
Georgia Institute of Technology
Atlanta, Georgia 30332

Received

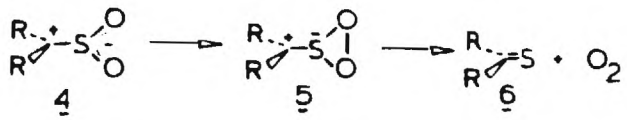
Abstract: *Dimethylimidazole thione 1,3-dioxide was prepared from 2-chloro-1,3-dimethylimidazolium chloride and 2-lithio dimethylimidazolium salts and found to decompose to dioxygen and the corresponding thione. N,N'-Dialkylthiourea dioxides also give the related thioureas and amidine upon heating in acetonitrile solution. Tetramethyl dimethoxyaminophosphine reacts with sulfur dioxide to produce the phosphine oxide and sulfide. These reactions are discussed in terms of an intermediate singlet sulfurane which fragments to triplet dioxygen via a intersystem crossing process.*

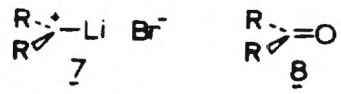
From both a biological[1] and chemical viewpoint the oxygen atom transfer reaction of 1,3- and 1,3-dipoles[2] containing one or more oxygen atoms has received considerable recent attention. Prominent among these reactive intermediates are persulfoxides, **1**, which result from the action of singlet oxygen on sulfides[3] or hydrogen peroxide on fluoro derivatives of dialkylsulfuranes.[4] It has been shown that **1** (R = alkyl) has the ability to transfer an oxygen atom to sulfides to give sulfoxides and more rapidly converts sulfoxides to sulfones. If **1** is derived from the dialkylsulfurane its electrophilicity is sufficient to effect epoxidation of alkenes.[4] In the absence of oxidizable reagents, **1** is ultimately converted into the sulfone, **3**, possibly via the electrocyclization product, the hypervalent thiadioxirane **2**. From studies of the solvent effects on efficiency of oxygen atom transfer the primary species present seems to be **1**.[3,5] However, when **1** (R = Ph) is generated via the sulfurane route in the presence of a triplet energy acceptor such as 9,10-dibromoanthracene, chemiluminescence of the latter is observed.[6] 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.

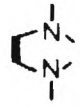


1 **2** **3**

Employing rather Edisonian reasoning we were convinced of the possibility that the reaction above could be reversed exothermically, i.e., **3** --> **2** --> O_2. If **3**, by proper substitution, would have less thermodynamic stability than **2**, such a reversal might be realized. With the knowledge[7] 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 sulfurane bonding array, a possible foward 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.





a, R= 

b, Me_2N-

c, NH_2-

d, n-BuNH-

It has been reported that diaminocyclopropenium[4] and dihydrodiazepinium[5] salts may be lithiated by n-butyl lithium or dichloromethyl lithium[6] at low temperatures to give substituted stabilized trichlorocarbenium ions which readily undergo SE reactions with weak electrophiles. Following these observations, in order to prepare **4a**, we treated an anhydrous diethyl ether suspension of N,N'-dimethylimidazolium bromide under an argon atmosphere with an excess of n-butyl lithium (1.6 M in hexane) to give **7a**. After 6 hours at 30° sulfur dioxide was introduced and upon standing for 20 hours unreacted starting material, lithium bromide, and **8a** was isolated (quantitative yield based on a 36.6% conversion).[10] 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 aprotic solvents only that solid N,N'-di(sec-butyl)thiourea S,S-dioxide decomposes to sulfur dioxide and the corresponding formamidine at 100° or that **4c** gives the analogous products in refluxing acetic acid.[14]

We find that **4c** *decomposes to thiourea, urea (2:3 ratio) and dioxygen in refluxing anhydrous acetonitrile with a 98% conversion after 0.7 hours. For* an nmr kinetic analysis, **6d** (mp. 85-6° (dec.))[15] was prepared by the hydrogen peroxide oxidation of N,N'-di(n-butyl)thiourea according to standard published procedures.[11] This derivative in acetonitrile provided the thiourea and foramidine (1:2.8 ratio) in a first order reaction with a composite k_1=1.0 x 10^{-4} (r=0.9972) at 45°.

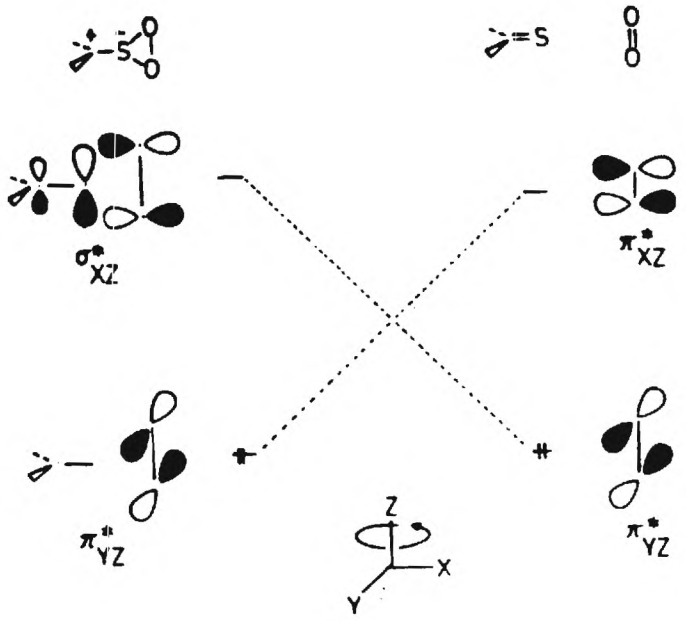


Figure 1. Orbital Correspondence for the Fragmentation of a Hypervalent Substituted Thiadioxirane to Dioxygen. Rotation of the O-O fragment occurs about the z-axis.

SCF-MO calculations reveal that the lowest energy mode of decomposition of **4c** is dissociation into the singlet carbene and sulfur dioxide complex (C-S bond length of 2.05 Å) lying only 2-3 kcal. above the bound dioxide. This result accounts for the equilibrium of **7a** and sulfur dioxide with **4a** leading to isolation of a considerable amount of starting imidazolium salt after 20 hours. The formamidine isolated in the decomposition of **4d** also 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[15] 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 a occupied-unoccupied orbital crossing occurs if a rotation about the z-axis of the oxygen pγ- and pπ-orbitals is assumed. This provides the orbital reactant to product correspondence (the stationary thione fragment acting as an orbital symmetry reference) shown in Figure **1**[16]. 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 triplet 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 reations, in which the triplet surface remains energetically below the singlet beyond the crossing point (Figure 2).

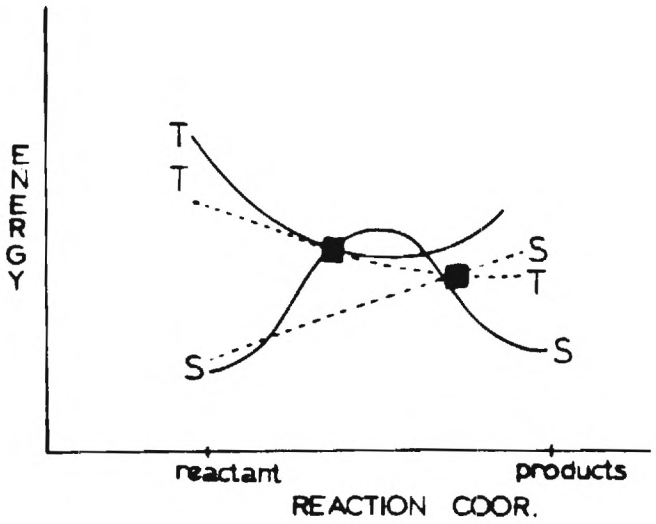
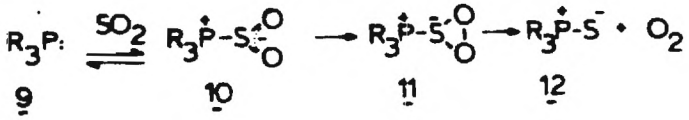
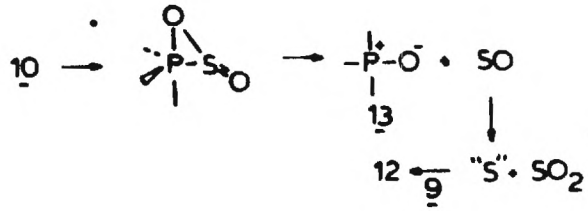


Figure 2. The Surfaces for Pericyclic Reactions. S is the lowest singlet state (ground state) and T the lowest triplet state. The solid line represents the path with two crossing points associated with most forbidden pericyclic reactions. The dotted line is characteristic of reactions producing a stable ground state triplet product such as dioxygen. If both states have the same symmetry intersystem crossing may occur in the shaded regions.

If intersystem crossing occurs before the rate determing stat 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 ratios for decomposition of **6d** in the presence of mono- or di-iodobenzene. This suggests that the crossing point does not meet the above criteron 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 π*-type which would stabilize a tricoordinate sulfur(+) bonding system is the phosphonium group. We explored the possibility of the reaction **9** --> **10** --> **11** --> **12**.





The treatment of **9**[17] (neat) with an excess of sulfur dioxide at −78° gave a 72% yield of the phosphine oxide (**13**) and sulfide (**12**) in a ratio of 3:4.[18] A 1:1 mixture of **12** and **13** could be accounted for by the reaction below[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 ordibromoethane the yield was unchanged but the ratio of **13** to **12** was 3:7.* It is amusing to speculate that in this case an external heavy atom catalyst was responsible for an increased intersystem crossing efficiency in the fragmentation of an intermediate such as **11**.

Acknowledgement

We wish to thank the NSF and NIH for generous financial support and Drs. Charles Liotta and Kent Barefield for their interest and suggestions.

References

(1) B.M. Hamilton, "In Molecular Mechanism of Oxygen Activation," O. Hayaishi, Ed., Academic Press, New York, 1974, p.405.

(2) Carbonyl oxides: H. Kwart and D.M. Hoffman, *J. Org. Chem.*, **31**, 419 (1966); B.A. Hamilton and J.R. Glacin, *J. Amer. Chem. Soc.*, **88**, 1564 (1966); R.W. Murray *et. al.*, *ibid.*, **101**, 1282 (1979). Pyridine N-oxides: D.M. Jerina, D.R. Boyd, and J.W. Daly, *Tetrahedron Lett.*, 45 (1970). Pernitroxides: C.J. Michejda and D.H. Campbell, *J. Amer. Chem. Soc.*, **98**, 6728 (1976).

(3) C.S. Foote, M.L. Kacher, and C. Gu, *ibid.*, **103**, 5949 (1981) and references therein.

(4) J.C. Martin and L.D. Martin, *ibid.*, **99**, 3511 (1977).

(5) Y. Ogata and Y. Sawaki, *ibid.*, **103**, 5947 (1981).

(6) P.D. Bartlett, T. Aida, H.-K. Chu, and T-S. Fang, *ibid.*, **102**, 5115 (1980).

(7) E.M. Burgess and A.J. Arduengo, *ibid.*, **99**, 2376 (1977).

(8) R. Weiss, C. Priesner, and H. Wolf, *Angew. Chem. Int. Ed. Engl.*, **17**, 445 (1978).

(9) C.D. Lloyd and H. McNab, *ibid.*, **15**, 459 (1976).

(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.

(11) W. Walter and G. Randau, *Justus Liebigs Ann. Chem.*, **722**, 80 (1969).

(12) Identified by mass spectroscopy.

(13) A satisfactory elemental analysis was obtained.

(14) J.J. Havel and R.O. Klutts, Syn. Comm., 389 (1974).

(15) MINDO/3 with geometry-energy optimization.

(16) An excellent discussion of favorable orbital orientation for [illegible] crossing may be found in L. Salem and L. Rowland, *Angew. Chem. Int. Ed.*, **11**, 92 (1972).

(17) Kindly provided by Dr. Kent Barefield.

(18) The balance of the reaction mixture was single unidentified GC containing product.

(19) A similar mechanism accounts for the formation of urea in the decomposition of **4c**.

Substituent Stabilized Thione S-Imides. The Effect of π-Donor Substituents on Reactivity

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School of Chemistry
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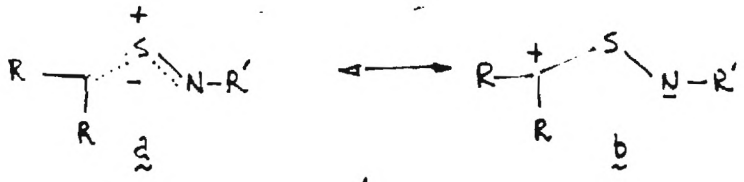
Since the first successful synthesis of isolable thione S-imides, 1, (best represented by canonical structures 1a and b) stabilized by a combination of Π-acceptor substituents[1] or a combination of Π-acceptor (R') and donor (R) groups[2] interest in this new sulfur functional group has continued. Studies 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.



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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 conventiently (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.

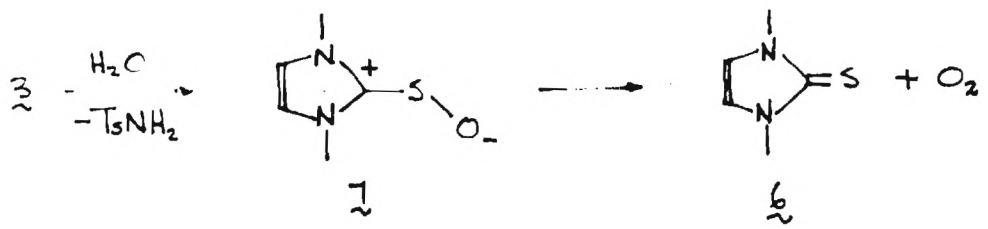
If the stabilizing substituents are inefficient in charge delocalization in either 1a or b the ylide structure no longer lies below the valence isomeric thiaziridine, 4, in potential energy and undergoes facile [1,3]-electrocyclization to give 4 which subsequently undergoes rapid loss of sulfur and formation of an imine, 5.[2,4]

4 5

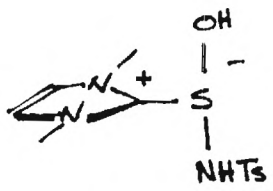
The difference in the thermal chemistry of 2 and 3 reflects this. Thione S-imide, 2, having a Π-donor substituent which delocalized positive change over a fewer number of atoms, readily (in refluxing THF or at 120° in the solid state) gives N-tosyl-N',N''-dimethylguanidine and sulfur while 3 with greater change delocalization is stable up to 145° (refluxing o-xylene). Both 2 and 3 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 2 and 3. The dimethylimidazolium substituted ylide reacts very rapidly ($t_{1/2}$ < 5 min) with H_2O/MeOH at 25° to quantitatively afford N,N'-dimethylimidizolthione (6) and tosylamide while 2 is unaffected by 20% HCl in MeOH/H_2O

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 (7), was not present. Attempts to prepare 5 by other routes proved fruitless but interesting. Thioamides have been oxidized to the corresponding stable S-oxides by a variety of peroxo-compounds[7]. Treatment of 6 with a 10-fold excess of MCPBA in CH_2Cl_2 at 25° resulted in a vigorous evalution of O_2 and rapid formation of m-chlorobenzoic acid while 6 was recovered unchanged. Similar results occurred with aqueous H_2O_2. We must conclude that 7 undergoes a facilile decomposition to dioxygen and 6 and thus the overall hydrolysis reaction of 3 may be represented by the sequence:



The difference in reactivity between 3 and 2 and the mechanism for the conversion of 3 to 7 may be explained in terms of an intermediate, 8, whose tricoordinate central hypervalent sulfur atom enjoys considerable stabilization



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by the equitorial Π-donor substituted carbocation.[8a] 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 equitorial Π-substituent. The lowest 3-center bonding orbital (σ) 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 σ-bond, thus 3 is more reactive than 2.

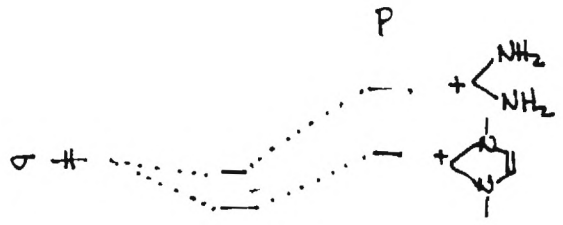
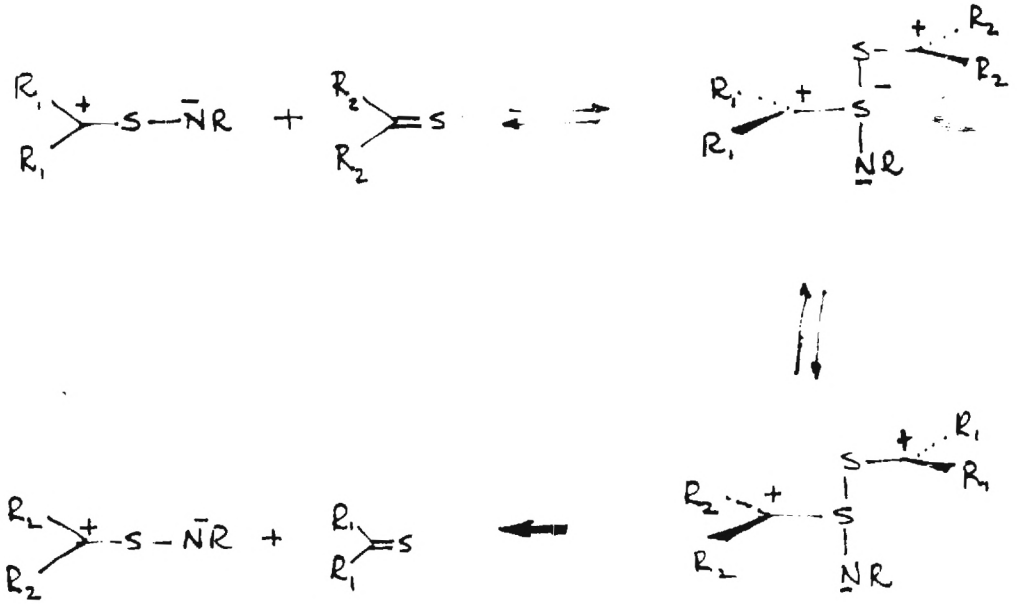
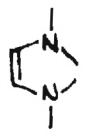


Figure I. Diagram for a hypervalent σ-bond and equitorial substituent p-orbital interaction.

The effect of the Π-donor substituent on the chemistry of ylides 3 and 2 may be demonstrated in another unusual reaction. As observed in the case of thione methylides,[8b] treatment of 3 with tetramethylthiourea in $MeCl_2$ solution at 30° rapidly and irreversibly affords 2 and 6. 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:



R_1 =  ; R_2 = Me_2N-

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 tetramethylsilane (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-p-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°. 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° 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° (dec.); ir (KBr) 3090 (C-H), 1260 and 900 cm^{-1}; Proton nmr (DMSO-d_6) δ 7.53 (s, 2H), δ 7.28 (q, 4H), δ 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 $C_{12}H_{15}N_3O_2S_2$: 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 $C_{12}H_{19}N_3O_2S_2$: 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 2 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 S-p-Toluenesulfonimide. Dimethylthioformamide[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°. 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°. When the addition was complete, the reaction mixture was cooled to -78° 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^{-1}. Fractional recrystallization with anhydrous THF separated the two compounds which were identified as p-toulenesulfonamide and N-dimethylaminomethylene-p-toluenesulfonimide (6.27 g): mp 134-135° (lit.[11] mp 133-135°).

9-Xanthione S-p-Toulenesulfonimide. 9-Xanthione[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° a red intermediate formed immediately; however, it dissipated over a period of 30 seconds. At -50° the red intermediate formed at a slower rate, but it also dissipated within 30 seconds. At -78° 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 m; 173-175° (lit.[13] mp 167-168°); 0.659 g of 9-xanthione and 0.571 g of p-toulenesulfonimide.

Thermal Decomposition of 2. Compound 2 (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] m; 143-145°).

These same products were isolated when 2 was suspended in refluxing THF for 24 hours.

Hydrolysis of 3. Thione S-imide 3 (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-toluene-sulfonimide and 1,3-dimethylimidazole-2-thione as established by nmr spectroscopy and thin layer chromatography (alumina, EtOAc/$Et_2\bar{O}$ 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-chloroperbenzoic 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 aqueious 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 volumn 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 $CDCl_3$ 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.

Acknowledgements. We sincerely wish to thank the National Institute of Health and the National Science Foundation for grant support.

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