The Preparation and Chemistry

of

Oxythio and Dithiocarbenes

THE PREPARATION AND CHEMISTRY OF OXYTHIO AND DITHIOCARBENES

By

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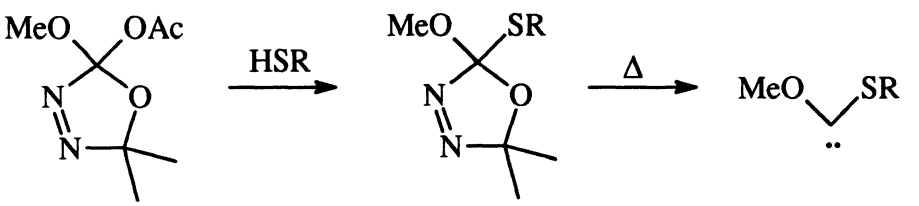
dedicated to my parents

Abstract

The chemistry of a variety of new oxythiocarbenes **33a-d**, generated upon thermolyses of oxythiooxadiazolines **31a-d** in solution, was studied.

Oxadiazolines **31a-d** were prepared by a substitution of the acetoxy substituent of oxadiazoline **13** with appropriate mercaptans. These oxadiazolines were found to form the corresponding oxythiocarbenes **33a-d** upon thermolysis at about 60-70 °C. The thermolysis temperature is about 30-40 °C lower than that of dioxyoxadiazolines. The first order rate constants for decomposition of **31a-c** in benzene at 60 °C were determined to be approximately (2.04-2.09) x 10^{-5} s^{-1}, which is about the same as that of dioxyoxadiazolines at 100 °C.

In order to demonstrate the existence of the reactive intermediates **33a-d**, several carbene traps were used. The formation of some interesting compounds from such trapping illustrates the synthetic utility of these carbenes. The reactions of **33a-d** were compared to those of the corresponding dioxycarbenes.



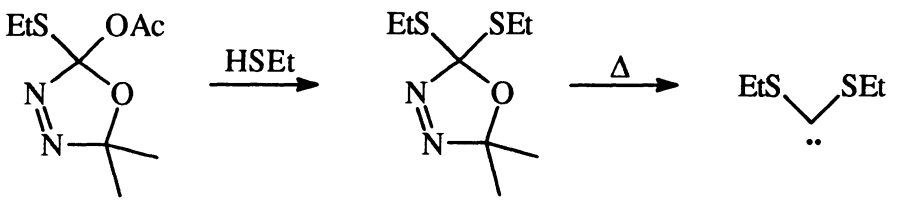
13 **31a-d** **33a-d**

R : **a** = Ph; **b** = CH_2Ph; **c** = Et; **d**= Me.

A method for preparation of 2-acetoxy-2-ethylthio-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**53**), which is the sulfur analogue of **13**, was developed.

This oxadiazoline was also found to form the corresponding carbene (acetoxyethylthiocarbene) upon thermolysis in solution. In the absence of any carbene trap, the carbene underwent a 1,2-acetyl shift. The first order rate constant for decomposition of **53** in benzene at 60 °C was determined to be 4.19×10^{-5} s^{-1}.

This oxadiazoline can lead to the syntheses of various dithiooxadiazolines (e.g. **61**) by substitution of the acetoxy group. These intermediates can potentially serve as precursors to the corresponding dithiocarbenes, such as **60**.



53 **61** **60**

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Chapter 1

Introduction

Most carbenes are highly reactive, short lived species that can only be generated in situ. Only a few carbenes are stable enough to allow some spectroscopic data to be taken.[1,2,3]

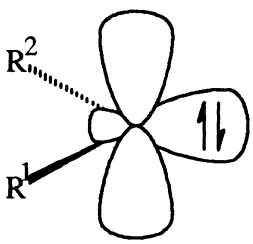
Some carbene reactions allow the introduction of functional groups that may be difficult to obtain by other methods. Carbene addition to double bonds is the best known route to generate various substituted cyclopropanes.[4,5,6] Other uses of carbenes include making bridged or multicyclic compounds.[10,11]

Since the chemistry of carbenes is so rich and diverse, the interest of many researchers in these species has been growing. In addition, the use of carbenes in organic synthesis has been increased dramatically.

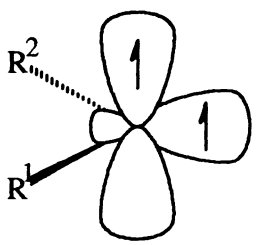
1.1 Carbene Structure

Carbenes are neutral and divalent carbon intermediates. They are made up of two covalent bonds and two non-bonding orbitals which contain the remaining two electrons of the central carbon atom.

Carbenes may adopt either singlet or triplet ground state electronic configurations, depending on the nature of the non-bonding orbitals. According to Hund's rule, if the electron pairing energy, ΔE_p, exceeds the energy difference between σ and π orbitals, the electrons should have parallel spins and occupy different orbitals. The result is a species with a triplet ground state. Conversely, if the energy difference between the orbitals exceeds the electron pairing energy, the electrons should have paired spins and occupy the same orbital. As a result, the ground state of the carbene is singlet.[7,8,9]



Singlet



Triplet

Singlet carbenes have a sp^2-like geometry with a strongly bent R^1-C-R^2 bond angle (< 120 °). However, triplet carbenes have more linear geometries but are still bent, with the R^1-C-R^2 bond angle greater than 120 ° but less than 180 °.

There are two factors that can determine the ground state configuration of a carbene: the bond angle between substituents R^1 and R^2 and the electronic effects of the substituents. For instance, when the R^1-C-R^2 bond angle is increased due to bulky substituents R^1 and R^2, the energy of the σ-orbital increases whereas the energy of the π-orbital remains approximately the same. As a result, this stabilizes the triplet state of the carbene. Furthermore, it was found that the ground state of carbenes with electron

withdrawing and π-donor substituents is usually singlet, whereas carbenes which carry substituents that are more electropositive than carbon, will normally have triplet ground state.[8,9] Therefore, based on these trends, it is predicted that oxythiocarbenes have singlet ground states.

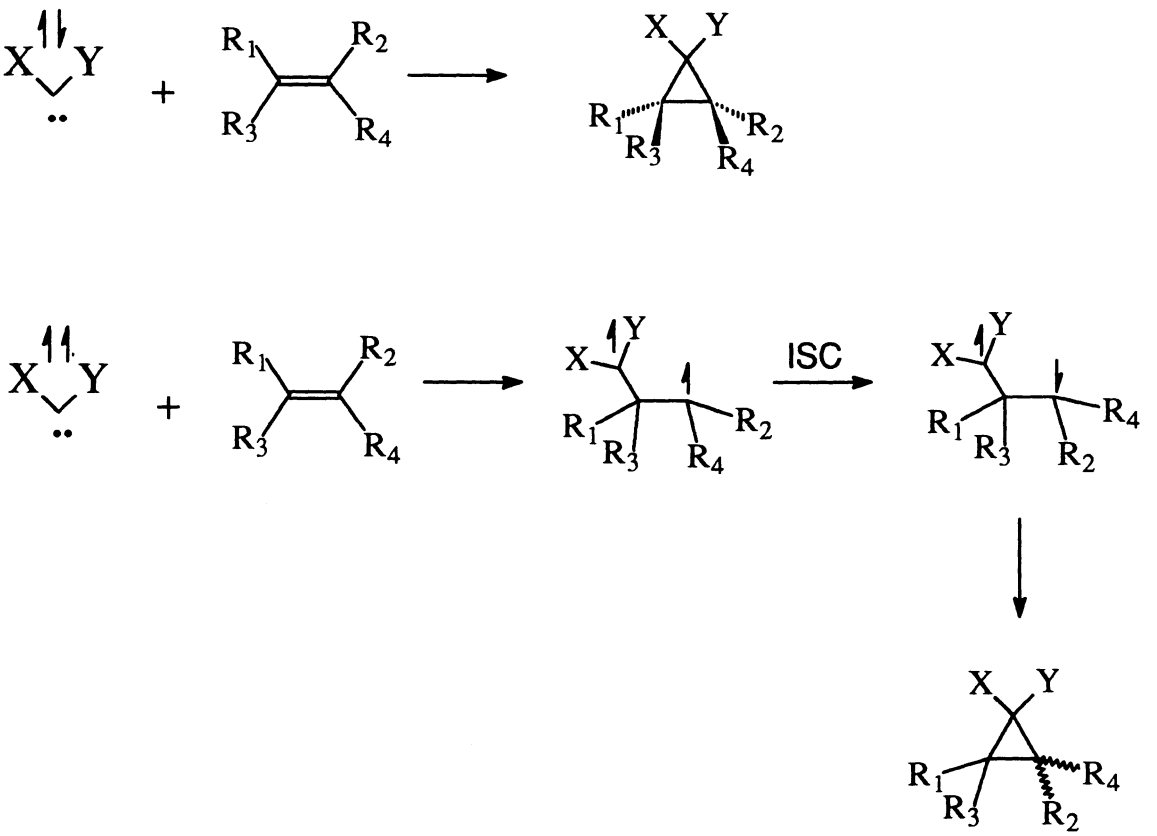
The states in which carbenes are formed depend on the method in which they are generated. Singlet carbenes are normally generated by thermolysis or photolysis in the absence of triplet sensitizers. In the presence of sensitizers, triplet carbenes can be generated. Thus, carbenes can sometimes be generated initially in either state regardless of which is the more stable form. If a singlet carbene was generated in the excited triplet state, after some time, it can decay to the singlet ground state.

Singlet and triplet carbenes react differently. Triplet carbenes usually behave as free radicals. They undergo reactions such as hydrogen abstraction, coupling of derived radicals and addition to unsaturated bonds in a stepwise and nonstereospecific manner.

Singlet carbenes typically undergo cyclopropanation reactions with retention of the stereochemistry about the double bond, since the movement of the pair of electrons occurs in a concerted or a very fast stepwise manner. Triplet carbenes, because of their biradical intermediate, undergo additions with loss of stereochemistry (Scheme 1). The addition happens in a stepwise manner because the two unpaired electrons cannot form a covalent bond immediately. One of the unpaired electrons forms a bond first with an electron from the double bond that has opposite spin, leaving two same spin unpaired electrons. These electrons cannot form a covalent bond until one of the electrons can reverse its spin (i.e.

intersystem crossing to the singlet state) to form a bond. During this time, free rotation about the C-C bond can occur which results in the loss of the stereochemistry from the double bond.[10] The stereochemistry resulting from these reactions often serves as a crude and simple way to distinguish between a singlet and a triplet carbene.

Scheme 1

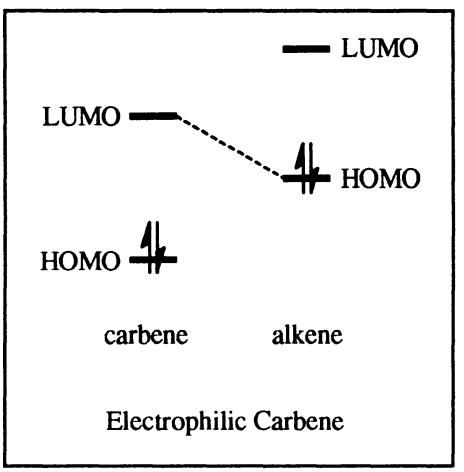


Singlet carbenes can be characterized as nucleophilic or electrophilic,[9] depending on the dominant orbital interactions.[14,15] For singlet carbenes, there are two possible orbital interactions: $\sigma - \pi^*$ (HOMO carbene - LUMO alkene) or p - π (LUMO carbene - HOMO alkene). The smallest orbital energy difference will determine which interaction is

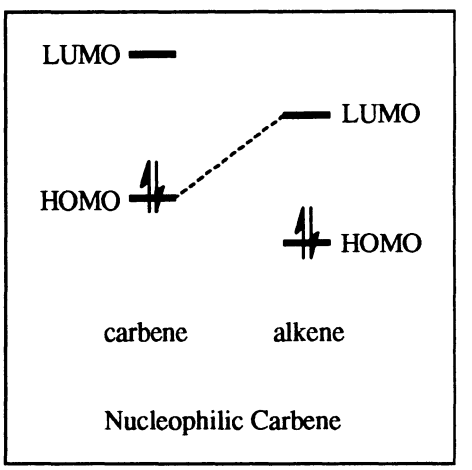
dominant for a particular carbene-alkene pair. The dominant interaction can vary from one substituent in the carbene to another.

Both electron withdrawing and electron donating substituents can stabilize a carbenic center. Electron withdrawing groups at the carbene carbon lower the LUMO energy making the p - π interaction between carbene and alkene dominant. The carbene thus becomes more electrophilic (Scheme 2). The majority of carbenes studied react as electrophiles.[11,12,13] On the other hand, if the carbene substituent is a π donor, the $\sigma - \pi^*$ (HOMO carbene - LUMO alkene) interaction becomes more significant, because electron donating groups raise the LUMO energy of the carbene by donation of electron density. As a result, the carbene becomes more nucleophilic (Scheme 3). For example, carbenes with OR, SR, or NR_2 substituents react as nucleophiles.[9] The p - π and $\sigma - \pi^*$ interactions are shown qualitatively below.

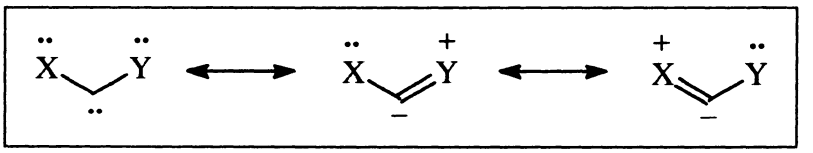
Scheme 2



Scheme 3

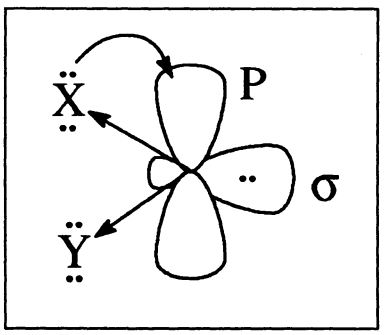


These electron donating substituents can stabilize the carbene in two ways : by resonance and by inductive effects (Scheme 4). The resonance effect pushes electron density onto the carbene carbon and increases the substituent's electronegativity.



Consequently, electron donating substituents withdraw electron density inductively from σ-orbitals along the covalent bonds and thus stabilize the carbenes.

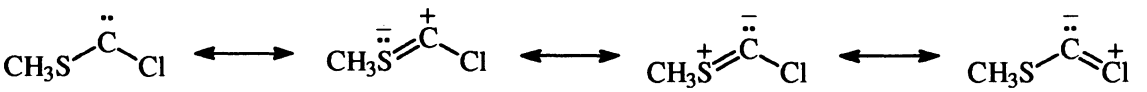
Scheme 4



The higher stability of heteroatom substituted carbenes results in a lower reactivity due to increased activation energy. Consequently, nucleophilic carbenes can undergo reactions selectively.

A broad range of carbene selectivities based on their reactivities with alkenes have been determined by Moss and the results have been put together in the widely recognized Moss Carbene Selectivity Spectrum.[16] The selectivity index value correlates quite well with chemistry of the carbenes, it allows one to predict the carbene behavior based on the knowledge of the substituents. The selectivity of chloro(methylthio)carbene has been

studied.[17] Thio substituents are unusual because σ_R^+ for the methylthio group varies widely from -0.55 to -0.95, experimentally. This broad range of σ_R^+ thus causes a significant range in the calculated value of the carbenic selectivity index (M_{CXY}) for methylthio carbenes, since $M_{CXY} = -1.10 \Sigma \sigma_R^+ + 0.53 \Sigma \sigma_I - 0.31$. The M_{CXY} for chloro methylthiocarbene was experimentally determined to be 0.91 for the addition to alkenes[17] which corresponds to $\sigma_R^+ = -0.39$. This is the least negative σ_R^+ value ever recorded for the methylthio substituent, which suggests that the carbene may have significant contributions from 'reverse' resonance structure as b.



a b c d

1.2 Sources of Dioxycarbenes

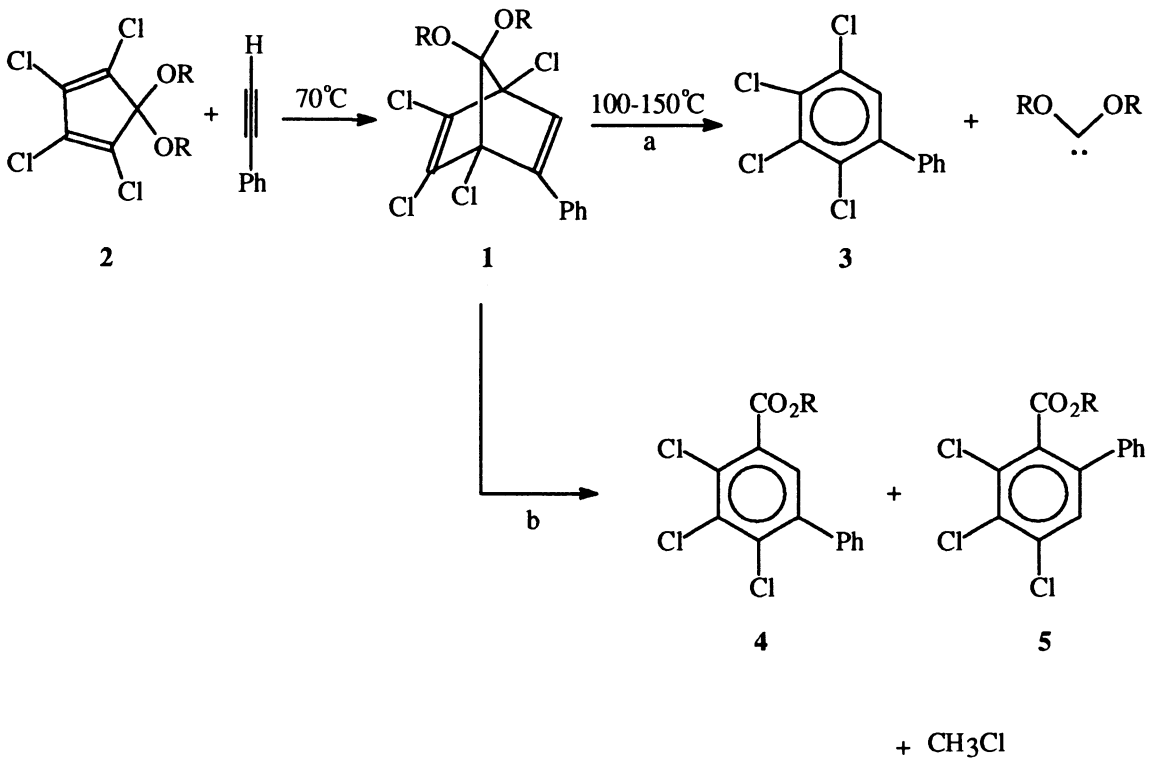
There are a wide variety of methods to generate carbenes. Only some of the sources of dioxycarbenes will be discussed here.

a) Norbornadienone Ketals

R. W. Hoffmann[18] and D. M. Lemal[19,20,21] developed this method in the early 1960's. The required norbornadienone ketals (**1**) were prepared by Diels-Alder addition of tetrachlorocyclopentadienone ketals (**2**) to phenylacetylene (Scheme 5) which can then undergo thermal cycloelimination to form carbenes. They used this method to generate

various dioxycarbenes. This method became the first source and remained the best source of dioxycarbenes for over a decade. Since then, a great deal of dioxycarbene chemistry has been studied.

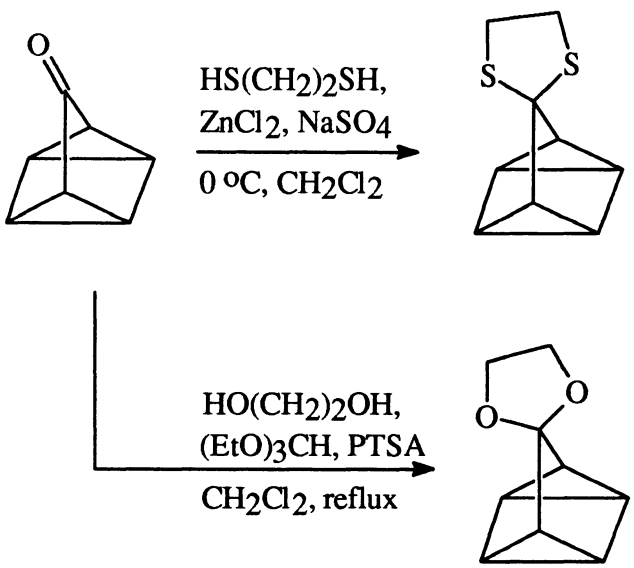
Scheme 5



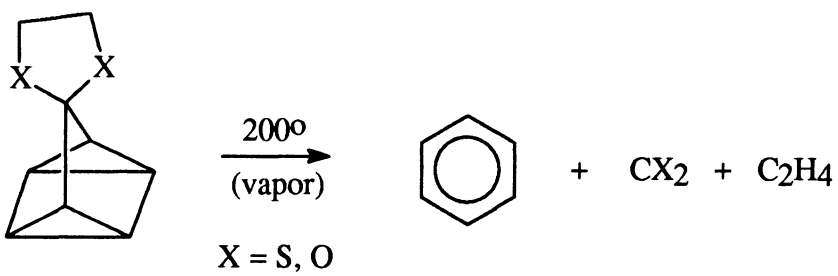
However, this method has a few limitations. It allows only symmetric carbenes to be generated, presumably because unsymmetric ketals **2** are difficult to synthesize. Furthermore, the thermal decomposition of **1** also yields the non-volatile biphenyl side product (**3**) which is difficult to remove. Pathway (b) can also compete with pathway (a) forming other side products (**4** and **5**). Consequently, the side products from thermolysis can interfere with the isolation of the carbene derived product.

b) Quadricyclanone Ketals

Lemal and coworkers[20] developed this method about the same time as the norbornadienone ketals (**1**). In fact, this system is the tautomer of ketals **1**. However, unlike the synthesis of **1**, direct ketalization of quadricyclanone was able to generate the corresponding ketals. Various quadricyclanone ketals including those that generate dithiocarbenes, was prepared as follows.



This method of generation of carbenes is not very useful, only pyrolysis of the ketals as vapor gives the carbene successfully.

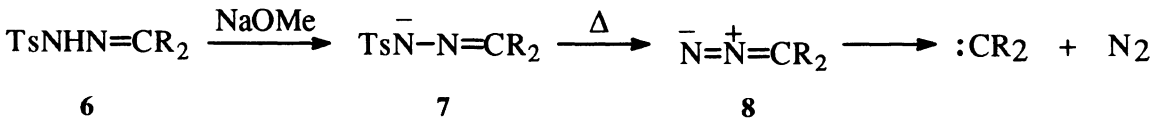


c) Tosylhydrazones

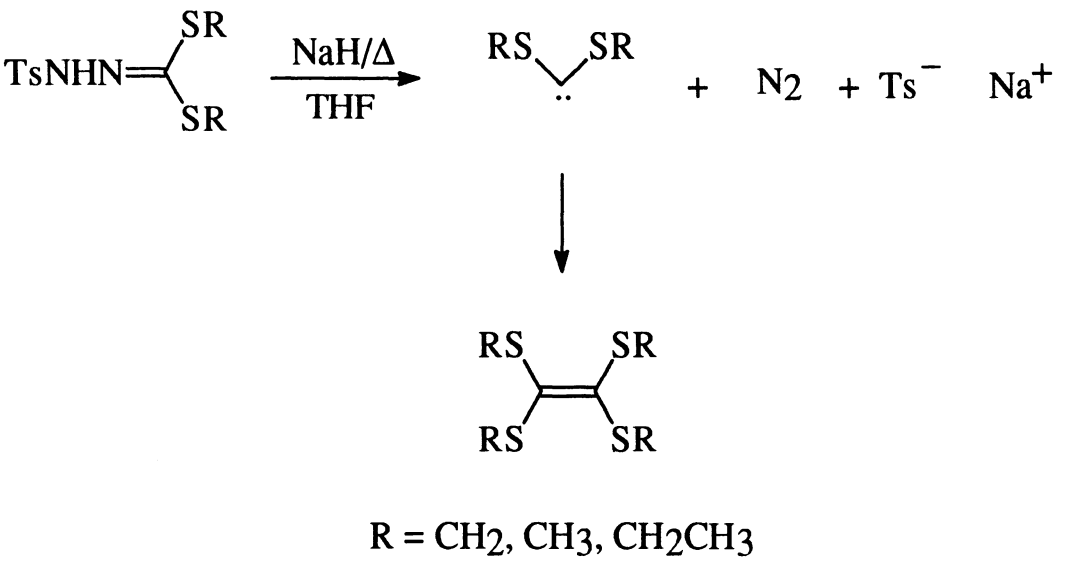
Toluene p-sulfonyl hydrazones **(6)** react with NaOMe to form tosylate salts **(7)**. **7** can be thermolyzed[22] or photolyzed[23] to afford the carbenes (Scheme 6). D. M. Lemal and coworkers reported the generation of dithiocarbenes thermally by this route[24] (Scheme 7).

Diazoalkanes **(8)** are the intermediates generated from **7**. These intermediates **8** are highly unstable and toxic. Therefore, they are normally formed in situ, which makes them less useful in synthesis.

Scheme 6



Scheme 7

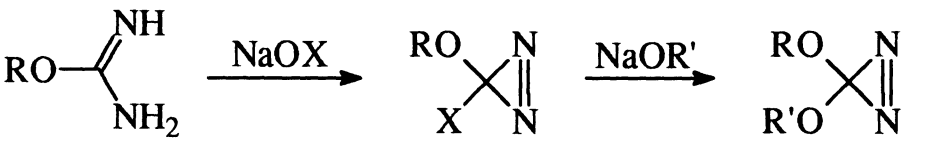


R = CH_2, CH_3, CH_2CH_3

d) Diazirines

Diazirines are quite important because various heteroatom substituted carbenes can be generated from them. This method became more useful after the publication of the diazirine exchange reaction which was developed by Moss.[25] This method provides a broad potential for making substituted carbenes.[26,27,28]

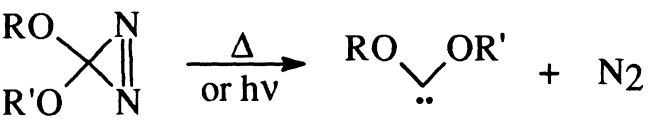
Scheme 8



9 **10**

X = Br, Cl

The halodiazirine (**9**), which is prepared by Graham oxidation of the corresponding amidine, reacts with a given alkoxide to form the dioxydiazirine (**10**) (Scheme 8). A wide range of asymmetric substituted dioxycarbenes can be made by this method.[28,29] Diazirines **10** are the only photochemical sources of dioxycarbenes.



10

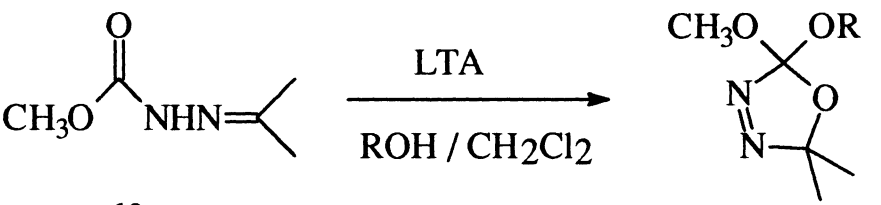
Even though **10** are useful sources of dioxycarbenes, they are unstable ($\tau_{1/2}$ at room temperature in pentane < 1 hour) and rather explosive. As a result, they are usually

used immediately after they are made and they are typically available only as highly dilute hydrocarbon solutions. These problems make diazirines unsuitable for synthetic work.

e) Oxadiazolines

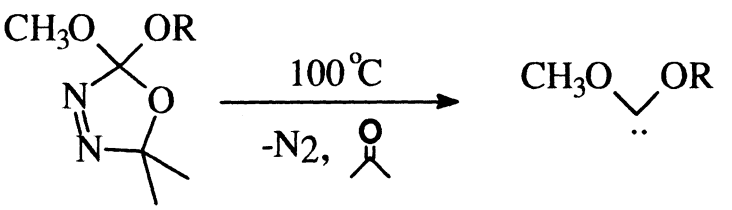
Oxadiazolines are ideal carbene precursors because they are easily prepared, stable and have long shelf lives. Their preparation was reported by Warkentin and coworkers.[30] They prepared various dioxyoxadiazolines (**11**) by oxidation of various hydrazones (**12**) with lead tetraacetate (LTA) in the presence of alcohol (Scheme 9).

Scheme 9



12 **11**

11 can be thermolyzed in either benzene or toluene at about 100 °C to generate the corresponding dioxycarbenes, by losing N_2 and acetone. These thermolyses in general do not form troublesome by-products, as the volatile by-products (N_2, acetone) generated can be removed easily. A wide range of unsymmetric **11** can be prepared.



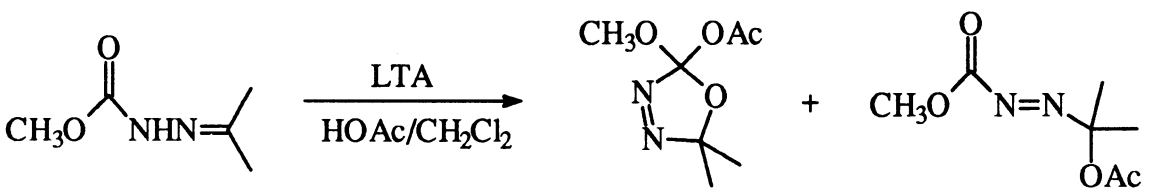
11

The method is limited by the need for purification of the oxadiazolines which sometimes result from messy oxidations. This method also allows only alcohols that are stable under oxidation condition to be used. As a result, phenoxy and thiol substituted oxadiazolines cannot be prepared by this route since phenols and thiols can be oxidized easily by reagents such as lead tetraacetate.

Acetoxyoxadiazoline Exchange Reaction

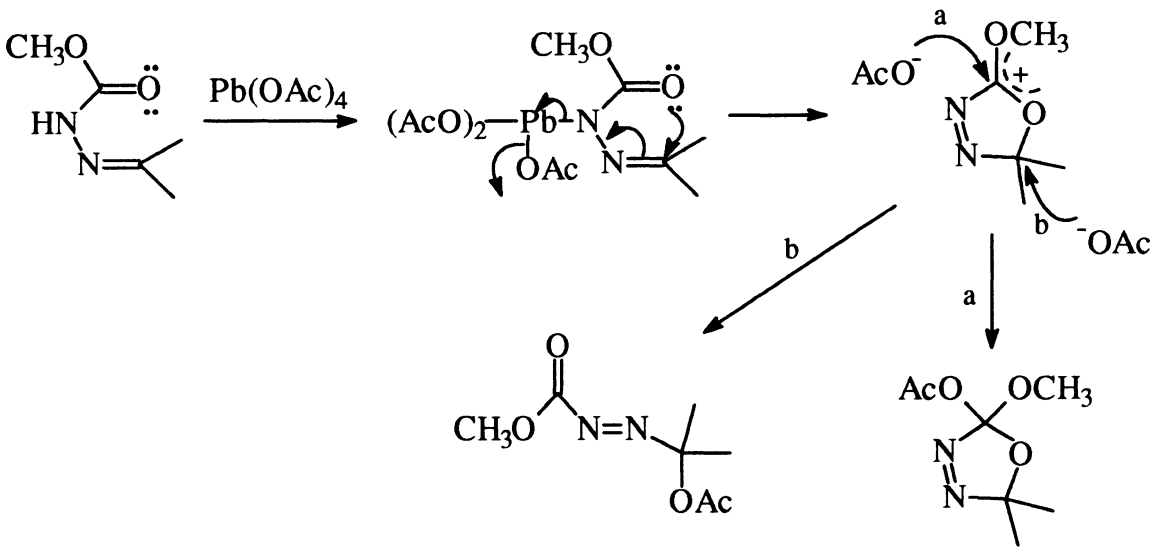
In order to overcome the problem of oxidizing the oxidation sensitive starting materials, the substituents have to be put on after the oxidation stage. This problem was solved by synthesizing 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**13**); the acetoxy substituent serves as a leaving group for later nucleophilic attack in the exchange. Warkentin and coworkers reported the preparation of **13** (Scheme 10).[31] Similar to the preparation of **11** in Scheme 9, hydrazone **12** is oxidized by lead tetraacetate except that reagents such as alcohols or phenol are not required during the oxidation.

Scheme 10



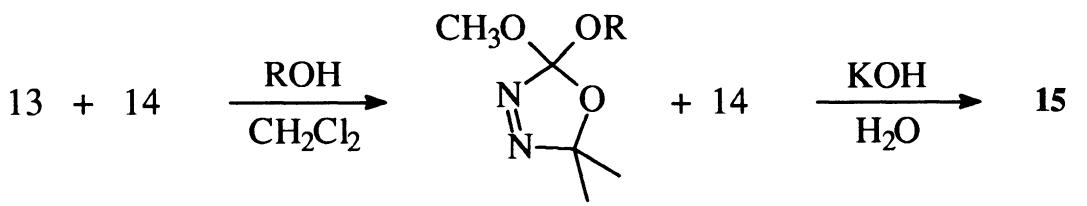
12 **13** (70 %) **14** (30 %)

The oxidation afforded a mixture of 70 % acetoxyoxadiazoline **13** and 30 % of the acyclic by-product **14**. The mechanism of the oxidation was proposed as follows.[32]



Purification of **13** can be done by slow bulb to bulb distillation. However, this was not always necessary. The mixture of **13** and **14** was exposed to an alcohol or phenol in CH_2Cl_2 at either room temperature or refluxing in CH_2Cl_2 (Scheme 11). The substitution reactions that convert 13 to 15 are probably S_N1 reactions.[31] Once the exchange is completed, **14** can be selectively hydrolyzed with aqueous KOH, giving the pure oxadiazoline **15**.

Scheme 11



15

R = CH_3, CH_2CH_3, CH_2Ph, Ph.

This method has been shown to be convenient for preparation of a wide variety of oxadiazolines. It is especially good for those nucleophilic capturing agents (e.g. phenol, mercaptans) that are not stable towards oxidizing agents. Oxadiazoline **13** also has a long shelf life.

1.3 Reactions of Carbenes

Singlet carbenes can undergo various characteristic reactions. The most common reactions in carbene chemistry are additions and insertions.

a) Additions

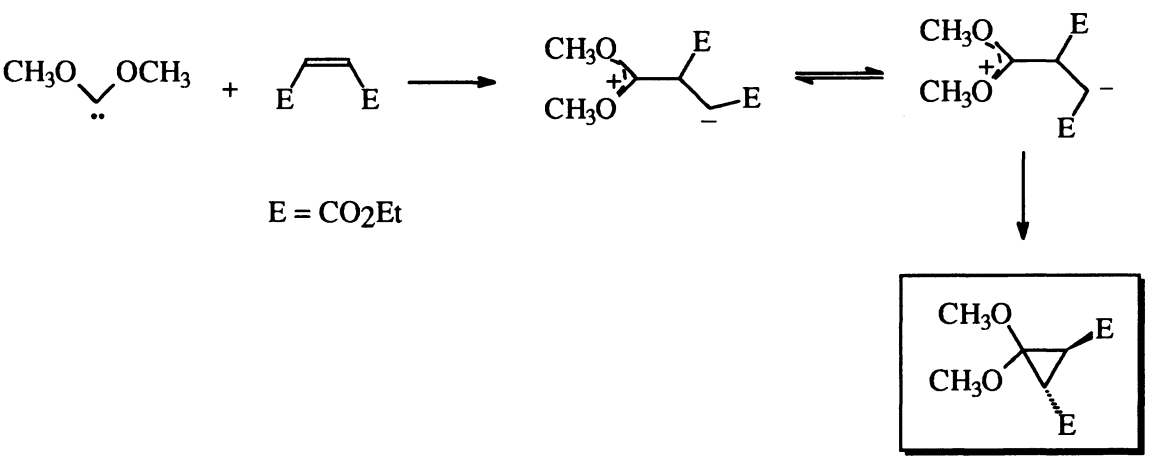
[1+2] Cycloaddition

i. Cyclopropanations

The addition of carbenes to alkenes is well established. Carbene philicities have been defined with reference to relative reactivities for carbene addition to alkenes.[16,33] Nucleophilic carbenes usually react faster with electron deficient alkenes, whereas electrophilic carbenes react faster with electron rich alkenes. While it was believed that singlet carbenes undergo addition to alkenes concertedly and stereospecifically, some systems appear to show non-stereospecific reactions.[4,34,35] R. W. Hoffmann reported the reaction of diethyl maleate with dimethoxycarbene (Scheme 12), which yielded *trans*-1,2-di(ethoxycarbonyl)-3,3-dimethoxycyclopropane.[34] The loss of stereochemistry contradicts

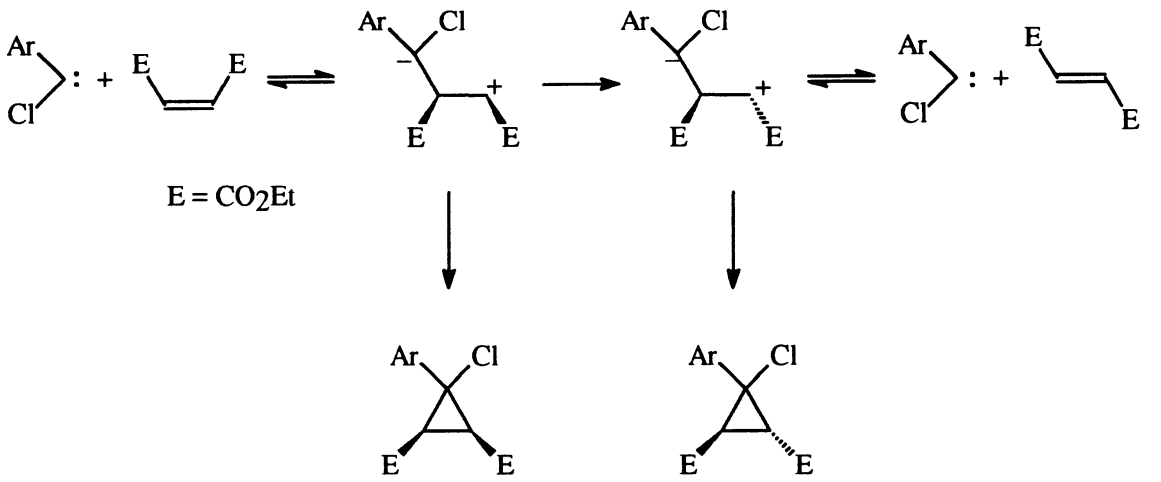
the idea that the addition is concerted. It could be due to a two-step addition mechanism, proceeding through a 1,3-dipolar intermediate or caused by isomerization through the 1,3-dipolar intermediate of a thermally unstable, initially formed *cis* adduct. For the mechanistic uncertainty, the observation was explained to be consistent with bond rotation in the carbene-alkene dipolar intermediate.

Scheme 12



Another non-stereospecific addition of a carbene to diethyl maleate was observed by Liu and coworkers[4] (Scheme 13). Decomposition of 3-chloro-3-phenyldiazirine in the presence of diethyl maleate was found to yield three cyclopropane products: two that retained the *cis* geometry of the alkene and one in which the carboethoxy groups were *trans*. In addition, it was found that fumarate was present in the reaction mixture after diazirine decomposition. They suggested the formation of a carbene-alkene dipolar intermediate whose lifetime was sufficiently long to allow bond rotation to occur and also the dissociation of the carbene-alkene dipolar intermediate after bond rotation had occurred, giving fumarate.

Scheme 13

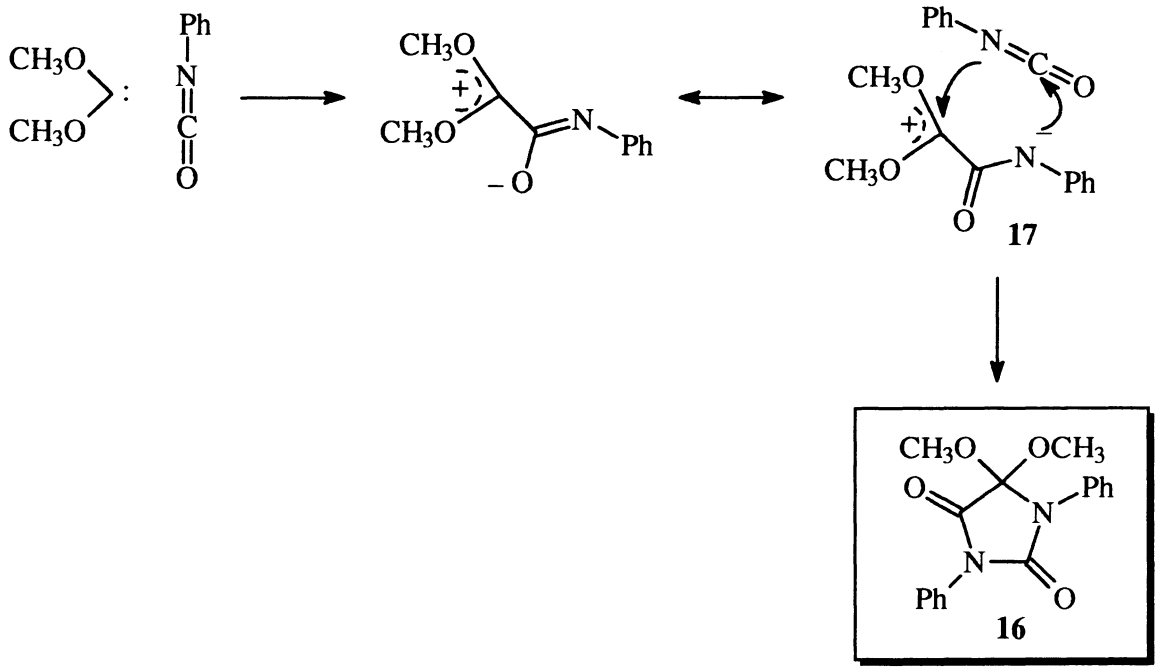


In order to determine the reaction stereochemistry of carbene-alkene addition, Moss and coworkers carried out the pyrolysis of 1,2,3,4-tetrachloro-7,7-dimethoxynorbornadiene in the presence of *cis* and *trans* β-deuteriostyrenes independently.[5] Comparison of the styrenes and the product compositions revealed that the addition of dimethoxycarbene to styrene was stereospecific. The results are consistent with the concerted mechanism, which is a typical singlet carbene behavior.

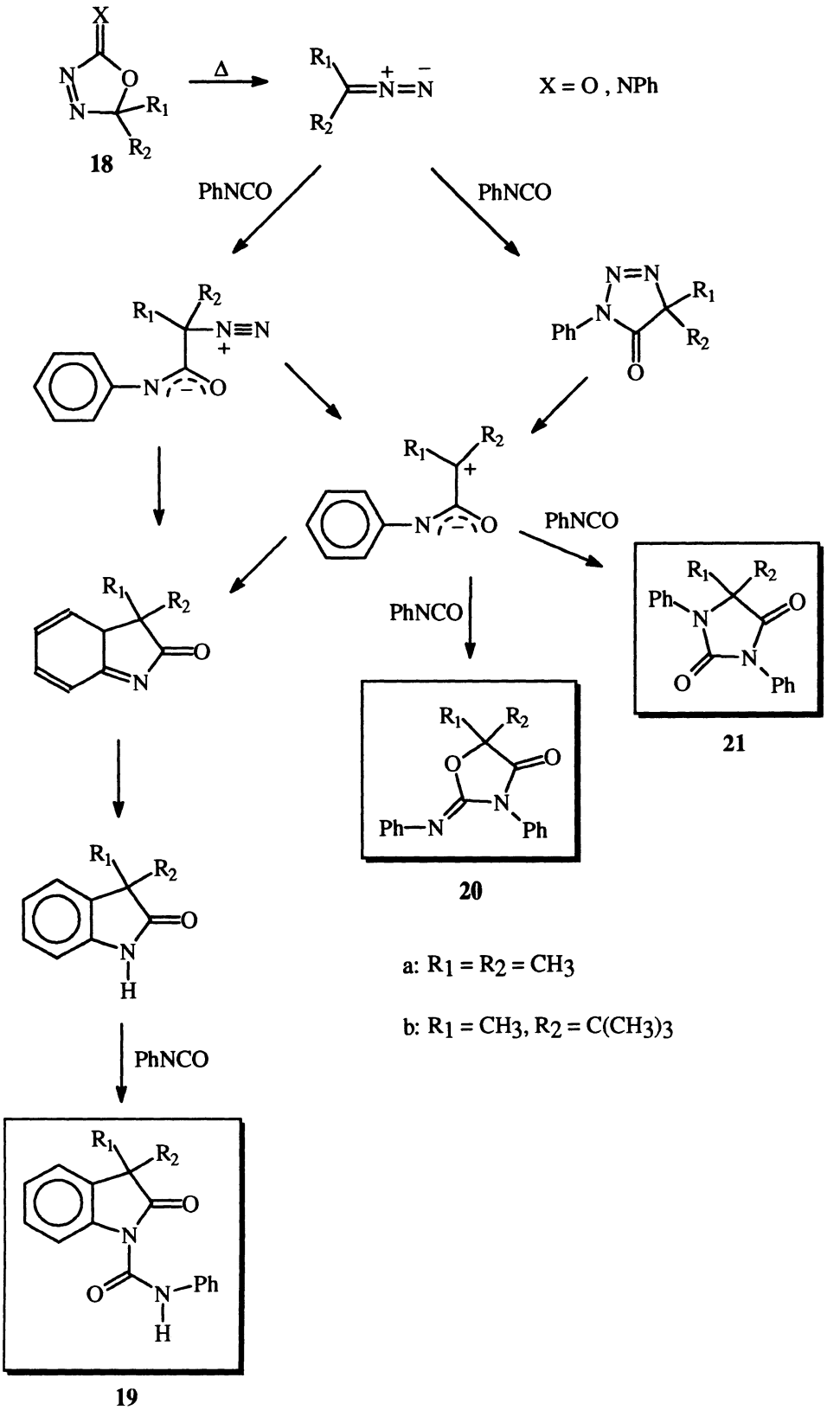
ii. Addition to Phenyl Isocyanate

Several products resulting from carbene reactions to phenyl isocyanate have been reported. R. W. Hoffmann[36] reported the addition of dimethoxycarbene to phenyl isocyanate to afford 1,3-diphenyl-5,5-dimethoxyhydantoin (**16**); a product that contains two units of phenyl isocyanate and one unit of carbene (2 : 1 adduct). The formation of this product was proposed to arise from addition of the carbene to phenyl isocyanate to

yield a 1,3-dipolar intermediate **17**. This intermediate then underwent regioselective addition with another equivalent of phenyl isocyanate to yield **16**. The mechanism is shown below:

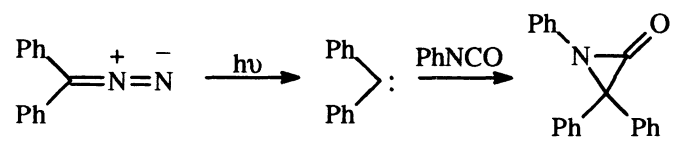


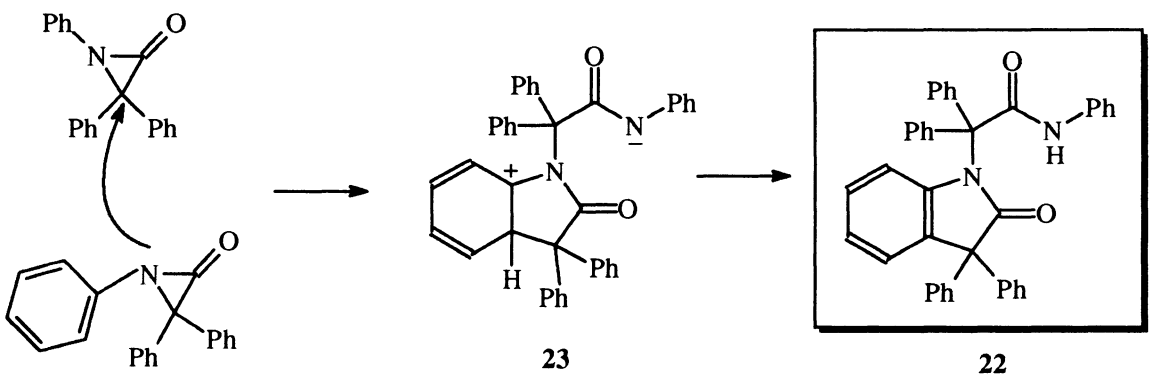
Another example of formal carbene addition to phenyl isocyanate was reported.[37] Thermolyses of various 5,5-dialkyl-Δ^3-1,3,4-oxadiazolin-2-ones (or 5,5-dialkyl-2-phenylimino- Δ^3-1,3,4-oxadiazolines) (**18**) in the presence of excess phenyl isocyanate afforded three products. The major product was 1-phenylcarbamoyl-3,3-dialkyloxindole (**19**) and the minor products were 2-phenylimino-3-phenyl-4-oxazolidone (**20**) and 1,3-diphenylhydantoin (**21**). The following mechanism of the formation of these products was proposed:


X = O , NPh
PhNCO
PhNCO
PhNCO
PhNCO
PhNCO
18
20
21
19
a: R1 = R2 = CH3
b: R1 = CH3, R2 = C(CH3)3

Sheehan and coworkers found 2-[1'(3,3-diphenyloxindolyl)]-2,2-diphenylacetanilide (**22**) arose from treatment of diphenyldiazomethane with phenyl isocyanate under ultraviolet irradiation[38] (Scheme 14). The formation of the acetanilide was explained by reaction of the photogenerated carbene from the diazomethane to phenyl isocyanate, forming the α-lactam which then dimerized with another α-lactam by attack of the lactam nitrogen on the α-carbon atom of another α-lactam.[39] This resulted in a zwitterionic intermediate **23**, which then underwent hydrogen migration to afford acetanilide **22**.

Scheme 14

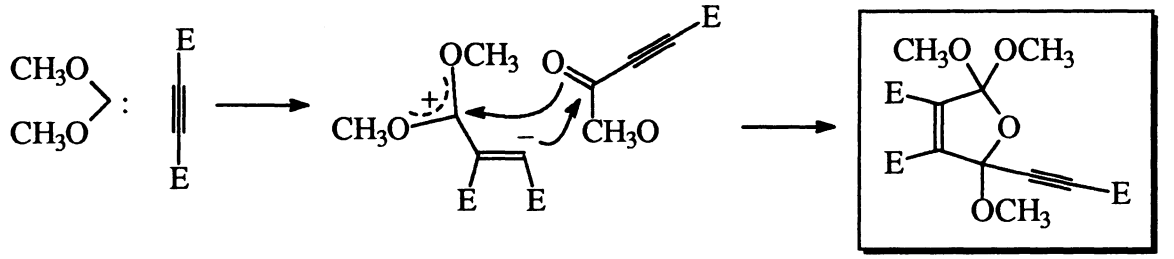




iii. Addition to DMAD

R. W. Hoffmann[34] reported the addition of dimethoxycarbene to dimethyl-acetylene dicarboxylate (DMAD) which yielded the substituted dihydrofuran **24** (Scheme 15). This product arose from the addition of the carbene to the triple bond of DMAD to form a 1,3-dipole intermediate which subsequently reacted with another equivalent of DMAD. The 1,3-dipolar added across the C=O bond to yield the final product.

Scheme 15



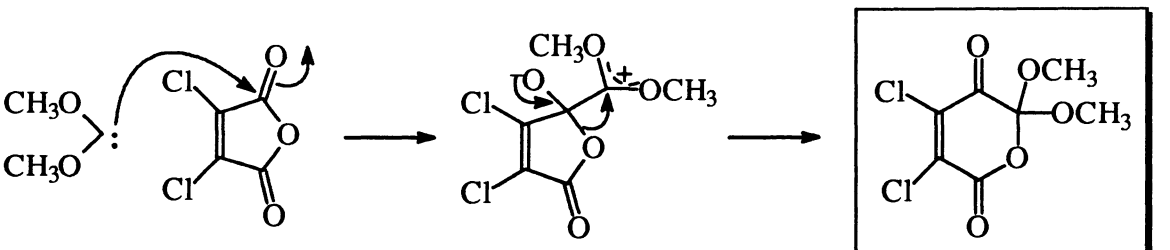
24

b) Insertions

i. Reaction with Heteroatom Unsaturated Systems

Reaction of carbenes with carbonyl compounds, e.g. dichloromaleic anhydride etc.; was examined by D. L. Pole and J. Warkentin[40] (Scheme 16). Nucleophilic attack of dimethoxycarbene on the C=O bond of the anhydride was proposed to generate a zwitterionic intermediate (**25**) which subsequently underwent ring expansion from a five to a six-membered ring system (**26**).

Scheme 16

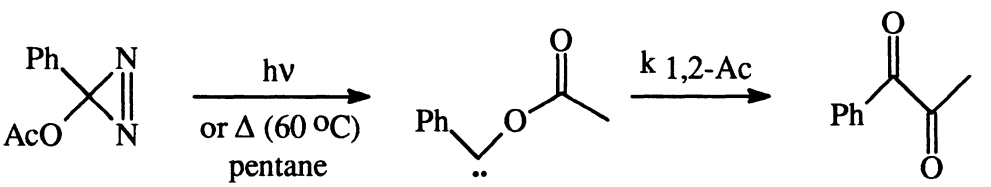


25 26

ii. 1,2-Acetyl Shift

Very little is known about 1,2-acyl shift in nucleophilic carbenes. Since an electron donating substituent stabilizes the carbene center, 1,2-acetyl shifts are not easily accessible. Moss reported that acetoxyphenylcarbene undergoes acetyl migration to form 3-phenyl-2,3-propanedione[41] (Scheme 17). This occurred because acetoxy is a weak donor.

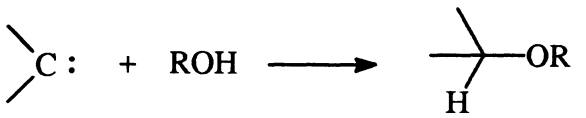
Scheme 17



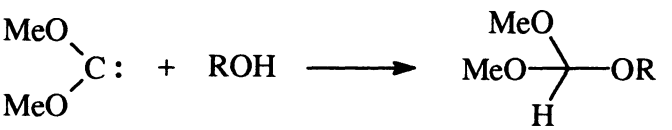
The rate constant for the rearrangement of the acyloxycarbene to dione was found to be $(1.3 \pm 0.2) \times 10^5\ s^{-1}$ by the pyridine probe method.[41a]

iii. O-H insertion

Carbenes react with alcohols to give ethers (eq. 1) or orthoformates (eq. 2), depending on the carbenes.



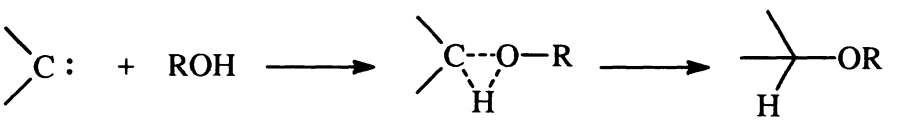
(Eq. 1)



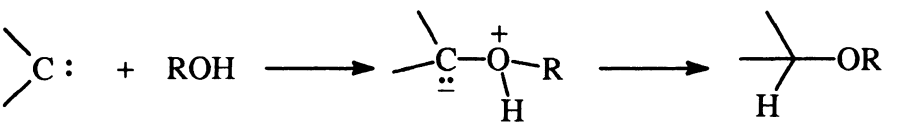
(Eq.2)

At least three mechanisms can be proposed.[42]

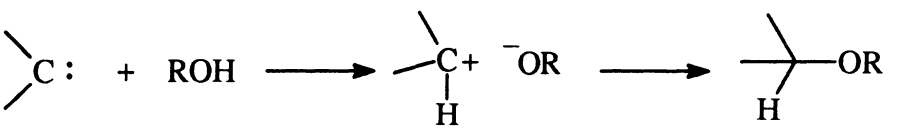
a. One-step insertion into the O-H bond.



b. Electrophilic attack of the carbene at oxygen, followed by proton transfer.

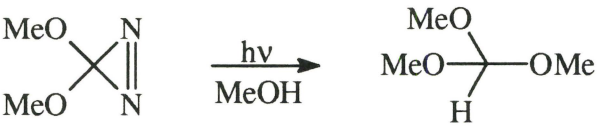


c. Protonation of the carbene to give an ion pair followed by ion pair collapse.



The electrophilic or nucleophilic character of the carbene determines the mechanism of the insertion. In general, nucleophilic carbenes whose reactivity is dominated by lone pair electrons should favor mechanism c or possibly a. Electrophilic carbenes, where the reactivity is centered in the vacant p-orbital, should prefer mechanism b or possibly a.

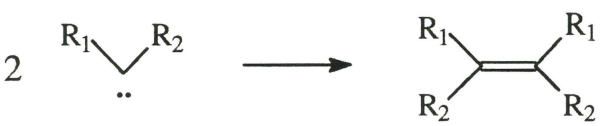
Moss and coworkers measured the kinetics of the OH insertion of dimethoxycarbene.[43]



The decay of dimethoxycarbene as a function of [methanol] in pentane at 20 °C was measured by laser flash photolysis. The kinetic isotope effect for insertion of DMC into MeOH(D) was determined to be 3.26 ± 0.49. The relatively large kinetic isotope effect observed indicates that the transition state involves substantial OH bond breaking which is consistent with either direct insertion (a) or carbene protonation (c).

c) <u>Dimerization</u>

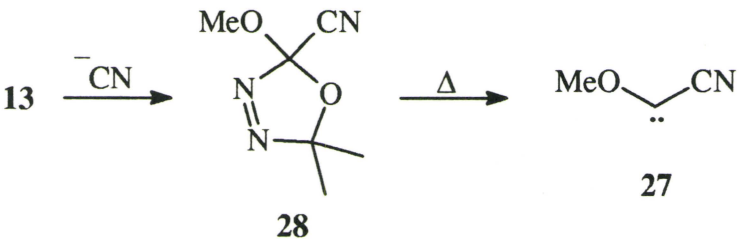
Carbenes can couple to each other to form dimers. This is usually one of the criteria used to prove the formation of carbenes in reactions.



Chapter 2

Results and Discussion

Initially, our aim was to expand the utility of the 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline exchange reaction[31] to generate interesting new substituted oxadiazolines. Our first attempt was to make cyanomethoxycarbene (**27**) by thermal decomposition of the corresponding oxadiazoline.



Carbene **27** is a push-pull carbene since the carbene center simultaneously carries both strongly donating and strongly withdrawing substituents. Moss and coworkers[27] carried out some geometry optimized HF/6-31G*//6-31G* calculations on carbene **27** and found that its geometry was strongly bent (O-C-C bond angle = 107.9 ^{0}), which indicates a singlet ground state configuration. They also calculated its carbene selectivity index (m_{CXY}) to be 1.11, which indicated that it should behave as an electrophile.

It is known that alcohols and phenols can be exchanged onto 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**13**) to form dioxyoxadiazolines.[31]

Therefore, the synthesis of 2-cyano-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**28**) was visualized to be possible by exchange of oxadiazoline **13** with tetraethylammonium cyanide. Unfortunately, unlike the exchange with other nucleophiles, such as alcohols, thiols or phenols, the exchange with cyanide did not yield the desired product.

Several attempts were made to synthesize oxadiazoline **28**, including a simple exchange method with oxadiazoline **13** and tetraethylammonium cyanide in CH_2Cl_2, to acid catalyzed exchange with a catalytic amount of previously dried p-toluene sulfonic acid (PTSA) at room temperature or at reflux temperature for 16 hours. It was noticed that as soon as tetraethylammonium cyanide was added into the solution of oxadiazoline **13** and PTSA, a vigorous reaction took place for about 1 minute and the reaction mixture became warm and slightly brown. Under either set of conditions, **13** was found to have been completely destroyed; no significant product was formed, however.

It was thought that the acetoxy substituent of oxadiazoline **13** may not be a good enough leaving group. Consequently, trimethylsilylcyanide was used instead since the trimethylsilyl group could bind quite tightly to the carbonyl oxygen of the acetoxy substituent, thereby facilitating the exchange by electrophilic catalysis. The reaction was carried out at room temperature or at 60 °C for 1 ½ days. Unfortunately, these approaches did not work either.

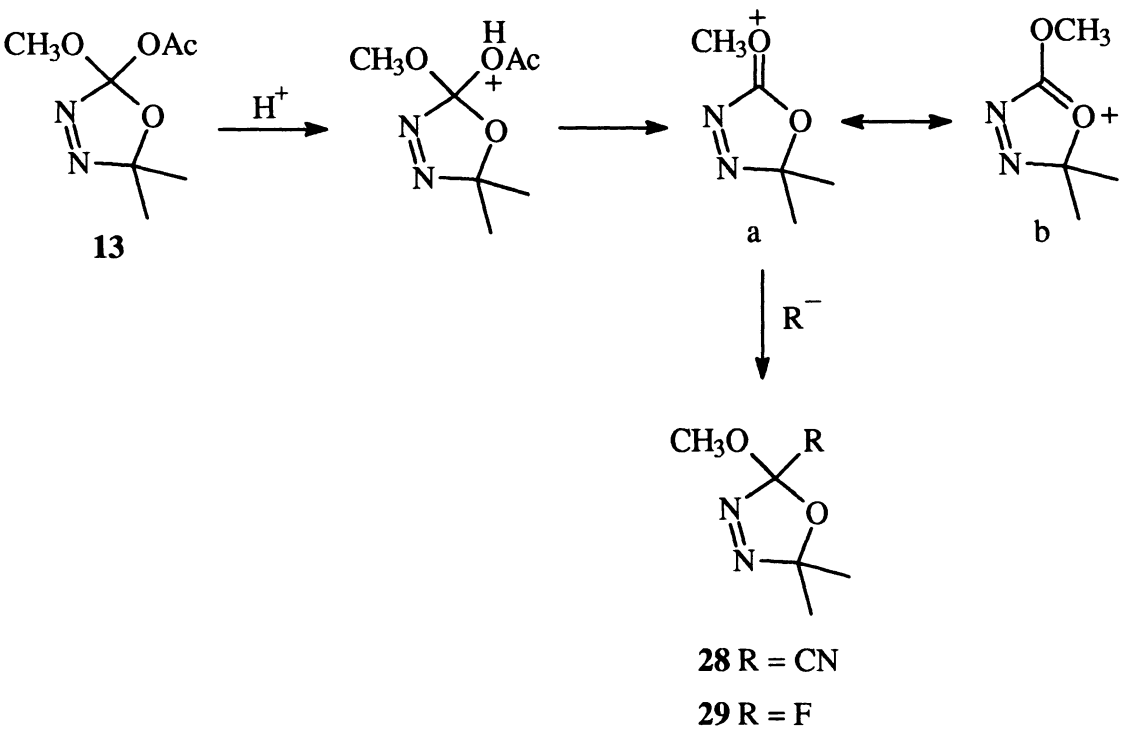
Other approaches, including use of different solvents such as THF or CH_3CN also failed. These aprotic solvents were chosen instead of many others available because they can be removed easily.

A promising procedure[44] used for a similar reaction found in the literature was also followed; a reaction of **13** with trimethylsilylcyanide and $BF_3 \cdot OEt_2$ in CH_2Cl_2 at ice temperature for 2 hours. All these approaches were attempted more than once, but did not give the desired product.

Several attempts to synthesize 2-fluoro-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (**29**) by reacting oxadiazoline **13** with tetrabutylammonium fluoride with and without PTSA, also failed.

Therefore, it was concluded that the exchanges of cyanide and fluoride with acetoxy of oxadiazoline **13** were not possible under the normal exchange condition.

Since the attempted exchanges were messy, it was difficult to determine what had occurred. The proposed mechanism of the exchange is shown as follows:



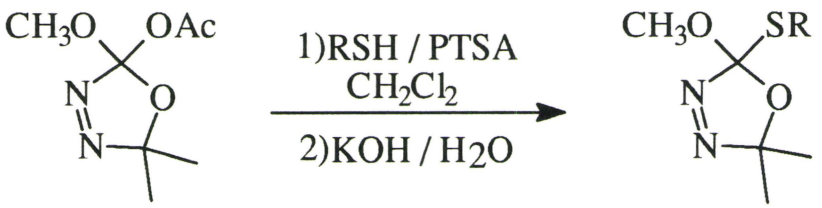
The failure of the exchange could be attributed to the attack of the nucleophile being too slow due to the very low concentration of cyanide and fluoride ions in the exchange media. As a result, the cationic intermediate (a or b) of the oxadiazoline did not have a long enough lifetime to be attacked by cyanide or fluoride ions. An alternative possibility is that the resultant oxadiazolines **28** and **29** may be highly unstable and decomposed quickly once formed.

Moss and coworkers had once studied various push-pull carbenes[26,27] such as cyanomethoxycarbene (**27**) and benzyloxycyanocarbene (**30**).[27] They generated carbene **30** from the corresponding diazirine precursor which was prepared by the exchange of 3-chloro-3-benzyloxydiazirine with *n*-$Bu_4N^+CN^-$. They were able to trap **30** when the exchange was performed with the presence of some electron rich alkenes. However, in the absence of a carbene trap, they found that the diazirine decomposed to a nitrile-containing, orange, viscous substance. They suggested that these diazirines were unstable. They did HF/3-21G//3-21G calculations on various diazirines with different substituents R_1 and R_2 (a. $R_1 = R_2 = H$; b. $R_1 = H$, $R_2 = MeO$, c. $R_1 = H$, $R_2 = CN$, $R_1 = CN$, $R_2 = MeO$) to determine the effect of cyano substitution on the stability of a diazirine, and found that the substitution lowers the LUMO (N=N π^* orbital) energy and was the lowest for cyanomethoxydiazirine. As a result, they concluded that the N=N π^* orbitals of alkoxycyanodiazirines may be good acceptors for nucleophilic addition. The cyanodiazomethanes, isomers of the cyanodiazirines, would likely be very unstable, readily decomposing to their carbenes.[27]

2.1 Synthesis of Oxythiooxadiazolines

The unsuccessful attempts in synthesizing oxadiazolines **28** and **29** led to the search for other carbene precursors. Quite a few dioxycarbenes had been studied, so it was interesting to investigate oxythiocarbenes since they were not reported in the literature. Progressing from oxygen to sulfur, which is a second row element in the periodic table, might lead to quite different properties and reactions of the carbene intermediates. The exchange by oxadiazoline **13** to synthesize dioxyoxadiazolines had been shown to give quite good yields, so thiols were the next logical step.

Exchange of the acetoxy substituent of oxadiazoline **13** with mercaptans was visualized in order to synthesize these oxythiooxadiazolines. Exchanges led to the formation of methylthio **(31d)**, ethylthio **(31c)**, benzylthio **(31b)** and phenylthio **(31a)** substituted oxadiazolines. Each of these oxythiooxadiazolines was successfully prepared by reacting crude oxadiazoline **13** with the corresponding mercaptans in acid catalyzed reactions. The by-product **14** in crude oxadiazoline **13** remained unreacted after the exchange, and was selectively hydrolyzed by treating the solution with aqueous potassium hydroxide. The hydrolysis yielded products that were in the aqueous phase and therefore pure **31** was readily obtained. The exchange is shown as follows:



13 (crude) **31 (a-d)**

Table 1 :

R	% yield (Exchange)
a= Ph	69
b = CH_2Ph	44
c = CH_2CH_3	60
d = CH_3	80

Chromatography was needed to obtain the pure oxadiazolines. All the pure oxadiazolines were clear liquids, except oxadiazoline **31a** which was a white solid with a melting point of 38-39 °C. The yields of the exchanges were quite high for most thiol compounds, and are listed in Table 1.

The method of identification for these oxythiooxadiazolines relied heavily on both ^{1}H and ^{13}C NMR. For oxadiazolines **31b** and **31c**, the methylene groups had diastereotopic protons since they were adjacent to a chiral center. The majority of the peaks agreed well with those found in the well characterized dioxyoxadiazolines. Most of the electron ionization spectra showed losses of methoxy and alkylthio groups from the oxadiazolines. It was noticed that the peak intensities for the losses of methoxy were smaller than those for the losses of alkylthio functional groups. However, there were some problems with a reliance on mass spectrometric data since most of the low resolution chemical ionization mass spectra (LRCIMS) for these compounds showed severe fragmentations. In fact, in half the oxadiazolines studied, neither $[M+H]^+$ nor $[M+NH_4]^+$ could be observed. However, there is no doubt that these compounds are indeed oxadiazolines **31a-d**.

2.2 Thermolysis in Benzene

2.2.1 Rate Constant Calculations

The rate constants for decomposition of oxadiazolines **31a-c** were measured. Each of these oxadiazolines was dissolved in benzene in a NMR tube. The solution was degassed by three freeze-pump-thaw sequences before the NMR tube was sealed and heated at 60 °C in a constant temperature oil bath. The decay of oxadiazoline as a function of time was followed by ^{1}H NMR using p-xylene as an internal standard. A plot of ln([oxadiazoline]$_t$ / [oxadiazoline]$_o$) versus time gave a straight line, which indicates that the oxadiazoline decays by first order kinetics. The results were shown in Table 2.

Table 2 :

R	k at 60 °C (10^{-5} s^{-1})	half life (h)
CH_2CH_3	2.07	9.30
CH_2Ph	2.09	9.21
Ph	2.04	9.44

These results indicate that changes in the substituents of the oxadiazoline have little effect on the rates of decomposition. This is probably because the substituents were not directly attached to the carbene center. However, the general effect of going from oxygen to sulfur was that the rates of decomposition for these oxythiooxadiazolines had increased dramatically compared to those of dioxyoxadiazolines. The rate constant for dimethoxyoxadiazoline at 100 °C was 1.19 x 10^{-5} s^{-1}.[29] The observation is consistent with the fact that sulfur stabilizes the anion at the adjacent carbon of ylide **32** better than the

oxygen analogue, thereby favoring the decomposition of oxadiazoline **31** to the ylide. Consequently, these oxythiooxadiazolines decompose faster and they can be thermolyzed at much lower temperature (e.g. 60 °C) which can be fairly useful when performing a thermolysis in the presence of a thermally sensitive carbene trap or when the expected products are thermally labile.

2.2.2 Products of Thermolysis in benzene

Products from the thermolyses of all the oxadiazolines **31a-d** were shown to be the following (Scheme 18):

Scheme 18

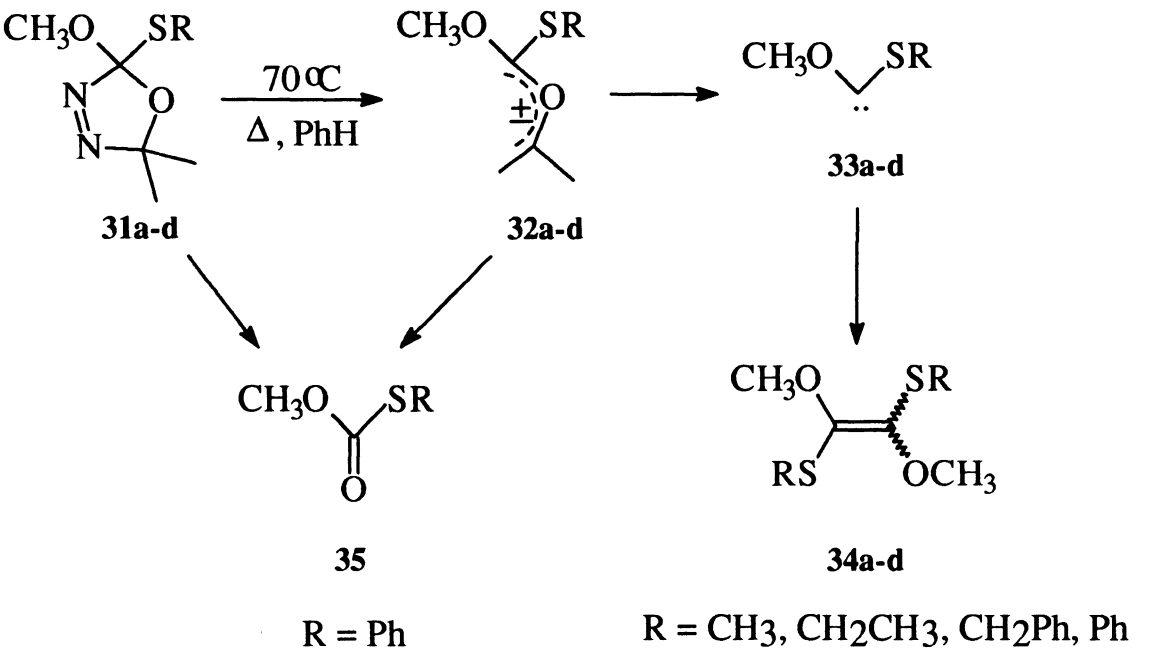


Table 3 :

R	dimer % yield isolated	crude ratio *trans/cis* dimer
Me	59	1.25
Et	65	1.39
C_6H_5	55	1.7
$CH_2C_6H_5$	59	1.32

These oxadiazolines lose nitrogen upon thermolysis, forming the corresponding ylides **32a-d** which then fragment to generate carbenes **33a-d** and acetone. These reactions were found to produce carbene dimers **34a-d**, which came from the coupling of two carbenes and thus confirmed the presence of carbenes **33a-d**. In the case of oxadiazoline **31a**, methyl (phenylthio)carbonate (**35**)[50] was also formed in 10 % yield. It may have come from initial fragmentation of the oxadiazoline through the cleavage of C-N and C-O bonds, forming the diazo compound and the carbonate. The formation of azine usually was taken as an indication that this happened. An alternative route to **35** could be the fragmentation of the ylide **32a** to give dimethylcarbene as by-product. Usually this can be confirmed by propene formation. Due to the fact that only very little of **35** was formed, it was quite difficult to tell for sure if azine or propene was produced. The proton spectrum was analyzed and no significant peaks besides those from the products **34a** and **35** were found. This made the formation of propene more probable, since azine is more easily detected by NMR spectroscopy.

As shown in Table 3, the ratio of *trans/cis* dimers in general showed only a minor substituent effect. We know that C-S bonds (about 1.81 angstrom) are significantly longer

than the same type of C-O bonds (about 1.43 angstrom).[45] It was found that in cases where the substituents are methylthio, ethylthio and benzylthio, there were only very small preferences for the *trans* isomers. This is due to the fact that the methyl substituent is relatively small and in the case of ethyl and benzyl substituents, the CH_2 groups can provide some bond flexibility to adopt the least interaction geometries between the adjacent sulfur substituents in the *cis* orientation. As a result, the difference in *trans* and *cis* is small. In the case for phenylthiocarbene, a slightly greater *trans* preference was observed. This was due to the fact that the bulky phenyl group was directly attached to sulfur. Although the C-S bonds are quite long, adjacent phenyl substituents will experience greater interactions if they are in the *cis* orientation, therefore favoring the *trans* orientation slightly more.

These carbene dimers were separated by chromatography, which was quite surprising at first because most dioxycarbene dimers were inseparable by chromatography. However, the separation of the *cis* and *trans*-1,2-dimethoxy-1,2-bis(methylthio)ethene **(34d)** was quite difficult. The ratios of these carbene dimers (Table 3) were calculated based on integrations of the product peaks in the crude by ^1H NMR with a standard of known concentration. These ratios are quite similar, only slightly lower in 1,2-dimethoxy-1,2-bis(phenylthio)ethene **(34a)** since some carbonate was also formed in the reaction.

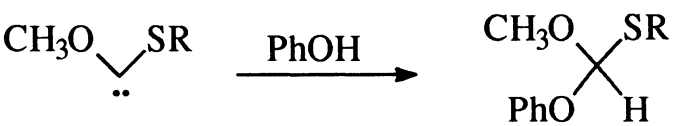
All these carbene dimers were characterized by proton and carbon NMR, IR and mass spectroscopy. The CI mass spectra for all these compounds revealed the $[M+H]^+$

peaks to be the base peaks. An X-ray crystal structure of **34b** was obtained to verify its stereochemistry (Appendix 1).

2.3 Carbene Trapping Experiments

2.3.1 Thermolysis in Phenol

In order to prove further that the thermal decomposition of the oxythiooxadiazolines **31a-d** indeed gave carbenes **33a-d**, those oxadiazolines were thermolyzed in the presence of phenol. The results of these thermolyses yielded the corresponding orthoesters **(36a-d)** which were formed by O-H insertion of the carbenes into the phenol. The mechanism of this reaction was presumably first protonation of the carbene to form a cation and then collapse with phenoxide ion to form the product.



33a-d **36a-d**

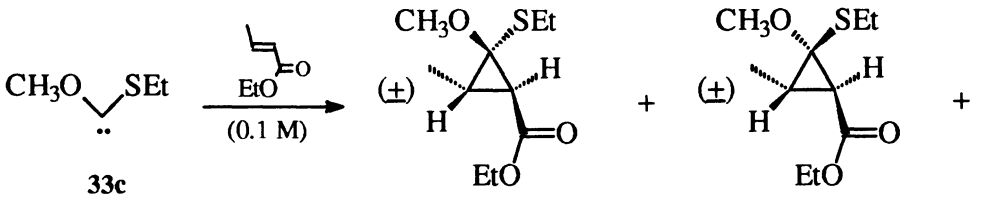
Table 4 :

R	% Yield
Me	61
Et	55
C_6H_5	85
$CH_2C_6H_5$	83

These thermolyses were quite clean and since only one product was formed in each case, purification could be achieved by removing any excess phenol by extracting the crude mixture with aqueous sodium carbonate. The yields shown in Table 4 were isolated yields. It was noticed that carbenes **33c** and **d** gave rather low yields, and the yields got higher with the bulky phenyl and benzyl substituents. The bulky substituents probably reduce hydrolysis of **36**. As these thermolyses were carried out in a water free environment, hydrolysis must have happened after the thermolysis. This is possible because before the base extraction, the reaction mixture was slightly acidic. Since the acidity of phenol (pKa = 9.89) is high enough, **36** could be easily hydrolyzed in the presence of trace amounts of water perhaps from the atmosphere.

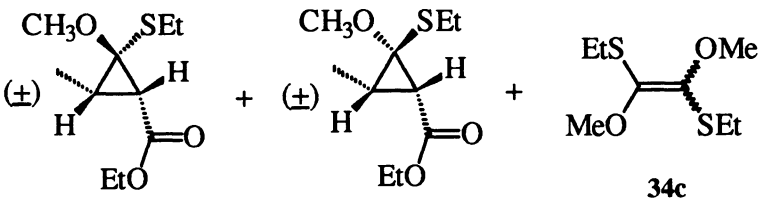
2.3.2 Thermolysis in Ethyl Crotonate

It is well known that carbenes add to double bonds to form cyclopropane derivatives. Oxadiazoline **31c** was thermolyzed in the presence of ethyl crotonate and the reaction yielded four substituted cyclopropane diastereomers (**37 i-iv**) and the carbene dimers **34c** shown as follows:



33c

37 i-iv



34c

The evidence for the formation of four cyclopropane adducts came from the proton NMR spectrum. It was found that there were four major methoxy signals in the ratio of 1 : 2 : 1.6 : 3.2, besides the very minor peaks for carbene dimers. The fact that four cyclopropanes were formed was quite surprising at first. Since the ethyl crotonate that was used contained predominantly the *trans* isomer, ideally, only two isomers were expected. The nonspecific stereochemistry must indicate that the addition was stepwise in manner, initially forming a 1,3-dipolar intermediate which then closed to form the cyclopropane. Or perhaps the cyclopropanes were initially formed in a concerted manner and later opened to the 1,3-dipole because of ring strain. In either case, the rotation in the dipole is the source for the loss of the stereochemistry.

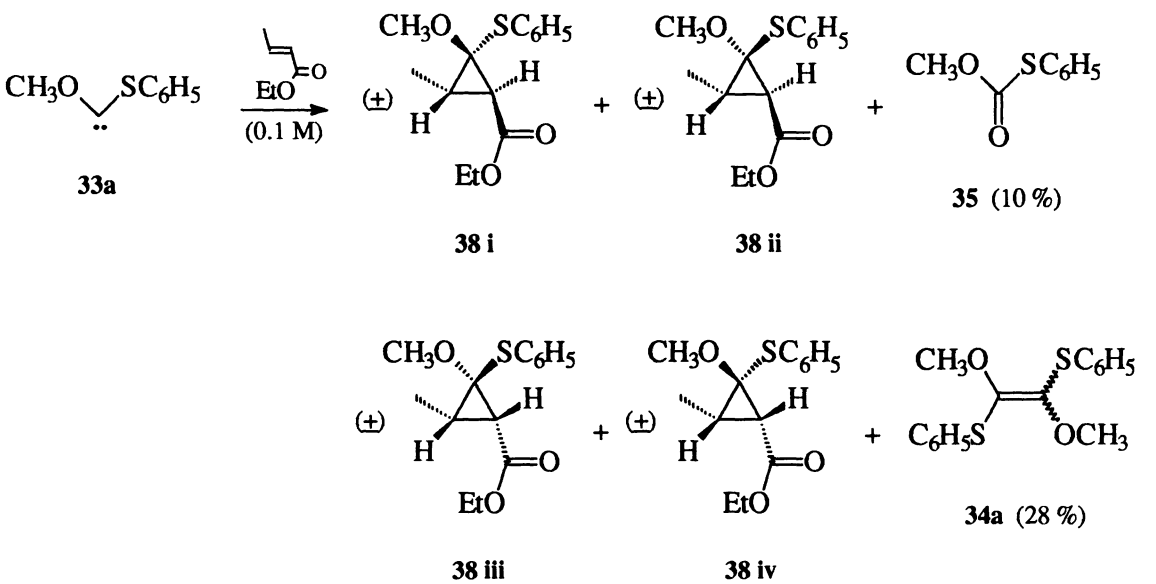
Although singlet carbene additions to double bonds in a stepwise fashion are somewhat unusual, there was some evidence observed by R. W. Hoffmann that seemed to suggest singlet carbenes can also react with double bonds in a stepwise manner.[34] He found only *trans* isomer when reacting dimethoxycarbene with diethyl maleate. The

observation with crotonate seemed to be consistent with R. W. Hoffmann's finding. The fact that more than two isomers of cyclopropanes were formed could be because the bulky substituents tried to avoid being on the same side.

There was also some evidence presented by Moss and coworkers which showed that the addition to a double bond occurred in a concerted manner because they obtained stereospecific products in reactions of dimethoxycarbene with various β-deuteriostyrenes.[5] This suggested that the ethoxycarbonyl group of the ethyl crotonate or diethyl maleate may have facilitated either the cyclopropane ring opening to the 1,3-dipolar intermediate or the direct formation of the 1,3-dipolar intermediate and caused the loss of stereochemistry.

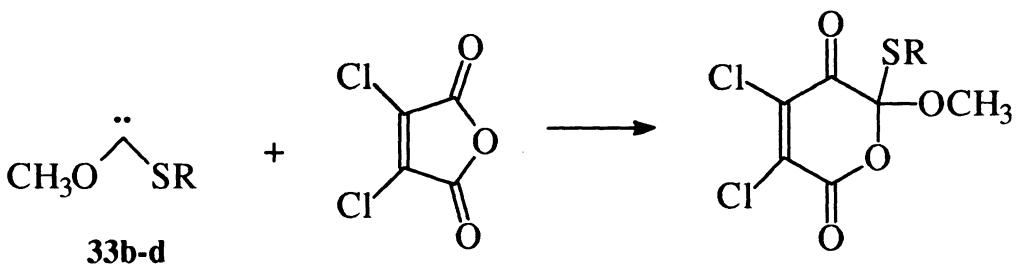
Unfortunately, the four adducts were not separable by chromatography. The total isolated yield of the cyclopropanes **37 i-iv** was 26 %, which was rather low probably because cyclopropanes are highly strained compounds and consequently the rate of reaction with ethyl crotonate is slow. As a result, the competing reaction which was carbene dimerization also took place; some carbenes generated in solution dimerized before they could be trapped by ethyl crotonate. This problem became more severe when the thermolysis was run at a higher temperature where carbene dimers were formed exclusively. Thermolysis at lower temperature (60 °C) was attempted but this did not eliminate the formation of the carbene dimers. Since **37 i-iv** could not be separated, it was not possible to characterize them individually. The molecular ion and $[M+H]^+$ were observed in EI and CI mass spectra, respectively, in the mixture.

Thermolysis of oxadiazoline **31a** was carried out also in the presence of ethyl crotonate under similar conditions. However, it was found in this case that only two of the four adducts (**38 i-iv**) were formed. The proton NMR spectrum showed the two major methoxy peaks in the ratio of 1 : 3.8 and the isolated yields were 7 % and 35 %. The reason for this could be due to the bulkiness of the phenyl substituent which is more sterically demanding and causes the formation of the other two cyclopropanes to be too unfavorable. However, out of the four possible cyclopropanes, it was not possible to distinguish which of the two isomers were actually formed in the reaction. Of the four possibilities, **38 iv** would be the least likely because it has the largest steric interactions with three other substituents on the same side of the cyclopropane ring. For the same reason as **33c**, some carbene dimers were also observed in this reaction.



2.3.3 Thermolysis in Dichloromaleic Anhydride

Carbenes are known to attack the carbonyl group of cyclic anhydrides to form an intermediate that undergoes ring expansion.[40] Similar to dimethoxycarbene, thermolysis of oxythiooxadiazolines in dichloromaleic anhydride gave the expected products (**39**) presumably by the same mechanism. These thermolyses yielded only one product in each case, which was the result of addition to the carbonyl group. Addition of the carbene to the electron deficient double bond was not observed. The yields and the melting points of the products are shown in Table 5.



33b-d **39b-d**

R= Me, Et, $CH_2C_6H_5$

Table 5 :

R	% Yield	melting point (° C)
Me	85	89 - 91
Et	89	71 - 74
$CH_2C_6H_5$	75	69 - 70

Since the thermolyses were relatively clean and only one product was formed in each case, these products **39b-d** were isolated by kugelrohr distillation under vacuum. The yields of these reactions were high and the products were all yellow solids. An X-ray

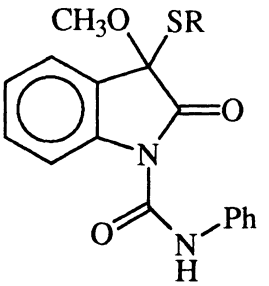
crystal structure for the product **39d** was obtained and confirmed the structure of these products (Appendix 2).

2.3.4 Thermolysis in Phenyl Isocyanate

Thermolyses of oxythiooxadiazolines **31a** and **31d** in the presence of excess phenyl isocyanate were attempted. These reactions were found to form three products in each case. The products were isolated by centrifugal chromatography. The first fraction, a minor product (**40**), which was later found to be a 2:1 adduct, travelled on the plate quite quickly. However, the 2:2 adducts, major products (**43**), were very polar and travelled on the plate extremely slowly. Only the diastereomers of the 2:2 adducts formed by carbene **33a** were separable. The 2:2 diastereomers of carbene **33d** were separated from other products and characterized as a mixture.

The products formed were somewhat different from what R. W. Hoffmann had obtained.[36] According to the LRCIMS taken for the products obtained from the two different carbenes, the minor product was confirmed to be a 2:1 adduct which contained one unit of carbene and two units of phenyl isocyanate in the molecule. The mass spectra showed that the major products consist of two units each of carbene and phenyl isocyanate (2:2 adducts).

The 2:1 adduct was identified as 1-phenylcarbamoyl-thiooxindole (**40**). The evidence for the structure was based on the ^{1}H and ^{13}C NMR spectra, infrared spectrum and the mass spectrum.



a: R = Ph
d: R = CH_3

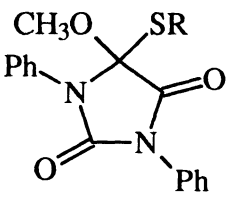
40

The LRCIMS of 2:1 adducts **40** resulting from methoxy(phenylthio)carbene and methoxy(methylthio)carbene showed m/z 390 and m/z 329, respectively which corresponded to $[M+H]^+$.

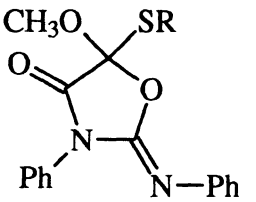
The infrared spectra of both **40a** and **d** revealed weak absoptions in the NH stretching region. In addition, there appeared an intense and somewhat broad band, which looked like there could be two overlapping carbonyl stretching bands at around 1748 cm^{-1} region. These bands can be attributed to the stretching of the two carbonyl groups in the molecule.

The ^1H NMR of **40** showed very interesting splitting patterns. In the low field, there was a doublet at about 8.3 ppm which integrated for one proton, and the coupling constant was about 8 Hz. This signal corresponds to the aromatic hydrogen that is close to the 1-phenylcarbamoyl functional group. In order to obtain maximum overlap between the nitrogen lone pair, the π-systems of the carbonyl groups and the π-system of the aromatic ring, the five membered ring will adopt a planar conformation. As a result, the aromatic hydrogen is held in the deshielding cone of the π-system and this caused the chemical shift

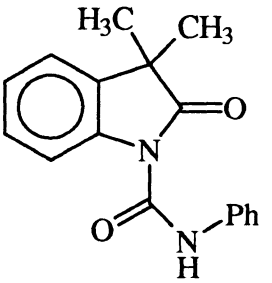
of the hydrogen to be higher than usual. Another characteristic feature appeared as a broad singlet about 10.4 ppm, which integrated for one proton. This broad singlet is attributed to the nitrogen bound hydrogen. These observations ruled out the hydantoin **41** and oxazolidone **42** structures.



41



42



19a

Comparison to the ^{1}H NMR spectrum of 1-phenylcarbamoyl-3,3-dimethyloxindole (**19a**)[37] showed strong similarities. The ^{13}C NMR of the 2:1 adducts **40a** and **d** were found to be quite similar. The signal at 174 ppm was attributed to the carbonyl carbon in the five-membered ring, whereas, the urea type carbonyl signal was found at about 149 ppm. Several fragments in the electron ionization mass spectra also supported the assignment, e.g. mass 162 was attributed to the $[Ph\text{-}NH\text{-}CO\text{-}N\text{-}CO]^{+}$ fragment.

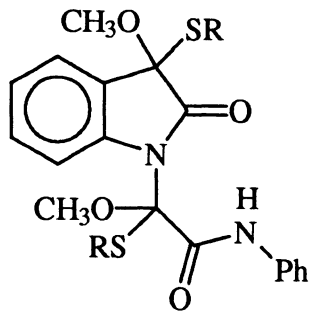
The major products which came from both reactions of **33a** and **33d** with phenyl isocyanate showed m/z 560 and m/z 436, respectively, in the LRCI mass spectrum. These masses were attributed to their $[M+NH_4]^{+}$ ions and the products were identified to be 2:2 adducts. Other evidence that the molecule contained two carbene units also came from the ^{1}H NMR. The products were later identified as two diastereomeric acetanilides.

The infrared spectra in each case showed two well separated carbonyl stretching bands, an intense band at 1746 cm^{-1} and one of medium intensity at 1718 cm^{-1}. In addition, there were some weak absoptions in the NH region.

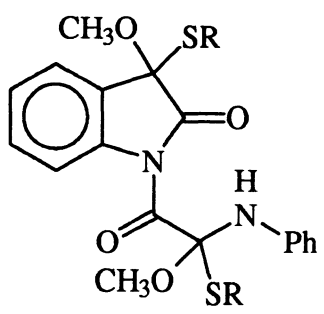
The ^1H NMR spectrum showed a pair of methoxy peaks and a pair of methylthio peaks of equal intensity. In the reaction of **33a** with phenyl isocyanate, there were only a pair of methoxy peaks. In the low field region, there was also a broad singlet at 7.6 ppm for the product from **33a** and at 8.3 ppm for the **33d**. These signals were each integrated to be one proton and were assigned as the amide hydrogens.

The ^{13}C NMR spectrum showed two carbonyl signals at 162 ppm and 172 ppm. These peaks were only apart from each other by approximately 10 ppm and revealed that they were in very similar chemical environments.

Based on these data, two structures (**43** and **44**) were predicted as follows.



43



44

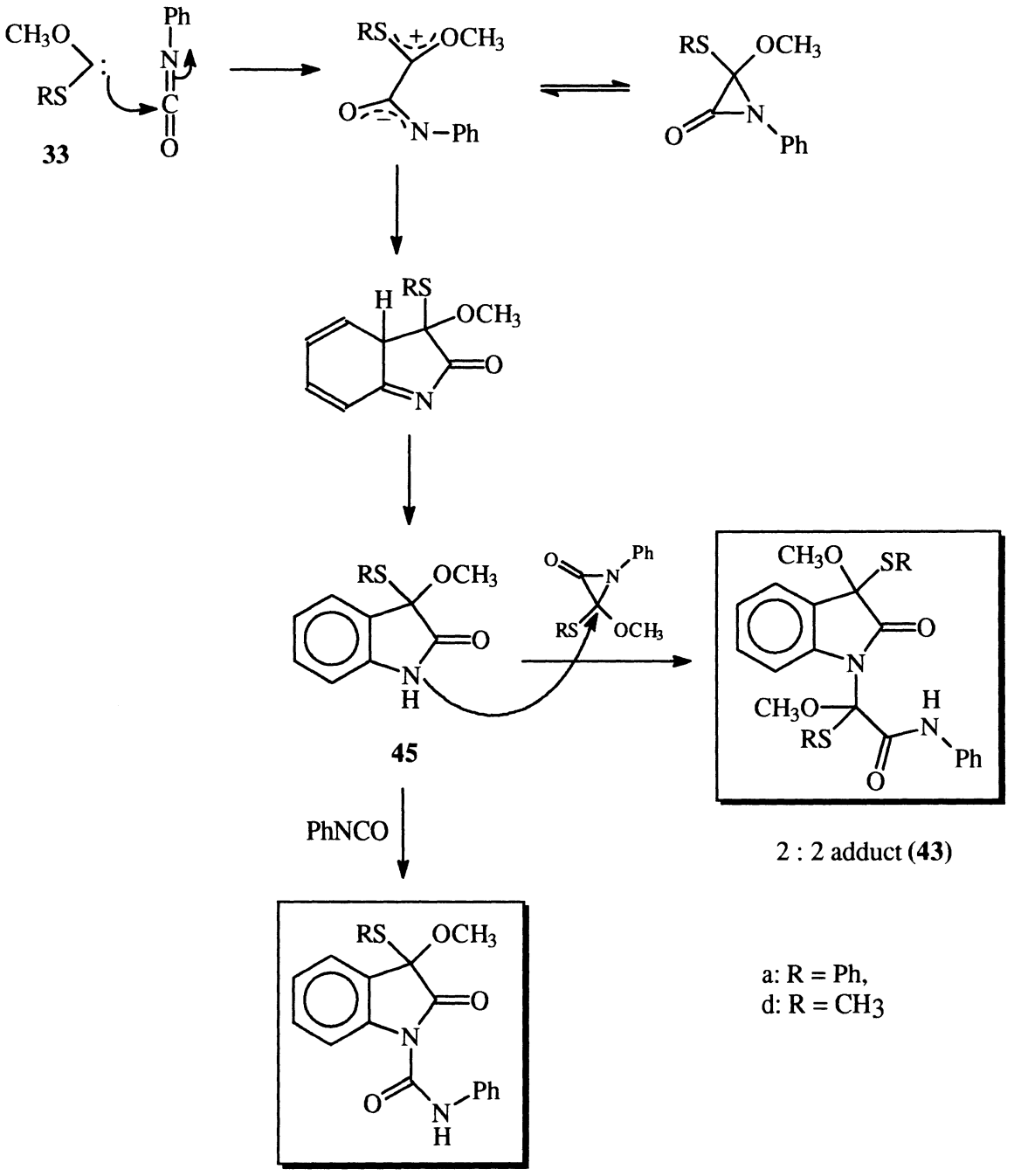
a: R = Ph,
d: R = CH_3

Since the doublet appearing in 2:1 adducts was not seen in any of the ^1H NMR spectra of the 2:2 adducts, structure **43** is predicted to be the correct one. In addition, the electron ionization spectra seemed to lead to the same conclusion. The mass spectra

showed medium to weak intensity peaks at m/z 119 or 120 (119 for R = Me; 120 for R = Ph), which indicated the $[PhNCO]^+$ or $[PhNCO+H]^+$ fragments, respectively. All 2:2 adducts showed expected molecular ions which confirmed the piece that is attached to the nitrogen in the five-membered ring.

Both **40** and **43** were fine, needle-like white solids. Unfortunately, several attempts to grow single crystals were not successful. Consequently, no X-ray crystal structures have been obtained to verify the structures. The spectroscopic evidence suggested the following products and mechanisms to achieve these products are shown as follows (Scheme 19).

Scheme 19



2 : 2 adduct (**43**)

2 : 1 adduct (**40**)

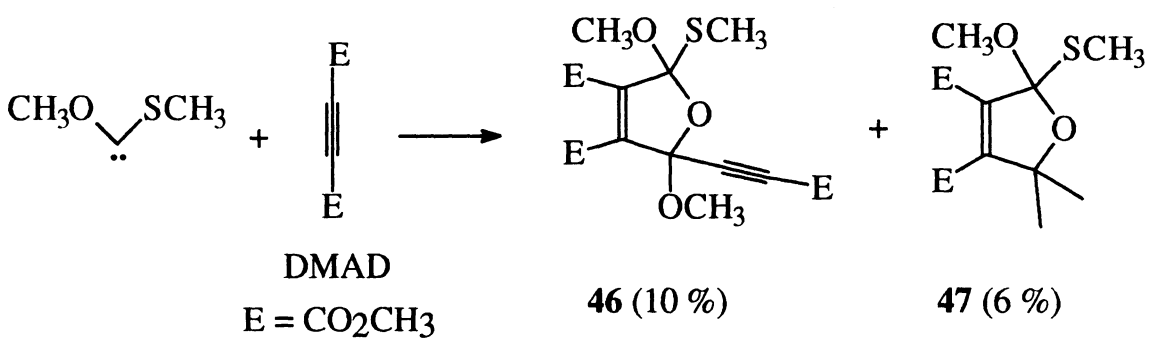
a: R = Ph,
d: R = CH_3

The carbene apparently reacted with an equivalent of phenyl isocyanate to form a 1,3-dipolar intermediate which is in equilibrium with the α-lactam. Since sulfur does not stabilize a cation as well as oxygen, the 1,3-dipolar intermediate is predicted to be unstable. Consequently, it undergoes intramolecular attack on the aromatic ring and then proton transfer to form oxindole **45**. The nitrogen of the oxindole is basic enough to react with either another equivalent of phenyl isocyanate or with the α-lactam to form **40** and **43**, respectively. Nucleophilic attack at C3 of an α-lactam has been proposed by Sheehan and coworkers.[38]

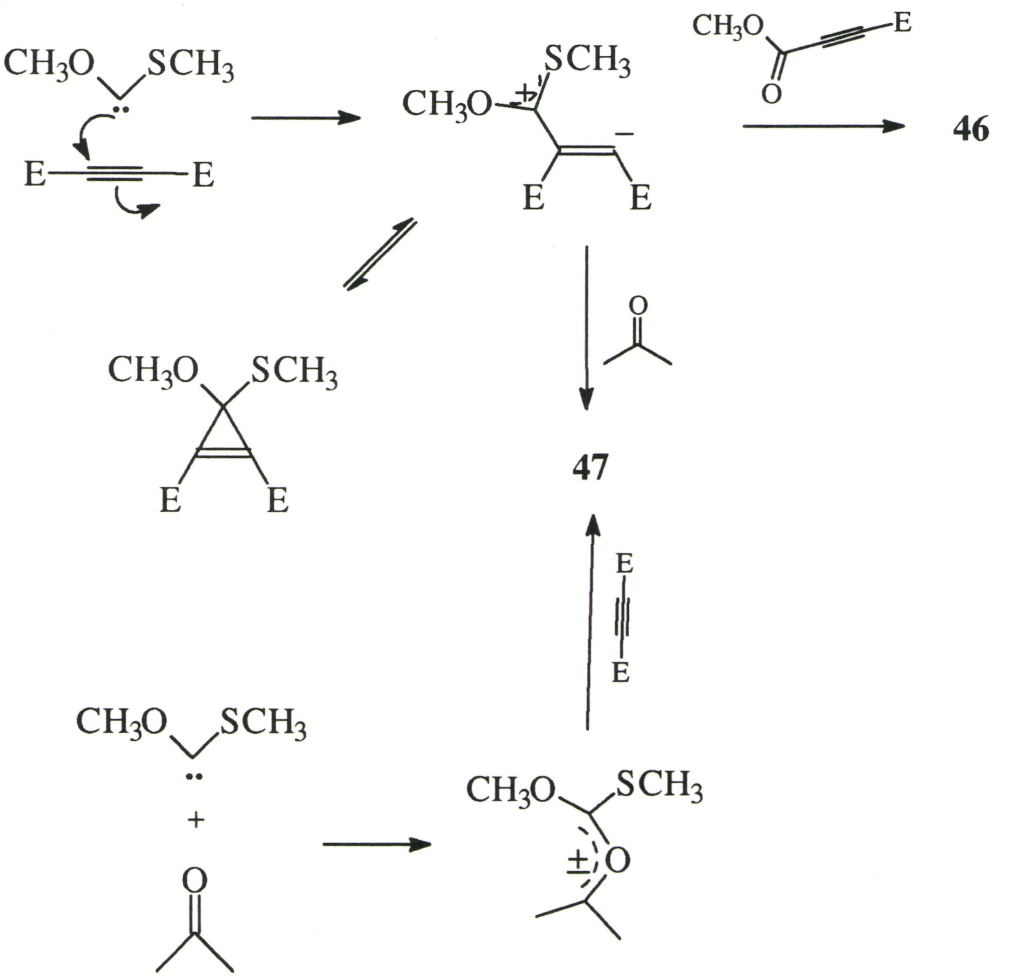
2.3.5 Thermolysis in DMAD

Thermolysis of oxadiazoline **31d** in the presence of DMAD was performed. The reaction was rather complicated and at least five products were found. Only two products could be firmly identified (Scheme 20). All other products seemed to result from a methyl-shift because ^{1}H NMR spectra showed no methylthio substituents in them.

Scheme 20



The following mechanism for this reaction is proposed. The addition of carbene to the triple bond of the DMAD yields a 1,3-dipolar intermediate which is in equilibrium with the cyclopropene. The 1,3-dipolar intermediate subsequently undergoes [3+2] cycloaddition with both DMAD and acetone (from the thermolysis) through the carbonyl group to afford **46** and **47**, respectively. The 1,3-dipolar intermediate can also add to DMAD and acetone to form the zwitterionic intermediates first and then undergo ring closure to yield the products. Product **47** may also come from the reaction of carbene with acetone to afford the carbonyl ylide, which either subsequently reacts with DMAD to form a zwitterionic intermediate that undergoes ring closure or undergoes [3+2] cycloaddition with DMAD.



R. W. Hoffmann looked at a similar reaction with dimethoxycarbene and DMAD.[34] He obtained only one product (**24**); the oxygen analogue of the 10 % product obtained here. The difference in products formed in both reactions demonstrated that the carbenes have quite different properties.

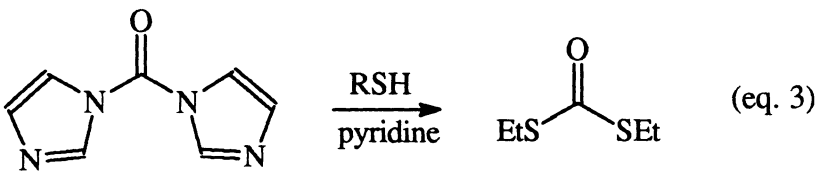
2.4 Dithiocarbenes

Dithiocarbenes were first made in the early 1960's by using tosylhydrazones[24] and quadricyclanone ketals[20] as carbene precursors. We have made some attempts to generate

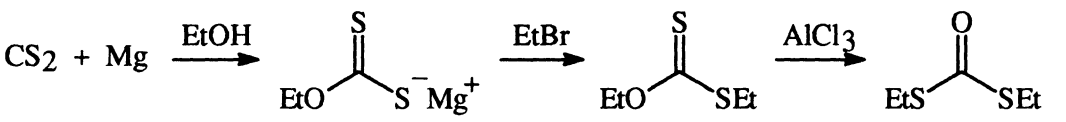
di(ethylthio)carbene by the oxadiazoline route.

2.4.1 Synthesis of Acetoxy(ethylthio)oxadiazoline

In order to generate the dithiocarbenes from an appropriate oxadiazoline precursor, the sulfur analogue of the hydrazone was required. The approach for the synthesis started with the preparation of a dithiolcarbonate (**48**). Two methods were used: 1,1-carbonyldiimidazole reacted with mercaptan (eq. 3) or a three step synthesis (eq. 4) shown below. The second method was later used routinely since it was more economical. In this method, magnesium was allowed to react with excess carbon disulfide in ethanol to yield magnesium ethyl xanthate (**49**). **49** was subsequently quenched by ethyl bromide to form diethyl xanthic ester (**50**)[46], which then underwent rearrangement to **48** by the catalysis of aluminum chloride.[47]



(eq. 3)

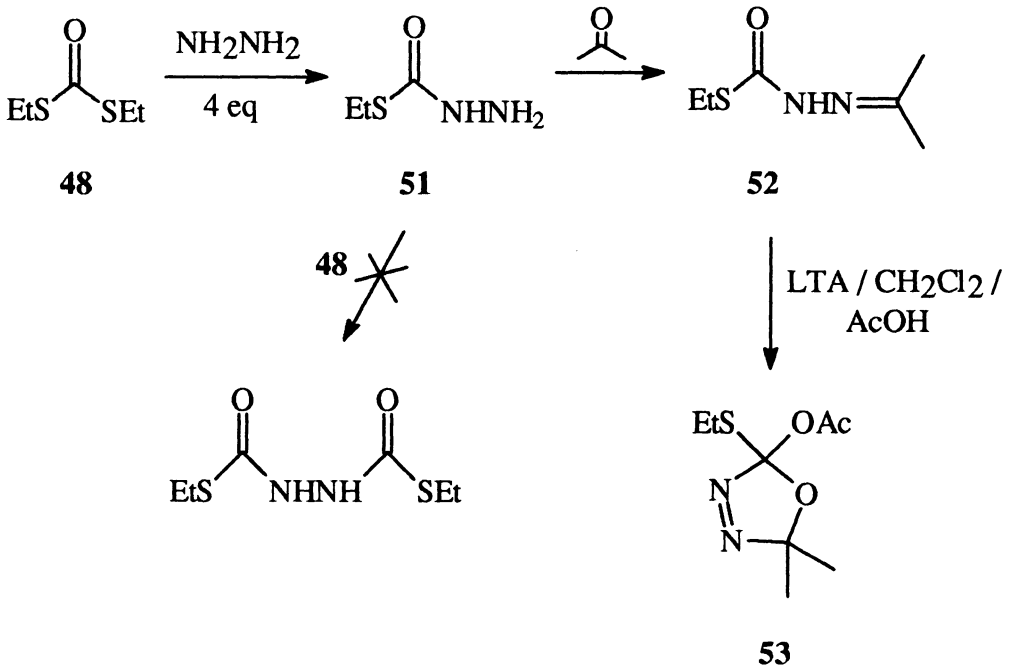


(eq. 4)

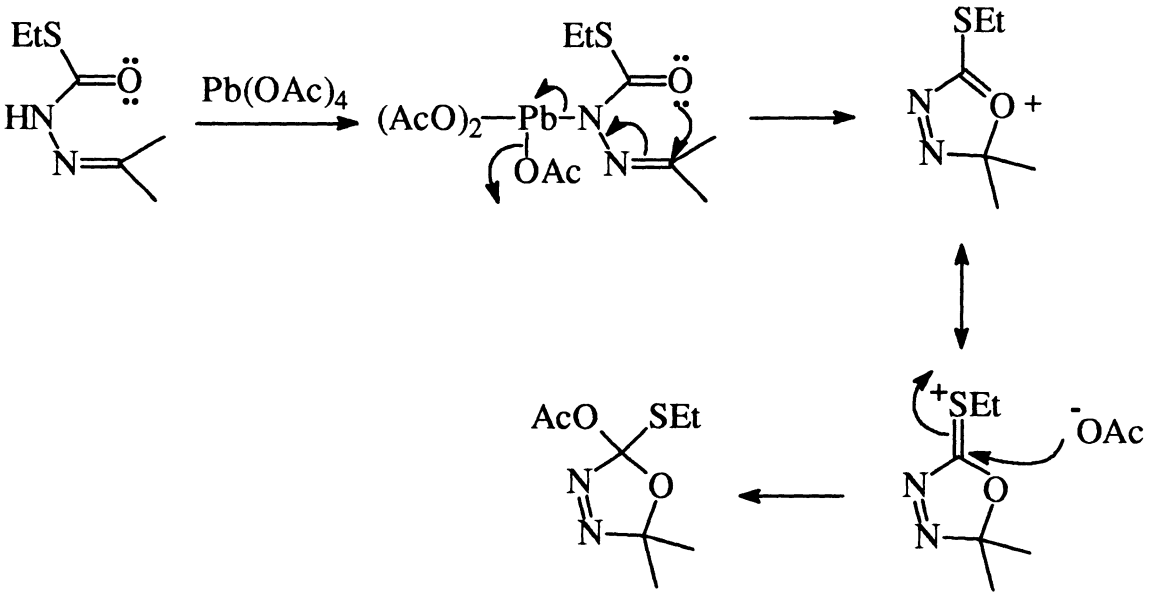
49 **50** **48**

The synthesis of the hydrazide **51** required an excess of hydrazine to be used so that most of the carbonate is converted rapidly to hydrazide and thereby eliminates the formation of

diacylated hydrazine. The hydrazide was then reacted with acetone to afford **52**. Oxidation of **52** with lead tetraacetate in an acid catalyzed reaction yielded the 2-acetoxy-2-ethylthio-Δ^3-1,3,4-oxadiazoline (**53**) in >95 % yield.



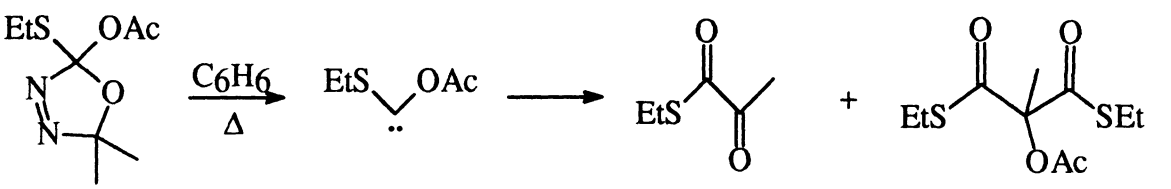
It was very surprising to find that no acyclic by-product was formed in this oxidation. Recall that in the oxidation of the oxygen analogue of the hydrazone,[31] the reaction gave only 70 % of oxadiazoline **13** and 30 % of acyclic by-product **14**. This observation is again consistent with sulfur being a poorer cation stabilizer than oxygen, therefore the cationic intermediate is more reactive than the oxygen analogue. Nucleophilic attack at the carbon adjacent to the sulfur, which leads to the formation of **53**, is perhaps faster than the attack at the sp^3 carbon due to steric effect. The following is the proposed mechanism of the lead tetraacetate oxidation.



2.5 Thermolysis in Benzene

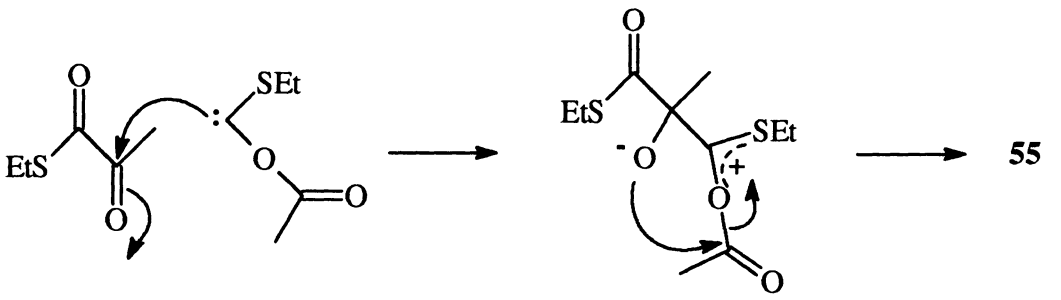
Thermolysis of oxadiazoline **53** in benzene without a carbene trap gave two products (Scheme 21). Product **54** resulted from 1,2-migration of the acyl group to the carbene center. Since **54** is quite reactive, it serves as a carbene trap which is prone to carbene addition and generates **55**. The following mechanism is proposed (Scheme 22).

Scheme 21



53 **54** **55** (42 %)

Scheme 22

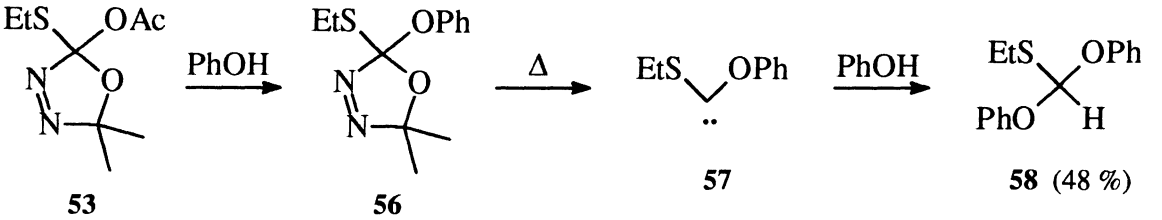


Since **55** is formed in competition with unimolecular formation of **54**, this suggests that nucleophilic addition to **54** is not very fast. The rate constant for decomposition of **53** was followed by ^{1}H NMR spectroscopy at the same temperature used for the previous oxythiooxadiazolines. The rate constant had increased two-fold as a result of the more electron withdrawing acetoxy group compared to methoxy. It was $k_{60}{}^{\circ}C = 4.19 \times 10^{-5}\ s^{-1}$, which corresponds to $t_{1/2} = 4.6$ hours.

2.6 Thermolysis in Phenol

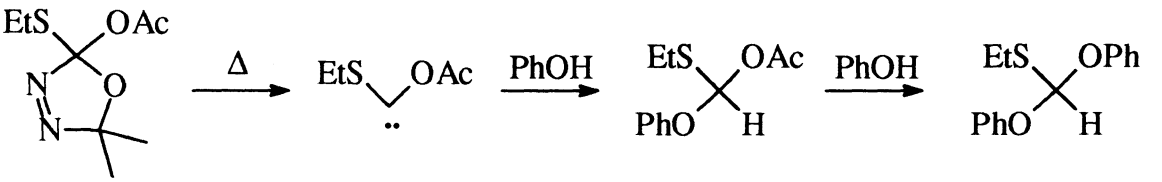
Initially, it was of interest to find out qualitatively how fast the acyl group migrates to the carbene center, by studying the competition between rearrangement and protonation of the carbene. However, the result was quite disappointing because the acetoxy of the oxadiazoline had exchanged with phenol. This process occurred first, which is in keeping with the observation that the exchange usually happened at a lower temperature than the thermolysis. The resultant (ethylthio)phenoxyoxadiazoline **(56)** was subsequently

thermolyzed to form carbene **57**. The carbene also inserted into the O-H bond of phenol to generate **58**.



53 **56** **57** **58** (48 %)

The less likely alternative would be that oxadiazoline **53** thermolyzed to form the carbene which then inserted into phenol. The initial product underwent substitution reaction by another phenol to form the final product. If this were the mechanism, it would require that the trapping of the carbene was faster than 1,2-acyl migration and also that thermolysis was faster than exchange.

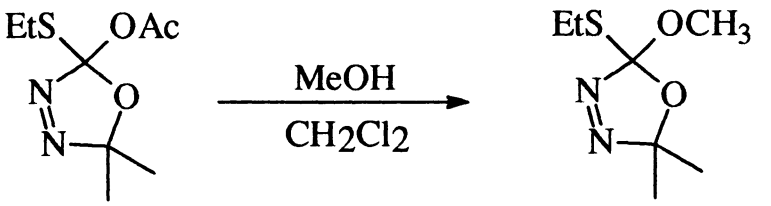


2.7 Exchange of Acetoxy(ethylthio)oxadiazoline

It is of interest to see if **53**, which is the sulfur analogue of the oxadiazoline **13**, can undergo exchange. Exchange has the potential of generating other thio-substituted oxadiazolines which may give the corresponding carbenes.

a. with Alcohol

The exchange of the oxadiazoline **53** with methanol was chosen. By comparison to the previously obtained proton NMR spectrum, the product was identified as oxadiazoline **31b** and the exchange yield was 92 %.

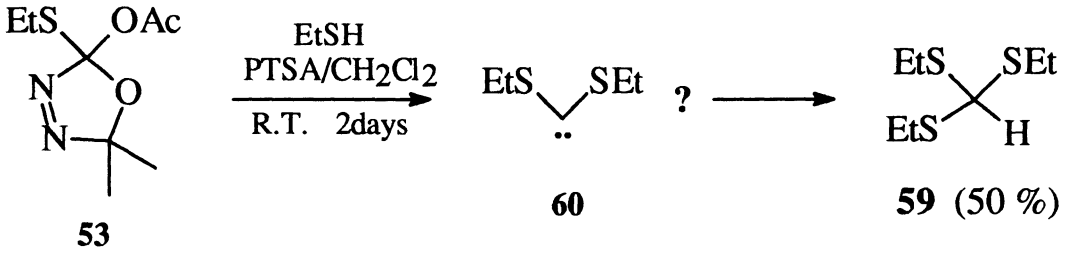


53 **31c**

b. with mercaptan

It is known that oxadiazolines **31a-d** thermolyze at lower temperatures than dioxyoxadiazolines. Therefore, it is expected that substituting the oxadiazoline with two thiol groups should make dithiooxadiazoline more reactive. Knowing this, the exchange was thought to be carried out best at room temperature.

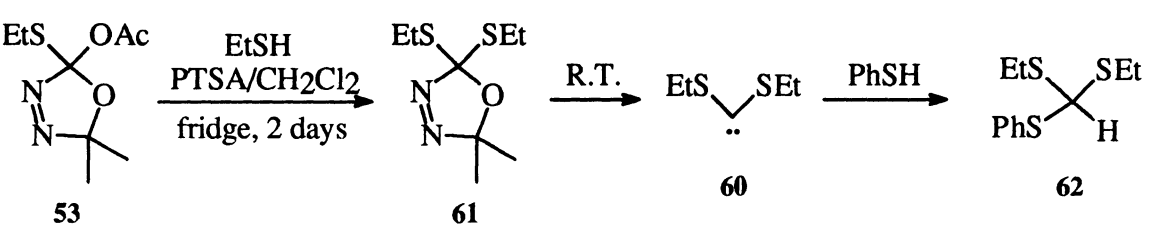
Exchange of the oxadiazoline **53** with ethane thiol at room temperature with a catalytic amount of PTSA was attempted. The dithiooxadiazoline was not expected to be unstable at 25 °C. Surprisingly, the product obtained was identified as triethylorthothioformate **(59)**[49]. The product was isolated by chromatography in 50 % yield. The formation of this product can be visualized as proceeding through insertion of dithiocarbene **60** into the S-H bond of ethyl mercaptan.



53 **60** **59** (50 %)

This observation illustrated that the dithiooxadiazoline was highly unstable as it decomposed to form the carbene even at room temperature. However, this fast rate of decomposition could be catalyzed by the acid. Therefore, the exchange reaction of oxadiazoline **53** was attempted with ethyl mercaptan without acid catalysis. Unfortunately, the oxadiazoline failed to exchange even after two weeks and the oxadiazoline remained unchanged.

In order to confirm that the di(ethylthio)oxadiazoline **(61)** was indeed formed, the exchange under similar conditions was carried out except that the reaction mixture was kept in a refrigerator during the exchange. Proton and carbon NMR spectra were taken for the crude mixture and it was confirmed that **61** was present. Another mercaptan, thiophenol, was added into this crude reaction mixture and left at room temperature for a day. Most of the dithiocarbene was trapped by thiophenol forming diethyl-phenylorthothioformate **(62)**. This is expected because thiophenol is more acidic than ethanethiol and should be a better trap.



53 **61** **60** **62**

This result confirmed the existence of the dithiocarbene. Since the formation of dimers is usually taken as diagnostic of carbene generation, thermolysis of **61** in benzene was attempted hoping to find carbene dimers. In order to do that, the fragile oxadiazoline **61** was carefully purified so that it was free of acid and excess ethyl mercaptan. First, the crude exchange mixture was extracted several times with ice-cold aqueous sodium bicarbonate to remove all the acid, dried with magnesium sulfate, filtered and then the solvent was evaporated at low temperature. The excess ethyl mercaptan was evaporated with pumping under vacuum for one hour, again at ice water temperature to prevent decomposition as much as possible. The purified oxadiazoline was dissolved in benzene, then transferred to a sealed tube. It was thermolyzed at 60 °C for 6 hours. Unfortunately, the thermolysis yielded **59** again. This happened probably because the pumping was carried out at a temperature so low that the vapor pressure of the ethyl mercaptan was insufficient to remove all the mercaptan.

The overall observation is that oxadiazoline **61** is very unstable, and that the thermolysis proceeds at room temperature, forming the carbene. Several S-H insertions have been observed, indicating that S-H insertion occurs in the same way as the O-H insertion.

Chapter 3

Summary

The utility of the exchange reaction of 2-acetoxy-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline to generate interesting new oxythiooxadiazolines **31a-d** was demonstrated. These oxythiooxadiazolines generate carbenes **33a-d** by losing nitrogen and acetone upon thermolysis at about 60-70 °C, which is about 30-40 °C lower than that of dioxyoxadiazolines. Most of these oxythiocarbene reactions with various carbene traps have shown very similar basic chemistry to analogous dioxycarbene reactions, only a few interesting differences were revealed.

Some attempts were made to generate dithiocarbene **60** from the oxadiazoline precursor which was prepared from 2-acetoxy-2-ethylthio-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline exchange reaction. There was some evidence that the dithiocarbene was generated since several S-H insertion products were obtained from the exchange. The dithiooxadiazoline **61** was found to be extremely unstable at room temperature and easily decomposed to di(ethylthio)carbene.

Chapter 4

Experimental

General

Proton nuclear magnetic resonance (^{1}H NMR) data were recorded on a Varian EM-390 90 MHz spectrometer, a Bruker AC-200 or a Bruker AC-300 spectrometer. Chemical shifts are reported in parts per million (δ) from an internal standard of tetramethylsilane (TMS) or relative to the residual solvent peak for benzene-d_6 at 7.15 ppm. Splitting patterns are designated as: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; bs, broad singlet. Coupling constants are reported in Hertz (Hz). Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were obtained at 50 MHz or 75 MHz on Bruker AC-200 or AC-300 spectrometers, respectively. The chemical shifts are reported relative to the center line of the triplet from chloroform-*d* at 77.0 ppm.

This standard procedure was followed for the rate constant measurements for decomposition of oxadiazolines **31a-c** and **53**. Oxadiazolines (ca. 0.02 g) were each dissolved in C_6H_6 (0.5 mL) containing p-xylene (internal standard), degassed (three freeze-pump-thaw cycles) and sealed in a NMR tube. Tubes were heated to 60 °C in a constant-temperature oil bath. The rate constants were determined by following the decay of the oxadiazoline signals by ^{1}H NMR spectroscopy.

Centrifugal chromatography was performed with silica gel (Merck Kieselgel 60

PF_{254}) coated plates (1 mm, 2 mm or 4 mm thick) spinning in a Chromatotron Model 7924T apparatus. Analytical thin layer chromatography was performed with silica plates (E. Merck, D-Plastikfolien, Kieselgel 60 PF_{254}). Column chromatographic separations were carried out using silica gel (E. Merck 60, 230-400 mesh). Preparative gas chromatography (prep-GC) separation was carried out with a HP 5890 GC with thermal conductivity detector (TCD) (phase: OV-17, size: 6'x0.25'', initial temperature: 100 °C, rate: 2.0 °C/minute, detector temperature: 175 °C, injector temperature: 160 °C). Gas chromatographic analyses were carried out with a Varian Vista 6000 GC with flame ionization detector (FID).

Gas chromatography Fourier Transformation Infrared (GC-FTIR) spectra were run on a HP 5890 GC connected to a Bio-Rad FTS-40 FTIR spectrometer with a Bio-Rad GC/C 32 GC interface. Infrared spectra (IR) were obtained on a Bio-Rad FTS-40 FTIR spectrometer. Peak intensities are designated qualitatively as: s, strong; m, medium; b, broad.

Gas chromatography mass spectra (GCMS) were obtained on a HP 5890 series II GC with a 5971A mass selective detector. Low resolution EI and CI mass spectra (LRMS) were obtained using a VG Analytical ZAB-E double focusing mass spectrometer.

Kugelrohr distillations were carried out with a BÜCHI GKR-50 instrument.

Melting points were determined on a Thomas Hoover capillary melting point apparatus.

Compounds reported without a reference to the literature are new.

X-Ray Crystallography

Crystals of **t-34b** and **39d** were grown from toluene.

Both x-ray crystallographic studies were carried out by Dr. J. F. Britten, McMaster University, Hamilton, Ontario. The x-ray crystallographic data for **t-34b** were collected on a Siemens P4 diffractometer with a rotating anode and graphite-monochromated Mo Kα radiation (λ = 0.71073 Å), whereas data for **39d** were collected on a Siemens P3 diffractometer with a standard anode and graphite-monochromated Ag Kα radiation (λ = 0.56086 Å). The background measurements were obtained by using a stationary crystal and stationary counter at the beginning and end of the scan, each for 25 % of the total scan time. The scan type used were θ-2θ. The scan speed were variable (3-60 ^{0}C/min), In both **t-34b** and **39d,** three standard reflections were measured after every 97 reflections showed no instrument instability and only minor crystal decay. Crystal data for **t-34b** and **39d** are listed in Appendix 1 and 2, respectively.

1.0. Synthesis of (Methoxycarbonyl)hydrazone of Acetone (12).

Methylhydrazinocarboxylate (10.02 g, 0.111 mol) was dissolved in acetone (30 mL) with stirring. Anhydrous $MgSO_4$ (3 g) was added to the solution and the mixture was stirred for 16 hours at room temperature. Upon completion, the mixture was filtered and the solvent was evaporated to afford **12**[48] as a white solid with melting point of 84-86 °C. ^{1}H NMR (90 MHz, $CDCl_3$) δ: 1.87 (s, 3H), 2.07 (s, 3H), 3.87 (s, 3H), 7.75 (bs, 1H).

2.0. Synthesis of 2-Acetoxy-2-methoxy-5,5-dimethyl -Δ^3-1,3,4-oxadiazoline (13).

Hydrazone **12** (5.07 g, 0.039 mol) was dissolved in CH_2Cl_2 (30 mL) with stirring. Acetic acid (1 mL) was added into the solution.[31] The solution was cooled in an ice bath and stirred prior to the addition of lead tetraacetate (18.4 g, 0.042 mol). The ice bath was removed after five minutes and the solution was stirred continuously for 1 hour at room temperature. Upon completion, the solids were removed by filtration and the filtrate was extracted three times with 5 % $NaHCO_3$. The combined CH_2Cl_2 layers were dried over anhydrous $MgSO_4$, the solids were removed by filtration and the solvent was evaporated using a rotary evaporator. The reaction yielded two products: 70 % of 2-acetoxy-2-methoxy-5,5-dimethyl -Δ^3-1,3,4-oxadiazoline **(13)** and 30 % of acyclic by-product **(14)**. The yields were determined by NMR spectroscopy and no extra signals were detected.

Oxadiazoline **13**[31]: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.55 (s, 3H), 1.66 (s, 3H), 2.11 (s, 3H), 3.61 (s, 3H).

Acyclic by-product **14**[31]: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.65 (s, 6H), 2.13 (s, 3H), 4.00 (s, 3H).

2.1. Synthesis of 2-Methoxy-5,5-dimethyl-2-phenylthio-Δ^3-1,3,4-oxadiazoline (31a).

A catalytic amount of p-toluenesulfonic acid (PTSA) (ca. 0.40g) was dried by azeotropic distillation (1 hour) of water from boiling benzene (10 mL) in a flask connected to a Dean and Stark trap containing molecular sieves. The solution was allowed to cool to room temperature before crude oxadiazoline **13** (total weigh = 5.0 g, 64 %, 0.017 mol of

13) and thiophenol (2.0 mL, 0.019 mol) dissolved in CH_2Cl_2 were added. The total volume (initial plus rinses) of CH_2Cl_2 was 40 mL. This final mixture was refluxed in a Dean and Stark apparatus for about 16 hours under N_2, then brought to room temperature. Some KOH pellets were added into the mixture and the whole stirred vigorously for about 2 hours to hydrolyze the oxidation by-product. Later, the mixture was extracted several times with water. The combined organic layers were dried over anhydrous $MgSO_4$. The solids were removed by filtration and the solvent evaporated by using a rotary evaporator, leaving a crude residue which was purified by centrifugal chromatography on a 4 mm plate eluting with hexane. The pure oxadiazoline **31a** was a white solid with melting point of 38-39 °C. The exchange yield was 69 % (2.79 g) based on oxadiazoline **13**.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.14 (s, 3H), 1.50 (s, 3H), 3.52(s, 3H), 7.28-7.34 (m, 3H), 7.57-7.63 (m, 2H); ^{1}H NMR (200 MHz, C_6D_6) δ: 0.97 (s, 3H), 1.15 (s, 3H), 3.25 (s, 3H), 6.93-6.96 (m, 3H), 7.68 -7.73 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 22.6 (CH_3), 25.0 (CH_3), 52.2 (OCH_3), 122.8 (C5), 128.8 (Ph), 129.0 (Ph), 129.2 (Ph), 135.7 (Ph), 137.2 (C2); IR (CCl_4, ν_{max}) cm^{-1}: 3064, 2993, 2943, 1477, 1441, 1366, 1264, 1238, 1204, 1128 (s), 1064(s), 1025, 976(m), 959(m), 911, 826, 692, 581, 516; MS (EI) m/z (rel. intensity): 207 $[M\text{-}OCH_3]^+$ (5), 169 (7), 153 (24), 137 (30), 129 $[M\text{-}SPh]^+$ (69), 109 $[SPh]^+$ (100).

2.2. Synthesis of 2-Benzylthio-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (31b).

This reaction was carried out in a manner similar to the synthesis of **31a**. Benzyl mercaptan (5.9 mL, 0.050 mol) was substituted for thiophenol. Crude oxadiazoline **13**

(15.0 g, 63 %, 0.050 mol of **13**), CH_2Cl_2 (120 mL) and previously dried PTSA (ca. 1.0 g) were used. Standard workup furnished crude product, which was subjected to centrifugal chromatography (4 mm plate, 5 % EtOAc/hexane). The pure oxadiazoline **31b** was obtained as a clear liquid in 44 % yield (5.58 g).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.53 (s, 3H), 1.57 (s, 3H), 3.40 (s, 3H), 4.09 (d, 1H, ^2J = -12.7 Hz), 4.20 (d, 1H, ^2J = -12.7 Hz), 7.24-7.36 (m, 5H); ^{1}H NMR (200 MHz, C_6D_6) δ: 1.20 (s, 3H), 1.24 (s, 3H), 3.17 (s, 3H), 4.08 (d, 1H, ^2J = -12.9 Hz), 4.20 (d, 1H, ^2J = -12.9 Hz), 6.96-7.09 (m, 3H), 7.21-7.26 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 23.1 (CH_3), 24.8 (CH_3), 34.8 ($S\underline{C}H_2Ph$), 51.5 (OCH_3), 122.6 (C5), 127.1 (Ph), 128.4 (Ph), 128.9 (Ph), 136.6 (C2), 137.1 (Ph); IR (CCl_4, ν_{max}) cm^{-1}: 3087, 3031, 2992, 2941, 2839, 1603, 1496, 1457, 1368, 1237, 1203, 1124 (s), 1069 (s), 979 (m), 910, 828, 703 (m); MS (EI) m/z (rel. intensity): 221 $[M\text{-}OCH_3]^+$ (2), 183 (5), 167 (14), 135 (17), 133 (37), 129 $[M\text{-}SCH_2Ph]^+$ (62), 91 $[CH_2Ph]^+$ (100), 73 (70); MS (CI, NH_3) m/z: 270 $[M+NH_4]^+$ (44), 253 $[M+H]^+$ (7).

2.3. Synthesis of 2-Ethylthio-2-methoxy-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline (31c).

The method in this experiment was similar to that used in the synthesis of **31a**. Crude oxadiazoline **13** (15.0 g, 70 %, 0.056 mol of **13**) and ethanethiol (97 %, 4.69 mL, 0.062 mol) were dissolved in CH_2Cl_2 (120 mL) and previously dried PTSA (ca. 1.06 g) was added. The solution was heated to 45 °C in a sealed tube for about 16 hours. Standard workup afforded crude product which was purified by chromatography (5 %

EtOAc/hexane) to give oxadiazoline **31c** as a clear liquid in 57 % isolated yield (6.05 g). ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.35 (t, 3H, ^{3}J = 7.5 Hz), 1.54 (s, 3H), 1.57 (s, 3H), 2.81 (dq, 1H, ^{2}J = -12.9, ^{3}J = 7.5 Hz), 2.95 (dq, 1H, ^{2}J = -12.9, ^{3}J = 7.5 Hz), 3.44 (s, 3H); ^{1}H NMR (200 MHz, C_6D_6) δ: 1.17 (t, 3H, ^{3}J = 7.4 Hz), 1.20 (s, 3H), 1.27 (s, 3H), 2.66 (dq, 1H, ^{2}J = -13.0, ^{3}J = 7.4 Hz), 2.88 (dq, 1H, ^{2}J = -13.0, ^{3}J = 7.4 Hz), 3.21 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 15.2 ($SCH_2\underline{C}H_3$), 23.0 (CH_3), 24.5 ($S\underline{C}H_2CH_3$), 24.7 (CH_3), 51.3 (OCH_3), 122.0 (C5), 136.9 (C2); IR (CCl_4, ν_{max}) cm^{-1}: 2991 (m), 2938 (m), 2874, 2837, 1456 (m), 1371, 1268, 1237, 1203 (m), 1180, 1124 (s), 1070 (s), 977 (m), 910 (m), 827, 625, 580; MS (EI) m/z (rel. intensity): 129 $[M\text{-}SCH_2CH_3]^+$ (8), 105 (10), 84 (28); MS (CI, NH_3): 189 $[M\text{-}H]^+$.

2.4. Synthesis of 2-Methoxy-5,5-dimethyl-2-methylthio-Δ^3-1,3,4-oxadiazoline (31d).

An excess amount of methyl mercaptan gas was dried by passing through a column packed with anhydrous $MgSO_4$, then liquidified into a tube immersed in dry ice. Crude oxadiazoline **13** (15.0 g, 63 %, 0.050 mol of **13**) and previously dried PTSA (ca. 1.0 g) were dissolved in CH_2Cl_2 (final volume = 120 mL). After transferring the solution into the tube containing the CH_3SH, the tube was sealed, then immersed in an oil bath at 45 °C for about 16 hours. Standard workup gave the crude product, which was purified by chromatography (4 mm plate, 5 % EtOAC/hexane). Oxadiazoline **31d** was isolated as a clear liquid in 80 % yield (7.07 g).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.55 (s, 3H), 1.57 (s, 3H), 2.33(s, 3H), 3.46 (s, 3H); ^{1}H

NMR (200 MHz, C_6H_6) δ: 1.20 (s, 3H), 1.25 (s, 3H), 2.09 (s, 3H), 3.20 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 12.9 (SCH_3), 23.2 (CH_3), 24.9 (CH_3), 51.4 (OCH_3), 122.6 (C5), 136.6 (C2); IR (CCl_4, ν_{max}) cm^{-1}: 2993, 2940, 2893, 2836, 1561, 1459, 1437, 1367, 1237, 1203, 1124 (s), 1072 (s), 999, 980, 949, 910, 827, 702, 682, 626, 581; MS (EI) m/z (rel. intensity): 176 $[M]^+$ (2), 145 $[M\text{-}OCH_3]^+$ (3), 129 $[M\text{-}SCH_3]^+$ (24), 90 (34), 75 (100); MS (CI, NH_3) m/z: 177 $[M+H]^+$ (12), 194 $[M+NH_4]^+$ (8).

3.1. Thermolysis of Oxadiazoline 31a in Benzene.

Oxadiazoline **31a** (0.209 g, 0.877 mmol) in benzene (10 mL) was refluxed under N_2 in an apparatus fitted with a Dean and Stark trap for 16 hours. Upon completion, the solvent was evaporated, and the residue was purified by chromatography on a 1 mm plate using hexane for elution. The reaction gave as major products, *cis* and *trans*-1,2-dimethoxy-1,2-bis(phenylthio)ethene (**c, t-34a**), which were separated from each other, and minor product, methyl phenylthiocarbonate (**35**)[50]. An authentic sample of **35** was prepared by treating methyl chloroformate with thiophenol in the presence of pyridine. ^1H NMR indicated the yields from oxadiazoline **13** versus internal standard of these products as 48 % of **t-34a**, 40 % of **c-34a** and 8 % of **35**. The isolated yields were 35 % (0.0467 g), 20 % (0.0267 g) and 7 % (0.0103 g), respectively.

The rate constant for decomposition of oxadiazoline **31a** at 60 °C was found to be 2.04×10^{-5} s^{-1} ($t_{1/2}$ = 9.45 hours, R^2 = 0.998).

trans-1,2-Dimethoxy-1,2-bis(phenylthio)ethene (**t-34a**): white solid, melting point 53-55

°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.55 (s, 6H), 7.17-7.42 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 58.5 (OCH_3), 126.7 (Ph), 129.0 (Ph), 129.5 (Ph), 133.6 (Ph), 142.8 (C=C); IR (CCl_4, ν_{max}) cm^{-1}: 3065, 3007, 2963, 2932, 2892, 2830, 1718, 1657, 1583 (m), 1479 (m), 1442 (m), 1206 (s), 1146 (s), 1121, 1081, 1023, 954, 909, 870, 832, 692 (s), 520; MS (EI) m/z (rel. intensity): 304 $[M]^+$ (100), 261 (94), 218 (33), 195 (13), 153 (29), 109 (75).

cis-1,2-Dimethoxy-1,2-bis(phenylthio)ethene (**c-34a**): clear liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.67 (s, 6H), 7.15-7.36 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 58.6 (OCH_3), 126.4 (Ph), 128.3 (Ph), 129.1 (Ph), 134.2 (Ph), 143.2 (C=C); IR (CCl_4, ν_{max}) cm^{-1}: 3066, 3004, 2965, 2935, 2894, 2832, 1581 (m), 1479 (m), 1442, 1264, 1198 (s), 1122 (s, br), 1085, 1025 (m), 1006, 959, 692 (m), 566; MS (EI) m/z (rel. intensity): 304 $[M]^+$ (100), 261 (95), 195 (15), 109 (80).

Methyl phenylthiocarbonate (**35**)[50]: clear liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.84 (s, 3H), 7.39-7.42 (m, 3H), 7.51-7.55 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 54.5 (OCH_3), 127.6 (Ph), 129.2 (Ph), 129.6 (Ph), 134.8 (Ph), 170.2 (C=O); IR (CCl_4, ν_{max}) cm^{-1}: 3066, 3008, 2954, 2888, 2836, 1730 (s), 1480, 1435, 1189 (m), 1143 (s, br), 1093, 1025, 689, 673, 532; MS (EI, GCMS) m/z (rel. intensity): 168 $[M]^+$ (38), 137 $[M\text{-}OCH_3]^+$ (3), 124 (16), 109 $[M\text{-}CO_2CH_3]^+$ (100), 91 (32), 78 (22), 69 (23), 65 (37).

3.2. Thermolysis of Oxadiazoline 31b in Benzene.

This reaction was carried out in the same manner as the thermolysis of oxadiazoline **31a** in benzene. Oxadiazoline **31b** (0.155 g, 0.615 mmol) in benzene (10 mL)

was refluxed under N_2 using a Dean and Stark trap. This reaction gave the corresponding *trans* and *cis*-1,2-bis(benzylthio)-1,2-dimethoxyethene, in a 1.3 : 1.0 ratio, respectively, by ^{1}H NMR integration. The crude product mixture was purified by chromatography on a 1 mm plate with hexane. The isolated yields of the *trans* and *cis* carbene dimers were 32 % (0.0205 g) and 27 % (0.01731 g), respectively.

The rate constant for decomposition of oxadiazoline **31b** at 60 °C was found to be 2.9 x 10^{-5} s^{-1} ($t_{1/2}$ = 9.2 hours, R^2 = 0.988).

trans-1,2-Bis(benzylthio)-1,2-dimethoxyethene **(t-34b)**: white crystalline solid, melting point 82-84 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.21 (s, 6H), 3.75 (s, 4H), 7.15-7.30 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 35.9 (S<u>C</u>H_2Ph), 57.9 (OCH_3), 126.9 (Ph), 128.3 (Ph), 128.8 (Ph), 138.6 (Ph), 143.5 (C=C); IR (CCl_4, ν_{max}) cm^{-1}: 3086, 3064, 3031, 3003, 2962, 2933, 2894, 2827, 1601, 1496, 1454, 1427, 1238, 1203 (s), 1136 (s), 1112, 1071, 954 (m), 700 (s), 672, 561; MS (EI) m/z (rel. intensity): 332 $[M]^+$ (4), 241 $[M\text{-}CH_2Ph]^+$ (45), 91 $[CH_2Ph]^+$ (100); MS (CI, NH_3) m/z: 333 $[M+H]^+$ (100), 350 $[M+NH_4]^+$ (74); X-ray crystallographic data were obtained (Appendix 1).

cis-1,2-Bis(Benzylthio)-1,2-dimethoxyethene **(c-34b)**: yellow liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.54 (s, 6H), 3.63 (s, 4H), 7.19-7.31 (m, 10H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 37.1 (S<u>C</u>H_2Ph), 58.6 (OCH_3), 127.0 (Ph), 128.3 (Ph), 129.0 (Ph), 137.9 (Ph), 144.1 (C=C); IR (CCl_4, ν_{max}) cm^{-1}: 3086, 3064, 3031, 3001, 2935, 2898, 2828, 1581, 1496, 1455, 1266, 1239, 1195 (m), 1141, 1105 (s), 1073, 1026, 957, 700 (s), 671, 562; MS (EI) m/z (rel. intensity): 332 $[M]^+$ (6), 241 $[M\text{-}CH_2Ph]^+$ (68), 91 $[CH_2Ph]^+$ (100); MS (CI,

NH_3) m/z: 333 $[M+H]^+$ (100), 350 $[M+NH_4]^+$ (28).

3.3. Thermolysis of Oxadiazoline 31c in Benzene.

A method similar to that employed in the thermolysis of oxadiazoline **31a** in benzene was used to examine the thermolysis of oxadiazoline **31c** (0.163 g, 0.856 mmol) which was refluxed in benzene (10 mL). The reaction produced *trans* and *cis*-1,2-bis(ethylthio)-1,2-dimethoxyethene in a 1.4 : 1.0 ratio, as measured by ^{1}H NMR integration. The *trans* and *cis* dimers were separated by chromatography (1 mm plate, hexane) to give isolated yields of 36 % (0.0304 g) and 29 % (0.025 g), respectively.

The rate constant for decomposition of oxadiazoline **31c** at 60 °C was found to be 2.07×10^{-5} s^{-1} ($t_{1/2}$ = 9.3 hours, R^2 = 0.967).

trans-1,2-Bis(ethylthio)-1,2-dimethoxyethene (**t-34c**): clear liquid; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.25 (t, 6H, ^{3}J = 7.3 Hz), 2.66 (q, 4H, ^{3}J = 7.3 Hz), 3.61 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 15.1 ($SCH_2\underline{C}H_3$), 25.4 ($S\underline{C}H_2CH_3$), 58.0 (OCH_3), 143.1 (C=C); IR (GC-FTIR, gas phase, ν_{max}) cm^{-1}: 3001, 2971 (m), 2939 (s), 2887, 2836, 1456 (br), 1381, 1266, 1200 (s), 1142 (s, br), 1053, 1021, 961, 804, 765; Raman (neat) cm^{-1}: 3000, 2962, 2929 (s), 2902, 2874, 2826, 1596 (s), 1449, 1428, 1113, 1055, 1003, 681, 656 (m); MS (EI) m/z (rel. intensity): 208 $[M]^+$ (15), 193 (4), 179 $[M-CH_2CH_3]^+$ (29), 165 $[M-COCH_3]^+$ (13), 151 (6), 135 (3), 119 (16), 84 (67), 75 (39), 49 (100); MS (CI, NH_3) m/z: 209 $[M+H]^+$ (100).

cis-1,2-Bis(ethylthio)-1,2-dimethoxyethene (**c-34c**): clear liquid; ^{1}H NMR (200 MHz,

$CDCl_3$) δ: 1.27 (t, 6H, ^3J = 7.3 Hz), 2.65 (q, 4H, ^3J = 7.3 Hz), 3.68 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.7 ($SCH_2\underline{C}H_3$), 26.4 ($S\underline{C}H_2CH_3$), 58.8 (OCH_3), 143.4 (C=C); IR (GC-FTIR, gas phase, ν_{max}) cm^{-1}: 2972, 2939 (m), 2887, 2836, 1579, 1457, 1381, 1265, 1194 (s), 1114 (s, br), 1026, 967, 863, 764; Raman (neat) cm^{-1}: 1581 (s), 1451, 1430, 1054, 968, 953, 679, 653 (s); MS (EI) m/z (rel. intensity): 208 $[M]^+$ (86), 193 (15), 179 $[M-CH_2CH_3]^+$ (100), 165 $[M-COCH_3]^+$ (45), 151 (31), 135 (2), 119 (16), 75 (33); MS (CI, NH_3) m/z: 209 $[M+H]^+$ (100).

3.4. Thermolysis of Oxadiazoline 31d in Benzene.

A method similar to that employed in the thermolysis of oxadiazoline **31a** in benzene was used to examine the thermolysis of oxadiazoline **31d** (0.37 g, 2.1 mmol) which was refluxed in benzene (15 mL). The reaction produced *trans* and *cis*-1,2-dimethoxy-1,2-bis(methylthio)ethene in a 1.2 : 1.0 ratio, as measured by ^1H NMR integration. The *trans* and *cis* dimers was separated by chromatography (hexane) to give isolated yields of 32 % (0.0613 g) and 27 % (0.0503 g), respectively.

The rate constant for decomposition of oxadiazoline **31d** at 60 °C was found to be 2.07×10^{-5} s^{-1} ($t_{1/2}$ = 9.3 hours, R^2 = 0.967).

trans-1,2-Dimethoxy-1,2-bis(methylthio)ethene **(t-34d)**: clear liquid; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.20 (s, 6H), 3.63 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.5 (SCH_3), 58.2 (OCH_3), 142.8 (C=C); IR (GC-FTIR, gas phase, ν_{max}) cm^{-1}: 3005, 2963, 2938 (m), 2909, 2837, 1445, 1319, 1203 (s), 1143 (s), 1023, 960, 807; MS (EI, GCMS) m/z (rel.

intensity): 180 $[M]^+$ (10), 165 $[M-CH_3]^+$ (22), 137 (74), 75 (100); MS (CI, NH_3) m/z: 181 $[M+H]^+$ (100).

cis-1,2-Dimethoxy-1,2-bis(methylthio)ethene (**c-34d**): ^1H NMR (200 MHz, $CDCl_3$) δ: 2.21 (s, 6H), 3.68 (s, 6H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 15.3 (SCH_3), 58.8 (OCH_3), 143.0 (C=C); IR (GC-FTIR, gas phase, ν_{max}) cm^{-1}: 3002, 2938 (m), 2838, 1584, 1445, 1315, 1194 (s), 1115 (s, br), 1030, 964, 866; MS (EI, GCMS) m/z (rel. intensity): 180 $[M]^+$ (10), 165 $[M-CH_3]^+$ (23), 137 (77), 75 (100); MS (CI, NH_3) m/z: 181 $[M+H]^+$ (100).

4. Thermolyses of Oxadiazoline 31a-d in the Presence of Phenol.

Phenol was dried by azeotropic distillation of water from boiling benzene for 1 hour in an apparatus fitted with a Dean and Stark trap containing molecular sieves. The solution was brought to room temperature before oxadiazoline was added into the stirring phenol solution. It was then refluxed under N_2 in the Dean and Stark apparatus for about 16 hours. Upon completion, the solution was cooled to room temperature and the benzene was evaporated. The remainder was dissolved in CH_2Cl_2, and extracted with 4 % Na_2CO_3. The organic layer was collected and dried over anhydrous $MgSO_4$. After the solids were removed by filtration and the solvent was evaporated, the carbene adduct was obtained.

4.1. From oxadiazoline **31a** (0.145 g, 0.610 mmol), phenol (ca. 0.12 g) and benzene (15 mL), there was obtained 0.128 g (85 %) of 1-methoxy-1-phenoxy-1-(phenylthio)methane (**36a**) as a clear liquid. ^1H NMR (200 MHz, $CDCl_3$) δ: 3.57 (s, 3H), 6.44 (s, 1H), 7.02-

7.07 (m, 3H), 7.24-7.32 (m, 5H), 7.47-7.58 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 51.5 (OCH_3), 109.0 (C1), 117.3, 122.9, 128.0, 129.0, 129.5, 132.3, 133.3, 156.1 (8 Ph); IR (CCl_4, ν_{max}) cm^{-1}: 3067, 3010, 2967, 2943, 2893, 2833, 1594 (m), 1491 (m), 1439, 1293, 1272, 1214 (s), 1171, 1081 (s, br), 1024 (s, br), 991, 914, 850, 693 (s), 508; MS (EI) m/z (rel. intensity): 231 $[M\text{-}CH_3]^+$ (5), 215 $[M\text{-}OCH_3]^+$ (4), 153 $[M\text{-}OPh]^+$ (100), 137 $[M\text{-}SPh]^+$ (92).

4.2. From oxadiazoline **31b** (0.104 g, 0.412 mmol), phenol (ca. 0.05 g) and benzene (10 mL), there was obtained 0.089 g (83 %) of 1-(benzylthio)-1-methoxy-1-phenoxymethane **(36b)** as a clear liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.42 (s, 3H), 3.74 (d, 1H, ^2J = -14.8 Hz), 3.83 (d, 1H, ^2J = -14.8 Hz), 6.15 (s, 1H), 6.95-7.01 (m, 5H), 7.18-7.28 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 33.5 ($S\underline{C}H_2Ph$), 51.1 (OCH_3), 105.7 (C1), 116.9, 122.6, 126.9, 128.3, 128.7, 129.3, 137.7, 156.0 (8 Ph); IR (CCl_4, ν_{max}) cm^{-1}: 3066, 3033, 2966, 2942, 2910, 2832, 1596 (m), 1494 (s), 1457, 1295, 1216 (s), 1198 (m), 1170, 1080 (s, br), 1033 (s), 991 (m), 915, 697 (s); MS (EI) m/z (rel. intensity): 229 $[M\text{-}CH_3O]^+$ (4), 167 $[M\text{-}PhO]^+$ (92), 137 $[M\text{-}SCH_2Ph]^+$ (85), 91 $[CH_2Ph^+]$ (100), 77 (32); MS (CI, NH_3) m/z: 259 $[M\text{-}H]^+$.

4.3. From oxadiazoline **31c** (0.10 g, 0.53 mmol), phenol (ca. 0.06 g) and benzene (20 mL), there was obtained 0.0573 g (55 %) of 1-(ethylthio)-1-methoxy-1-phenoxymethane **(36c)** as a clear liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.32 (t, 3H, ^3J = 7.4 Hz), 2.68 (dq,

2H, ^{3}J = 7.4 Hz, overlapping quartets with ^{2}J<-0.01 Hz), 3.49 (s, 3H), 6.32 (s, 1H), 7.00-7.09 (m, 3H), 7.25-7.34 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 15.1 ($SCH_2\underline{C}H_3$), 23.3 ($S\underline{C}H_2CH_3$), 51.3 (OCH_3), 106.5 (C1), 117.1, 122.7, 129.4, 156.2 (4 Ph); IR (CCl_4, ν_{max}) cm^{-1}: 3069, 2969, 2880, 2832, 1595, 1494 (m), 1295, 1216 (s), 1197 (m), 1170, 1080 (s), 1026 (m), 983 (m), 916 (m), 852, 692, 645, 591; MS (EI) m/z (rel. intensity): 198 $[M]^+$ (1), 167 $[M-OCH_3]^+$ (5), 137 $[M-SCH_2CH_3]^+$ (38), 105 $[M-PhO]^+$ (100), 77 (28); MS (CI, CH_4) m/z: 199 $[M+H]^+$.

4.4. From oxadiazoline **31d** (0.102 g, 0.581 mmol), phenol (ca. 0.07 g) and benzene (11 mL), there was obtained 0.0649 g (61 %) of 1-methoxy-1-(methylthio)-1-phenoxymethane **(36d)** as a clear liquid. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.14 (s, 3H), 3.48 (s, 3H), 6.22 (s, 1H), 7.00-7.08 (m, 3H), 7.22-7.34 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 11.4 (SCH_3), 51.4 (OCH_3), 106.9 (C1), 117.1, 122.8, 129.4, 156.1 (4 Ph); IR (CCl_4, ν_{max}) cm^{-1}: 3069, 3004, 2966, 2923, 2894, 2833, 1595 (m), 1494 (s), 1435, 1294, 1217 (s), 1196 (m), 1170, 1079 (s), 1034 (s), 971 (m), 915, 846, 692; MS (EI, GCMS) m/z (rel. intensity): 153 $[M-OCH_3]^+$ (6), 137 $[M-SCH_3]^+$ (29), 91 (100), 86 (31), 84 (46), 77 (22), 49 (58).

5. Thermolysis of Oxadiazoline 31a and c in the Presence of Ethyl Crotonate.

A mixture of oxadiazoline and ethyl crotonate in dry benzene was sealed in a tube and heated in an oil bath at 70 °C for about 16 hours. After evaporation of the solvent, the crude product was purified by centrifugal chromatography (hexane) on a 1 mm plate

which had been previously washed with triethylamine.

5.1. The reaction was carried out with the following compounds: oxadiazoline **31a** (0.120 g, 0.504 mmol), ethyl crotonate (96 %, 0.08 mL, 0.605 mmol) and benzene (10 mL). The separation yielded five products: a pair of substituted cyclopropanes **(38)** (35 %, 0.0469 g major isomer vs. 7 %, ca. 0.0094 g minor isomer), a pair of *cis* and *trans* carbene dimers (10 % **c-34a**, 0.0076 g and 18 % **t-34a**, 0.0137 g, respectively), and **35** (11 %, 0.0075 g).

1-(Ethoxycarbonyl)-2-methoxy-3-methyl-2-(phenylthio)cyclopropane (major diastereomer): ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.27 (dd, 3H, ^3J = 10.4, ^4J = 6.5 Hz), 1.28 (t, 3H, ^3J = 7.2 Hz), 1.83 (d, 1H, ^3J = 6.8 Hz), 2.27 (m, 1H, ^3J = 6.8, ^4J = 6.5 Hz), 3.37 (s, 3H), 4.19 (dq, 2H, ^3J = 7.2 Hz), 7.44-7.48 (m, 2H), 7.15-7.28 (m, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2 ($OCH_2\underline{C}H_3$), 28.9 (CH_3), 36.5 ($O\underline{C}H_2CH_3$), 54.9 (OCH_3), 60.9, 78,2, 110.7 (C1, C2 and C3), 126.1, 128.6, 128.8, 134.7 (4 Ph), 168.7 (C=O); IR (CCl_4, ν_{max}) cm^{-1}: 3064, 2981 (m), 2965 (m), 2934 (m), 2903, 2878, 2829, 1735 (m), 1584, 1480 (m), 1444 (m), 1416, 1367, 1318 (s), 1265 (m), 1228 (m), 1201 (m), 1170 (s, br), 1117 (m), 1098 (m), 1049 (m), 1024, 998 (m), 911, 864, 692; MS (EI) m/z (rel. intensity): 266 $[M]^+$ (3), 235 $[M\text{-}OCH_3]^+$ (18), 221 (32), 220 (100), 205 (25), 193 $[M\text{-}CO_2C_2H_5]^+$ (85), 161 (47), 157 $[M\text{-}SPh]^+$ (89), 129 (45), 109 (50), 69 (47); MS (CI, NH_3) m/z: 284 $[M+NH_4]^+$ (74), 267 $[M+H]^+$ (39).

1-(Ethoxycarbonyl)-2-methoxy-3-methyl-2-(phenylthio)cyclopropane (minor diastereomer) (peaks were subtracted from the spectrum of the diastereomeric mixtures):

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.15 (t, 3H, ^{3}J = 7.1 Hz), 1.27 (dd, 3H), 1.87 (d, 1H, ^{3}J = 7.2 Hz), 2.03 (m, ^{3}J = 7.2, ^{4}J = 6.2 Hz), 3.48 (s, 3H), 4.02 (m, 2H), 7.17-7.58 (m, 5H).

5.2. The reaction was carried out with the following compounds: oxadiazoline **31c** (0.193 g, 1.02 mmol), ethyl crotonate (96 %, predominantly *trans* from Aldrich, 0.65 mL, 5.22 mmol) and benzene (10 mL). The separation (centrifugal chromatography, on 1 mm plate, hexane) gave **t-34c** and **c-34c** and four diastereomers of the cyclopropane derivatives (**37 i-iv**). The collective yield of all four cyclopropane diastereomers was 26 % (0.0577 g). 1-(Ethoxycarbonyl)-2-ethylthio-2-methoxy-3-methylcyclopropane (in diastereomeric mixtures, **37 i-iv**): ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.22-1.35 (m, containing $SCH_2\underline{CH_3}$, CH_3, $OCH_2\underline{CH_3}$), 1.69 (d, ^{3}J = 6.9 Hz), 1.72 (d, ^{3}J = 5.7 Hz), 1.92 (m, 1H), 2.08 (dq, ^{4}J = 6.5, ^{3}J = 13.0 Hz), 2.66 (m, $S\underline{CH_2}CH_3$), 3.31 (s, OCH_3), 3.40 (s, OCH_3), 3.62 (s, OCH_3), 3.69 (s, OCH_3), 4.15 (q, ^{3}J = 7.1 Hz), 4.16 (q, ^{3}J = 7.1 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.1, 14.2, 14.7, 15.0, 24.5, 24.7, 25.4, 25.6, 28.2, 30.1, 35.7, 36.9, 53.7, 54.2, 54.3, 57.9, 58.6, 60.5, 77.8, 109,4, 109.6, 143.0, 143.3, 168.7, 169.4; IR (CCl_4, ν_{max}) cm^{-1}: 2977 (m), 2932 (m), 2871, 2828, 1735 (s), 1450, 1379, 1317, 1264, 1227, 1200, 1169 (s), 1119 (m), 1052, 996, 913, 865, 702, 578; MS (EI) m/z rel.(intensity): 218 $[M]^+$ (11) 189 $[M-C_2H_5]^+$ (10), 187 $[M-OCH_3]^+$ (17), 145 $[M-CO_2C_2H_5]^+$ (100), 129 (15), 105 (28); MS (CI, NH_3) m/z: 219 $[M+H]^+$.

6.1. Thermolysis of Oxadiazoline 31c in the Presence of Ethyl Acrylate.

Oxadiazoline **31c** (0.20 g, 1.0 mmol) and ethyl acrylate (0.14 mL, 1.3 mmol) in dry benzene (10 mL) were thermolyzed at 70 °C for about 16 hours in a sealed tube. After evaporation of the solvent, the crude product was purified by preparative GC. The isolated yields of the substituted cyclopropanes were less than 20 %.

1-(Ethoxycarbonyl)-2-ethylthio-2-methoxycyclopropane **(63)**, mixture of diastereomers in 1.5:1 ratio: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.22-1.37 (m, SCH_2CH_3, OCH_2CH_3), 1.46-1.57 (m, 3H), 1.81 (dd, ^4J = 5.8, ^3J = 6.6 Hz), 2.14 (m, 2H), 2.59-2.78 (m, SCH_2CH_3), 3.31 (s, OCH_3), 3.34 (s, OCH_3), 4.15 (q, 2H, ^3J = 7.1Hz), 4.16 (q, 2H, ^3J = 7.1Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2, 14.9, 21.6, 21.8, 25.0, 25.3, 30.5, 31.5, 53.4, 54.0, 54.8, 60.9, 129.6, 168.6; IR (CCl_4, ν_{max}) cm^{-1}: 2983, 2934, 2878, 2829, 1738 (s), 1455, 1446, 1375, 1350, 1261 (m), 1201, 1175 (s), 1147 (m), 1094, 1065 (m), 1035, 977, 889, 827, 690; MS (EI) m/z (rel. intensity): 204 $[M]^+$ (22), 175 $[M-C_2H_5]^+$ (21), 159 (14), 143 $[M-SCH_2CH_3]^+$ (13), 131 $[M-CO_2C_2H_5]^+$ (48), 86 (69), 84 (100).

7.1. Thermolysis of Oxadiazoline 31b in the Presence of Dichloromaleic Anhydride.

A mixture of oxadiazoline **31b** (0.205 g, 0.811 mmol) and dichloromaleic anhydride (0.15 g, 0.899 mmol) in dry benzene (10 mL) was heated in a sealed tube at 80 °C for about 16 hours. After evaporation of the solvent, the excess anhydride was removed by kugelrohr distillation at ca. 40 °C under vacuum (ca. 0.1 mm Hg). The pure carbene-anhydride adduct **39b** was collected at an oven temperature of ca. 70 °C as a

yellow crystalline solid in 75 % yield (0.2033 g). Its melting point was 69-70 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.54 (s, 3H), 3.75 (s, 2H), 7.29 (s, br, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 35.0 ($S\underline{C}H_2Ph$), 52.5 (OCH_3), 108.9 (C6), 127.7, 128.7, 129.1, 135.0 (4 Ph), 136.8 (C3), 141.3 (C4), 152.6 (C2), 173.5 (C5); IR (CCl_4, ν_{max}) cm^{-1}: 3087, 3032, 2949, 2894, 2840, 1762 (s, br), 1721 (s), 1583 (s), 1497, 1457, 1273 (m), 1234 (m), 1196 (m), 1163 (s), 1040 (s, br), 982 (m), 908, 885, 701 (s), 666 (m); MS (EI) m/z (rel. intensity): 337 (3), 335 (7), 333 [M (^{35}Cl, ^{35}Cl)+H]$^+$ (10), 259 (18), 214 (12), 213 (9), 212 (68), 211 (29), 210 [(M (^{35}Cl, ^{35}Cl)+H)-SCH_2Ph]$^+$, 98), 209 [M (^{35}Cl, ^{35}Cl)-SCH_2Ph]$^+$ (35), 185 (15), 184 (7), 183 (74), 182 (12), 181 (100), 123 (24), 91 (21); MS (CI, NH_3) m/z: 354 (17), 352 (68), 350 (100), 337 (9), 335 (27), 333 (36).

7.2. Thermolysis of Oxadiazoline 31c in the Presence of Dichloromaleic Anhydride.

A mixture of oxadiazoline **31c** (0.197 g, 1.03 mmol) and dichloromaleic anhydride(0.190 g, 1.14 mmol) in dry benzene (10 mL) was heated in a sealed tube at 70 °C for about 16 hours. After evaporation of the solvent, the pure carbene-anhydride adduct **39c** was obtained by kugelrohr distillation as a yellow crystalline solid in 89 % yield (0.250 g). Its melting point was 71-74 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.24 (t, 3H, ^{3}J = 7.5 Hz), 2.52 (dq, 1H, ^{2}J = -12.8, ^{3}J = 7.5 Hz), 2.60 (dq, 1H, ^{2}J = -12.8, ^{3}J = 7.5 Hz), 3.69 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.6 ($SCH_2\underline{C}H_3$), 24.7 ($S\underline{C}H_2CH_3$), 52.5 (OCH_3), 109.0 (C6), 136.6 (C3), 141.2 (C4), 152.7 (C2), 173.6 (C5); IR (CCl_4, ν_{max}) cm^{-1}: 2950, 2881, 1807, 1761 (s), 1722 (m),

1583, 1266, 1236, 1196, 1160 (m), 1102, 1040 (s, br), 982, 909, 886, 667; MS (EI) m/z (rel. intensity): 275 (2), 273 (4), 271 [M (^{35}Cl, ^{35}Cl)+H]$^+$ (6), 213 (13), 211 (27), 209 (18), 185 (20), 183 (73), 181 (100); MS (CI, NH_3) m/z: 292 (4), 290 (13), 288 [M (^{35}Cl, ^{35}Cl)+NH_4]$^+$ (20), 275 (20), 273 (95), 271 [M (^{35}Cl, ^{35}Cl)+H]$^+$ (100).

7.3. Thermolysis of Oxadiazoline 31d in the Presence of Dichloromaleic Anhydride.

A mixture of oxadiazoline **31d** (0.208 g, 1.2 mmol) and dichloromaleic anhydride (0.22 g, 1.3 mmol) in dry benzene (10 mL) was heated in a sealed tube at 70 °C for about 16 hours. After evaporation of the solvent, purification by kugelrohr distillation, gave the pure corresponding carbene-anhydride adduct **39d** as a yellow crystalline solid in 85 % yield (0.2575 g). Its melting point was 89-91 °C; X-ray crystallographic data were obtained (Appendix 2).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.06 (s, 3H), 3.70 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 12.9 (SCH_3), 52.2 (OCH_3), 108.6 (C6), 136.5 (C3), 141.2 (C4), 152.6 (C2), 172.7 (C5); IR (CCl_4, ν_{max}) cm^{-1}: 3502, 2995, 2948, 2839, 1805 (m), 1762 (s, br), 1721 (s), 1631, 1584 (s), 1460, 1436, 1271 (s), 1236 (s), 1196 (s), 1162(s, br), 1042 (s, br), 990 (s), 962, 909, 887, 826, 670 (m); MS (EI) m/z (rel. intensity): 225 (2), 223 (5), 221 (15), 213 (3), 211 (13), 209 (18), 201 (2), 199 (13), 197 (18), 185 (9), 183 (45), 181 (71); MS (CI, NH_3) m/z: 278 (6), 276 (20), 274 [M (^{35}Cl, ^{35}Cl)+NH_4]$^+$ (28), 261 (15), 259 (66), 257 [M (^{35}Cl, ^{35}Cl)+H]$^+$ (100).

8.1. Thermolysis of Oxadiazoline 31a in the Presence of Phenyl Isocyanate.

Oxadiazoline **31a** (0.204 g, 0.858 mmol) and phenyl isocyanate (0.19 mL, 1.74 mmol) in dry benzene (8 mL) were sealed in a tube and heated in an oil bath at 70 °C for about 16 hours. After evaporation of the solvent, MeOH was added to the residue and the whole stirred for about an hour. The MeOH was evaporated and the remainder was subjected to centrifugal chromatography (5 % EtOAc/hexane) on a 1 mm plate. The separation gave three products: 10 % (0.0335 g) of **40a**, 39 % (0.0908 g) of **43a-1**, and 28 % (0.0652 g) of **43a-2**.

1-Phenylcarbamoyl-3-methoxy-3-(phenylthio)oxindole (**40a**): white solid, melting point 139-140 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.56 (s, 3H), 7.03-7.15 (m, 3H), 7.33-7.58 (m, 9H), 8.32 (d, 1H, ^3J = 8.2 Hz), 10.36 (bs, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 53.8 (OCH_3), 87.9 (C3), 116.8, 120.6 , 124.2, 124.4, 124.7, 124.8, 128.6, 128.8, 129.1, 130.0, 130.9, 136.6, 136.8, 138.5 (14 Ph), 149.0 (NCON), 173.6 (C2); IR (CCl_4, ν_{max}) cm^{-1}: 3260 (br), 3064 (br), 2948, 2891, 2832, 1748 (s, br), 1600 (m), 1552 (s), 1503, 1470 (m), 1448, 1340, 1310, 1277, 1243, 1204, 1163 (m), 1112, 1088, 1022, 970, 913, 693 (m), 574, 505; MS (EI) m/z (rel. intensity): 314 $[M-C_6H_4]^+$ (3), 281 $[M-SPh]^+$ (16), 162 $[C_6H_5NH(CO)N(CO)]^+$ (100), 119 $[PhNCO]^+$ (54), 91(18); MS (CI, NH_3) m/z: 391 $[M+H]^+$.

2-[1'-(3-Methoxy-3-(phenylthio)oxindolyl)]-2-methoxy-2-(phenylthio)acetanilide (**43a-1**): white solid, melting point 169-171 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.52 (s, 3H), 3,58 (s, 3H), 6.86-7.54 (m, 20H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 51.2 (OCH_3), 54.2 (OCH_3),

87.7 (C3), 99.0 (C10), 111.7, 119.6, 119.9, 123.5, 124.6, 124.8, 125.1, 128.6, 128.7, 128.8, 129.0, 129.6. 129.9, 130.3, 136.1, 136.8, 137.4, 139.7 (18 Ph), 162.2 (C=O), 172.2 (C2); IR (CCl_4, ν_{max}) cm^{-1}: 3411, 3362, 3063, 3034, 2962, 2943, 2891, 2833, 1746 (s), 1718 (m), 1604 (m), 1527 (s), 1468, 1442 (m), 1336, 1311, 1279, 1243, 1183, 1158, 1086 (m, br), 1075 (m), 986, 909 (s), 692 (m), 503; MS (EI) m/z (rel. intensity): 447 (18), 433 $[M\text{-}SPh]^+$ (26), 405 (55), 272 (13), 162 (100), 146 (37), 120 (65), 110 (81), 109 (67), 77 (40).

.2-[1'-(3-Methoxy-3-(phenylthio)oxindolyl)]-2-methoxy-2-(phenylthio)acetanilide (**43a-2**): white solid, melting point 171-173 °C; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.62 (s, 3H), 3.68 (s, 3H), 6.80 (dd, 2H, ^3J = 41.2, ^3J = 25.3 Hz), 7.01-7.38 (m, 13H), 7.51-7.55 (m, 4H), 7.62 (s, br, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 51.4 (OCH_3), 53.6 (OCH_3), 87.7 (C3), 99.6 (C10), 112.1, 119.6, 123.2, 124.2, 124.6, 125.0, 128.5, 128.7, 128.8, 129.0, 129.4, 129.6, 129.8, 130.0, 136.4, 137.0, 137.3, 139.5 (18 Ph), 161.9 (C=O), 171.9 (C2); IR (CCl_4, ν_{max}) cm^{-1}: 3413, 3396, 3061, 2961, 2891, 2830, 1744 (s), 1719 (m), 1604 (m), 1525 (s), 1468, 1442 (m), 1337, 1312 (m), 1281, 1243, 1193, 1117, 1087, 1066 (m, br), 986, 909, 824, 691 (m), 504; MS (EI) m/z (rel. intensity): 433 $[M\text{-}SPh]^+$ (22), 405 (34), 272 (13), 162 (100), 110 (26), 109 (31), 77 (32); MS (CI, NH_3): 560 $[M+NH_4]^+$.

8.2. Thermolysis of Oxadiazoline 31d in the Presence of Phenyl Isocyanate.

A mixture of oxadiazoline **31d** (0.501 g, 2.84 mmol) and phenyl isocyanate (0.63 mL, 5.80 mmol) in dry benzene (25 mL) was refluxed under N_2 for about 16 hours. After

evaporation of the solvent, MeOH was added to the residue and the solution was stirred for an hour. The MeOH was evaporated and the crude residue was subjected to centrifugal chromatography (hexane). The separation afforded **40d** in 8 % yield (0.07472 g) and a mixture of **43d-1** and **43d-2** in 34 % yield (0.199 g) after recrystallization in MeOH.

1-Phenylcarbamoyl-3-methoxy-3-(methylthio)oxindole (**40d**): white solid, melting point 106-108 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.38 (s, 3H), 3.43 (s, 3H), 7.14-7.61 (m, 8H), 8.37 (d, 1H, ^3J = 8.0 Hz), 10.48 (br, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 10.9 (SCH_3), 53.1 (OCH_3), 83.5 (C3), 117.0, 120.6, 124.3, 124.4, 124.7, 125.1, 129.1, 131.2, 136.9, 138.8 (10 Ph), 149.1 (NCON), 174.1 (C2); IR (CCl_4, ν_{max}) cm^{-1}: 3298 (br), 3259 (br), 3145, 3082, 2959, 2931, 1748 (s), 1601 (s), 1553 (s), 1501, 1466 (m), 1448 (m), 1339 (m), 1311, 1277 (m), 1242 (m), 1209, 1166 (m), 1154, 1108 (m), 1087, 1024, 691, 677, 575, 506; MS (EI) m/z (rel. intensity): 328 $[M]^+$ (6), 281 $[M-SCH_3]^+$ (50), 207 (4), 162 $[PhNH(CO)N(CO)]^+$ (100), 146 (6), 119 (25); MS (CI, NH_3) m/z: 346 $[M+NH_4]^+$ (14), 329 $[M+H]^+$ (17).

2-[1'-(3-Methoxy-3-(methylthio)oxindolyl)]-2-methoxy-2-(methylthio)acetanilide, a mixture of **43d-1** and **43d-2** in a 2:1 ratio: white solid, melting point 181-182 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.12 (s, SCH_3), 2.39 (s, SCH_3), 3.33 (s, OCH_3), 3.54 (s, OCH_3), 8.41 (s, br), 2.13 (s, SCH_3), 2.36 (s, SCH_3), 3.40 (s, OCH_3), 3.53 (s, OCH_3), 8.23 (s, br), 7.08-7.61 (m, 17H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 10.8, 12.5, 51.2, 51.3, 53.4, 53.9, 82.6, 83.1, 96.6, 96.7, 109.0, 110.0, 111.0, 112.4, 112.8, 119.8, 119.9, 123.9, 124.6,

124.7, 124.9, 125.1, 129.1, 129.2, 130.8, 136.4, 136.6, 140.1, 162.9, 163.1, 172.9; IR (CCl_4, ν_{max}) cm^{-1}: 3414 (br), 3061, 2931, 2832, 1746 (s), 1717 (s), 1604 (m), 1525 (s), 1465, 1442 (m), 1338, 1309, 1279, 1243, 1196, 1180, 1117, 1095 (br), 1073, 690; MS (EI) m/z (rel. intensity): 387 $[M\text{-}OCH_3]^+$ (4), 371 $[M\text{-}SCH_3]^+$ (85), 343 (100), 298 (10), 270 (40), 210 (45), 208 (99), 162 (94), 119 (19), 77 (20); MS (CI, NH_3) m/z: 436 $[M+NH_4]^+$.

9. Thermolysis of Oxadiazoline 31d in the Presence of Dimethyl Acetylene Dicarboxylate (DMAD).

A mixture of oxadiazoline **31d** (0.329 g, 1.87 mmol) and DMAD (0.46 mL, 3.74 mmol) in benzene (20 mL) was sealed in a tube and heated at 70 °C for about 16 hours. Upon completion, the solvent was evaporated and the crude mixture was subjected to centrifugal chromatography (5 % EtOAc/hexane). The separation afforded at least five products, but only two products were identified.

2-Methoxy-2-methylthio-5,5-dimethyl-3,4-bis(methoxycarbonyl)-2,5-dihydrofuran (**47**), 6 % (0.0323 g) isolated yield: ^1H NMR (300 MHz, $CDCl_3$) δ: 1.54 (s, 3H), 1.57 (s, 3H), 2.11 (s, 3H), 3.48 (s, 3H), 3.81 (s, 3H), 3.86 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.1 (SCH_3), 26.0 (CH_3), 27.3 (CH_3), 51.3 (OCH_3), 52.5 (CO_2CH_3), 52.7 (CO_2CH_3), 88.5 (C5), 116.7, 137.7, 141.8 (C2, C3, and C4), 162.2 (C=O), 163.0 (C=O).

3,4-Furandicarboxylic acid, 2,5-dihydro-2,5-dimethoxy-2-methylthio-5-(3-methoxy-3-oxo-1-propynyl)-dimethyl ester (**46**), 10 % (0.0699 g) isolated yield: ^1H NMR (300 MHz,

$CDCl_3$) δ: 2.12, 2.13 (2xs, 3H), 3.49 (s, 3H), 3.62, 3.63 (2xs, 3H), 3.81(s, 3H), 3.85 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 12.4, 12.6, 52.8, 52.9, 53.0, 53.1, 77.9, 78.1, 78.3, 78.6, 102.1, 118.8, 132.9, 133.0, 143.1, 143.3, 152.8, 159.5, 159.6, 161.7; IR (CCl_4, ν_{max}) cm^{-1}: 3008, 2952, 2894, 2839, 1730 (s, br), 1681, 1458, 1436, 1328, 1266 (s), 1235 (m), 1183, 1116, 1098, 1077, 1038, 1020, 988, 956, 918, 873, 692, 578; MS (EI) m/z (rel. intensity): 374 $[M]^+$ (2), 343 $[M-OCH_3]^+$ (9), 327 $[M-SCH_3]^+$ (100), 315 $[M-CO_2CH_3]^+$ (7), 157 (61), 59 $[CO_2CH_3]^+$ (22); MS (CI, NH_3): 375 $[M+H]^+$ (8), 392 $[M+NH_4]^+$ (7).

10. Synthesis of Diethyl Xanthic Ester (50).

The procedure of H. S. Fry[46a] was followed with some modifications. A mixture of magnesium (6.0 g, 0.25 mol), carbon disulfide (60 mL, 1.0 mol) and absolute ethanol (250 mL) was refluxed under N_2 for 2 hours. After cooling to room temperature, ethyl bromide (41 mL) was added to the solution. It was refluxed again for another 2 hours, then brought to room temperature. Sulfuric acid (5 %, 500 mL) was added to the stirring solution. The resultant solution was extracted with ether (3 times, 200 mL each). The combined organic layers were extracted with 10 % Na_2CO_3 (300 mL) followed by water and finally dried over anhydrous $MgSO_4$. After removal of the $MgSO_4$ solid by filtration and evaporation of the solvent, the crude product was purified by distillation under vacuum (ca. 0.3 mm Hg) at 65 °C. The pure xanthate **50**[46b] was obtained as a light yellow liquid in 85 % (31.53 g) yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.35 (t, 3H, ^{3}J = 7.4 Hz), 1.42 (t, 3H, ^{3}J = 7.2 Hz), 3.13 (q, 2H, ^{3}J = 7.4 Hz), 4.65 (q, 2H, ^{3}J = 7.2 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 13.4 ($SCH_2\underline{C}H_3$), 13.8 ($OCH_2\underline{C}H_3$), 30.1 ($S\underline{C}H_2CH_3$), 69.7 ($O\underline{C}H_2CH_3$), 215.0 (C=S).

11. Synthesis of Di(ethylthiol)carbonate (48).

The procedure of T. Kawata et. al.[47] was followed with some modifications. Xanthate **50** (14.0 g, 0.093 mol) and $AlCl_3$ (12.5 g in total, added portionwise into the solution) were refluxed in a mixture of benzene (10 mL) and chloroform (40 mL) under N_2 for two hours. After cooling to room temperature, ice water was cautiously added into the solution. The resultant mixture was then extracted with ether (3 times, 100 mL each). The combined organic layers were washed with water and dried over anhydrous $MgSO_4$. After removal of the $MgSO_4$ solid by filtration and evaporation of the solvent, the crude product was purified by distillation under vacuum (ca. 0.3 mm Hg) at 30-34 °C afforded carbonate **48**[47] as a yellow liquid in 52 % yield (7.27 g).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.30 (t, 6H, ^{3}J = 7.4 Hz), 3.00 (q, 4H, ^{3}J = 7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.9 ($SCH_2\underline{C}H_3$), 24.9 ($S\underline{C}H_2CH_3$), 189.2 (C=O).

12. Synthesis of (Ethylthiocarbonyl)hydrazone of Acetone (52).

Carbonate **48** (3.5 g, 0.023 mol) and hydrazine hydrate (4.55 mL, 0.093 mol) were dissolved in methanol (50 mL). This mixture was stirred with anhydrous $MgSO_4$ for about 16 hours. After removal of the anhydrous $MgSO_4$ by filtration and evaporation of the

solvent by using a rotary evaporator, the excess hydrazine was removed by distillation under vacuum, leaving the hydrazide **51** as a white, semicrystalline solid. The hydrazide was dissolved in acetone (40 mL) and stirred with 5 g of anhydrous $MgSO_4$ for about 16 hours. After removal of the $MgSO_4$ by filtration and evaporation of the solvent, hydrazone **52** was obtained as a yellow solid. After drying by vacuum pump, the yield was 2.91 g (78 %). The melting point of the hydrazone was 65-69 °C.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.31 (t, 3H, ^3J = 7.4 Hz), 1.89 (s, 3H), 2.03 (s, 3H), 2.89 (q, 2H, ^3J = 7.4 Hz), 9.17 (bs, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 15.1 ($SCH_2\underline{C}H_3$), 16.6 (CH_3), 23.2 ($S\underline{C}H_2CH_3$), 25.3 (CH_3), 121.8 (N=C), 135.1 (C=O).

13. Synthesis of 2-Acetoxy-2-ethylthio-Δ^3-1,3,4-oxadiazoline (53).

Hydrazone **52** (2.23 g, 0.014 mol) was stirred in CH_2Cl_2 (50 mL) until dissolved and acetic acid (0.45 mL) was added to the solution. The solution was cooled in an ice bath before addition of lead tetraacetate (6.52 g, 0.0147 mol). The ice bath was subsequently removed and the mixture was stirred for an additional hour at room temperature. The mixture was filtered and the filtrate was extracted 3 times with 5 % $NaHCO_3$ (50 mL each). The combined organic layers were dried over anhydrous $MgSO_4$. After removal of the $MgSO_4$ solid by filtration, the solvent was evaporated, giving the oxadiazoline **53**, as a bright, yellow liquid in 97 % (2.95 g). There was absolutely no acyclic by-product found.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.36 (t, 3H, ^3J = 7.5 Hz), 1.56 (s, 3H), 1.66 (s, 3H), 2.13 (s, 3H), 2.91 (dq, 1H, ^2J = 7, ^3J = 7.5 Hz), 3.05(dq, 1H, ^2J = 7, ^3J = 7.5 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.8 ($SCH_2\underline{C}H_3$), 21.2, 22.7, 22.9 (3 CH_3), 24.6 ($S\underline{C}H_2CH_3$), 124.8 (C5), 133.1 (C2), 166.4 (C=O); MS (EI) m/z (rel. intensity): 159 $[M\text{-}OAC]^+$ (41), 148 (14), 103 (100), 89 (66), 59 $[AcO]^+$ (77).

14. Thermolysis of Oxadiazoline 53 in Benzene.

A solution of oxadiazoline **53** (0.327 g, 1.5 mmol) in benzene (10 mL) was heated in a sealed tube at 70 °C for about 16 hours. Upon completion, a GCMS trace of the crude was taken, it showed two products: 3-ethylthio-2,3-propanedione **(54)** and 2-acetoxy-2,2-(diethylthiocarbonyl)ethane **(55)**. However, after evaporating the solvent by using a rotary evaporator, a second GCMS trace revealed only **55**. The solvent-free crude mixture was subjected to centrifugal chromatography (petroleum ether) yielding **55** in 45 % yield (0.0894 g).

Using the standard procedure described earlier, the rate constant for decomposition of oxadiazoline **53** at 60 °C was found to be 4.19x 10^{-5} s^{-1} ($t_{1/2}$ = 4.6 hours, R^2 = 0.998).

3-Ethylthio-2,3-propanedione **(54)**: MS (EI, GCMS) m/z (rel. intensity): 132 $[M]^+$ (2), 104 $[M\text{-}C_2H_4]^+$ (33), 89 $[M\text{-}COCH_3]^+$ (4), 58 (7), 59 (7), 60 $[CH_3(CS)H]^+$ (7), 61 (7), 43 $[COCH_3]^+$ (100).

2-Acetoxy-2,2-bis(ethylthiocarbonyl)ethane (**55**): ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.22 (t, 6H, ^{3}J = 7.4 Hz), 1.83 (s, 3H), 2.17 (s, 3H), 2.87 (q, 4H, ^{3}J=7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.0 ($SCH_2\underline{C}H_3$), 20.9, 21.3 (2 CH_3), 23.6 ($S\underline{C}H_2CH_3$), 91.3 (C2), 168.4 (OC=O), 194.9 (SC=O); IR (CCl_4, ν_{max}) cm^{-1}: 2973, 2935, 2877, 1764 (s), 1709 (s, br), 1879 (s, br), 1451 (m), 1420, 1371 (m) 1266 (m) 1224 (s), 1130 (m), 1049, 1019, 992 (m), 966, 920 (m), 873, 599; MS (EI) m/z (rel. intensity): 222 (2), 203 $[M\text{-}SCH_2CH_3]^+$ (17), 175 $[M\text{-}(CO)SCH_2CH_3]^+$ (4), 151 (3), 133 (9), 114 (4), 105 (14), 89 $[(CO)SCH_2CH_3]^+$ (7), 43 (100); MS (CI, NH_3) m/z: 282 $[M+NH_4]^+$ (100), 265 $[M+H]^+$ (17).

15. Thermolysis of Oxadiazoline 53 in the Presence of Phenol.

Oxadiazoline **53** (0.136 g, 0.623 mmol) and previously dried phenol (0.13 g) were thermolyzed in benzene (15 mL) at 80 °C for about 16 hours in a sealed tube. After evaporating the solvent, the residue was subjected to centrifugal chromatography (hexane) afforded 1-ethylthio-1,1-diphenoxymethane **58** as a clear liquid in 48 % (0.0769 g) yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.34 (t, 3H, ^{3}J = 7.5 Hz), 2.82 (q, 2H, ^{3}J = 7.5 Hz), 6.73 (s, 1H), 7.04-7.11 (m, 6H), 7.22-7.32 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.0 ($SCH_2\underline{C}H_3$), 23.4 ($S\underline{C}H_2CH_3$), 105.4 (C1), 117.8, 123.2, 129.5, 155.4 (4 Ph); IR (CCl_4, ν_{max}) cm^{-1}: 3070, 3040, 2972, 2877, 1595 (s), 1491 (s), 1301, 1204 (s, br), 1172 (m), 1031 (s, br), 987 (s), 896, 863, 692 (s); MS (EI) m/z (rel. intensity): 231 $[M\text{-}C_2H_5]^+$ (3), 199 $[M\text{-}SCH_2CH_3]^+$ (10), 167 $[M\text{-}OPh]^+$ (100).

16. Exchange of Oxadiazoline 53 in Methanol.

Methanol (0.2 mL) was added into a solution of oxadiazoline **53** (0.115 g, 0.527 mmol) in CH_2Cl_2 (5 mL). This mixture was allowed to stand at room temperature for 48 hours. The crude mixture was then extracted with 5 % $NaHCO_3$ (3 times, 15 mL each). The organic layer was collected and dried over anhydrous $MgSO_4$. After filtration, the solvent was evaporated, and purification of the residue with centrifugal chromatography (hexane) gave oxadiazoline **31c** in 92 % yield.

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.35 (t, 3H, ^{3}J = 7.5 Hz), 1.54 (s, 3H), 1.57 (s, 3H), 2.81 (dq, 1H, ^{2}J = -12.9, ^{3}J = 7.5 Hz), 2.95 (dq, 1H, ^{2}J = -12.9, ^{3}J = 7.5 Hz), 3.44 (s, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 15.2 ($SCH_2\underline{C}H_3$), 23.0 (CH_3), 24.5 ($S\underline{C}H_2CH_3$), 24.7 (CH_3), 51.3 (OCH_3), 122.0 (C5), 136.9 (C2).

17a. Exchange of Oxadiazoline 53 with Ethanethiol at Room Temperature.

Ethanethiol (0.10 mL, 1.4 mmol) and dried PTSA (ca. 0.03 g) were added into a solution of oxadiazoline **53** (0.279 g, 1.28 mmol) in CH_2Cl_2 (10 mL). This mixture was allowed to stand at room temperature for 41 hours. The mixture was then chromatographed (hexane), affording triethylorthothioformate **59**[49], as a clear liquid in 50 % yield (0.126 g).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.29 (t, 9H, ^{3}J = 7.4 Hz), 2.74 (q, 6H, ^{3}J = 7.4 Hz), 4.89 (s, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2 ($SCH_2\underline{C}H_3$), 25.8 ($S\underline{C}H_2CH_3$), 53.6 (C1); IR (CCl_4, ν_{max}) cm^{-1}: 2972 (s), 2928 (s), 2872, 2825, 1625, 1451 (s), 1421, 1376, 1264 (s),

1181, 1145, 1052, 973, 694; MS (EI) m/z (rel. intensity): 196 $[M]^+$ (2), 135 $[M-SCH_2CH_3]^+$ (100), 107 (18), 45 (25).

17b. Exchange of Oxadiazoline 53 with Ethanethiol at Low Temperature.

The exchange of oxadiazoline **53** (0.3006 g, 1.38 mmol) with ethanethiol (0.10 mL, 1.35 mmol) in the presence of PTSA (ca. 0.03 g) and 10 mL of CH_2Cl_2 was repeated at low temperature (refrigerator). The reaction yielded 2,2-bis(ethylthio)-5,5-dimethyl-Δ^3-1,3,4-oxadiazoline **(61)** in 77 % yield (0.233 g).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.29 (t, 6H, ^3J = 7.4 Hz), 1.61 (s, 6H), 2.74 (q, 4H, ^3J = 7.4 Hz); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.6 ($SCH_2\underline{C}H_3$), 24.1 (CH_3), 25.5 ($S\underline{C}H_2CH_3$), 123.3 (C5), 128.7 (C2); IR (CCl_4, ν_{max}) cm^1: 2972 (s, br), 2931 (s), 2873 (s), 2828, 1755, 1714, 1653, 1454 (s), 1422, 1379 (m), 1367 (m), 1264 (m), 1234 (m), 1205, 1174, 1067 (s, br), 1055 (m, br), 973, 909 (m), 845 (m), 594.

18. Oxadiazoline 61 Trapping with Thiophenol.

An excess of thiophenol (0.21 mL) was added to the crude mixture of oxadiazoline **61** (0.233 g, 1.06 mmol). The mixture was allowed to stand at room temperature for 36 hours. The product mixture was subjected to centrifugal chromatography (hexane), affording diethyl phenylorthothioformate **(62)** in 65 % yield (0.168 g).

^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.28 (t, 6H, ^3J = 7.4 Hz), 2.78 (q, 4H, ^3J = 7.4 Hz), 5.07 (s, 1H), 7.25-7.34 (m, 3H), 7.51-7.59 (m, 2H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 14.2

($SCH_2\underline{C}H_3$), 26.3 ($S\underline{C}H_2CH_3$), 57.7 (C1), 128.1, 128.8, 132.8, 134.1 (4 Ph); IR (CCl_4, ν_{max}) cm^{-1}: 3076, 3063, 3020, 2972 (s, br), 2929 (s), 2873, 2827, 1583, 1480 (m), 1453 (m), 1441 (m), 1421, 1377, 1264 (m), 1174, 1142, 1087, 1067, 1063, 1026, 974, 910, 691 (s); MS (EI) m/z (rel. intensity): 245 $[M+H]^+$ (3), 244 $[M]^+$ (2), 243 $[M-H]^+$ (3), 183 $[M-SCH_2CH_3]^+$ (18), 135 $[M-SC_6H_5]^+$ (100), 107 (12).

Appendix 1

Table I-1. Crystal data and structure refinement for **t-34b**.

Empirical formula	$C_{18} H_{20} O_2 S_2$
Formula weight	332.46
Crystal size (mm)	0.4 x 0.4 x 0.4
color	colorless
Temperature (K)	228 (2)
Wavelength (Å)	0.71073
Crystal system	monoclinic
Space group	$P2_1 / c$
Unit cell dimensions	
a (Å)	8.8974 (5)
b (Å)	7.5626 (8)
c (Å)	13.0719 (12)
α (^{0})	90
β (^{0})	93.795 (7)
γ (^{0})	90
Volume (Å^3), Z	877.65 (13), 2
Density (calculated) (Mg/m^3)	1.258
Absorption coefficient (mm^{-1})	0.307
F(000)	352
Theta range for data collection (^{0})	2.29 to 24.99
Limiting indices	$-1 \le h \le 10, -1 \le k \le 8, -15 \le l \le 15$
Reflections collected	2158
Independent reflections	1539 [R(int) = 0.0754]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1539 / 0 / 141

Goodness-of-fit on F^2	1.043
Final R indices [I>2σ (I)]	R1 = 0.0431, wR2 = 0.1227
R indices (all data)	R1 = 0.0460, wR2 = 0.1249
Extinction coefficient	0.004 (5)
Largest diff. peak and hole ($Å^{-3}$)	0.287 and -0.300

Table I-2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **t-34b**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
S(1)	5929(1)	1533(1)	8763(1)	32(1)
O(1)	5459(1)	1951(2)	10756(1)	31(1)
C(1)	5311(2)	796(2)	9945(1)	26(1)
C(3)	4641(2)	3410(2)	8534(1)	35(1)
C(4)	3037(2)	2795(2)	8365(1)	34(1)
C(5)	2500(2)	2171(3)	7410(2)	44(1)
C(6)	1050(3)	1497(3)	7259(2)	61(1)
C(7)	128(3)	1452(4)	8066(3)	71(1)
C(8)	641(3)	2083(4)	9011(2)	69(1)
C(9)	2092(2)	2764(3)	9165(2)	50(1)
C(10)	6988(2)	2278(3)	11123(2)	41(1)

Table I-3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **t-34b**.

	x	y	z	U(eq)
H(3A)	4753(23)	4174(34)	9142(16)	47(6)
H(3B)	4988(22)	3991(30)	7932(17)	40(5)
H(5)	3084(26)	2206(36)	6867(19)	59(7)
H(6)	748(31)	1071(41)	6576(23)	75(8)
H(7)	-934(34)	1053(43)	7960(22)	81(8)
H(8)	18(46)	1916(52)	9530(33)	119(13)
H(9)	2550(29)	3248(33)	9868(23)	60(7)
H(10A)	7475(27)	1194(40)	11334(20)	64(7)
H(10B)	6959(26)	3079(35)	11710(20)	52(6)
H(10C)	7507(25)	2841(33)	10573(18)	50(6)

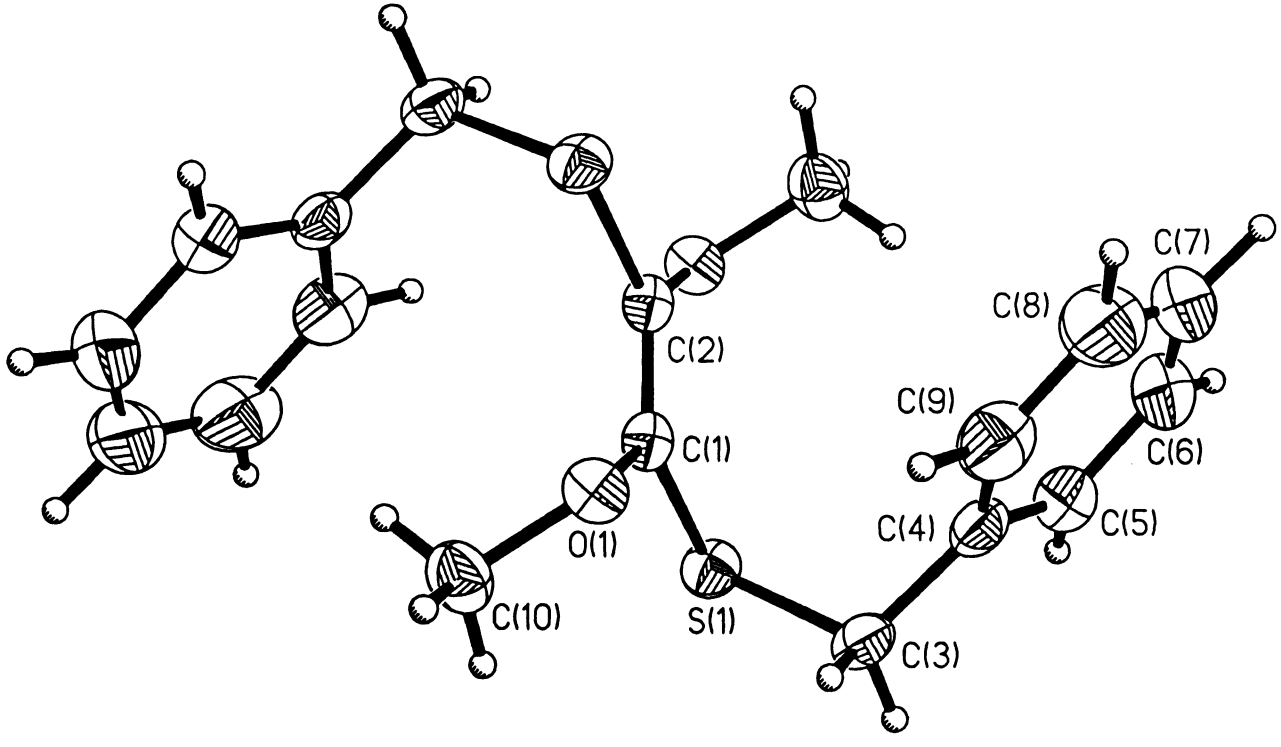
Table I-4. Bond lengths (Å) and angles (^{0}) for **t-34b.**

S(1)-C(1)	1.764(2)	C(4)-C(9)	1.385(3)
S(1)-C(3)	1.836(2)	C(4)-C(5)	1.390(3)
O(1)-C(1)	1.373(2)	C(5)-C(6)	1.389(3)
O(1)-C(10)	1.434(2)	C(6)-C(7)	1.379(4)
C(1)-C(2)#	1.337(3)	C(7)-C(8)	1.374(5)
C(3)-C(4)	1.503(3)	C(8)-C(9)	1.393(4)
C(1)-S(1)-C(3)	99.20(8)	C(9)-C(4)-C(3)	120.8(2)
C(1)-O(1)-C(10)	114.11(13)	C(5)-C(4)-C(3)	120.2(2)
C(2)#-C(1)-O(1)	120.6(2)	C(6)-C(5)-C(4)	120.9(2)
C(2)#-C(1)-S(1)	122.3(2)	C(7)-C(6)-C(5)	119.7(3)
O(1)-C(1)-S(1)	117.09(12)	C(8)-C(7)-C(6)	120.0(2)
C(4)-C(3)-S(1)	111.16(11)	C(7)-C(8)-C(9)	120.5(2)
C(9)-C(4)-C(5)	118.9(2)	C(4)-C(9)-C(8)	120.1(2)

Symmetry transformations used to generate equivalent atoms:
C(2) is related to C(1) by -x+1,-y,-z+2

Table I-5. Anisotropic displacement parameters (Å^2 x 10^3) for **t-34b.** The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U11 + ... + 2 h k a^* b^* U12]$

	U11	U22	U33	U23	U13	U12
S(1)	32(1)	37(1)	27(1)	3(1)	9(1)	1(1)
O(1)	33(1)	32(1)	29(1)	-7(1)	5(1)	0(1)
C(1)	24(1)	31(1)	23(1)	-1(1)	4(1)	5(1)
C(3)	43(1)	26(1)	35(1)	5(1)	2(1)	-1(1)
C(4)	36(1)	27(1)	39(1)	9(1)	4(1)	6(1)
C(5)	42(1)	45(1)	44(1)	8(1)	-1(1)	-1(1)
C(6)	47(1)	61(2)	71(2)	10(1)	-15(1)	-4(1)
C(7)	35(1)	69(2)	109(2)	31(2)	-4(1)	0(1)
C(8)	45(1)	74(2)	92(2)	23(2)	30(1)	13(1)
C(9)	50(1)	50(1)	53(1)	7(1)	16(1)	12(1)
C(10)	40(1)	39(1)	42(1)	-8(1)	-5(1)	-3(1)



Symmetry transformations used to generate equivalent atoms:
C(2) is related to C(1) by -x+1,-y,-z+2

Appendix 2

Table II-1. Crystal data and structure refinement for **39d**.

Empirical formula	$C_7 H_6 Cl_2 O_4 S$
Formula weight	257.08
Crystal size (mm)	0.45 x 0.40 x 0.20
Color	yellow
Temperature (K)	293 (2)
Wavelength (Å)	0.56086
Crystal system	monoclinic
Space group	$P2_1 / n$
Unit cell dimensions	
a (Å)	7.758 (2)
b (Å)	8.954 (2)
c (Å)	14.733 (3)
α (^{0})	90
β (^{0})	98.48 (3)
γ (^{0})	90
Volume (Å^3), Z	1012.2 (4), 4
Density (calculated) (Mg/m^3)	1.687
Absorption coefficient (mm^{-1})	0.426
F(000)	520
Theta range for data collection (^{0})	2.11 to 20.05
Limiting indices	$0 \leq h \leq 9, 0 \leq k \leq 10, -17 \leq l \leq 17$
Reflections collected	2069
Independent reflections	1931 [R(int) = 0.0212]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1931 / 0 / 152

Goodness-of-fit on F^2	0.843
Final R indices [I>2σ (I)]	R1 = 0.0324, wR2 = 0.0636
R indices (all data)	R1 = 0.0597, wR2 = 0.0697
Extinction coefficient	0.001 (2)
Largest diff. peak and hole ($Å^{-3}$)	0.172 and -0.172

Table II-2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for **39d**. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
O(1)	108(2)	11324(2)	3336(1)	46(1)
O(2)	212(2)	13345(2)	4167(1)	59(1)
C(2)	987(3)	12319(3)	3913(2)	42(1)
Cl(3)	3873(1)	13355(1)	4929(1)	76(1)
C(3)	2874(3)	12091(3)	4174(2)	43(1)
Cl(4)	5924(1)	10792(1)	4047(1)	67(1)
C(4)	3728(3)	11005(3)	3817(2)	43(1)
O(5)	3515(2)	9009(2)	2773(1)	62(1)
C(5)	2791(3)	9904(3)	3186(2)	42(1)
S(6)	305(1)	8699(1)	4056(1)	48(1)
O(6)	134(2)	9503(2)	2263(1)	53(1)
C(6)	826(3)	9904(2)	3132(2)	42(1)
C(7)	1022(6)	6916(3)	3702(3)	68(1)
C(8)	-1739(5)	9423(6)	2060(3)	75(1)

Table II-3. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$ x 10^3) for **39d**.

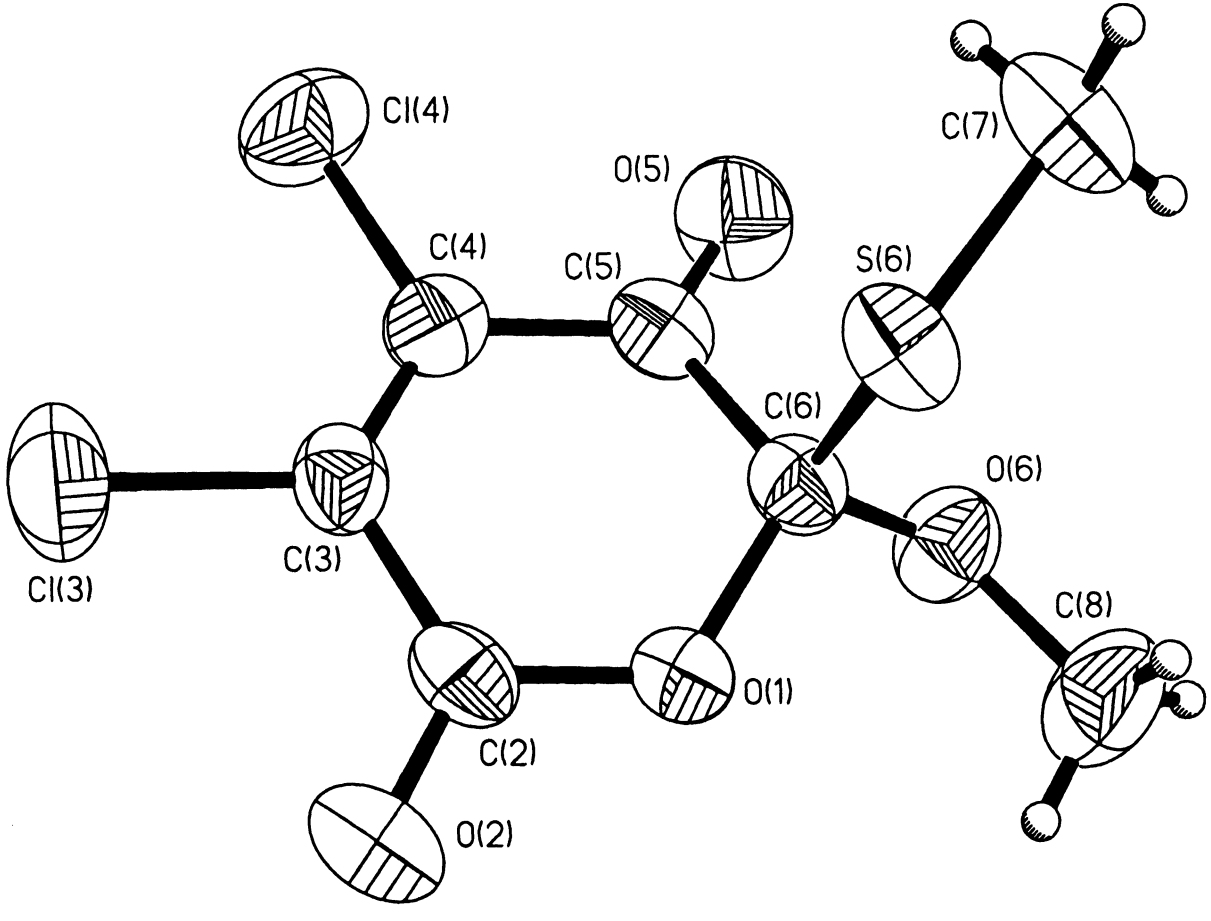
	x	y	z	U(eq)
H(7A)	2214(52)	6969(39)	3674(24)	106(14)
H(7B)	413(47)	6733(38)	3139(26)	106(14)
H(7C)	879(43)	6293(37)	4162(23)	92(12)
H(8A)	-2149(51)	8876(42)	2524(29)	122(17)
H(8B)	-2193(46)	10315(39)	2134(25)	102(14)
H(8C)	-1935(46)	9036(39)	1473(25)	109(14)

Table II-4. Bond lengths (Å) and angles (^{0}) for **39d**.

O(1)-C(2)	1.346(3)	C(4)-C(5)	1.471(3)
O(1)-C(6)	1.438(3)	O(5)-C(5)	1.196(3)
O(2)-C(2)	1.188(3)	C(5)-C(6)	1.515(3)
C(2)-C(3)	1.472(3)	S(6)-C(7)	1.793(3)
Cl(3)-C(3)	1.692(2)	S(6)-C(6)	1.829(2)
C(3)-C(4)	1.328(3)	O(6)-C(6)	1.360(3)
Cl(4)-C(4)	1.698(3)	O(6)-C(8)	1.442(4)
C(2)-O(1)-C(6)	122.8(2)	O(5)-C(5)-C(4)	123.1(2)
O(2)-C(2)-O(1)	118.6(2)	O(5)-C(5)-C(6)	121.2(2)
O(2)-C(2)-C(3)	123.7(2)	C(4)-C(5)-C(6)	115.7(2)
O(1)-C(2)-C(3)	117.7(2)	C(7)-S(6)-C(6)	101.3(2)
C(4)-C(3)-C(2)	122.2(2)	C(6)-O(6)-C(8)	117.1(2)
C(4)-C(3)-Cl(3)	122.9(2)	O(6)-C(6)-O(1)	108.6(2)
C(2)-C(3)-Cl(3)	114.9(2)	O(6)-C(6)-C(5)	107.7(2)
C(3)-C(4)-C(5)	120.8(2)	O(1)-C(6)-C(5)	114.0(2)
C(3)-C(4)-Cl(4)	123.2(2)	O(6)-C(6)-S(6)	116.4(2)
C(5)-C(4)-Cl(4)	116.0(2)	O(1)-C(6)-S(6)	103.3(2)
		C(5)-C(6)-S(6)	107.0(2)

Table II-5. Anisotropic displacement parameters (Å^2 x 10^3) for **39d**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U11 + ... + 2 h k a^* b^* U12]$

	U11	U22	U33	U23	U13	U12
O(1)	42(1)	36(1)	59(1)	-2(1)	4(1)	4(1)
O(2)	72(1)	39(1)	68(1)	-2(1)	17(1)	11(1)
C(2)	55(2)	28(1)	44(2)	7(1)	11(1)	0(1)
Cl(3)	84(1)	63(1)	79(1)	-22(1)	0(1)	-20(1)
C(3)	51(2)	37(1)	41(1)	3(1)	3(1)	-9(1)
Cl(4)	40(1)	81(1)	77(1)	12(1)	6(1)	-2(1)
C(4)	39(1)	45(2)	45(1)	10(1)	9(1)	-5(1)
O(5)	59(1)	64(1)	69(1)	-15(1)	25(1)	5(1)
C(5)	50(2)	39(1)	41(1)	4(1)	16(1)	1(1)
S(6)	60(1)	37(1)	50(1)	-2(1)	19(1)	-4(1)
O(6)	52(1)	63(1)	43(1)	-9(1)	3(1)	-2(1)
C(6)	46(2)	37(1)	42(2)	-4(1)	7(1)	1(1)
C(7)	97(3)	35(2)	77(3)	-1(2)	25(2)	0(2)
C(8)	58(2)	94(3)	68(3)	-17(2)	-8(2)	-4(2)


Cl(4)
O(5)
C(7)
C(4)
C(5)
S(6)
C(6)
O(6)
Cl(3)
C(3)
C(8)
O(1)
C(2)
O(2)

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