THE CHEMISTRY OF THIONE S-IMIDES

A THESIS

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THE CHEMISTRY OF THIONE S-IMIDES

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GLOSSARY OF ABBREVIATIONS

DME	1,2-dimethoxyethane
DMSO	dimethylsulfoxide
Hz	Hertz
ir	infrared
m-CPBA	*meta*-chloroperbenzoic acid
nm	nanometer
nmr	nuclear magnetic resonance
ppm	parts per million
THF	tetrahydrofuran
TLC	thin-layer chromatography
TMS	tetramethylsilane
uv	ultraviolet

SUMMARY

The research described herein was to develop synthetic methods for the preparation of a new heterocumulene, the thione S-imide; and to investigate the chemical properties of this new system with emphasis on delineating its ability to undergo cycloaddition reactions.

Reaction of N-(trimethylsilyl)benzamide with sulfur dichloride afforded benzamide-N-sulfenyl chloride (28). (Attempts to prepare an N-thioamide by the dehydrohalogenation of 28 were unsuccessful.) Compound 28 reacted rapidly with diphenyl diazomethane at -30° to give N-benzoyl-chlorodiphenylmethanesulfenamide (26). Treatment of 26 with triethylamine at -78° resulted in the isolation of 2,2,5-triphenyl-1,3,4-oxathiazole (38), and no concrete evidence was obtained to support the intermediacy of benzophenthione S-benzoylimide (24) in this reaction.

Reaction of 28 with 9-diazofluorene at -30° gave N-benzoyl-9-chloro-fluorenesulfenamide (27). Treatment of 27 with triethylamine at -78° resulted in the formation of fluorenethione S-benzoylimide (25) which could be isolated as a metastable solid at room temperature; however, in solution at ca. -30°, 25 underwent electrocyclic ring closure to 5'-phenylspiro(fluorene-9,2'[1',3',4']oxathiazole) (39).

When 25 was treated with N-isobutenylpyrrolidine at -78° there was obtained 2'-benzoyl-3'-pyrrolidine-4',4'-dimethylspiro(fluorene-9,5'[1',2']isothiazolidine) (47). The isothiazolidine structure of

47 was firmly established by spectral and chemical data.

Reaction of **25** with *N*-propenylpiperidine at -78° afforded 2'-benzoyl-3'-piperidine-4'-methylspiro(fluorene-9,5'[1',2']isothiazolidine) (**55**).

The thione *S*-imide **25** was also found to react with the terminal double bond of 1-diethylaminobutadiene to give 2'-benzoyl-3'-(*trans*-*N*-ethenyldiethylamine)spiro(fluorene-9,5'[1',2']isothiazolidine) (**58**).

The reaction of **25** with the above enamines is proposed to proceed initially by formation of 1,2-cycloadducts (across the S=N bond of the heterocumulene) which would then undergo a Stevens rearrangement to afford the isolated isothiazolidines.

An unstable sulfonium ylid, 2-phenyl-4-fluorenylide-5-methyl-6-diethylamino-1,4,3-oxathiazine (**60**) was obtained from the reaction of **25** with 1-(diethylamino)-1-propyne.

The addition of 1,1,3,3-tetramethyl-2-thiourea to a methanolic solutions of chloramine-T gave an excellent yield of 1,1,3,3-tetramethyl-2-thiourea *S*-*p*-toluenesulfonimide (**69**). Compound **69** underwent thermal decomposition to give *N*-[bis(dimethyl)amino]methylene-*p*-toluenesulfonamide (**74**). The reaction of **69** with dimethyl acetylenedicarboxylate afforded a moderate yield of 1,1-[bis(dimethyl)amino]-2,3-dicarbomethoxy-1-propene-3-thione *S*-*p*-toluenesulfonimide (**74**).

The reaction of dimethylthioformamide and 9-xanthione with chloramine-T afforded unstable thione *S*-imides which rapidly decomposed to *N*-dimethylaminomethylene-*p*-toluenesulfonamide (**76**) and *N*-xanthylidene-*p*-toluenesulfonamide (**78**), respectively.

CHAPTER I

INTRODUCTION

Since the first reported synthesis of an isocyanate in 1848[1], the preparation and investigation of heterocumulenes has contributed immensely to synthetic organic chemistry. The synthetic importance of this class of compounds arises from the ambivalent nature of the heterocumulene linkage where nucleophilic, electrophilic and electrocyclic addition reactions are possible. At present over two dozen

$$X{=}Y{=}Z \qquad \overset{-}{X}{-}Y{\equiv}\overset{+}{Z}$$

$$X,\ Y \text{ or } Z = C,\ CR_2,\ O,\ NR,\ S,\ SO \text{ and } SO_2$$

heterocumulenes have been reported; and those containing tetravalent sulfur as the central atom are shown in Table 1.

Table 1. Heterocumulenes Containing Tetravalent Sulfur

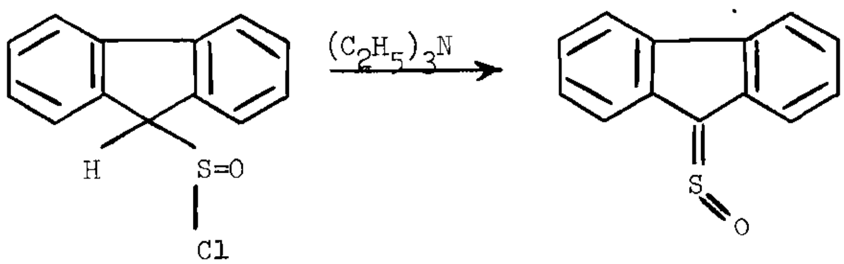
$R_2C{=}S{=}CR_2$, thione ylids	RN=S=NR, sulfurdiimides
$R_2C{=}S{=}NR$, thione S-imides **1**	RN=S=O, N-sulfinylamine
$R_2C{=}S{=}O$, sulfines	O=S=O, sulfur dioxide

The studies reported in this dissertation are concerned with the synthesis of a new heterocumulene, the thione *S*-imide **1**. Isoelectronic and closely related to sulfines, thione *S*-imides* might be expected to show similar reactivity and stability.

$$R_2C{=}S{=}NR$$

1

Sulfines have been prepared by the dehydrohalogenation of a precursor sulfinyl chloride such as **2**[2,3]; the oxidation of monomeric



2

thioketones[4,5] and the thioketene **3**[58]; and, most recently, by the base

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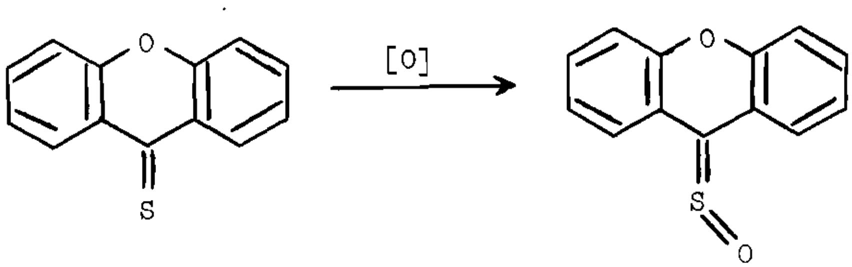
*Thione *S*-imide is the name recommended and used for indexing of **1** by the Chemical Abstracts Service.

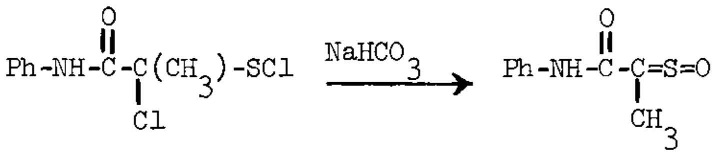
The author is grateful to Dr. K. L. Loening, Director for Nomenclature of the Chemical Abstracts Service, for his assistance in naming structure **1**.

$$[(CH_3)_3C]_2C{=}C{=}S \xrightarrow{[O]} [(CH_3)_3C]_2C{=}C{=}S{=}O$$

3



hydrolysis of α-chlorosulfenyl chlorides[6]. For the most part the sulfines thus produced are relatively stable and can be isolated and

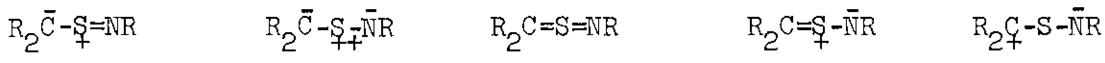


characterized at room temperature.

The stability of sulfines (4) is dependent on charge delocalization in the resonance contributors 4a, 4b, 4c, and 4d. Structure

$R_2\bar{C}-\overset{+}{S}{=}O$	$R_2\bar{C}-\overset{++}{S}-\bar{O}$	$R_2C{=}S{=}O$	$R_2C{=}\overset{+}{S}-O^-$	$R_2\overset{+}{C}-S-O^-$
4a	4b	4	4c	4d

4d would be expected to contribute to only a minor degree, particularly if the substituents on carbon destabilize a positive charge*. Molecular orbital calculations indicate that the stability of sulfines is governed predominantly by delocalization of the negative charge on the carbon atom in the resonance structures 4a and 4b[3]. Similar arguments involving structures 1a through 1d may be raised to predict the stabilities of thione *S*-imides (1) when the substituent on nitrogen is electron withdrawing.



1a 1b 1 1c 1d

Prior to 1972, the only reported reaction which might have provided a thione *S*-imide was the reaction of benzenesulfonylazide (6) and xanthione (7) in refluxing xylene to give as proposed intermediates 8 and 9[8]. However, the only products isolated were sulfur and benzenesulfonimidoxanthene (10). The possibility

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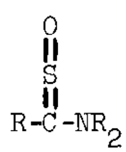
*If the substituents on carbon become sufficiently electron donating, structure 4d would become more influential in the resonance scheme. The stability of thioamide *S*-oxides (5)[7] is surely dependent on the contribution of 4d.



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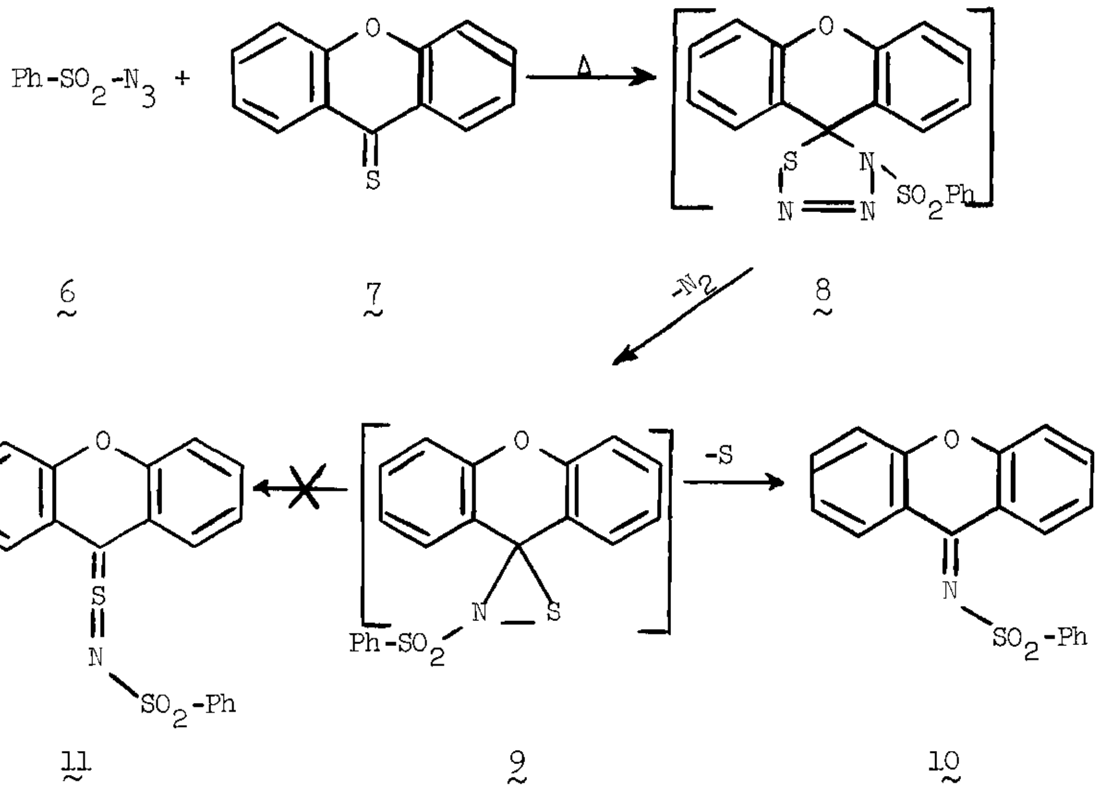
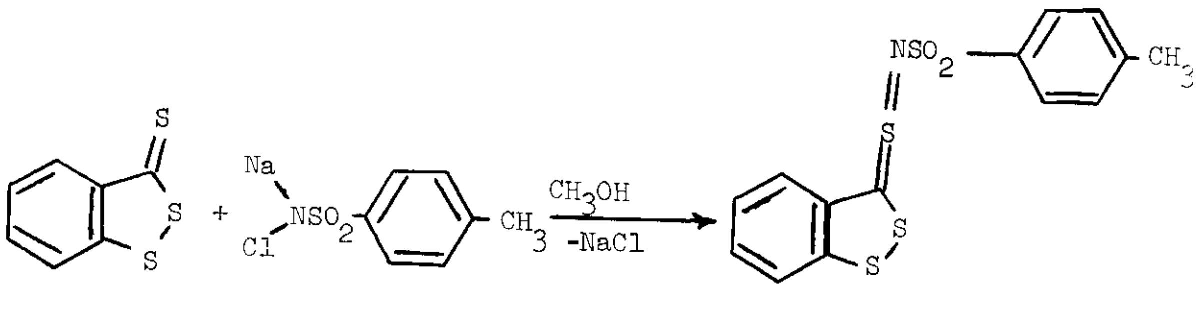


exists that xanthione S-benzenesulfonimide (11) may have been the initial adduct arising from the reaction of the nitrene 12 and 7. Under the conditions of the reaction 11 may have closed to the thiaziridine 9 which would decompose to the isolated products.

$$\underset{12}{Ph\text{-}SO_2\text{-}\ddot{N}:} \quad + \quad 7 \longrightarrow [11] \longrightarrow [9]$$

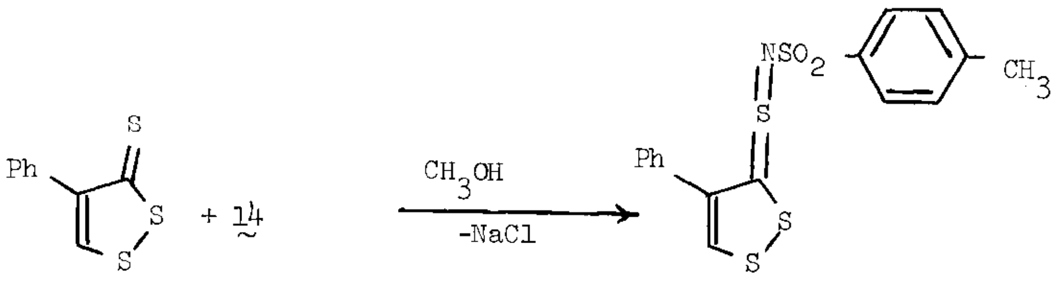
While the research described herein was in progress there appeared a report of the preparation of the N=S=C function by the reaction of 1,2-benzodithione-3-thione (13) and chloramine-T (14)[9].

In a similar manner 17 was prepared from 4-phenyl-1,2-dithiole-3-



13 14 15

thione (16). Except for the decomposition of 15 to the imine 18



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upon melting or treatment with a catalytic amount of acid, no other chemical properties of these molecules were described. The thiaziridine 19 was proposed as the intermediate in this desulfurization process.

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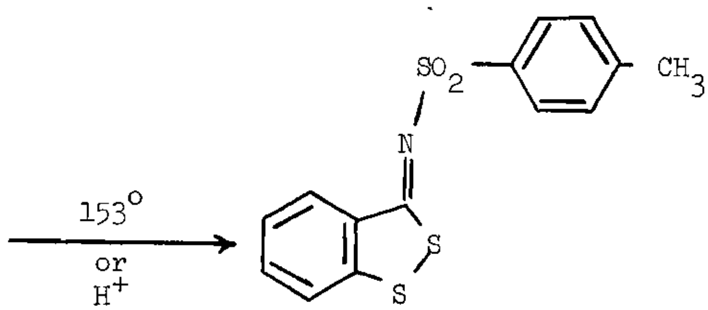

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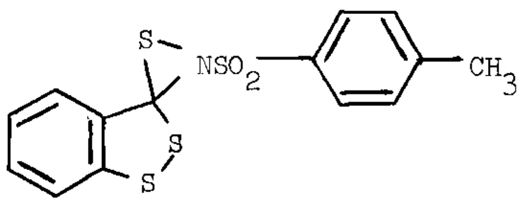

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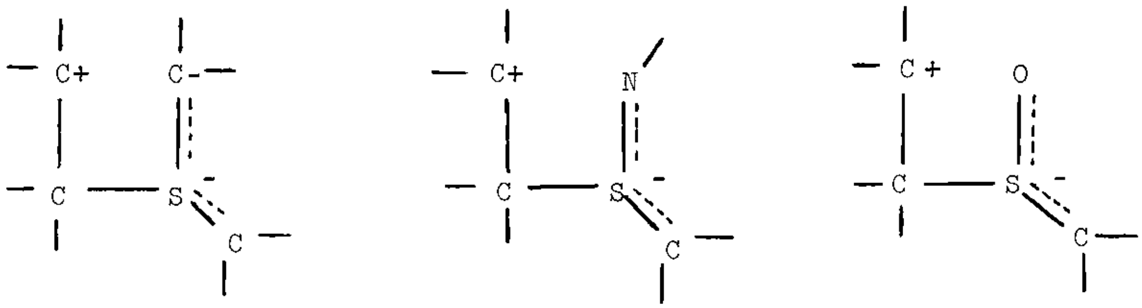
One of the major contributions of heterocumulenes has been the ability of several members of this class to participate in cycloaddition reactions to yield four, five and six-membered ring products[10]. Thione S-imides might be expected to undergo non-concerted cycloadditions due to the electronegativities of the components in the carbon-sulfur-nitrogen multiple bond linkage. A second factor which

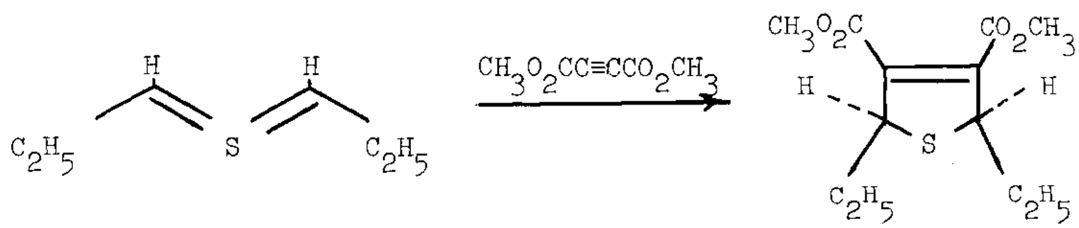
$$R_2\bar{C}-\underset{++}{S}-\bar{N}R$$

influences reactivity in polar cycloaddition reactions is the transition state charge stabilization which is also dependent on electronegativity. On this basis thione S-imides would be expected to exhibit electro-



philic reactivity between thione ylids and sulfines for similar substitution.

The thione ylids that have been studied were found to behave as 1,3-dipoles to yield five-membered ring products such as 20[11]. One may expect, however, that with appropriate substitution thione ylids



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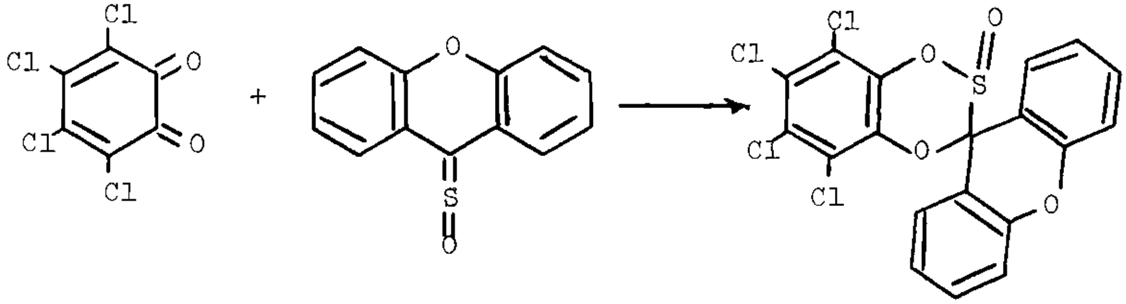
would also participate in nonconcerted 1,2-cycloadditions. On the other hand, sulfines undergo a Diels-Alder type reaction with _ortho_-quinones and 1,3-dienes to give six-membered ring sulfoxides 21[12] and 22[13]. The only report of an attempted 1,2-dipolar cycloaddition was that of Sheppard and Diekmann who obtained the interesting zwitterionic 1:1 adduct 23 from the reaction of 9-fluorenthione _S_-oxide and morpholinocyclohexene[2].



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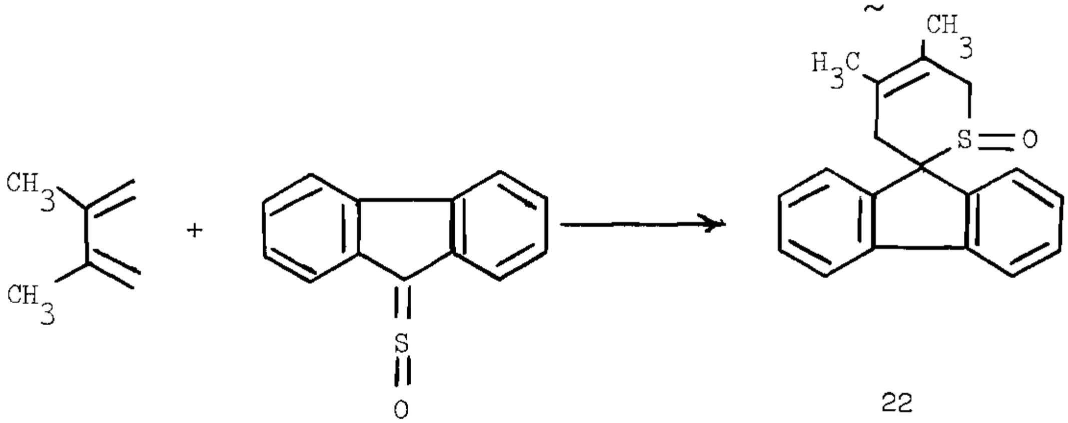

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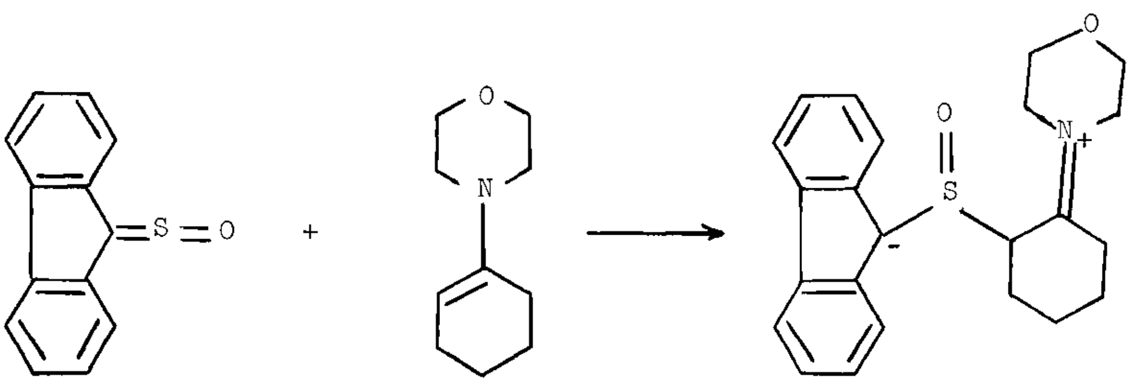
Since cycloaddition reactions employing thione S-imides might lead to interesting heterocyclic molecules, the purpose of the



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research described herein was to develop convenient synthetic routes for this new heterocumulene; and to investigate its chemical properties with emphasis on delineating its ability to undergo cycloaddition reactions.

CHAPTER II

INSTRUMENTATION AND EQUIPMENT

Thiophene free benzene was distilled from sodium metal before use. Tetrahydrofuran (THF) and dimethoxyethane (DME) were distilled from sodium metal and benzophenone. Triethylamine and acetonitrile were dried by distilling from powdered phosphorus pentoxide. Methanol was distilled from magnesium methoxide prior to use. Ether, anhydrous and USP, was purchased commercially in one pound cans and used without additional purification. All other liquid organic reagents and solvents were purified according to established procedures[14] and distilled prior to use. All inorganic chemicals used were commercally available reagent grade. Sulfur dichloride was distilled under vacuum (1mm) at ambient temperatures, and only the first half of the distillate which condensed at -78° was collected.

When anhydrous reaction conditions were required, the necessary glassware was dried for at least four hours in an oven maintained at $125^{\circ}C$. An inert atmosphere was established with purified nitrogen which was dried by passing through a coiled tube immersed in a dry ice-acetone bath. In all cases where triethylamine hydrochloride was precipitated, its identity was confirmed by melting point and comparison of its infrared spectra with an authenic sample. In cases where sodium chloride was precipitated, its identity was confirmed by standard flame tests. Unless otherwise indicated, yields of triethylamine hydrochloride and sodium chloride were approximately quantitative. In all cases where the possibility existed that more than one product might be formed in a reaction, the crude reaction mixture was subjected to nmr and ir analysis; and, unless otherwise indicated, only the products isolated and characterized were observed in the crude mixture.

Concentration of solvents under reduced pressure was done using a Buchi Rotavapor rotary evaporator. Solid-liquid phase chromatography was accomplished using alumina (Fisher, 80-200 mesh) or florisil (Fisher, 60-100 mesh) as indicated. Thin layer chromatography was performed using silica gel G (according to Stahl; E. Merck AG, Darmstadt) on 3" x 1" microscope slides and in each case the liquid phase is indicated.

Mass spectra were obtained using either a Varian Associates Model M-66 medium resolution mass spectrometer with a 70 electron volt source or a Hitachi Perkin-Elmer RMU-7L high resolution mass spectrometer with an 80 electron volt source. Nuclear magnetic resonance spectra (nmr) were acquired using a Varian Associates Model A-60D nuclear magnetic resonance spectrometer. Deuterochloroform ($CDCl_3$) and deuterodimethylsulfoxide (DMSO-d_6), containing 1 percent of tetramethylsilane as an internal standard, were used as solvents. Chemical shifts are reported in units of $\delta(\delta = 10 - \tau)$ and the abbreviations s, d, t, q, and m refer to singlet, doublet, triplet, quartet and multiplet, respectively. For a multiplet a single value for the chemical shift is given which is the center of gravity of the multiplet. Infrared spectra were obtained on a Perkin-Elmer Model 457 recording spectrophotometer using either 0.1 mm sodium chloride cells, sodium chloride plates or a potassium bromide wafer. Ultraviolet spectra were recorded using one centimeter balanced cells on a Beckman DB-GT or Carey Model 14 recording spectrophotometer. Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Melting points are reported in degrees centigrade.

Elemental analysis (C, H, N and S) were performed by Atlantic Microlab, Inc., Atlanta, Georgia.

CHAPTER III

EXPERIMENTAL

Benzamide-N-sulfenyl Chloride

N-(Trimethylsilyl) benzamide (29)

N-(Trimethylsilyl) benzamide was prepared by modification of the procedure of Derkach and Smetankina[15]. Freshly distilled (bp 58-59^{o}) chlorotrimethylsilane (21.7 g, 0.20 mole) was added dropwise over a period of one hour under nitrogen to 24.2 g (0.20 mole) of benzamide and 22.3 g (0.22 mole) of triethylamine in 150 ml of anhydrous ether and 75 ml of anhydrous THF. When the addition was complete, stirring was continued for two hours and then the precipitated triethylamine hydrochloride was removed by filtration. After washing the precipitate with two 50 ml portions of anhydrous ether, the combined filtrate was concentrated with a rotary evaporator under reduced pressure to a colorless oil. Vigorous stirring of the oil with dry hexane caused the crystallization of 38 g (98 percent) of N-(trimethylsilyl) benzamide (29): mp 62-65^{o} (lit. mp[15] 63-65^{o}).

Benzamide-N-sulfenyl Chloride (28)

N-(Trimethylsilyl) benzamide (29)(38 g, 0.196 mole) in 175 ml of anhydrous ether was added dropwise under nitrogen over a three hour period to 30.3 g (0.294 mole) of freshly distilled sulfur dichloride in 35 ml of anhydrous ether and 50 ml of pentane maintained at zero degrees. After about one-third of 29 had been added, a yellow precipitate began to separate from the reaction mixture. When the addition was complete, the reaction mixture was stirred at zero degrees for an additional six hours. Pentane (175 ml) was then added and the reaction mixture was cooled to -30° for one hour. The precipitate which had separated from the solution was collected by filtration under a nitrogen atmosphere and dried under reduced pressure at zero degrees to yield 30.9 g (84 percent) of benzamide-N-sulfenyl chloride (28) as bright yellow micro needles: mp 105-108° (dec); uv max (THF) 209 nm (ε7070), 237 nm (ε12,900) and 350 nm (ε140); ir ($CHCl_3$) 3200 (N-H) and 1670 cm^{-1} (C=O); nmr (DMSO-d_6) δ11.66 (s, 1H, NH), 7.97 (m, 2H, aromatic CH) and 7.50 (m, 3H, aromatic CH).

Anal. Calculated for C_7H_6NOSCl: C, 44.80; H, 3.22; N, 7.46; S, 17.09. Found: C, 44.68; H, 3.29; N, 7.52; S, 17.13.

Compound 28 has been kept for three months without appreciable deterioration if it was tightly sealed under an inert atmosphere and stored below zero degrees.

N, N'-Thiobenzamidemorpholine (30)

Benzamide-N-sulfenyl chloride (3g, 0.016 mole) in 10 ml of anhydrous THF was added dropwise over a period of 20 minutes under nitrogen to 2.8 g (0.032 mole) of morpholine in 25 ml of THF maintained at -78°. When the addition was complete, stirring was continued for an additional hour. The precipitated morpholine hydrochloride (1.94 g, 98 percent) was removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure to a yellow oil. The oil was dissolved in a minimum volume of hot benzene - hexane; and, upon cooling, 2.08 g of N, N'-thiobenzamidemorpholine (30) separated as colorless plates. When the mother liquor was concentrated to half volume and allowed to stand for 12 hours an additional 0.175 g of 30 crystallized to give a total yield of 2.25 g (59 percent): mp 117-118°; ir ($CHCl_3$) 3410 and 3300 (N-H) and 1680 cm^{-1} (C=O); nmr ($CDCl_3$) δ8.12 (s, 1H, NH), 7.81 and 7.43 (m, 5H, aromatic CH), 3.62 (m, 4H, $(CH_2)_2O$) and 3.17 (m, 4H, $(CH_2)_2N$); mass spectrum (70 eV) m/e (rel intensity) 238 (33), 121 (73), 105 (100), 86 (44).

Anal. Calculated for $C_{11}H_{14}N_2O_2S$: C, 55.44; H, 5.92; N, 11.76; S, 13.45. Found: C, 55.52; H, 5.98; N, 11.73; S, 13.35.

Compound 30 was also prepared by the dropwise addition of 10 g (0.065 mole) of morpholine-N-sulfenyl chloride[17] under nitrogen to 9.3 g (0.065 mole) of the sodium salt of benzamide (prepared by the addition of benzamide to an equamolar amount of sodium hydride in refluxing DME) suspended in 150 ml of DME. When the addition was complete, the solution was filtered and the filtrate was concentrated with a rotary evaporator under reduced pressure to a yellow powder. Recrystallization from benzene-hexane gave 7.1 g (46 percent) of 30.

N, N'-Thiobenzamideaniline (31)

Benzamide-N-sulfenyl chloride (2g, 0.011 mole) in 15 ml of anhydrous THF was added dropwise over a period of 45 minutes under nitrogen to 2.05 g (0.022 mole) of aniline in 15 ml of THF at -78°. When the addition was complete the reaction was stirred for an additional hour, and it was then warmed to room temperature. The precipitated aniline hydrochloride (1.30 g, 92 percent) was removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure to a brown residue. The residue was dissolved in ether, decolorized with Norit, and the ether was removed under reduced pressure to give a colorless powder. Two recrystallizations from benzene - hexane gave 1.43 g (54 percent) of *N*, *N'*-thiobenzamideaniline (**31**) as colorless needles: mp 148-150° (dec); ir ($CHCl_3$) 3490 (broad, N-H), 1675 (C=O) and 1600 cm^{-1} (C=C); nmr (DMSO-d_6) δ10.12 (s, 1H, NH), 8.39 (s, 1H, NH), 7.93 (m, 2H, aromatic protons) and 7.15 (m, 8H, aromatic CH); mass spectrum (70 eV) *m/e* (rel intensity) 244 (4), 121 (77), 105 (100), 93 (64).

Anal. Calculated for $C_{13}H_{12}N_2OS$: C, 63.90; H, 4.95; N, 11.47; S, 13.13. Found: C, 63.71; H, 5.02; N, 11.38; S, 13.22.

Attempted Preparation of N-Thiobenzamide

Triethylamine (1.62 g, 0.016 mole) was added to 3.0 g (0.016 mole) of benzamide-*N*-sulfenyl chloride in 35 ml of THF maintained at -78°. The reaction mixture was warmed to room temperature, filtered, and the filtrate was concentrated with a rotary evaporator under reduced pressure to a brown residue. Recrystallization of the residue from benzene gave 1.3 g of colorless needles which were subsequently identified as *N*, *N*-thiobisbenzamide (**33**): mp 185-187° (dec) (lit mp[16] 187-189°). The mother liquor from the recrystallization was concentrated with a rotary evaporator under reduced pressure to a brown oil. The oil was distilled in a Hickmann still (bath temperature, 50°; 3 mm) to give 0.418 g of benzonitrile[21]. No other identifiable products were isolated.

In another experiment 2,3-dimethylbutadiene was added to the reaction mixture at -78° immediately after the addition of triethylamine. However, only **33** and benzonitrile were isolated. Similar results occurred when enamines or 1,1-diphenylethylene were added as trapping reagents. The use of other bases (potassium *tert*-butoxide, sodium hydride, lithium diisopropylamide, ethyldiisopropylamine) with the above trapping reagents also gave **33** and benzonitrile as the only isolable products. However, when *tert*-butyllithium was employed as the base, in addition to **33** and benzonitrile, an 8 percent yield of *N*-(thio-*tert*-butyl) benzamide (**34**) was isolated: mp 173-174°; ir ($CHCl_3$) 3410 (N-H) and 1690 cm^{-1} (C=O); nmr ($CDCl_3$) δ 7.84 (m, 2H, aromatic CH), 7.48 (m, 3H, aromatic CH), 7.0 (s, 1H, NH) and 1.33 (s, 9H, $(CH_3)_3C$); mass spectrum (70 eV) *m/e* (rel intensity) 209 (3.2), 153 (75), 105 (100), 57 (66).

Anal. Calculated for $C_{11}H_{15}NOS$: C, 63.12; H, 7.31. Found: C, 63.21; H, 7.31.

Benzophenthione S-Benzoylimide

N-Benzoyl-chlorodiphenylmethanesulfenamide (**26**)

Diphenyl diazomethane[18] (1.03 g, 0.0053 mole) in 10 ml of anhydrous THF was added dropwise over a period of 30 minutes under nitrogen to 1.0 g (0.0053 mole) of benzamide-*N*-sulfenyl chloride in 25 ml of THF maintained at -30°. When the evolution of nitrogen had ceased (*ca*. 10 minutes after the addition was complete) the solvent was removed with a rotary evaporator under reduced pressure. The resulting residue was dissolved in a minimum volume of anhydrous ether and cooled to -30°. After standing overnight, 0.178 g (11 percent) of N-benzoyl-chlorodiphenylmethanesulfenamide (26) had separated as light yellow needles: mp 110-117° (dec); ir ($CHCl_3$) 3410 (N-H) and 1675 cm^{-1} (C=O); nmr (Acetone-d_6) δ 7.34 (m, 6H) and 6.83 (m, 10H).

Compound 26 rapidly decomposed upon exposure to moisture or if allowed to stand at room temperature. Noticeable decomposition had also occurred after three days at -30°. The instability of 26 precluded elemental analysis.

Treatment of 26 with Triethylamine: Isolation of 2,2,5-Triphenyl-1,3,4-oxathiazole (38)

Triethylamine (0.59 g, 0.0053 mole) was added at once to 1.87 g (0.0053 mole) of 26 under a nitrogen atmosphere and at -78°. Although a precipitate of triethylamine hydrochloride formed immediately, no color changes were observed. After warming to room temperature the triethylamine hydrochloride was removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure. The resulting residue was recrystallized from ether-hexane to give 0.52 g (31 percent) of 2,2,5-triphenyl-1,3,4-oxathiazole (38) as colorless plates: mp 118-120°; ir ($CHCl_3$) 1605 (C=N) and 1575 cm^{-1} (C=C); nmr ($CDCl_3$) δ7.98 (m, 2H) and 7.38 (m, 13H); mass spectrum (70 eV) m/e (rel intensity) 182 (9.2), 103 (100).

Anal. Calculated for $C_{20}H_{15}NOS$: C, 75.68; N, 4.76; N, 4.41; S, 10.10. Found: C, 75.53; H, 4.81; N, 4.45; S, 9.95.

Attempted Trapping of Benzophenthione S-Benzoylimide (24)

A THF solution (35 ml) of 1.87 g (0.0053 mole) of 26 and 0.664 g (0.0053 mole) of N-isobutenylpyrrolidine[19] maintained at -78° under a nitrogen atmosphere was treated at once with 0.59 g (0.0053 mole) of triethylamine. After warming to room temperature, the precipitated triethylamine hydrochloride was removed by filtration, and the filtrate was concentrated with a rotary evaporator under reduced pressure. An infrared spectrum of the resulting residue revealed that the only product present was 2,2,5-triphenyl-1,3,4-oxathiazole (38).

Fluorenethione S-Benzoylimide

N-Benzoyl-9-chloro-9-fluorenesulfenamide (27)

9-Diazofluorene[20] (3.06 g, 0.016 mole) in 20 ml of anhydrous THF was added dropwise over a period of one hour under nitrogen to 3.0 g (0.016 mole) of benzamide-N-sulfenyl chloride in 50 ml of THF maintained at -30°. When the addition was complete, stirring was continued until the evolution of nitrogen had ceased (ca. 15 minutes), and then the THF was removed with a rotary evaporator under reduced pressure. The resulting residue was dissolved in anhydrous ether and cooled to -30°. After four hours the light yellow crystals that had separated from the solution were collected. Washing the crystals with three 25 ml portions of anhydrous ether gave 4.28 g (76 percent) of N-benzoyl-9-chloro-9-fluorenesulfenamide (27) as colorless needles: mp 114-116° (dec); ir (KBr) 3280 (N-H) and 1660 cm^{-1}

(C=O); nmr (DMSO-d_6) δ8.10 (s, 1H, NH) and 7.48 (m, 13H, aromatic CH).

Anal. Calculated for $C_{20}H_{15}NOSCl$: C, 68.27; H, 4.01; N, 3.98; S, 9.11. Found: C, 68.36; H, 4.10; N, 3.94; S, 9.19.

Although **27** decomposes upon exposure to moisture or if allowed to stand over a two day period at room temperature, it has been stored for up to two months without appreciable decomposition at -30°.

Treatment of **27** with Triethylamine: Isolation of 5'-Phenylspiro (fluorene-9,2'[1',3',4']oxathiazole) (**39**)

Triethylamine (0.283 g, 0.0028 mole) was added at once to 1.0 g (0.0028 mole) of **27** maintained at -78° under nitrogen. The precipitated triethylamine hydrochloride was removed from the resulting red reaction mixture by rapid filtration at -78°. The colored filtrate was then allowed to warm slowly to ambient temperatures. At ca. -30° the solution decolorized. The THF was removed with a rotary evaporator under reduced pressure, and the resulting residue was recrystallized from ether-hexane at -30° to give 0.283 g (46 percent) of 5'-phenylspiro(fluorene-9,2'[1',3',4']oxathiazole) (**39**) as colorless needles: mp 100-103° (dec). An analytical sample was prepared by a second recrystallization from ether - hexane: mp 102-103° (dec); uv max (dioxane) 213 nm (ε34,000), 230 nm (ε50,200), 237 nm (ε46,400), 278 nm (ε17,800), 287 nm (shoulder, ε16,200) and 306 nm (shoulder, ε9670); ir ($CHCl_3$) 1605 (C=N) and 1575 cm^{-1} (C=C); nmr ($CDCl_3$) δ7.58 (m, 13H, aromatic CH);

mass spectrum (70 eV) m/e (rel intensity) 315 (20), 196 (9.2), 180 (100), 135 (32), 103 (19).

Anal. Calculated for $C_{20}H_{13}NOS$: C, 76.16; H, 4.15; N, 4.44; S, 10.17. Found: C, 76.06; H, 4.22; N, 4.38; S, 10.24.

Upon standing at room temperature over a two week period 39 decomposed to give benzonitrile, 9-fluorenone and elemental sulfur. These components were separated by column chromatography over florisil and identified by comparison with authenic samples[21].

Isolation of Fluorenethione S-benzoylimide (25)

Compound 27 (0.350 g) was dissolved in 10 ml of anhydrous THF and cooled to -78° under a nitrogen atmosphere. Triethylamine (0.110 gram) was added by syringe and the solution was filtered under nitrogen into a receiving flask which was also at -78°. After removing an alliquot for uv analysis (uv max (THF, -78°) 484 nm), 15 ml of dry hexane was added to the red colored filtrate causing the precipitation of fluorenethione S-benzoylimide (25) as red needles. The crystals were collected at -78° under a nitrogen atmosphere and allowed to warm slowly to room temperature. Although the crystals appeared to be stable at ambient temperatures, any mechanical perturbation resulted in the instantaneous transformation to 5'-phenylspiro(fluorene-9,2'[1',3',4']oxathiazole) (39).

Reaction of 25 with Anhydrous HCl

An anhydrous THF solution (35 ml) of fluorenethione S-benzoylimide (25), which had been prepared in situ from 3.16 g (0.009 mole) of 27 and 0.91 g (0.009 mole) of triethylamine at -78°, was treated with a slow stream of anhydrous HCl until the red color of 25 had dissipated. After warming to room temperature the precipitated triethylamine hydrochloride was removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure. The resulting residue was recrystallized from anhydrous ether to give 2.6 g (82 percent) of N-benzoyl-9-chloro-9-fluorenesulfenamide (27): mp 114-116° (dec)[21].

Reaction of 25 with N-Isobutenylpyrrolidine

9-Diazofluorene[20] (5.11 g, 0.027 mole) in 50 ml of anhydrous THF was added dropwise over a period of one hour under nitrogen to 5.0 g (0.027 mole) of benzamide-N-sulfenyl chloride in 100 ml of THF maintained at -30°. When the addition was complete and the evolution of nitrogen had ceased, the solution was cooled to -78° and 2.96 g (0.029 mole) of triethylamine was added at once. To the resulting red reaction mixture was added 3.66 g (0.029 mole) of N-isobutenylpyrrolidine[19] which caused the solution to decolorize immediately. After warming to room temperature the precipitated triethylamine hydrochloride (3.57 g, 96 percent) was removed by filtration and the filtrate was concentrated with a rotary evaporator to a brown viscous oil. The crude residue was triturated with 800 ml of anhydrous ether and the etheral solution was decanted from an insoluble brown tar. The volume of the ether was reduced to 300 ml with a rotary evaporator under reduced pressure and the solution was then allowed to stand at -30°. After 24 hours, 6.60 g of 2'-benzoyl-3'-pyrrolidine-4',4'dimethylspiro(fluorene-9,5'[1',2']isothiazolidine) (47) was collected as colorless plates. When the mother liquor was concentrated to a volume of 100 ml and allowed to stand at -30°, an additional 0.93 g of 47 crystallized to give a total yield of 7.53 g (64 percent): mp 185-187° (dec); uv max ($CHCl_3$) 228 nm (ε25,300), 265 nm (ε15,400) and 310 nm (ε2890); ir ($CHCl_3$) 1635 (C=O) and 1600 cm^{-1} (C=C); nmr ($CDCl_3$) δ7.47 (m, 13H, aromatic CH), 5.62 (s, 1H, 3'-CH), 3.23 (m, 4H, $(CH_2)_2N$), 1.76 (m, 4H, $(CH_2)_2$), 1.66 (s, 3H, 4'-CH_3) and 0.58 (s, 3H, 4'-CH_3); mass spectrum (70 eV) m/e (rel intensity) 440 (1.2), 315 (65), 206 (10), 202 (8.4), 135 (100), 125 (62).

Anal. Calculated for $C_{28}H_{28}N_2OS$: C, 76.32; H, 6.40; N, 6.36; S, 7.28. Found: C, 76.11; H, 6.59; N, 6.40; S, 7.14.

Hydrolysis of 47

Compound 47 (0.440 g, 0.001 mole) was dissolved in 35 ml of THF and 25 ml of a 2N sodium hydroxide solution. After stirring for 24 hours at room temperature the reaction mixture was neutralized with concentrated hydrochloric acid and then extracted with 50 ml of chloroform. The chloroform extract was dried with magnesium sulfate and concentrated with a rotary evaporator under reduced pressure. The resulting residue was dissolved in 25 ml of ether; 10 ml of hexane was added and the ether was slowly evaporated under reduced pressure until crystallization began. The recrystallizing flask was then allowed to stand at -30°. After 24 hours, 0.032 g of colorless needles were collected by filtration and subsequently identified as benzamide[21]. The filtrate was concentrated with a rotary evaporator under reduced pressure to yield a light yellow oil. Chromatography on 10 g of florisil using methylene chloride as the elutant afforded a colorless oil which was crystallized from hexane giving colorless needles of 9-isobutyraldehyde-fluorene (50) (0.021 g, 10 percent): mp 143-146^{o}; ir ($CHCl_3$) 1725 (aldehyde C=O) and 1600 cm^{-1} (C=C); nmr ($CDCl_3$) δ9.78 (s, 1H, CHO), 7.55 (m, 8H, aromatic CH), 6.83 (s, 1H, 9-CH) and 1.01 (s, 6H, $C(CH_3)_2$); mass spectrum (70 eV) m/e (rel intensity) 236 (2.9), 207 (16), 165 (100). Calculated mass: 236.120. EMD: 236.118.

Oxidation of 47 with One Equivalent of m-Chloroperbenzoic Acid

Purified m-chloroperbenzoic acid[22] (0.230 g, 0.0013 mole) in five ml of methylene chloride was added dropwise over a period of 15 minutes to 0.605 g (0.0013 mole) of 47 in 10 ml of methylene chloride maintained at zero degrees. When the addition was complete the reaction mixture was warmed to room temperature and stirred for 48 hours. At the end of this period the reaction mixture was cooled to zero degrees and the precipitated m-chlorobenzoic acid was removed by filtration. The filtrate was extracted with 25 ml of a 5 percent aqueous sodium thiosulfate solution, 25 ml of a 10 percent aqueous sodium bicarbonate solution and 25 ml of water. The methylene chloride extract was then dried with magnesium sulfate and concentrated with a rotary evaporator under reduced pressure. The resulting residue was dissolved in 35 ml of anhydrous ether. Ten ml of hexane was added and the solution was slowly concentrated with a rotary evaporator under reduced pressure. When crystals began to separate from the solution, the flask was removed from the rotary evaporator and allowed to stand at -30^{o}. After 16 hours, 0.320 g (56 percent) of 2'-benzoyl-3'-pyrrolidine-4',4'-dimethylspiro(fluorene-9,5'[1',2'] isothiazolidine)-1'-oxide (51) was collected as colorless needles: mp 210-213° (dec); uv max ($CHCl_3$) 235 nm (ε28,300), 270 nm (ε19,300) and 280 nm (shoulder, ε16,200); ir ($CHCl_3$) 1665 (C=O), 1600 (C=C) and 1290 cm^{-1} (S=O); nmr ($CDCl_3$) δ7.61 (m, 13H, aromatic CH), 5.94 (s, 1H, 3'-CH), 3.31 (m, 4H, $(CH_2)_2N$), 1.85 (s, 3H, 4'-CH_3), 1.80 (m, 4H, $(CH_2)_2$) and 0.66 (s, 3H, 4'-CH_3); mass spectrum (70 eV) m/e (rel intensity) 456 (2.1), 250 (100), 206 (44), 105 (65).

Anal. Calculated for $C_{28}H_{28}N_2O_2S$: C, 73.65; H, 6.18; N, 6.14; S, 7.02. Found: C, 73.54; H, 6.22; N, 6.08; S, 7.07.

Oxidation of 47 with Excess m-Chloroperbenzoic Acid

Purified m-chloroperbenzoic acid[22] (0.78 g, 0.0045 mole) in 15 ml of methylene chloride was added dropwise over a period of 10 minutes to 1.0 g (0.002 mole) of 47 in 15 ml of methylene chloride maintained at zero degrees. When the addition was complete the reaction mixture was warmed to room temperature. After 24 hours, TLC (silica gel, $CHCl_3$ - hexane, 4:1, v:v) indicated the presence of unreacted 47, compound 51 and a third unknown component. An additional 0.25 g of m-chloroperbenzoic acid was added to the reaction mixture and stirring was continued for 72 hours at room temperature. At the end of this period the reaction mixture was cooled to zero degrees and the precipitated m-chlorobenzoic acid was removed by filtration. The filtrate was extracted with 25 ml of a 5 percent aqueous sodium thiosulfate solution, 25 ml of a 10 percent aqueous sodium bicarbonate solution and 25 ml of water. The methylene chloride extract was dried with magnesium sulfate and concentrated with a rotary evaporator under reduced pressure. The resulting residue was recrystallized from methylene chloride - hexane affording 0.362 g (64 percent) of 4', 4'-dimethylspiro(fluorene-9,5'[1',2']dihydroisothiazole)-1'-oxide (53) as colorless micro needles: mp 168-169^{o}; uv max ($CHCl_3$) 241 nm (ε12,800), 272 nm (ε15,100) and 282 nm (shoulder, ε12,800); ir ($CHCl_3$) 1595 (C=N) and 1295 cm^{-1} (S=O); nmr ($CDCl_3$) δ7.46 (m, 9H, aromatic CH and 3'-CH), 1.67 (s, 3H, 4'-CH_3) and 0.96 (s, 3H, 4'-CH_3); mass spectrum (70 eV) m/e (rel intensity) 281 (2.1), 280 (6.9), 233 (9.3), 206 (100), 191 (92), 165 (83).

Anal. Calculated for $C_{17}H_{15}NOS$: C, 72.56; H, 5.37; N, 4.98; S, 11.40. Found: C, 72.37; H, 5.41; N, 4.90; S, 11.35.

Reaction of 25 with N-Propenylpiperidine

9-Diazofluorene[20] (2.05 g, 0.011 mole) in 15 ml of anhydrous THF was added dropwise over a period of one hour under nitrogen to 2.0 g (0.011 mole) of benzamide-N-sulfenyl chloride in 35 ml of THF maintained at -30^{o}. When the addition was complete and the evolution of nitrogen had ceased the solution was cooled to -78^{o} and 1.11 g (0.011 mole) of triethylamine was added at once. To the resulting red reaction mixture was added 1.5 g (0.012 mole) of N-propenylpiperidine[23] which caused the solution to decolorize immediately. After warming to room temperature, the precipitated triethylamine hydrochloride (1.51 g, 99 percent) was removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure. After the last traces of solvent had been removed, an nmr of the residue revealed that only the trans-isomer of the adduct was present. The residue was dissolved in 200 ml of anhydrous ether, and the solution was clarified by filtering through a celite pad. The volume of the ether was reduced with a rotary evaporator under reduced pressure to ca. 125 ml and the solution was then allowed to stand at -30°. After 24 hours, 3.15 g of 2'-benzoyl-3'-piperidine-4'-methylspiro(fluorene-9,5' [1',2'] isothiazolidine) (55) was collected as colorless plates. When the mother liquor was concentrated to a volume of ca. 50 ml, an additional 0.325 g of 55 was obtained to give a total yield of 3.47 g (71 percent): mp 159-161° (dec); uv max ($CHCl_3$) 242 nm (ε28,800), 263 nm (ε16,600) and 310 nm (ε3000); ir ($CHCl_3$) 1637 (C=O) and 1600 cm^{-1} (C=C); nmr ($CDCl_3$) δ 7.46 (m, 13H, aromatic CH), 5.60 (d, 1H, *J* = 8 Hz, 3'-CH_a), 3.17 (m, 5H, 4'-CH_b and $(CH_2)_2N$), 1.59 (s, 6H, $(CH_2)_3$) and 0.56 (d, 3H, *J* = 6.5 Hz, 4'-CH_3); mass spectrum (70 eV) *m/e* (rel intensity) 440 (1.3), 287 (46), 192 (35), 165 (30), 105 (100), 84 (38).

Anal. Calculated for $C_{28}H_{28}N_2OS$: C, 76.32; H, 6.40; N, 6.36; S, 7.28. Found: C, 76.28; H, 6.47; N, 6.33; S, 7.33.

Oxidation of 55 with m-Chloroperbenzoic Acid

Purified *m*-chloroperbenzoic acid[22] (0.160 g, 0.0009 mole) in 10 ml of methylene chloride was added dropwise over a period of 20 minutes to 0.410 g (0.0009 mole) of 55 in 15 ml of methylene chloride maintained at zero degrees. When the addition was complete, the solution was stirred at zero degrees for 24 hours. At the end of this period, the reaction mixture was diluted to a volume of 50 ml with methylene chloride and extracted with 50 ml of a 10 percent aqueous soidum thiosulfate solution, 50 ml of a 10 percent aqueous sodium bicarbonate solution and 50 ml of water. The methylene chloride extract was dried with magnesium sulfate and concentrated with a rotary evaporator under reduced pressure. After attempts to crystallize the resulting residue were unsuccessful it was chromatographed on 10 g of florisil. Eluting with hexane - methylene chloride (2:1, v:v) afforded 0.140 g (34 percent) of 2'-benzoyl-3'-piperidine-4'-methylspiro(fluorene-9,5'[1',2']isothiazolidine)-1'-oxide (56): mp 206-212° (dec). An analytical sample was prepared by recrystallization from ether - hexane to give 56 as colorless rods: mp 218-219° (dec); uv max ($CHCl_3$) 247 nm (ε18,000), 274 nm (ε12,400) and 284 nm (shoulder, ε10,700); ir ($CHCl_3$) 1665 (C=O), 1600 (C=C) and 1295 cm^{-1} (S=O); nmr ($CDCl_3$) δ7.60 (m, 13H, aromatic CH), 5.78 (d, 1H, *J* = 8.5 Hz, 3'-CH_a), 3.32 (m, 5H, 4'-CH_b and $(CH_2)_2N$), 1.55 (s, 6H, $(CH_2)_3$) and 0.77 (d, 3H, *J* = 7 Hz, 4'-CH_3); mass spectrum (70 eV) *m/e* (rel intensity) 456 (1.3), 408 (4.2), 289 (97), 274 (100), 192 (42), 124 (61), 84 (26).

Anal. Calculated for $C_{28}H_{28}N_2O_2S$: C, 73.65; H, 6.18; N, 6.14; S, 7.02. Found: C, 73.51; H, 6.20; N, 6.08; S, 7.14.

Reaction of 25 with 1-Diethylaminobutadiene

9-Diazofluorene[20] (2.05 g, 0.011 mole) in 15 ml of anhydrous THF was added dropwise over a period of one hour under nitrogen to 2.0 g (0.011 mole) of benzamide-*N*-sulfenyl chloride in 35 ml of THF maintained at -30°. When the addition was complete and the evolution of nitrogen had ceased, the solution was cooled to -78° and 1.11 g (0.011 mole) of triethylamine was added at once. To the resulting red reaction mixture was added 1.40 g (0.011 mole) of 1-diethylaminobutadiene[24] which caused the solution to decolorize immediately. After warming to room temperature, the precipitated triethylamine hydrochloride (1.41 g, 92 percent) was removed by filtration and the filtrate was concentrated with a rotary evaporator under reduced pressure. The resulting dark brown residue was triturated with 250 ml of anhydrous ether. The ethereal solution was decolorized with Norit and then it was concentrated on a rotary evaporator under reduced pressure to a volume of *ca.* 75 ml. After standing at -30° for 16 hours, 1.79 g (36 percent) of 2'-benzoyl-3'-(*trans*-*N*-ethenyldiethylamine)spiro(fluorene-9,5'[1',2'] isothiazolidine) (58) had crystallized from the solution as colorless plates: mp 123-124° (dec); uv max ($CHCl_3$) 247 nm (ε18.500), 264 nm (ε19,100) and 311 nm (ε4410); ir ($CHCl_3$) 1645 (C=C-N), 1630 (C=O) and 1600 cm^{-1} (C=C); nmr* ($CDCl_3$) δ7.51 (m, 13H, CH_a), 6.51 (d, 1H, J = 13.5 Hz, CH_b), 5.70 (m, 1H, J = 8 Hz, CH_c), 4.42 (d of d, 1H, $J_{b,d}$ = 13.5 Hz, $J_{d,c}$ = 5.5 Hz, CH_d), 3.07 (q, 4H, J = 7.5 Hz, CH_e), 2.92 (m, 2H, CH_f) and 1.11 (t, 6H, J = 7.5, CH_g).

Reaction of 25 with 1-(Diethylamino)-1-propyne

9-Diazofluorene[20] (2.05 g, 0.011 mole) in 15 ml of anhydrous THF was added dropwise over a period of one hour under nitrogen to 2.0 g (0.011 mole) of benzamide-*N*-sulfenyl chloride in 35 ml of THF maintained at -30°. When the addition was complete and the evolution of nitrogen had ceased, the solution was cooled to -78° and 1.11 g (0.011 mole) of triethylamine was added at once. To the resulting red reaction mixture was added 1.22 g (0.011 mole) of 1-(diethylamino)-1-propyne[25]. Within

* See page 56, this thesis for nmr assignments.

five minutes the solution had become orange and it was allowed to warm to room temperature. A yellow precipitate was collected by filtration and was found to weigh 0.651 g greater than the theoretical amount of triethylamine hydrochloride. The filtrate was concentrated with a rotary evaporator under reduced pressure to yield a brown oil. Attempts to obtain a crystalline product from the oil were unsuccessful; however, distillation of the oil in a Hickmann still (bath temperature, 50°, 3 mm) afforded a colorless liquid which was identified as benzonitrile[21].

An nmr spectrum of the yellow precipitate indicated the presence of triethylamine hydrochloride and a 1:1 adduct of 25 and 1-(diethylamino)-1-propyne. The precipitate was washed with 100 ml of water and 0.398 g of an insoluble yellow-orange powder, mp 121-124° (dec), was collected. The adduct was recrystallized by dissolving the powder in a minimum volume of methylene chloride - hexane followed by slowly concentrating the solution with a rotary evaporator under reduced pressure until crystallization began. In this manner, 0.211 g (4.5 percent) of 2-phenyl-4-fluorenylide-5-methyl-6-diethylamino-1,4,3-oxathiazine (60) was collected as yellow needles: mp 125-126° (dec); uv max ($CHCl_3$, 0°) 242 nm (ε20,500), 253 nm (ε25,900) 261 nm (ε33,600), 278 nm (shoulder, ε12,500), 327 nm (ε9450), 311 nm (ε9770) and 375 nm (shoulder, ε5800); ir (KBr) 1590, 1525 and 1500 cm^{-1} (C=C and C=N); nmr ($CDCl_3$, -30°) δ7.58 (m, 13H, aromatic CH), 3.75 (q, 2H, *J* = 7.3 Hz, $CH_3\underline{CH_2}N$), 3.60 (q, 2H, *J* = 7.3 Hz, $CH_3\underline{CH_2}N$), 2.72 (s, 3H, 5-CH_3), 1.54 (t, 3H, *J* = 7.3 Hz, $\underline{CH_3}CH_2N$) and 1.06 (t, 3H, *J* = 7.3 Hz, $\underline{CH_3}CH_2N$), a singlet at δ5.34 (2H) was assigned to methylene chloride. The area of this signal did not diminish after 60 had been subjected to reduced pressure (0.1 mm) for 24 hours.

Anal. Calculated for $C_{27}H_{26}N_2OS \cdot CH_2Cl_2$: C, 65.75; H, 5.52; N, 5.48; S, 6.26. Found: C, 65.97; H, 5.28; N, 5.23; S, 6.18.

Although 60 was stable in the crystalline state and in solution below zero degrees, it rapidly decomposed at the melting point or in solution at room temperature. Upon decomposition 60 gave benzonitrile[21] and a trace of difluorenylidene (detected by TLC) as the only identifiable products.

Reaction of Benzamide-N-sulfenyl Chloride with 9-Diazoxanthene

9-Diazoxanthene[26] (2.0 g, 0.010 mole) in 20 ml of anhydrous THF was added dropwise over a period of one hour under nitrogen to 1.80 g (0.010 mole) of benzamide-N-sulfenyl chloride in 35 ml of THF maintained at -78°. Rapid evolution of nitrogen ensued, and as the addition progressed a colored precipitate formed. When the addition was complete the reaction mixture was filtered to give 0.182 g of an orange powder, mp $282-284^{\circ}$, which was subsequently identified as 9-xanthoneketazine[27]. The filtrate was concentrated with a rotary evaporator under reduced pressure to afford a brown residue from which benzonitrile[21] and N, N-thiobisbenzamide (33)[16] were obtained as the only isolable products.

1,1,3,3-Tetramethyl-2-thiourea S-p-Toluenesulfonimide (69)

1,1,3,3-Tetramethyl-2-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 (14) dissolved in 100 ml of methanol maintained at zero degrees. When the addition was complete the reaction mixture was stirred at zero degrees 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 percent)) 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 percent) of 1,1,3,3-tetramethyl-2-thiourea S-p-toluenesulfonimide (69) to separate as a colorless powder: mp 133-134° (dec); uv max ($CHCl_3$) 243 nm (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); nmr ($CDCl_3$) δ7.74 (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 (70 eV) 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. Calculated 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 69 decomposes within a few days at room temperature, it can be stored for extended periods of time if maintained at temperatures below zero degrees.

Compound 69 is recovered unchanged after being dissolved in aqueous and dilute acidic solutions.

Thermal Decomposition of 69

Compound 69 (0.20 g, 0.0007 mole) was placed neat 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 percent) of colorless needles which were subsequently identified as N-[bis(dimethyl)amino]methylene-p-toluenesulfonamide (73), mp 140-143° (lit. mp[28] 143-145°).

Elemental sulfur and 73 were also the only products isolated when 69 was suspended in refluxing THF for 24 hours.

Hydrolysis of 69

Compound 69 (1.0 g, 0.0033 mole) was dissolved in 20 ml of a 50 percent aqueous sulfuric acid solution. After standing for three days at zero degrees, the solution was neutralized with sodium carbonate which caused the precipitation of 0.347 g (61 percent) of p-toluenesulfonamide [21]. The remaining solution was extracted with three 50 ml portions of chloroform. The combined chloroform extracts were dried with sodium sulfate and concentrated with a rotary evaporator under reduced pressure to reveal that no additional products had been extracted from the aqueous solution.

Reaction of 69 with Dimethyl Acetylenedicarboxylate

Dimethyl acetylenedicarboxylate (1.12 g, 0.0079 mole) in 10 ml of methylene chloride was added dropwise over a period of 30 minutes to 2.0 g (0.0066 mole) of 69 in 35 ml of methylene chloride maintained at zero degrees. When the addition was complete stirring was continued for two hours at zero degrees and then the methylene chloride was removed with a rotary evaporator under reduced pressure. The resulting red-brown residue was dissolved in a minimum volume of hot anhydrous acetonitrile and the solution was then allowed to stand at -30°. After three days the light tan solid which had separated from the solution was collected. Recrystallization from acetonitrile gave 1.12 g (38 percent) of 1,1-[bis(dimethyl)amino]-2,3-dicarbomethoxy-1-propene-3-thione S-p-toluenesulfonimide (74) mp 207-210° (dec). An analytical sample was prepared by two additional recrystallizations from acetonitrile to afford 74 as off-white prisms: mp 211-213° (dec); uv max ($CHCl_3$) 242 nm (ε20,800), 305 nm (ε25,300) and 335 nm (shoulder, ε10,900); ir (KBr) 1740, 1675 (C=O), 1595 (N=S=C) and 1385, 1170 cm^{-1} (SO_2-N); nmr (DMSO-d_6) δ7.65 (d, 2H, J = 8.5 Hz, aromatic CH), 7.29 (d, 2H, J = 8.5 Hz, aromatic CH), 3.72 (s, 3H, CO_2CH_3), 3.56 (s, 3H, CO_2CH_3), 3.03 (s, 12H, $[(CH_3)_2N]_2$) and 2.34 (s, 3H, p-CH_3); mass spectrum (80 eV), molecular ion, theoretical: 443.118. Found: 443.113.

Anal. Calculated for $C_{18}H_{25}N_3O_6S_2$: C, 48,74; H, 5.68; N, 9.47; S, 14.46. Found: C, 48.88; H, 5.74; N, 9.48; S, 14.42.

Hydrolysis of 74

Compound 74 (0.387 g, 0.009 mole) was dissolved in 25 ml of a 50 percent aqueous sulfuric acid solution and allowed to stand for three days. Sodium bicarbonate was then added part-wise to the solution. When the solution had reached pH 5, a precipitate began to form. The solid (0.172 g) was collected by filtration and identified as unreacted 74. The slightly acidic filtrate was neutralized with additional sodium bicarbonate and extracted with three 50 ml portions of methylene chloride. The combined methylene chloride extracts were dried with sodium sulfate and concentrated with a rotary evaporator under reduced pressure to afford 0.072 g of a colorless solid which was identified as *p*-toluenesulfonamide[21].

Dimethylthioformamide S-*p*-Toluenesulfonimide

Dimethylthioformamide[29] (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 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-toluenesulfonamide[21] and N-dimethylaminomethylene-p-toluenesulfonamide (76) (6.27 g): mp 134-135° (lit. mp[30] 133-134°).

9-Xanthione S-p-Toluenesulfonimide

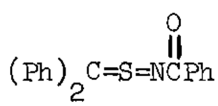
9-Xanthione[31] (1.59 g, 0.0075 mole) in 35 ml of methylene chloride was added dropwise to 2.11 g (0.0075 mole) of chloramine-T. The addition was done at various temperatures. At -30° a red intermediate formed immediately; However, it dissipated over a period of 30 seconds. At -50° the red intermediate 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 percent ethanol gave 0.026 g of N-xanthylidene-p-toluenesulfonamide (78), mp 173-175° (lit. mp[32] 167-168°); 0.659 g of 9-xanthione[21] and 0.571 g of p-toluenesulfonamide[21].

CHAPTER IV

DISCUSSION OF RESULTS

The purpose of this research was to develop synthetic routes for the preparation of thione S-imides and to study their synthetic utility. As discussed in Chapter I, thione S-imides should be sufficiently stable, at least at low temperatures, to be prepared and then treated with suitable reactants so as to obtain new heterocyclic or heterolinear molecules.

Since the stability of thione S-imides would seem to be dependent on the ability of the carbon atom in the heterocumulene linkage to stabilize a negative charge (see page 4), the preparation of benzophenthione S-benzoylimide (24) and 9-fluorenthione S-benzoylimide (25) was set as the initial synthetic goal. A logical means of entry to 24 and 25 would be the 1,3-dehydrohalogenation of the α-chlorosulfenamides 26 and 27 with a tertiary amine to give the desired thione



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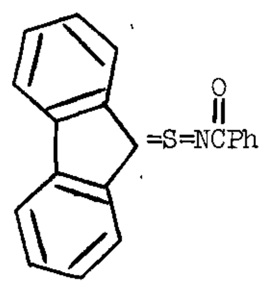

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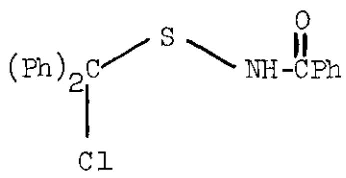

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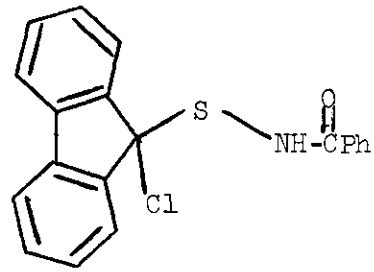


27

S-imide and a tertiary amine hydrochloride.

The preparation of other heterocumulenes by the dehydrohalogenation of suitable precursors has ample precedence. Ketenes are quite simply prepared by the reaction of acyl halides with amine bases[33]. Sulfenes were first prepared by the dehydrohalogenation of sulfenyl chlorides possessing an α-hydrogen substituent[34]; and sulfines may be likewise prepared by the reaction of triethylamine on a sulfinyl chloride bearing an α-hydrogen[2,3].

The key interagent required for the synthesis of 26 and 27 was benzamide-N-sulfenyl chloride (28), a molecule containing the heretofore unknown function -NH-SCl. This compound was successfully prepared by

28

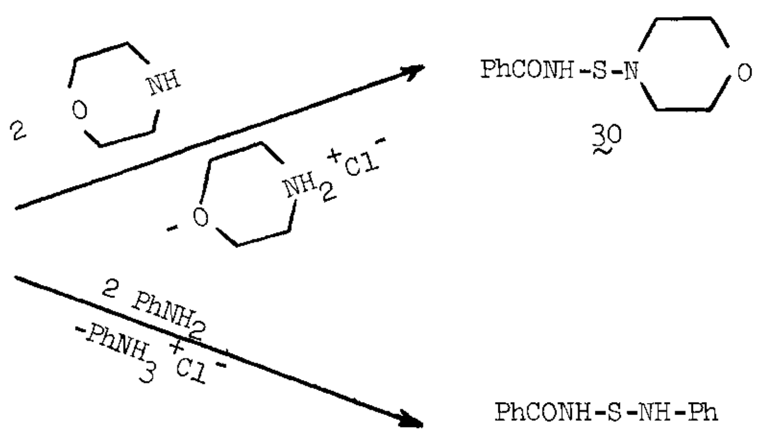
the reaction of N-(trimethylsilyl)benzamide (29)(prepared by a modification of the procedure of Derkach and Smetankina[15]) with sulfur dichloride in ether - pentane solution. Pure **28** precipitated from the above reaction mixture as a yellow crystalline solid in 80-85 percent yield.

$$\underset{\mathbf{29}}{PhCONH\text{-}Si(CH_3)_3} + SCl_2 \longrightarrow \underset{\mathbf{28}}{PhCONH\text{-}SCl} + ClSi(CH_3)_3$$

The structure of **28** was established by examination of its infrared and nmr spectra. The infrared spectrum showed an absorption for N-H stretching at 3200 cm^{-1} and a carbonyl stretching frequency at 1670 cm^{-1}. The nmr spectrum displayed a broad singlet at δ11.66 (1H) for NH and aromatic-CH multiplets at 7.97 (2H) and 7.50 (3H).

In addition, **28** reacted rapidly with two equivalents of morpholine or aniline to give N,N'-thiobenzamidemorpholine (**30**) and N,N'-thiobenzamideaniline (**31**), respectively. Compound **30** was

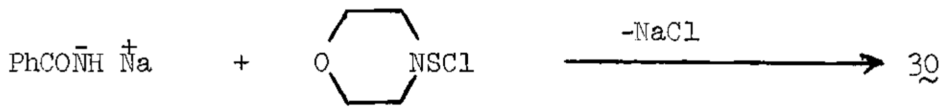
28



31

also prepared independently from the soidum salt of benzamide and morpholine-N-sulfenyl chloride[35].

Although the attractive possibility exists that 28 upon



dehydrohalogenation may lead to a N-thioamide derivative 32, attempts to trap such an intermediate in which a variety of bases and trapping reagents were employed were unsuccessful. In every case only

$$PhC(=O)N{=}S$$

32

N,N-thiobisbenzamide (33)[16,21] and benzonitrile[21] were isolated. However, when tert-butyllithium was employed as the base, N-(thio-

$$28 \xrightarrow{\text{base}} PhCONH\text{-}S\text{-}NH\text{-}COPh \; + \; PhC{\equiv}N$$

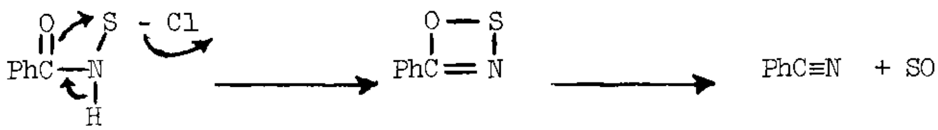
33

tert-butyl)benzamide (34) was isolated in addition to 33 and benzonitrile. Although the mechanism for the formation of 33 is not clear,

$$PhCONH\text{-}SC(CH_3)_3$$

34

benzonitrile is probably formed through the intermediacy of 35. The sulfur monoxide produced is unstable and disproportionates to elemental sulfur and sulfur dioxide[36]. An analogous mechanism involving sulfur



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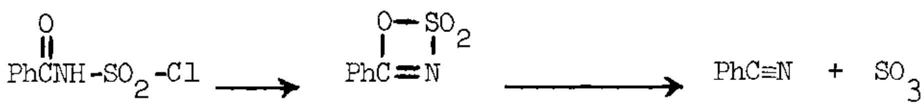
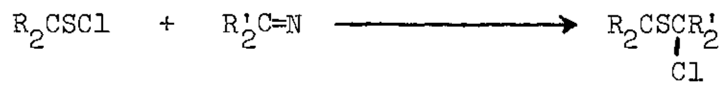
trioxide elimination has been proposed for the formation of benzonitrile from benzoylsulfamoyl chloride (36)[37].



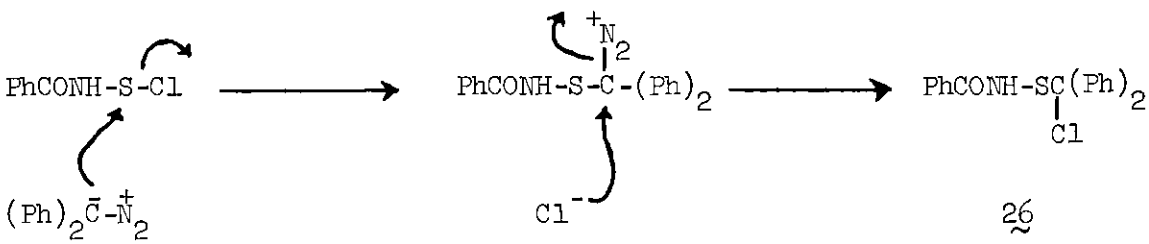
36

The ability of sulfenyl chlorides to undergo reaction with diazo compounds to give products such as 37 is well documented[38]. The sulfenyl chloride 28 was found to behave in a similar manner in its reaction with diphenyldiazomethane in THF solution at -30° to give



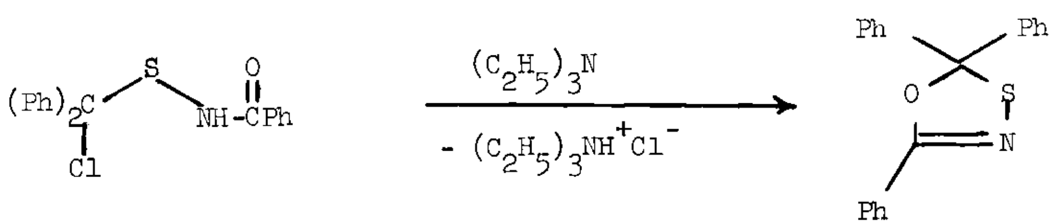
37

N-benzoyl-chlorodiphenylmethanesulfenamide (26). Compound 26 was isolated in low yield as a colorless crystalline solid displaying an infrared N-H and carbonyl stretching frequency at 3410 and 1675 cm^{-1}, respectively.



26

Triethylamine reacted rapidly with 26 in THF solution at -78° without visible formation of a colored intermediate to yield an equivalent of triethylamine hydrochloride and 2,2,5-triphenyl-1,3,4-oxathiazole (38). The oxathiazole 38 was characterized by its infrared



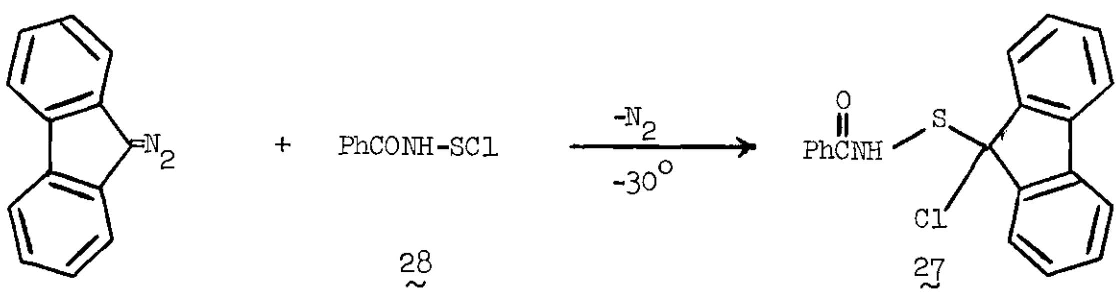
26

38

spectrum which contained a C=N absorption at 1605 cm^{-1} and aromatic C=C absorption at 1575 cm^{-1}. The mass spectrum was most informative, displaying fragments at m/e 182 ($C_{13}H_{10}O^+$) and 103 ($C_7H_5N^+$).

Since thione S-imides such as 24 were predicted to behave as electrophilic π-systems similar to sulfines[2], an attempt was made to trap benzophenthione S-benzoylimide (24) with electron rich olefins. However, when 26 was treated with triethylamine in the presence of an enamine, the oxathiazole 38 was the only product isolated. Although the thione S-imide 24 may have existed as a transitory intermediate which underwent internal cyclization more rapidly than cycloaddition, the possibility exists that 38 may have been formed from 26 by an intramolecular 1,4-elimination.

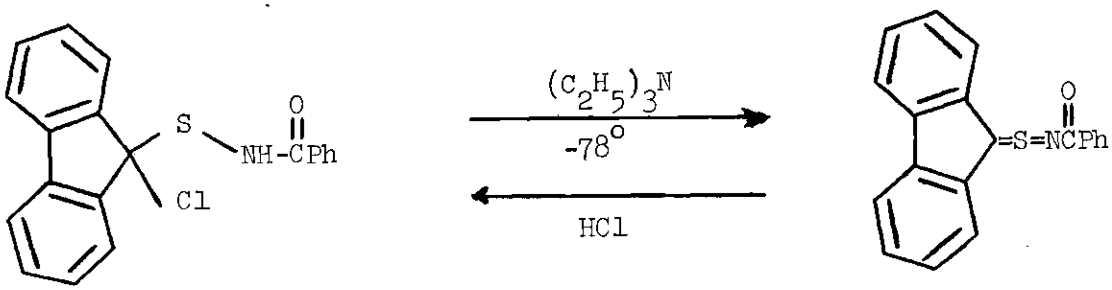
The instability of 24 may have been due to insufficient charge stabilization by the phenyl substituents on the heterocumulene carbon. If this was the case stability might be provided by employing the fluorenyl ring system as the substituent. To this end, N-benzoyl-9-chloro-9-fluorenesulfenamide (27) was prepared by the addition of 9-diazofluorene to benzamide-N-sulfenyl chloride (28) in THF solution at -30°.



28 27

Compound 27 was isolated in good yield as a colorless solid which decomposed at room temperature or upon exposure to atmospheric moisture. The infrared spectrum of 27 displayed an N-H and a carbonyl absorption at 3280 and 1660 cm^{-1}, respectively, and the nmr spectrum exhibited a singlet at δ8.10 (NH) and a multiplet at 7.48 (aromatic CH).

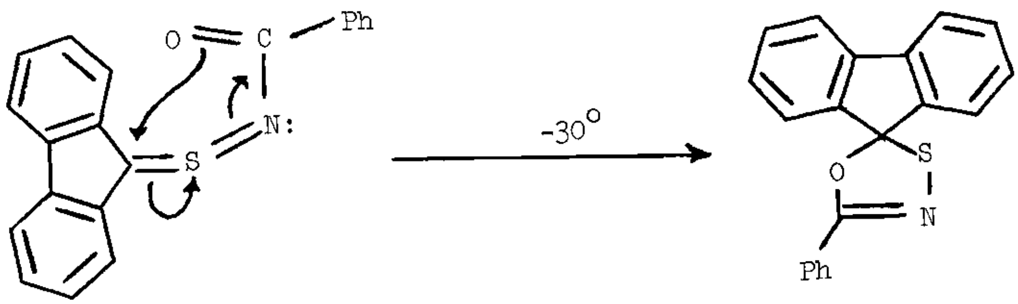
Treatment of 27 with triethylamine at -78° provided a deep red (λ_{max} 484 nm) solution of 9-fluorenethione S-benzoylimide (25)*. Unlike sulfines[12], passage of anhydrous HCl into the solution of 25 at -78° resulted in the rapid reformation of the precursor 27



27 25

* Although 27 may be isolated, its isolation is not required for the preparation of 25. A one step synthesis of 25 from benzamide-N-sulfenyl chloride may be employed by generating 27 *in situ* followed by treatment of the reaction mixture with triethylamine at -78°.

When a solution of 25 was allowed to warm to ca. -30° the color was discharged and a 46 percent yield of the electrocyclic closure product 5-phenylspiro(fluorene-9,2'[1',3',4']oxathiazole) (39) was isolated.



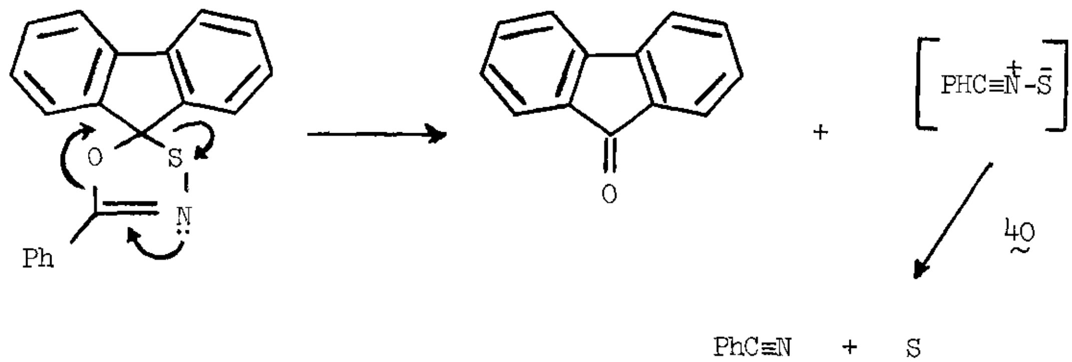
39

The spirooxathiazole 39 was characterized by its infrared spectrum which was similar to that of the oxathiazole 38. The mass spectrum was also consistent with the proposed structure, displaying a molecular ion at m/e 315 and fragments at 196 ($C_{13}H_8S^+$), 180 ($C_{13}H_8O^+$) and 103 ($C_7H_5N^+$).

Furthermore, on standing at room temperature, 39 decomposed to give fluorenone, benzonitrile and sulfur. A mechanism for this decomposition may involve the intermediacy of benzonitrile sulfide (40)[39].

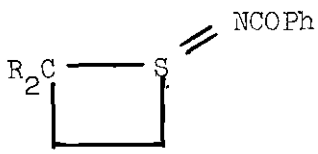
Although 25 underwent rearrangement at temperatures greater than -30° in solution, it was isolated as a metastable solid at room temperature after crystallizing from the reaction mixture at -78°.

However, the slightest amount of mechanical deformation of the crystals of 25 resulted in the instantaneous transformation to 39.



With substantial evidence at hand that the colored intermediate was 9-fluorenethione S-benzoylimide (25), attention was turned to the use of 25 in cycloaddition reactions. Mechanistic considerations revealed the possibility of obtaining five different cycloadducts from the reaction of 25 with suitable olefins. Four-membered ring adducts 41 and 42 would result from 1,2-cycloaddition across the C=S or S=N bond. Five-membered ring adducts 43 would result from 1,3-cycloaddition across the C=S=N linkage. A six-membered ring adduct 44 would be the result of 1,4-cycloaddition involving the S=N-C=O linkage. And 1,5-cycloaddition, although rare[40], might occur across the entire π-system of 25 to yield seven-membered ring adducts such as 45.

Initial studies revealed that the cycloadditive reactivity of 25 at -30° was not sufficient to compete against internal cyclization



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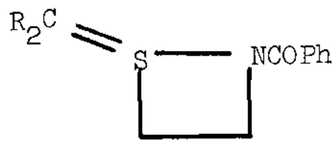

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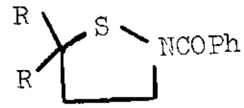

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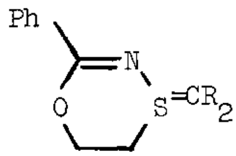

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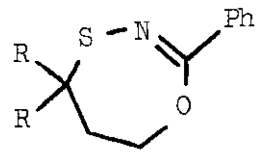


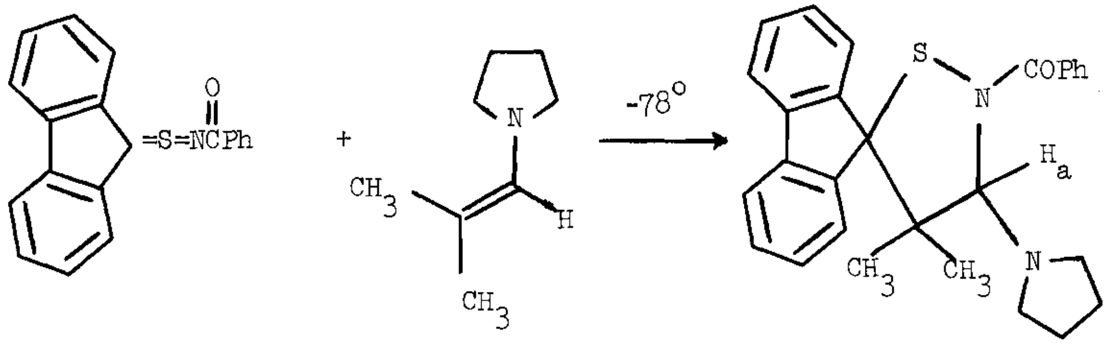
45

R,R = fluorenyl

for the capture of electrophiles such as phenyl diazomethane or diphenyl ketene, and nucleophiles such as vinyl ethers and ketene acetals. However, 25 reacted rapidly with the more nucleophilic alkenes, enamines and ynamines, at -78°.

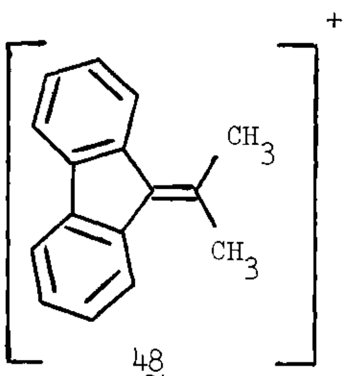
When 25, generated *in situ* at -78° in a THF solution, was treated with *N*-isobutenylpyrrolidine (46) the solution decolorized immediately and there was obtained 2'-benzoyl-3'-pyrrolidine-4',4'-dimethylspiro(fluorene-9,5'[1',2']isothiazolidine) (47) as the only isolable product.

The nmr spectrum of 47 displayed an aromatic multiplet at 7.47



25 46 47

(13H), a singlet for H_a at 5.62 (1H) and non-equivalent methyl singlets at 1.66 (3H) and 0.58 (3H). The pyrrolidine ring exhibited multiplets at 3.23 (4H) and 1.76 (4H). The infrared spectrum contained a tertiary amide C=O absorption at 1635 cm^{-1} [41]. The mass spectrum was most informative, revealing a molecular ion at m/e 440 and fragments at m/e 206 and 202 corresponding to 48 and 49. Fragment 49 would result by loss of sulfur from a fragment having the composition $C_{12}H_{14}N_2OS^+$. The major fragmentation mode resulted from



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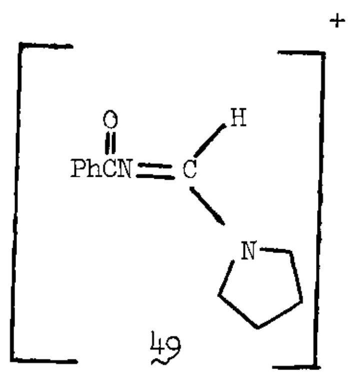
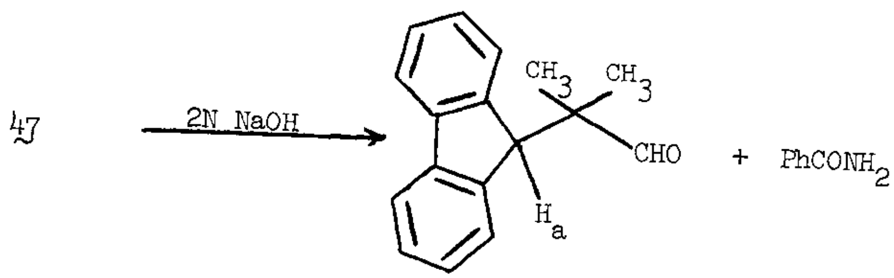


49

cleavage of the ring system into its chemical precursors (m/e 315 and 125).

The possibility of 47 having a structure analogous to 42 or 44 may be discounted since the ultraviolet spectra (page 24) of the adduct is not characteristic of fluorenyl sulfonium ylids[42]. A structure analogous to 41 is improbable since the C=O absorption for acyl iminosulfuranes has been observed at 1600-1540 cm^{-1} in the infrared[43]. Since the C=N linkage may show infrared absorptions in the range 1690-1630 cm^{-1} [44], spectral data does not adequately distinguish between a five-membered ring adduct and a seven-membered ring structure such as 45. However, sufficient chemical evidence was also obtained to support an isothiazolidine ring structure for 47.

Hydrolysis of 47 in 2N sodium hydroxide afforded 9-isobutyraldehydefluorene 50 and benzamide as the only isolable products.

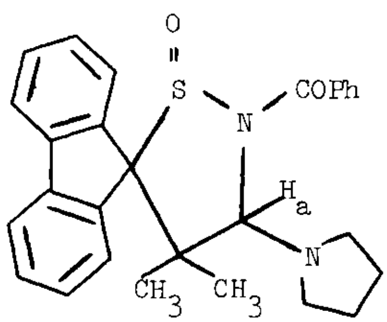


50

The structure of 50 is based on its nmr, infrared and mass spectral data. The nmr displayed a singlet for the aldehydic proton at δ9.78 (1H). Singlets were also observed for H_a at δ6.83 (1H) and for the methyl groups at 1.01 (6H). The infrared spectrum displayed an aldehyde C=O absorption at 1725 cm^{-1} and the theoretical exact mass is 236.120 as compared to the experimentally determined value of 236.118.

Oxidation of 47 with one equivalent of m-chloroperbenzoic acid (m-CPBA) provided 2'-benzoyl-3'-pyrrolidine-4',4'-dimethylspiro(fluorene-9,5'[1',2']isothiazolidine)-1'-oxide (51) in moderate yield.

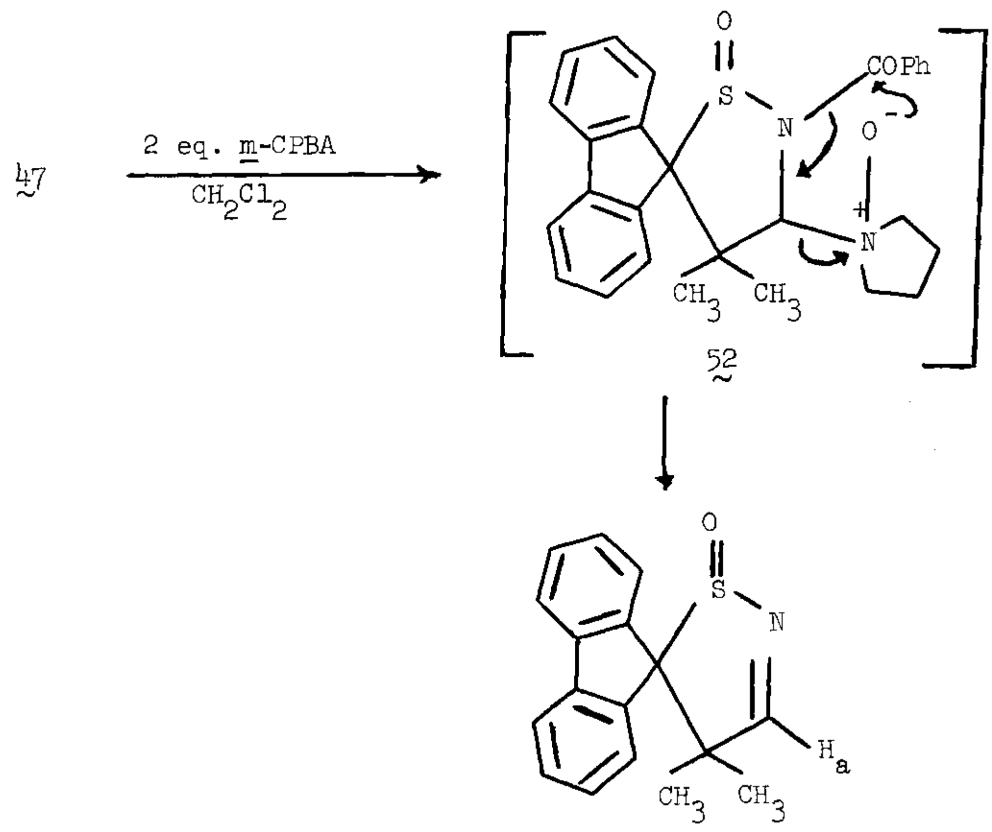
The mass spectrum of 51 was consistent with the structure



51

shown and the infrared spectrum contained a C=O absorption at 1665 cm^{-1} and a strong S=O absorption at 1290 cm^{-1}. The nmr spectrum of 51 was similar to that of 47 except for a downfield shift of 0.32 ppm for H_a, 0.19 ppm for the lower field methyl and 0.08 ppm for the higher field methyl. Although a downfield shift of these signals would be expected due to the inductive effect of the sulfoxide function in the ring, the greater shift of the downfield methyl, as compared to the upfield methyl, is probably the result of its being in a cis-orientation with the sulfoxide oxygen.

The addition of excess m-CPBA to 47 resulted in the formation of 4',4'-dimethylspiro(fluorene-9,5'[1',2']dihydroisothiazole)-1'-oxide (53) in 64 percent yield. This oxidative elimination may be the result of decomposition of the intermediate N-oxide 52, as shown.

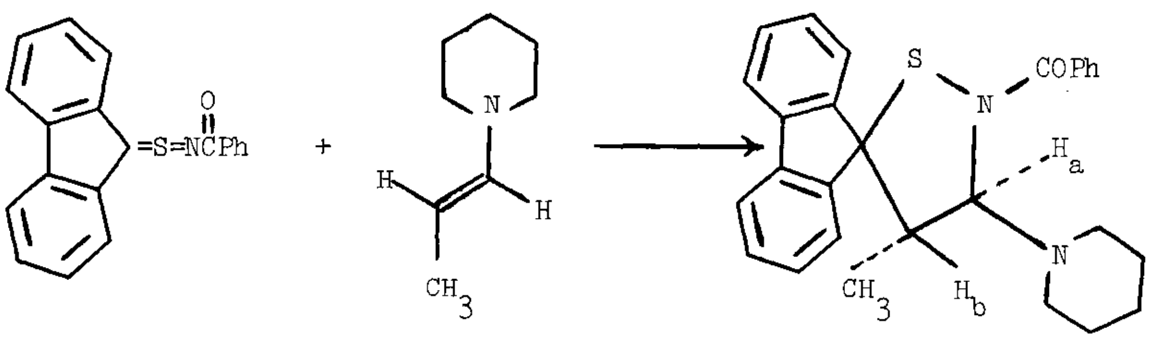


53

The nmr spectrum of 53 displayed a multiplet at δ7.46 (9H) composed of the fluorenyl ring protons and H_a. In addition, singlets at δ1.67 (3H) and 0.96 (3H) accounted for the nonequivalent methyl groups. The infrared spectrum displayed a C=N stretching absorption at 1595 cm^{-1} and the mass spectrum exhibited a molecular ion at m/e 281 and principal fragments at m/e 233 ($C_{17}H_{15}N^+$) and 206 ($C_{16}H_{14}^+$).

The oxidative elimination to give 53 confirms the structure assigned to 47 since the only other possible adduct capable of this elimination mechanism would have a structure analogous to 42.

Although the reaction of heterocumulenes with enamines possessing β-hydrogens often leads to acyclic adducts[10], treatment of 25 with N-propenylpiperidine (54) at -78° resulted in the exclusive formation of 2'-benzoyl-3'-piperidine-4'-methylspiro(fluorene-9,5'[1',2']iso-

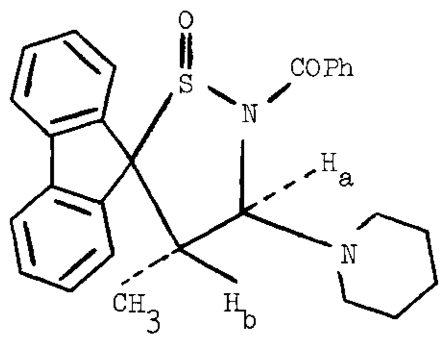


25 54 55

thiazolidine) (55) in good yield.

The nmr spectrum of 55 displayed signals centered at δ7.46 (m, 13H, aromatic CH), 5.60 (d, 1H, J = 8 Hz, H_a), 3.17 (m, 5H, H_b and

$(CH_2)_2N$), 1.59 (s, 6H, $(CH_2)_3$) and 0.56 (d, 3H, _J_ = 6.5 Hz, CH_3). Although 55 is tentatively assigned as having a _trans_-relationship for H_a and H_b, the possibility cannot be eliminated that it actually possesses _cis_-stereochemistry since the coupling constant of H_a,H_b is intermediate in the ranges expected for _cis_ or _trans_ isomers of flexible five-membered rings[45]. The infrared spectrum of 55 was similar to that of 47, having a C=O stretching absorption at 1637 cm^{-1}. The mass spectrum exhibited a molecular ion at _m/e_ 440 and the fragmentation pattern was consistent with the structure shown.



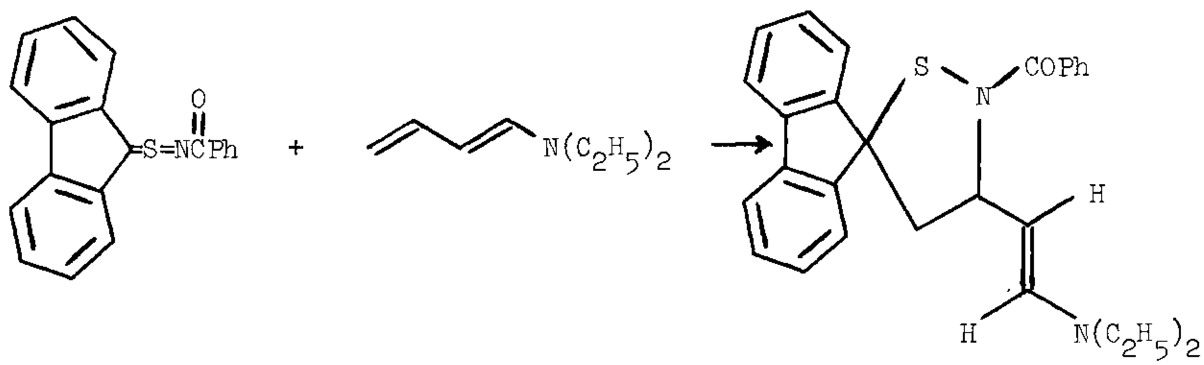
56

Compound 55 was also readily oxidized with _m_-CPBA to 2'-benzoyl-3'-piperidine-4'-methylspiro(fluorene-9,5'[1',2']isothiazolidine)-1'-oxide (56), _albiet_ in lower yield than the oxidation of 47 to 51.

The infrared spectrum of 56 was similar to that of 51, containing C=O and S=O stretching absorptions at 1665 and 1295 cm^{-1}, respectively. The nmr spectrum displayed signals at δ7.60 (m, 13H, aromatic CH), 5.78 (d, 1H, _J_ = 8.5 Hz, H_a), 3.32 (m, 5H, H_b and $(CH_2)_2N$), 1.55 (s, 6H,

($(CH_2)_3$) and 0.77 (d, 3H, J = 7 Hz, CH_3). The cis-relationship of the oxide function to H_b and the C.3'-piperidine is tentatively assigned based on the observed nmr downfield shift of H_b and the H_a,H_b coupling constant[45].

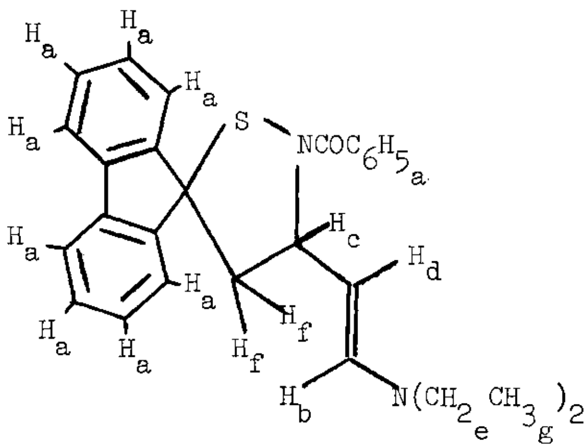
In an attempt to determine if 25 would behave as a dienophile similar to sulfines[13], 25 was treated with 2,3-dimethylbutadiene. No reaction occurred below -30° and only the oxathiazole 39 was isolated. The thione S-imide 25 did react rapidly at -78° with 1-diethylamino-butadiene (57); however, no 1,4-cycloadducts were detected. The only



25 57 58

product was 2'-benzoyl-3'-(trans-N-ethenyldiethylamine)spiro(fluorene-9,5[1',2']isothiazolidine) (58) which was isolated in 37 percent yield.

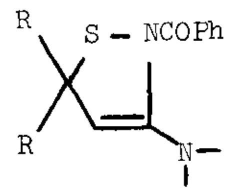
Since attempts to purify 58 for complete analysis were unsuccessful, the structure assigned to 58 is based primarily on its nmr spectrum. The assignment of trans-stereochemistry in the enamine double bond is based on the coupling constant observed for H_b (J = 13.5 Hz).



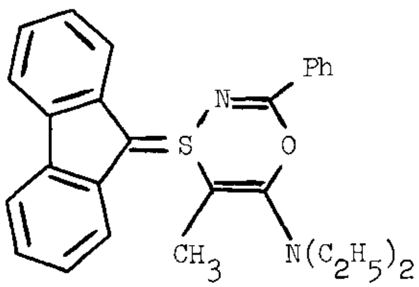
H	δ	mult
a	7.51	m
b	6.51	d
c	5.70	m
d	4.42	dd
e	3.07	q
f	2.92	m
g	1.11	t

Additional support for the structure assigned to 58 was obtained from its infrared spectrum which contained a characteristic C=C stretching absorption of an enamine at 1645 cm^{-1} [46] and a tertiary amide C=O absorption at 1630 cm^{-1} [41]. Furthermore, the ultraviolet spectrum of 58 (page 30) was very similar to those of adducts 47 (page 24) and 55 (page 28).

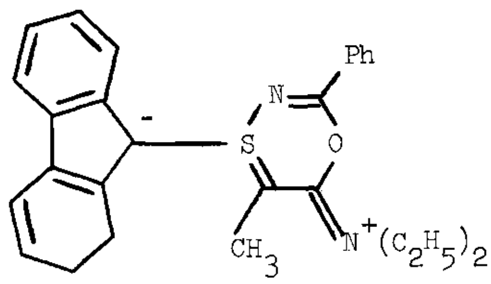
Based on the isothiazolidine adducts obtained from the reaction of 25 with enamines, the reaction of 25 with ynamines might possibly yield dihydroisothiazoles such as 59. However, when 1-(diethylamino)-1-propyne was added to a THF solution of 25 at -78°, 2-phenyl-4-fluoren-



R,R = fluorenyl 59



60



61

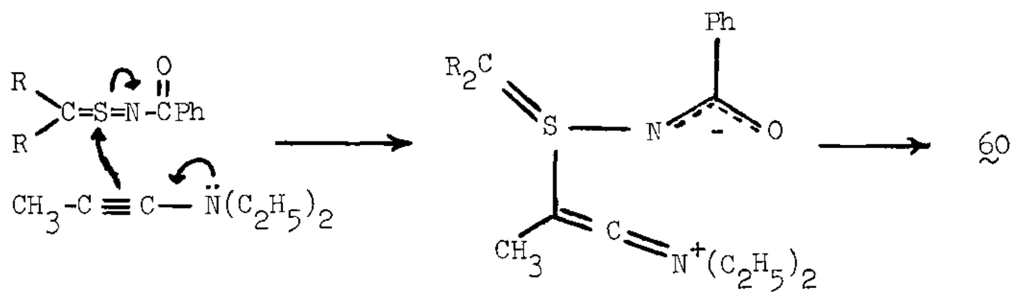
ylide-5-methyl-6-diethylamino-1,4,3-oxathiazine (60) was the only adduct isolated.

The fluorenyl ylid 60 was isolated as a yellow crystalline solid which decomposed in solution at room temperature or at the melting point (125-126°). The ultraviolet spectrum of 60 was similar to 9-dimethylsulfonium fluorenylide[47] displaying λ_{max} (ε) at 242 (20,500), 253 (25,900), 261 (33,600), 278 (12,500), 327 (9450), 311 (9770) and 375 nm (5800). The nmr spectrum contained aromatic protons centered at δ7.58 (m, 13H), a methyl singlet at 2.72 (3H), and non-equivalent N-ethyl groups displaying quartets at 3.75 (2H, J = 7.3 Hz) and 3.60 (2H, J = 7.3 Hz) and triplets at 1.54 (3H, J = 7.3 Hz) and 1.06 (3H, J = 7.3 Hz).

The infrared spectrum of 60 was transparent between 1600-2900 cm^{-1} and displayed C=C and C=N absorptions at 1590, 1525 and 1500 cm^{-1} and suggests that the charge delocalized structure 61 is the best representation of the structure since 60 should show a characteristic enamine C=C absorption between 1630-1660 cm^{-1} [46].

Upon thermal decomposition 60 affords benzonitrile, a trace of difluorenylide and a plethora of other products which have not been identified.

The mechanism that is believed to be in effect for the reaction of 25 with 1-(diethylamino)-1-propyne is initial nucleophilic attack of the ynamine on the central sulfur atom of the heterocumulene linkage

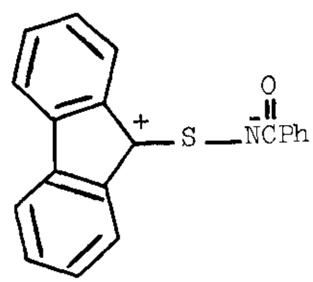


R,R = fluorenyl

62

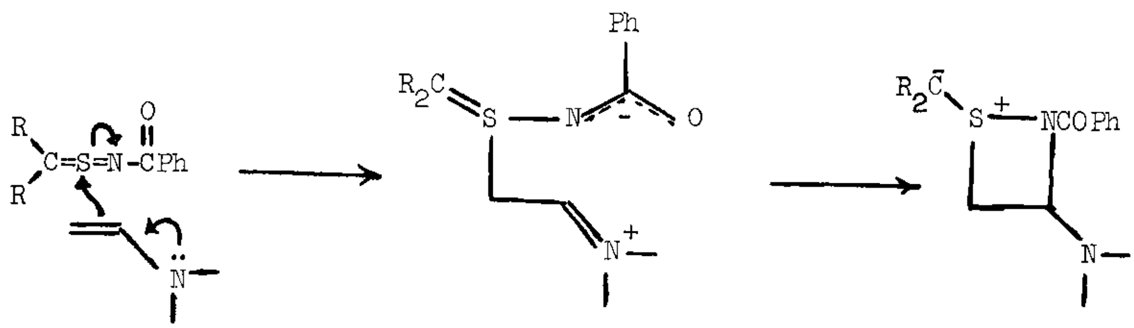
to give a 1,4-dipolar intermediate 62[48], followed by closure to the sulfonium ylid 60.

Although the mechanism for the reaction of the thione S-imide 25 with enamines appears to proceed *via* 1,3-cycloaddition, three



63

arguments can be raised against such a mechanism. The first is that for 1,3-cycloaddition to occur would require 25 to be polarized as shown in 63. Polarization in this manner would impart antiaromatic character to the fluorenyl ring system which would seem to reduce the possibilities of 63 being a major contributing resonance structure. Secondly, if the reaction between enamines and 25 did proceed by 1,3-cycloaddition then the reaction between 25 and an ynamine would have been expected to yield a dihydroisothiazole adduct such as 59. Thirdly, Kuehne has shown that the reaction of 1,3-dipoles such as nitrile oxides and azides with the morpholine enamine derivative of 10-methyl-$\Delta^{1(9)}$-2-octalone gives products resulting from cycloaddition across the double bond adjacent to the amine function; whereas heterocumulenes such as sulfenes add across the terminal double bond[49] similar to what was observed in the reaction of 25 with 1-diethylamino-butadiene.

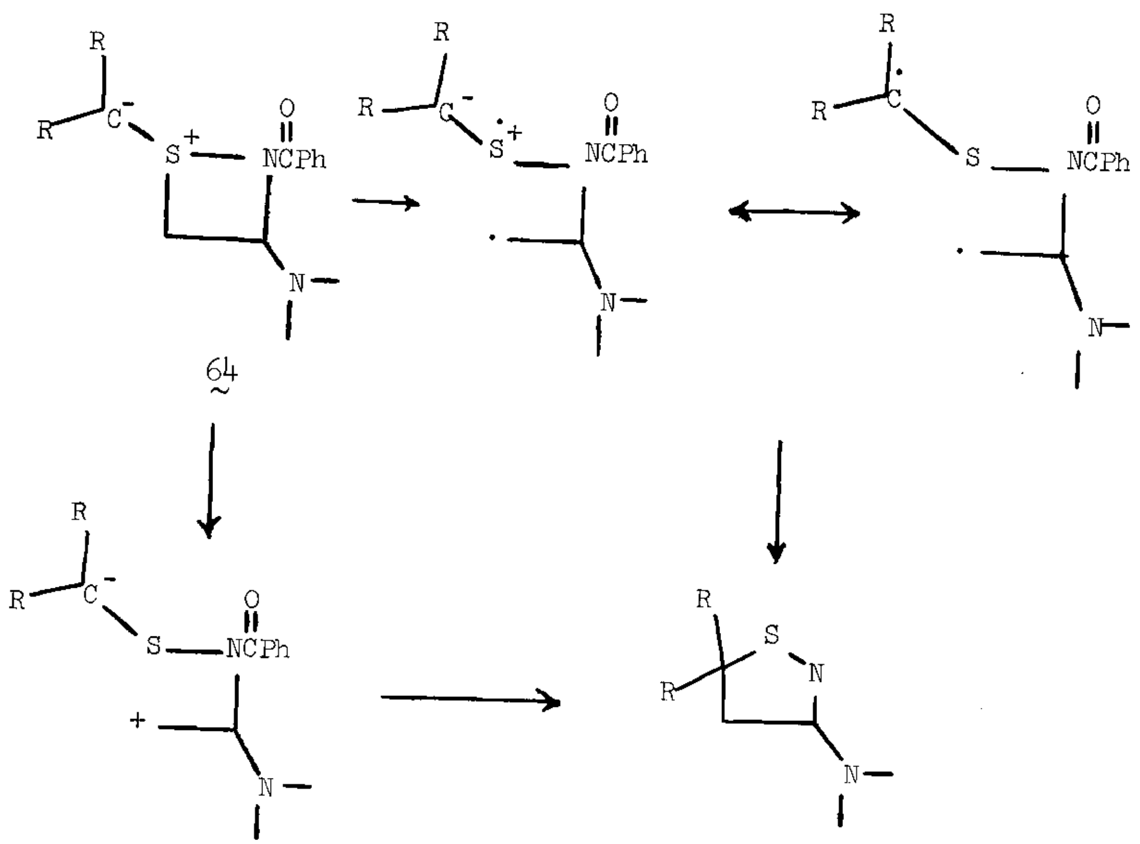


R,R = fluorenyl

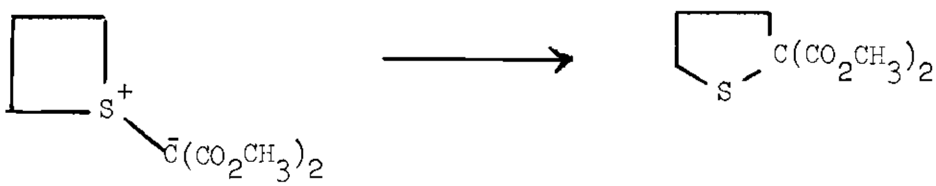
64

The mechanism that is possibly occurring in the reaction of 24 with enamines is initial 1,2-cycloaddition to give four-membered ring adducts such as 64. Although a non-concerted mechanism is depicted based on the zwitterionic adduct obtained in the reaction of the analogous sulfines with enamines[2], a concerted $[\pi 2_s + \pi 2_a]$ cycloaddition might be involved since antarafacial interaction could result from participation of a favorably disposed unoccupied sulfur d-orbital with the ethylenic component[50].

Adduct 64 would then undergo a Stevens rearrangement involving either a radical[51] or polar intermediate[52] to yield the isothiazolidine products.



Ring expansion involving sulfur ylids has precedence. Ando, et al. found that the copper catalyzed thermal reaction of diazomalonate in thietane afforded 66 which was speculated to be the result of rearrangement of the intermediate sulfonium ylid 65[53]. And Minami, et al. showed that the iminosulfurane 67 obtained from the reaction of diphenylsulfur diimide with diphenyl ketene readily rearranged to 68[52].

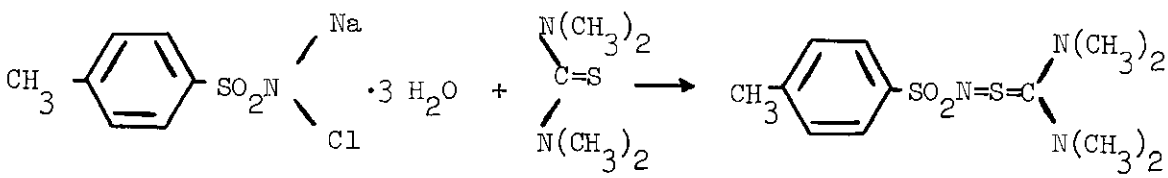


65 66

67 68

Studies to extend the synthesis of thione S-imides via the intermediary reaction of benzamide-N-sulfenyl chloride (28) with other diazo compounds met only with disappointments. Diazo compounds less reactive than 9-diazofluorene or diphenyl diazomethane failed to react with 28, and the reaction of the more nucleophilic 9-diazoxanthene with 28 resulted in the formation of benzonitrile, N,N-thiobisbenzamide (33) and 9-xanthoneketazine[27] as the only isolable products.

Encouraged by the report of Oae and Tamagaki that the C=S=N linkage may be prepared by the reaction of thiones with chloramine-T[9], the reaction of 1,1,3,3-tetramethyl-2-thiourea with chloramine-T (14) was investigated. The addition of 1,1,3,3-tetramethyl-2-thiourea to a methanolic solution of 14 at 0° led to the formation of a quantitative yield of sodium chloride and the isolation of 1,1,3,3-tetramethyl-2-thiourea S-p-toluenesulfonimide (69) in 91 percent yield.



14 69

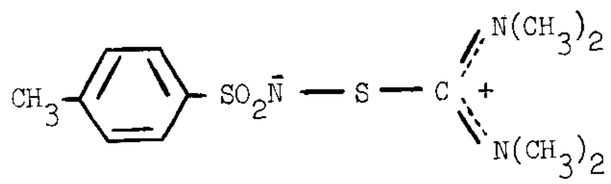
The thione S-imide 69 was obtained as a colorless powder which was moderately stable at room temperature, but which can be stored for extended periods of time below 0°. The nmr spectrum of 69 displayed doublets for the aromatic protons at δ7.74 (2H) and 7.21 (2H), a singlet for the tetramethylamino protons at 3.12 (12H) and a singlet for the tosyl methyl protons at 2.37 (3H). The infrared spectrum exhibited SO_2 absorptions at 1395 and 1165 cm^{-1}. In addition, a strong absorption at 1580 cm^{-1} has been tentatively assigned to the N=S=C function*. A cryoscopic molecular weight determination in *tert*-

* Oae and Tamagaki report an infrared absorption in the same region for 15.[9]

butyl alcohol revealed that **69** was monomeric in nature.

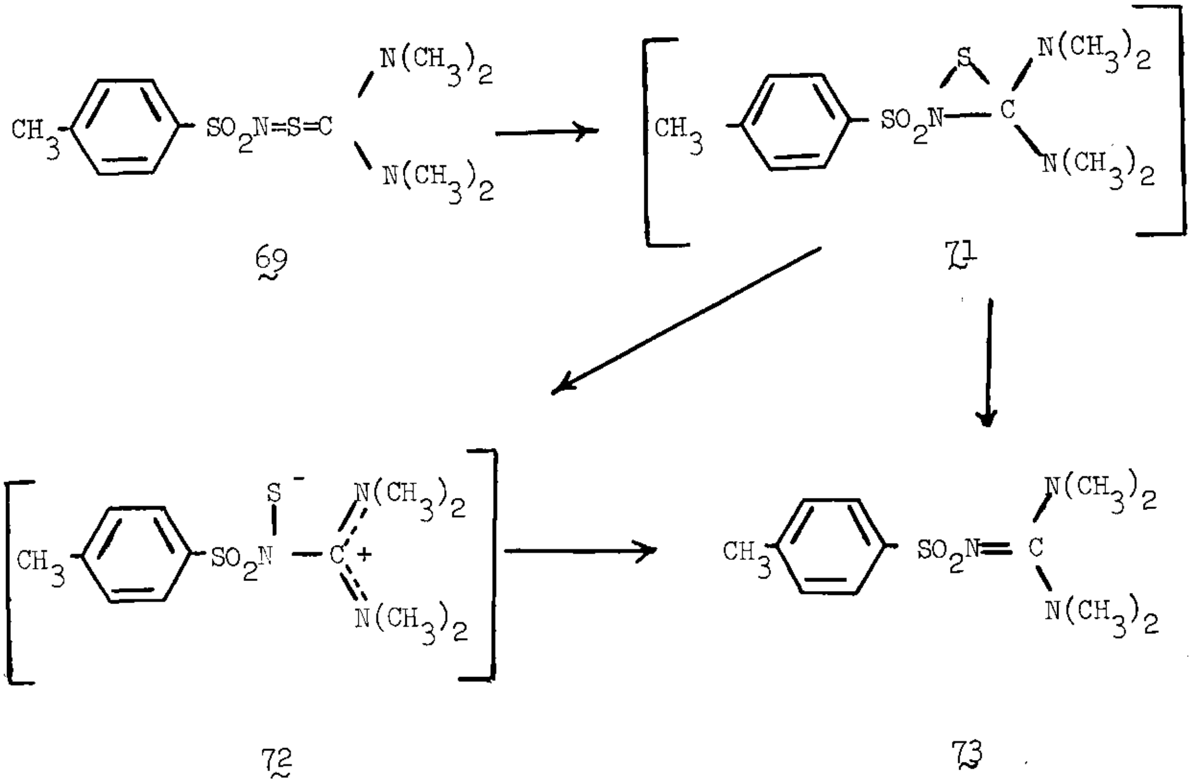
A temperature dependent nmr study on **69** revealed that rotation about the C-N bond of the tetramethylamino groups was sufficiently hindered at -65° to resolve the singlet into a 1:1 doublet. As the temperature was further decreased to -80° a third signal was observed to move upfield from the higher field signal of the doublet, and at -100° the tetramethylamino protons had resolved into an unsymmetrical triplet with a signal area ratio of 2:1:1.

The stability of **69** would seem to be dependent on the ability of the amine substituents to stabilize the positive charge in the delocalized structure **70**. A similar argument can be raised to explain the stability of thioamide _S_-oxides (page 4)[7].



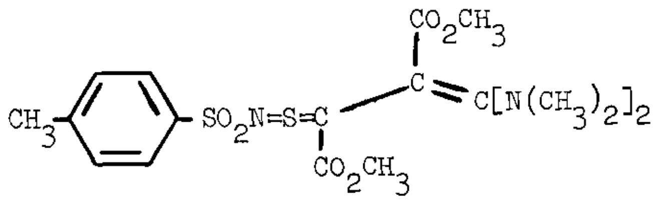
70

At the melting point (133-134°) or when suspended in refluxing THF, **69** rapidly decomposes to give sulfur and _N_-[bis(dimethyl)amino] methylene-_p_-toluenesulfonamide (**73**), mp 141-143° (lit. mp[28] 143-145°). The mechanism of decomposition most likely involves the intermediacy of the thiaziridine **71** which would either eliminate sulfur in a nonlinear cheletropic fragmentation[54], or undergo ring opening to give 72 followed by loss of sulfur, as shown.



Oae and Tamagaki reported that the dithio ester S-tosylimide 15 underwent decomposition to the corresponding imine 18 through a proposed thiaziridine intermediate[9]. In an analogous manner, sulfines photolyticly decompose to a ketone or aldehyde and sulfur through the probable intermediacy of an oxathiairane[55].

The thiourea S-imide 69 was found to be stable in neutral and dilute acid solutions; however, it hydrolyzes over a three day period in 50 percent sulfuric acid to give p-toluenesulfonamide[21] as the only isolable product.

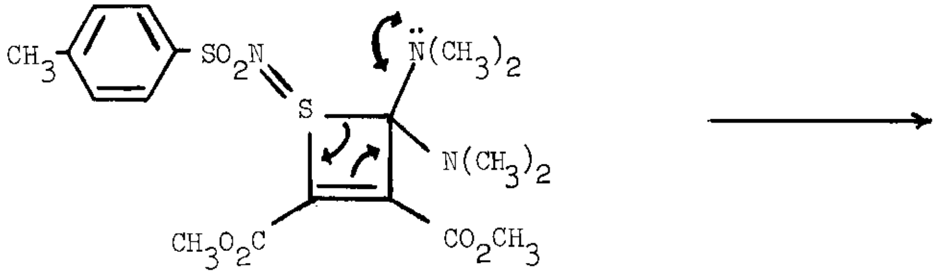


74

Unlike fluorenthione S-benzoylimide (25), compound 69 failed to react with nucleophilic olefins. However, 69 reacted rapidly with dimethyl acetylenedicarboxylate to afford a high melting 1:1 adduct 74 in 38 percent yield.

The structure 1,1-[bis(dimethyl)amino]-2,3-dicarbomethoxy-1-propene-3-thione S-p-toluenesulfonimide is assigned to 74 based primarily on a broad infrared absorption at 1596 cm^{-1} which has been tentatively attributed to the N=S=C function (page 62). The nmr spectrum of 74 displayed doublets for the aromatic protons at 7.65 (2H) and 7.29 (2H), singlets for the carbomethoxy protons at 3.72 (3H) and 3.56 (3H), a singlet for the tetramethylamino protons at 3.03 (12H) and a singlet for the tosyl methyl protons at 2.34 (3H). The mass spectrum displayed a molecular ion at 443.113 as compared to the theoretical value of 443.118.

Compound 74 is probably formed by ring opening of an initial 1,2-cycloadduct 75, with the lone pair of electrons on the amino substituents greatly facilitating the proposed opening.

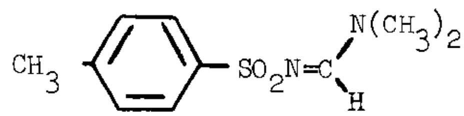


75

74

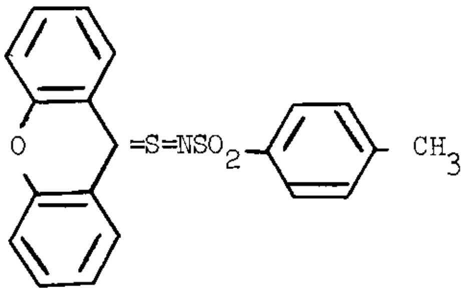
As was the case with 69, hydrolysis of 74 led to the formation of p-toluenesulfonamide[21].

Although two amino substituents adequately stabilize a positive charge on the carbon of the N=S=C linkage, replacement of one of the amino substituents by hydrogen resulted in loss of stability. Thus, the reaction of chloramine-T (14) and dimethylthioformamide at -30° in methanol resulted in the precipitation of sodium chloride followed rapidly by that of sulfur. Work-up of the reaction mixture yielded only N-dimethylaminomethylene-p-toluenesulfonamide (76)[30] and p-toluenesulfonamide[21].



76

Similar results were obtained when chloramine-T (14) was reacted with 9-xanthione in methanol at -30°; however, an intermediate red color formed which rapidly disappeared. Isolated from the reaction mixture was *N*-xanthylidene-*p*-toluenesulfonamide (**78**)[32], *albiet*. in low yield, *p*-toluenesulfonamide[21] and xanthone[21]. The latter two



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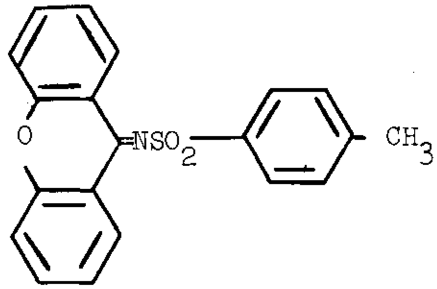

78

products probably arise by hydrolysis of the intermediate thione *S*-imide **77** since **78** is stable to aqueous conditions[32].

CHAPTER V

CONCLUSIONS

Thione S-imides have been prepared in three steps from N-(trimethylsilyl)benzamide (29). The reaction of sulfur dichloride with 29 gave benzamide-N-sulfenyl chloride (28). N-benzoyl-chlorodiphenylmethanesulfenamide (26) and N-benzoyl-9-chloro-9-fluorenesulfenamide (27) was then prepared by the addition of diphenyl diazomethane and 9-diazofluorene to 28. Treatment of 27 with triethylamine gave 2,2,5-triphenyl-1,3,4-oxathiazole (38) via. the proposed transitory intermediacy of benzophenthione S-benzoylimide (24). Treatment of 27 with triethylamine afforded 9-fluorenthione S-benzoylimide (25) which underwent electrocyclic ring closure to 5'-phenylspiro(fluorene-9,2'[1',3',4']oxathiazole) (39) at -30°.

At -78°, 25 was intercepted with N-isobutenylpyrrolidine and N-propenylpiperidine to give spiroisothiazolidines 47 and 55 which were characterized by spectral and chemical data. Compound 25 reacted with the terminal double bond of 1-diethylaminobutadiene to afford 2'-benzoyl-3'-(trans-N-ethenyldiethylamine)spiro(fluorene-9,5'[1',2']isothiazolidine) (58). The products 47, 55 and 58 are proposed to be the result of a Stevens rearrangement of initial 1,2-cycloadducts such as 64. The reaction of 25 with 1-(diethylamino)-1-propyne afforded 2-phenyl-4-fluorenylide-5-methyl-6-diethylamino-1,4,3-oxathiazine (60).

1,1,3,3-tetramethyl-2-thiourea S-p-toluenesulfonimide (69) has been prepared by the reaction of 1,1,3,3-tetramethyl-2-thiourea with chloramine-T (14). Compound 69 was relatively stable at room temperature and reacted with dimethyl acetylenedicarboxylate to afford 1,1-[bis(dimethyl)amino]-2,3-dicarbomethoxy-1-propene-3-thione S-p-toluenesulfonimide (74) which is proposed to be the result of ring opening of the initial 1,2-cycloadduct 75. Compound 69 thermally decomposed via. proposed thiaziridine intermediate to give N-[bis(dimethyl)amino]methylene-p-toluenesulfonamide (73).

Reaction of dimethylthioformamide and xanthione with chloramine-T resulted in the formation of unstable thione S-imides which rapidly decomposed to the imines 76 and 78, respectively.

Attempts to prepare the N-thioamide 32 by dehydrohalogenation of 28 were unsuccessful.

Portions of this research have been reported previously[56,57].

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VITA

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He was graduated from the Fernandina Beach High School, Fernandina Beach, Florida in June, 1965, and received his Bachelor of Science degree from the Florida State University, Tallahassee, Florida in June, 1969. He immediately began graduate work in the School of Chemistry at the Georgia Institute of Technology, Atlanta, Georgia.

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