This is to certify that the

thesis entitled

THE PHOTOCHEMISTRY OF NITROGEN
AND SULFUR HETEROCYCLES:
N-SUBSTITUTED-2-BENZOTHIAZOLINONES

presented by

JOSEPH GEORGE BUCHER III

has been accepted towards fulfillment
of the requirements for

Ph.D. degree in CHEMISTRY

Major professor

Date JULY 24, 1978


MSU

THE PHOTOCHEMISTRY OF NITROGEN AND SULFUR HETEROCYCLES: N-SUBSTITUTED-2-BENZOTHIAZOLINONES

By

Joseph George Bucher III

A DISSERTATION

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

DOCTOR OF PHILOSOPHY

Department of Chemistry

1978

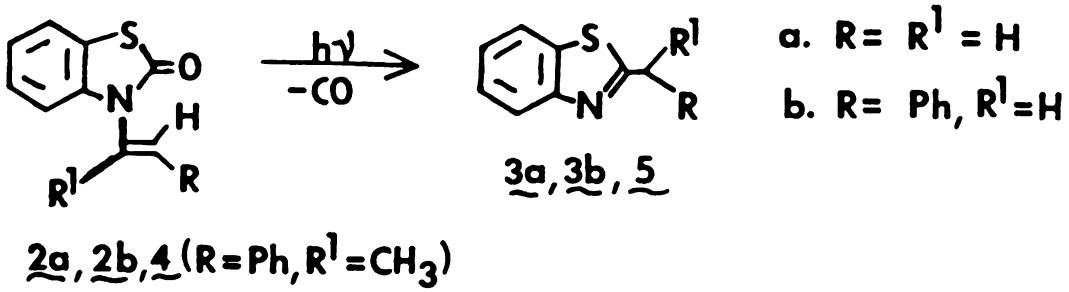
ABSTRACT

THE PHOTOCHEMISTRY OF NITROGEN
AND SULFUR HETEROCYCLES:
N-SUBSTITUTED-2-BENZOTHIAZOLINONES

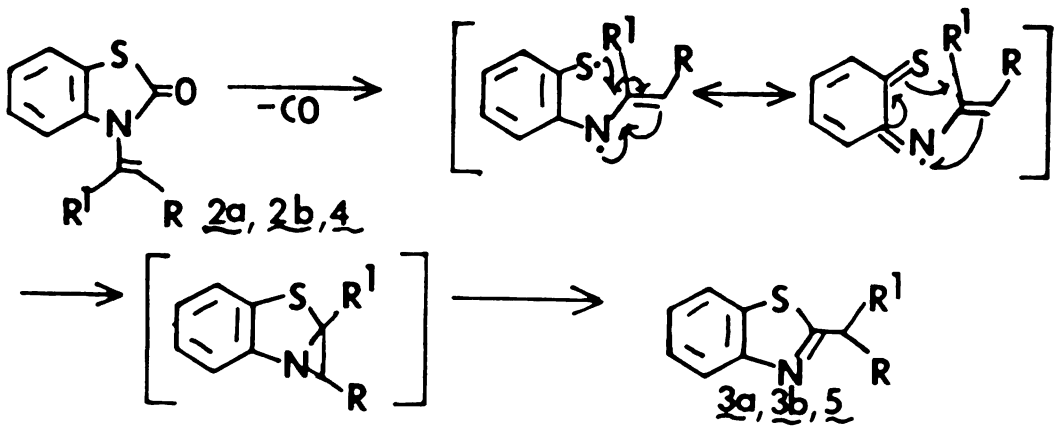
By

Joseph George Bucher III

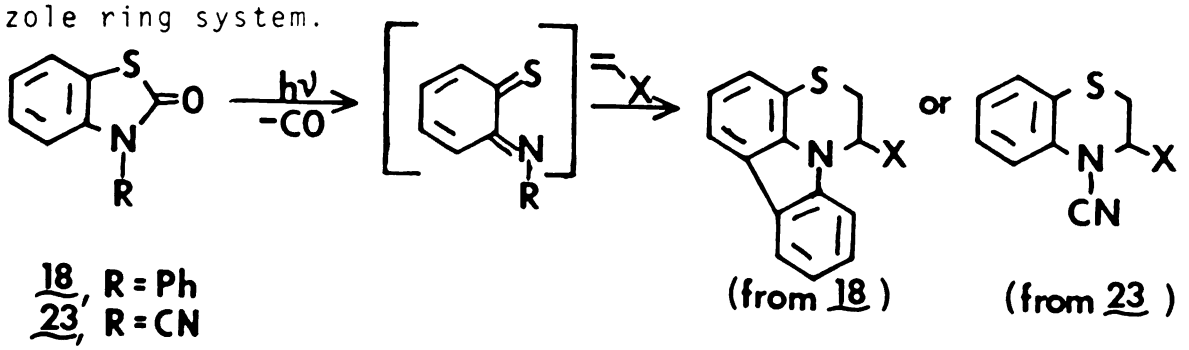
The title compounds were found to photochemically extrude carbon monoxide. The resulting intermediates rearranged or were trapped, depending upon the type of nitrogen substituent present. Irradiation of those compounds bearing a vinyl type substituent on nitrogen (2a, 2b, 4) resulted in rearrangement to benzothiazole derivatives.



Mechanistic experiments indicate the possibility of an aziridine intermediate, presumably formed from a "photochemical Diels-Alder" type rearrangement of the photodecarbonylated species. This rearrangement may be either concerted or stepwise and *via* either a diradical or *ortho*-quinoid intermediate.



When the nitrogen of 2-benzothiazolinone bears a phenyl (18) or cyano (23) group, the expulsion of carbon monoxide affords an intermediate proposed to be a new hetero ortho-quinoid. This intermediate was efficiently trapped with a variety of very electron-rich dieophiles (e.g., vinyl ethers and silyl enol ethers) to afford benzothiazine derivatives. The N-phenyl compound (18) also produces an unexpected carbazole ring system.



Mechanistic experiments indicate that photodecarbonylation of 18 occurs via a singlet reaction and that carbazole formation results from a triplet reaction. In the photolysis of 23 the existence of a very long lived intermediate was demonstrated by varying the amount of added trap. The addition of trap to the intermediate appeared to be completely regioselective within experimental error.

The synthetic potential of these new hetero ortho-ortho-quinoid intermediates was also studied by examining their reaction toward various olefin traps.

To Marg

ACKNOWLEDGEMENTS

I wish to express my deepest appreciation to my research director, Dr. Lynn R. Sousa, whose knowledge, experience, and patience have helped to make my educational experience at Michigan State University very gratifying.

I also wish to thank my colleagues for their assistance in preparing me for this degree. I wish them the best of luck in the future.

I would like to acknowledge the National Science Foundation, the Research Corporation, and Michigan State University for financial support in the form of research and teaching assistantships.

Finally, and most sincerely, I wish to express my heartfelt thanks to my wife, Margaret, for her invaluable help and support.

PREFACE

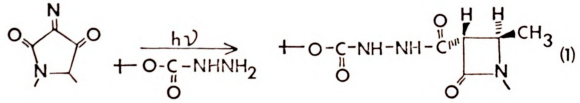
The determination of the absolute structure of penicillin during World War II opened a new era in medicine, namely that of β-lactam antibiotics. With this new and valuable structural information, chemists have strived for new syntheses and derivatives of the important β-lactam ring system.

The β-lactam or 2-azetidinone ring system was first isolated and identified in 1907 by Staudinger[1] et al. from the cycloaddition reaction of diphenyl ketene with imines. Until World War II, little work was done with these compounds since they had no obvious importance. The structure elucidation of penicillin generated new interest in the β-lactam ring system and within the next fifteen years many novel syntheses of 2-azetidinones were developed.[2] Unfortunately, these new procedures lacked the important feature of producing the correct stereochemistry, and therefore, biologically inactive 2-azetidinones were formed. It was not until 1959 that Sheehan[3] et al. developed a method of closing an amino acid to the cis β-lactam with dicyclohexylcarbodimide in his penicillin synthesis. Since then, additional and more practical stereospecific syntheses have been developed.[4]

Recently, light has been used to prepare β-lactams. This approach is reasonable since light is known to form strained systems. Light also has the advantages of being

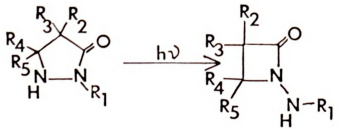
useful at low temperatures and of causing selective reaction which is dependent on the chromophore that has been excited.

Light has been used for various stages of β-lactam syntheses. Stork[5] and Lowe and Ridley[6] used it as a reaction initiator in the photolysis of diazopyrrolidenediones. Nitrogen was photoextruded, and the resulting carbene rearranged by known carbene chemistry (a Wolff rearrangement) to a 2-azetidinone (equation 1).



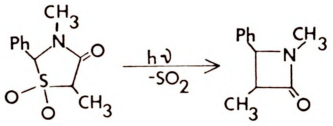
(1)

Light has also been used to initiate a molecular rearrangement, as in the case of Ege's[7] and Johnson and Hatch's[8] ring contraction of pyrazolidineones (equation 2).



(2)

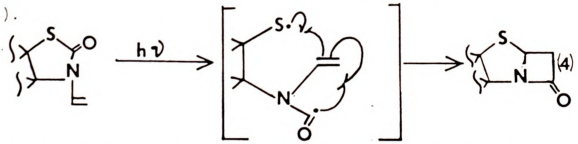
Recently, Sousa and Johnson[9] developed a novel and apparently stereospecific photochemical generation of β-lactams by photoextrusion of sulfur dioxide from dioxothiazolidines (equation 3).



(3)

This concept of small molecule extrusion has become an important aspect of the work to be described in this thesis, and may well be a reasonable approach to many other photosyntheses involving ring contraction or trapping reactions.

N-vinyl-2-thiazolidinone and other similar derivatives could conceivably rearrange to a penam ring system (equation 4).



(4)

Photolysis of these compounds proved not to yield 2-azetidinones, but the photochemistry of these systems appeared interesting and potentially useful.

This thesis will discuss the photochemistry of some N-substituted 2-benzothiazolinones, with an emphasis on mechanism and synthetic potential. Chapter One will deal with those derivatives that undergo intramolecular rearrangements, and Chapter Two will center on those compounds involving intermolecular trapping.

TABLE OF CONTENTS

CHAPTER ONE

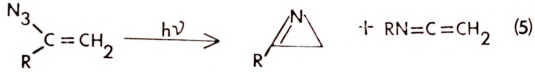
THE PHOTOCHEMISTRY OF N-VINYL-2-BENZOTHIAZOLINONES

INTRODUCTION

Photoextrusion of small molecules has been of interest to photochemists for a long period of time. The loss of these molecules usually results in a diradical, zwitterionic or neutral, noncharge-separated intermediate that can either rearrange, fragment further, or combine with other available molecules. Some of the more commonly extruded species include molecular nitrogen, sulfur dioxide, carbon dioxide and carbon monoxide. Many of these reactions produce interesting and useful products.

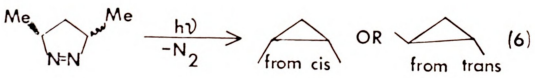
Diazo compounds[10] are known to expell molecular nitrogen photochemically to afford an intermediate carbene which proceeds to do known carbene chemistry. An example of this was noted in the preface, where it was indicated that diazopyrrolidenediones were converted to 2-azetidinones through a Wolff rearrangement.[5,6]

Azides are similar to diazo compounds in that photoextrusion of nitrogen gives a nitrene, the nitrogen analog of a carbene. This intermediate reacts in the predictable fashion of other nitrenes. For example, when azide alkenes are irradiated an azirine is formed along with an azoallene (equation 5).[11]



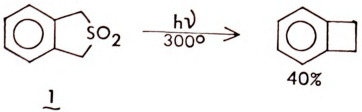
(5)

Loss of nitrogen by irradiation of pyrazolines has proven to be a useful, stereospecific preparation of cyclopropanes.[12] Irradiation of cis or trans 3,5-dimethylpyrazoline produces a cyclopropane retaining the appropriate stereochemistry (equation 6).



(6)

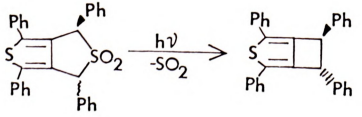
Sulfur dioxide is generally an easy molecule to expell photochemically.[13] When the 1,3-dihydroisothianaphthene-2,2-dioxide (1) is irradiated, loss of sulfur dioxide yields a benzocyclobutene (equation 7).[14]



(7)

1

A thieno[c]cyclobutene was produced on irradiation of sulfone (2) (equation 8).[15]



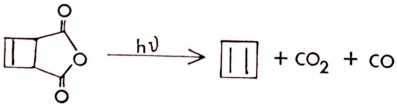
(8)

In the preface it was shown that dioxothiazolinones will photoextrude sulfur dioxide to yield a 2-azetidinone stereospecifically.[9]

Decarboxylation is another fairly common photoreaction. Extrusion of carbon dioxide by irradiation of γ-lactones is another example of cyclopropane preparation[16] (equation 9). This reaction is not selective, giving a mixture of isomers which makes it less desirable than the pyrazoline reaction.

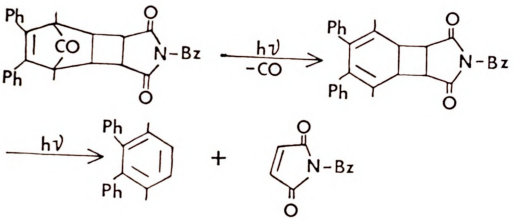
(9)

Cyclobutadiene has also been reported to result from photodecarboxylation and decarbonylation, of a bicycloadipic anhydride derivative[17] (equation 10).

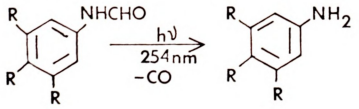


(10)

Probably the most common photoextrusion reaction is that of decarbonylation. It has been used as an approach to aromatic compounds[18] (equation 11), and as a procedure for deprotection of anilines by decarbonylation of formanilides (equation 12).[19]



(11)



(12)

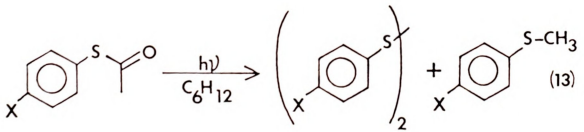
The formation of ortho-quinodimethide type compounds, or intermediates, is also reported to result from photodecarbonylation. This will be discussed in Chapter Two.

Heterocycles are ideally suited for photochemical expulsion of stable molecules. The lone pairs of electrons and the electronegativities of the heteroatoms can help to stabilize the charge or radical character left behind in the intermediate. The literature contains additional examples to supplement those already cited.[20]

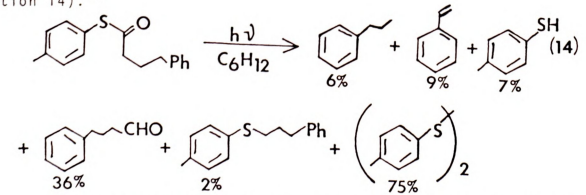
In this chapter the photochemistry of some N-substituted-2-benzothiazolinones will be discussed, specifically those

that involve an intramolecular rearrangement along with photo-extrusion of carbon monoxide. The photochemistry of this type of compound has not been previously reported. The photochemistry of thiol esters and amides has been studied and may offer insight toward predicting the photochemistry of benzothiazolinone derivatives.

Irradiation of some 4-substituted phenyl thiol acetates afforded products resulting from cleavage of the S-acyl bond and extrusion of carbon monoxide (equation 13).[21]



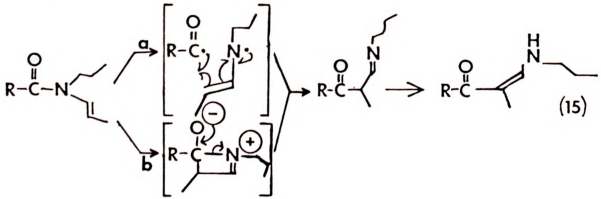
When 4-tolyl thiol-4-phenylbutyrate was irradiated, products resulting from S-acyl bond cleavage predominated with some minor products resulting from Norrish type II reactions (equation 14).[21]



These experiments indicate that S-acyl bonds are quite photolabile and would be expected to break quickly in compounds like benzothiazolinones. Other experiments with thiol

radicals indicate that they attack terminal olefins in the expected manner, following the Kharasch rule to give the more stable intermediate radical.[22,23]

Simple amides are relatively photostable. When formamide, acetamide, and N-methylacetamide are irradiated the primary cleavage is the R-acyl bond, not the N-acyl bond.[24] When a vinyl or aryl group is substituted on the amide, nitrogen N-acyl cleavage will occur fairly readily. One classic example is the work done by Yang and Lenz involving what appears to be a photo Fries rearrangement of enamides.[25] The simplest mechanism proposes an N-acyl cleavage followed by a recombination to the olefinic bond in what ultimately results in a 1,3 acyl shift (equation 15a). An alternate mechanism involves attack of the π-bond, with nitrogen lone pair assistance, on the carbonyl carbon followed by cleavage of the N-acyl bond (equation 15b).

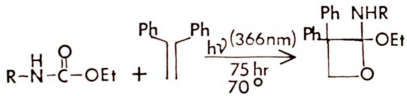


(15)

Other examples of photochemical amide N-acyl bond cleavage are known.[26]

There has been limited study of the photochemistry of carbamates or urethanes. These compounds are similar to the

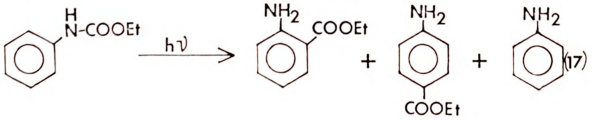
thiolcarbamate system found in benzothiazolinones. Photolysis of ethyl carbamates in the presence of 1,1-diphenylethylene results in a photocycloaddition product[27] (equation 16).



(16)

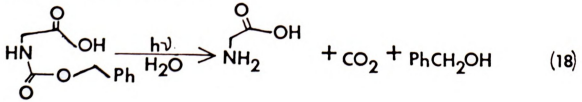
Apparently no decarbonylation products were observed.

When N-aryl-carbamates are irradiated (254 nm light), as in N-aryl enamides, the N-acyl bond will cleave as in the case of N-phenyl carbamates where a photo Fries rearrangement occurs[28] (equation 17).



(17)

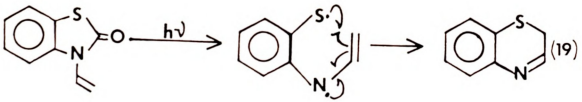
The use of benzyl carbamate protecting groups is an example of N-acyl bond cleavage with assistance from another acyl group [29] (equation 18).



(18)

The apparent ease of S-acyl bond, as well as N-acyl bond cleavage of enamides or N-aryl amides makes a single bond

cleavage difficult to predict for 2-benzothiazolinones, however, it is reasonable to predict photodecarbonylation to occur. For an N-vinyl-2-benzothiazolinone, a rearrangement following the Kharasch rule would be expected to yield a [1,4] benzothiazine (equation 19).

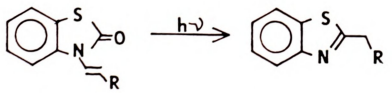


(19)

If a single bond broke, then a variety of possible pathways can exist, from photo-Fries rearrangements to α-lactam and β-lactam formation. The following section will discuss what actually happens to N-vinyl-2-benzothiazolinone derivatives on photolysis and will try to rationalize why some of the possible pathways were not followed.

RESULTS AND DISCUSSION

The first photoreaction to be studied for this project was that of N-vinyl-2-benzothiazolinone (2a). This compound was prepared by nucleophilic displacement of bromide from ethylene bromide by the sodium salt of 2-benzothiazolinone (prepared by treating 2-benzothiazolinone with sodium sand[30]) followed by dehydrobromination with potassium t-butoxide. When 2a was irradiated in 2-propanol with Vycor filtered light for two hours a 3% yield of 2-methylbenzothiazole (3a), identical with an authentic sample, was obtained. The same reaction done in acetonitrile produced a 22% yield of this product (equation 20).



a. R=H
b. R=Ph (20)

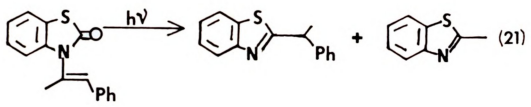
2a,b 3a,b

A large amount of intractible material (mainly aromatic by PMR) was formed in both photoreactions. No evidence was observed for α or β-lactam formation in this or any of the following photoreactions. The low yield of 3a was found not to be attributable to a secondary photoreaction since irradiation of 3a under similar conditions resulted in recovery of 75% of the initial 3a.

In order to study the generality of the rearrangement, trans-N-(2-phenylethenyl)-2-benzothiazolinone (2b) was

photolysed in the same manner. Compound 2b was prepared by nucleophilic displacement of chloride from α-chloroacetophenone by the sodium salt of 2-benzothiazolinone, followed by reduction of the intermediate ketone with sodium borohydride and dehydration of the resulting alcohol with phosphorous pentoxide. The trans stereochemistry of the product was indicated by comparison of the chemical shifts of the vinyl hydrogens in the PMR with calculated values.[31] Irradiation of 2b in 2-propanol afforded a 28% yield of 2-benzylbenzothiazole (2b), which was identical to an authentic sample.[32] In acetonitrile a 30% yield of this product was obtained.

Photolysis of N-(1-methyl-2-phenylethenyl)-2-benzothiazolinone (4) was carried out to see if anything could be learned about migrating groups. This compound was prepared in the same way as 2b with α-bromopropiophenone used in the first step. The E and Z isomers of 4 were formed in a ratio of 3:1 and the E isomer was used for the photolyses since the Z isomer was not crystaline and difficult to purify. The stereochemistries of these products were indicated by comparison of the vinyl hydrogen chemical shifts to calculated values.[31] Irradiation of 4 in acetonitrile produced two products: 2-(2-phenylethyl)-2-benzothiazole (5) and 2-methylbenzothiazole (3a) in 4.6% and 6.8% yields, respectively (equation 21). These compounds were separated by preparative thin layer chromatography.

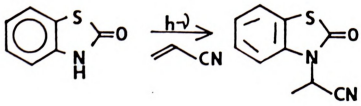


(21)

4 5 3a

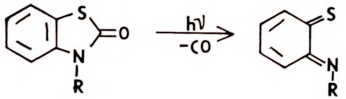
Compound 5 was identical with an authentic sample prepared by methylation of 2-benzylbenzothiazole (3b). The band containing compound 3a had spectral data comparable to an authentic sample of 3a along with small additional signals that were attributed to impurities in that band. One interesting impurity gave a peak at m/e of 267 in the mass spectrum. This could correspond to an isomer of 5.

Apparently the conjugated vinyl group on nitrogen is necessary for photodecarbonylation to occur in the above reactions. Irradiation of N-methyl-2-benzothiazolinone for two hours, with or without acrylonitrile present (to trap a potential intermediate), indicated no loss of starting material within experimental error. When 2-benzothiazolinone is irradiated in the presence of acrylonitrile no decarbonylation was observed, but a product resulting from addition of the trap to 2-benzothiazolinone, N-(1-cyanoethyl)-2-benzothiazolinone, was isolated (equation 22).



(22)

The possibility of a new ortho-quinoid intermediate exists from photodecarbonylation of 2-benzothiazolinones (equation 23).

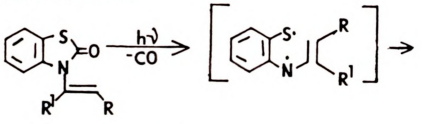


(23)

When N-(2-phenylethenyl)-2-benzothiazolinone (2b) was irradiated with either an electron-rich dienophile (ethylvinyl ether) or an electron poor dienophile (acrylonitrile) in attempts to trap this intermediate only the benzothiazole product was obtained. This indicates that either the intermediate will add only a limited selection of traps or that the intramolecular rearrangement is much faster than incorporation of any external trap. Chapter Two will discuss similar intermediates in more detail and will show that these related intermediates are trappable.

The benzothiazole products were not expected from the photoreactions of 2 and 4. If the photodecarbonylation is assumed to occur first, then one would expect the vinyl group to bridge the nitrogen and sulfur to afford the Diels-Alder type product of a benzothiazine (6) (equation 24). This might be rationalized by a Michael-type attack by the vinyl group on the sulfur. If a radical intermediate were assumed, which is a useful way to predict Diels-Alder and Michael reaction products, one would expect the sulfur radical to

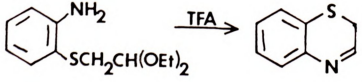
attack the terminal carbon of the vinyl group to afford 5 (Kharash rule).[23]



2a,b;4(R=Ph, R¹=CH₃) → 6a–c (24)

a. R=R¹=H
b. R=Ph, R¹=H
c. R=Ph, R¹=CH₃

Few attampts have been made to prepare 2H-1,4-benzothiazine (6a), and those that were tried produced the wrong compound. The first reported preparation of 5a was by Langlet,[33] who heated 2-aminothiophenol with ethylene bromide in glacial acetic acid. His structure proof was found to be incorrect in 1968 by Santacroce et al.,[34] who determined that 2-methylbenzothiazole was actually prepared. Recently Prota et al.[35] claim to have prepared this elusive benzothiazine by treating 1(o-aminophenylthio)-2,2-diethoxyethane (7) with trifluoroacetic acid (equation 25).

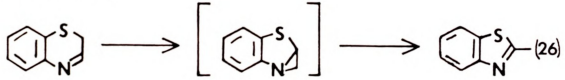


7 → 6a (25)

Only PMR data supported this structure. It is not surprising, in light of this previous work, that 6a was not found in the photoreactions of 2a.

When Santacroce determined the correct structure for Langlet's reaction he suggested that 6a undergoes a ring

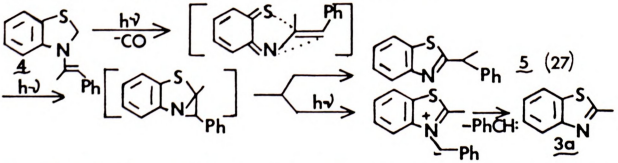
contraction to 3a. This process could occur as shown below (equation 26).



6a 3a

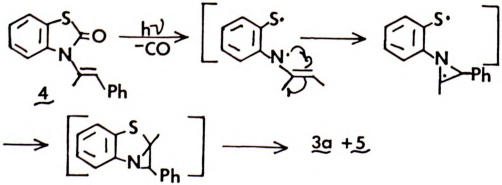
This mechanism is consistent with the products from the photoreactions of 2a and 2b, but it does not explain the products observed from the photolysis of 4. The proposed benzothiazine intermediate 6c is a known compound,[36] yet it is not observed in the reaction mixture obtained by irradiation of 4. The photolability of 6c was not determined, thus if it were very photoreactive it might not be observed. Also, the benzothiazine contraction mechanism does not explain the formation of 3a from photolysis of 4.

Another mechanism that can account for the photoproducts from 4 is that from a photochemical Diels-Alder reaction. After photoextrusion of carbon monoxide, the vinyl group adds so that the sulfur bonds to the internal carbon and the nitrogen bonds to the terminal carbon (equation 27).



The intermediate aziridine could open and shift a methyl group to give 5, or it could lose a phenyl carbene species to give

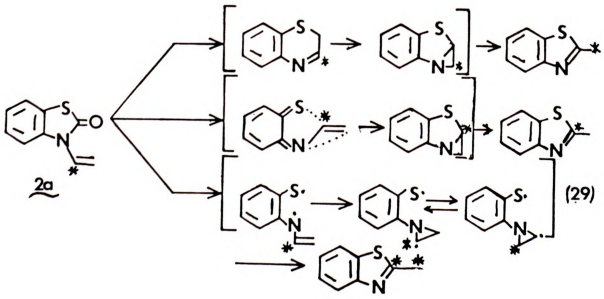
3a via an azomethine ylide. Aziridines are known to undergo a photochemical ring opening to an ylide which can usually be trapped with an electron poor dipolarophile.[37] No attempts were made to trap an intermediate ylide from photolysis of 4. It is reasonable to predict that the ylide could decompose to the phenyl carbene in the same manner as is proposed for the generation of carbenes from epoxides.[38a] One might expect to observe phenyl carbene reaction products in the photolysate mixture from insertion into carbon hydrogen bond, addition to H-bonds, or possibly addition to stilbene.[38b] No products of this nature were observed, however, this observation is not conclusive when one considers the small amounts that may be present. This mechanism appears to be rather unlikely. The excitation energy necessary to extrude carbon monoxide should result in a ground state which would have to absorb another photon to allow the photochemical Diels-Alder to occur. This problem can be overcome by considering a stepwise process instead. The same results can be rationalized by rearrangement of a diradical intermediate following photodecarbonylation (equation 28).



(28)

It is interesting to note that the aziridine intermediate has a molecular weight equal to the molecular ion (at m/e 267) in the mass spectrum of the impurity found in the thin layer chromatography band containing 3a from the photolysis of 4. Preliminary attempts to prepare this aziridine intermediate by addition of phenyl carbene to 2-methybenzothiazole failed. Photochemical generation of phenyl carbene from phenyldiazomethane[38b] and stilbene oxide[38a] failed to add to the imine π-bond of 2-methylbenzothiazole. This is not surprising since the literature is very limited in examples of aziridine syntheses involving carbene addition to imines.[39]

An experiment that could distinguish between the above mechanisms is a labeling study which could be carried out in the future. By labeling one of the vinyl carbons of 2a and observing its position in the photoproduct, one could further determine if any of the above mechanisms are correct (equation 29).



Although the thermal Diels-Alder mechanism appears unlikely in light of the photoproducts observed from 4, it would be more firmly ruled out by not finding the label in the methyl group of the product, as shown above. The photochemical Diels-Alder reaction should put the label in the thiazole ring. The stepwise mechanism would scramble the label into both positions assuming that a tight radical pair or cage effect were not present, and that 1,2 hydrogen shifts are rapid. The cage effect would make a distinction between the last two mechanisms impossible.

The original synthesis of N-vinyl-2-benzothiazolinone (2a) could not be used to make the labeled compound. The symmetry of ethylene bromide makes selectivity of substitution impossible. Other halides like 1,1 dibromoethane may work, but the best direction would probably be to attach one carbon at a time to the nitrogen.

This novel photoreaction warrants further study not only for the mechanism of rearrangement but also for the potential ortho-quinoid intermediate. This intermediate will be discussed in Chapter Two.

EXPERIMENTAL

General. ^{1}H-NMR spectra (PMR) were measured with a Varian T-60 spectrometer. ^{13}C-NMR spectra (CMR) were obtained on a Varian CFT-20 or Bruker WH-180 spectrometer. Multiplicities were determined by off resonance decoupling. Both types of NMR used tetramethylsilane (TMS) as an internal standard. Infrared spectra (IR) were recorded on a Perkin-Elmer 237B grating infrared spectrophotometer. Ultraviolet spectra (UV) were obtained on a Unicam SP-800 or Cary-17 spectrometer. Mass spectra (MS, 70 eV) were obtained on a Hitachi Perkin-Elmer RMU-6D spectrometer. Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Microanalyses were performed by Instranal Laboratories, Rensselaer, New York.

Gravity columns were packed with alumina (Fisher, 80-200 mesh), silica gel (Mallinckrodt silica C-77 or Davison Chemical, 60-200 mesh), or Florisil (Fisher, 100-200 mesh) all mixed with fluorescent dye (Brinkman, Lumilux). Analytical thin layer chromatography plates were aluminum oxide (Baker, IB-F) or silica gel (Baker, 1B2-F). All preparative thin layer chromatography plates were prepared from silica gel (EM Reagents, 60PF-254, 1 mm) or aluminum oxide (EM Reagents, 60PF-254, 1 mm).

Tetrahydrofuran (THF) was distilled from sodium and benzophenone. Dimethylformamide (DMF) was dried over 3A molecular sieves. Tertiary butyl alcohol was distilled from

calcium hydride and stored over 3A molecular sieves. Acetonitrile (UV) was obtained from Burdick and Jackson Laboratories, Muskegon, Michigan, distilled from potassium carbonate and stored over 3A molecular sieves. Isopropyl alcohol (UV) was obtained from Burdick and Jackson Laboratories, Muskegon, Michigan, and stored over 3A molecular sieves.

All photolyses were performed with argon bubbling through the solution during irradiation. All compound preparations were carried out under a nitrogen atmosphere.

Quantitative NMR. Internal standard quantitative proton NMR was used for analysis of photolysis products when the spectrum indicated a clean signal of known hydrogen content and a clean base line where the internal standard would appear. The standards were easy to purify, easy to remove from the sample, unreactive toward the sample, and had a chemical shift in a "clean" region of the spectrum. They were usually, but not necessarily, liquid and contained only one kind of hydrogen (i.e., singlet in the pmr). Some common standards include acetonitrile (δ2.0), acetone (δ2.0), nitromethane (δ4.3), methylene chloride (δ5.1) and dioxane (δ4.56).

A known amount of standard (usually 2-5 μL) was syringed directly into the NMR sample and mixed thoroughly. The spectrum was taken with careful integration of the standard and appropriate sample signal. The integration values were applied to the following equation:

$$\frac{M_s H_s I_u}{H_u I_s} = M_u$$

Where: M_u = moles of sample (unknown)

M_s = moles of added standard

H_u = number of hydrogens per molecule responsible for sample signal

H_s = number of hydrogens per molecule responsible for standard signal

I_u = integration value for sample

I_s = integration value for standard

Preparation of 2-benzothiazolinone.[40] A mixture of Urea (96 g, 1.6 mol) and 2-aminothiophenol (100 g, 0.8 mol) was heated at 150°C for 3 h and then at 220°C for an additional 3 h. The resulting material was dissolved in 600 mL of THF and filtered. The solvent was removed from the filtrate at reduced pressure and the residue was crystalized from abs ethanol. The crude crystals were sublimed (135°C), 0.2 torr) overnight. The sublimated crystals were recrystalized from abs ethanol to yield 53.6 g (44%) of product (mp 136-139°C, lit[41] 136-138°C). Spectral data were as previously reported.[42]

Preparation of N-(2-bromoethyl)-2-benzothiazolinone. A solution of 2-benzothiazolinone (5.0 g, 33 mmol) in 100 mL of THF was added to sodium sand[30] (0.75 g, 33 mmol) in 25 mL of THF. After 5 h of stirring, 125 mL of DMF was added and the resulting solution was added over a 27 h period to a solution of

ethylene bromide (61.0 g, 325 mmol) in 125 mL of THF and 125 mL of DMF. The solvents were removed at reduced pressure from the resulting solution. The residue was dissolved in methylene chloride, filtered through celite, and the filtrate solvent was removed at reduced pressure. The residue was crystalized and recrystalized from ether and pentane to yield 3.8 g (46%) of product (mp 63-64°C). The spectral data are: IR ($CHCl_3$) 1670, 1590, 1480, 1450 cm^{-1}; PMR ($CDCl_3$, TMS) δ3.5 (t, 2H), 4.3 (t, 2H), 6.9-7.5 (m, 4H); MS m/e (rel intensity) 259 (34), 164 (32), 151 (99), 150 (32), 136 (100); UV (abs ethanol) λ_{max}^{nm} 221 (ε 14000), 243 (ε 5200), 283 (ε 2600), 290 (ε 2600); Anal. calcd for C_9H_8BrNOS: C, 41.88; H, 3.12. Found: C, 42.08; H, 3.12.

Preparation of N-vinyl-2-benzothiazolinone (2a). A solution of potassium t-butoxide (2.5 g, 22.5 mmol) in 150 mL of t-butyl alcohol was added to a 60°C solution of N-(2-bromoethyl)-2-benzothiazolinone (5.0g, 19.5 mmol) in 55 mL of t-butyl alcohol. The solution was refluxed for 66 h, cooled, filtered through celite, and the filtrate solvent was removed at reduced pressure. The residue was crystalized and recrystalized from ether and pentane to yield 1.0 g (30%) of 2a (mp 39-40°C). The spectral data are: IR (melt) 1680, 1640, 1590, 1470, 1560, 1350, 1325, 1305, 1220, 1180, 1050, 955, 875, 745 cm^{-1}; PMR ($CDCl_3$, TMS) δ5.2-6.9 (m, 3H, AMX system), 7.0-7.4 (m, 4H); MS m/e (rel intensity) 179 (6), 178 (11), 177 (100), 149 (64); UV (abs ethanol) λ_{max}^{nm} 216 (ε 5440), 283 (ε 299), 289 (ε 286);

Anal. calcd for C_9H_7NOS: C, 61.00; H, 3.98; N, 7.90. Found: C, 61.29; H, 3.95; N, 8.03.

Photolysis of N-vinyl-2-benzothiazolinone (2a) in 2-propanol. A solution of 2a (102 mg, 0.58 mmol) in 150 mL of 2-propanol was purged with argon for 15 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution (<39°C). The residue contained 4.9 mg (3.1%) of 2-methylbenzothiazole (3a) as determined by quantitative PMR (CH_2Cl_2). The PMR also indicated a large amount of unidentifiable aromatic residue. The product was identified by comparison to an authentic sample (Aldrich).

Photolysis of N-vinyl-2-benzothiazolinone (2a) in acetonitrile. A solution of 2a (104 mg, 0.59 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through vycor. The solvent was removed at reduced pressure (<40°C) from the resulting solution and the residue contained 21.6 mg (14.5%) of 2-methylbenzothiazole and 3.2 mg of recovered 2a as the only identifiable compounds. The PMR indicated other aromatic material was present. The yields were determined by quantitative PMR (CH_3NO_2, 5 μL) and the product was identified by comparison to an authentic sample (Aldrich).

Preparation of N-(benzoylmethyl)-2-benzothiazolinone. A solution of 2-benzothiazolinone (3.0 g, 20 mmol) in 50 mL of THF was added to sodium sand[30] (0.45 g, 20 mmol) in 30 mL of THF. After stirring for 2.5 h, 80 mL of DMF was added followed by a solution of α-chloroacetophenone (3.0 g, 19 mmol) in 80 mL of THF and 70 mL of DMF. After stirring overnight the solvent was removed at reduced pressure from the resulting solution. The residue was dissolved in methylene chloride, filtered through celite, and the filtrate solvent was removed at reduced pressure. The residue was recrystalized from abs ethanol to yield 4.8 g (89%) of product (mp 162-163.5°C). The spectral data are: IR ($CDCl_3$) 1710, 1675, 1600, 1475, 1450, 1330, 1180, 1000 cm^{-1}; PMR ($CDCl_3$, TMS) δ5.25 (s, 2H), 6.6-8.0 (m, 9H); MS m/e (rel intensity) 269 (17), 136 (15), 105 (100), 77 (30); UV abs ethanol) λ_{max}^{nm} 223 (ε 13300), 245 (ε 16900), 282 (ε 3780), 289 (ε 3510); Anal. calcd for $C_{15}H_{11}NO_2S$: C, 66.93; H, 4.12. Found: C, 67.05; H, 4.08.

Preparation of N-(2-hydroxy-2-phenylethyl)-2-benzothiazolinone. A solution of sodium borohydride (0.37 g, 9.5 mmol) in 30 mL of dry methanol was added to a refluxing solution of N-(benzoylmethyl)-2-benzothiazolinone (5.0 g, 18.6 mmol) in 30 mL of dry methanol. After 3 h the reaction mixture was quenched with 50 mL of 0.1 N sodium hydroxide and extracted with three 50 mL-portions of methylene chloride. The organic layers were combined, washed twice with saturated sodium chloride, and dried over sodium sulfate. The solvent was removed at reduced

pressure and the residue was crystalized and recrystalized from benzene to yield 4.5 g (89%) of product (mp 100-101°C). The spectral data are: IR ($CHCl_3$) 3425, 1675, 1590, 1490, 1475, 1430, 1175 cm^{-1}; PMR ($CDCl_3$, TMS) δ3.1 (d, 1H, washes out with D_2O), 4.0 (d, J=6 Hz, 2H), 5.0 (quar., J=6 Hz, 4 Hz, 1H; w/ D_2O, t, J=6 Hz, 1H), 6.8-7.5 (m, 9H); MS m/e (rel intensity) 271 (7), 165 (100), 134 (40); UV (abs ethanol) λ_{max}^{nm} 223 (ε 12300), 247 (ε 4500), 283 (ε 1960), 290 (ε 2060); Anal. calcd for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83. Found: C, 66.57; H, 4.91.

Preparation of trans-N-(2-phenylethenyl)-2-benzothiazolinone (2b). A solution of N-(2-hydroxy-2-phenylethyl)-2-benzothiazolinone (4.0 g, 14.8 mmol) in 100 mL of dry xylene was heated to 100°C and phosphorous pentoxide (2.0 g) was added over a 4.5 h period. The reaction mixture was cooled and filtered through celite. The filtrate was washed twice with saturated sodium bicarbonate and saturated sodium chloride and dried over sodium sulfate. The solvent was removed at reduced pressure and the residue was chromatographed on a silica gel column (300 g). The second band, eluted with methylene chloride, yielded 1.74 g (46.5%) of 2b, which was recrystalized from abs ethanol (mp 96-97°C). The spectral data are: IR ($CHCl_3$) 1675, 1630, 1580, 1470, 950 cm^{-1}; PMR ($CDCl_3$, TMS) δ7.0-7.5 (m); MS m/e (rel intensity) 255 (7), 254 (19), 253 (100), 225 (40), 224 (91); UV (abs ethanol) λ_{max}^{nm} 286 (ε 6500), 253 (ε 16400), 217 (ε 37500); Anal. calcd

for $C_{15}H_{11}NOS$: C, 71.12; H, 4.38. Found: C, 71.44; H, 4.39.

Photolysis of N-(2-phenylethenyl)-2-benzothiazolinone (2b) in 2-propanol. A solution of 2b (101 mg, 0.40 mmol) in 150 mL of 2-propanol was purged with argon for 1 h and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure (<40°C) from the resulting solution. The residue contained 25.3 mg (28.3%) of 2-benzylbenzothiazole (3b) by quantitative PMR (CH_2Cl_2), which also indicated a large amount of aromatic material. No other signals were present. The product was identified by comparison to an authentic sample (see below).

Photolysis of N-(2-phenylethenyl)-2-benzothiazolinone (2b) in acetonitrile. A solution of 2b (101 mg, 0.40 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution. The residue contained 27.5 mg (30.6%) of 2-benzylbenzothiazole (3b) by quantitative PMR (dioxane) and other unidentifiable aromatic material. The product was identified by comparison to an authentic sample (see below).

Preparation of phenyl acetylchloride.[32] Thionyl chloride (18 mL, 0.25 mol) was slowly added to phenyl acetic acid (27.2 g, 0.2 mol). The resulting solution was refluxed for 3.5 h and then distilled. The fraction collected at 96-98°C (17 mm) yielded approximately 40 mL of product.

Preparation of 2-benzylbenzothiazole (3b).[32] Dry hydrogen gas was bubbled into 2-aminothiophenol (13.75 g, 12.1 mL, 0.11 mol) until no liquid was evident. Phosphorous pentoxide (46.9 g, 0.33 mol) and phenyl acetyl chloride (17.8 g, 15.2 mL, 0.11 mol) were added and the thick slurry was heated at 175°C for 8 min. The resulting gum was cooled and 1N sodium hydroxide was added until the solution was basic to pH paper. The aqueous solution was extracted with three 200 mL-portions of ether. The ether layers were combined and dried over sodium sulfate. After the ether was removed at reduced pressure, the residue was vacuum distilled. The fraction collected at 145-150°C (0.25 mm) yielded approximately 11.7 g (45%) of (3b). The spectral data are: IR (neat) 3040, 3000, 1600, 1515, 1490, 1450, 1430, 1310, 1240, 1100, 1060, 1025, 1010, 855, 755, 725, 700 cm^{-1}; PMR ($CDCl_3$, TMS) δ4.3 (s, 2H), 7.0-8.0 (m, 9H); MS m/e (rel intensity) 225 (100), 224 (89), 121 (17), 91 (32), 65 (44).

Photolysis of N-(2-phenylethenyl)-2-benzo-thiazolinone (2b) with acrylonitrile. A solution of 2b (104 mg, 0.41 mmol) and acrylonitrile (4.0 g, 5 mL, 76 mmol) in 150 mL of methanol

(distilled and dried over 3A molecular sieves) was purged with argon for 85 min and irradiated for 30 min with a 450 W Hanovia medium pressure mercury lamp through a Vycor filter. The solvent was removed at reduced pressure (<40°C) from the resulting solution and the residue contained 2-benzylbenzothiazole and 2b as the only identifiable products by PMR. A moderate amount of aromatic and aliphatic material was also noted in the PMR.

Photolysis of N-(2-phenylethenyl)-2-benzothiazolinone (2b) with ethylvinylether. A solution of 2b (102 mg, .40 mmol) and ethylvinylether (3.8 g, 5.0 mL, 53 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 1 h with 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution and the residue contained 2-benzylbenzothiazole (7.2 mg) and starting material as the only identifiable products. An appreciable amount of aromatic and aliphatic residue was noted in the PMR. The yield of 2-benzylbenzothiazole was determined by quantitative PMR (CH_3CN, 2 μL).

Preparation of α-bromopropiophenone. Bromine (27 g, 170 mmol) was added dropwise to a solution of propiophenone (21 g, 160 mmol) in 45 mL of ether. The solution was distilled at reduced pressure and the fraction boiling at 92.5° (0.6 torr) yielded approximately 30 g (88%) of product. The spectral data were identical with the literature.[43]

Preparation of N-(1-benzoylethyl)-2-benzothiazolinone. A solution of 2-benzothiazolinone (10.0 g, 66 mmol) in 120 mL of the THF was added to sodium sand[30] (1.5 g, 66 mmol) in 30 mL of THF. After stirring for 3 h, 150 mL of DMF was added followed by a solution of α-bromopropiophenone (10 mL, 67 mmol) in 100 mL of THF and 100 mL of DMF. After an additional 1.5 h of stirring the solvent was removed at reduced pressure from the resulting solution. The residue was dissolved in methylene chloride, filtered through celite and the filtrate solvent was removed at reduced pressure. The residue was recrystalized from 95% ethanol to yield 14.8 g (79%) of produce (mp 105-106°C). The spectral data are: IR ($CDCl_3$) 1670, 1580, 1450, 1375, 1300, 1225, 1180, 1125, 975 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.65 (d, H=8 Hz, 3H), 6.0 (quar., J=8 Hz, 1H) 6.7-7.4 (m, 4H), 7.6-7.9 (m, 2H); MS m/e (rel intensity) 283 (30), 178 (91), 150 (100), 105 (71), 77 (73); Anal. calcd. for $C_{16}H_{13}NO_2S$: C, 67.82; H, 4.62. Found: C, 67.93; H, 4.65.

Preparation of N-(2-hydroxy-1-methyl-2-phenylethyl)-2-benzothiazolinone. A solution of N-(1-benzoylethyl)-2-benzothiazolinone (5.0 g, 17.7 mmol) and sodium borohydride (0.5 g, 12.6 mmol) in 50 mL of 2-propanol was refluxed under nitrogen for 4 h. The solution was quenched with 75 mL of 0.1 N sodium hydroxide and extracted with methylene chloride. The organic layer was washed with saturated sodium chloride solution, and dried over sodium sulfate for 1 h. The solvent was removed at reduced pressure to yield approximately 4 g (79%)

of product in the form of a glass. The spectral data are: IR ($CDCl_3$) 3325, 1745, 1650, 1590, 1450, 1300, 1190, 1030 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.5 (d, 3H), 3.6 (bs, 1H, washed out with D_2O), 5.3 (bquar., 1H), 6.807.6 (m, 9H).

Preparation of N-(1-methyl-2-phenylethenyl)-2-benzothiazolinone (4). A solution of N-(2-hydroxy-1-methyl-2-phenylethyl)-2-benzothiazolinone (4.0 g, 14 mmol) and phosphorous pentoxide (3.0 g, 21 mmol) in 100 mL of dry xylenes was refluxed for 18 h. The solution was cooled, washed twice with saturated sodium bicarbonate, once with saturated sodium chloride and dried over sodium sulfate. The solvent was removed at reduced pressure and the residue was chromatographed on a silica gel column (200 g) with methylene chloride. The single moving band was crystalized and recrystalized from 95% ethanol to yield 0.8 g (20%) of the E-isomer of 4 (mp 106.5-107.5). The oil that remained in the mother liquor of the recrystalizing solvent appeared to be the Z-isomer of 4 which later crystalized (mp 89-95°C). The spectral data for E-4 are: IR ($CDCl_3$) 1675, 1595, 1475, 1340, 1300, 1225, 1200, 1130, 1030, 1020 cm^{-1}; PMR ($CDCl_3$, TMS) δ2.25 (s, 3H), 6.55 (s, 1H), 6.8-7.4 (m, 9H); MS m/e (rel intensity) 267 (74), 151 (40), 116 (100), 115 (37), 91 (32); UV (abs ethanol) λ_{max}^{nm} 289 (ε 3510), 280 (ε 4740); Anal. calcd for $C_{16}H_{14}NOS$: C, 71.88; H, 4.90; N, 5.24. Found: C, 71.63; H, 4.92; N, 5.22. The spectral data for Z-4 are: IR ($CHCl_3$) 1660, 1585, 1465, 1185 cm^{-1}; PMR ($CDCl_3$) δ2.2 (s, 3H), 6.6-7.4 (m, 10H); MS m/e (rel intensity) 267 (78), 151 (41), 116 (100), 115 (27), 91 (25).

Photolysis of E-N-(1-methyl-2-phenylethenyl)-2-benzothiazolinone (4). A solution of 4 (203 mg, 0.76 mmol) in 350 mL of acetonitrile was purged with argon for 25 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution. The residue was separated by preparative thin layer chromatography (silica gel, 0.25% methanol in methylene chloride) and was found to contain 4 (7.9 mg, fastest moving band), 2-(1-phenylethyl)-benzothiazole (5) (8.3 mg, .035 mmol, second band), and 2-methylbenzothiazole (3a) (7.7 mg, .052 mmol, slowest moving band), along with a large amount of intractable material that contributed aliphatic and aromatic signals in the PMR. All yields were determined by quantitative PMR. Compounds 4 and 5 were identified by comparison to authentic samples. The spectral data for the band containing 3a are: IR (neat) 1660, 1520, 1430, 1300, 1240, 1170, 1150, 1050, 830, 750, 725, 700, 650 cm^{-1}; PMR ($CDCl_3$) δ2.8 (s, 3H), 7.0-7.4 (m, 2H), 7.5-7.9 (m, 2H); PMR (CD_3CN) δ2.7 (s, 3H), 7.0-7.5 (pent. (m), 2H), 7.7-7.9 (m, 2H); MS m/e (rel intensity) 239 (27), 238 (17), 151 (7), 150 (20), 149 (100), 148 (18), 109 (13), 108 (33), 82 (10), 69 (28), 63 (17). The IR is comparable with a literature example[44] except for the absorptions at 1660 and 830 cm^{-1}. The PMR spectra in both solvents are identical to the PMR spectra of an authentic sample (Aldrich) run in those solvents except for a small difference in the integrations of the aromatic regions. The mass spectrum is comparable to a literature example[45] except for the m/e's at 239 and 238.

Preparation of 2-(1-phenylethyl)-benzothiazole (5). A solution of 2-benzylbenzothiazole (1.17 g, 1 mL, 5.2 mmol) in 9 mL of THF was added to a stirring suspension of sodium hydride (0.25 g of 50% suspension in mineral oil, 5.2 mmol, washed three times with 5 mL portions of dry pentane) in 5 mL of THF. After 40 min methyl iodide (1.5 g, 0.65 mL, 10.4 mmol) was added and the suspension was left to stir for 18 h. The resulting yellow slurry was boiled in the hood to remove any excess methyl iodide and then the remaining solvent was removed at reduced pressure. The residue was dissolved in 50 mL of methylene chloride, filtered through celite, and the filtrate washed twice with water and dried over sodium sulfate. The solution was filtered and the solvent was removed at reduced pressure. The residue was chromatographed on a silica gel column (100 g) with methylene chloride. The first band yielded 1.04 g (84%) of 5 (mp 39-40°C). The spectral data are: IR (neat) 1600, 1510, 1490, 1450, 1430, 1365, 1310, 1235, 1120, 1025, 1010, 755, 725, 700 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.8 (d, J=6 Hz, 3H), 4.5 (quar., J=6 Hz, 1H), 6.9-7.9 (m, 9H); MS m/e (rel intensity) 239 (100), 224 (46), 162 (22), 124 (17), 105 (41), 91 (19).

Preparation of N-methyl-2-benzothiazolinone. A solution of 2-benzothiazolinone (5.0 g, 33 mmol) in 50 mL of THF was added to sodium sand[30] (0.75 g, 33 mmol) in 50 mL of THF. After 3 h, 100 mL of DMF was added, followed by a solution of methyl iodide (4.0 mL, 67 mmol) in 50 mL of THF and 50 mL

of DMF. After stirring overnight the excess methyl iodide was evaporated in the hood and the remaining solvents were removed at reduced pressure. The residue was dissolved in methylene chloride, washed twice with water, and dried over sodium sulfate. The solvent was removed at reduced pressure and the residue was crystalized and recrystalized from petroleum ether (30° - 60°) to yield 4.4 g (73%) of product (mp 75-76°C, lit.[46] 76°C). The spectral data are: IR ($CHCl_3$) 1670, 1590, 1475, 1325, 1220, 1125 cm^{-1}; PMR ($CDCl_3$, TMS) δ3.35 (s, 3H), 6.7-7.4 (m, 4H); MS m/e (rel intensity) 165 (94), 136 (100); UV (abs ethanol) λ_{max}^{nm} 290 (ε 3000), 284 (ε 3000), 245 (ε 5600). The IR and PMR were identical with the literature.[47]

Photolysis of N-methyl-2-benzothiazolinone. A solution of N-methyl-2-benzothiazolinone (20.6 mg, 0.13 mmol) in 0.4 mL of deuteroacetonitrile in a quartz 5 mm PMR tube was purged with argon for 20 min and irradiated for 6 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. PMR analysis revealed no loss of starting material within experimental error.

Photolysis of N-methyl-2-benzothiazolinone and acrylonitrile. A solution of N-methyl-2-benzothiazolinone (102 mg, 0.62 mmol) and acrylonitrile (4.1 g, 5 ml, 76 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 4 h with a 450 W Hanovia medium pressure mercury lamp through

Vycor. The solvent was removed at reduced pressure and the residue was separated by preparative thin layer chromatography (silica gel, CH_2Cl_2). The only moving band was identified as N-methyl-2-benzothiazolinone (approximately 75% recovered) by PMR.

Photolysis of 2-benzothiazolinone and acrylonitrile. A solution of 2-benzothiazolinone (102 mg, 0.67 mmol) and acrylonitrile (4.1 g, 5 mL, 76 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution and the residue was separated by preparative thin layer chromatography (silica gel) with methylene chloride. The top band was unidentified by PMR. The second band proved to be N-(1-cyanoethyl)-2-benzothiazolinone (11.7 mg, 8.6%). The yield was determined by quantitative PMR (CH_3NO_2, 4 μL). The spectral data for the product are: IR (neat) 2310, 1675, 1590, 1470 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.8 (d, J=7 Hz, 3H), 5.8 (quar. J=7Hz, 1H), 7.3 (m, 4H); MS m/e (rel intensity) 204 (6), 161 (33), 151 (43), 150 (100).

Photolysis of 2-methylbenzothiazole. A solution of 2-methylbenzothiazole (110 mg, 0.74 mmol) in 330 mL of 2-propanol was purged with argon for 30 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through quartz. The solvent was removed at reduced pressure from the resulting

solution. The residue contained 2-methylbenzothiazole (83 mg, 75%) by quantitative PMR (CH_3NO_2). No other identifiable products were detected.

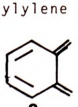
CHAPTER TWO

THE PHOTOCHEMISTRY OF N-PHENYL AND N-CYANO-2-BENZOTHIAZOLINONES

INTRODUCTION

The intermolecular trapping reaction is an important tool in organic chemistry, both mechanistically and synthetically. The concept of this process is relatively simple. When a reactive intermediate is believed to be present in a reaction, an additional compound may be introduced to react with the intermediate prior to completion of the original reaction path. This, in effect, stops the reaction progress early and allows one to examine an internal step of the reaction sequence. The use of iron tricarbonyl to trap cyclobutadiene is a classic example of a trapping reaction.[48] The use of olefins to trap dipolar species is another common example of mechanistic use of this reaction.[49] The Diels-Alder reaction may also be expressed in terms of a trapping reaction, but now as a synthetic tool, as well as a mechanism determining device.

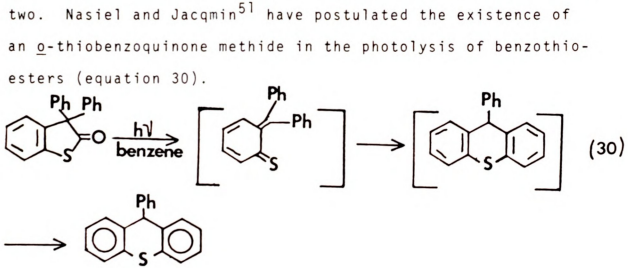
One type of intermediate species that is generally substaniated by examination of a trapping product is the ortho-quinoid dimethide or o-xylylene (8). These usually unstable



8

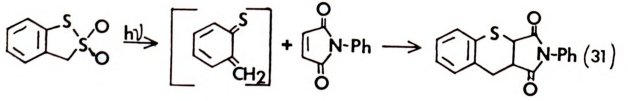
species are prepared mainly by thermal or photodecarbonylation.[50] Although they are generally studied for mechanistic understanding, o-xylylenes may be useful as synthetic intermediates, especially if hetero ortho-quinoid systems can be generated.

There are only a few examples of ortho-quinoid species involving one exocyclic heteroatom, and fewer still involving two. Nasiel and Jacqmin[51] have postulated the existence of an o-thiobenzoquinone methide in the photolysis of benzothioesters (equation 30).



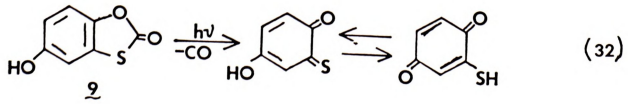
(30)

The intermediate was trapped intramolecularly to afford 9-phenylthioxanthene. Photodesulfonylation of 3H-1,2-benzodithiole-2,2-dioxide apparently affords a similar intermediate that is efficiently trapped with N-phenylmalemide to yield a thiochroman derivative[52] (equation 31).



(31)

Chapman and McIntosh[53] postulated a 2-hydroxy-5-oxo-1,3-cyclohexadiene-6-thione on photolysis of the monothiocarbonate (9) (equation 32).

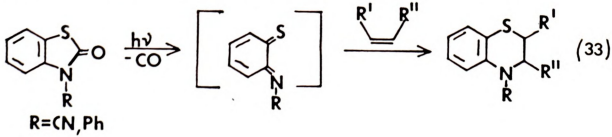


(32)

9

This intermediate was never isolated and was characterized by its spectroscopic properties. We have not found any reports involving an ortho-quinoid species with exocyclic nitrogen and sulfur. This combination could prove to be a useful synthetic intermediate (vide infra).

In 2-benzothiazolinones, the nature of the substituent on nitrogen is important in determining the reactivity of the intermediate formed after photodecarbonylation. In Chapter One, it was shown that an easily manipulated substituent on nitrogen with a reactive π system (e.g., a vinyl group) would intramolecularly rearrange to a benzothiazole derivative. When an unreactive or aromatic group is present on nitrogen (e.g., cyano or phenyl) the prospect of rearrangement is reduced (phenyl would have to lose its aromaticity), and intermolecular trapping becomes a definite possibility. Selection of an appropriate dienophile trap could result in a benzothiazine or phenothiazine derivative (equation 33).

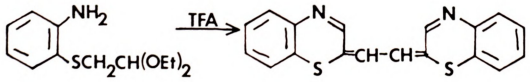


(33)

Benzothiazines and phenothiazines are known for their biological activity, as well as their use as synthetic dye intermediates. The above process may be a useful approach to their synthesis.

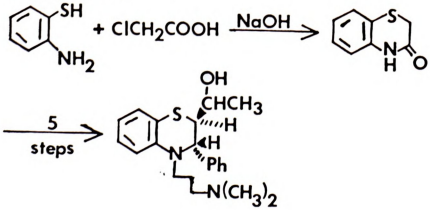
In order to evaluate the utility of this new photochemical approach to these heterocycles, it is necessary to review the established procedures for their preparation. The biological activity of these compounds will also be discussed to help place synthetic goals in perspective.

Benzothiazines are well known as precursors to cyanine dyes,[54] as well as for their antihistaminic activity.[55] They are generally prepared by condensation of o-aminothiophenol with α-haloaldehyde, ketone, or carboxylic acid derivatives. For example, Thomson et al.[56] treated an amino acetal, prepared from o-aminothiophenol,[34] with trifluoroacetic acid to afford a red thiazine dye (equation 34).



(34)

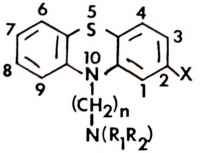
In the synthesis of a new class of antiinflammatory agents Krapcho and Turk[57] treated o-aminothiophenol with α-chloroacetic acid to yield an oxobenzothiazine. This intermediate was converted to the desired product in five additional steps (equation 35).



(35)

The above examples of 1,4-benzothiazines are typical syntheses and can be used to afford moderate to good yields of desired products. However, the availability of α-halo carbonyl compounds, especially those involving a dialkyl substituted α-carbon limits the processes to generation of simple derivatives. A promising alternative is described by Carelli,[36] whereby treatment of bis(o-aminophenyl)disulfide with ordinary ketones produces good yields of benzothiazines. Unfortunately, this work is relatively new and has not been proven for more hindered systems.

Phenothiazine syntheses are much more abundant because of the widespread use of these compounds in pharmacology and medicine.[58] The active derivatives generally incorporate a dialkylamine function on the nitrogen as illustrated in 10. It has also been observed that substitution at the 2-position (para to the sulfur) substantially increases activity.



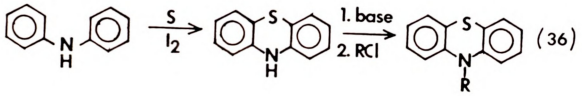
X=H, Cl, CF_3, OCH_3, etc.

n=2,3

10

The simplest preparation of phenothiazine involves sulfurization of diphenylamine. This reaction is a modification of the Ferrario-Ackermann reaction of phenoxy ethers.[59] By mixing diphenylamine with sulfur and iodine, phenothiazine is

produced and it can be N-alkylated by treatment with a strong base (e.g., sodium hydride or ethylmagnesium bromide) followed by addition of the appropriate aminoalkyl halide (equation 36).



(36)

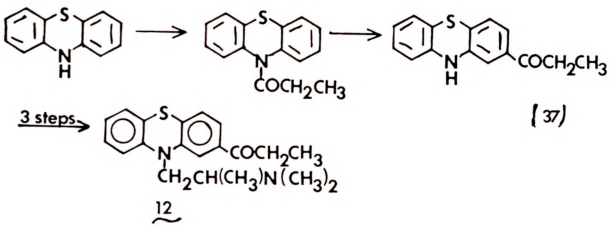
11

Some useful compounds of this type include pyrathiazine (11, R = CH_2CH_2-N⟨ ⟩) and phomethazine (11, R = $CH_2CH(CH_3)N(CH_3)_2$) both of which act as antihistamines. Diethiazine (11, R = $CH_2CH_2N(Et)_2$) and ethopropazine (11, R = $CH_2CH(CH_3)N(Et)_2$) exhibit anti-Parkinsonian activity, as well as antihistaminic activity.

It was previously mentioned that substitution in the 2 position promotes a marked increase in the activity of phenothiazines. This substitution is accomplished in one of three ways: direct electrophilic substitution, coupling of two appropriately substituted aromatic compounds (Smiles rearrangement) and sulfurization of a substituted diphenylamine.

Propiomazine (12) is prepared by the direct electrophilic substitution route. Phenothiazine is N-acylated with propionyl chloride to act as a protecting group, and to deactivate the nitrogen to allow the para directing sulfur to predominate in the substitution step. Friedel-Crafts acylation is accomplished next, followed by saponification to the amine.

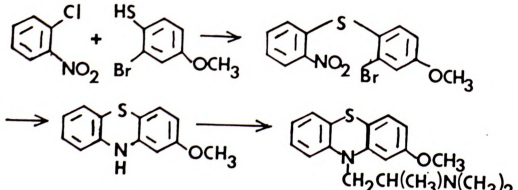
Alkylation of the nitrogen, as before, completes the synthesis (equation 37).



(37)

12

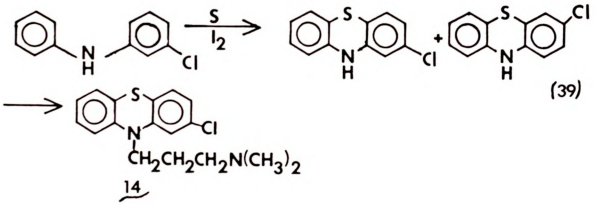
The Smiles rearrangment was used to prepare methopromazine (13). Nucleophilic aromatic substitution on o-chloronitrobenzene with 2-bromo-4-methoxythiophenol produces an intermediate sulfide. After reduction of the nitro group the sulfide is cyclized to a phenothiazine ring system. N-alkylation affords the product (equation 38).



(38)

13

Sulfurization of 3-chlorodiphenylamine was used in the synthesis of chloropromazine (14). The intermediate 2-chlorophenothiazine was N-alkylated to produce the product (equation 39).



(39)

14

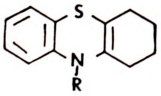
It is interesting to note that the phenothiazine derivatives discussed up to 14 contain a dialkylethylamine side chain. These compounds generally exhibit antihistaminic activity. Compounds containing a dialkyl propyl amine function, like 14, are proving to be remarkable neuroleptic (antipsychotic) agents.

The advantage of phenothiazine syntheses lies in their moderate to good yields. There is a large range of derivatives that can be prepared by simply modifying the side chain on nitrogen. The reaction conditions may be a disadvantage to these syntheses. The use of high temperatures and strong bases could have an adverse effect on delicate functionality which makes the feasibility of more complex structures less likely.

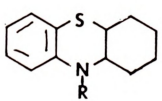
The synthesis and use of partially saturated phenothiazine derivatives is relatively limited to the old literature.[34,60]

Few examples of these compounds are known and recent studies do not acknowledge or investigate their biological activity. The activity of some of these compounds was compared to the analogous phenothiazines and benzothiazine about two decades ago. The information received will be discussed later.

The basic procedure for preparation of 1,2,3,4-tetrahydrophenothiazines (15) is the same as preparing benzothiazines; that is, condensing α-halocyclohexanones with o-aminothiophenol and simple cyclohexanones with bis(o-aminophenyl)disulfide.[34,60] The hexahydro derivatives (16) can be prepared by reduction of the tetrahydro compounds with lithium aluminum hydride.[60] A sulfone derivative, which has been claimed to be a useful



15



16

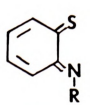
pharmaceutical intermediate, is prepared by heating 2-halocyclohexyl-o-aminothiophenol sulfone.[61]

Very little has been published involving comparison studies of the biological activities of the above compound types (i.e., benzothiazines, phenothiazines, and tetrahydrophenothiazines). In 1957 a study of the toxicity, antiacetylcholine and antihistaminic activities of various N-dialkylamine substituted benzothiazines, phenothiazines and tetrahydrophenothiazines was prepared.[62] In general, the toxicity of these

agents was decreased substantially when a chlorine was substituted for the hydrogen meta to the nitrogen. It also appeared that antihistaminic activity was greater than anti-acetylcholine activity in most cases. The activity of tetrahydrophenothiazines was equal to or greater than that of the benzothiazines, but less than that of the phenothiazines. With the chlorine substituted derivatives tetrahydrophenothiazines were about equal in activity to the phenothiazines, but the saturated analogs were less toxic. Another study in 1958[63] indicated that phenothiazines were more effective analgesic agents than either of the other two compound types.

Based on the above data it would appear that phenothiazines deserve more synthetic attention, though a number of workable syntheses have been developed. The tetrahydro derivatives also show promise with their lower toxicity, and introduction of new synthetic methods for their preparation may spur new interest in their pharmacology. Benzothiazines also cannot be disregarded in light of the recent discovery of their anti-inflammatory activity.

Preparation of these heterocycles by the trapping of a photo-generated iminothionocyclohexadiene intermediate (17) is an interesting prospect.



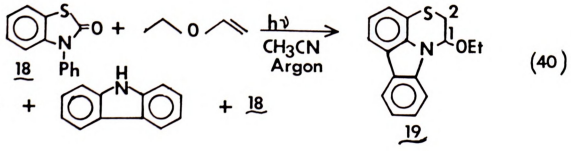
17

One can take advantage of low temperatures and other mild conditions to run these reactions. The benzothiazolinone starting materials are easy to prepare and there are a wide variety of traps available that do not absorb the light necessary for generation of 17. The potential disadvantage of this type of procedure is that photoreactions are often inefficient and afford low to moderate yields of products.

We have found that both N-phenyl-2-benzothiazolinone and N-cyano-2-benzothiazolinone photodecarbonylate, and in the presence of electron-rich olefins, afford products that appear to result from the trapping of an ortho-quinoid intermediate. The N-phenyl compound is also oxidized to an unexpected carbazole ring system. This chapter will focus on the photoreactions of N-phenyl and N-cyano-2-benzothiazolinone. Novel products will be rationalized mechanistically, and the synthetic applicability of this new reaction intermediate will be studied.

RESULTS AND DISCUSSION

When N-phenyl-2-benzothiazolinone (18) and ethylvinyl-ether in acetonitrile are irradiated for two hours with Vycor filtered light, carbazole, a new compound (19) which proved to be 1-ethoxy-1,2-dihydro-[1,4]thiazino[2,3,4-jk]carbazole, and unreacted 18 are recovered from the resulting solution (equation 40).[64] Both carbazole and compound 19 were identified by comparison with authentic samples. Compound 19 analysed for $C_{16}H_{15}NOS$. The proton nuclear magnetic resonance spectrum (PMR) for 19 indicated an ethoxy group (δ1.15, t, 3H and δ3.3, multiplet, 2H), a methine (δ 5.9, t, 1H) coupled to a methylene (δ3.15, t, 2H), and a carbazole-like aromatic region. The ethoxy methylene multiplet results from the diastereotopic nature of the hydrogens. The ring methylene triplet appears to be a set of overlapping doublets resulting from the diastereotopic nature of these hydrogens. The infrared spectrum (IR) was very similar to that of carbazole and the mass spectrum indicated a molecular ion at m/e 269 and a base peak at m/e 167 which is the molecular ion for carbazole.



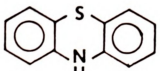
(40)

The position of the ethoxy group posed an interesting structure elucidation problem. Due to the similarity of the nitrogen and sulfur deshielding effects simple PMR could not be used to distinguish between a structure with the ethoxy in the 1 position or in the 2 position (see equation 41). This problem was solved by comparing the off-resonance decoupled ^{13}C NMR (CMR) spectrum of 19 with that of its sulfone derivative, prepared by potassium permanganate oxidation of 19. The chemical shift of the ring methylene carbon of 19 at δ31.03 moved downfield to δ53.23 in the sulfone derivative (a 22.2 ppm shift) while the methine chemical shift of 19 at δ76.73 moved to only δ80.88 in the sulfone derivative (a 4.15 ppm shift). This experiment clearly indicates that the ring methylene is closer to the sulfur than the methine, and thus the structure for 19 is correct as drawn. Again, lack of distinction between deshielding effects of sulfones and amines as well as between sulfones and sulfides prevented conclusive evidence for structure 19 from PMR data.

Irradiation of 18 in acetonitrile without the dienophile present produced carbazole and recovered 18 in roughly the same yield as when the dienophile is present. It appears that carbazole formation does not depend on the presence of the dienophile trap and that the intermediate to 19 goes to unidentified material if it is not trapped. Other less electron-rich dienophiles (e.g., cyclohexene and acrylonitrile) were ineffective at trapping. Attempts to use ketene diethyl acetal resulted only in unidentified mixtures.

A few mechanistic experiments were performed. The photoreaction to give 19 was neither quenched by piperylene nor sensitized by acetone; however, the formation of carbazole was quenched and sensitized by piperylene and acetone, respectively. These data indicate that the photoreaction to give carbazole involves a triplet state reaction. The reaction also appears to be completely regioselective within experimental error.

Thermally (750°C) 18 is known to give carbazole through a phenothiazine (20) intermediate.[65]

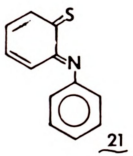


20

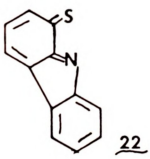
The presence of 20 was not observed in the photolyses of 18, but can not be ruled out. Phenothiazine was found to be relatively photolabile when subjected to the conditions of the photolyses of 18. It is unlikely, though, that 20 is an intermediate which leads to 19 or carbazole since its irradiation with or without a trap present did not afford these products.

The nature of the intermediates is unclear. In the thermal reaction, an ortho-quinoid species (21) was proposed to explain the formation of phenothiazine. This intermediate could also be considered in the photochemical reaction if it

is assumed that trapping is faster than rearrangement to phenothiazine. Another possible intermediate is the carbazole version (22) of ortho-quinoid 21.



21



22

The lack of phenothiazine or other rearranged products related to those of Chapter One may be a result of an initial bridging to the carbazole ring structure. This may or may not be immediately oxidized. This bridging would prohibit the phenyl ring from approaching the sulfur. It would not be surprising for this bridging reaction to be very rapid, since diphenylamine is reported to form carbazole photochemically.[66] When diphenyl amine is subjected to the conditions used in the photolysis of 18, it is consumed rapidly and affords only carbazole in modest yield after two hours.

As was indicated before, carbazole appears to be formed from a triplet reaction of 18 and compound 19 from a singlet reaction. This could result from loss of OCS from 18 in the former reaction and loss of CO in the latter. Mass spectral analysis of the gasses generated during photolysis indicated

the presence of CO. The presence of OCS was not observed, but that may be because it is relatively photolabile.[67]

The oxidation step in the reaction sequence to 19 without the apparent presence of an oxidizing agent is puzzling. In the photolysis of diphenylamine, Grellmann[66] observes an intermediate with a visible absorbance (610 nm) which disappears when the solution is subjected to air. He claims that this intermediate is a dihydrocarbazole that is rapidly air oxidized to carbazole. The UV spectrum of a carefully prepared photolysate mixture of 18 and ethylvinylether which had been purged with argon for at least 20 min prior to irradiation, and irradiated with continual argon purging (purging before irradiation for times ranging from 15 min to 40 min had little effect on product yields) indicated no absorbance at or near 610 nm even at a concentration up to ten times that of Grellmann's. The likelihood that oxygen is unnecessary for the oxidation to take place suggests the presence of alternate oxidizing agents. It should be noted that the photoreaction of 18 to give carbazole need not involve an oxidizing agent. Loss of OCS from 18 with aromatic ring closure followed by 1,3 and 1,5 hydrogen shifts would afford carbazole.

Carbonyl compounds can be thought of as oxidizing agents, since it is well known that they abstract hydrogen via their n-π^* excited states.[68] This is generally limited to aldehydes and ketones, however some examples of esters and amides

which undergo Norrish type II reactions have been reported.[69] No evidence has been found for any reduced derivatives of 18, however since little is known about this envisioned intermediate it would not be surprising for it to have decomposed to the intractable material recovered from the photolysate.

Another potential oxidizing agent may come from the extruded molecules. Carbonyl sulfide (COS) is not generally known as an oxidizing agent, but recent patents claim that various alkanes can be oxidized in the presence of COS and a heavy metal catalyst.[70] It is possible that the COS presumedly generated in the carbazole reaction could oxidize the intermediate leading to 19. Alternatively, carbonyl sulfide is known to photofragment to carbon monoxide and excited sulfur.[67] This excited sulfur could abstract the hydrogens from the intermediate leading to 19 and become hydrogen sulfide. The presence of hydrogen sulfide was not detected in the mass spectrum of the effluent gasses of the photolysis of 18. Actually, the large amount of COS necessary to account for the observed yield of 19 makes the prospects for this oxidizing agent unfavorable.

The intermediate resulting from the extrusion of carbon monoxide from 18 may also be a candidate for an oxidizing agent. The intermediate could abstract hydrogens from the intermediate preceeding 19 and afford 1-mercaptocarbazole. This process would involve the use of two molecules of 18

for every molecule of 19 produced. The presence of 1-mercaptocarbazole was not observed in the photolysates of 18, which appears to rule out this possibility also.

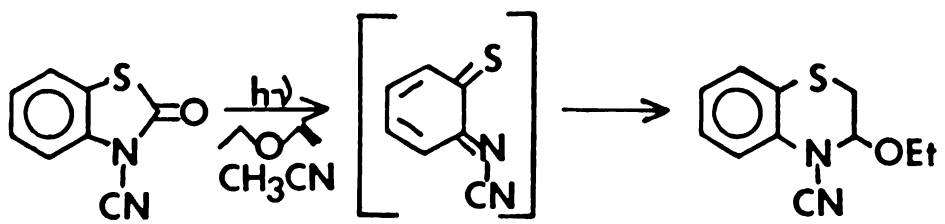
To summarize, the product 19 appears to occur from a singlet reaction with loss of carbon monoxide, coupling of the aromatic rings, oxidation to a carbazole ring system, and addition of ethylvinylether. The order of these steps has not been determined although it is reasonable to assume that loss of carbon monoxide occurs before trapping with ethylvinylether. The formation of carbazole appears to involve a triplet reaction with loss of carbonyl sulfide, coupling of the aromatic rings, and either rearrangement or a redox reaction. Again, the order of the steps was not determined. One important aspect of the photoreactions of 18 is the apparent generation of an ortho-quinoid intermediate. This intermediate has potential synthetic applications and further study is warranted.

The photoreaction of N-phenyl-2-benzothiazolinone (18) produces only thiazino carbazoles, which currently are of unknown utility. This reaction could be modified to form a variety of new compounds simply by substituting on the aromatic rings prior to photolysis. The products can also be modified by use of different electron-rich olefins as traps. This facet of the reaction, namely the trapping process, can be used in a less complicated manner to prepare classes of compounds of known pharmacological and

industrial value.

Substitution of the phenyl group of 18 by another active functional group, for example a cyano group, can avert the formation of the carbazole system and produce a new trappable ortho-quinoid species. This modification makes a new approach to N-substituted benzothiazines and related biologically active compounds feasible. These new compounds can be quite versatile, since the cyano group can be transformed into a variety of other functional groups.

N-cyano-2-benzothiazolinone (23) was prepared by reacting the sodium salt of 2-benzothiazolinone with cyanogen bromide. Compound 23 was identified by the strong IR absorption at 2240 cm^{-1}, indicative of a nitrile, and by a molecular ion at m/e 176 in the mass spectrum. Unlike 18, when 23 is irradiated in the presence of ethyl vinyl ether with Vycor filtered light, it decomposes in less than one half hour. Irradiation of 23 in the presence of ethyl vinyl ether with Corex filtered light affords a moderate yield of a new product, 4-cyano-3-ethoxy-1,2-dihydro-4H-1,4-benzothiazone (24) in 1.5 h (equation 41).



(41)

23 23a 24

Compound 24 has a PMR spectrum very similar to 19 in the alkyl region. The IR indicates that the nitrile is present (2210 cm^{-1}) and the mass spectrum shows a molecular ion at m/e 220. The position of the ethoxy group was determined in the same way as that in 19, by analysis of off-resonance decoupled CMR data of 24 and its sulfone derivative.

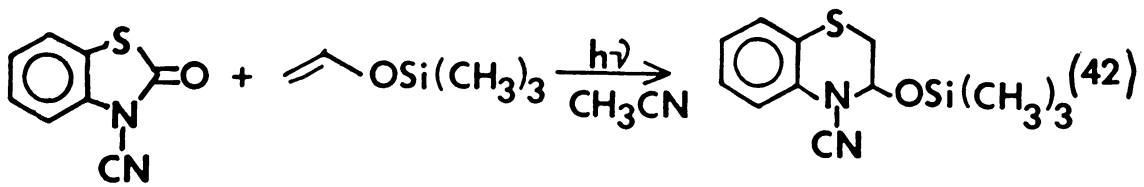
When attempting to determine the optimum ratio of trap to 23 for a maximum yield of 24, an interesting fact was learned. There was not an appreciable decline in yield of 24 until the trap to 23 ratio was decreased to 1:3. This indicates that a very long lived intermediate is formed prior to trapping. The maximum yield of 24 is attained with a thirtyfold excess of trap and is only 36%. This indicates that 23 does not totally photodecarbonylate to the desired intermediate. When the ratio of trap to 23 is less than 10:1, solid is observed suspended in the previously clear photolysate. This solid was found to be insoluble in ethyl vinyl ether, which tends to rule out its concealed presence in the photolysates containing higher concentrations of trap. It is reasonable to assume that ethyl vinyl ether interferes with the formation of this unidentified solid.

In order to determine the scope of this photoreaction, various electron-rich olefins were prepared and added in place of ethyl vinyl ether in the photolysis solution. These traps were selected for their ease and generality

of preparation, as well as for the modifiable functionality that they would provide after reaction. They included cyclohexene, vinyloxytrimethylsilane and related derivatives, and an enamine, 3-(4-morpholinyl)-2-pentene.

Cyclohexene proved, as in the photolysis of 18, to be ineffective at trapping the intermediate. It would appear that an extremely electron-rich dieophile, like the vinyl ethers, is necessary for the trapping reaction to occur. A seemingly prolific source of this type of trap can be found in silyl enol ethers. These compounds are very similar to vinyl ethers except that they offer the advantage of hydrolysis to the alcohol after the photoreaction. Silyl enol ethers can be prepared from virtually any enolizable aldehyde or ketone.

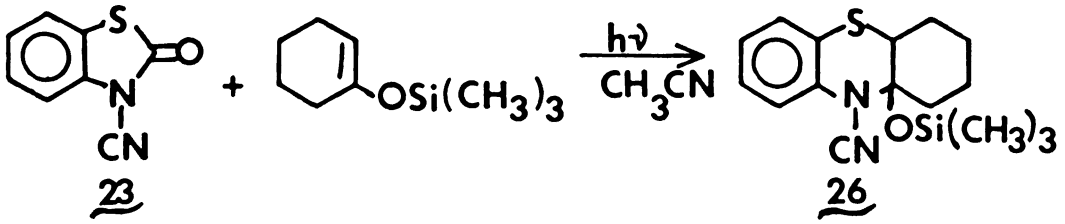
The simplest example of a silyl enol ether is vinyloxytrimethylsilane. This compound can be prepared by cleaving tetrahydrofuran with n-butyl lithium to obtain the enol ether of acetaldehyde, which can then be silated with chlorotrimethylsilane.[71] When 23 is irradiated in the presence of vinyloxytrimethylsilane, the formation of a new compound, 4-cyano-3-trimethylsiloxy-1,2-dihydro-4H-1,4-benzothiazine (25) is apparent (equation 42).



23 25

Compound 25 has a PMR very similar to that of 24 without the ethyl group, and also has a strong singlet coincident with TMS. This compound hydrolyses upon thin layer chromatography on silica gel and further evidence for its existence is provided by the resulting alcohol. The IR shows absorption at 3450 cm^{-1} to indicate the presence of the alcohol and again the nitrile absorption is observed (2210 cm^{-1}). The mass spectrum shows a molecular ion at m/e 192. The position of the hydroxy group on the molecule was assumed, based on the off-resonance decoupled CMR studies of 19 and 24.

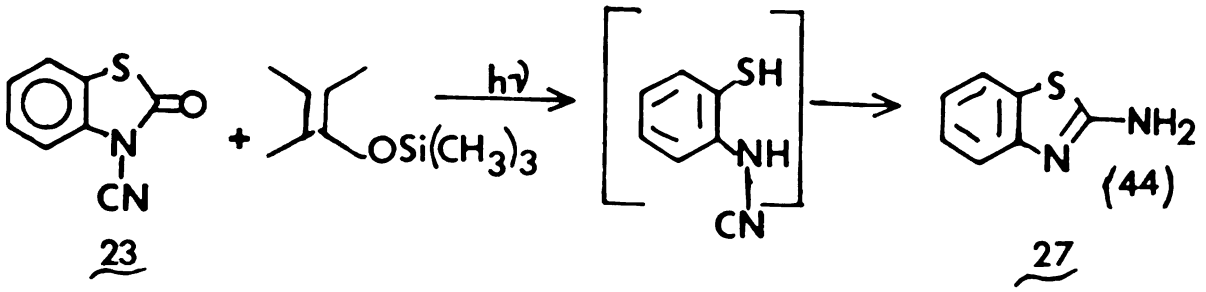
In order to determine if phenothiazines are attainable, 1-trimethylsiloxycyclohexene was tried as a trap. This compound was prepared by refluxing cyclohexanone, triethylamine, and chlorotrimethylsilane in dimethylformamide and distilling the product.[72] When 23 was irradiated in the presence of this trap, evidence of a limited nature was obtained for the expected compound, 10-cyano-10a-trimethylsiloxy-1,2,3,4,4a,10a-hexahydrophenothiazine (26) (equation 43).



(43)

The residue from this photolysis, obtained after stripping away the solvent, provided a slowly moving band on a preparative silica gel thin layer chromatography plate. The IR obtained from this band indicated an OH (3300 cm^{-1}) and a nitrile (2200 cm^{-1}). The PMR of this band was not too helpful, although it showed broad signals in the aliphatic region. The mass spectrum indicated a molecular ion at m/e 246 and fragments at m/e 203 and 150 which correspond to loss of HOCN and C_6H_8O, respectively. All of these data are consistent with the alcohol derivative for the expected compound 26.

Preparations for highly substituted benzothiazines are rare, due to the limited availability of α-disubstituted-α-halo-ketones and aldehydes (vide supra). A solution to this difficulty was sought by using the heavily substituted silyl enol ether, 2-methyl-3-trimethylsiloxy-2-butene. This compound was prepared by refluxing 3-methyl-2-butanone, triethyl amine, and chlorotrimethylsilane in dimethylformamide and distilling the product.[72] Irradiation of 23 in the presence of this trap produced no evidence for a trapped product. Separation of the photolysate residue by preparative silica gel thin layer chromatography isolated 2-aminobenzothiazole (27) (equation 44).



The completely aromatic PMR, the mass spectrum (m/e 150, molecular ion) and the IR which indicated an amino group (3360 and 3450 cm^{-1}) and no nitrile were identical to literature spectra for this compound.[73a,b]

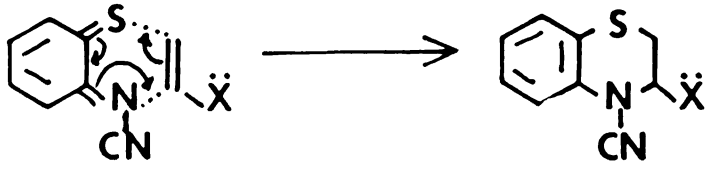
It is interesting to note that 27 has never been observed in previous photoreactions of 23. The mass of this compound is consistent with reduction of the previously proposed ortho-quinoid intermediate. A viable reducing agent is the 2-methyl-3-trimethylsiloxy-2-butene present in solution, which contains nine readily abstractable allylic hydrogens. Once the intermediate is reduced, the nucleophilic sulfur is free to intramolecularly attack the nitrile and ultimately arrive at 27. The presence of 27 offers new supporting evidence for the proposed ortho-quinoid intermediate.

Enamines are also another source of electron-rich dieneophiles. These compounds can be prepared generally from a secondary amine and almost any enolizable aldehyde or ketone although the reaction fails with acetaldehyde or monosubstituted acetones because of their facile self aldol condensation.[74] Reaction of enamines would allow placement of a nitrogen in the 3 position of a benzothiazine. The lack of

reactions to alter alkyl substituents on amines could limit the versatility of this reaction, especially when substitution of the hydroxy group of 25 with an appropriate amine could reach the same goal.

Compound 23 was irradiated in the presence of 3-morpholino-2-pentene[74] and no trapping product was evident. This could be because this enamine absorbs some of the light normally absorbed by 23 (enol ethers do not abosrb light in the same regions as 23) or possibly the enamine is not electron-rich enough. Little is known about enamines as dienophiles since most Diels-Alder reactions and ortho-quinoid trappings are done with electron poor olefins.

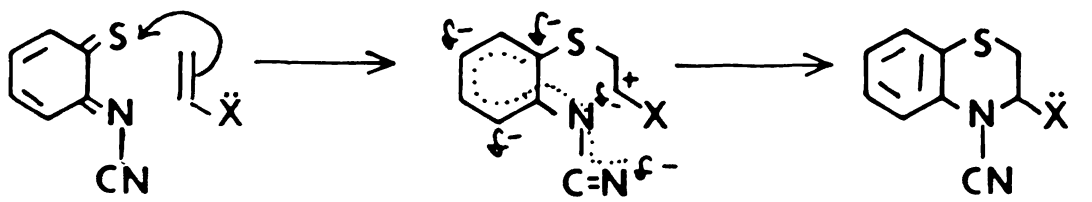
The complete regioselectivity of the reaction resulting from trapping the ortho-quinoid intermediate is interesting. This selectivity can be explained by both concerted and stepwise mechanisms. A polar Diels-Alder reaction could be occuring (equation 45). This process makes the regioselectivity of the reaction difficult to predict although prediction may be possible from an MO calculation. A stepwise mechanism can be considered and may help to explain the orientation.



(45)

One can also consider the intermediate as an extended Michael system. Nucleophilic attack by the olefin on sulfur will be

stabilized by resonance, the electronegative iminonitrogen, and the nitrile. This imino nitrogen can attack the electron deficient carbon on the trap, to complete the reaction sequence (equation 46). Without the nitrile on nitrogen, attack of the trap on the imino nitrogen might be expected since the sulfur could stabilize the residual charge much better than an unsubstituted nitrogen.



(46)

These proposed mechanisms can be tested by examining the products from the photoreactions of 23 and isomeric cis and trans electron-rich olefins, for instance, cis and trans-1-ethoxypropene. A stereospecific reaction would indicate a concerted pathway whereas a set of stereoselective reactions would indicate a stepwise process.

The obvious capabilities of this fascinating photoreaction need further study. Other dienophiles, like thiol vinyl ethers and certainly other enamines may prove to form useful intermediates. Other nitrogen substituents on the starting benzothiazolinone may also allow for a more versatile reaction. For instance, the use of a vinylogous nitrile would put many of the active benzothiazines in easy reach (see introduction). This novel reaction may be just the beginning of a new approach to heterocyclic synthetic photochemistry.

EXPERIMENTAL

General

All of the information contained in the general experimental of Chapter One is also valid in the following.

Internal Standard Quantitative HPLC

The amounts of recovered N-phenyl- and N-cyano-2-benzothiazolinone from photolyses were determined by internal standard HPLC. All data was obtained from a partisil 10/50 (Altec) column at 50% stroke using stop-flow injections through a Valvseal septumless injector (Precision Sampling), detected on an Altex model 151 UV detector (0.8-0.16 sensitivity, 254 nm) and recorded on a Linear Instruments Corp. integrating recorder. Solvents used were methylene chloride (for N-cyano-2-benzothiazolinone) and 0.25% acetonitrile in methylene chloride (for N-phenyl-2-benzothiazolinone).

An internal standard was selected that did not interfere with the sample signal. A response factor was determined from the peak areas (integrations) of a mixture of equal weights of sample and internal standard by applying the following formula:

$$\frac{\text{amt. of std.}}{\text{amt. of sample}} \times \frac{\text{int. of sample}}{\text{int. of std.}} = \text{response factor}$$

For the phenyl compound benzophenone gave a response factor of 0.263 and for the cyano compound acetophenone gave

a response factor of 0.283.

The sample solution was chromatographed first to determine if any impurity existed in the internal standard area. A measured quantity of standard was added to the sample solution and the peak areas obtained from this solution were applied to the following equation:

$$\frac{\text{wt. of std.}}{\text{int. of std.-impurity}} \times \frac{\text{int. of sample}}{\text{response factor}} = \text{wt. of sample}$$

The peak area of the standard was corrected for impurities by applying the following equation:

$$\frac{\text{int. of impurity (obtained from sample w/o std.)}}{\text{int. of sample (obtained from sample w/o std.)}} \times \text{int. of sample (w/ std.)} = \text{impurity}$$

Preparation of N-phenyl-2-benzothiazolinone (18). N-phenyl-2-benzothiazolinone (18) was prepared by literature methods.[75] The spectral data were: IR ($CDCl_3$) 1690, 1660, 1585, 1495, 1470, 1345, 1290, 1140, 1025, 960, 840 cm^{-1}; PMR ($CDCl_3$, TMS) δ6.5-7.5 (m); MS m/e (rel intensity) 227 (100), 199 (47), 198 (81); UV (95% ethanol) λ_{max}^{nm} 290 (ε 2400), 283 (ε 2400), 242 (ε 8200).

Photolysis of N-phenyl-2-benzothiazolinone (18) and ethylvinylether. A solution of 18 (100 mg, 0.44 mmol) and ethylvinylether (10mL, 76 g, 106 mmol, Aldrich, redistilled) in 150 mL of acetonitrile was purged with argon for 15 min and

irradiated with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure (<40°C) from the resulting yellow suspension. The residue was chromatographed on a Florosil column (100 g). Carbazole (6.2 mg, 8.4%) and 1-ethoxy-1,2-dihydro-[1,4]thiazino[2,3,4-jk]carbazole (19) (37.0 mg, 31%) were eluted with methylene chloride and recovered 18 (19.4 mg, 19.4%) was eluted with 1% methanol in methylene chloride. Yields for carbazole and 19 were determined by quantitative NMR (methylene chloride) and recovered 18 by internal standard HPLC. Spectral data for carbazole and 19 were consistent with authentic samples. Physical and spectral data for are: mp 75.5-76.0°C; IR ($CHCl_3$) 1600, 1575, 1480, 1450, 1430, 1380, 1325, 1185, 1130, 1090, 1070 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.2 (t, 3H), 3.2 (t, 2H), 3.62 (m, 2H), 5.95 (t, 1H) 7.0-8.0 (m, 7H); CMR ($CDCl_3$) δ14.60 (q), 29.57 (t), 64.81 (t), 83.94 (d), 112.14, 117.69, 120.42, 123.54, 126.04, 127.69, 131.61; MS m/e (rel intensity) 269 (15), 224 (22), 167 (100), 86 (59), 84 (93); UV (abs ethanol) λ_{max}^{nm} 345 (ε 5400), 332 (ε 4880), 293 (ε 17,400), 283 (ε 9600), 274 (ε 13,200), 265 (ε 16,800), 253 (ε 27,600); Anal. calcd for $C_{16}H_{15}NOS$: C, 71.35; H, 5.61; N, 5.70. Found: C, 71.12; H, 5.66; N, 5.11; MS of effluent gasses, m/e 72 (ethylvinylether), 41 (acetonitrile), 40 (argon), 28 (carbon monoxide).

Preparation of 1-ethoxy-3,3-dioxo-1,2-dihydro[1,4]thiazino-[2,3,4-jk]carbazole (19a). A solution of 19 (77 mg, 0.29 mol) in 15 mL of glacial acetic acid was cooled to 0°C and a

solution of potassium permanganate (60 mg, 0.38 mmol) in 2 mL of water was added. After 5 min sodium bisulfite (~0.5 g) was added. Methylene chloride and water were added to the acid solution and the aqueous layer was separated and extracted with two additional 10 mL-portions of methylene chloride. The organic layers were combined, dried over sodium sulfate and filtered. The filtrate solvent was removed at reduced pressure. The resulting oil was separated by preparative thin layer chromatography (silica gel, methylene chloride). The slowest moving band was identified as 19a (16 mg, 18%). The spectral data are: IR ($CDCl_3$) 1600, 1475, 1450, 1430, 1310, 1125 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.2 (t, 3H), 3.6 (m, 4H), 6.1 (t, 1H), 7.0-8.2 (m, 7H); CMR ($CDCl_3$) δ14.77 (q), 53.23 (t), 64.59 (t), 80.85 (d), 109.80, 119.37, 120.34, 121.03, 121.28, 122.68, 122.86, 124.26, 124.57. 127.33; MS m/e (rel intensity) 301 (1), 284 (3), 227 (32), 198 (26), 167 (15), 149 (17), 110 (18), 103 (35), 75 (48), 72 (100), 68 (52).

Photolysis of N-phenyl-2-benzothiazolinone (18). A solution of N-phenyl-2-benzothiazolinone (18) (100 mg, 0.44 mmol) in 160 mL of acetonitrile was purged with argon for 15 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed and reduced pressure (<40°C) from the resulting yellow suspension and the residue was chromatographed on a Florosil column (100 g). Carbazole (17 mg, crude yield) was eluted with methylene chloride and recovered 18 (20 mg) was eluted with 1% methanol in methylene chloride. Both compounds were identified by

comparison to authentic samples.

Exploratory photolysis of N-phenyl-2-benzothiazolinone (18) and acrylonitrile in the presence of piperylene. A solution of N-phenyl-2-benzothiazolinone (18) (106 mg, 0.47 mmol), acrylonitrile (5 ml, 4.05 g, 76.4 mmol), and piperylene (2 ml, 1.4 g, 20.6 mmole) in 140 mL of acetonitrile was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting brown solution. The residue was chromatographed on a silica gel column (100 g) with 1% methanol in methylene chloride. Recovered 18 (18.6 m, 18%) was the only identifiable compound recovered.

Exploratory photolysis of N-phenyl-2-benzothiazolinone (18) with cyclohexene. A solution of 18 (101 mg, 0.44 mmol) and cyclohexene (10 ml, 8.1 g, 0.1 mmol) in 170 mL of acetonitrile was purged with argon for 30 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution and the brown residue was chromatographed on a Florisil column (50 g). Carbazole (3.8 mg, 7.7%) was eluted with methylene chloride and recovered 18 (32.9 mg) with 1% methanol in methylene chloride. The yield of carbazole was determined by quantitative NMR (CH_2Cl_2, 1 μL).

Exploratory photolysis of N-phenyl-2-benzothiazolinone (18) with ketene diethylacetal, evidence for 1,3,5-triethoxybenzene: A solution of 18 (100 mg, 0.44 mmol) and ketene

diethylacetal (10 mL, 7.9 g, 68 mmol) in 150 mL of acetonitrile was purged with argon for 30 min and irradiated for 6 h with a 450 W Hanovia medium pressure mercury lamp through Corex. The solvent was removed at reduced pressure (< 40°C) from the resulting solution and the residue was treated with 50% aqueous acetic acid at 25°C for 2 h. Methylene chloride and water were added to the acid solution and the aqueous layer was separated and extracted with additional methylene chloride. The organic layers were combined, extracted with 1.0 N sodium hydroxide, and dried over sodium sulfate. The methylene chloride was removed at reduced pressure and the residue was chromatographed on a silica gel column (100 g). Carbazole (3 mg) and an oil that appeared to be 1,3,5 triethoxybenzene (11 mg), and recovered 18 were eluted with methylene chloride. The spectral date for 1,3,5 triethoxybenzene are: IR ($CDCl_3$) 2975, 2900, 1600, 1455, 1390, 1295, 1180, 1060, 820 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.35 (t, J=8 Hz, 9H), 3.85 (quar., J=8 Hz, 6H), 5.95 (s, 3H); CMR ($CDCl_3$) δ14.65, 63.29, 93.81, 160.69; MS m/e (rel intensity) 210 (97), 127 (100), 69 (89).

The basic extract was neutralized with 1.0 N HCl and extracted with methylene chloride. The organic layer was separated and the solvent was removed at reduced pressure. The residue was chromatographed on a silica gel column (100 g). No identifiable products were eluted with methylene chloride.

Photolysis of N-phenyl-2-benzothiazolinone (18) and ethylvinylether with piperylene: A solution of 18 (100 mg, 0.44 mmol), ethylvinylether (10 mL, 7.6 g, 106 mmol) and piperylene (2 mL, 1.4 g, 20.6 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution and the residue was chromatographed on a florisil column (50 g). The thiazinocarbazole 19 (29.9 mg, determined by quantatitive NMR, CH_3NO_2, 3) was eluted with methylene chloride and recovered 18 (31.3 mg, determined by internal standard HPLC) was eluted with 1% methanol in methylene chloride.

Photolysis of N-phenyl-2-benzothiazolinone (18) and ethylvinylether in acetone. A solution of N-phenyl-2-benzothiazolinone (18) (97 mg, 0.43 mmol) and ethylvinylether (10 mL, 7.6 g, 106 mmol) in 150 mL of acetone was purged with argon for 30 min and irradiated for 7.5 h with a 450 W Hanovia medium pressure mercury lamp through Pyrex. The solvent was removed at reduced pressure from the resulting solution and the residue analyzed by HPLC. It proved to contain carbazole (2.15 mg, 3%) and recovered 18 (82.7 mg, 85%).

Photolysis of phenothiazine (20) in acetonitrile: A solution of phenothiazine (100 mg, 0.5 mm) in 150 mL acetonitrile was purged with argon for 40 min and then irradiated for 2 h

with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution and the residue was eluted through a plug of florisil with methylene chloride. The filtrate solvent was removed at reduced pressure leaving a yellow residue (64.2 mg) which appeared to be phenothiazine by analytical TLC comparison to an authentic sample.

Exploratory photolysis of phenothiazine with ethylvinyl-ether: A solution of phenothizine (100 mg, 0.50 mmol) and ethylvinylether (10 ml, 7.6 g, 106 mmol) was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Vycor. The solvent was removed at reduced pressure from the resulting solution and PMR analysis of the residue indicated only phenothiazine as an identifiable component. No yield was determined.

Photolysis of diphenylamine: A solution of diphenylamine (102 mg, 0.61 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure lamp through a Vycor filter. The solvent was removed at reduced pressure from the resulting solution and the residue was chromatographed on 100 g of silica gel with methylene chloride elution. PMR analysis of the single moving band indicated only carbazole (26.0 mg, 26%) as determined by quantitative PMR (CH_3NO_2, 4 μL). No starting material was detected.

Preparation of N-cyano-2-benzothiazolinone (23): A solution of 2-benzothiazolinone (1.0 g, 6.6 mmol) in 25 mL of THF was added to a stirred suspension of sodium sand[30] (0.15 g, 6.6 mmol) in 25 mL of THF. After 2 h (H_2 evolution had ceased) a solution of cyanogen bromide (1.0 g, 9.4 mmol) in 25 mL of THF was added dropwise. After 20 h the solvent was removed at atmospheric pressure. The resulting solid was dissolved in methylene chloride, filtered through celite and the filtrate evaporated at reduced pressure. The resulting solid was chromatographed on a Florisil column (30 g) with methylene chloride. The first band proved to contain the product which was recrystalized from 95% ethanol (0.9 g, 77.5%) mp 114-115°C. The spectral data are: IR ($CHCl_3$) 2240, 1725, 1675, 1470, 1330, 1190, 1170 cm^{-1}; PMR ($CDCl_3$) δ7.3 (s); MS m/e (rel intensity) 176 (100), 148 (83), 96 (25), 78 (25); UV (95% ethanol) λ_{max}^{nm} 283 (2075), 276 (2170); Anal. calcd for $C_8H_4N_2OS$: C, 54.54; H, 2.29; N, 15.90. Found: C, 54.74; H, 2.18, N, 15.91.

Photolysis of N-cyano-2-benzothiazolinone (23) in the presence of ethylvinylether. A solution of N-cyano-2-benzothiazolinone (23) (104 mg, 0.59 mmol) and ethylvinylether (10 mL, 7.6 g, 106 mmol) in 150 mL of acetonitrile was purged with argon for 25 min and irradiated for 1.5 h with a 450 W Hanovia medium pressure mercury lamp through Corex. The solvent was removed at reduced pressure from the resulting solution and the residue was analysed by quantitative NMR (acetonitrile,

4 μL) for 4-cyano-2-ethoxy-2,3-dihydro-4H-1,4-benzothiazine (24) (43.9 mg, 35.6%). The residue was then separated by preparative thin layer chromatography (silica gel, CH_2Cl_2) and the fastest moving band was recovered 23 (9.2 mg) by internal standard HPLC. The second band (24) was recrystalized from ether/pentane to give an analytical sample (mp 75.5-76.0°C). The spectral data for 24 are: IR ($CDCl_3$) 2210, 1575, 1475, 1440, 1390, 1325, 1175, 1060 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.25 (t, 3H), 3.15 (dd, 2H), 3.9 (d quart., 2H), 5.3 (t, 1H), 6.8-7.4 (m, 4H); CMR ($CDCl_3$) δ14.60 (q), 29.87 (t), 64.81 (t), 83.94 (d), 112.14, 117.69, 120.42, 123.84, 126.04, 127.69, 131.61; MS m/e (rel intensity) 220 (91), 175 (29), 163 (100), 136 (54); Anal. calcd for $C_{11}H_{12}N_2OS$: C, 59.98; H, 5.49; N, 12.72. Found: C, 60.13; H, 5.62; N, 12.77.

Photolyses of N-cyano-2-benzothiazolinone (23) with varying amounts of ethylvinylether. Each photolysis was carried out as described above with 23 (100 mg, 0.57 mmol) and varying amounts of ethylvinylether as described below. The yield of 24 was determined by quantitative PMR ($(CH_3)_2CO$, 1 μL) of the crude residue obtained by removing the photolysate solvent at reduced pressure. The results are given as: mL of added ethylvinylether (molar ratio of trap to 23), yield of 24 (%): 2.5 mL (46:1), 43.6 mg (35%); 1.25 mL (23:1), 43.6 mg (35%); 0.625 mL (12:1), 43.4 mg (35%); 0.30 mL (6:1), 39.5 mg (32%); 0.15 mL (3:1), 35.9 mg (29%), 0.075 mL (1.5:1),

34.1 mg (27%); 0.042 mL (0.75:1), 32.9 mg (26%); 0.014 mL (0.26:1), 14.3 mg (11%).

Preparation of 4-cyano-3-ethoxy-1,1-dioxo-2,3-dihydro-1,4-benzothiazine (24a). A solution of potassium permanganate (57 mg, 0.36 mmol) in 2 mL of water was added quickly to a stirring solution of 24 (81 mg, 0.36 mmol) in glacial acetic acid at 0°C. After 5 min sodium bisulfite (approximately 0.5 g) was added to the brown suspension. After the solution became colorless it was separated with methylene chloride and water. The aqueous layer was extracted with two additional portions of methylene chloride. The organic layers were combined and dried over sodium sulfate. The liquid was filtered and the methylene chloride and residual acetic acid were removed at reduced pressure. The solid residue was recrystalized from chloroform/hexanes. Yield 44.6 mg (49%) (MP 149-152°C w/decomp.) The spectral data are: IR ($CHCl_3$) 2210, 1590, 1475, 1440, 1320, 1150, 1120, 1060 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.3 (t, 3H), 3.4-4.1 (m, 4H), 5.4 (dd, 1H), 7.0-7.9 (m, 4H); CMR ($CDCl_3$) δ14.62 (q), 54.06 (t), 67.24 (t), 86.63 (d), 109.63, 117.94, 124.54, 124.93, 127.69, 133.31, 134.66; MS m/e (rel intensity) 252 (85), 225 (23), 207 (57), 159 (100), 132 (60), 131 (89), 118 (89), 117 (75), 104 (36), 90 (76), 44 (70).

Photolysis of N-cyano-2-benzothiazolinone (23) with cyclohexene. A solution of 23 (100 mg, 0.57 mmol) and cyclohexene (10 mL, 8.1 g, 0.1 mol) in 150 mL of acetonitrile was

purged with argon for 20 min and irradiated for 1.5 h with a 450 W Hanovia medium pressure mercury lamp through Corex. After solvent was removed from the resulting solution no identified products were observed by PMR or TLC (silica gel/ CH_2Cl_2) of the residue, except for 23. The PMR indicated a large amount of aliphatic material.

Preparation of vinyl oxytrimethylsilane.[71] A solution of THF (120 mL, 1.5 mol) and n-butyl lithium in hexanes (330 mL of a 1.52 M solution, 0.5 mol) was refluxed for 1 h. The solution was cooled, and the solvents were removed at reduced pressure. Dry ether (125 mL) was added to the residue and the solution was cooled to 0°C. A solution of chlorotrimethylsilane (60.7 g, 70 mL, 0.55 mol) in 125 mL of dry ether was added over 1 h. After an additional hour the solution was distilled and the fraction 172-175°C (25 mL, 193 g, 17%) proved to be product by comparison with an authentic sample (Petrarch Systems, Inc., Levittown, Pennsylvania).

Photolysis of N-cyano-2-benzothiazolinone (23) and vinyloxytrimethylsilane. A solution of 23 (100 mg, 0.57 mmol) and vinyloxytrimethylsilane (14 mL, 10.8 g, 93 mmol) in 150 mL of acetonitrile was purged with argon for 40 min and irradiated for 1 h with a 450 W Hanovia medium pressure mercury lamp through Corex. The solvent was removed at reduced pressure from the resulting solution and the residue was separated by preparative thin layer chromatography (silica gel,

CH_2Cl_2). The top band was identified as 23 (38.5 mg, 39%) by quantitative HPLC and the slowest moving band appeared to contain a new compound, 4-cyano-3-hydroxy-1,2-dihydro-4H-1,4-benzothiazine (25) (9.9 mg, 9%). The yield of 25 was determined by quantitative PMR (CH_2Cl_2, 2 μL) and some was lost during workup. The spectral data for 25 are: IR ($CDCl_3$) 3300, 2200, 1585, 1575, 1480, 1440, 1380, 1280, 1250, 1175, 1040, 1000 cm^{-1}; PMR ($CDCl_3$, TMS) δ3.0 (t, 2H), 3.6 (bs, 1H), 5.6 (t, 1H), 6.6-7.3 (m, 4H); MS m/e (rel intensity), 192 (80), 163 (100), 150 (47), 136 (50), 124 (38).

Preparation of 1-trimethylsiloxycyclohexene.[72] A solution of triethylamine (97.0 g, 133.6 mL, 960 mmol), chlorotrimethylsilane (52.3 g, 61.1 mL, 480 mmol) and cyclohexanone (39.2 g, 41.7 mL, 400 mmol) in 300 mL of DMF was refluxed for 24 h. The solution was filtered, and the filtrate was treated with 200 mL of 1 N sodium bicarbonate and extracted with 100 mL of dry pentane. The sodium bicarbonate/pentane treatment was applied two additional times to the aqueous layer. The pentane layers were combined and dried over sodium sulfate. The pentane solution was decanted from the drying agent and after removal of the pentane at reduced pressure was distilled. The fraction collected at 79-80° (24 mm) (lit.[76] 77.5°C, 28 mm) yielded approximately 40 mL (36 g, 51%) of product d_4^{20} 0.878 (lit.[76] d_4^{20} 0.891). The spectral data are: IR (neat) 1670, 1450, 1365, 1335, 1260, 1250, 1180, 980, 900, 845 cm^{-1}; PMR ($CDCl_3$, TMS) δ0.5 (s, 9H), 1.6-2.6 (m, 8H), 5.0-5.4 (m, 1H); MS m/e

(rel intensity) 170 (46), 169 (22), 155 (39), 142 (17), 128 (35), 75 (100), 73 (59), 45 (17).

Photolysis of N-cyano-2-benzothiazolinone (23) and 1-trimethylsiloxycyclohexene (preliminary experiment). A solution of 23 (104 mg, 0.59 mmol) and 1-trimethylsiloxycyclohexene (20.5 mL, 18.0 g, 106 mmol) in 150 mL of acetonitrile was purged with argon for 25 min and irradiated for 1 h with a 450 W Hanovia medium pressure mercury lamp through Corex. The solvent was removed at reduced pressure from the resulting solution and the residue was separated by preparative thin layer chromatography (silica gel, CH_2Cl_2). The top band appeared to be 23 and the slowest moving band appeared to contain a new compound, 10-cyano-10a-hydroxy-1,2,3,4,4a,10a-hexahydrophenothiazine (26). The spectral data for 26 are: IR (neat) 3300, 2910, 2840, 2200, 1775, 1710, 1580, 1475, 1435, 1250, 1115, 830, 740; PMR ($CDCl_3$, TMS) δ1.0-2.8 (bm), 4.9 (bs, 1H), 6.9-7.8 (m), 8.0 (d); MS m/e (rel intensity) 246 (95), 229 (43), 203 (57), 150 (100), 124 (51), 110 (68), 55 (89).

Preparation of 2-methyl-3-trimethylsiloxy-2-butene.[72] A solution of triethylamine (97.0 g, 133.6 mL, 960 mmol), chlorotrimethylsilane (52.3 g, 61.1 mL, 480 mmol) and 3-methyl-2-butanone (34.4 g, 42.7 mL, 400 mmol) in 300 mL of DMF was refluxed for 48 h. The resulting suspension was cooled to room temperature and filtered. The filtrate was diluted with

200 mL of dry pentane followed by 200 mL of 1 N sodium bicarbonate. After separation of the organic layer the aqueous layer was treated twice more with pentane and sodium bicarbonate. The organic layers were combined, washed twice with 1 N sodium bicarbonate and dried over sodium sulfate. The residue that resulted from removal of the solvent from the dried solution was distilled. The fraction collected between 129-144° C (lit.[76] 133°C) yielded approximately 40 mL (32.5 g, 55%) of product d_4^{20} 0.813 (lit.[76] d_4^{20} 0.803). The spectral data are: IR (neat) 2940, 2880, 1680, 1245, 1180, 1005, 960, 850, 830, 750 cm^{-1}; PMR ($CDCl_3$, signals relative to $-Si(CH_3)_3$) δ0.0 (s, 9H), 1.4 (s, 6H), 1.55 (s, 3H); MS m/e (rel intensity) 158 (37), 143 (45), 75 (98), 73 (100), 45 (15).

Photolysis of N-cyano-2-benzothiazolinone (23) and 2-methyl-3-trimethylsiloxy-2-butene. A solution of 23 (101 mg, 0.58 mmol) and 2-methyl-3-trimethylsiloxy-2-butene (2.54 mL, 2.07 g, 13.1 mmol) in 150 mL of acetonitrile was purged with argon for 30 min and irradiated for 1.5 h with a 450 W Hanovia medium pressure mercury lamp through Corex. The solvent was removed at reduced pressure from the resulting solution and the residue was separated by preparative thin layer chromatography (silica gel, CH_2Cl_2). The top band was recovered 23. The slowest moving band appeared to be 2-aminobenzothiazole (74 mg, crude yield). The spectral data for the slowest moving band are: IR ($CHCl_3$) 3450, 3360, 1615,

1525, 1445, 1300, 1180, 1120, 1010 cm^{-1}; PMR ($CDCl_3$) δ1.0-2.4 (bm, intractable material), 6.5-7.6 (bm); MS m/e (rel intensity) 150 (100), 123 (23), 96 (28), 69 (15), 45 (6). The MS was identical with the literature.[73a] The PMR was comparable to the literature[73b] except for the impurity in the aliphatic region. The IR was similar to the literature[73b] but the literature spectrum was recorded from a kBr pellet.

Preparation of 3-(4-morpholinyl)-2-pentene. The title compound was prepared by a literature method.[74] The spectral data are: IR (neat) 2940, 1645, 1450, 1315, 1300, 1260, 1215, 1140, 1120, 1100, 1000, 885 cm^{-1}; PMR ($CDCl_3$, TMS) δ1.0 (t, J=7 Hz, 3H), 1.55 (d, J=7 Hz, 3H), 2.15 (quar., J=7 Hz, 2H), 2.65 (t, J=5 Hz, 4H), 3.65 (t, J=5 Hz, 4H), 4.35 (quar., J=7 Hz, 1H); MS m/e (rel intensity) 155 (93), 140 (84), 106 (70), 58 (100), 41 (87); UV (CH_3CN) λ_{max}^{nm} 220 (ε 5600).

Photolysis of N-cyano-2-benzothiazolinone (23) and 3-(4-morpholinyl)-2-pentene (preliminary experiment). A solution of 23 (101 mg, 0.44 mmol) and 3-morpholine-2-pentene (2.02 g, 2.2 mL, 13.25 mmol) in 150 mL of acetonitrile was purged with argon for 20 min and irradiated for 2 h with a 450 W Hanovia medium pressure mercury lamp through Corex. The solvent was removed at reduced pressure from the resulting solution. The residue was separated on a silica gel column (50 g) with methylene chloride. The slowest moving band was separated by preparative thin layer chromatography (silica gel, CH_2Cl_2).

The only moving band was an unidentified mixture. The spectral data for this band are: IR (neat) 3275, 3125, 2950, 1630, 1525, 1440, 1300, 1105, 1060, 1005, 825, 780, 750 cm^{-1}; PMR ($CDCl_3$, TMS) δ0.8-1.4 (bm), 2.0-3.0 (bm), 3.6 (bs), 5.6 (bs), 6.8-7.6 (m), 7.9 (bs).

LIST OF REFERENCES

LIST OF REFERENCES

1. H. Staudinger, Ann. Chem., 356, 51 (1907).

2. For a recent review of β-lactam syntheses see: A.K. Mukerjee and R.C. Srivastava, Synthesis, 327 (1972).

3. J.C. Sheehan and K.R. Henry-Logan, J. Amer. Chem. Soc., 81, 5838 (1959).

4. R.B. Woodward, K. Heusler, J. Gosteli, P. Naegeli, W. Oppolzer, R. Ramage, S. Ranganathan, and H. Vorbrüggen, J. Amer. Chem. Soc., 88, 852 (1966); R.F. Abdulla and K.H. Fuhr, J. Heterocyclic Chem., 13, 427 (1976); J.E. Baldwin, M.A. Christie, S.B. Haber, and L.I. Kruse, J. Amer. Chem. Soc., 98, 3045 (1976); D.B.R. Johnston, S.M. Schmitt, F.A. Bouffard, and B.G. Christensen, J. Amer. Chem. Soc., 100, 313 (1978).

5. G. Stork and R.P. Szajewski, J. Amer. Chem. Soc., 96, 5787 (1974).

6. G. Lowe and D. Ridley, J. Chem. Soc., Perkin Trans. I, 2024 (1973).

7. S. Ege, Chem. Commun., 759 (1968).

8. P. Johnson and C. Hutch III, J. Org. Chem., 40, 909, (1975).

9. M. Johnson, Ph.D. Thesis, Michigan State University, E. Lansing, Michigan, 1978.

10. (a) K.H. Saunders, "The Aromatic Diazo-Compounds and Their Technical Applications", Longmans, Green, and Co., New York, 1936, Chap. IX. (b) W. Kirmse, "Carbene Chemistry", 2nd ed., Academic Press, New York, 1971, pp 18-24.

11. G. Smolinsky, J. Org. Chem., 27, 3557 (1962).

12. (a) R. Moore, A. Mishla, and R.J. Crawford, Can. J. Chem., 46, 3305 (1969). (b) S.V. Andrews and A.C. Day, Chem.

Commun., 667 (1966). (c) J. Sanjiki, H. Kato, and M. Ohta, Chem. Commun., 496 (1968).

13. For a review of sulfone photochemistry see: E. Block, Quar. Rep. on Sulfur Chem., 4, 321 (1969).

14. Y. Odaira, K. Yamaji, and S. Tsutsumi, Bull. Chem. Soc. Japan, 37, 1410 (1969).

15. M.P. Cava, M.V. Lakshmikanthan, and M. Behforouz, J. Org. Chem., 39, 206 (1974).

16. R.S. Givens and W.F. Oettle, J. Amer. Chem. Soc., 93, 330 (1971).

17. G. Maier and B. Hoppe, Tetrahedron Lett., 861 (1973).

18. C.M. Anderson, J.B. Bremner, H.H. Westberg, and R.N. Warrener, Tetrahedron Lett., 1585 (1969).

19. R.K. Barnett and T.D. Roberts, Chem. Commun., 758 (1972).

20. O. Buchart (ed.), "Photochemistry of Heterocyclic Compounds", John Wiley and Sons, Inc., 1976; H. Schultz, Z. Naturforch, 28b, 339 (1973); H. Kato, S. Nakazawa, T. Kiyosawa and K. Hirakawa, J. Chem. Soc., Perkins Trans. I, 672 (1976).

21. J.R. Grunwell, N.A. Marron, and S.J. Hanhan, J. Org. Chem, 38, 1559 (1973).

22. K. Griesbaum, Angew. Chem. internat. Edit., 9, 273 (1970).

23. K. Boustany, J. Chem. Eng. Data, 17, 104 (1972).

24. S.R. Bosco, A. Cirillo, and R.B. Timmons, J. Amer. Chem. Soc., 91, 3140 (1969).

25. N.C. Yang and G.R. Lenz, Tetrahedron Lett., 4897 (1967).

26. I. Ninomiya, T. Naito, and T. Mori, J. Chem. Soc., Perkin Trans. I, 505 (1973); Y. Katsuhara, H. Maruyama, Y. Shigemitsu and Y. Odaira, Tetrahedron Lett., 1323 (1973).

27. T. Tsutsomi and S. Tominaga, Tetrahedron Lett., 3175 (1969).

28. D. Bellus and K. Schaffner, Helv. Chim. Acta, 51, 221 (1968).

29. J.A. Barltrop and P. Schofield, J. Chem. Soc., 4758 (1965).

30. L.F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, John Wiley and Sons, Inc., New York, 1967, pp 1022-3.

31. The PMR chemical shift values for the vinyl hydrogens of 2b and 4 were calculated by adding the appropriate substituent values found in table 3-6 of D.H. Williams and I. Fleming, "Spectroscopic Methods in Organic Chemistry", 2nd ed., McGraw Hill, Ltd., London, 1973, p. 137, to the vinyl hydrogen chemical shift values of 2a.

32. Compound 3b was prepared according to the procedure of F. Hammer, J. Chem. Soc., 1480 (1956).

33. Langlet, Bihang till Svenska Vet. Akad. Handlingar, 22II, N. 1, s. 20; Beilstein, 27, 44.

34. C. Santacroce, D. Sica, and R.A. Nicolaus, Gazz. Chim. Ital., 98, 85 (1968).

35. F. Chioccara, E. Novellino, G. Prota, Chem. Commun., 50 (1977), and references cited therein.

36. V. Carelli, P. Marchini, M. Cardellini, F. Micheletti Moracci, G. Liso, and M.G. Lucarelli, Ann. Chim. Rome, 59 (11), 1050 (1969).

37. R. Husigen, W. Scheer, and H. Huber, J. Amer. Chem. Soc., 89, 1753 (1967).

38. (a) H. Dietrich and G.W. Griffin, Tetrahedron Lett., 153, (1968); (b) W. Kirmse, "Carbene Chemistry", 2nd ed., Academic Press, New York, 1971, pp 84-88.

39. E.K. Fields and J.M. Sandri, Chem. Ind., 1216 (1959); P.K. Kadaba and J.O. Edwards, J. Org. Chem., 25, 1431 (1960).

40. W.J. Close, J. Amer. Chem. Soc., 73, 95 (1951).

41. A.W. Hofmann, Chem. Ber., 12, 1128 (1879).

42. "Coblentz Society Spectra", Sadtler Research Laboratories, Inc., Philadelphia, 1975, IR spectrum no. 6019; "The Sadtler Standard Spectra", Sadtler Research Laboratories, Inc., Philadelphia, 1976, NMR spectrum no. 11083.

43. ibid., grating IR spectrum no. 3661; NMR spectrum no. 496.

44. ibid., grating IR spectrum no. 29765.

45. E. Stenhagen, S. Abrahamsson, and F.W. McLafferty, "Registry of Mass Spectral Data", Vol. 1, John Wiley and Sons, Inc., New York, 1974, mass spectrum no. 384-7.

46. E. Besthorn, Chem. Ber., 43, 1519 (1910).

47. "The Sadtler Standard Spectra", Sadtler Research Laboratories, Inc., Philadelphia, 1978, NMR spectrum no. 26796;

"Coblentz Society Spectra", Sadtler Research Laboratories, Inc., Philadelphia, 1975, IR spectrum no. 9159.

48. R.G. Amiel, P.C. Reeves, and R. Pettit, Chem. Commun., 1028 (1967).

49. R. Huisgen, Angew. Chem. internat. Edit., 2, 565 (1963); A. Padwa, ibid., 15, 123 (1976).

50. D.S. Weiss, J. Amer. Chem. Soc., 97, 255 (1975) and references cited therein.

51. J. Nasiel and G. Jacqumin, Tetrahedron, 28, 597 (1972).

52. A.K. Bhattacharya, Diss. Abstr. Int. B., 36 (9), 4477 (1976).

53. O.L. Chapman and C.L. McIntosh, Chem. Commun., 383 (1971).

54. G. Prota, E. Ponsiglione, and R. Ruggiero, Tetrahedron, 30, 2781 (1974); R.H. Thomson, Angew. Chem. internat. Edit., 13, 305 (1974).

55. S. Umio and H. Noguchi, Japan Patent 6,927,588 (1969); S. Winthrop and R. Gaudry, Canadien Patent 694,002 (1964); S. Winthrop and R. Gaudry, U.S. Patent 2,989,528 (1961); F. Kiichi and W. Hiroyasu, Japan Patent 5241 (1958).

56. F. Chioccara, G. Prota, and R.H. Thomson, Tetrahedron, 32, 1407 (1976).

57. J. Krapcho and C.F. Turk, J. Med. Chem., 16, 776 (1973).

58. The phenothiazine syntheses and references to their activity are taken from: D. Lednicer and L.A. Mitscher, "The Organic Chemistry of Drug Synthesis", John Wiley and Sons, Inc., New York, 1977, Chap. 19, unless otherwise referenced.

59. S. Schneller, Int. J. Sulfur Chem. B, 7, 155 (1972).

60. V. Carelli, P. Marchini, M. Cardellini, F. Micheletti Moracci, G. Liso, and M. Lucarelli, Tetrahedron Lett., 4619 (1969).

61. O. Hromatka and J. Augl, German Patent 1,088,055 (1960).

62. K. Fugii, Y. Kowa, and G. Hayaski, Yakugaka Zasshi, 77, 362 (1957).

63. G. Hayaski, T. Kowa, K. Fujii, and M. Tasaka, Yakugaka Zasshi, 78, 716 (1958).

64. Published in part: L. Sousa and J. Bucher III, Tetrahedron Lett., 2267 (1978).

65. D. Lin, M. Thomson, and D. DeJongh, Can. J. Chem., 53, 2293 (1975).

66. E. Forster and K. Grellmann, Chem. Phys. Lett., 14, 536 (1972).

67. A.R. Knight, O.P. Strausz, S.M. Malm, and H.E. Gunning, J. Amer. Chem. Soc., 86, 4243 (1964).

68. J.A. Barltrop and J.D. Coyle, "Excited States in Organic Chemistry", John Wiley and Sons, Ltd., London, 1975, p 193.

69. J.G. Calvert and J.N. Pitts, "Photochemistry", John Wiley and Sons, Inc., New York, 1966, pp 434-41, 460-2.

70. W.O. Haag and J.N. Miale, U.S. Patent 3,875,252 (1975); U.S. Patent 3,821,278 (1975); U.S. Patent 3,787,517 (1974).

71. R.J. Crawford, Diss. Abstr. Int. B, 31 (9), 5254 (1971).

72. H.O. House, L.J. Czuba, M. Gall, and H.D. Olmstead, J. Org. Chem., 34, 2324 (1969).

73. (a) E. Stenhagen, S. Abrahamsson, and F.W. McLafferty, "Registry of Mass Spectral Data", Vol. 1, John Wiley and Sons, Inc., New York, 1974, mass spectrum no. 392-10; (b) "The Sadtler Standard Spectra", Sadtler Research Laboratories, Inc., Philadelphia, 1976, NMR spectrum no. 18705, grating IR spectrum no. 15563.

74. G. Stork, A. Brizzolura, H. Landesman, J. Szmuszkovicz, and R. Terrell, J. Amer. Chem. Soc., 85, 207 (1963).

75. H. Passing, J. Prakt. Chem., 153, 1 (1939).

76. R. Bourhis and E. Frainnet, Bull. Soc. Chim. France, 3552 (1967).