# Mono(trimethylsilyl) Bisketenes: Cycloaddition and Electrophilic Addition Reactions

by

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# Abstract

The 1,2-bisketenes 2-phenyl-3-trimethylsilyl-1,3-butadiene-1,4-dione and 2,3-di-tert-butyl-1,3-butadiene-1,4-dione were generated by photolysis of the corresponding cyclobutenediones in yields of 87-99%, and 5-15%, respectively, as relatively long-lived intermediates at room temperature. The 2-ethoxy-3-trimethylsilyl 1,2-bisketene generated similarly was only observed as a transient species by time resolved infrared spectroscopy. These bisketenes were not stable at high temperature and reformed the cyclobutenediones. 3,4-Di-tert-butylcyclobutenedione was also prepared by dehydrochlorination of the corresponding succinyl chloride at high temperature.

The reactions of 1,2-bisketenes with nucleophiles such as alcohols and amines were studied and the reactions were found to go by stepwise processes, and in some cases the monoketene formed could be observed and even isolated.

The reactions of bisketenes with electrophiles were studied. The reaction of 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione with bromine was found to occur by attack at $C_\alpha$ and resulted in a 1,4-addition. This 2,3-bis(trimethylsilyl) bisketene was also found to react with *t*-BuCl to give a monoalkyl substituted bisketene.

Cycloaddition reactions of some 1,2-bisketenes were also studied, and those were found not to give Diels-Alder reactions with various dienophiles. 2,3-Bis(trimethylsilyl)-1,3-butadiene-1,4-dione was found to react with acetaldehyde give a ketenyl lactone which upon heating gave a vinyl ketene after loss of $CO_2$. The more reactive 2-phenyl-3-trimethylsilyl-1,3-butadiene-

1,4-dione was found to react with electron-rich alkynes to give furanone derivatives under photolysis conditions or heating. With the reactive alkyne ethoxytrimethylsilylethyne 4+2 cycloaddition to form a benzoquinone was the major pathway. The reaction of bisketenes with diazo compounds gave furanone and cyclopentene-3,5-dione derivatives.

# Acknowledgments

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# Contents

# *Chapter 1*

# The Chemistry of Bisketenes

## 1.1 Carbon suboxide

Diels and Wolf[1a] synthesized the first stable, isolable bisketene, carbon suboxide **1** in 1906, while studying the action of phosphorus pentoxide on diethyl malonate at 300 °C. The following year[1b] Diels published another much more productive method, which involves the dehydration of malonic acid with phosphorus pentoxide. However, since decarboxylation of malonic acid occurs under the reaction conditions, the generated carbon suboxide was contaminated by acetic acid and carbon dioxide.[1b] Staudinger and his co-workers demonstrated that carbon suboxide could be prepared by dehalogenation of dibromomalonyl chloride[2a] and by dehydrochlorination of malonyl chloride[2b] in 1908. Birkofer and Sommer[3a] have improved the synthesis by starting with bis(trimethylsilyl) malonate and using phosphorus pentoxide as a dehydrating reagent, and carbon suboxide is formed in reasonable yield. Other methods that have been used in laboratory preparations of carbon suboxide **1** (Fig. 1) include the thermolysis of O,O-diacetyltartaric anhydride in *vacuo* at 600-700 °C (46-68%) or under normal pressure at 770 °C (ca. 45% yield),[3b] and the pyrolysis of diethyl oxaloacetate in the presence of acetic anhydride at 850-880 °C(48% yield).[3c]

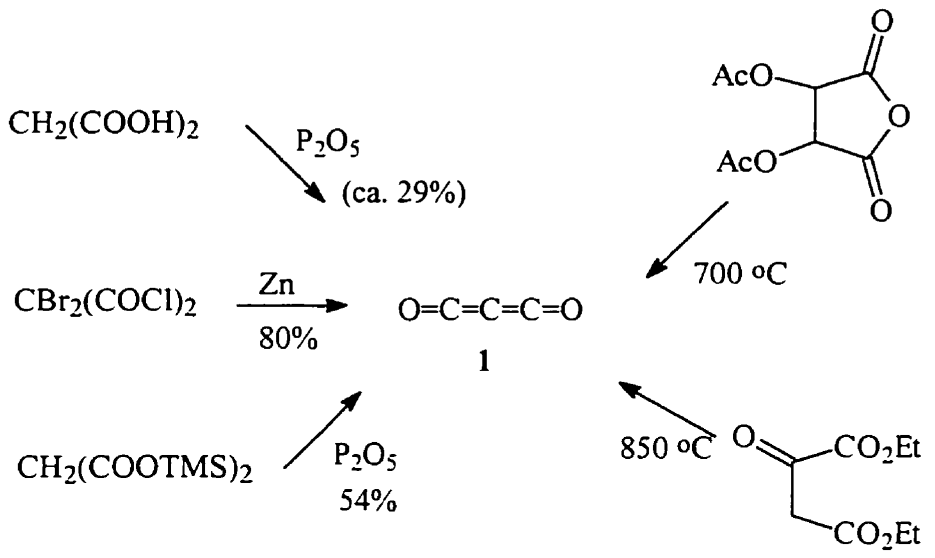



**Figure 1**

This is a unique, highly strained molecule, and carbon suboxide is the only stable member of the linear dioxides of carbon which has been isolated and characterized besides $CO_2$, although there have been a lot of efforts to prepare and study the other members of this series of compounds. The chemistry of carbon suboxide has been regularly reviewed. [4]

## 1.2 Aldo- and ketobisketenes

Considering the structure of ketenes, monosubstituted ketenes $R_1HC=C=O$ have been classified as aldoketenes in reference to aldehydes, and disubstituted ketenes $R_1R_2C=C=O$ have been referred to as ketoketenes, in reference to ketones. Aldoketenes are generally not stable and dimerize easily to β-lactones, but ketoketenes are more stable. Diarylketenes, in particular

$Ph_2C=C=O$, are normally isolable, and are stable for short periods. Ketoketenes dimerize mainly to 1,3-cyclobutanediones, and occasionally to β-lactones depending on the reaction conditions.

Staudinger[5a] reported that adipyl chloride was dehydrochlorinated to yield as the product a dimer of the expected bisketene **2** (Fig. 2), the structure of which was not determined. Sauer[5b] reported that the intermediate **3** could be trapped with ethanol before work-up, and a 40% yield of ethyl 2-cyclopentanone carboxylate was obtained. Dehydrochlorination of adipyl chloride in the presence of aldehydes or ketones yields the 1,3-dioxin-4-one **4**.[5c] The structure of the bisketene dimer was shown by Baldwin[5d] to be **5**, which can be formulated as the product of the reaction of the proposed intermediate **3** with **2**, and by other routes. The intermediate **3** was proposed to be the acylketene **3a**, however as the intermediate was not directly observed, other possibilities such as the β-lactone **3c** can also be considered. Oxet-2-one **3b**, a 4π electrocyclic ring closure product of α-oxoketene **3a** can be ruled out, as such oxet-2-ones are very unstable and have only been observed in an argon matrix.[5e] Some acylketenes are stable, isolable compounds, and oxo-ketene **3a** has been generated and trapped in an argon matrix.[5f] The intermediate **3** could be trapped at room temperature with ethanol and gives the corresponding ester, however alternative routes for the formation of the ester are possible.

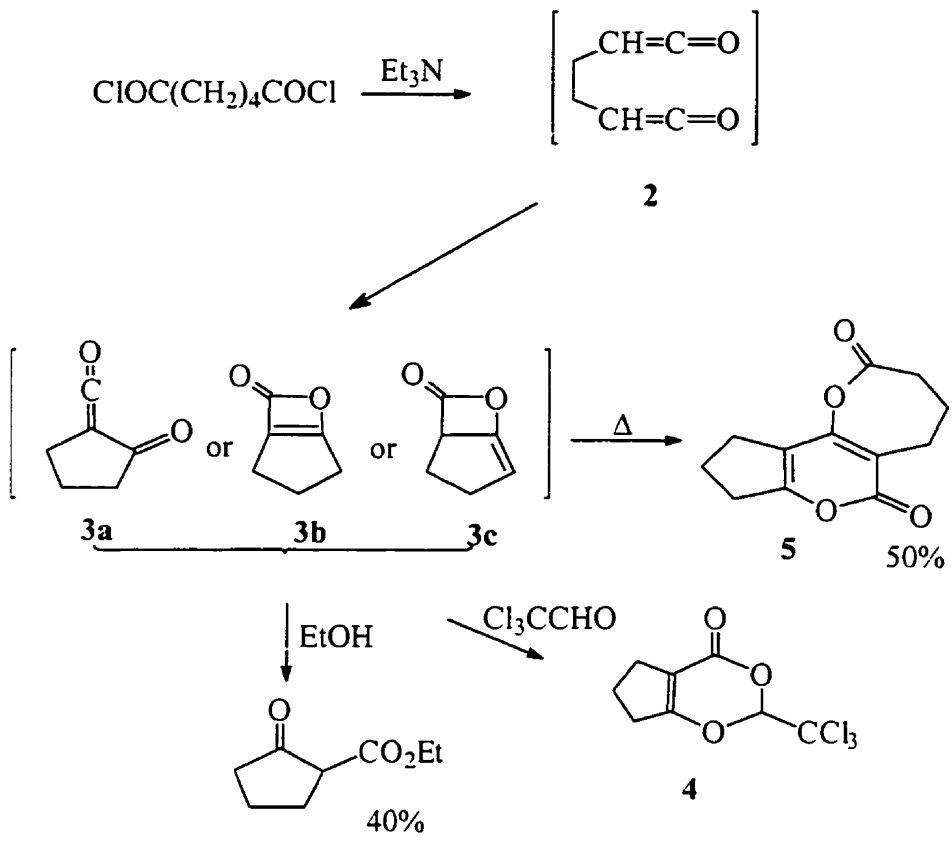



**Figure 2**

Suberoyl chloride (Fig. 3), on the other hand, was converted by Et3N to polymeric ketene derivatives and also forms the β-lactone **7**.[5b] Under conditions of high dilution, suberoyl chloride has been dehydrohalogenated to form a macrocyclic bisketene dimer **8**,[6a,b] which was converted by EtOK to the 1,8-cyclotetradecanedione **9** in 10% yield. The β-lactone **7**, which may be formulated as forming from an intramolecular dimerization of the bisketene **6**, was also obtained, and on treatment with EtOK formed cycloheptanone in 33% yield.[6a,b] Baldwin[6c] has further studied this reaction, and found that under

controlled conditions the β-lactone **7** was the major product and could be separated in a 71% yield.

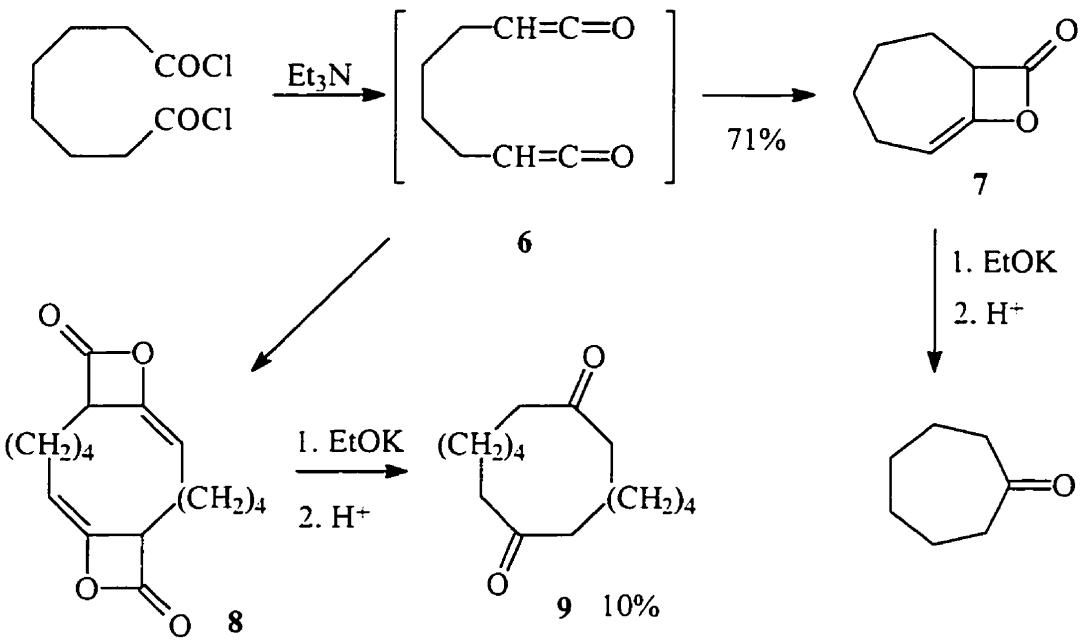



**Figure 3**

Although the reactions in Fig. 2 and Fig. 3 are shown as involving bisketenes, these reactions could proceed by formation of monoketenes, which lead to the observed products (Fig. 4).

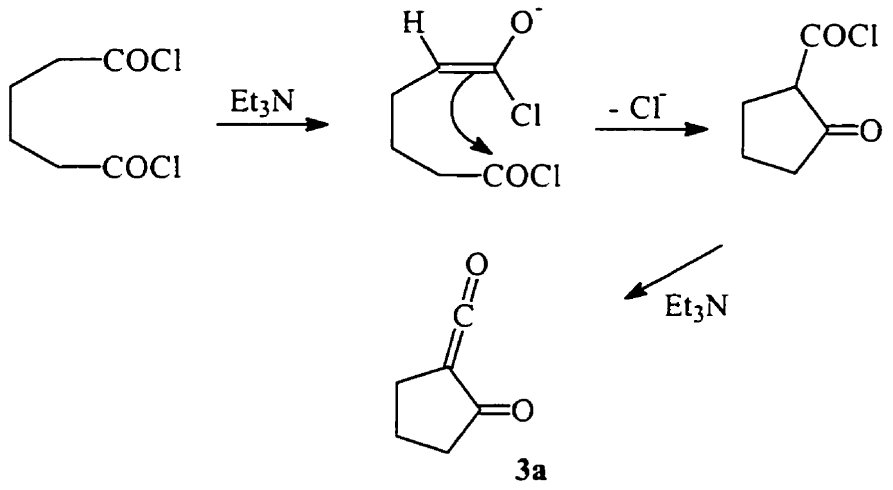
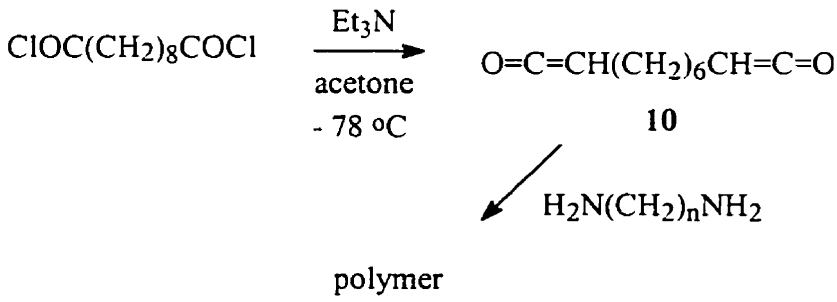


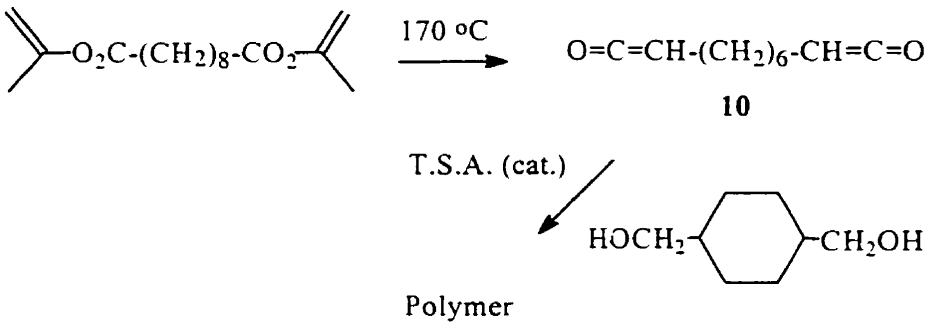

**Figure 4**

Garner and Fasulo[7a,b] reported that sebacyl bisketene **10** was synthesized and copolymerized in solution to polymeric products (Eq. 1). The sebacyl bisketene was progressively more stable as the temperature at which it was synthesized was lowered from 0 to - 78 °C. It was reported that sebacyl bisketene could be generated in the absence of solvent at - 78 °C and would remain active at that temperature for a prolonged time. However, this bisketene was not directly observed.



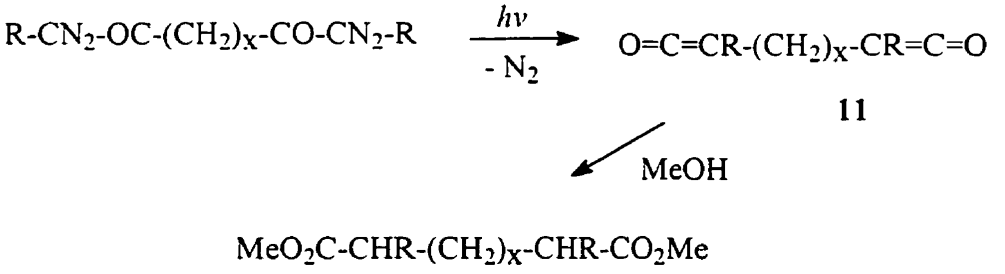

(1)

Diisopropenyl sebacate was reported to be converted to the bisketene **10** at 170 °C, which then was copolymerized in situ with 1,4-bis(hydroxymethyl) cyclohexane (*cis* and *trans* mixture) with a catalytic amount of p-toluenesulfonic acid (Eq. 2).[7c]




(2)

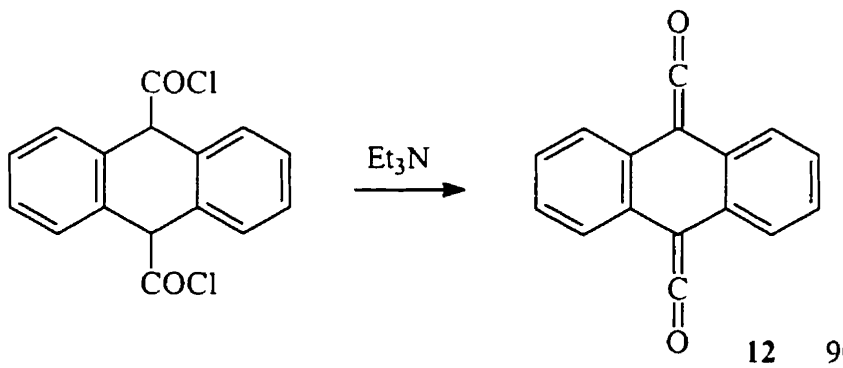
Attempts to make bisketenes **11** by double Wolff rearrangements were reported (Eq. 3).[8] These bisketenes were suggested as intermediates and were trapped with methanol in situ. However, it is quite possible that the reactions go by stepwise pathways, and the bisketenes **11** might never have been generated.




(3)

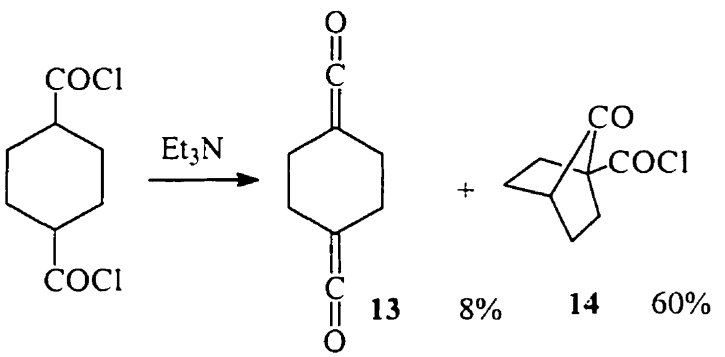
However, a variety of isolable bisketenes can be prepared provided they are of the disubstituted, "ketoketene" type, rather than the monosubstituted, "aldoketene" variety. Since ketene functional groups show marked reactivity toward other ketene groups by ketene dimerization and polymerization, it is necessary, in order to obtain stable, isolable bisketenes, that the two ketene moieties in the molecule should have a reasonable stability toward each other. One simple strategy is that the two monoketene moieties themselves should correspond to isolable and stable monoketenes, so that the bisketene may be successfully isolated.

Blomquist and Meinwald[9] reported the first successful synthesis and isolation of a monomeric bisketene, namely anthraquinoketene **12**. The bisketene **12** was prepared in 90% yield by the dehydrochlorination of 9,10-dihydroanthracene-9,10-dicarbonyl chloride with triethylamine at room temperature (Eq. 4). The bisketene proved to be a reasonably stable, orange-red, crystalline solid which reacted readily with oxygen as well as with water, methanol, and aniline.




**12** 90% (4)

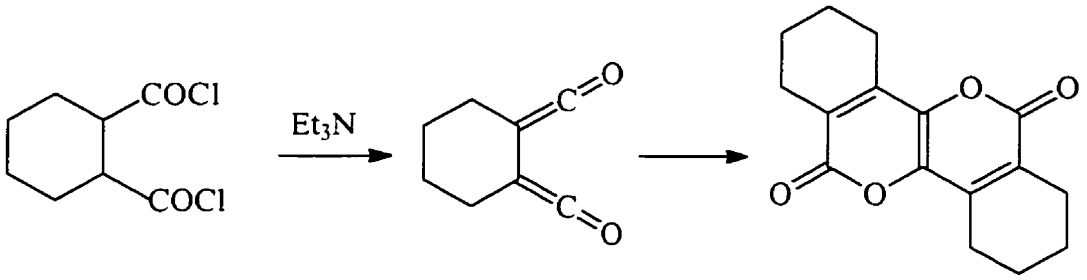
Hatchard and Schneider[10a] reported the synthesis and isolation of 1,4-cyclohexanedimethenone **13** in 8% yield by dehydrochlorination of hexahydroterephthaloyl chloride with triethylamine (Eq. 5). A second product obtained in this reaction was 7-oxobicyclo-[2.2.1]-heptane-1-carbonyl chloride **14** which could be obtained in 60% yield under controlled conditions. The bisketene **13** was a yellow crystalline solid, which was relatively stable at low temperature and could be purified by low temperature sublimation. However on warming to room temperature, it polymerized spontaneously to oligomers containing spirocyclic cyclohexane and cyclobutanedione structures.[10b] The reaction of pyridine adducts of **13** with polymers such as poly(ethylene oxide) containing OH and other nucleophilic groups gave rise to higher molecular weight polymers,[10c] and with diamines polyamides were formed.[10d]



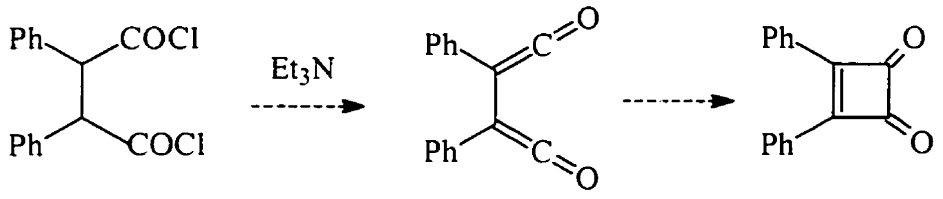

**13** 8% **14** 60% (5)

Blomquist and Le Goff[11] attempted the synthesis of 1,2-cyclohexane-dimethenone **15**, but the interesting dimer **16** was obtained in 6% yield along with a large amount of polymeric tars (Eq. 6). The bisketene **15** was not detected in the monomeric form. It is interesting that the reaction of 2,3-diphenyl succinyl chloride with triethylamine in benzene did not give the

bisketene **17** and the dione **18** as expected,[12] instead only complex unidentified products resulted (Eq. 7).




**15** **16** 6% (6)




**17** **18** (7)

Some other bisketenes [(**19a**, **20a**, **20b**, **20c**),[13a] (**20d**),[13b] (**21**)[13e] were prepared by the dehydrochlorination method from the respective acid chlorides. These ketenes are stable and could be isolated. The bisketene **19b** was generated by the dehalogenation method as a reactive intermediate.[13c] These ketenes demonstrate that the stability of the monoketene moiety in the molecule plays an essential rule in the stability of bisketenes (Fig. 5).

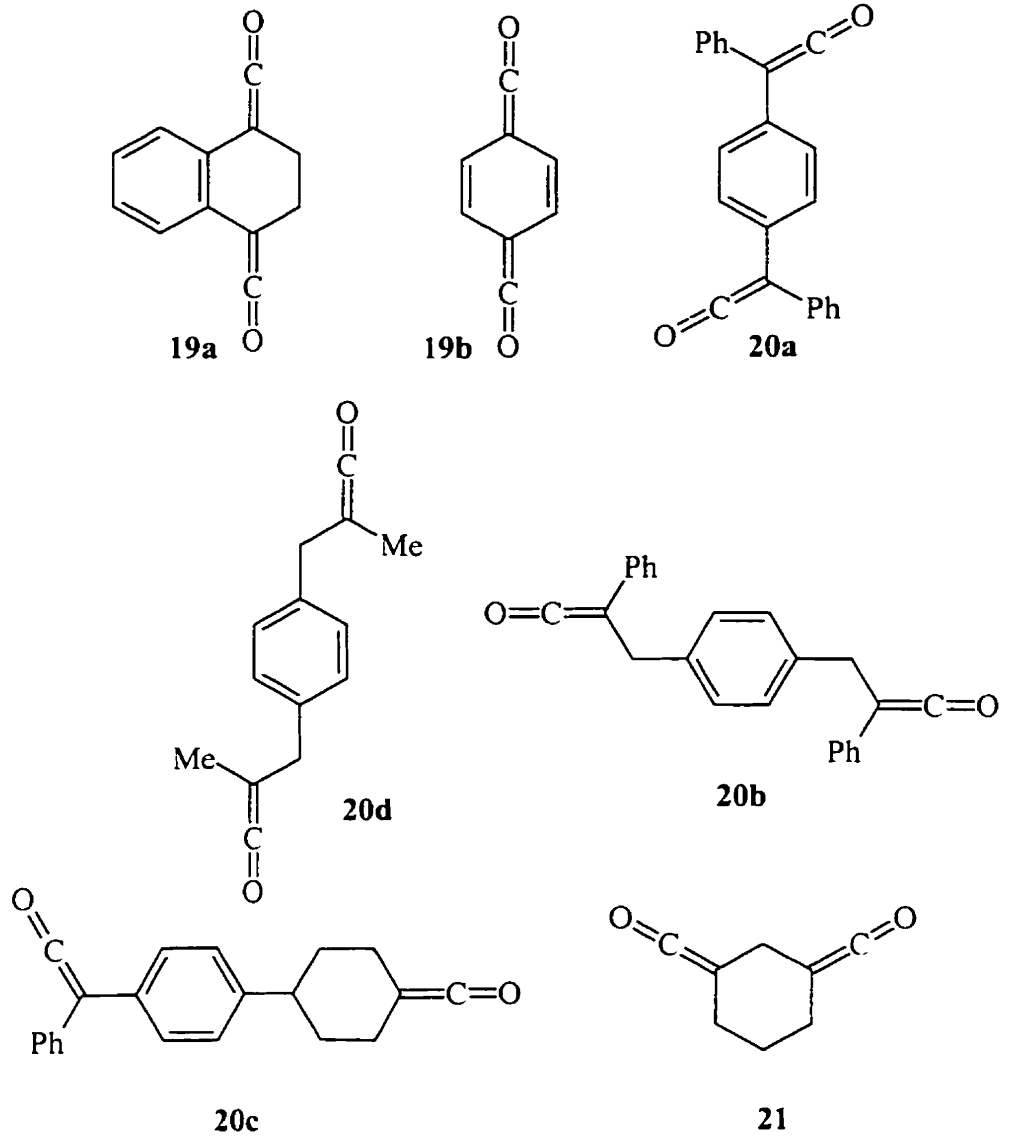
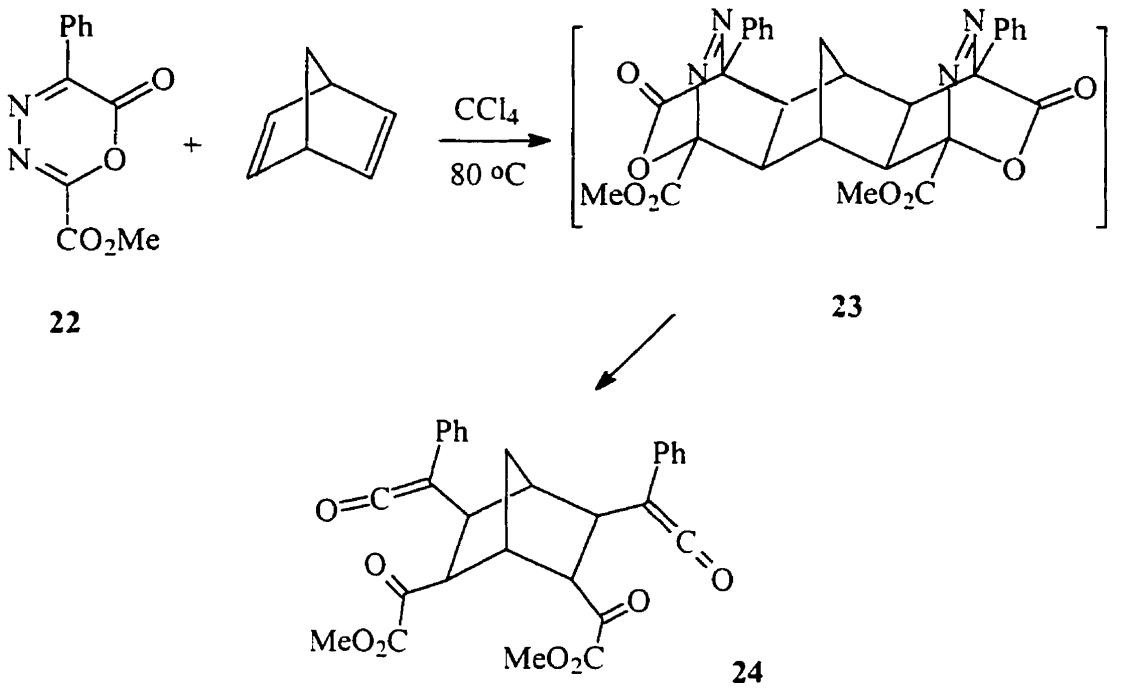


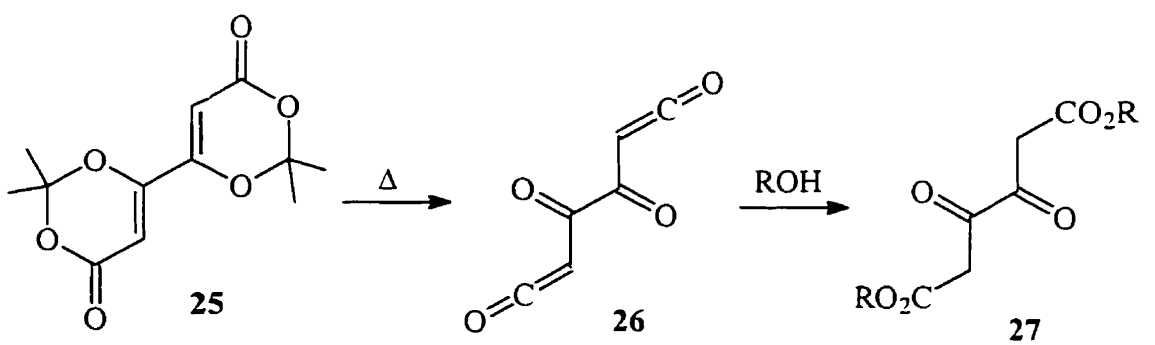

**Figure 5**

The reaction of 6-oxo-5-phenyl-1,3,4-oxadiazin-2-carboxylate **22** with norbornadiene afforded the Diels-Alder adduct **23**,[14] which decomposed in solution at the temperature of the reaction conditions to give the bis(γ-oxoketene) **24** as a stable compound in solution (Eq. 8). Thermolysis of the

bisdioxenone **25** in the presence of alcohols gave diesters **27** and may formally be represented as proceeding through the bisketene **26** (Eq. 9),[15] although stepwise reactions probably occurred.




(8)

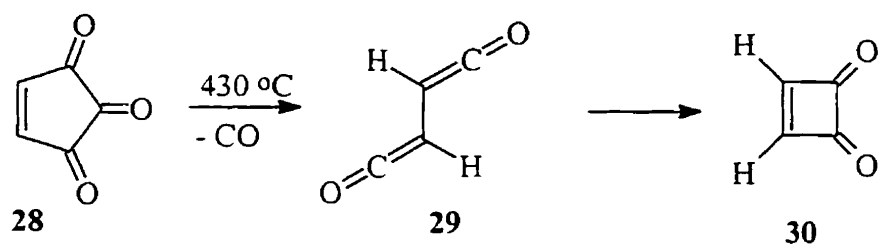



(9)

## 1.3 Bisketenes from cyclobutenediones

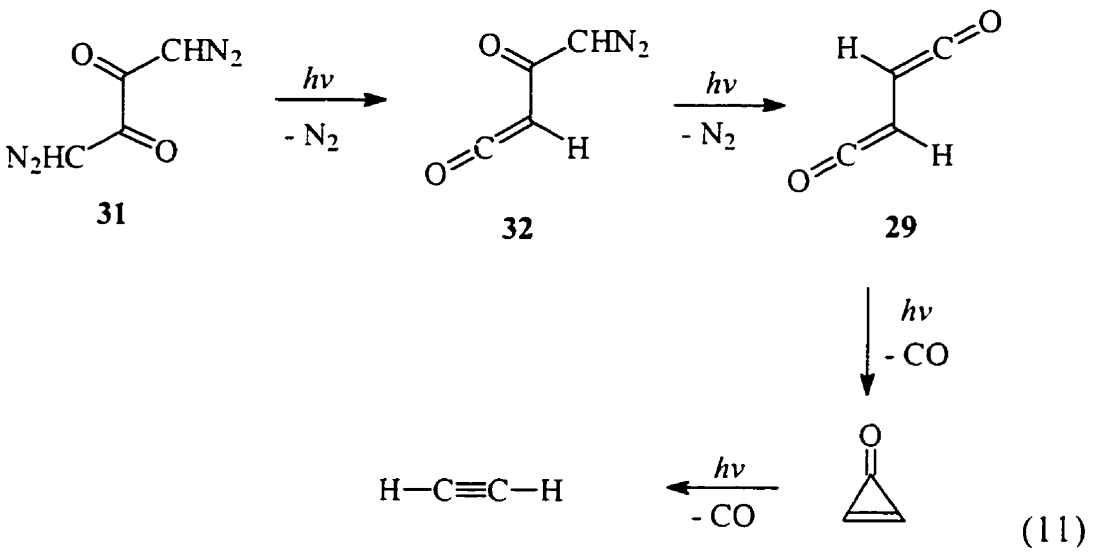
The search for 1,2-bisketenes, which have four carbon atoms compared to three for carbon suboxide, led to the study of the photochemistry of cyclobutenediones. However the parent bisketene **29** has not yet been made by this route, but was generated by other methods.[16,17] These bisketenes were generally generated as reactive intermediates or observed at low temperature.

The parent bisketene **29**, 1,3-butadiene-1,4-dione (1,2-bisketenyl) was first generated by Kasai, et al.[16] Flash pyrolysis of **28** at 430 °C in *vacuo* and deposition of the pyrolysate in methylene chloride cooled at - 78 °C gave **30** in a 9% yield, together with polymeric materials (Eq. 10). The formation of **29** by decarbonylation was confirmed by ring closure to **30** as well as by trapping of **29** with methanol to give dimethyl succinate.



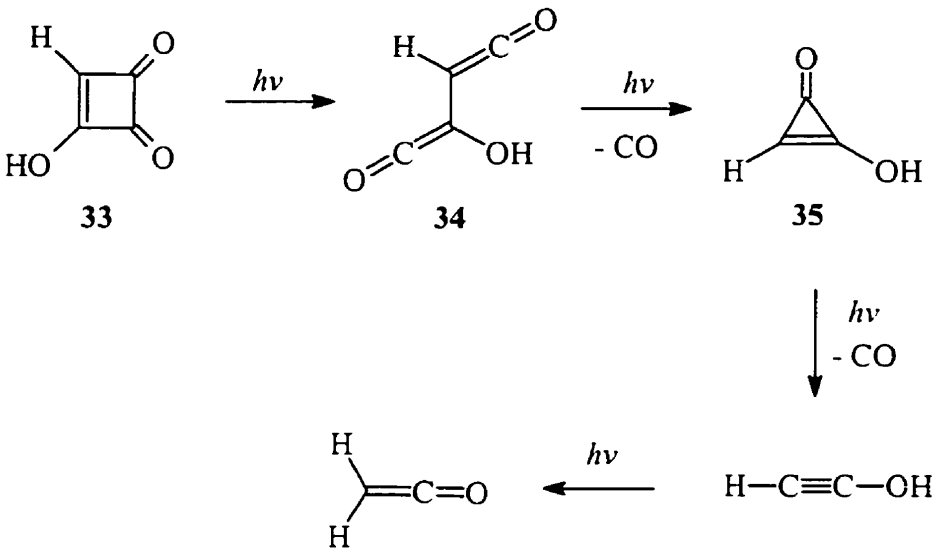

**28** **29** **30** (10)

Irradiation of the diazo ketone **31** in an argon matrix gave a stepwise Wolff rearrangement to the parent bisketene **29** *via* the oxo-ketene intermediate **32** (Eq. 11). Further irradiation of **29** gave the decarbonylation products cyclopropenone and acetylene.[17] The products **29, 32,** and cyclopropenone were all characterized by their IR spectra.

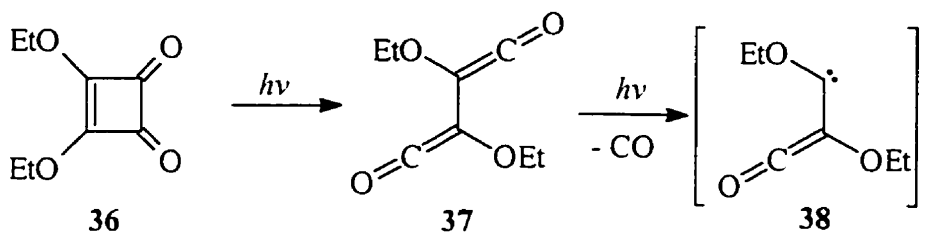



31 32 29 (11)

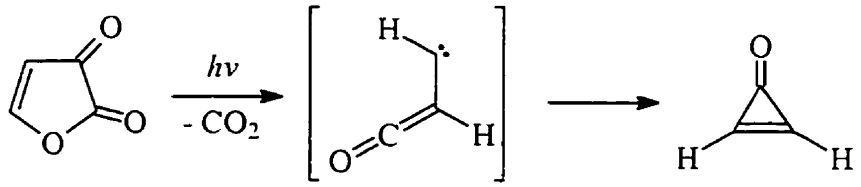
Irradiation of 3-hydroxycyclobutene-1,2-dione **33** (semisquaric acid) in an argon matrix cleanly yields ethynol in three photochemical steps (Eq. 12). The first photolysis product of **33**, 2-hydroxy-1,3-butadiene-1,4-dione **34** (hydoxybisketenyl), exhibits two very strong relatively broad carbonyl bands at 2112 and 2135 $cm^{-1}$.[18] Photolysis of the diethoxy analog **36** in ether gave the cyclopropenone **39** (Eq. 13). In ethanol the presumed bisketene intermediate **37** gave the succinate diester.[19] Bisketenes **34** and **37** under further irradiation gave cyclopropenones **35** and **39**, presumably *via* carbene intermediates such as **38**. The photolysis of furan-2,3-diones also leads to cyclopropenones, and this has been proposed to occur *via* carbene intermediates analogous to **38** (Eq. 14).[42]


H
O
HO
O
33
hv
H
C=O
O=C
OH
34
hv
- CO
O
H
OH
35
hv
- CO
H
C=C=O
H
hv
H—C≡C—OH

(12)

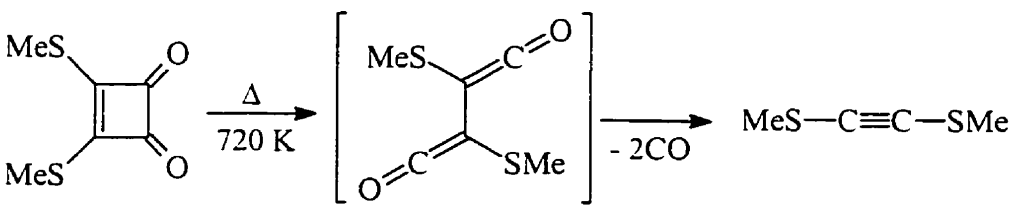

EtO
O
EtO
O
36
hv
EtO
C=O
O=C
OEt
37
hv
- CO
EtO
O=C
OEt
38
O
EtO
OEt
39
hv
- CO
EtO—C≡C—OEt

(13)

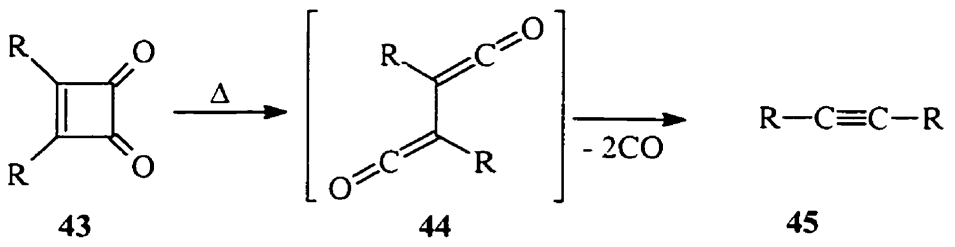


(14)

The photolysis and thermolysis of cyclopropenones is known to give acetylenes,[34] and cyclobutenediones have also been used to prepare novel acetylenes. Thermolysis of the cyclobutenedione **40** at 720 K occurred with bisdecarbonylation, and gave the alkyne **42** (Eq. 15). Similar results were obtained for the bis($CH_3Se$) and dichloro-substituted cyclobutenediones.[20] Flash pyrolysis at 650 °C of alkynyl-substituted cyclobutenediones **43** leads to bisdecarbonylations and formation of alkynes **45** (Eq. 16). These reactions likely proceed through the bisketene intermediates **44** which undergo thermal decarbonylation.[21]



**40** **41** **42** (15)

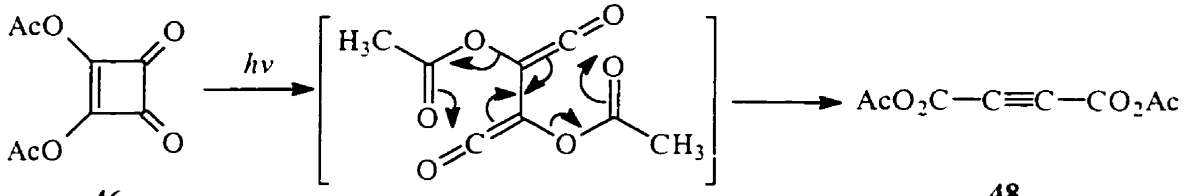



**43** **44** **45**

R = PhC≡C, PhC≡CC≡C

(16)

Irradiation of **46** gave the acetylene **48**, and this result was explained as occurring through the bisketene **47** as a first unobserved intermediate, which then reacts by a novel bis[3,3] sigmatropic rearrangement to give the acetylene **48** (Eq. 17).[22]




**46** **47** **48**

(17)

Refluxing of 3-phenyl-1,2-cyclobutenedione in methanol led to dimethyl 2-phenylsuccinate and the butenolide **50** (Fig. 6), and this may be explained as resulting from two competing reaction routes, namely formation of the bisketene **49** which gives the ester, or by addition of methanol to the cyclobutenedione followed by ring opened to the vinylketene, which could afford the succinate ester and the butenolide **50**.[23]

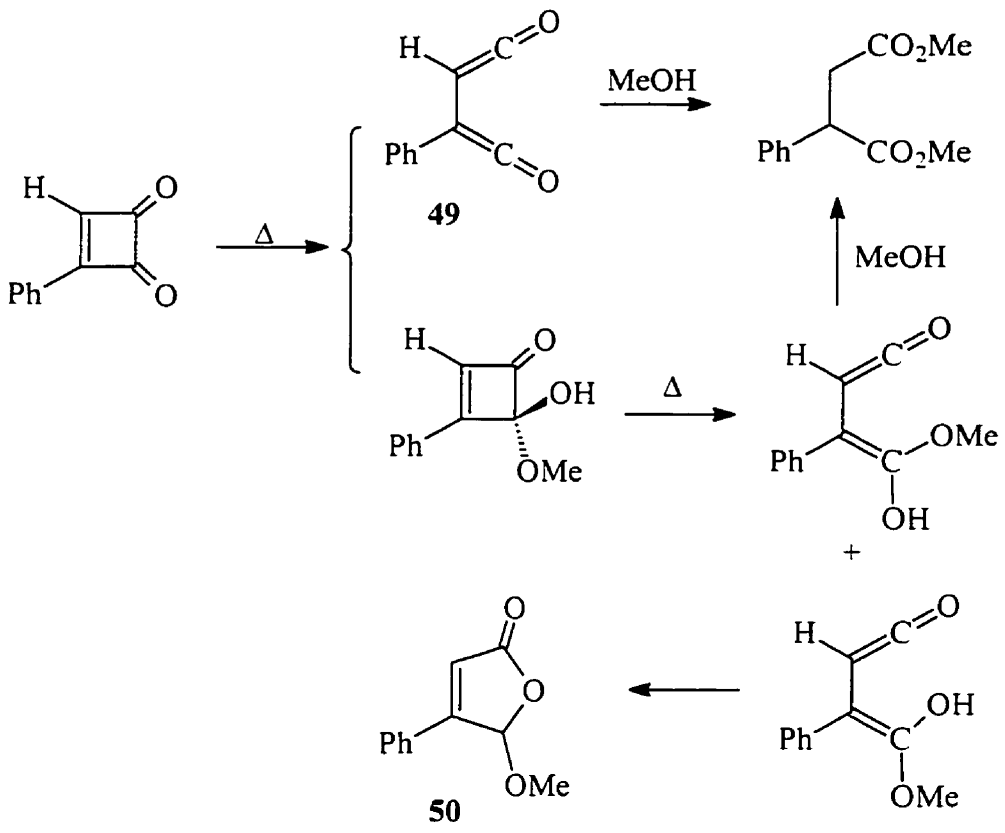
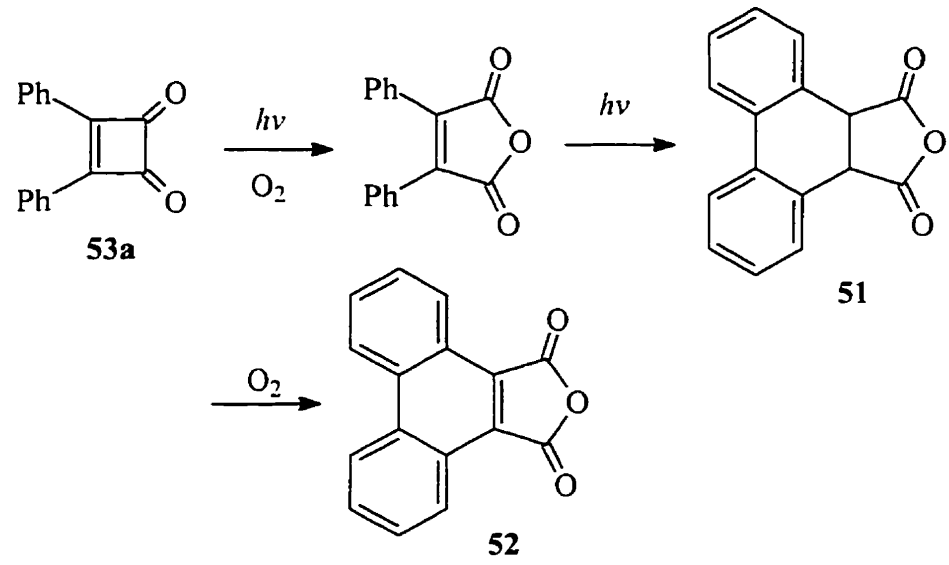



**Figure 6**

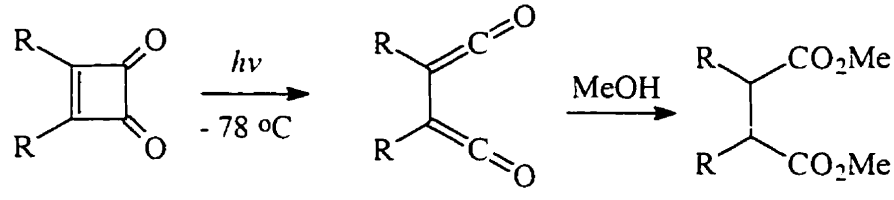
Photolysis of 1,2-diphenylcyclobutenedione resulted in the rapid formation of the phenanthrene 9,10-dicarboxylic anhydride **52** and its 9,10-dihydro-derivative **51** (Eq. 18). The same products were obtained by irradiation of diphenylmaleic anhydride, which was assumed to be an intermediate in this conversion.[24a] Obata and Takizawa[24b] separated the diphenylmaleic anhydride in 4% yield.




**53a** **51** **52**

(18)

Obata and Takizawa[25] reported the direct observation of the bisketene intermediate **54** by IR spectroscopy during photolysis of the dione **53** at -78 °C (Eq. 19, 20). Irradiation of a benzene solution of the dione **53a** together with **57** gave the imino dione **56** in 86% yield. When a solution of the dione **53a** (R = Ph) in dry methanol was irradiated, dimethyl diphenylsuccinate **55** [meso form (67%) and dl form (17%)] were obtained.



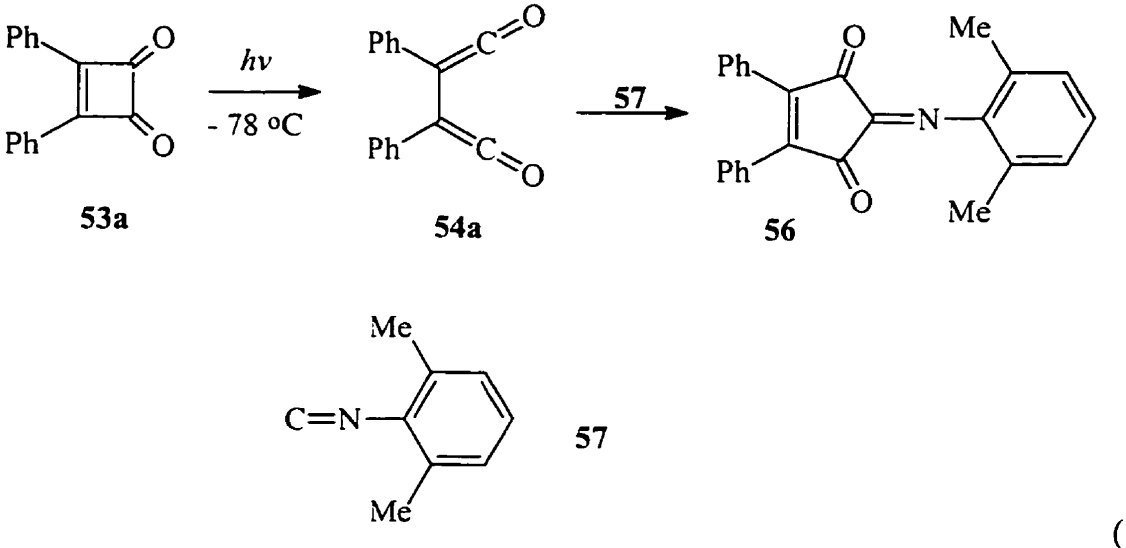

**53**

a, R = Ph

b, R = Me

**54** **55**

(19)




53a 54a 56 57

(20)

As part of their continuing interest in the reactions and rearrangements of α-ketenylcyclobutanones, R. D. Miller and his coworkers[26] have studied the cycloaddition of bisketenes with cyclopentadiene (Fig. 7). Irradiation of the cyclobutenedione **53a** in neat cyclopentadiene led to the isolation of the lactone **61** (R = Ph) in 83% yield as a single isomer. The structure of the lactone was confirmed by single-crystal X-ray analysis. As the size of the substituents in the 3,4-position of the cyclobutenedione was reduced, the resulting butenolides **61** were isolated as epimeric mixtures. Trapping the reaction mixture (R = Ph) with ethanol at -20 °C gave meso- and (±)-diethyl 2,3-diphenyl-succinates (40%), the keto ester **62** (35%), and the butenolide **61** as a minor product (< 3%). These results demonstrated that the butenolide **61** resulted from the rearrangement of **60** which was formed by the bisketene [2+2] cycloaddition, and that **61** did not arise from an insertion reaction of a carbene intermediate **59**.

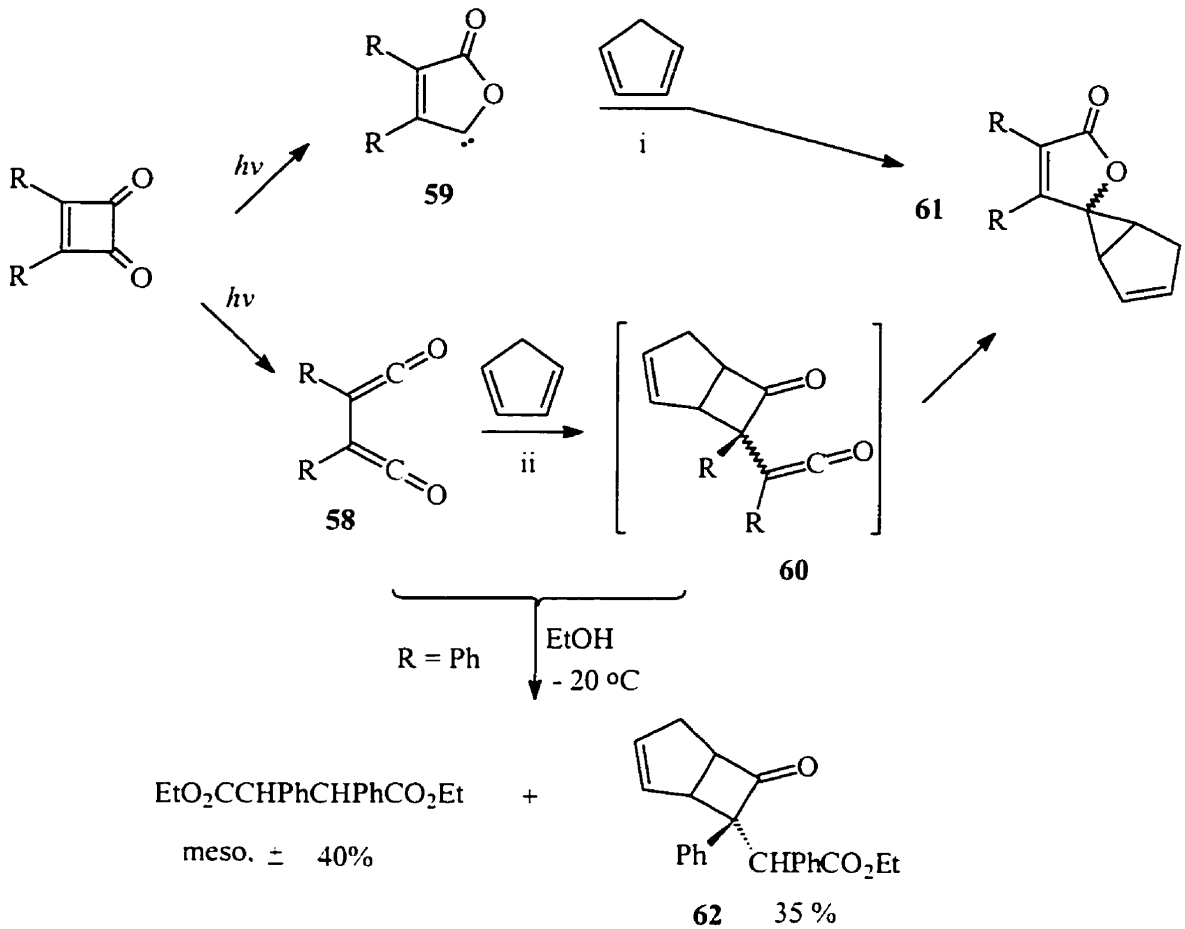
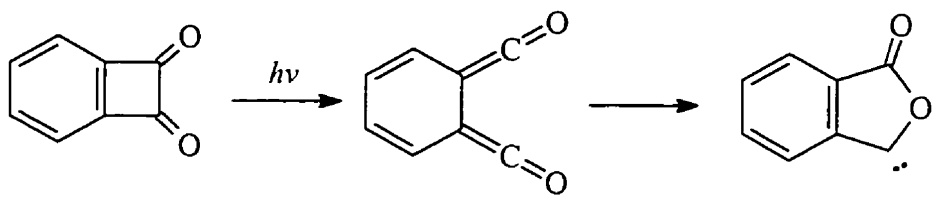



**Figure 7**

## 1.4 Bisketenes from benzocyclobutenediones

The photochemistry of benzocyclobutenedione **63** has been the subject of several detailed investigations under solution conditions,[27a-c] as a thin film[27d] and in glassy matrix at - 196 °C,[28] in an argon matrix[29] and under laser flash conditions at room temperature.[30]

The bisketene **64** was identified using UV detection as a relatively long-lived intermediate ($\tau$ > 100 ms) in the laser flash photolysis study (Eq. 21).[30a] In collaborative studies between our group and Lusztyk and Wagner[30b] the kinetics of the ring closure of **64** to **63** have been measured using time-resolved infrared spectroscopy. Oxocarbene **65** has not been observed directly and its existence is still the subject of some controversy.




**63** **64** **65** ( 21)

Directly trapping the bisketene **64** after its generation in an argon methanol matrix followed by warming up to room temperature gave methyl *o*-formylbenzoate **66** (ca. 38%), butenolide **67** (ca. 45%), and phthalate **68** (ca. 17%) (Fig. 8).[31] The formation of **68** was assumed to result from oxidation of a non-observed dihydrophthalate. Butenolide **67** may be formally explained by methanol insertion by the carbene intermediate **65**, but it is more likely formed from methanol addition to the bisketene **64** to give the intermediate **70**, which rearranges to **67** via **71** (Fig. 8). The formation of the *o*-formylbenzoate **66** was explained by a 1,4-addition of the methanol to the bisketene **64** via the transition state **69**.[31] Rearrangement of **70** is another possible route to **66**. Photolysis of the ethyl ester analog of the *o*-formylbenzoate **66** resulted in a quantitative conversion to the ethoxy analog of butenolide **67**, which was the only separated product upon irradiation of the dione **63** with ethanol.[27e]

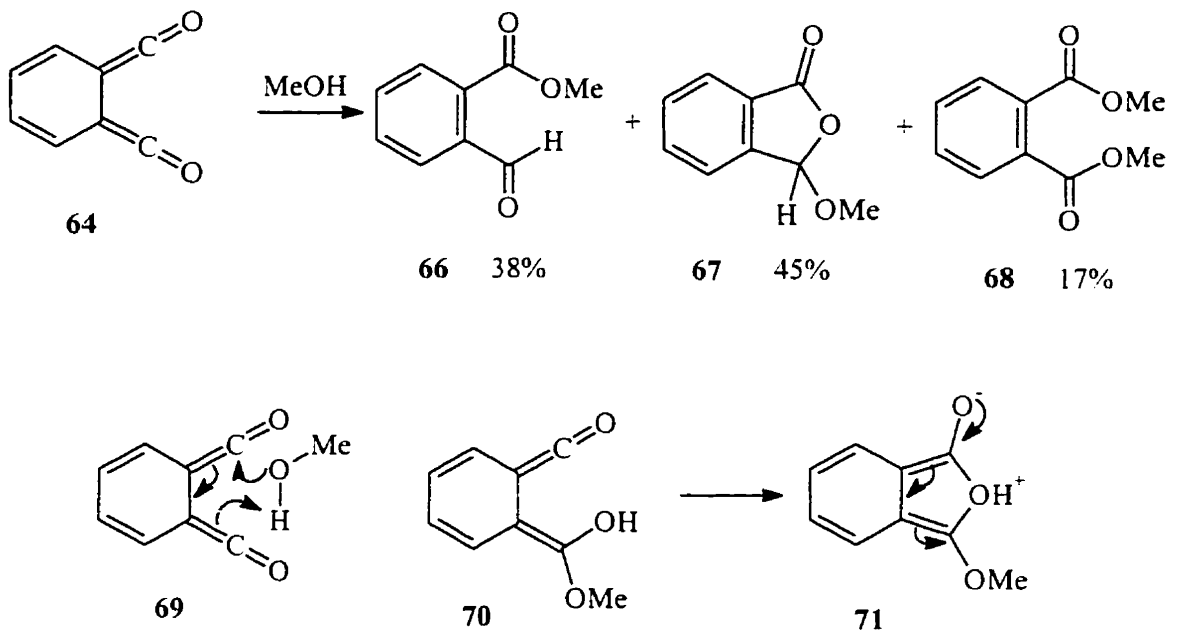
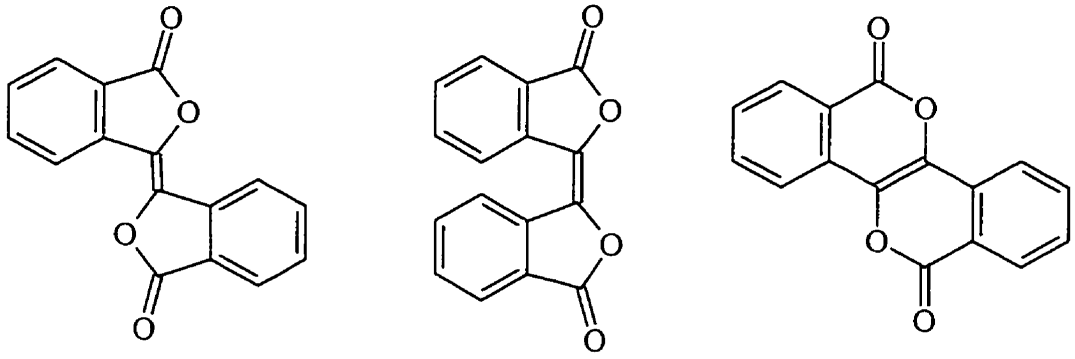


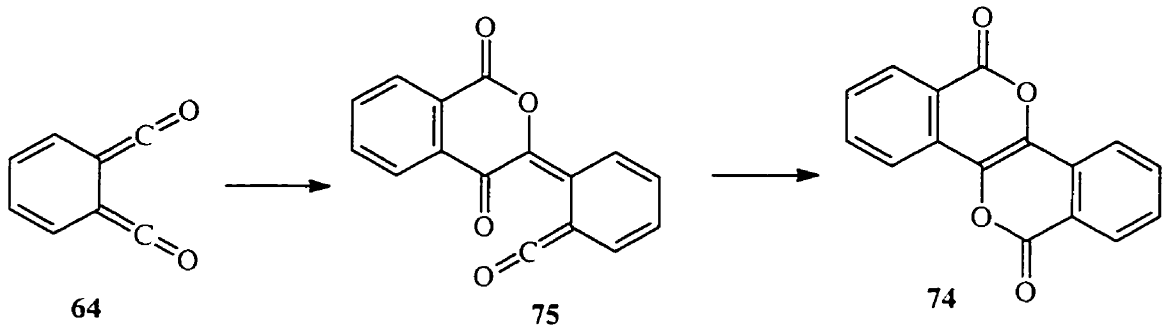

**Figure 8**

Upon photolysis of the dione **63** in the absence of trapping agents dimers **72-74** are formed (Fig. 9).[27a-c,32] The bisisocoumarin **74** was proposed to be the result of a dimerization of the bisketene through the [4+2] cycloaddition intermediate **75** (Eq. 22). The trans-biphthalyl **72** and cis-biphthalyl **73** may be described as resulting from the dimerization of the proposed carbene intermediate **65**.[27c] However, the possibility that these are formed through the bisketene **64** intermediate by one of the alternative pathways shown (Eq. 23) or other mechanisms cannot be ruled out.



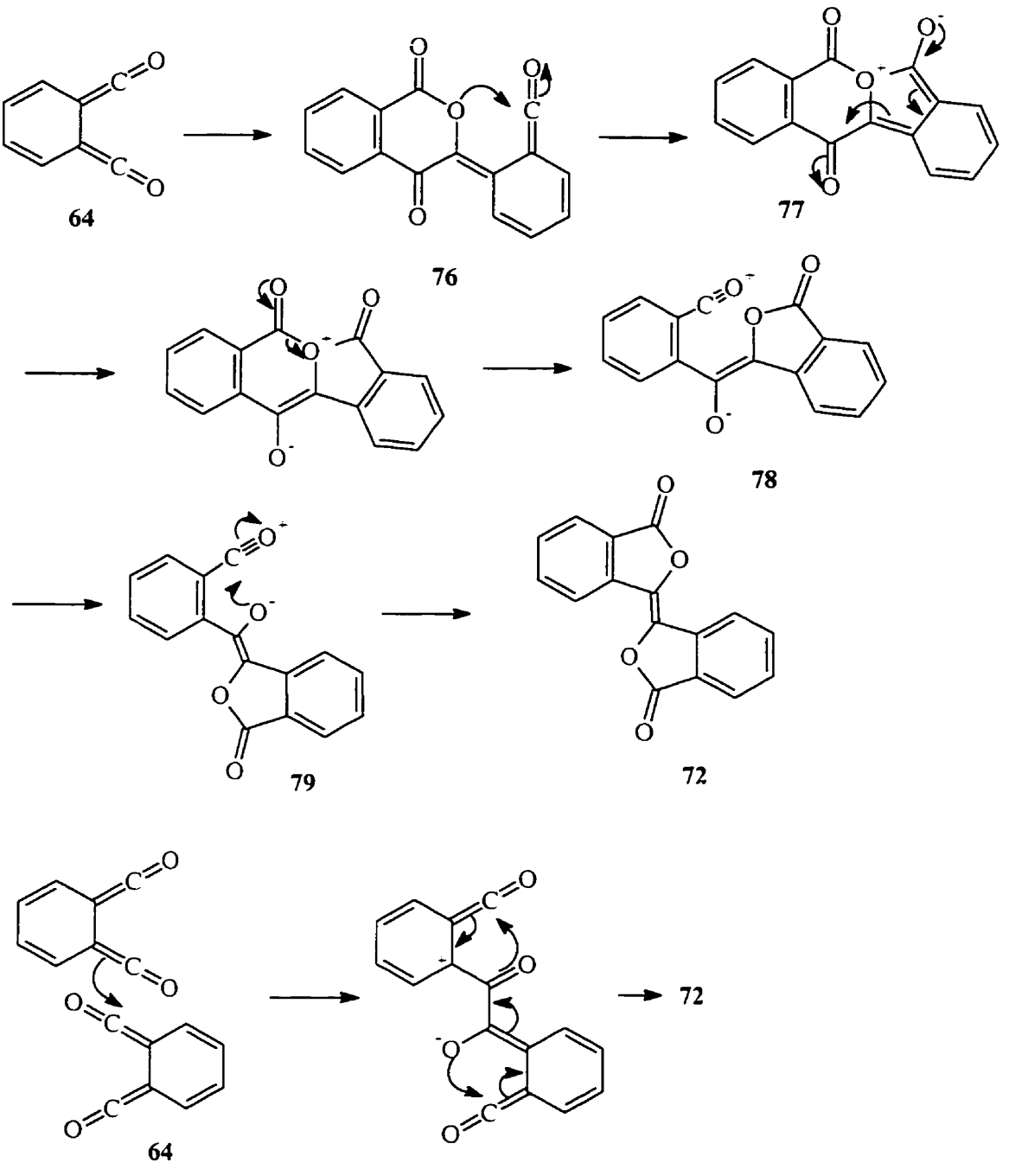
72 73 74

**Figure 9**



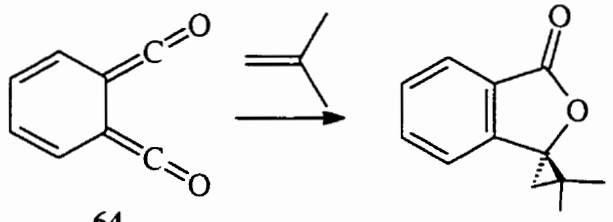
64 75 74

(22)

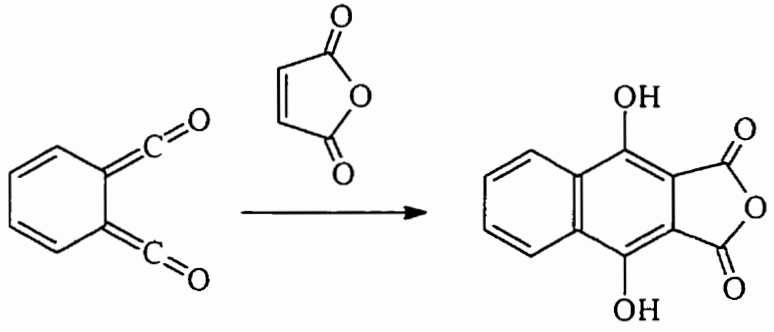



(23)

Olefin reactions with **64** to give spirocyclopropanyl butenolides such as **80** have been observed,[27b,c] and these were proposed to be the results of trapping of the oxocarbene **65** (Eq. 24). However these may also be explained by an initial [2+2] cycloaddition similarly to Miller's proposal (Fig. 7).[26] Products resulting from trapping of the bisketene by electron deficient olefins such as maleic anhydride to give [4+2] addition products such as anhydride **81** have also been reported (Eq. 25).[27b,c]



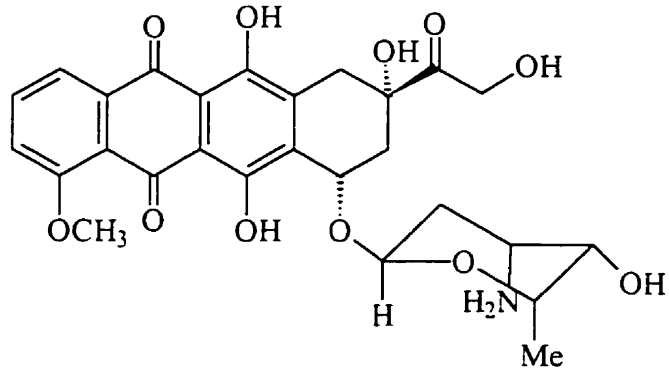
**64** **80** 65% (24)



**64** **81** 67% (25)

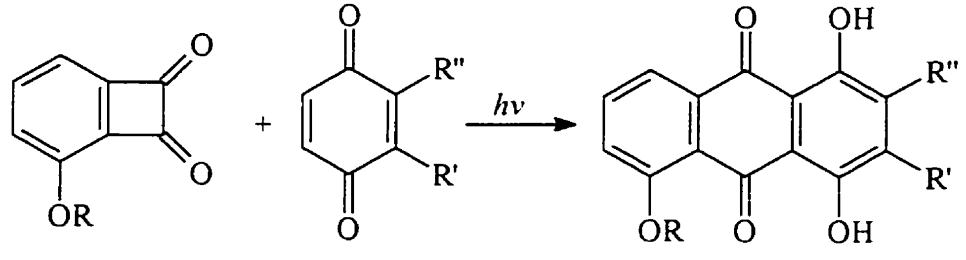
Jung and Lowe[33] reported synthetic approaches to the potent antineoplastic agent adriamycin (Fig. 10) involving Diels-Alder reaction of photochemically generated bisketenes (Eq. 26). The ether **82** (R = $CH_2OCH_3$) was photolyzed in the presence of several quinones **83**, and the desired

anthraquinone products **84** were obtained, albeit in yields that were low for unexplained reasons. These methods also resulted in a straightforward total synthesis of the natural products isolandicin and digitopurpone.



**adriamycin**

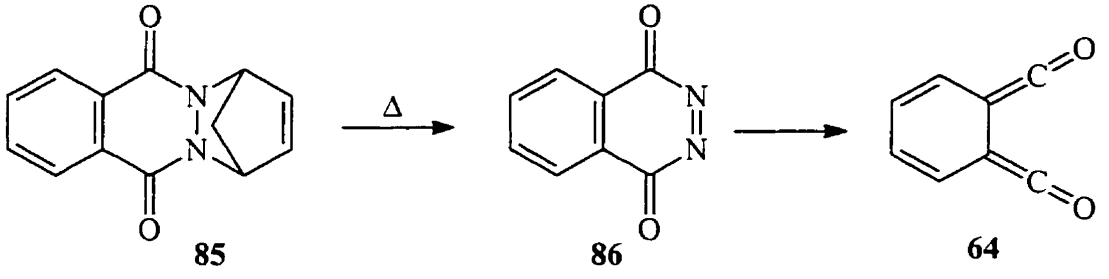
**Figure 10**



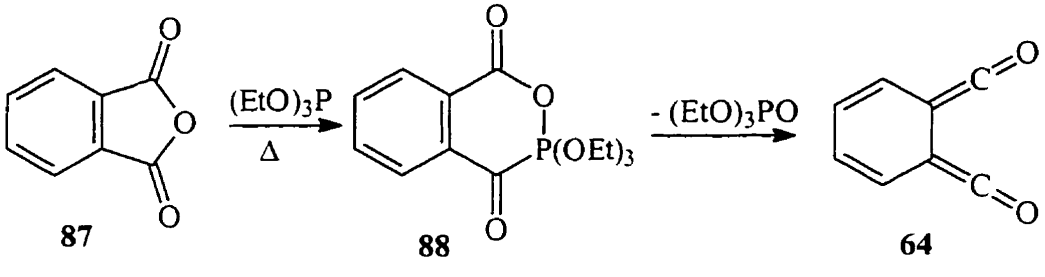
**82** **83** **84** 4.8-13.5% (26)

Other methods for generation of the bisketene **64** include pyrolysis of **85** to give the retro Diels-Alder reaction intermediate **86** which lost nitrogen to give the bisketene **64** (Eq. 27).[10b] The reaction of the anhydride **87** with

phosphite has also been reported to lead to bisketene intermediate **64**, possibly by a route involving the intermediate **88** (eq. 28).[35] The bisketene **64** has not been observed in these reactions, but was converted to the dione **63**, or led to the formation of dimers **72-74**.




**85** **86** **64** (27)




**87** **88** **64** (28)

## 1.5 Other bisketenes

The photolysis of the dione **89** in methanol afforded the acid anhydride **92** in a 72% yield (Fig. 11).[36] Since the photolysis of anhydride **91** under the same conditions as employed for the dione **89** afforded **92** in an 82% yield, **91** was a probable intermediate of the reaction. The photochemical reaction of the dione with benzylamine in dry THF afforded the imide **94** via **93**. The

intermediacy of **93** in the latter photolysis was supported by a separate photolysis of an authentic sample of imide **93** to afford **94**. However, the oxidation step was not discussed, but probably involved reaction with atmospheric oxygen.[36]

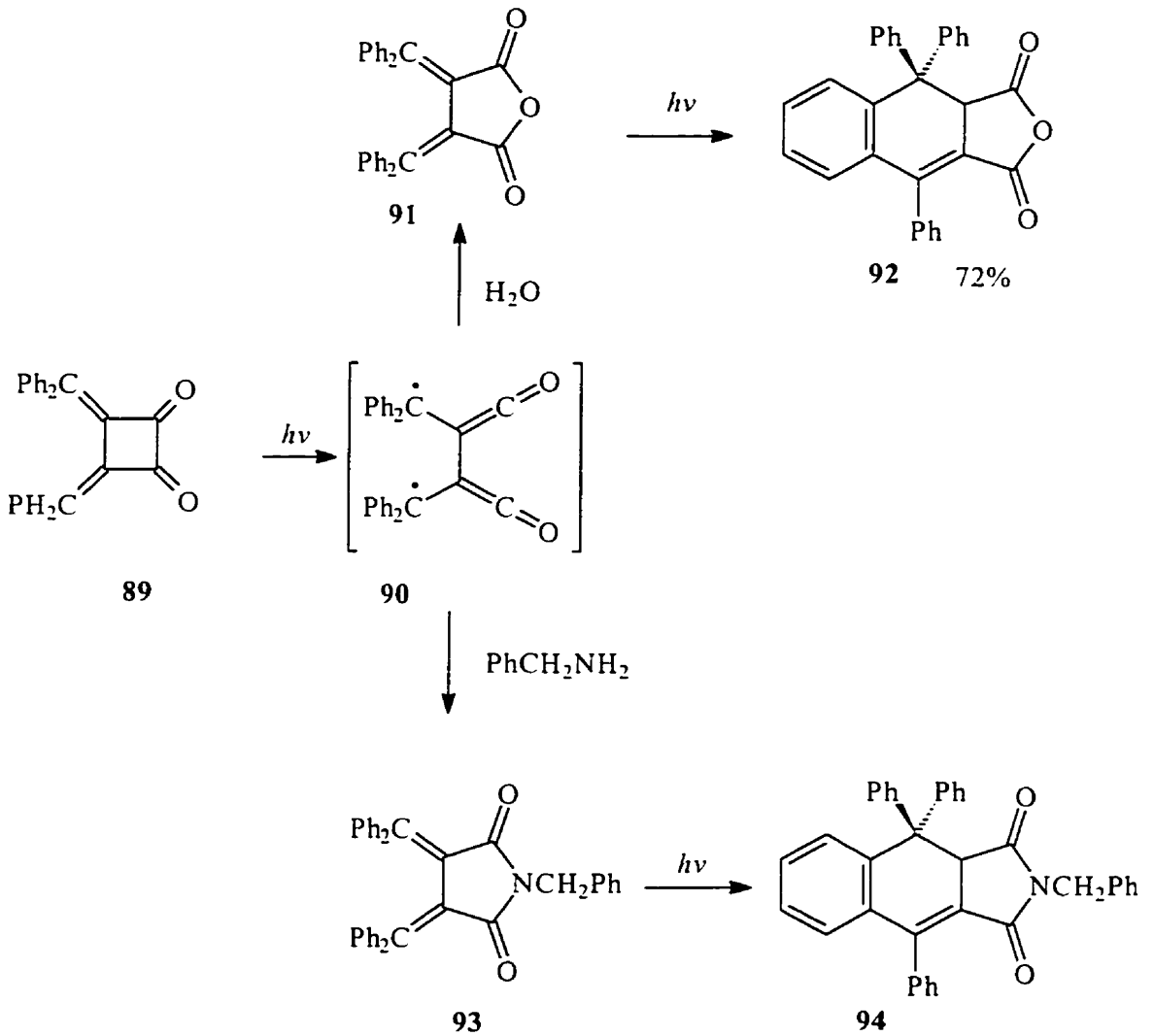
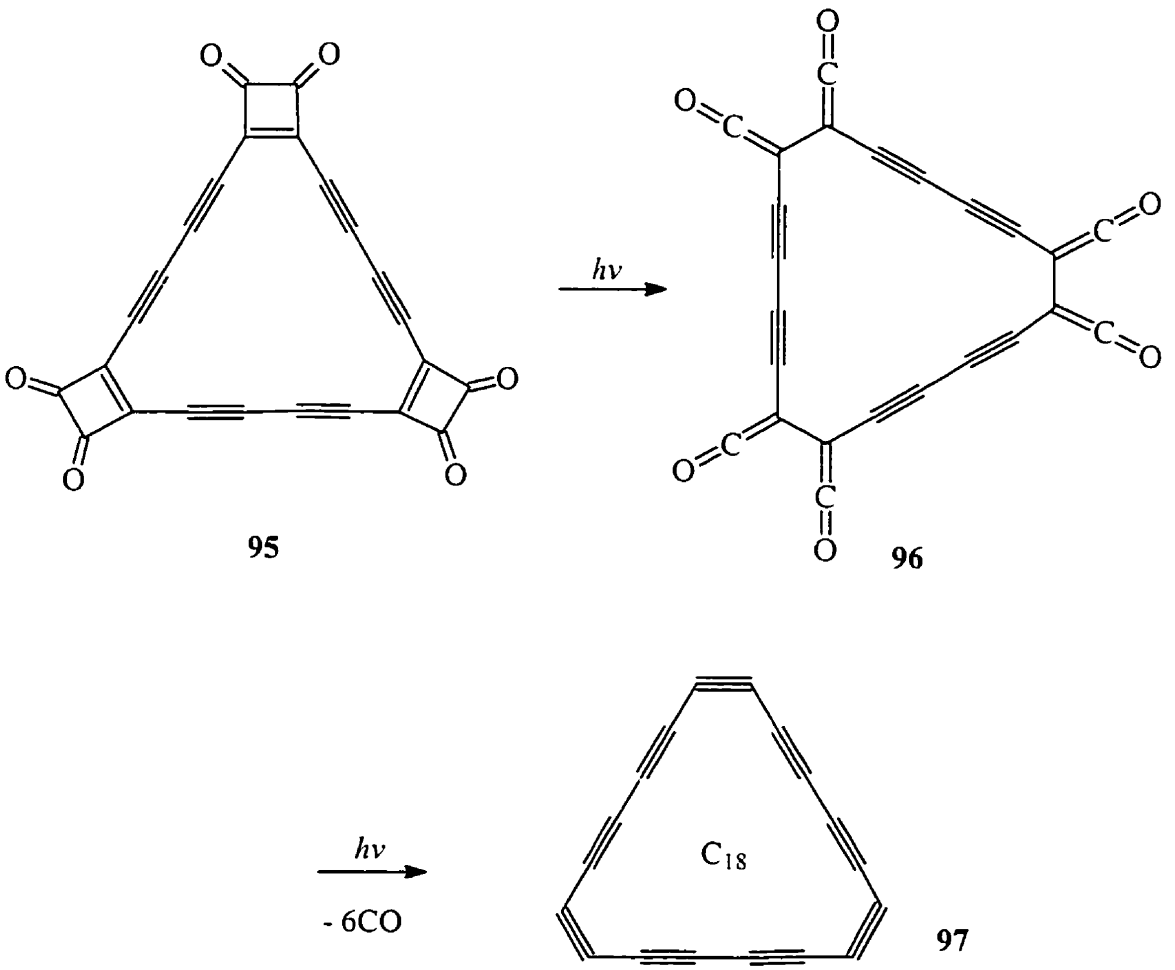


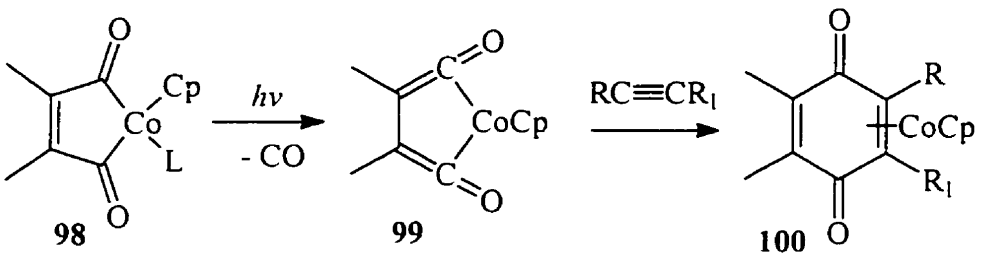

**Figure 11**

Irradiation ($\lambda > 338$ nm) of the dione **95** in a 1,2-dichloroethane glass at 30 K generated within six minutes an IR band at 2115 $cm^{-1}$ which may arise from the hexaketene **96** (Eq. 29). Further irradiation resulted in the loss of CO and presumably the carbon macrocycle **97**.[37]




(29)

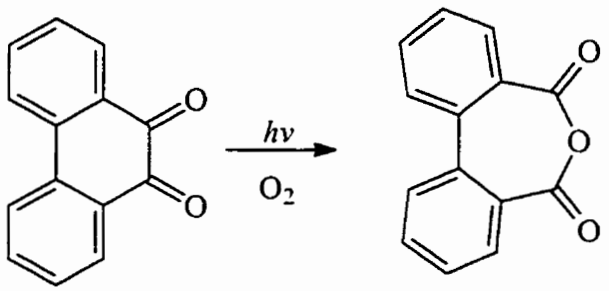
Photolysis of the metal complex **98** (L = CO) resulted in the extrusion of CO and gave the metal complexed bisketene **99** in 78% yield (Eq. 30).[38] The structure of **99** was confirmed by a single-crystal analysis. However, the C-C-O bond angles (145.5°, 142.8°) indicate substantial rehybridization of the carbonyl carbons from sp toward $sp^2$. Bisketene complex **99** reacted under mild conditions with a variety of alkynes to give excellent isolated yields of $\eta^5$-CpCo-($\eta^4$-1,4-benzoquinone) compounds **100**, which might be formed through the maleoyl cobalt species **98** (L = alkyne), instead of a direct bisketene [4+2] reaction.[38]



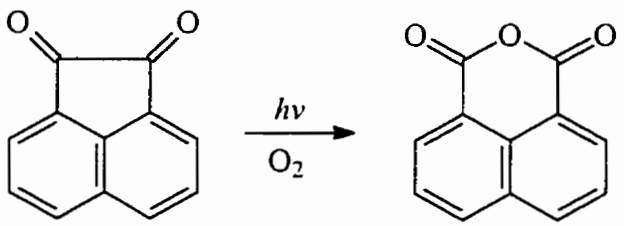

**98** **99** **100**

Cp = cyclopentadienyl (30)

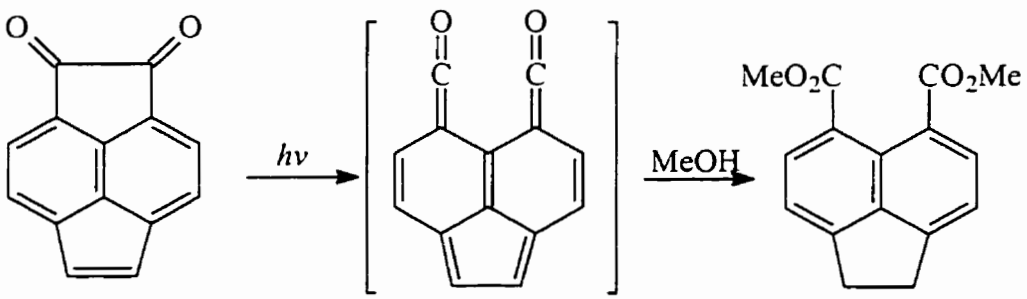
Exposure of a benzene or acetonitrile solution of phenanthraquinone **101** or acenaphthaquinone **103** to sunlight in the presence of oxygen resulted in the formation of biphenyl-2,2'-dicarboxylic anhydride **102** and naphthalene-1,8-dicarboxylic anhydride **104**, respectively (Eq. 31 and Eq. 32). Both these reactions might proceed by formation of the related bisketenes.[24a] Irradiation of a methanolic solution of pyracyloquinone **105** leads to formation of dimethyl 5,6-acenapthenedicarboxylate **107** in 30% yield. The reaction was suggested to proceed *via* the bisketene quinoid tautomer **106** (Eq. 33).[39]




**101** **102** (31)




**103** **104** (32)




**105** **106** **107** (33)

The irradiation of *o*-benzoquinones **108** at low temperature monitored by infrared and ultraviolet spectroscopy revealed that the photodecarbonylation to

cyclopentadienones **109** is highly sensitive to the substituents on the benzoquinone, and the competitive α-fission to give the interesting bisketenes **110** become more important in simpler benzoquinones (Fig. 12). For the benzoquinone **108a**, four ketene bands observed at 2022, 2129, 2136, and 2146 $cm^{-1}$ have been attributed to the four possible rotamers (**110a** or **111a**) available by rotation about the C-C single bond at - 170 °C. The possibility that carbon monoxide can be formed in the photodecarbonylation of bisketenes **110a** initially formed was excluded, since a plot of intensities of carbon monoxide and bisketene **110a** absorption as a function of irradiation of time indicate that both compounds are primary photo products of *o* -benzoquinone **108a**.[40]

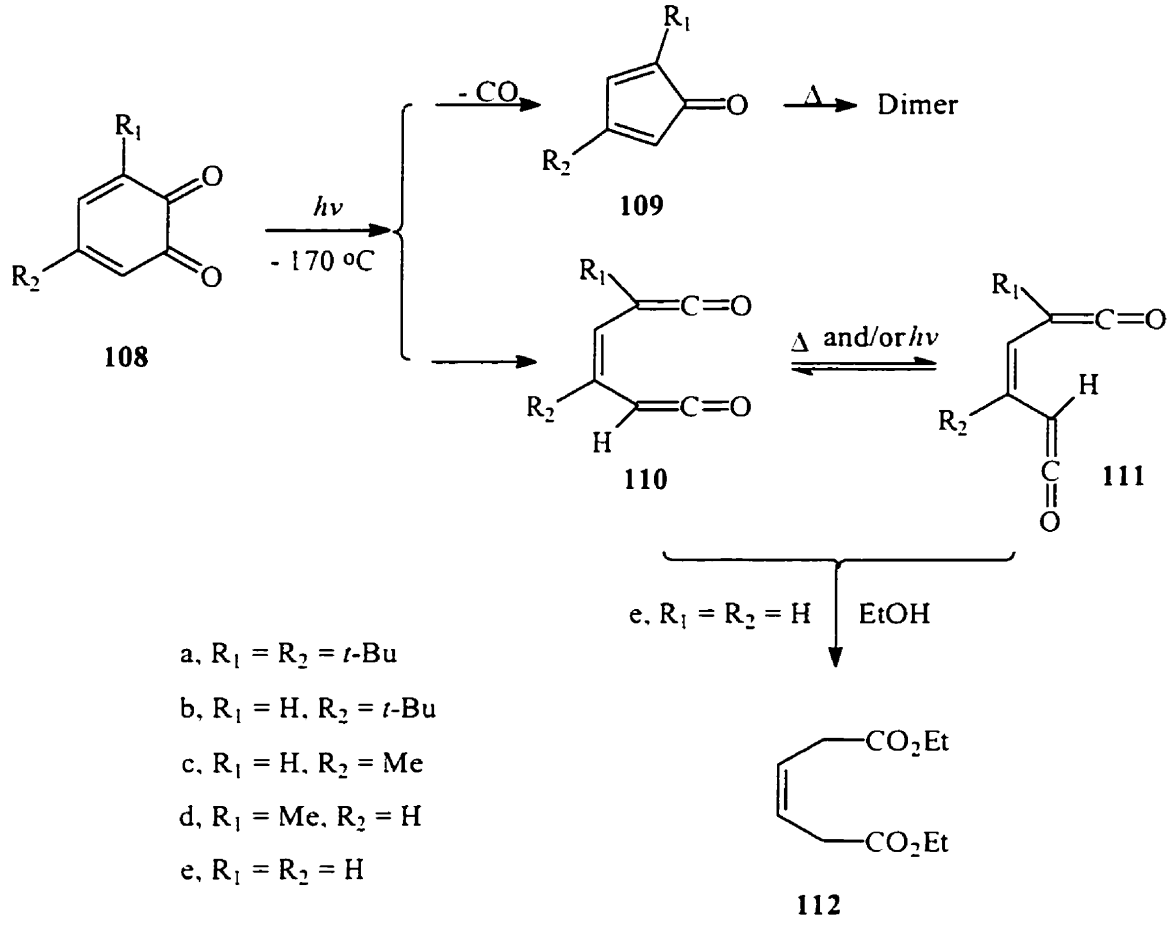
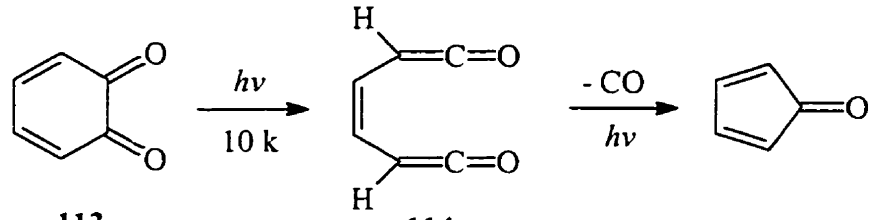



**Figure 12**

Irradiation of *o*-quinone **113** with a lamp $\lambda > 300$ nm gave the bisketene **114** observed by IR spectroscopy at 10 K in an argon matrix (Eq. 34). Formation of cyclopentadienone was not observed with further irradiation. However, when shorter wavelength irradiation (254 nm) was used, the bisketene gave decarbonylation to produce cyclopentadienone. These results indicated that at least for *o*-quinone itself under these conditions, the generation of the cyclopentadienone was through a bisketene intermediate. [41]




113 114 (34)

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# *Chapter 2*

# Preparation of Cyclobutenediones

## 2.1 Introduction

Cyclobutenediones are highly versatile starting materials for the synthesis of a variety of carbocyclic and heterocyclic products. Examples are the compounds (**2-7**) shown in Fig. 1, which are among the results of the most recent progress made by Liebeskind[1], Moore[2] and others[3]. An essential aspect of the utility of cyclobutenediones as synthetic precursors to other molecules is the ready availability of generally substituted and functionalized cyclobutenediones[4].

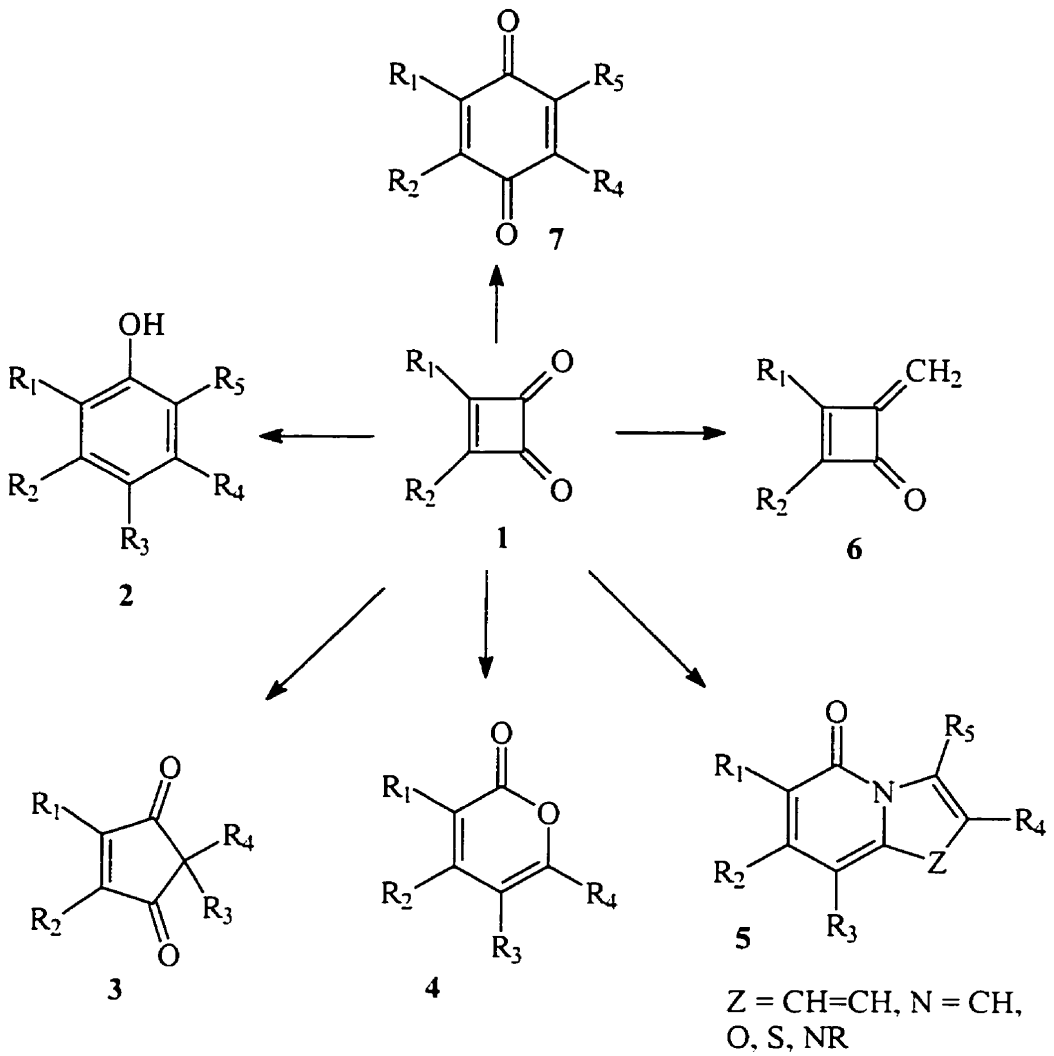
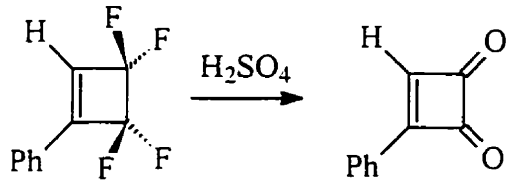



**Figure 1**

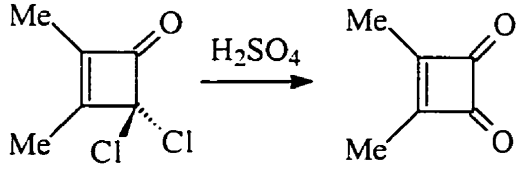
### 2.1.1 Cyclobutenediones from hydrolysis

The majority of methods for preparing cyclobutenediones rely on the hydrolysis of geminal dihalides (Eq. 1,2) or ketals (Eq. 3), which are available from a variety of photo or thermal [2+2] reactions. The methods have been reviewed by Schmidt and Ried[4b-e]. In most cases the hydrolysis was carried out

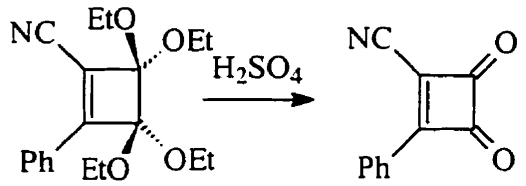
using Brønsted acids (normally concentrated sulfuric acid). However other reagents such as $AgBF_4$ have also been used. 3,4-Bis(diphenylmethylene)cyclobutene-1,2-dione **15** was obtained in almost quantitative yield by treatment of **14** with $AgBF_4$ in wet THF (Eq. 4). Interestingly, increasing the water content to 10% gave **16** as the major product (44%) together with some dione **15** (27%)[5]. Substituting $AgClO_4$ for $AgBF_4$ in wet THF gave the succinic anhydride **17** in (85%) yield (Eq. 5). In this latter reaction, the dione **15** is proposed to be formed initially and then oxidized by $HClO_4$ produced in the course of the reaction. This is substantiated by the ready oxidation of the dione with $HClO_4$, as well as with aqueous $H_2O_2$ and $HNO_3$[5].



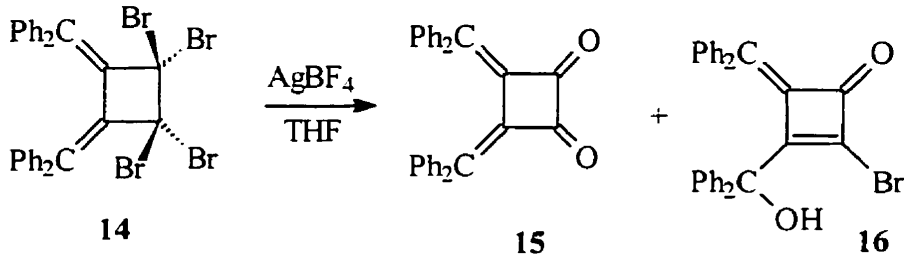

**8** **9** (1)



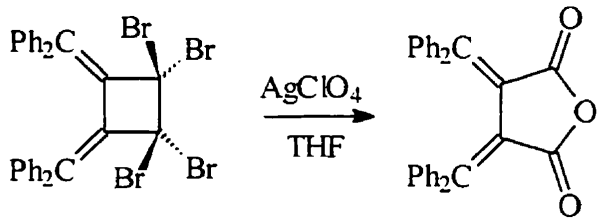

**10** **11** (2)




12 13 (3)




14 15 16 (4)

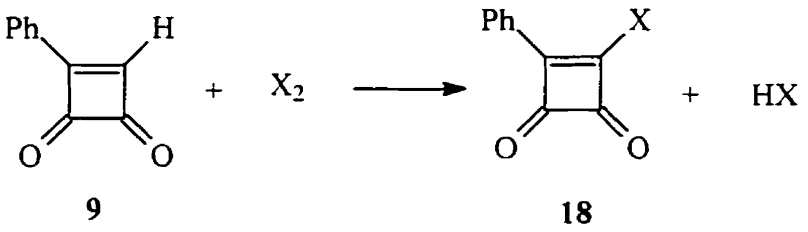



14 17 (5)

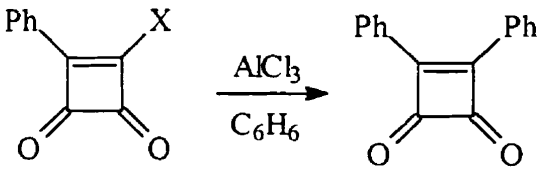
### 2.1.2 Cyclobutenediones from other cyclobutenediones

The conversion of one cyclobutenedione into another has also been a fruitful method of preparation. Dihalo or monohalocyclobutenediones have the potential of Friedel-Crafts reactions (Eq. 6,7), and have been reacted with a large variety of nucleophiles (Eq. 8). Many cyclobutenediones were obtained by this method[4]. A recent report by Shoji Eguchi and his coworkers[6] utilizes squaric acid (**21**), which is a commercially available and relatively cheap starting material. The dichloride **22** was obtained in 54% yield by the $SOCl_2$-dimethylformamide (DMF) method (Eq. 9). Dichloride **22** and a bulky allylsilane **23** were treated with titanium tetrachloride at - 78 °C in

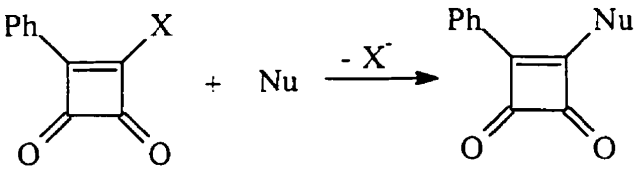
dichloromethane for 5 min to afford the dione **24** as the predominant product, which resulted from 1,4-addition to the enone moiety of the dione **22**, followed by dechlorosilylation (Eq. 10). However with less substituted allylsilanes, the major product was from the 1,2-addition to the dione **22**.



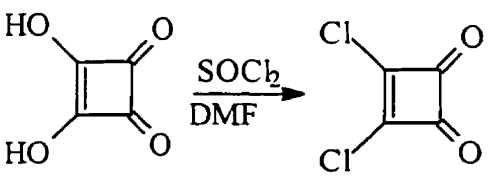

**9** **18** (6)



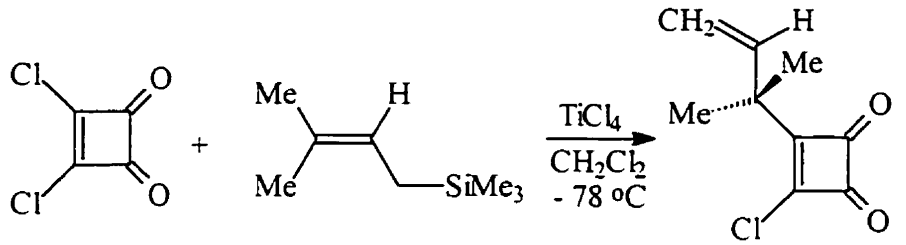

**18** **19** (7)




**18** **20** (8)

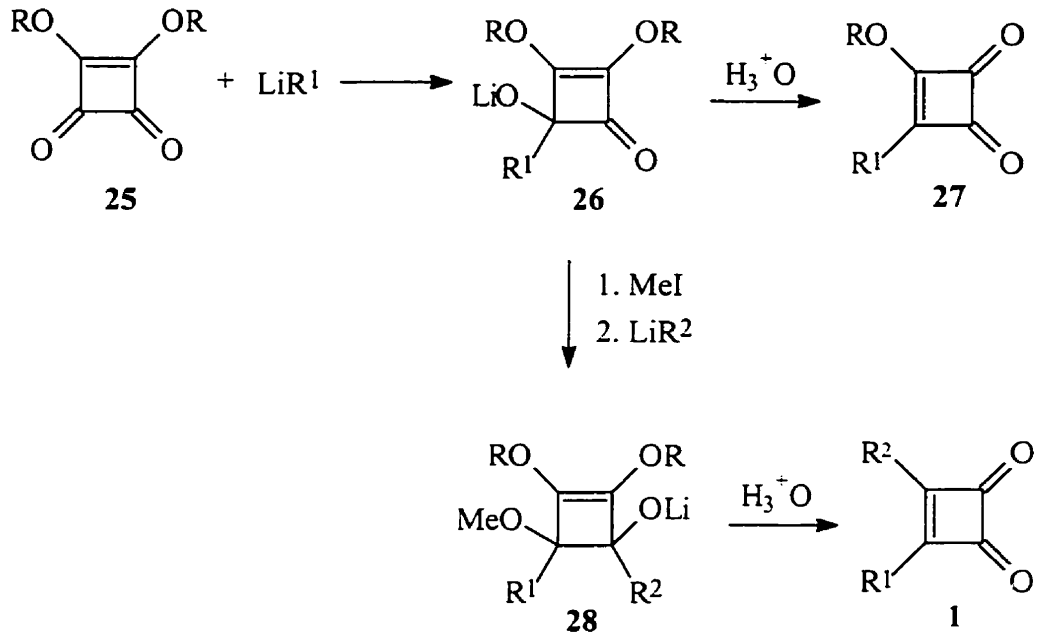



**21** **22** (9)

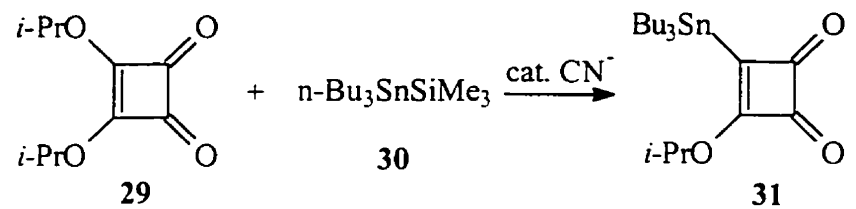



22 23 24 68% (10)

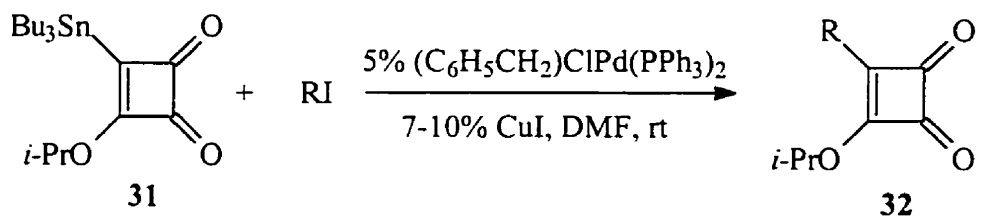
Another category of these methods is based on the conversion of squaric acid esters **25** into other cyclobutenediones **1** by reaction with organolithium reagents (Eq. 11). Liebeskind and Feng[7a] have also introduced organotin chemistry into this field. Treatment of 3,4 -diisopropoxycyclobutenedione **29** with n-$Bu_3SnSiMe_3$ and catalytic cyanide furnished 3-isopropoxy-4-(tri-*n*-butylstannyl)cyclobutenedione **31** in 65% yield (Eq. 12). This compound cross-coupled with organic iodides (aryl, vinyl, alkynyl) under the influence of cocatalytic palladium/Cu species to provide 3-isopropoxy-4-substituted cyclobutenediones **32** in good yields (57-99%) (Eq. 13). Attempts to extend the method to monoalkyl substituted cyclobutenediones failed to give the stannylcyclobutenediones; however an alternative method was introduced through the use of the cyclobutenedione monoacetals **33**. Treatment of the monoacetal **33** with n-$Bu_3SnSiMe_3$ and catalytic cyanide generated the stannylcyclobutenedione monoacetal **34** in 72% yield (Eq. 14). Cross-coupling of **34** with a variety of organic iodides was accomplished by utilizing the previously described Pd/Cu system (Eq. 15), providing a method for regiospecific synthesis of monoacetals **35** of disubstituted cyclobutenediones and furnishing substrates that on hydrolysis provide the parent cyclobutenediones **36** (Eq. 16).


RO
OR
O
O
+ LiR1
LiO
R1
H3+O
25
26
27
1. MeI
2. LiR2
MeO
OLi
R2
28
1

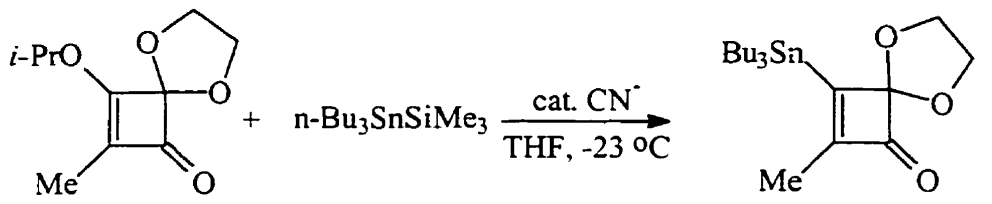
(11)


i-PrO
i-PrO
+ n-Bu3SnSiMe3
cat. CN-
Bu3Sn
29
30
31

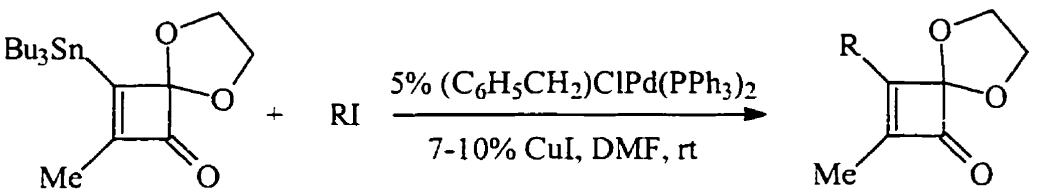
(12)


Bu3Sn
i-PrO
+ RI
5% (C6H5CH2)ClPd(PPh3)2
7-10% CuI, DMF, rt
R
31
32

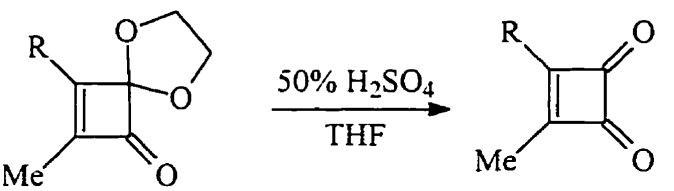
(13)




33 34 (14)

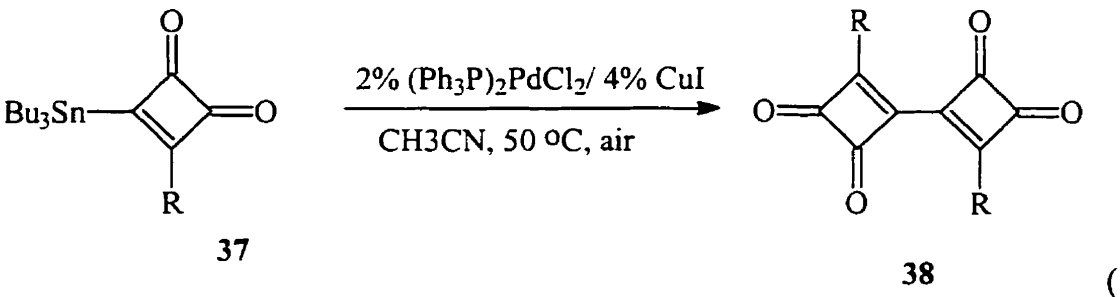



34 35 (15)

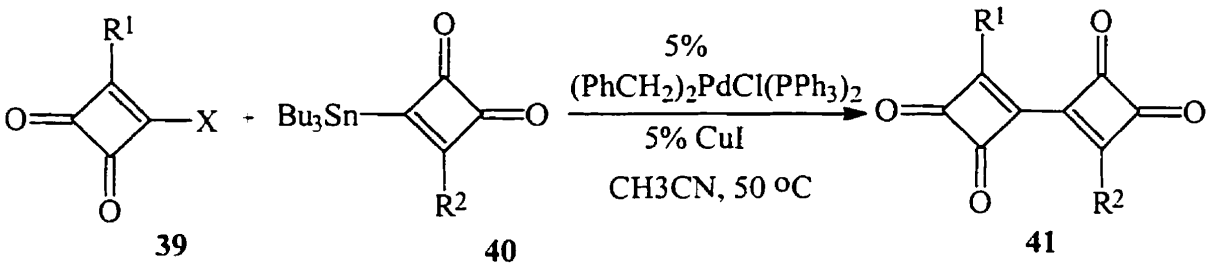



35 36 (16)

Liebeskind, et al.,[7b] have applied these methods to the synthesis of 4,4'-bi(cyclobutene-1,2-diones) (named bisquaryls by reference to squaric acid and biaryls). The symmetrically substituted bisquaryls **38** were prepared by a palladium-catalyzed oxidative dimerization of (tri-n-butylstanyl) cyclobuten-1,2-diones **37** (Eq. 17) and the unsymmetrically substituted bisquaryls **41** were prepared by a palladium-copper cocatalyzed cross-coupling of 3-substituted-4-(tri-n-butylstanyl)-3-cyclobutene-1,2-diones **40** with 3-halo-4-substituted-3-cyclobutene-1,2-diones **39** (Eq. 18). The novel parent bisquaric acid was obtained as a very strong Brønsted acid that apparently fully ionizes on dissolution; only one $pK_a$ value ($pK_2$ = - 4.49) was observed. It was assumed that $pK_1$ was beyond the range of study.



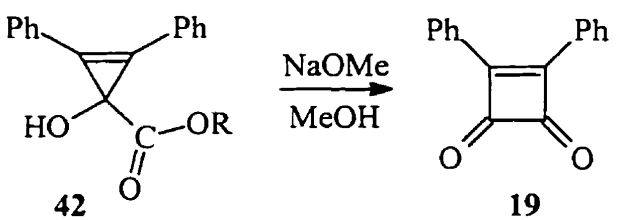

37 38 (17)



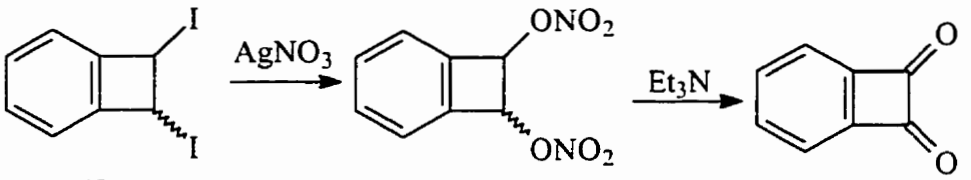

39 40 41 (18)

### 2.1.3 Other methods

Cyclobutenediones have been prepared by ring enlargement of cyclopropene derivatives. 3-Alkoxycarbonyl-3-hydroxycyclopropenes **42** were reported to give a base catalysed rearrangement to form the cyclobutenediones **19** (Eq. 19).[8] An interesting method was reported to prepare the benzocyclobutenedione **45**. The diiodide **43** was treated with silver nitrate to give the dinitrate **44** which was decomposed to the cyclobutenedione **45** (Eq. 20).[9] Other methods which involved bisketene intermediates were reviewed in Chapter 1.




42 19 (19)

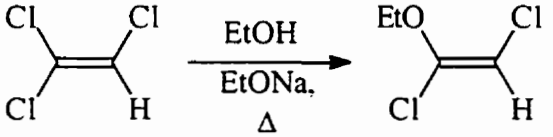



43 44 45 (20)

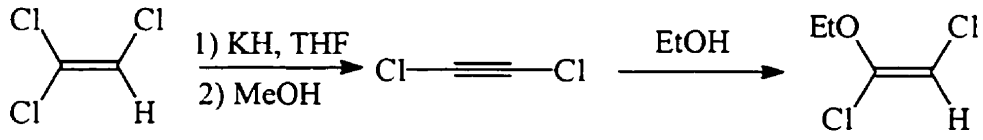
## 2.2 Results and discussion

### 2.2.1 Preparation of acetylenes

1-Ethoxy-2-trimethylsilylacetylene was prepared as described below. For the initial attempt to prepare *trans* -1,2-dichloro-1-ethoxyethene, a literature method[10] was used (Eq. 21). Trichloroethene was reacted with sodium ethoxide in ethanol under reflux and gave the product in low yield (30%). The reaction was monitored by $^1$H NMR and it appeared that the reaction ceased after two hours and prolonged refluxing time gave no increase in the yield. Therefore another known method[11] was used for preparing the reaction intermediate dichloroacetylene (a toxic gas), which was then reacted directly with a large excess of ethanol, presumably catalysed by potassium ethoxide generated in situ, to give *trans* -1,2-dichloro-1-ethoxyethene in good yield (82%) (Eq. 22).

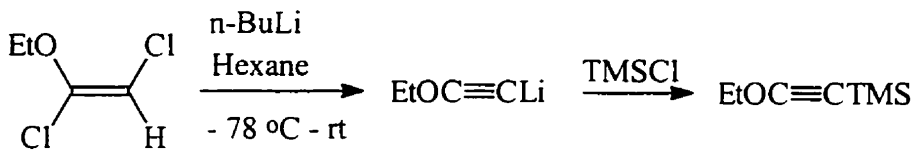



(21)



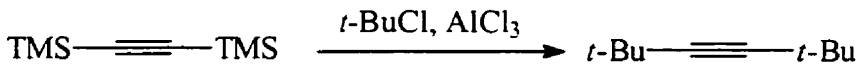

(22)

For the preparation of 1-trimethylsilyl-2-ethoxyacetylene starting from *trans*-1,2-dichloro-1-ethoxyethene, no exactly analogous method was found. However treatment of *trans*-1,2-dichloro-1-ethoxyethene with *n*-butyllithium (2.2 eq) at -78 °C followed by trapping with chlorotrimethylsilane gives 1-trimethylsilyl-2-ethoxyacetylene in good yield (86%) (Eq. 23).




(23)

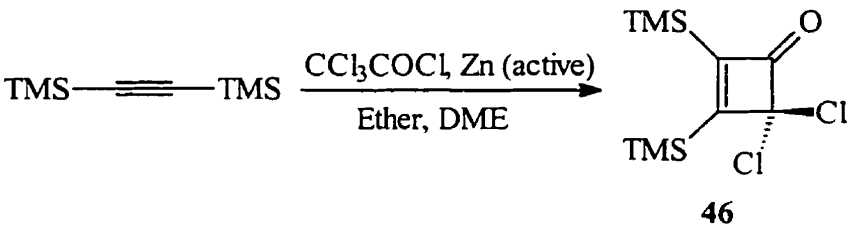
Di-*tert*-butylacetylene was prepared from bis(trimethylsilyl)acetylene with *t* -BuCl by using aluminum chloride as catalyst by a known method.[12] The reaction was found to give a better yield at - 78 °C instead of the reported - 23 °C (Eq. 24).



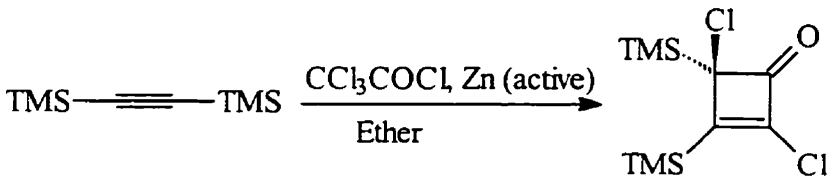

(24)

### 2.2.2 [2+2] Cycloaddition reactions of acetylenes with dichloroketene

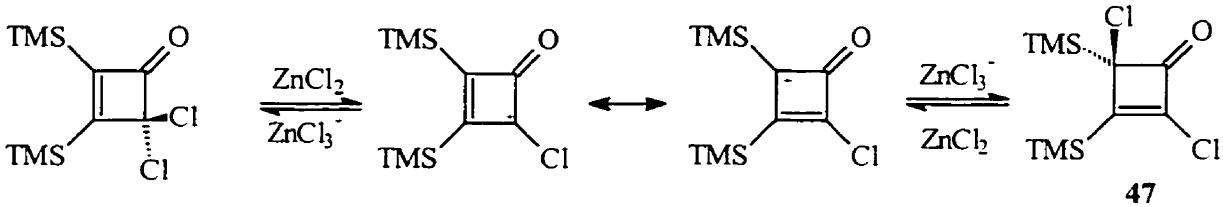
The reaction of the 1,2-bis(trimethyl)silylacetylene with dichloroketene generated from $CCl_3COCl$ and activated Zn in ether and DME as co-solvent gave 4,4-dichloro-2,3-bis(trimethylsilyl)cyclobutenone **46**[13] as the only separated product (Eq. 25). The rearranged cyclobutenone **47** was obtained upon prolonged reaction time and with ether as solvent (Eq. 26). The rearrangement of 4,4-dichlorocyclobutenone **46** by a 1,3-chlorine shift catalyzed by $ZnCl_2$ formed during the reaction is a well known process (Fig. 2). The use of DME as a cosolvent is recommended to inhibit rearrangement, as DME coordinates with $ZnCl_2$ and lowers its activity as a catalyst. The Zn dust was initially activated by a literature method by preparing the Zn-Cu couple.[14] Later reported methods for activation of zinc dust by heating for 2 hr at 140 °C[15] and the use of ultrasound[16] were utilized, and these greatly assist in the generation of the dicholoroketene. All these methods work well. As we realized the Zn-Cu couple was activated in a similar manner by a vacuum drying process, we reasoned that the heating process probably helped to remove the oxide on the Zn dust surface, in addition to the water. Most conveniently the Zn dust in this reaction was activated simply by heating the flask with a soft flame for10 min with stirring under a nitrogen or Ar atmosphere before the reaction, and this also served to flame dry the glassware.




**46** (25)



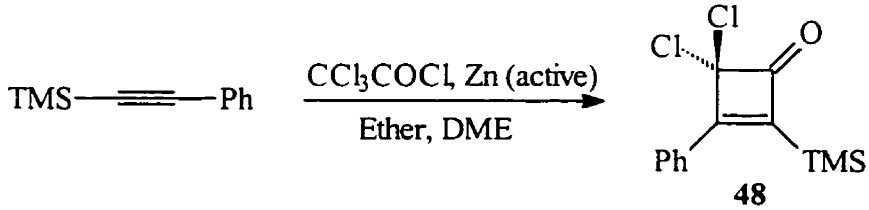

47 (26)




46 47

**Figure 2**

The reaction of phenyltrimethylsilylacetylene with dichloroketene generated from CCl3COCl and activated Zn dust as described above gave the cyclobutenone **48** in good yield (Eq. 27).[13] The regioselectivety could be explained by a stepwise ketene [2+2] mechanism as shown in Figure 4. The carbocation which was stabilized by a phenyl group was favored, and led to the observed product. For a detailed discussion of this mechanism see Chapter 6.




48 (27)

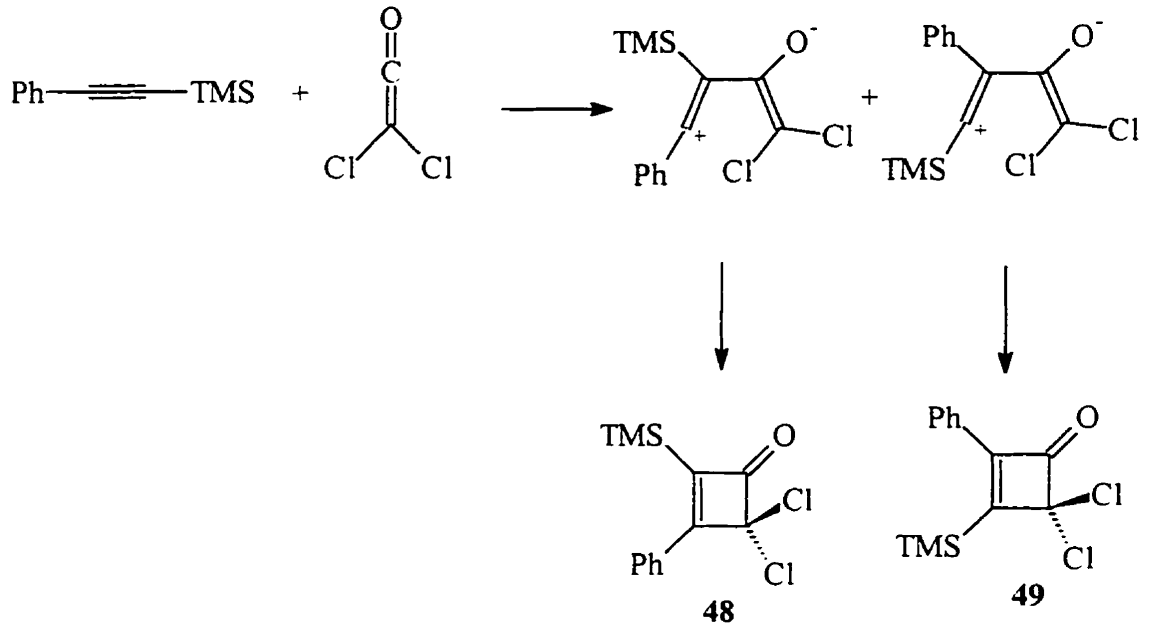
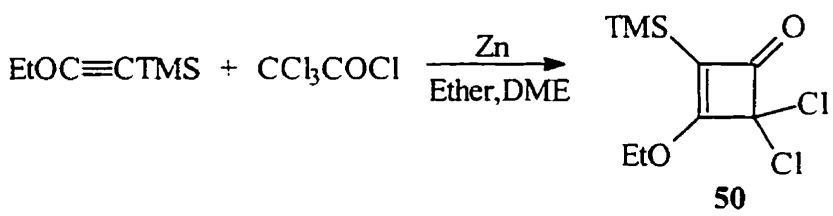



**Figure 3**

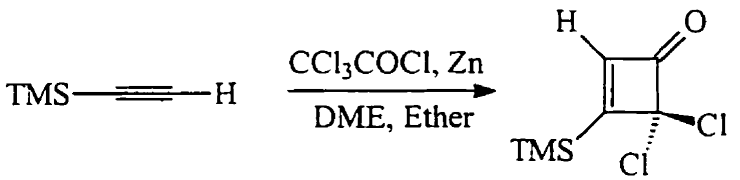
The electron rich trimethylsilylethoxyacetylene reacted with dichloroketene readily and gave 4,4-dichloro-2-trimethylsilyl-3-ethoxycyclobutenone **50**[13] in good yield (82%) (Eq. 28). The regiochemistry can be explained as in the case of the phenyltrimethylsilylacetylene.




(28)

Acetylene itself does not undergo a [2+2] cycloaddition with dichloroketene, however with one TMS substituent the reaction occurs and

gives the cyclobutenone **51** in 57% yield (Eq. 29). The reaction was monitored by $^1$H NMR, and it was observed that the acetylene was not totally consumed even with a large excess of dichloroketene, indicating a slow rate of reaction of the [2+2] process. It is interesting to notice that the regioselectivity here (Fig. 4) favored generation of the carbocation in the α-position to the silicon, which is normally considered as relatively unfavorable, but is favored here as the other carbocation would be in the α- position to a single proton, and it is much less stable. Danheiser and Sard[13] have observed that the regioselectivity of this reaction was greater than 99%. The relatively low yield of this reaction suggests that this reaction has reached the electron demand limit of the dichloroketene [2+2] reaction.




**51** (29)

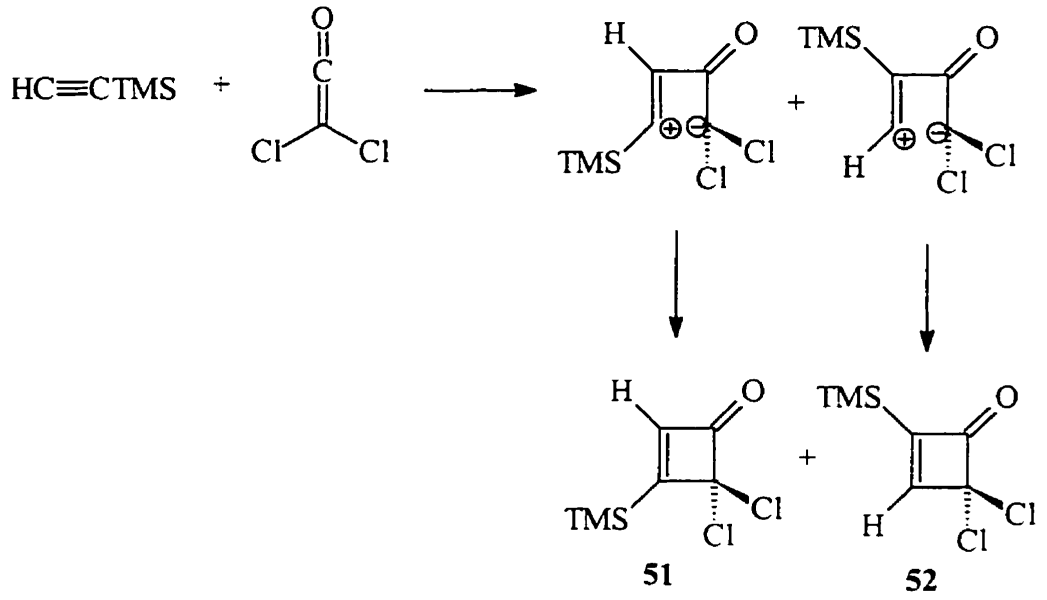
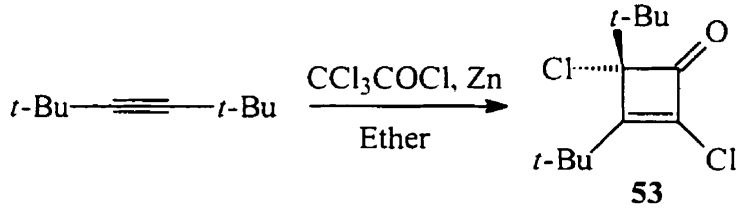



**Figure 4**

The crowded 1,2-di-*tert*-butylacetylene was found to react under these conditions and gives the cyclobutenone **53** (Eq. 30). It is interesting to find that this [2+2] reaction goes well and gives a good yield (77%) of the cyclobutenone. This reaction demonstrates the low steric demand of the perpendicular approach of the ketene to the triple bond (see Chapter 6 for a depiction of this mechanism).

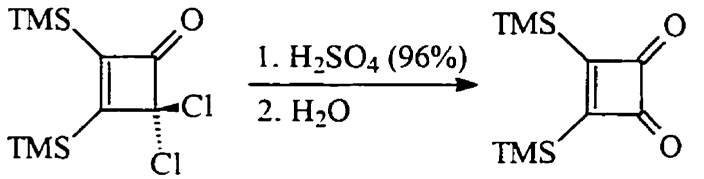



(30)

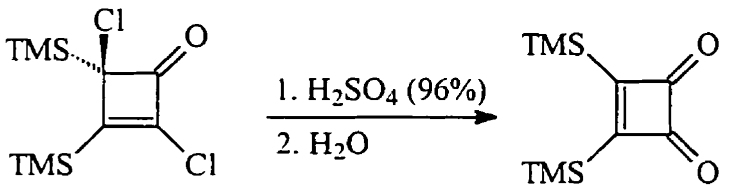
### 2.2.3 Preparation of the cyclobutenediones

It is interesting to find that both cyclobutenones **46** and **47** give the 1,2-cyclobutenedione **54** by hydrolysis with concentrated (96%) sulfuric acid (Eq.

31,32). The reaction temperature was crucial, and the best yield (80%) was obtained at 40-50 °C.




**46** **54** (31)




**47** **54** (32)

The mechanism of the hydrolysis step may be explained as in Figure 5. Chloride loss gives the same carbocation from the two different starting cyclobutenones. This carbocation could be trapped by sulfuric acid or by water and then converted to the cyclobutenedione (Fig. 5). Since the dione is formed before workup, the low yield observed when higher temperatures are used could result from formation of the dione which is destroyed by thermal ring opening and electrophilic attack on the bisketene (see Chapter 5).

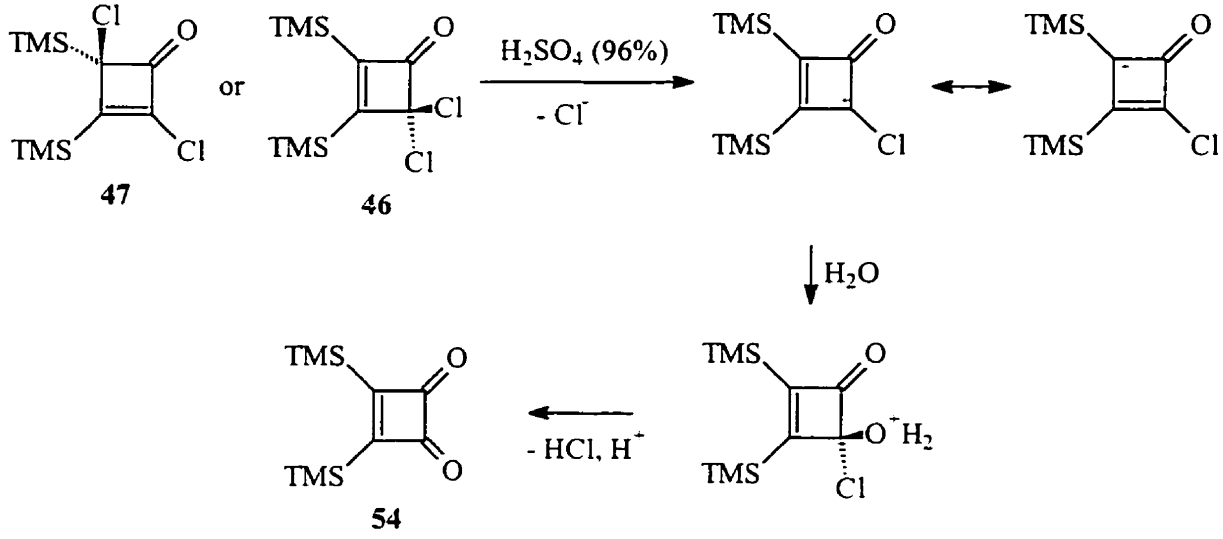
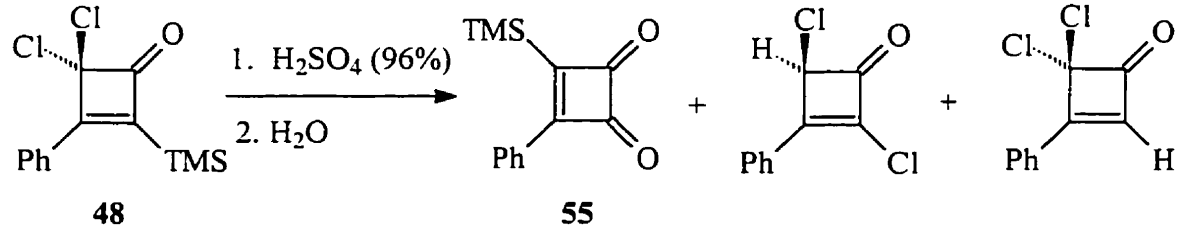
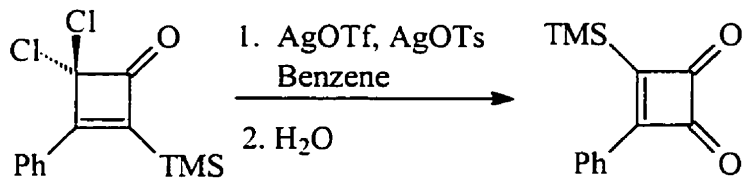



**Figure 5**

The phenyl substituted cyclobutenone **48** upon hydrolysis at 95 °C gave the cyclobutenedione (Eq. 33), albeit in a low yield of 43% due to the side reaction of desilylation. It is interesting to note that the desilylated cyclobutenone was not further hydrolysed to the cyclobutenedione and this process may require higher temperature and longer reaction time. Later on this reaction was improved by using a silver salt promoted hydrolysis method (Eq. 34) to give the dione **55** in good yield (73%). The cyclobutenedione **55** was obtained as yellow crystals and was stable upon heating,

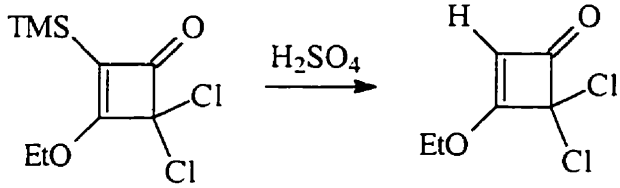



(33)




**48** **55** (34)

Attempted hydrolysis of 4,4-dichloro-2-trimethylsilyl-3-ethoxycyclobutenone **50** by using sulfuric acid only resulted in the product 4,4-dichloro-3-ethoxycyclobutenone **56** (Eq. 35). That might help us understand the hydrolysis mechanism better, as the ethoxy group stabilizes the adjacent carbocation center formed by protonation (Fig. 6), thereby bypassing the reaction pathway for the formation of the dione and resulting in the observed desilylation product. The same reasoning can to be used to explain the low yield of the phenyl substituted dione **55** due to competing desilylation (Eq. 33).




**50** **56** (35)

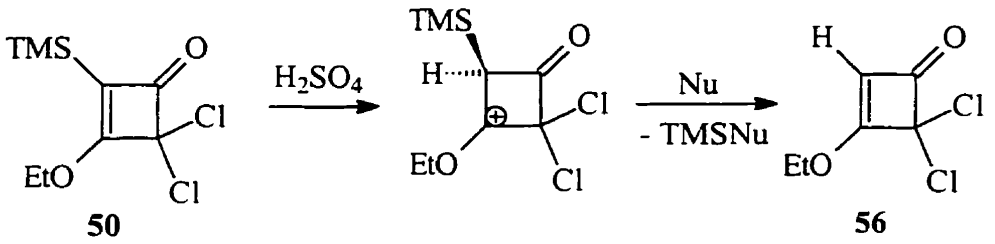
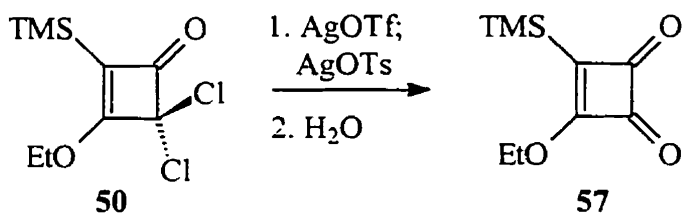


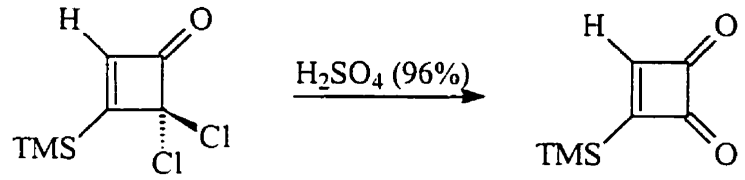

**Figure 6**

In sulfuric acid there are two processes competing with each other, that is chloride ionization and protonation. To obtain the final product 3-trimethylsilyl-4-ethoxycyclobutenedione **57**, we need to avoid the protonation process, and this is done by the use of silver salt assisted hydrolysis. The first reagent we tried was silver trifluoromethanesulfonate (triflate), and in this reaction the starting material 4,4-dichloro-2-trimethylsilyl-3-ethoxycyclobutenone **50** was consumed in three hours, but this resulted in a low yield of **57** (10%), possibly due to the oxidizing ability of the Ag+ which destroyed the initially formed dione. Eventually we found that the best reagent was using both AgOTf and AgOTs in a one to one ratio, which resulted in a good yield of **57** (74%) (Eq. 36). The dione **57** was observed to be formed before hydrolysis.

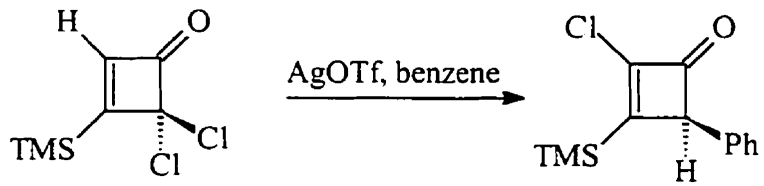



(36)

An attempt to use the sulfuric acid method to hydrolyze 4,4-dichloro-3,-trimethylsilylcyclobutenone **51** was not successful, and resulted in low yield (<5%). The dione was also not stable on silica gel. The reaction was monitored by $^{1}H$ NMR and it was found that the cyclobutenone **51** was consumed, but product **58** was only recovered in low yield, and may have been destroyed by the sulfuric acid before work up (Eq. 37). Attempted use of the silver method to hydrolyze 4,4-dichloro-3-trimethylsilylcyclobutenone **51** with silver triflate resulted in the unexpected product 2-chloro-3-trimethylsilyl-4-phenylcyclobutenone **59** as the only observed product (Eq. 38). This might occur because the carbocation formed during hydrolysis is very reactive so that it reacts with the solvent benzene before or after it was trappped by triflate (Fig. 7). Changing the reaction solvent to THF or carbon tetrachloride was not successful, as the reaction became very slow, and the expected product 3-trimethylsilyl-cyclobutenedione was not observed.




**51** **58** (37)




**51** **59** (38)

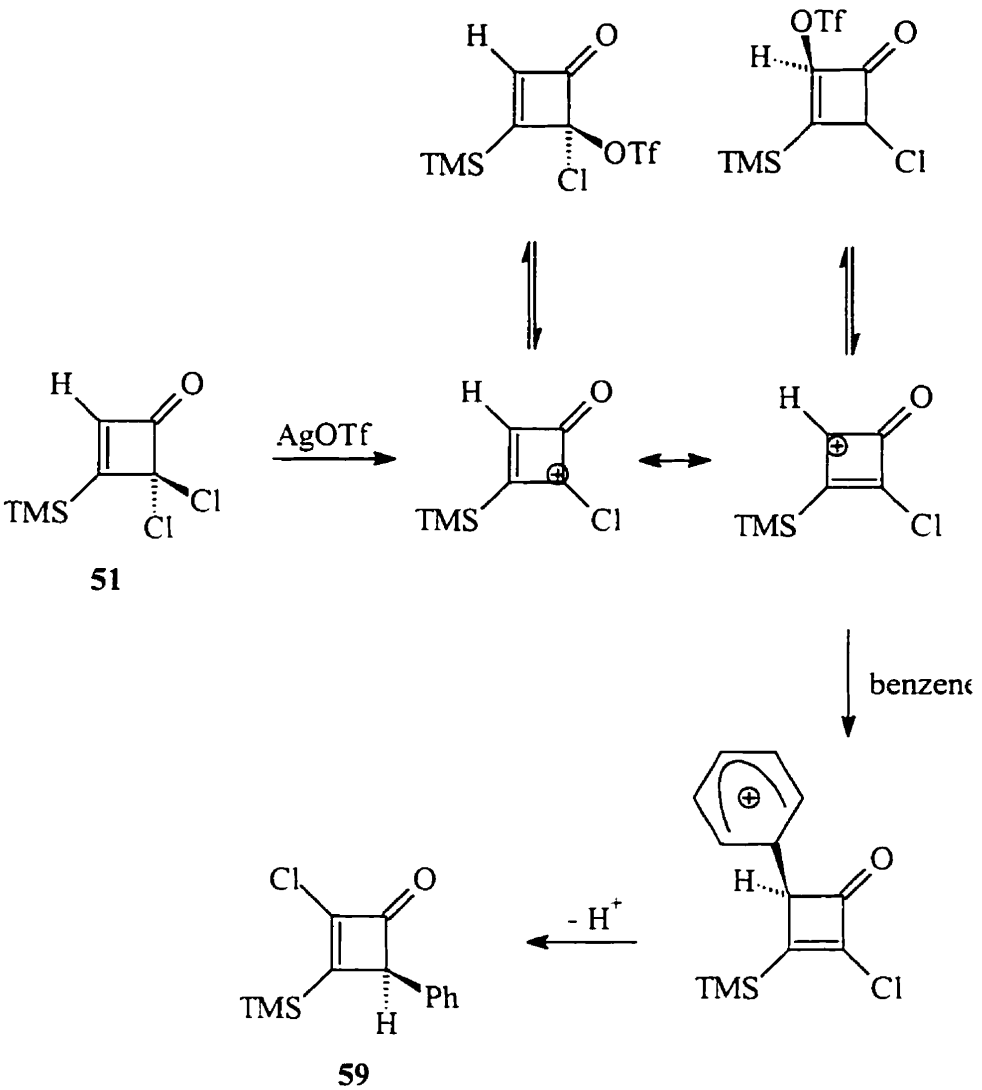
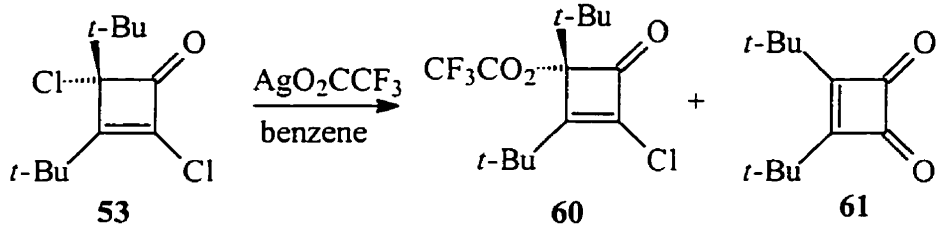



**Figure 7**

The bulky dione **61** was obtained in moderate yield (47%) by using the silver salt hydrolysis method, demonstrating the generality of this method. It is interesting to note that by using silver trifluoroacetate the dione **61** and the trifluroacetate ester **60** were both obtained, thus indicating that the trifluoroacetate is a poor leaving group under these reaction conditions, and is stable on silica gel and to aqueous workup (Eq. 39).




53 60 61 (39)

## 2.3 Experimental

Unless indicated materials were obtained from Aldrich and used without purification. Diethyl ether, THF and DME were distilled from sodium and benzophenone. Deuterated chloroform was dried by 4 $^{o}$A molecular sieves. Glassware was flame dried and cooled under an atmosphere of nitrogen or argon. All reactions involving air sensitive materials were conducted under nitrogen atmosphere or argon. Analyses and separation by VPC were done using OV-17 columns. $^{1}$H NMR and $^{13}$C NMR were performed on Varian Gemini 200 and/or 400 instruments. Infrared spectra were measured on a Nicolet FTIR spectrometer. Elemental analysis was by Galbraith Laboratories. The zinc-copper couple were prepared according to a published method.[14] Zinc activation was preferably carried out by flame drying the zinc dust with a soft flame from a Bunsen burner under a nitrogen or argon atmosphere with magnetic stirring.

**E-1,2-Dichloro-1-ethoxyethene.** Trichloroethene (13.1 g, 0.1 mol) was added to potassium hydride (35% in mineral oil, 14 g, 0.12 mol) (KH was washed with 30 mL pentane and 3×30 mL anhydrous THF) in anhydrous THF (100 mL) cooled in a water bath under nitrogen protection, and then methanol

(100 μL, 79 mg, 2.5 mmol) was added using a syringe, and the mixture was stirred at room temperature for 6 h. Anhydrous ethanol (20 mL) was added in one portion and the mixture was stirred at room temperature overnight. The reaction mixture was diluted with water (500 mL) and extracted by ether (3 x 50 mL), and the ether layers were combined and washed with water (3 x 50 mL), dried over $MgSO_4$, the solvent was removed by fractional distillation, and the product was collected at 120-124 °C, giving the product E-1,2-dichloro-1-ethoxyethene[10] as a colorless oil (11.5 g, 0.082 mol, yield 82%). $^1H$ NMR ($CDCl_3$) δ 1.35 (t, 3, $J_{1,2}$ = 7.04 Hz), 4.10 (q, 2, $J_{1,2}$ = 7.04 Hz), 5.53 (s, 1).

**Trimethylsilylethoxyacetylene.** E-1,2-Dichloro-1-ethoxyethene (1.33 g, 9.43 mmol) was dissolved in hexane (10 mL) and then *n*-BuLi in hexane (2.2 eq, 1.15 M) was added at -78 °C (acetone/$CO_2$) under nitrogen protection and the mixture was stirred while warming to room temperature and was kept stirring for another 2 hr. Chlorotrimethylsilane (2.48 g, 22.8 mmol, 1.1 eq) was added over 5 min and the solution was stirred overnight at room temperature. The reaction mixture was diluted with hexane (40 mL), washed with water (3 x 20 mL), dried over $MgSO_4$, and the solvent was removed by a rotary evaporator to give the crude product which was further purified by thin layer chromatography (on silica gel eluted by 3% ethyl acetate in hexane) giving the product trimethylsilylethoxyacetylene (1.15 g, 8.1 mmol, 86%). $^1H$ NMR ($CDCl_3$) δ 0.13 (s, 9), 1.37 (t, 3, $J_{1,2}$ = 7.04 Hz), 4.13 (q, 2, $J_{1,2}$ = 7.04 Hz).

**Representative method[14] for 4,4-dichlorocyclobutenones.** A 100 mL three-necked round-bottomed flask was charged with 2.0 g (0.03 mol) of Zn

dust which was then activated by a soft flame heating for 10 min under stirring. After the flask was cooled to room temperature, 40 mL of anhydrous ether, and phenyltrimethylsilylacetylene (0.01 mol) were added in one portion. Trichloroacetyl chloride (1.4 mL, 0.013 mol) in 15 mL of anhydrous DME (dimethoxyethane) and was added dropwise with stirring to the reaction mixture over one hour. The reaction was left at room temperature under stirring for 16 hr. The resulting dark brown mixture was filtered through a sintered glass Buchner funnel and the black solid separated was thoroughly washed with 20 mL of ether. The filtrate was washed successively with 20 mL of NaCl saturated solution, 20 x 3 mL of ice cold saturated $NaHCO_3$ solution, 20 x 2 mL of saturated sodium chloride solution, and was then dried over anhydrous $MgSO_4$. The solvent was removed by a rotary evaporator, and gave 4.0 g of crude product. The crude product was purified by flash chromatography, eluted by a solvent hexane/ethyl acetate (100/5) and gave colorless solid product **2-trimethylsilyl-3-phenyl-4,4,-dichlorocyclobutenone 48**[13] (2.4 g, 84 mmol, 84%), mp 72.5 °C.

The following were prepared similarly.

**2,3-Bis(trimethylsilyl)-4,4,-dichlorocyclobutenone (46)**[13,17] (2.3 g, 82 mmol, 82%) mp 35.0-35.5 °C, $^1$H NMR ($CDCl_3$) δ 0.28, 0.42. $^{13}$C NMR ($CDCl_3$) δ -1.64, -1.06, 96.8, 169.1, 184.1, 196.7.

**4,4-Dichloro-2-trimethylsilyl-3-ethoxycyclobutenone (50)**[13] was chromatographed on silica gel (eluted by 10% ethyl acetate in hexane) to give colorless solid (2.2 g, 8.7 mmol, 87%): $^1$H NMR ($CDCl_3$) δ 0.24 (s, 9), 1.15 (t, 3, $J_{1,2}$ = 7.1 Hz), 4.68 (q, 2, $J_{1,2}$ = 7.1 Hz); $^{13}$C NMR ($CDCl_3$) δ -1.63, 14.99, 70.22, 87.59, 127.75, 180.73, 184.94; IR ($CDCl_3$) 1770 (vs), 1579 (vs) cm$^{-1}$;

EIMS *m/z* 252 ($M^+$, 28), 237 ($M^+$-$CH_3$, 16), 208 ($M^+$-$CH_3$,$CH_3CH_2$, 10), 134 ($M^+$-$CH_3CH_2O$,TMS, 45), 189 ($M^+$-Cl,CO, 22), 93 ($TMSCl^+$-$CH_3$, 37), 73 ($TMS^+$, 100); HRMS calcd for $C_9H_{14}O_2SiCl_2$ 252.0140, found 252.0154.

**4,4-Dichloro-3-trimethylsilylcyclobutenone (51)**[13] (1.2 g, 57 mmol, 57%).

**Representive method for 2,4-dichlorocyclobutenones.** A 100 mL three-necked round-bottomed flask was charged with 2.0 g (0.03 mole) of Zn dust, which was activated by a soft flame heating for 10 min under stirring. After the flask was cooled to room temperature, 40 mL of anhydrous ether and the di-tert-butylacetylene (0.01 mol) were added in one portion. Trichloroacetyl chloride (1.4 mL, 0.013 mol) in 15 mL of anhydrous ether was added dropwise to the reaction mixture over one hour. The reaction was left at room temperature under stirring for 16 hr. The resulting dark brown mixture was filtered through a sintered glass buchner funnel and the black solid separated was thoroughly washed with 20 mL of ether. The filtrate was washed successively with 20 mL of NaCl saturated solution, 20 x 3 mL of ice cold $NaHCO_3$ saturated solution and 20 x 2 mL of saturated sodium chloride solution, then dried over anhydrous $MgSO_4$. The solvent was removed by a rotary evaporator and gave crude product which was purified by flash chromatography, eluted by a solvent hexane/ethyl acetate (100/5), and gave colorless solid product, **3,4-di-*tert*-butyl-2,4-dichlorocyclobutenone 53** (1.9 g, 7.7 mmol, 77%): mp 38.5 °C; $^1$H NMR ($CDCl_3$) δ 1.08 (s, 9), 1.34 (s, 9); $^{13}$C NMR ($CDCl_3$) δ 27.2, 28.6, 35.8, 37.9, 92.8, 128.6, 182.6, 186.8; IR ($CDCl_3$)

1785 (vs), 1568 (s) $cm^{-1}$; EIMS m/z 248 (2), 194 (15), 192 (20), 157 (29), 57 (100); HRMS m/z calcd for $C_{12}H_{18}Cl_2O$ 248.0735, found 248.0726.

**3,4-Bis(trimethylsilyl)-2,4,-dichlorocyclobutenone (47)** (2.4 g, 8.6 mmol, 86%): $^1H$ NMR ($CDCl_3$) δ 0.17 (s, 9), 0.34 (s, 9); $^{13}C$ NMR ($CDCl_3$) δ -2.68, -1.38, 77.40, 139.1, 182.9, 183.2; IR (CDCl3) 1787 (vs) $cm^{-1}$; EIMS *m/z* 280 ($M^+$, 3), 237 ($M^+$-CH3, CO, 7), 172 ($M^+$-Cl, TMS, 37), 73 $TMS^+$, 100); HRMS *m/z* calcd for $C_{10}H_{18}OCl_2$ 280.0273, found 280.0276.

**3,4-Bis(trimethylsilyl)cyclobutenedione (54).**[17] A solution of 3,4-bis(trimethylsilyl)-2,4-dichlorocyclobutenone **47** (1.0 g, 3.56 mmol) in 5 mL of ether was added in 10 min to sulfuric acid (96%, 3 mL) at 45 °C using a water bath, then the reaction was kept at 45-50 °C for 30 min and the reaction mixture was cooled by a dry ice/acetone bath and added to 100 mL of an ice and water mixture, the solution was extracted three times with 50 mL portions of ether, and the combined ether extract was washed three times with 50 mL portions of distilled water, dried over MgSO4, and concentrated on the rotary evaporator. The crude product was purified by recrystalization from ether, and gave the dione **54** (0.64 g, 2.85 mmol, 80%) as a bright yellow green solid , mp 50-52 °C $^1H$ NMR ($CDCl_3$) δ 0.37. $^{13}C$ NMR ($CDCl_3$) δ -1.6, 201.9, 217.1.

**3-Trimethylsilyl-4-phenylcyclobutenedione (55).** A solution of 4,4-dichloro-2-trimethylsilyl-3-phenylcyclobutenone (1.0 g, 3.5 mmol) in 5 mL of anhydrous ether was added dropwise to 2.5 mL of stirred concentrated H2SO4 at 95 °C. The solution was kept at 95 °C for 30 minutes, cooled with dry ice/acetone, and added to 100 mL of an ice and water mixture. The solution was extracted three times with 50 mL portions of ether, and the combined ether extract was washed three times with 50 mL portions of distilled water,

dried over MgSO4, and concentrated on the rotary evaporator. The crude product (0.73 g) was purified by flash chromatography, using 1/1 hexane / dichloromethane to give cyclobutenedione **55** (0.36g, 1.26 mmol, 35%) as a bright yellow green solid, mp 102.8-103.2 °C: $^{1}$H NMR ($CDCl_3$) δ 0.45 (s, 9), 7.50-8.00 (m, 5); $^{13}$C NMR ($CDCl_3$) δ -1.4, 129.8, 130.0, 134.0, 157.2, 198.4, 199.9, 201.0, 203.2. IR ($CDCl_3$) 1776 (s), 1601 (s), 1541(m) $cm^{-1}$; UV (hexane) $\lambda_{max}$ 287 nm; EIMS *m/z* 230 ($M^+$, 10), 174 ($M^+$-2CO, 39), 159 ($M^+$-2CO-Me,100); HRMS m/z calcd for $C_{13}H_{14}SiO_2$ 230.0763, found 230.0758. Anal. Calcd for $C_{13}H_{14}SiO_2$ (230.34): C, 67.79; H, 6.13; Si, 12.19. found: C, 67.65; H, 6.12; Si, 11.31.

**3-Trimethylsilyl-4-ethoxycyclobutenedione (57).** 4,4-Dichloro-2-trimethylsilyl-3-ethoxycyclobutenone 50 (0.55 g, 2.06 mmol) was dissolved in benzene (10 mL), and silver trifluoromethanesulfonate (0.67 g, 2.6 mmol) and silver toluenesulfonate (0.73 g, 2.6 mmol) were added in one portion, and then the reaction mixture was heated to reflux for 3 h. The silver chloride precipitate was filtered, and the solution was diluted with ether (100 mL), and washed with distilled water (3x30 mL), dried over $MgSO_4$, and the solvent was removed by a rotary evaporator to give the crude product which was further purified by thin layer chromatography (on silica gel eluted using a solvent of 3% ethyl acetate in hexane), to give the 3-trimethylsilyl-4-ethoxycyclobutenedione **57** as a yellow colored oil (0.30 g, 1.52 mmol, 74%): $^{1}$H NMR ($CDCl_3$) δ 0.32 (s, 9), 1.49 (t, 3, $J_{1,2}$ = 7.2 Hz), 4.78 (q, 2, $J_{1,2}$ = 7.2 Hz); IR ($CDCl_3$) 1776 (s), 1755 (s), 1557(s) $cm^{-1}$; $^{13}$C NMR ($CDCl_3$) δ -2.3, 15.6, 70.5, 186.9, 194.9, 197.3, 204.8; EIMS *m/z* 199 ($M^+$+1, 0.5), 183 ($M^+$-

$CH_3$, 1), 170 ($M^+$-CO, 4.5), 141 (TMSCCOEt$^+$-1, 30), 73 ($TMS^+$, 100); HRMS calcd for $C_8H_{11}O_3Si$ ($M^+$-$CH_3$) 183.0477, found 183.0480.

**4,4-Dichloro-3-ethoxycyclobutenone (56).**[18] 4,4-Dichloro-2-trimethylsilyl-3-ethoxycyclobutenone (**50**) (50 mg, 0.198 mmol) was dissolved in sulfuric acid (96%, 0.5 mL), and then heated in a water bath (55 $^oC$) for 30 min. The reaction mixture was poured into ice (20 mL), and diluted to 50 mL with water (0 $^oC$), extracted with ether (2x30 mL), and the ether layer was washed with water (4x30 mL) and dried over $MgSO_4$. The solvent was removed by a rotary evaporator to give 4,4-dichloro-3-ethoxycyclobutenone **56** as a colorless oil (30.2 mg, 0.167 mmol, 84%). $^1H$ NMR ($CDCl_3$) $\delta$ 1.57 (t, 3, $J_{1,2}$ = 7.08 Hz), 4.42 (q, 2, $J_{1,2}$ =7.08 Hz), 5.29 (s, 1).

**2-Chloro-3-trimethylsilyl-4-phenylcyclobutenone (59).** 4,4-Dichloro-3-trimethylsilylcyclobutenone (**51**) (46.8 mg, 0.224 mmol) was dissolved in benzene (2 mL), and silver trifluoromethanesulfonate (113 mg, 0.439 mmol) was added in one portion. The reaction mixture was heated to reflux and kept refluxing for 48 h. The white precipitate was filtered and the solvent was removed by using a rotary evaporator gave the crude oil product which was further purified by thin layer chromatography (on silica gel using 3% ethyl acetate in hexane as eluent) to give 2-chloro-3-trimethylsilyl-4-phenylcyclobutenone **59** as a colorless oil (48 mg, 0.19 mmol, 85%). $^1H$ NMR ($CDCl_3$) $\delta$ 0.18 (s, 9), 4.69 (s, 1), 7.10-7.35 (m, 5); $^{13}C$ NMR ($CDCl_3$) $\delta$ -2.0, 67.9, 127.4, 127.9, 128.7, 136.0, 140.5, 180.5, 184.4; IR ($CDCl_3$) 1723 (vs), 1644 (s), 1604 (m), 1564 (s) $cm^{-1}$; EIMS *m/z* 250 ($M^+$, 100), 235 ($M^+$-Me,

89), 199 ( $M^+$-Me, HCl, 99), 141 ( $M^+$-TMS, HCl, 52), 95 ($M^+$-Ph, Cl, CO, 37); HRMS calcd for $C_{13}H_{15}OSiCl$ 250.0580, found 250.0570.

**3,4-Di-*tert*-butylcyclobutenedione (61).** 2,4-Dichloro-di-*tert*-butyl-cyclobutenone (**53**) (0.5 g, 2.0 mmol) was dissolved in benzene (10 mL), and silver trifluoroacetate (0.9 g, 4.1 mmol) was added in one portion, and then the reaction mixture was heated to reflux for 6 hr. The silver chloride precipitate was filtered, and the solution was diluted with ether (100 mL), and washed with distilled water (30 × 3mL), dried over $MgSO_4$, and the solvent was removed by a rotary evaporator to give the crude product which was further purified by thin layer chromatography (on silica gel eluted using a solvent of 3% ethyl acetate in hexane), to give the dione **61** as a yellow colored solid (182 mg, 0.94 mmol, 47%), mp 57.5-58.0 °C, $R_f$ 0.33 (10% ethyl ecetate in hexane), and trifluoroacetate **60** (150 mg, 0.46 mmol, 23%), $R_f$ 0.44 (10% ethyl ecetate in hexane). Dione **61**: $^1$H NMR ($CDCl_3$) δ 1.44 (s, 18); $^{13}$C NMR ($CDCl_3$) δ 28.9, 35.4, 198.9, 206.4; IR ($CDCl_3$) 1770 (bvs), 1576 (s) $cm^{-1}$; EIMS *m/z* 194 (45), 138 (10), 123 (100), 95 (26), 81 (54), 57 (66); HRMS *m/z* calcd for $C_{12}H_{18}O_2$ 194.1307, found 194.1305. Trifluoroacetate **60**: $^1$H NMR ($CDCl_3$) 1.17 (s, 9), 1.37 (s, 9); $^{13}$C NMR ($CDCl_3$) 26.5, 27.9, 35.4, 36.6, 105.2, 105.5, 111.2, 116.9, 122.6 (q, J = 285 Hz), 133.8, 154.5, 155.3, 156.2, 157.0 (q, J = 42.8), 182.1, 183.2; IR ($CDCl_3$) 1798 (vs), 1576 (s) $cm^{-1}$; EIMS *m/z* 326 (3), 311 (2), 270 (18), 210 (5), 173 (8), 156 (10), 84 (18), 57 (100); HRMS *m/z* calcd for $C_{14}H_{18}ClF_3O_3$ 326.0897, found 326.0912.

## 2.4 References

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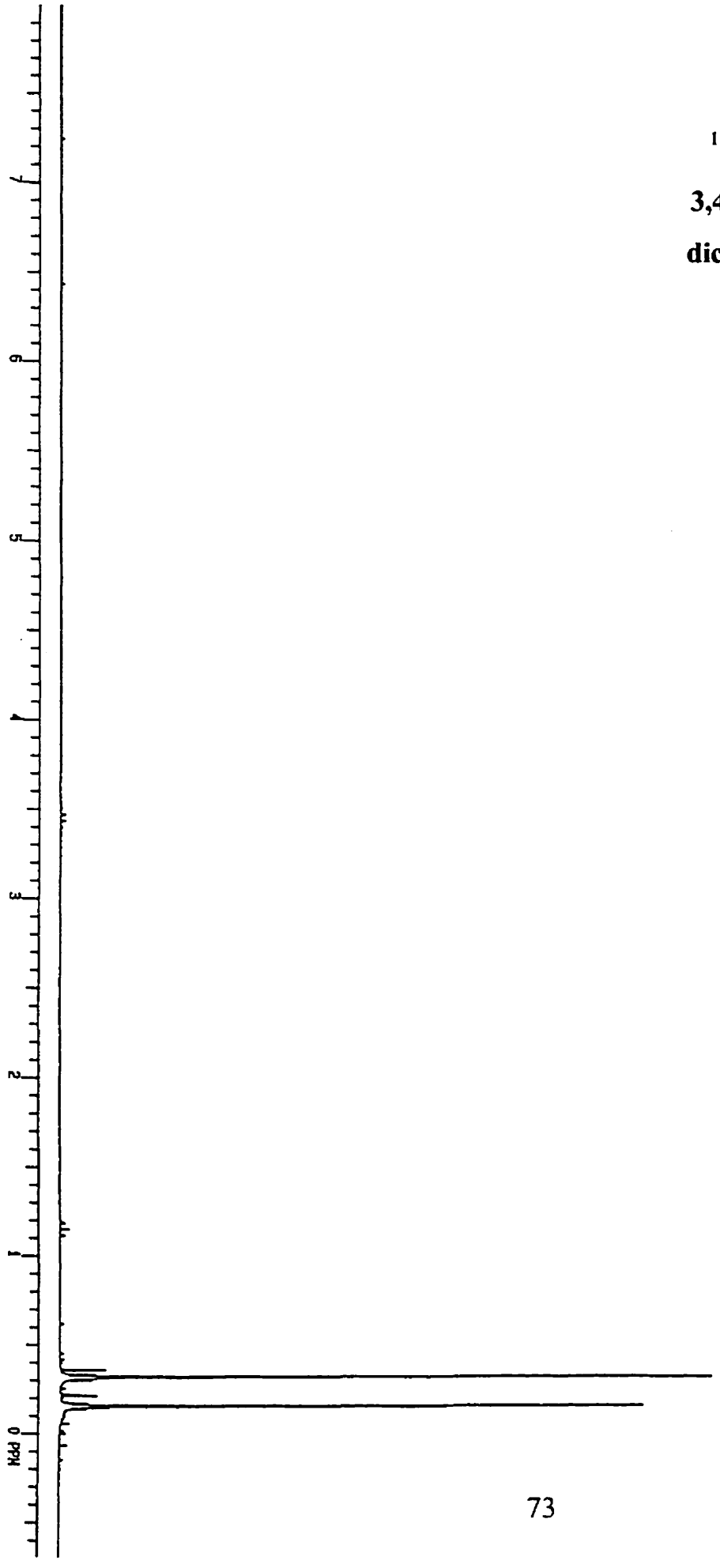
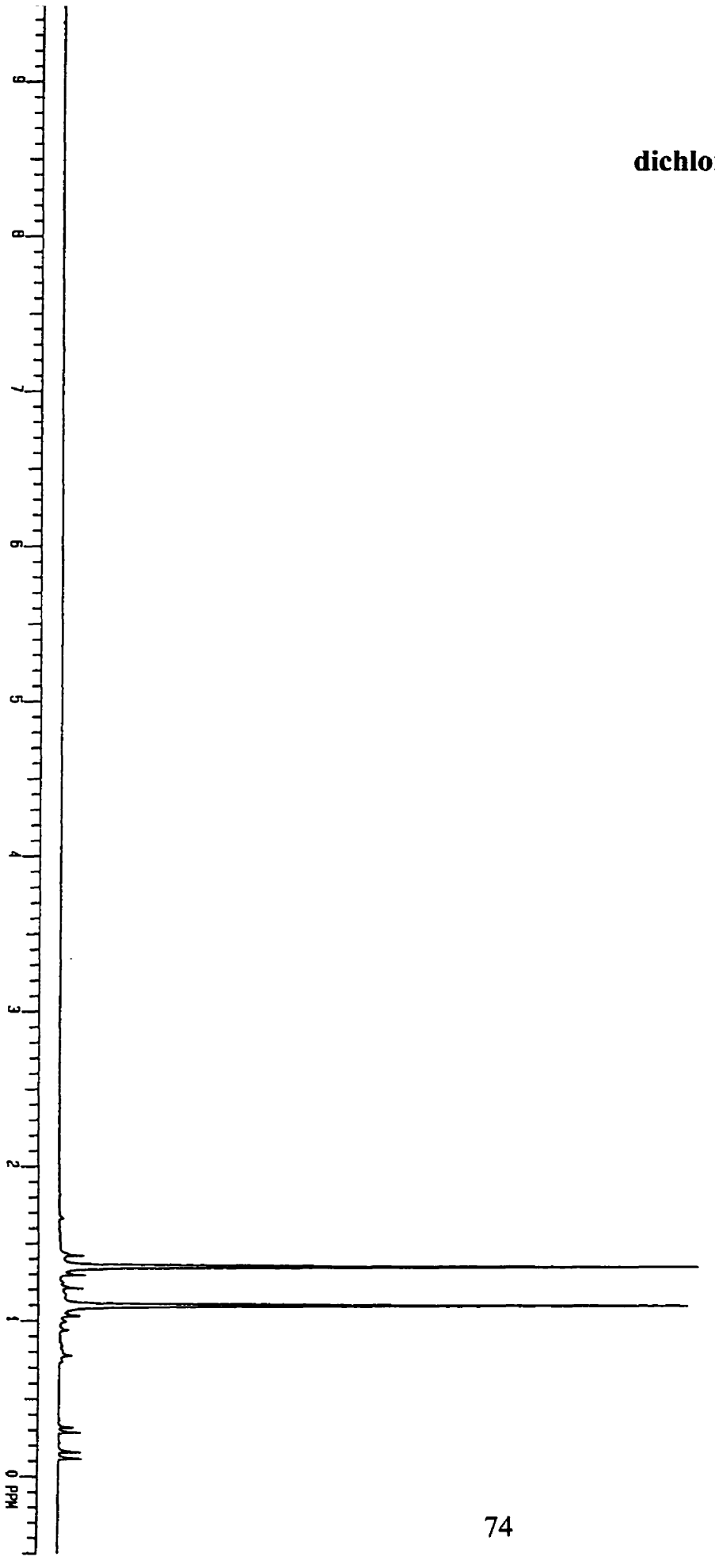
**Appendix 1**

**$^{1}H$ and $^{13}C$ NMR Spectra**

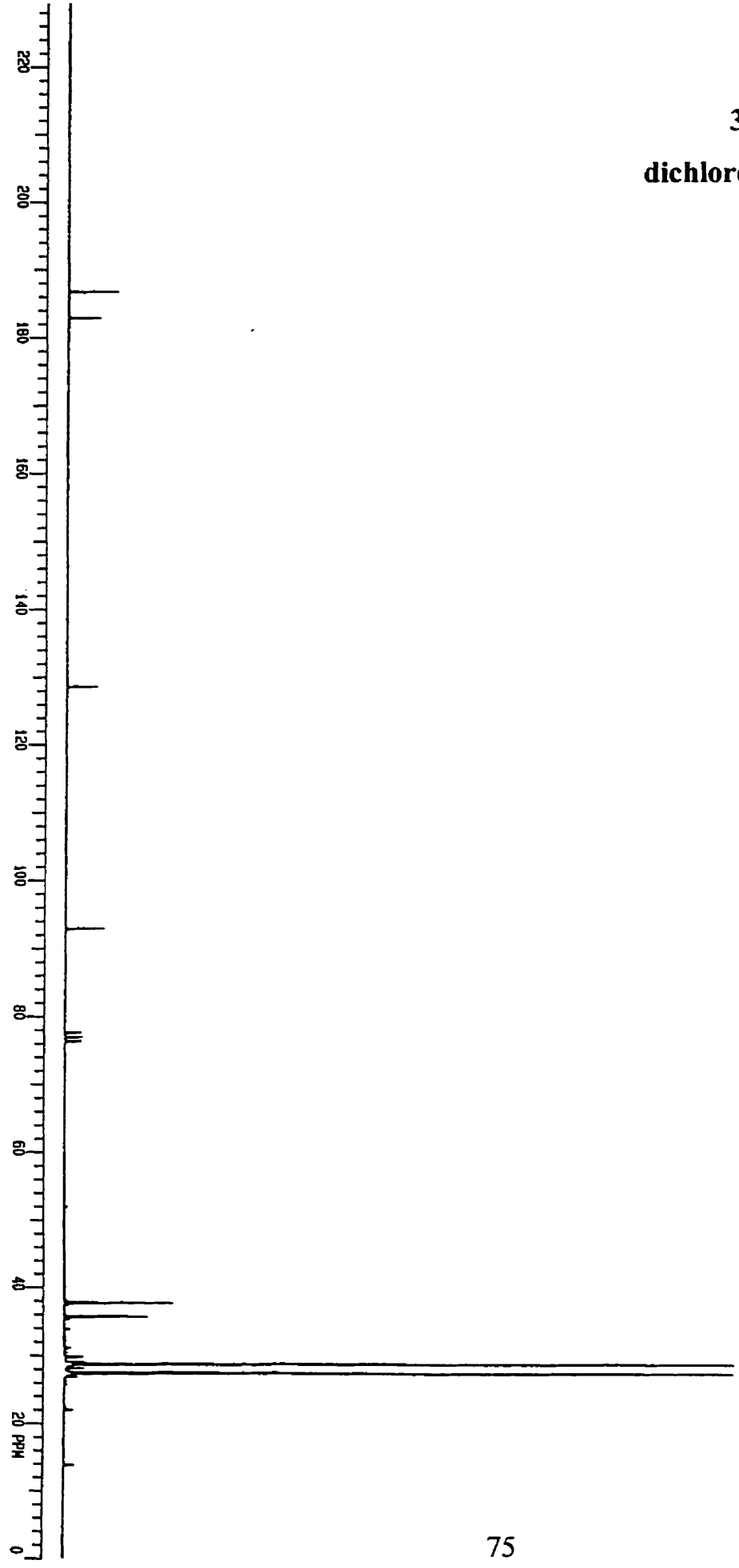
**3,4-Bis(trimethylsilyl)-2,4,-dichlorocyclobutenone (47)**

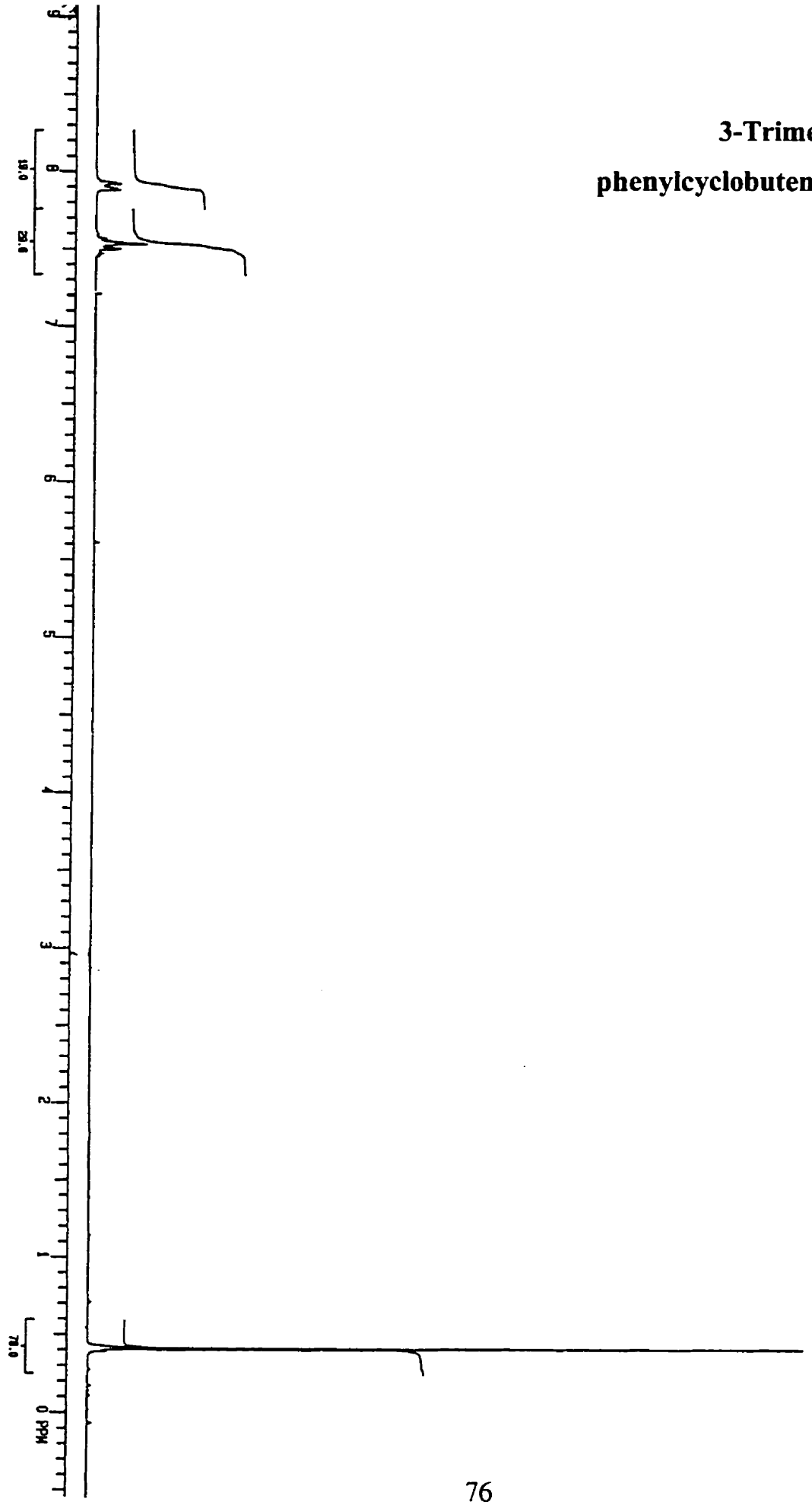


**3,4-Di-*tert*-butyl-2,4-dichlorocyclobutenone (53)**



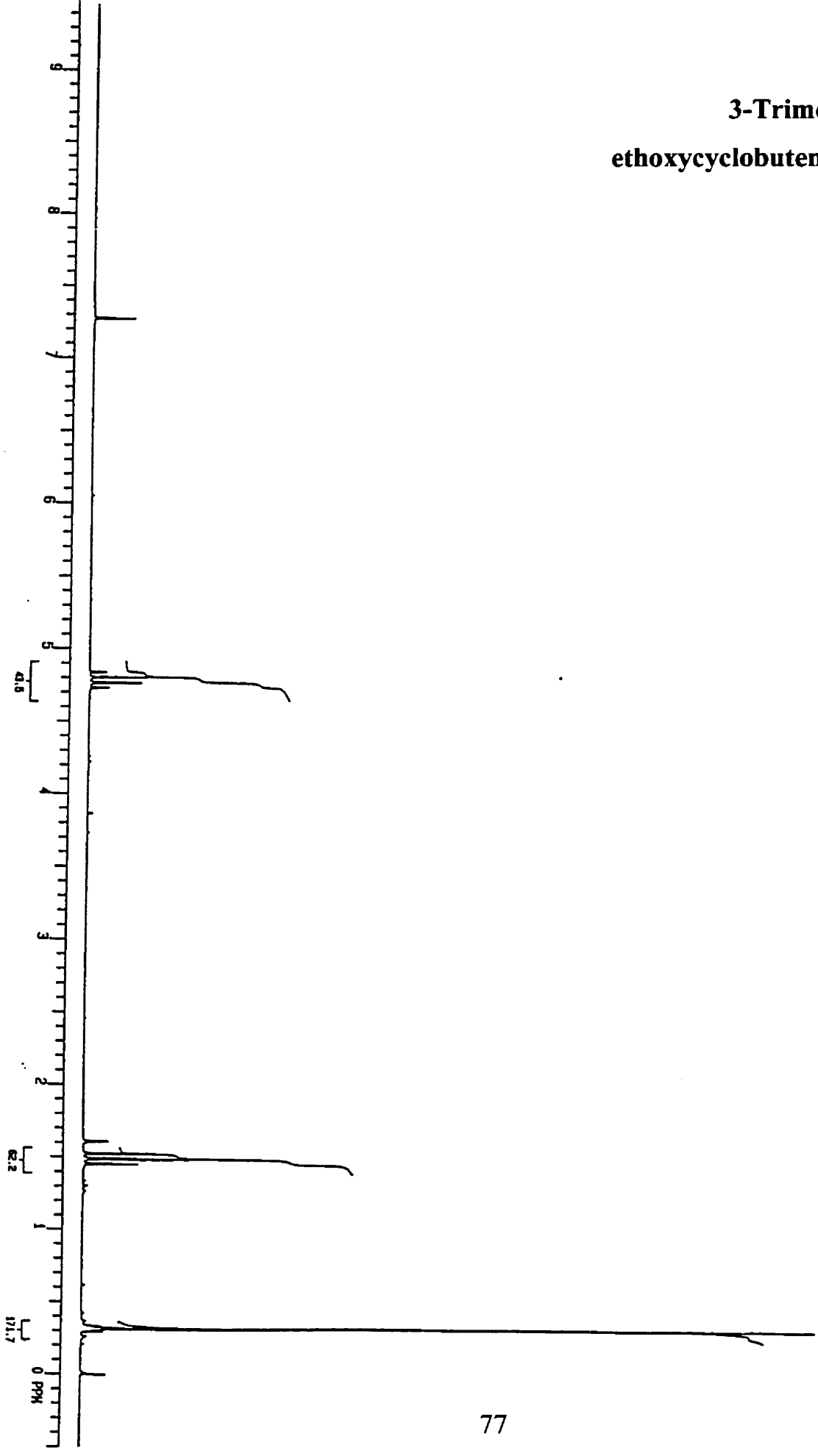
**3,4-Di-*tert*-butyl-2,4-dichlorocyclobutenone (53)**



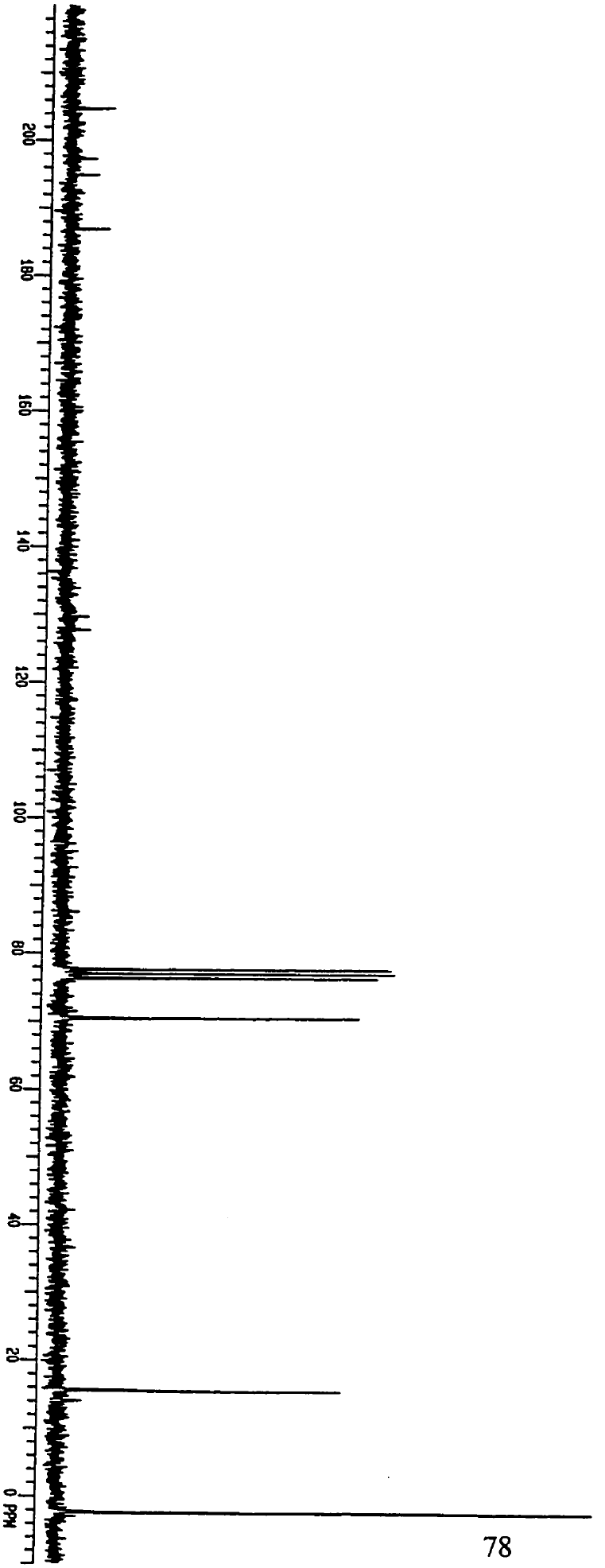


**3-Trimethylsilyl-4-phenylcyclobutenedione (55)**

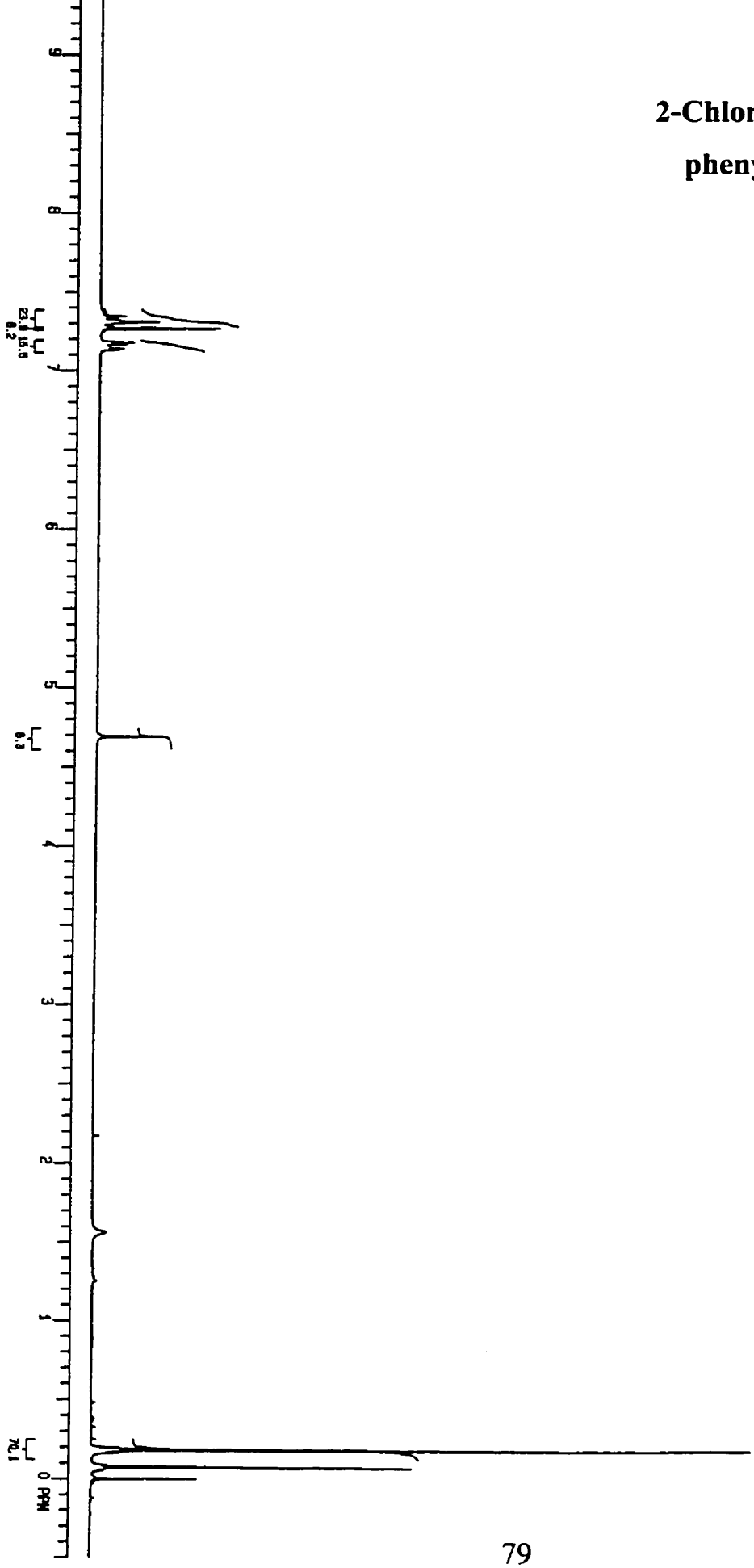
**3-Trimethylsilyl-4-ethoxycyclobutenedione (57)**



**3-Trimethylsilyl-4-ethoxycyclobutenedione (57)**



**2-Chloro-3-trimethylsilyl-4-phenylcyclobutenone (59)**



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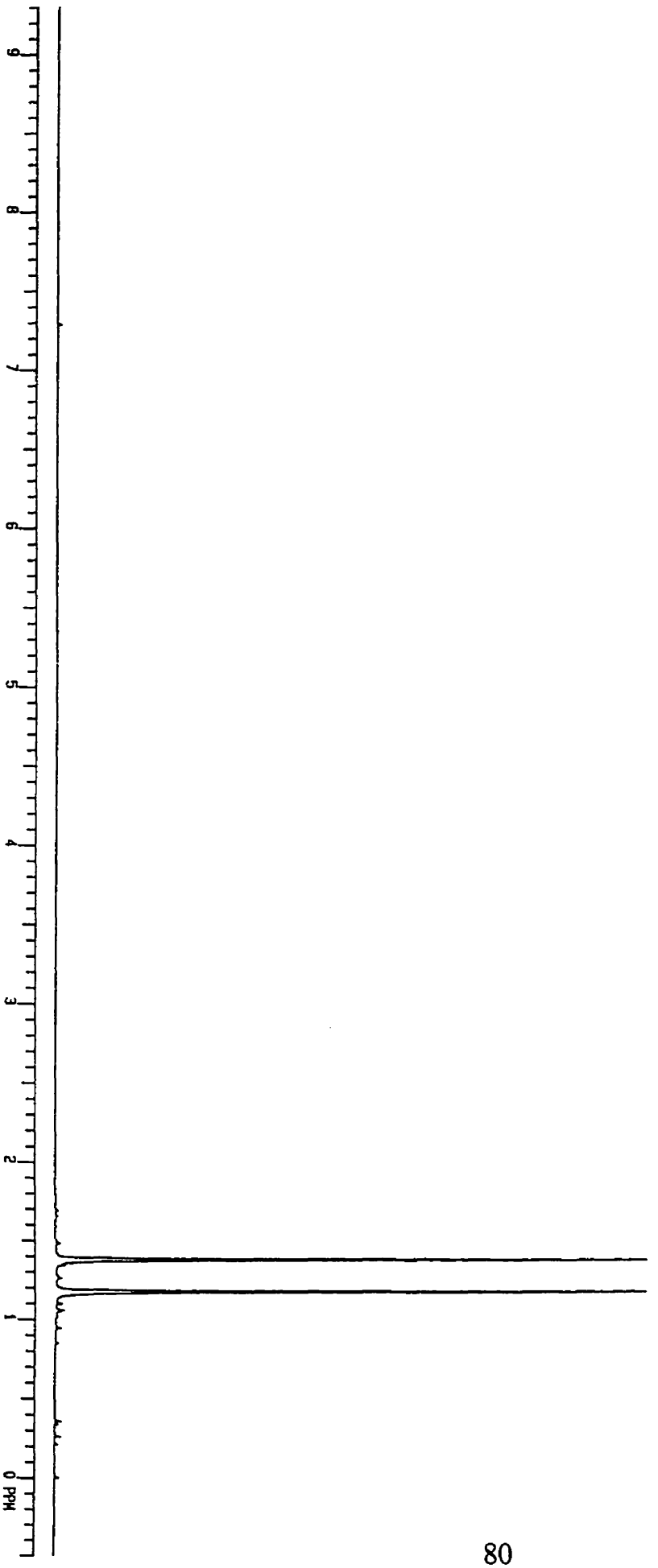

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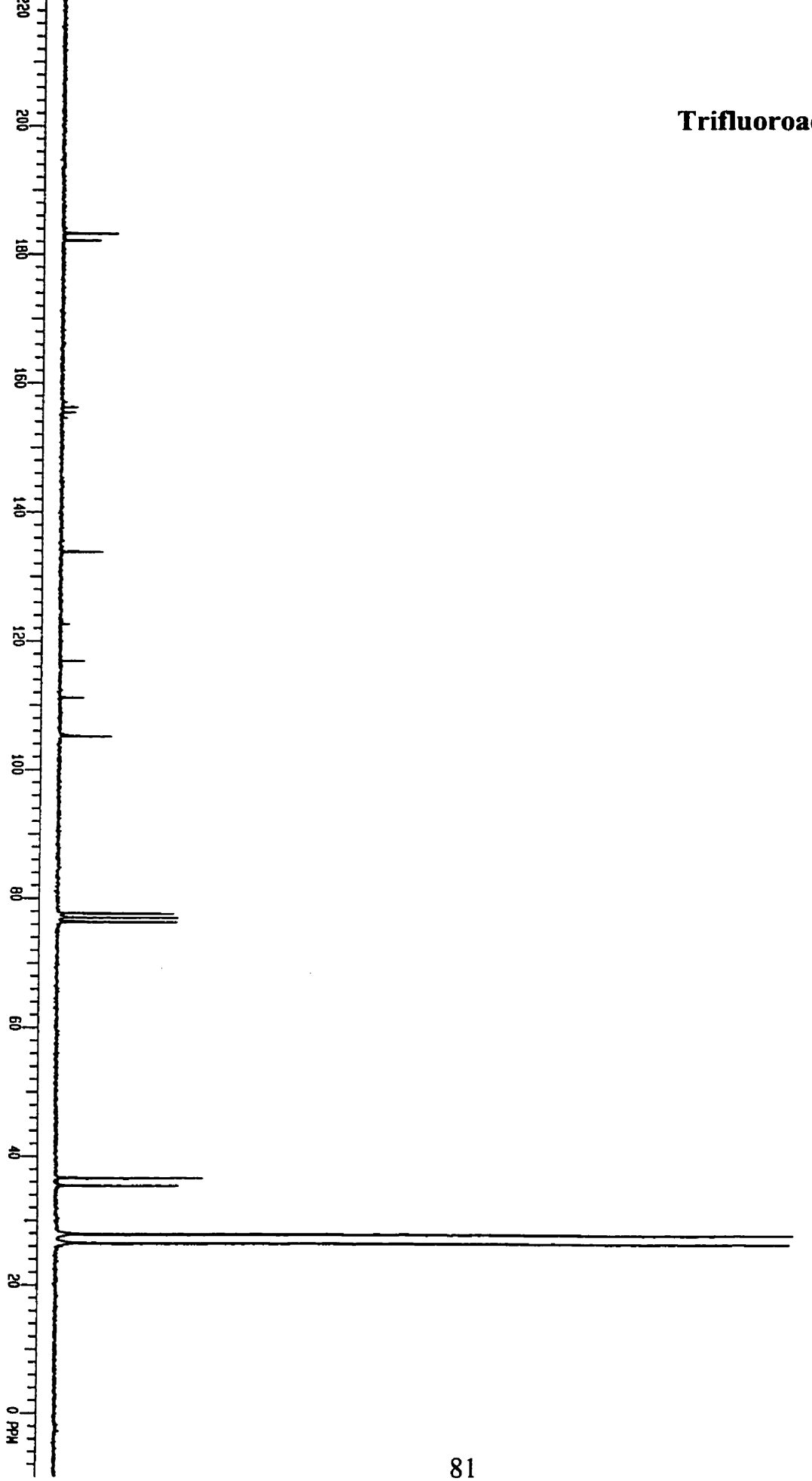
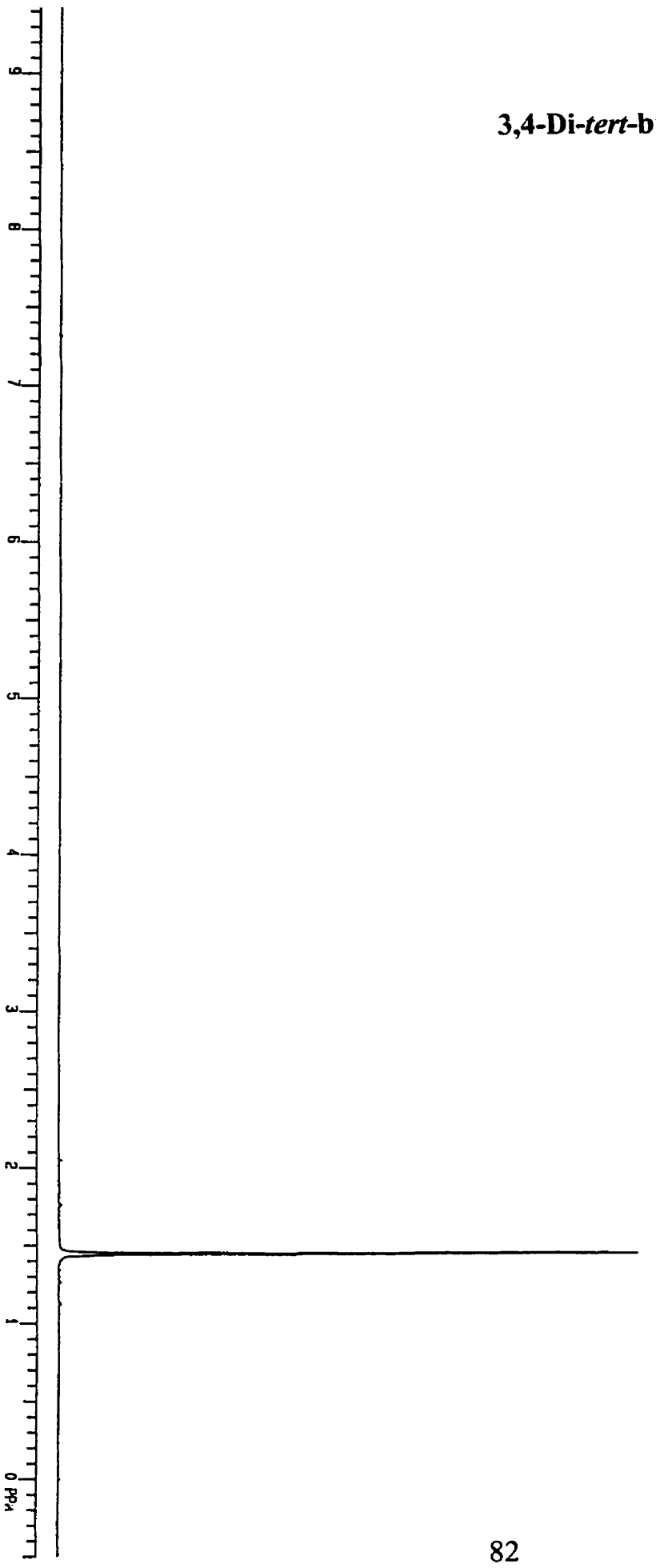
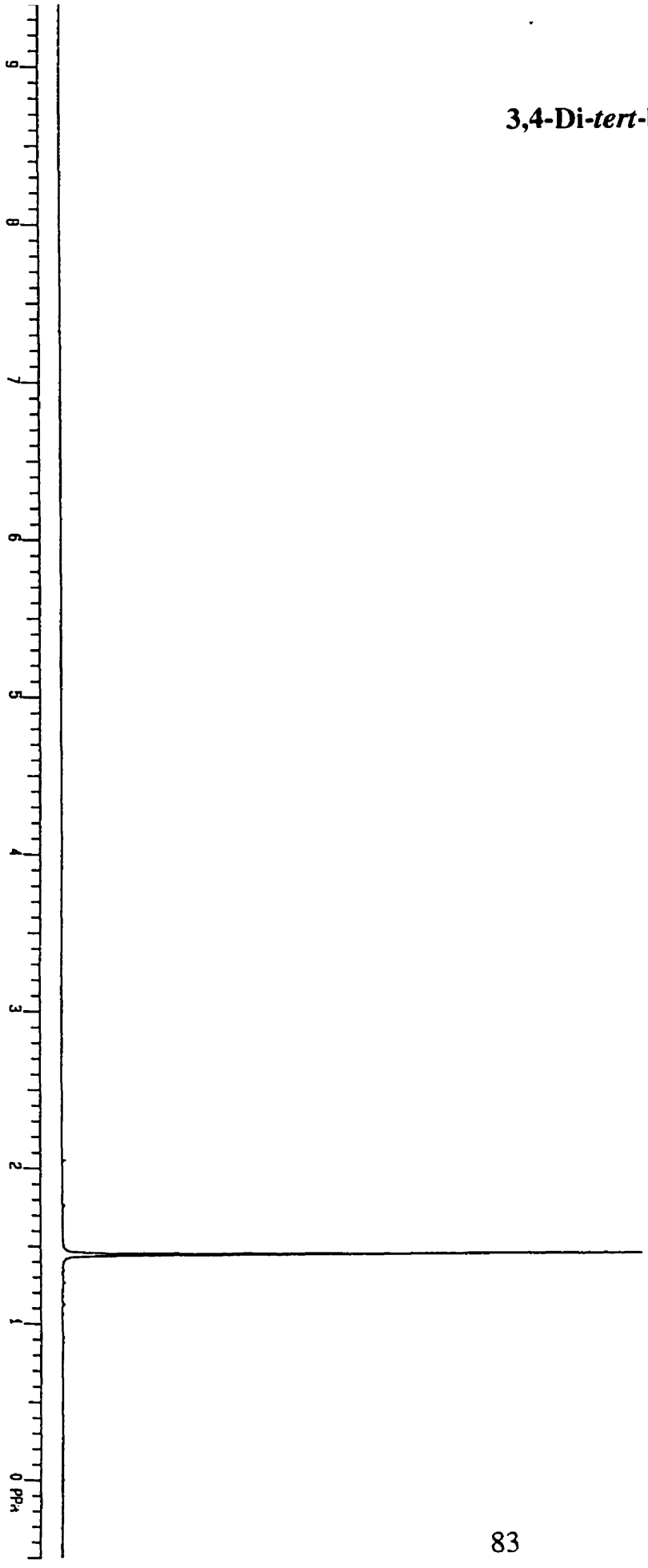


**3,4-Di-*tert*-butylcyclobutenedione (61)**



**3,4-Di-*tert*-butylcyclobutenedione (61)**

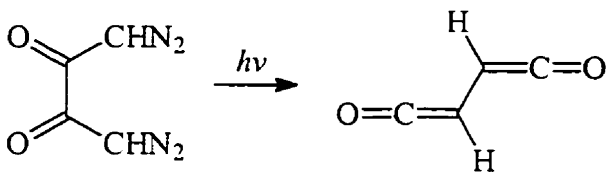


# *Chapter 3*

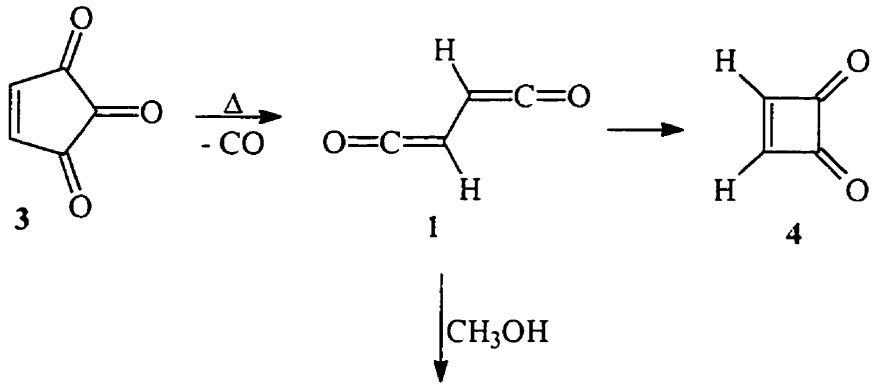
# Preparation of Bisketenes

## 3.1 Introduction

Bisketenes have long been the targets of chemical investigations. A detailed discussion has been given in Chapter 1. The parent 1,3-butadiene-1,4-dione (**1**)[1a,b] is a reactive species that when formed by photolysis of the bis(diazo)diketone **2** in an Ar matrix at 10 K could be identified[1a] by its IR band at 2125 $cm^{-1}$. Pyrolysis of **3** at 430 °C also gave **1** as evidenced by cyclization to **4** and trapping with $CH_3OH$ to give dimethyl succinate **5**.[1b]




**2** **1** (1)




(2)

The prediction was made by this laboratory[2a] that with an appropriate choice of substituents bisketenes may become more stable than the isomeric cyclobutenediones. The basis of this prediction was ab initio calculations that indicated that **1** is only 6.9 kcal/mol less stable than **4**, and that electropositive substituents exert large stabilizing influences on ketenes and could favor the acyclic structure.[2a] For example, the $SiH_3$ group has a calculated isodesmic ketene stabilizing energy of 7.6 kcal/mol (Eq. 3).[2a] However, the calculated energies of the individual species indicate that bisketene **1** is destabilized relative to ketene and butadiene by 11.9 kcal/mol (Eq. 4). [2a,f]

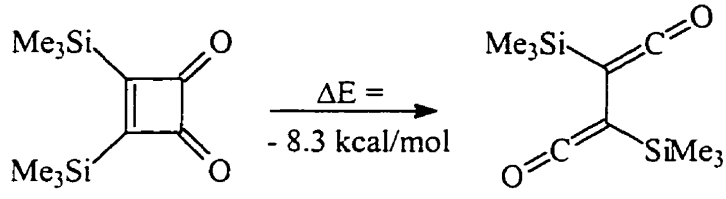
$$SiH_3CH{=}C{=}O + CH_2{=}CH_2 \xrightarrow[7.6\ kcal/mol]{\Delta E =} SiH_3CH{=}CH_2 + CH_2{=}C{=}O \qquad (3)$$

$$\underset{\mathbf{1}}{(CH{=}C{=}O)_2} + 2CH_2{=}CH_2 \xrightarrow[-\ 11.9\ kcal/mol]{\Delta E =} 2CH_2{=}C{=}O + \underset{anti}{(CH{=}CH_2)_2} \qquad (4)$$

These considerations led to the prediction that 1,2-bis(ketenes) could be prepared that were more stable than the isomeric cyclobutene-1,2-dione and, in

particular, that the use of the known ketene stabilizing influence of the $Me_3Si$ group[2,5] would permit the preparation of **5**. Assuming additivity of substituent effects and an equivalence of the properties of the substituents $SiH_3$ and $Me_3Si$ leads to an initial estimate that **5** would be 8.3 kcal/mol more stable than **6** (Eq. 5). A more direct calculation indicates a $\Delta E$ of -4.9 kcal/mol for two $SiH_3$ groups.[4]

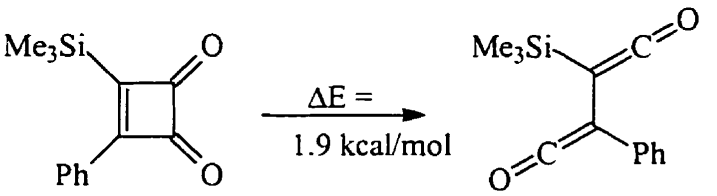
This prediction has been confirmed, using the ketene stabilizing effect of silicon substitution.[3] The dione **6** was converted to bisketene **5** quantitatively upon heating, and also upon photolysis with 350 nm light together with some decarbonylation.[3] A comparison of the calculated and measured activation energies for thermal ring opening was made.[4] The calculated $E_{act}$ value 27.2 kcal/mol for the dione **6** is in reasonable agreement with the experimental $\Delta H^{\neq}$ value of 29.4 kcal/mol.[4]



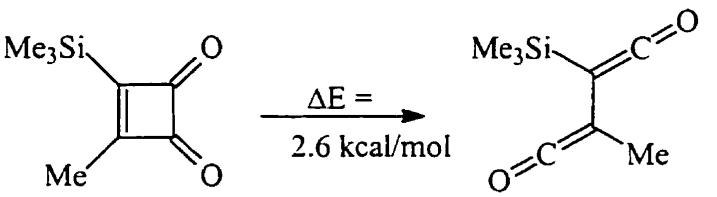

**6** **5** (5)

Being encouraged by these results, we decided to study the unsymmetrically substituted bisketenes. It is of interest to examine the properties of bisketenes substituted with a single stabilizing silyl substituent and another substituent with different properties. Calculations of the effect of the phenyl and methyl groups on ketene stability compared to the effects on an alkene indicate that these groups are destabilizing as ketene substituents relative to hydrogen by 2.6 and 3.3 kcal/mol, respectively. Assuming an additivity of substituent effects leads to estimates that 3-

phenylcyclobutenedione is 9.5 kcal/mol more stable than the bisketene, but that 3-phenyl and 3-methyl-4-(trimethylsilyl)cyclobut-3-ene-1,2-diones **8** and **10** will be more stable than the corresponding bisketenes **7** and **9** by only 1.9 and 2.6 kcal/mol, respectively.



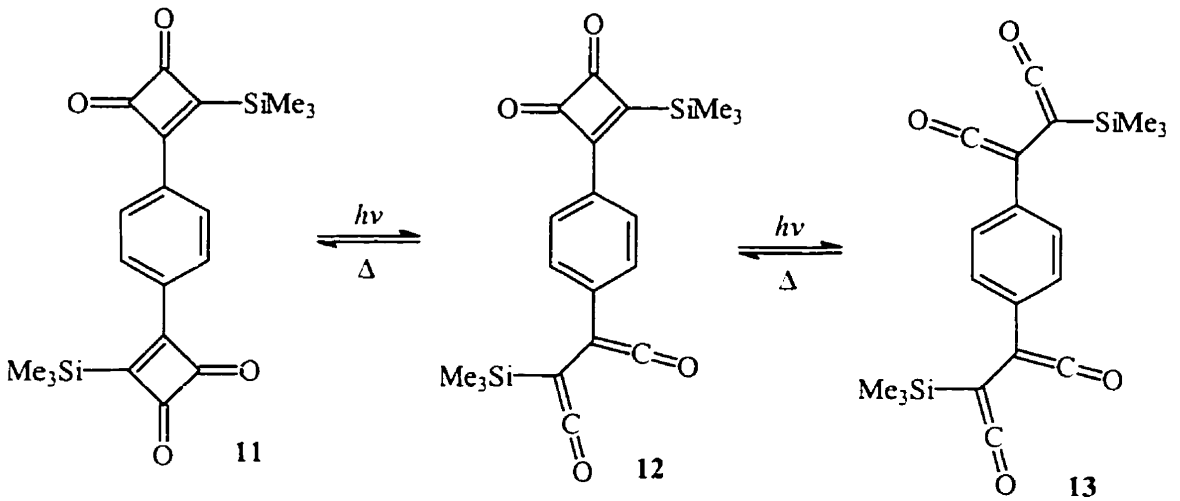

**8** **7** (6)




**10** **9** (7)

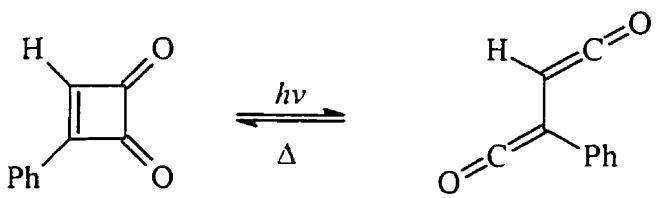
As noted below (Section 3.2), this prediction was verified experimentally. The bisketenes **7** and **9** were obtained in 87-99% and 55% yield, respectively, upon photolysis with 350 nm light. [6]

A long-lived tetraketene **13** stabilized by $Me_3Si$ groups has also been prepared in this lab.[9a] Photolysis of **11** with 350 nm light led to the formation of **13** as evidenced by its spectroscopic properties. The formation of **13** probably occurs by a stepwise process via the bisketene **12** (Eq. 8).

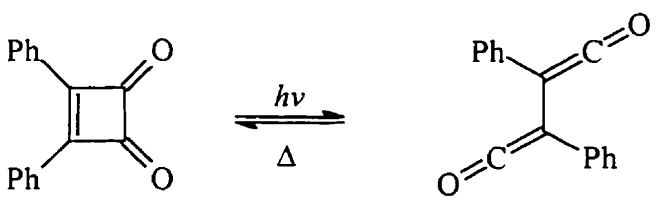



( 8)

The unstabilized phenyl and diphenyl bisketenes **15** and **17** generated by photolysis of the cyclobutenediones **14** and **16**, respectively, have been recently found to be long lived at room temperature, with half lives for ring closure at 25 °C in hydrocarbon solvents of 1.1 h and 18 s, respectively. [7]



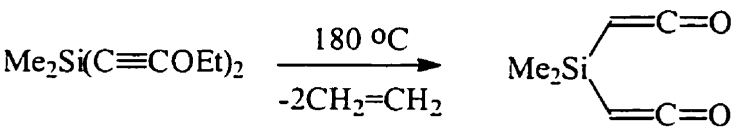

**14** **15** (9)



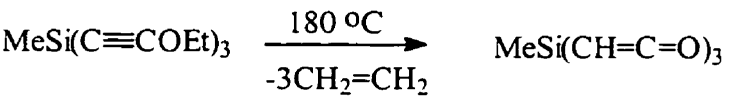

**16** **17** (10)

The first stable and persistent 1,3-bisketene **19** and trisketene **21** have been prepared in this lab recently.[10] The 1,3-bisketene **19** was prepared by

pyrolysis of the alkynyl ether **18** at 180 °C in a gas chromatograph (Eq. 11). The trisketene **21** was prepared by a similar way by pyrolysis of the alkynyl ether **20** (Eq. 20). Calculations indicate that there is no diminution of the ability of silicon to stabilize ketenes even when a second or third moiety is added.[10]

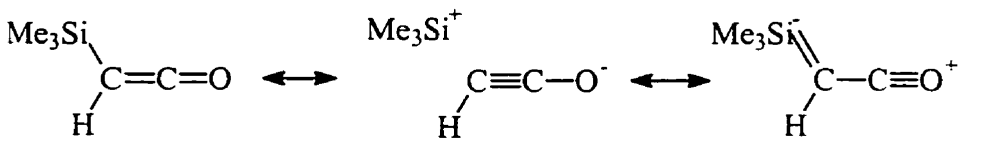



**18** **19** (11)




**20** **21** (12)

There is disagreement about the origin of the stabilizing influence of silyl substituents on ketenes. It was suggested by Brady and Cheng[12] that this effect arose from hyperconjugative donation from C-Si bond into the in-plane p orbital of the carbonyl group, as represented by the resonance structure **22A**. This proposal was disputed by Runge, who instead argued that the silicon acted as a dπ-pπ electron acceptor, as represented by **22B**.[13] These two mechanisms give opposite predictions of the direction of electron redistribution in ketenes due to silyl group substitution.



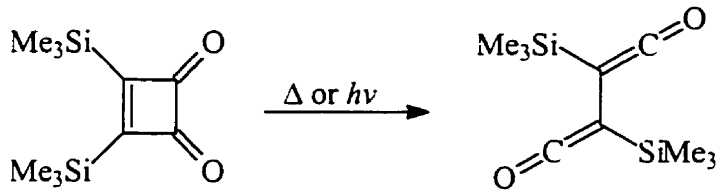

**22** **22A** **22B**

**Figure 1**

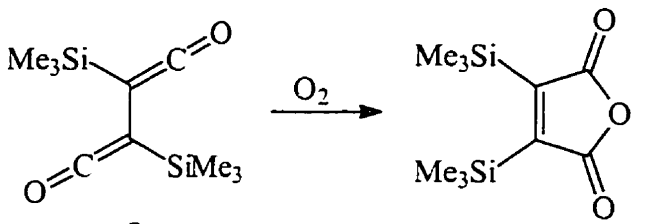
*Ab initial* molecular orbital calculations of the geometries and energies of silylketenes are not definitive as to the stabilization of these compounds.[2a,b] This effect is related to the stabilization of β-silyl carbocations and radicals,[14] and the interaction shown in **22A** is an example of "neutral hyperconjugation", as recently discussed by Lambert and Singer. [14d]

Nuclear magnetic resonance spectroscopy is a powerful tool for the examination of electronic distributions in molecules. A recent systematic study of the $^{13}C$, $^{17}O$, and $^{29}Si$ NMR of the silyl ketenes and bisketenes available in this lab reveal that the chemical shifts are all consistent with decreased negative charge on silicon, and increased negative charge on the carbonyl carbon and oxygen, when compared to model non-silylated ketenes, or to silylated alkenes.[11] The charge distribution is highly supportive of an important role for the "neutral hyperconjugation" interaction shown in **22A**.

The bisketene **5** was obtained both from heating and photolysis of the cyclobutenedione **6** (Eq. 13). The easy way of making this bisketene was to use a preparative VPC, and typically more than 100 mg may be obtained in one run. The bisketene **5** was obtained as yellow colored solid, with a melting point about 5 °C. It is thermodynamically stable relative to **6** and may be stored in a refrigerator for months under argon. It is sensitive to air and is gradually oxidized to black colored unidentified product. From this complex mixture a low yield of bis(trimethylsilyl)maleic anhydride was separated (Eq. 14).[3]




6 5 (13)




5 (14)

Calculations show that in all cases the bisketenes prefer twisted, almost perpendicular conformations, as opposed to the planar *s*-**E** or *s*-**Z** conformations.[8] These conclusions are confirmed experimentally by the measured photoelectron spectrum of **5**, which is uniquely consistent with a twisted conformation, and by the dipole moment of **5** of 2.7 D, compared to the value of 1.7 D for $Me_3SiCH=C=O$.[8b] This significant dipole moment excludes an *s*-**E** conformation and is consistent with the twisted conformation. The unexpected conclusion that the *s*-**E** conformation is not favored cannot be ascribed primarily to steric effects, as the calculations show that the twisted conformation is favored even for the parent bisketene **1**. The instability of the planar structure may be attributed to the unfavorable π-π repulsion between the electrons in the p orbitals at the central carbons of the bisketenes, due to the high negative charge density (*vide supra*) on these carbons, and the absence of any plausible conjugatively stabilizing interaction in a planar 1,3-dienyl unit.

### 3.2 Results and discussion

The phenyl substituted cyclobutenedione **8** was obtained as yellow crystals and was stable upon heating. However on photolysis at 350 nm there was a color change to a deeper yellow and a new UV absorption at $\lambda_{max}$ 257 nm appeared, while that at 287 nm due to the dione essentially disappeared. Evidence for the structure of bisketene **7** includes the presence of the strong ketene bands in the IR at 2076 $cm^{-1}$, which is compared to the band at 2084 $cm^{-1}$ for **5**. $^{1}H$ NMR indicated clearly the disappearance of the cyclobutenedione peaks and the reappearance of new peaks at δ 0.23 (TMS) and 7.05-7.40 (Ph). The $^{13}C$ NMR shows the very distinctive peaks for the $Me_3Si$- and Ph-substituted ketenyl carbons at δ 7.9 and 33.5 respectively. The bisketene was obtained in 87-99% yield, depending upon the concentration of the sample and the irradiation time. Basically it is a quite clean reaction as long as 350 nm light was used and the solvent was absolutely dry. When shorter wavelengths of light such as 300 nm and 254 nm were used, decarbonylation to the alkyne became significant. This is because the bisketene **7** has a low $\lambda_{max}$ wavelength absorption (257 nm), but little absorption at 350 nm.

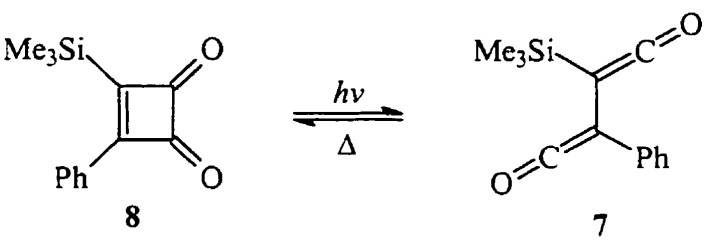
Upon heating of **8** in $CDCl_3$, followed by rapid cooling, the presence of the phenyl substituted bisketene **7** could be detected by the appearance of the $^{1}H$ NMR peak of the $Me_3Si$ at δ 0.23 and of the IR band at 2076 $cm^{-1}$. The relative concentrations of **7** and **8** were determined by integration of the NMR spectra, and the data were used to calculate equilibrium constants and thermodynamic parameters (Table 1).[6] These equilibrium constant measurements were carried out by A. D. Allen.

Table 1 Thermal Equilibration of **7** and **8** in $CDCl_3$[6]

| T (°C) | [**8**]/[7] | K[a] |
|---|---|---|
| 161.3 | 2.2 (±0.1)/97.8 | $2.25 \times 10^{-2}$ |
| 161.0 | 2.8 (±0.1)/97.2 | $2.88 \times 10^{-2}$ |
| 143.1 | 1.4 (±0.2)/98.6 | $1.42 \times 10^{-2}$ |
| 142.2 | 1.6 (±0.2)/98.4 | $1.63 \times 10^{-2}$ |
| 100.5 | 0.5 (±0.10/99.5 | $5.02 \times 10^{-3}$ |
| 100.3 | 0.9 (±0.1)/99.1 | $9.08 \times 10^{-3}$ |
| 25.0[b] | 0.06/99.94 | $6.00 \times 10^{-4}$ |

[a]$\Delta G^{o}$ (25 °C) = 4.4 kcal/mol; $\Delta H^{o}$ = 6.9 ± (1.3) kcal/mol; $\Delta S^{o}$ = 8.5 ± (3.2) kcal/mol×K.

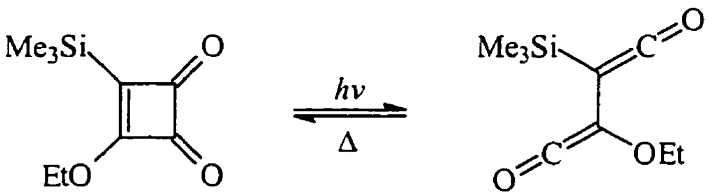
[b]Extrapolated.




**8** **7** (15)

To explore the limits for generation of 1,2-bisketene by the ring opening process of the corresponding cyclobutenediones, we decided to examine a substituent that is highly destabilizing toward ketenes. The ethoxy substituent was chosen and was expected on the basis of molecular orbital calculations to greatly destabilize the bisketene. It was of interest to see in this case whether the bisketene could be observed by $^{1}$H-NMR and/or IR spectroscopy at room temperature.

With the dione **23** in hand, we tried to photolyse it to generate the bisketene **24**, however no **24** was observed. However, upon using the method of laser flash photolysis (LFP) generation of the bisketene **24** was detected by time-resolved infrared spectroscopy (TRIR), which showed the distinctive IR bands of the bisketene at 2090 and 2104 $cm^{-1}$.[7] This experiment was carried out by J. Lusztyk and B. Wagner at the Steacie Institute of Molecular Sciences in Ottawa.

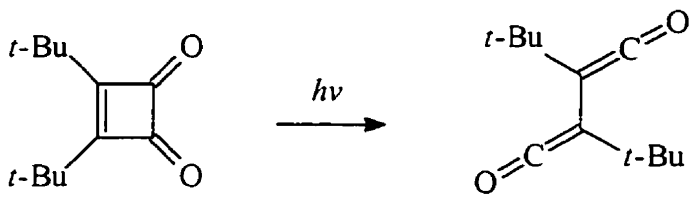



**23** **24** (16)

So far all the bisketenes that could be observed at room temperature had at least one silyl group as a stabilizing substituent. It is of interest to examine the steric effect of large substituents such as those in di-*tert*-butyl 1,2-bisketene, as the di-tert-butyl monoketene t-$Bu_2C$=C=O is stable indefinitely at room temperature. It is conceivable that the strain in 3,4-di-tert-butyl-1,2-cyclobutenedione would render the bisketene more stable.

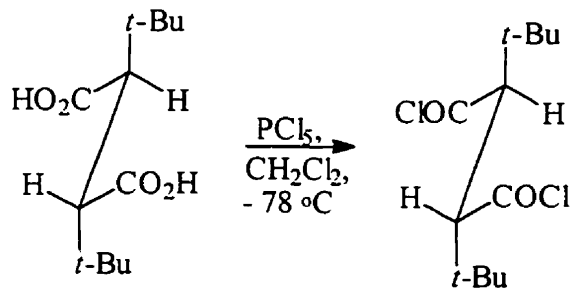
The dione **25** (Chap. 2) was a low melting yellow solid. Upon heating to 180 $^{o}C$, no change in the $^{1}H$ NMR spectrum was observed. However when the dione **25** was irradiated in $CDCl_3$ with 350 nm lamps bisketene **26** could be observed to the extent of 5% conversion by $^{1}H$ NMR and IR, as evidenced by the appearance of peaks at $\delta$ 1.17 and 2101 $cm^{-1}$, respectively. The bisketene **26** was observed to form much faster when lower wavelength 300 nm lamps

were used, but a large amount of acetylene also appeared due to the decarbonylation reaction. Benzophenone was also used as a triplet sensitizer, and it also made the ketene formation much faster but with a large amount of the acetylene. The generation of the bisketene **26** (14%) was also observed by photolysis of the dione **25** in $C_6D_6$ with 350 nm light as evidenced by the appearance of peaks at $^1H$ NMR δ 1.21 and IR 2099 $cm^{-1}$. Heating the bisketene in $CDCl_3$ to observe the reformation of the cyclobutenedione failed, with formation of the known succinic anhydride **29**.



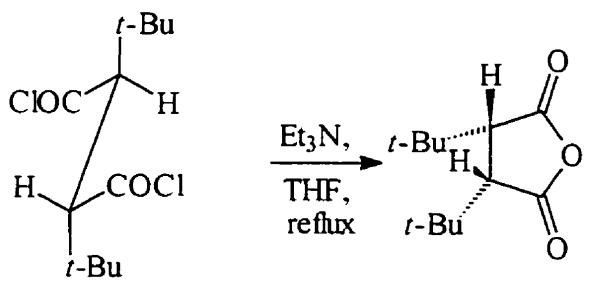

**25** **26** (17)

The reaction of the meso diacid[15] **27** with $PCl_5$ at -78 °C gave the succinyl chloride **28** in good yield (80%). However reaction of **27** with thionyl chloride gave only the cis anhydride **29**. The succinyl chloride **28** could be purified by an aqueous work up, which indicated a low reactivity towards $H_2O$ due to the presence of two bulky *t*-butyl groups.

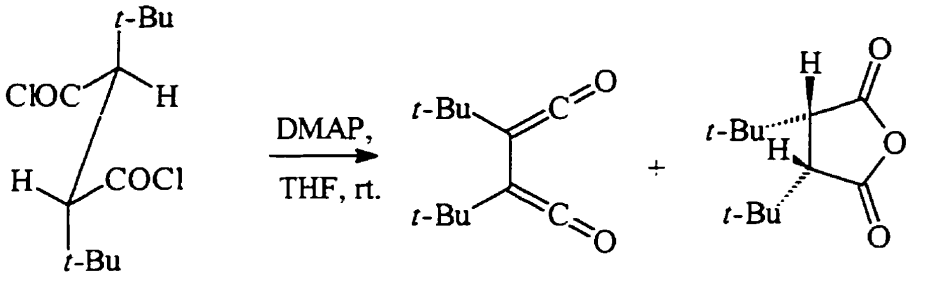



**27** **28** (18)

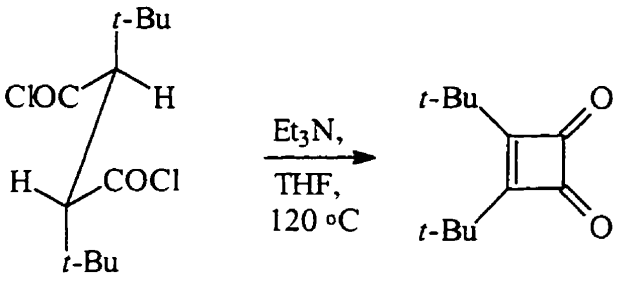
Attempted generation of the bisketene through bisdehydrochlorination using triethylamine failed even under reflux in THF or benzene. The reaction was very slow, and the succinyl chloride was consumed in a week but the cis anhydride was the only observed product. Dehydrochlorination did however occur when the reaction mixture was sealed in an ampoule and heated to 120 $^{o}$C for 16 hours in THF. The dione **25** was obtained in 70% yield, along with the anhydride **29**. This reaction clearly indicated the dione **25** was generated from the bisketene **26** initially formed from the dechlorination reaction upon heating. Reaction at room temperature with DMAP as the base for 2 hours gave as the major product 90% of the anhydride **29**, which contained 10% of the bisketene, as indicated by the $^{1}$H NMR signal at $\delta$ 1.17 and the IR band at 2101 cm$^{-1}$ as observed in the photolysis of the dione. Attempts to increase the yield of the bisketene failed.




**28** **29** (19)




**28** **26** **29** (20)




**28** **25** (21)

In conclusion, the phenyl substituted bisketene was observed to be long-lived at room temperature but could be converted back to the dione upon heating, and the equilibrium constant for this interconversion was measured at elevated temperatures. The bisketene was destabilized electronically by the phenyl group as compared to trimethylsilyl, as predicted by ab initio molecular orbital calculations.

The ethoxy trimethylsilyl substituted bisketene was even less stable, as expected on the basis of molecular orbital calculations, and could not be observed by conventional methods. The bisketene, however, was observed by LFP techniques as a transient species.

The bisketene with bulky di-tert-butyl substituents could be formed to the extent of 5-15% by photolysis of the corresponding dione, and the dione form was confirmed to be the stable form by the formation of the dione from dehydrochlorination of the related succinyl chloride at high temperature.

These results indicated that the steric effect of the bulky t-butyl groups was not sufficient to favor the bisketene at equilibrium compared to the cyclobutenedione.

Future work in the generation of long-lived bisketenes could include the study of other electronically stabilizing substituents such as stannyl groups. Other bulky substituents could be used to examine the steric effect, such as adamantyl and/or 2,4,6-trimethylphenyl substituents. With proper choice of substituents, it is possible that long-lived and even persistent 1,2-bisketenes with bulky substituents could be obtained due to steric repulsion in the cyclobutenediones.

## 3.3 Experimental

Photolyses were carried out using a Rayonet RPR-100 reactor. The general procedures are given in Chapter 2.

**2-Trimethylsilyl-3-phenyl-1,3-butadiene-1,4-dione (7).** A solution of 3-trimethylsilyl-4-phenylcyclobutenedione **8** (74.2 mg, 0.322 mmol) in 0.5 mL $CDCl_3$ in an NMR tube under a $N_2$ atmosphere was photolyzed 1.5 hours with 350 nm light. The $^1$H-NMR due to dione decreased, and new signals appeared corresponding to 87% isomerization to the bisketene. $^1$H NMR ($CDCl_3$) δ 0.23 (s, 9), 7.05-7.40 (m, 5H); $^{13}$C NMR ($CDCl_3$) δ -0.23, 7.9, 33.5, 124.4, 125.1, 129.4, 134.0, 178.8, 202.2.; IR ($CDCl_3$) 2076 (s), 2042 (w) $cm^{-1}$; UV $\lambda_{max}$ (hexane) 257 nm.

**2,3-Di-*tert*-butyl-1,3-butadiene-1,4-dione (26) ($CDCl_3$).** A solution of 2,3-di-*tert*-butylcyclobutenedione **25** (10 mg, 0.052 mmol) in 0.5 mL $CDCl_3$ in an NMR tube under a $N_2$ atmosphere was photolyzed 25 hour with 350 nm light. New $^1H$ NMR signals appeared corresponding to 5% isomerization to the bisketene, along with the residual dione. $^1H$ NMR ($CDCl_3$) δ 1.17 (s, 18); IR ($CDCl_3$) 2101 (s) $cm^{-1}$.

In another experiment benzophenone (2 eq) was used and the reaction mixture was photolysed 6 hr to give 15% of the bisketene, 35% of the di-*tert*-butylacetylene and residual dione, as indicated by the $^1H$ NMR spectrum.

**2,3-Di-*tert*-butyl-1,3-butadiene-1,4-dione (26) ($C_6D_6$).** A solution of 2,3-di-*tert*-butyl-cyclobutenedione **25** (10 mg, 0.052 mmol) in 0.5 mL $C_6D_6$ in an NMR tube under a $N_2$ atmosphere was photolyzed 50 hour with 350 nm light. New $^1H$ NMR signals appeared corresponding to 14% isomerization to the bisketene, along with residue dione. Bisketene **26**: $^1H$ NMR ($C_6D_6$) δ 1.21 (s, 18); IR ($C_6D_6$) 2099 (s) $cm^{-1}$. Dione **25**: $^1H$ NMR ($C_6D_6$) δ 1.03 (s, 18);

**meso-2,3-Di-*tert*-butylsuccinyl chloride (28).** The meso-di-*tert*-butylsuccinic acid[15] (0.1 g, 0.435 mmol) was suspended in dichloromethane (20 mL) and cooled with a acetone/dry ice bath and $PCl_5$ (3 eq) was added in one portion. The reaction was allowed to warm to room temperature in three hours. The solvent was removed and the residue redissolved in ether (30 mL), and the precipitate was removed by filtration. The ether solution was washed five times with water (10 mL) and dried over MgSO4. The solvent was removed and the residue was redissolved in hexane (20 mL) and the remaining residue was removed by filtration. The solvent was removed and gave **28** (93.0 mg, 35 mmol, 80%): $^1H$ NMR ($CDCl_3$) δ 1.18 (s, 18), 3.27 (s, 2); $^{13}C$ NMR

($CDCl_3$) δ 29.1, 36.1, 67.2, 174.5; IR ($CDCl_3$) 1801 (bvs) $cm^{-1}$; EIMS *m/z* 251 (2), 231 (6), 118 (10), 111 (31), 57 (100); HRMS *m/z* calcd for $C_{11}H_{17}O_2Cl_2$ ($M^+$ -$CH_3$) 251.0606, found 251.0600.

**2,3-Di-*tert*-butyl-1,3-butadiene-1,4-dione (26).** The succinyl chloride **28** (10 mg) was dissolved in THF (5 mL), and DMAP (2 eq) in THF (1 mL) was added in 5 min at room temperature. The solvent was removed after 3 hr of reaction and the residue was redissolved in $CDCl_3$ (0.5 mL) and the $^1H$ NMR showed the signal δ 1.17 ascribed to the bisketene (10%) along with the signals at δ 1.05 (s, 18) and 2.60 (s, 2) ascribed to the cis-anhydride 90% (see Chapter 4) and residual DMAP. The reaction mixture in $CDCl_3$ also showed the IR absorption at 2101 $cm^{-1}$.

**2,3-Di-*tert*-butylcyclobutenedione (25).** Succinyl chloride **28** (80 mg, 0.30 mmol) was dissolved in anhydrous THF (5 mL), and $Et_3N$ (61 mg, 0.6 mmol) in THF (1 mL) were added in one portion. The solution was sealed in a vial and heated to 120 °C for 16 hr. The precipitate was removed by filtration and the solvent was removed. The residue was purified by a thin layer chromatography with elution with 5% ethyl acetate in hexane to give the dione (41 mg, 0.21 mmol, 70%): $^1H$ NMR ($CDCl_3$) δ 1.44 (s, 18); $^{13}C$ NMR ($CDCl_3$) δ 28.9, 35.4, 198.9, 206.4. The identification was confirmed by comparison with an authentic sample made in Chapter 2.

The $^1H$ NMR spectrum of the crude product also showed the signals at δ 1.05 (s, 18) and 2.60 (s, 2) of the cis anhydride (see Chapter 4)

## 3.4 References

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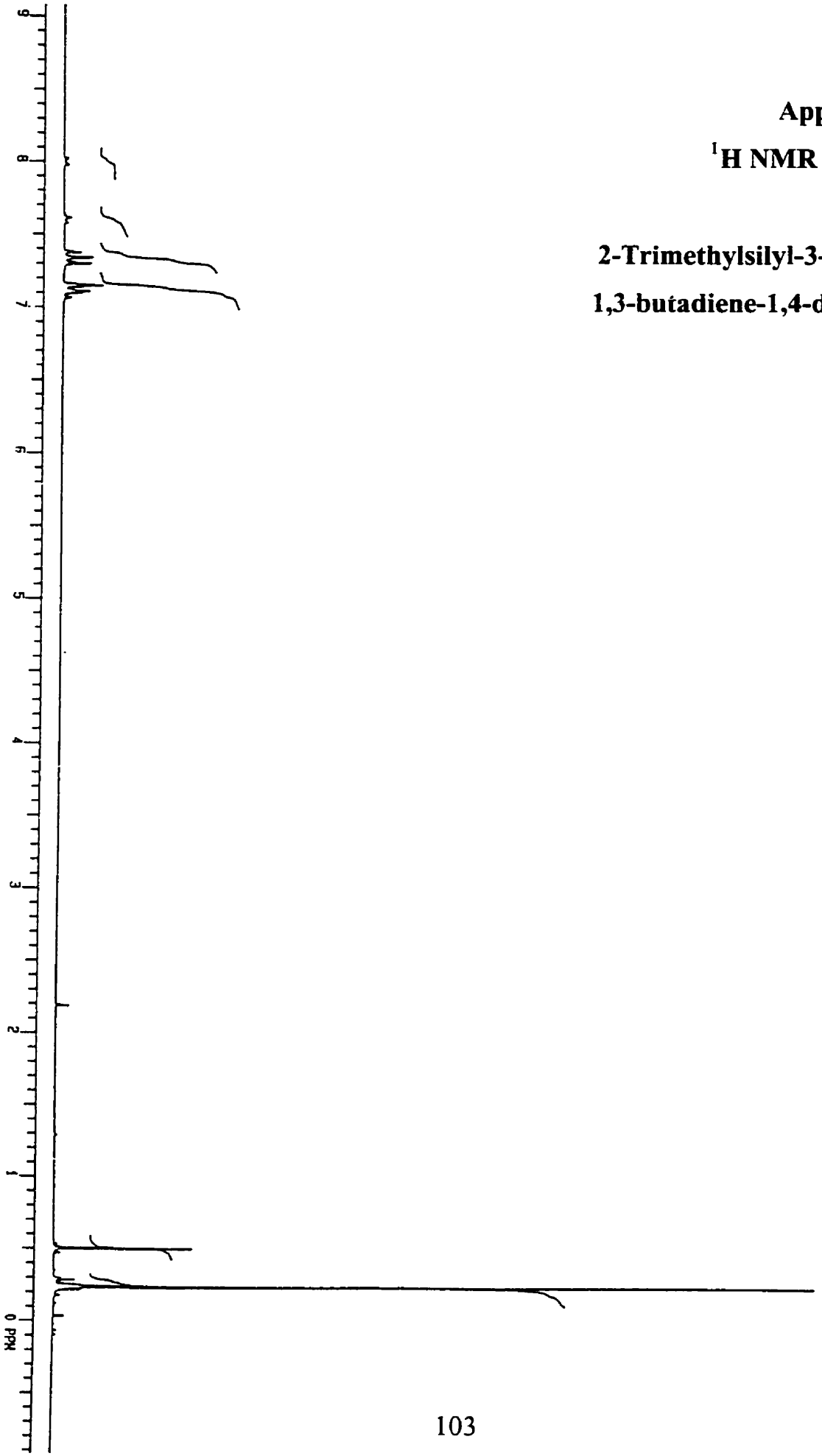
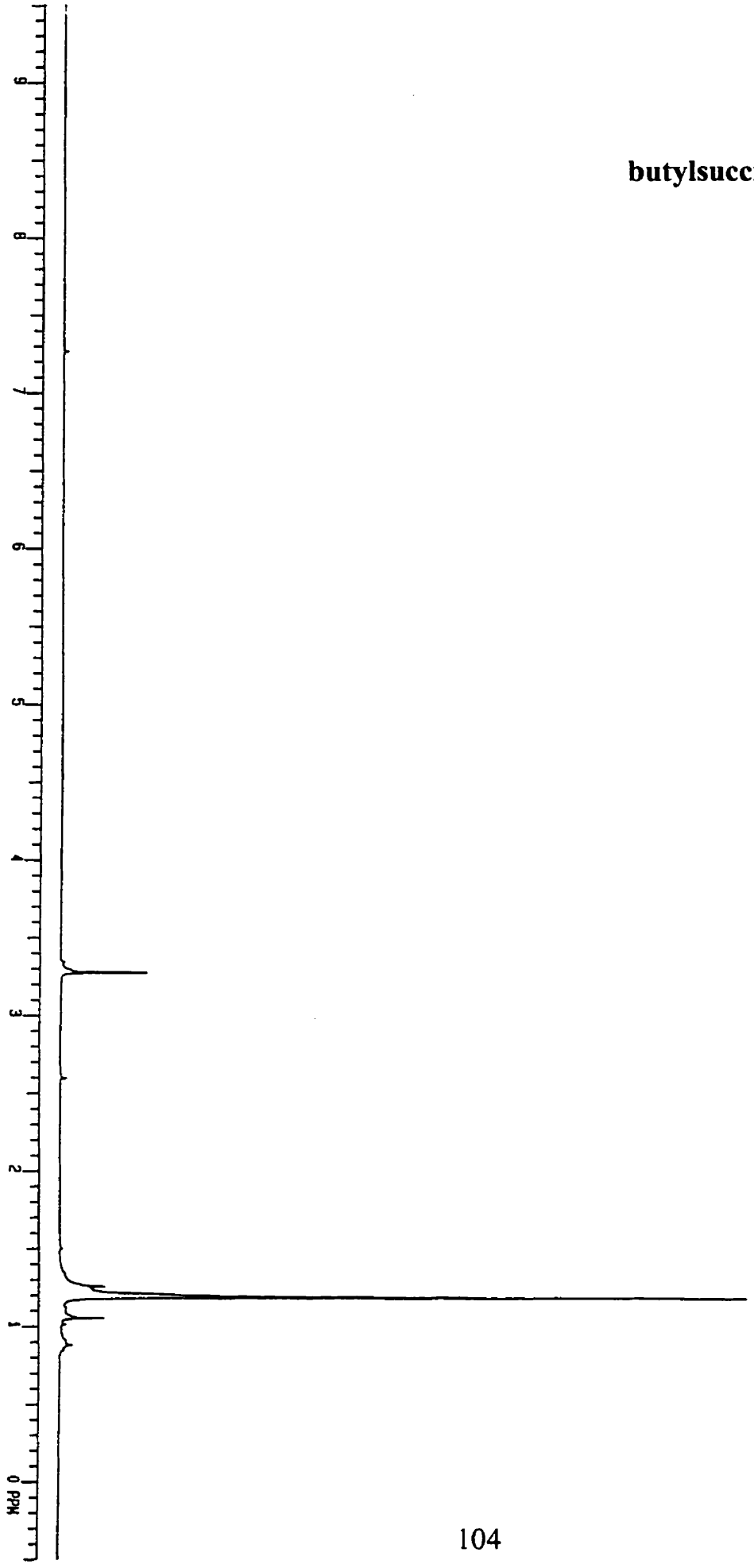
## Appendix 1

## $^1$H NMR Spectra

**2-Trimethylsilyl-3-phenyl-1,3-butadiene-1,4-dione (7)**



**meso-2,3-Di-*tert*-butylsuccinyl chloride (28)**



# *Chapter 4*

# Nucleophilic Reactions of Bisketenes

## 4.1 Introduction

Consideration of the resonance structures of ketenes (Fig. 1) indicates that nucleophilic attack will occur at $C_\alpha$ because of the high positive charge present on that *sp*-hybridized carbon. The mechanisms of such additions have been discussed in detail in previous reviews,[1] and so only a brief introduction is considered here which will help to interpret the nucleophilic addition reactions of the bisketenes studied.

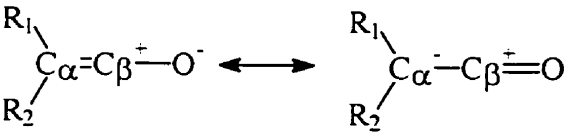


**Figure 1:** Resonance structures of ketenes

The most common types of nucleophilic additions are those involving oxygen, nitrogen, and sulfur nucleophiles such as water, alcohols, amines, and thiols,[1a] and the addition of carbon nucleophiles, especially organolithium species including lithium enolates.[2-7]

The mechanism of neutral hydrolysis of ketenes is depicted in Fig. 2.[1,8-10] with polar transition state **1**, and possible zwitterionic and enediol intermediates **2** and **3** leading to the carboxylic acid product.

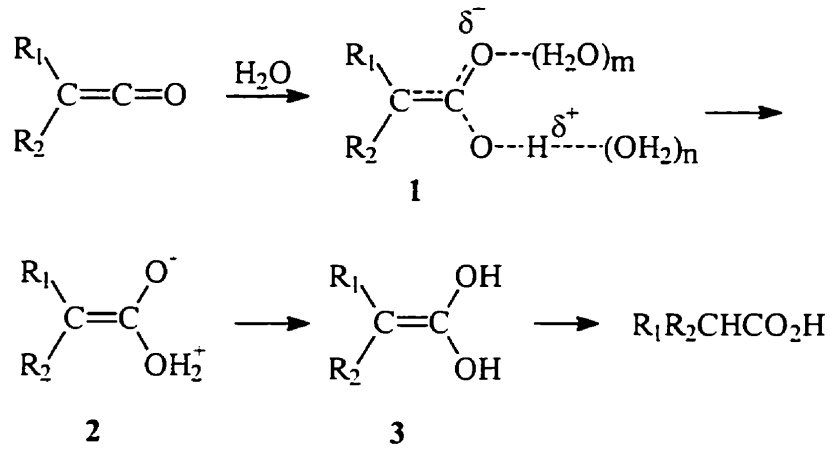



**Figure 2:** Hydration mechanism for ketenes in neutral solution

Attack occurs in the ketene plane on the LUMO at $C_\alpha$ because of the large coefficient of the LUMO at this carbon. Only minor rate effects are observed for monoalkyl ketenes compared to the parent ketene. Thus for $CH_2$=C=O, *n*-BuCH=C=O, and *t*-BuCH=C=O, in which one side is unhindered in all cases, the relative hydration reactiveties are 1.0, 2.2, and 0.4, respectively.[8,11] However in *t*-$Bu_2$C=C=O in which there is a large *tert*-butyl group on each side of the ketene the relative reactivity is reduced to $4\times10^{-6}$ relative to the parent ketene.[8,9] The conjugating Ph group produces an acceleration of $10^2$ of the rate compared to the parent ketene.[12] This result was explained as resulting from stabilization of the enolate-like transition state being more important than the stabilization of the ground state by the phenyl group. The enediol intermediate **3** (Fig. 2) in some cases could be directly observed, for example, in the hydration of $Ar_2$C=C=O (Ar = 2,4,6-$Me_3C_6H_2$

and 2,3,4,5,6,-$Me_5C_6$), the endiols were observed as reasonably long-lived intermediates.[13]

The acid-catalyzed reaction was explained as proceeding by a different pathway as shown in Fig. 3. This process is proposed to occur by rate-determining attack of a proton at $C_\beta$ perpendicular to the ketene plane leading to an acylium ion (Fig. 3), which was trapped by water leading to the final product acid.[1b]

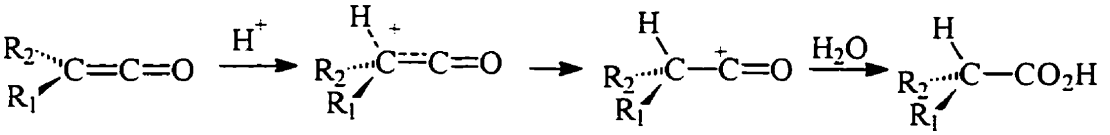


**Figure 3:** Acid-catalyzed hydration of ketenes

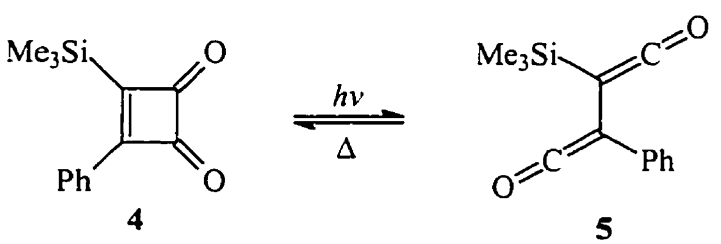
Despite the large number of kinetic studies of the reactions of ketenes with alcohols,[1] the mechanism of this reaction is still controversial. In most cases the experimental data can explained by the intervention of an enolate-like transition state formed by addition to the C=O bond. However an alternative explanation that the reaction occurs through a cyclic 4-membered transition state involving addition to the C=C bond has also been suggested.[14,18]

## 4.2 Results and discussion

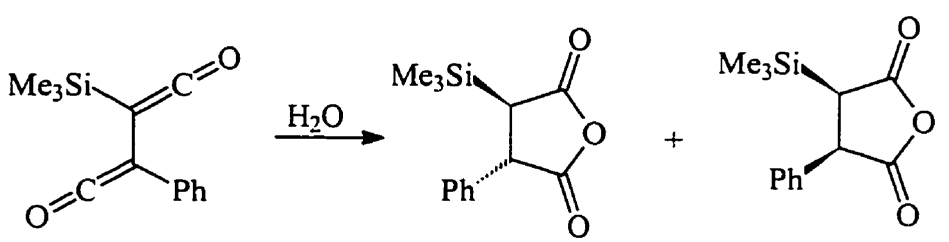
As bisketenes are bifunctional molecules, and are highly reactive toward nucleophiles such as alcohols and amines, these species have the potential of being used in polymer synthesis as coupling reagents in the synthesis of polyesters and polyamides. Therefore it is of interest to study the reaction with simple alcohols and amines to provide a basic understanding of these reactions.

Because of the mechanistic interest in kinetic studies involving the reaction with water, product studies of this reaction were also carried out.

The reaction of the bisketene **5** (formed from photolysis of the dione **4** as shown in Eq. 1) in $CDCl_3$ with $H_2O$ produced a mixture of the stereoisomeric succinic anhydrides *E*-**6** and *Z*-**6** in a variable ratio that depend upon the reaction conditions (Eq. 2). The stereoisomers were readily differentiated on the basis of the $J_{H\text{-}H}$ values for vicinal protons, which are 3.6 and 10.4 Hz, respectively, for the structures assigned as *E*-**6** and *Z*-**6**. The structural assignments are based on those found for the corresponding 2,3-bis(trimethylsilyl)succinic anhydrides, for which X-ray crystal structure determinations reveal dihedral angles of 108° between the C-H bonds in the *E*-isomer and 38.8° in the *Z*-isomer[15], and the $\cos^2\phi$ values of these angles, 0.10 and 0.61, respectively, were consistent with the observed coupling constants, according to the Karplus equation ($^3J = A\cos^2\phi + C$ ($\phi = 0 - 90°$); $^3J = A'\cos^2\phi + C'$ ($\phi = 90 - 180°$).

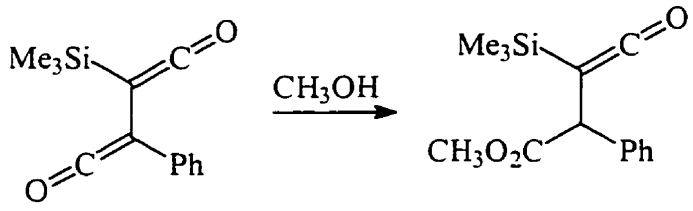



**4** **5** (1)



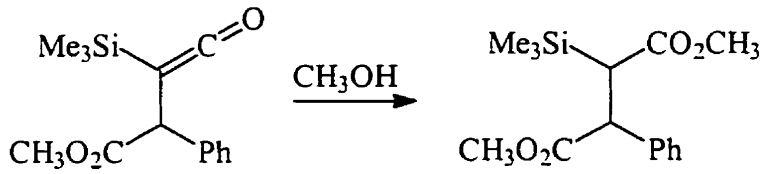

**5** *E*-**6** *Z*-**6** (2)

The bisketene **5** was generated by photolysis of the dione in $CDCl_3$ in an NMR tube and 1.6 equivalent of $CH_3OH$ was added at - 78 °C, followed by warming to RT and evaporation of the solvent. After addition of more $CDCl_3$, the photolysis and methanolysis procedure was repeated one or two times, resulting in formation of the monoketene **7** in a yield of 95% as observed by $^1H$ NMR measurements, together with residual diketone (Eq. 3). The monoketene was purified by VPC and obtained pure as a rather stable colorless liquid. The structure of **7** was confirmed by the IR absorption at 2093 $cm^{-1}$, the $^{13}C$ NMR signal for Cβ of the ketene moiety at δ 8.5, and by other consistent spectral data.

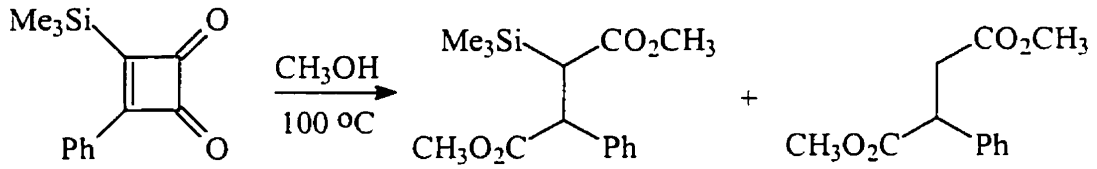



**5** **7** (3)

Reaction of the monoketene **7** with methanol in $CDCl_3$ at room temperature for 10 hours gave the two diastereoisomeric dimethyl succinates **8** in a 2/1 ratio (Eq. 4), which were isolated after separation by liquid chromatography. These were also formed by heating the diketone **4** in methanol at 100 °C for 18 hours, and were observed along with the desilylated ester **9**, in relative yields of 28, 26, and 20%, respectively (Eq. 5).



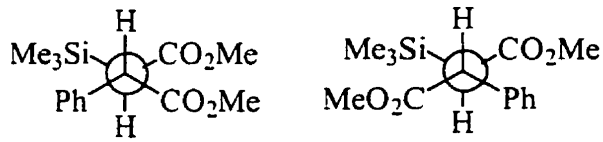

**7** **8** (4)




**4** **8** **9** (5)

Tentative assignments of the *threo* and *erythro* isomers of the diester **8** were made from their NMR spectra. The principal differences were the $^1$H chemical shifts for the *threo* and *erythro* isomers of the $Me_3Si$ groups at δ -0.21 and 0.13, of the OMe groups at δ 3.60 and 3.68 for *threo*-**8** and 3.38 and 3.62 for *erythro*-**8**, and the TMS*CH* proton signals at δ 2.96 and 3.10, respectively. The coupling constant between the protons at C2 and C3 was 12.4 Hz in each case, and these compounds are proposed to exist predominantly in the conformers shown. The higher field $Me_3Si$ group in *threo*-**8** and the $CO_2CH_3$ group in *erythro*-**8** are attributed to a shielding influence of the aryl ring on the protons. Nuclear Overhauser effect (nOe) measurements show that irradiation of the $Me_3Si$ group peaks produced a significant (1.4%) enhancement of the absorption of the Ph protons of *threo*-**8** and a small effect (0.4%) on the phenyl protons of *erythro*-**8**; separate irradiation of the OMe groups of the *threo*-**8** produced no effect on the $Me_3Si$ signal, whereas irradiation of the δ 3.38 and

3.62 MeO groups of *erythro*-**8** produced 0.1% and 0.3% enhancements of the $Me_3Si$ resonances, respectively, consistent with these assignments.




*threo*-**8** *erythro*-**8**

The kinetics of the reaction of **5** in 5 and 10% EtOH in $CH_3CN$ solution at 25 °C were measured by A. D. Allen by observing the decrease in the UV absorption at 257 nm. The rate constants obtained were 0.0408 and 0.156 $s^{-1}$, respectively. By analogy with the reaction with MeOH (Eq. 3), this reaction is considered to be formation of the ethyl ester analog of **7**.

The initial reaction of **5** with nucleophiles at the phenyl substituted ketenyl unit is consistent with the 1.9 x $10^4$ fold greater reactivity of PhCH=C=O with neutral water[8,16] compared to $Me_3SiCH$=C=O.[17] The rate constant for reaction of **5** in 5% EtOH/$CH_3CN$ (approximately 1 M) of 0.0408 $s^{-1}$ may be compared to the reported[18] rate constant of $Ph_2C$=C=O in 0.99 M EtOH in dioxane of 0.00629 $s^{-1}$. By this comparison, the bisketene **5** is approximately sixfold more reactive toward nucleophilic addition than $Ph_2C$=C=O, which is 17-fold less reactive than PhCH=C=O.

Bulky groups R cause major decreases in the reactivity of arylketenes ArRC=C=O compared to PhCH=C=O.[4,10] Thus PhC(Pr-*i*)=C=O is almost 4000 times less reactive than PhCH=C=O toward $H_2O$. Based on the comparisons made in the previous paragraph, it appears that the bisketene **5** is within a factor of 10 of being as reactive as PhCH=C=O, and yet on steric

grounds, a much lower reactivity of **5** would have been expected. Two conceivable causes for the evident high reactivity are transition state stabilization and ground state destabilization. However, the transition state for EtOH addition to **5** would have the character of **25**, which would be dominated by conjugation of the negatively charged oxygen with the phenyl group, just as for comparable addition to PhCH=C=O.[16] Extended conjugation involving the ketenyl unit as in **25a** suffers from unfavorable acyl anion character, and therefore enhanced electronic stabilization of the transition state for addition to **5** appears improbable (Fig. 4).

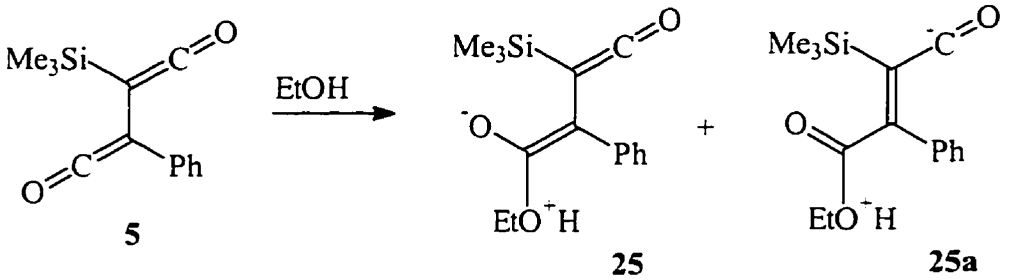



**Figure 4**

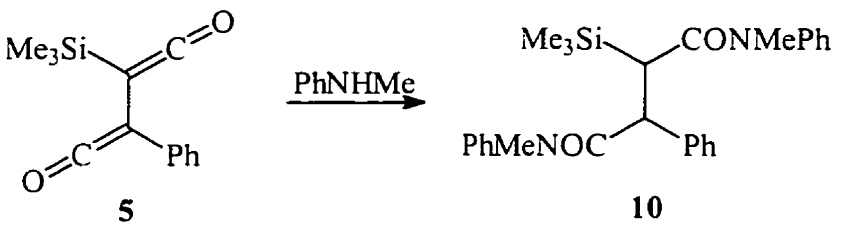
Ground state destabilization does appear to be plausible cause of the high reactivity of **5** relative to model monoketenes. It has been pointed out, based on published calculated energies,[22] that the parent bisketene is destabilized relative to ketene and butadiene, by 11.9 kcal/mol (Eq. 6).

$$(CH{=}C{=}O)_2 \;+\; 2CH_2{=}CH_2 \xrightarrow[-\,11.9\ \text{kcal/mol}]{\Delta E =} 2CH_2{=}C{=}O \;+\; (CH{=}CH_2)_2 \qquad (6)$$

The instability of the parent bisketene relative to 1,3-butadiene noted in equation 6 is evidently due to the same cause as the preference of the bisketene for a geometry in which the two ketenyl units are almost orthogonal. In the

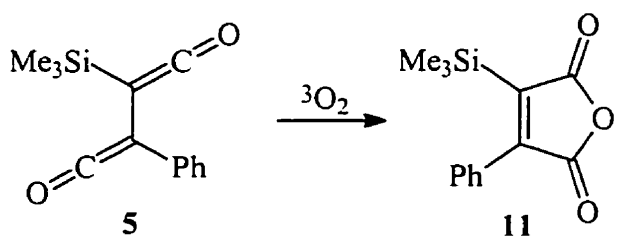
case of **5**, steric factors would further contribute to a preference for a perpendicular conformation. Thus it is known that silyl groups at the 2- and 3-position of 1,3-butadiene cause a preference for twisted conformations[20], and the factors favoring planar 1,3-butadiene conformation are small in any case.[21] However the origin of the preference for the non-planar stucture is not primarily steric, but is due to electronic causes. Thus even for the parent there is a calculated to be a significant preference for the twisted conformation, by 2.4 kcal/mol compared to the anti-conformation (see Chapter 3).[19]

Addition to the bisketene **5**, obtained by photolysis of **4**, of N-methylaniline at 0 °C gave a diamide **10** as the only isolated product, in 30% yield (Eq. 7). Because only one of the stereoisomers was obtained, the stereochemistry could not be reliably assigned.




**5** **10** (7)

Reaction of **5** with $^3O_2$ produced the maleic anhydride **11** (Eq. 8). This corresponds to the reaction for **2** with $^3O_2$, and a mechanism for this process has been presented.[15]




**5** **11** (8)

The reaction of the bisketene 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione **12** with aniline gave the formation of the monoketene N-phenyl 2,3-bis(trimethylsilyl)-4-oxobut-3-enamide **13** (60%), as monitored by $^{1}H$ NMR (Fig. 5). The formation of the monoketene **13** was confirmed by the observation of the α-carbon of the monoketene at δ 179.7, by $^{13}C$ NMR and by the ketenyl IR absorption at 2087 $cm^{-1}$. The monoketene is not stable at room temperature, and decomposes to unidentified products. Attempted purification of the monoketene by rotary thin layer chromatography failed, and gave a product tentatively identified on the basis of its spectral properties as the monoamide of succinic acid **14**.[24] In one case, presumably because the eluant contained a small amount of methanol, methyl 3- or 2-trimethylsilyl-4-oxo-4-(phenylamino)butanoate (**15a** or **15b**) was separated. The regiochemistry could not be determined with certainty based on the known data. All these results give further evidence of the formation of the monoketene.

The reaction of **12** with N-methylaniline was very slow, and no product was observed after two weeks.

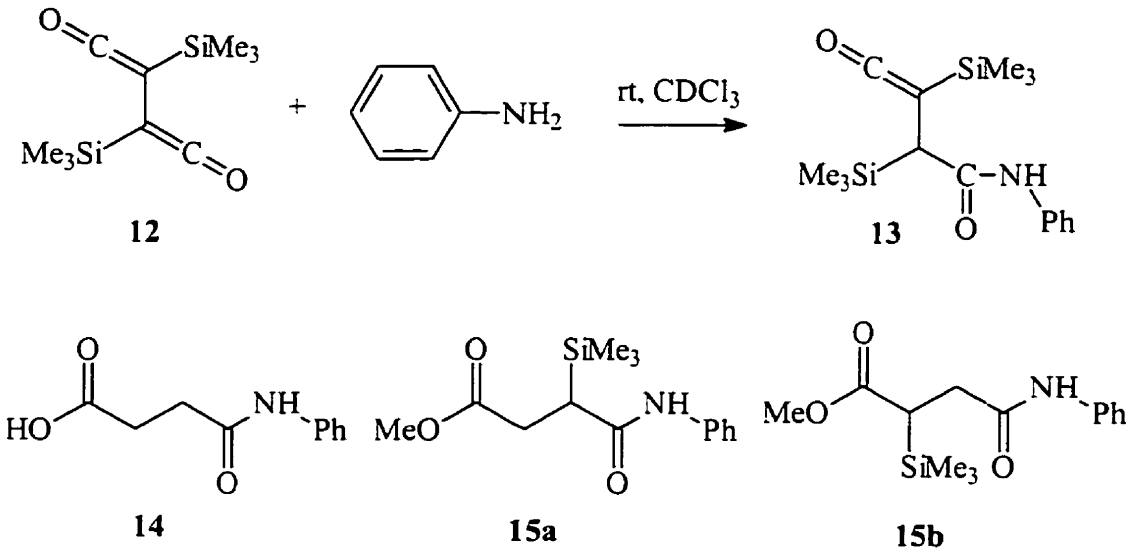
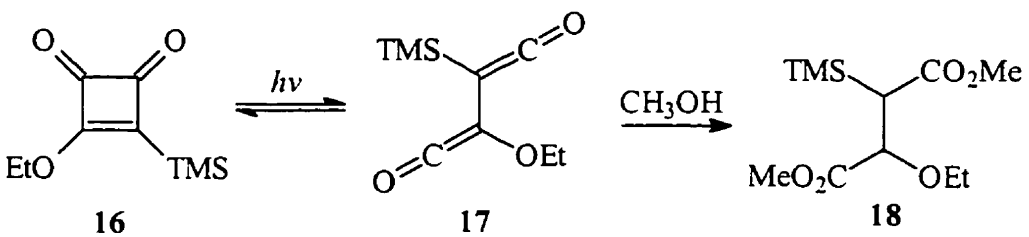



**Figure 5**

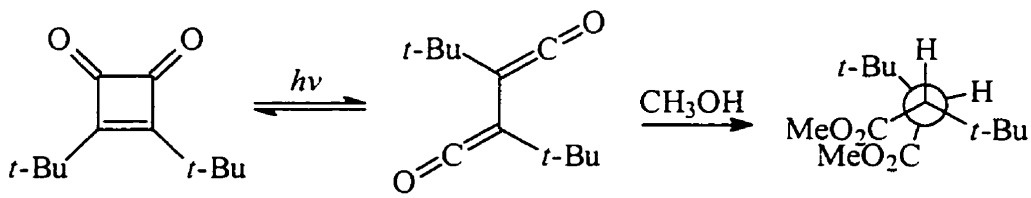
The bisketene **17** formed as a transient species from the photolysis of the dione **16** was successfully trapped in situ with methanol (Eq. 9). Reaction with a 5-fold excess of MeOH gave complete conversion of **16** after photolysis for 2 hour at 6 °C. The major products were the two diesters (**18**) in a ratio of 7.2/1 (Eq. 9). The major diester product was successfully separated by thin layer chromatography. This material displayed a 2,3 H,H coupling constant of 9.8 Hz, which is intermediate between the values of 12 and 6 Hz found for anti and gauche protons, respectively, in succinate esters. When we used the poorer nucleophile *t*-butanol the reaction of **17** was found to be very slow and gave a mixture of unidentified products.



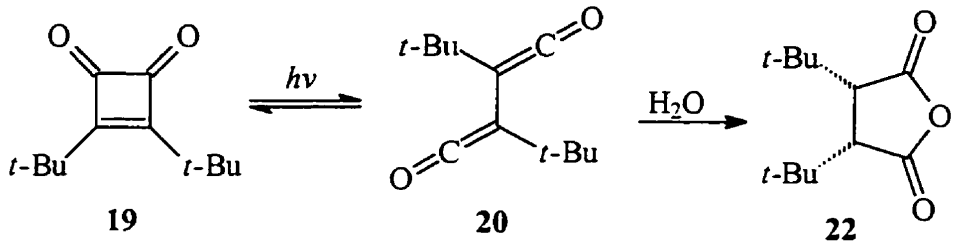

(9)

Photolyses of the dione **19** with methanol and with water give the succinate diester **21** and the cis anhydride **22** as the only products, respectively (Eq. 10, 11). Diester **21** was previously reported by Rhodes, et al.[25] however no spectra are available for comparison. The assignment of structure **21** was carried out by measuring the vicinal H,H coupling constant visible on the $^{13}C$ satellite peaks[26] which gave $J_{1,2}$ = 1.2 Hz and J ($^{1}H$-$^{13}C$) = 130.4 Hz. By comparison meso 3,4-di-*tert*-butylsuccinyl chloride (see Chapter 3), prepared from the authentic *meso* acid showed $J_{1,2}$ = 11.3 Hz and J ($^{1}H$-$^{13}C$) = 141.1 Hz. There **21** was indicated to have the d,l structure, and the low coupling constant evidently results from a preference for a conformation with a dihedral angle near 90° between the C-H bonds. The assignment of the structure **22** was made by comparison to the $^{1}H$ NMR spectrum of an authentic cis anhydride,[23] and was identical with the product from photolysis of the dione **19**.

The reaction of bisketene **20** generated by photolysis of the dione **19** using 350 nm light (see Chapter 3) with excess methanol also afforded the diester **21** in 8% yield based on the dione **19.** This result confirmed the formation of the bisketene and also indicated a 8% conversion of the dione **19** to the bisketene **20**.

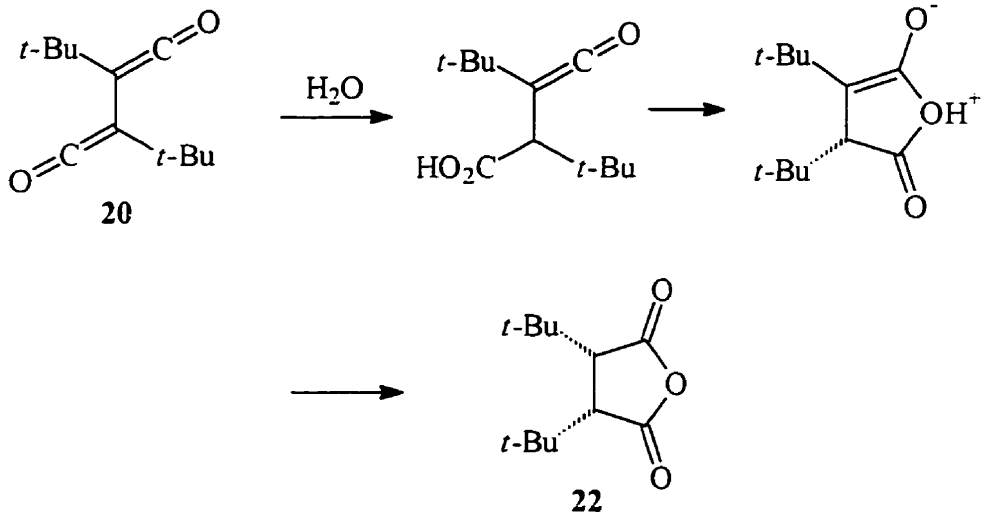



**19** **20** d,l-**21** (10)




19 20 22 (11)

The formation of the cis anhydride may be explained by the process shown in equation 12, which is similar to that suggested for the 2,3-bis(trimethylsilyl) bisketene **12**. Initial attack of water gives the ketenyl carboxylic acid, which then cyclizes. The stereochemistry of the final product is determined by the protonation of the resulting intermediate, and attack anti to the vicinal *tert*-butyl group would give the observed cis-product. Hydration of **12** gives a mixture of cis and trans anhydrides.[15b]




20 22 (12)

In conclusion, the long-lived phenyl trimethylsilyl 1,2-bisketene was found to react with methanol in a stepwise process, and the diester was obtained without desilylation. The reaction with amines was also successful, in contrast to the bis(trimethylsilyl)-1,2-bisketene which often reacted with the

loss of a silyl group in the products. Because of the high reactivity and greater product stability using the phenyl trimethylsilyl bisketene this may be a better coupling reagent in polymer synthesis. 3-ethoxy-4-trimethylsilyl cyclobutenedione and 3,4-di-tert-butyl cyclobutenedione were found to react with methanol and water under photolysis, presumably through the 1,2-bisketenes, and in the latter case gave highly stereoselective product formation of the (±)-diester and the cis anhydride.

Future work could include study of the phenyl trimethylsilyl bisketene as a polymer coupling reagent and the study of the synthesis of polyesters and polyamides with a stable silyl substituent in the polymer chain, which might show some novel properties and result in possible application in industry. As the reaction is stepwise it is possible to design the synthesis of polymers with two different alcohols or amines.

## 4.3 Experimental

Photolyses were carried out using a Rayonet RPR-100 reactor. The general procedures are given in Chapter 2.

**Methyl 4-oxo-2-phenyl-3-(trimethylsilyl)-3-butanoate (7).** A solution of the bisketene **5** prepared as in Chapter 3 was cooled to -78 °C, and $CH_3OH$ (20 μL, 0.50 mmol) was added with shaking. The solution was allowed to warm to RT over 10 minutes, the solvent was evaporated at room temperature, the resulting residue was redissolved in $CDCl_3$, and the above photolysis and methanolysis were repeated. Purification by VPC on an OV-17 column at 200 °C gave pure monoketene **7** (57.3 mg, 0.218 mmol, 68%): $^1$H NMR ($CDCl_3$) δ

0.00 (s, 9), 3.68 (s, 3), 4.00 (s, 1), 7.20-7.50 (m, 5); $^{13}C$ NMR ($CDCl_3$) δ -0.6, 8.5, 47.7, 53.3, 128.3, 128.4, 129.1, 139.5, 173.9, 194.1; IR ($CDCl_3$) 2093 (vs), 1709 (s) $cm^{-1}$; EIMS *m/z* 262 ($M^+$, 2), 247 ($M^+$-Me, 35), 219 ($M^+$ -Me-CO, 11), 203 ($M^+$-COOMe, 73), 73($TMS^+$, 100); HRMS m/z calcd for $C_{14}H_{18}O_3Si$ 262.1025, found 262.1009.

**Dimethyl 2-trimethylsilyl-3-phenylsuccinates (8).** Reaction of the monoketene (9.8 mg, 0.037 mmol) in 0.5 mL $CDCl_3$ containing methanol (20 μL, 16 mg, 0.5 mmol) in an NMR tube for 10 hours at RT gave complete conversion to a 1/2 mixture of the two stereoisomers *erythro*-**8** and *threo*-**8**, as assigned by $^1H$ NMR (see text). These esters were also prepared by reaction of the dione (120 mg, 0.521 mmol) in 4.5 mL $CH_3OH$ for 18 hours in a sealed tube at 100 °C. After evaporation of the solvent, $^1H$ NMR analysis showed the presence of *erythro*-**8**, *threo*-**8**, and dimethyl 2-phenylsuccinate in a ratio of 1/1/1.1. The esters were separated by radial chromatography using 5% ethyl acetate in hexane to give *erythro*-**8** (42.3 mg, 0.144 mmol, 28%) and *threo*-**8** (16 mg, 0.0654 mmol, 10%). *Erythro*-**8**: mp 59-61 °C; $^1H$ NMR ($CDCl_3$) δ 0.13 (s, 9), 3.10 (d, 1, J = 12.4 Hz), 3.38(s, 3), 3.62 (s, 3), 4.02 (d, 1, J = 12.4 Hz), 7.24-7.34 (m, 5); $^{13}C$ NMR ($CDCl_3$) δ -2.09, 41.05, 49.72, 50.89, 52.15, 127.35, 127.86, 128.43, 138.98, 173.21, 173.26; IR ($CDCl_3$) 1719(s), 1731(s) $cm^{-1}$; EIMS *m/z* 294 ($M^+$, 0.7), 279 ($M^+$-Me, 6), 235 (M+-COOMe, 23), 131 (100), 73 ($TMS^+$, 26); HRMS m/z calcd for $C_{15}H_{22}O_4Si$ 294.187, found 294.1275. *Threo*-**8**: $^1H$ NMR ($CDCl_3$) δ -0.21 (s, 9), 2.96 (d, 1, J = 12.4 Hz), 3.60 (s, 3), 3.69 (s, 3), 4.09 (d, 1, J = 12.4 Hz), 7.25-7.35 (m, 5); $^{13}C$ NMR ($CDCl_3$) δ -2.14, 41.02, 50.34, 51.31, 52.31, 127.95, 128.72, 128.81,

136.96, 174.41, 175.03; IR ($CDCl_3$) 1736(s), 1710(s) $cm^{-1}$; EIMS *m/z* 279 ($M^+$-Me, 7), 235 ($M^+$-COOMe, 28), 131 (100), 73 ($TMS^+$, 14); HRMS *m/z* calcd for $C_{15}H_{22}O_4Si$ 294.187, found 294.1267.

**2-Phenyl-3-trimethylsilylsuccinic anhydride (6).** Diketone **4** (44.2 mg, 0.20 mmol) in 0.5 mL $CDCl_3$ in an NMR tube was photolyzed 1 hour at 350 nm at 6 °C, and then 20 μL $H_2O$ was added; the tube was then stored 24 hours in the refrigerator, the solution was dried over $MgSO_4$, and the solvent evaporated. The product was redissolved in 0.5 mL $CDCl_3$ and the procedure repeated. Examination of the product by $^1H$ NMR revealed formation of the anhydride *E*-**6** (85%) along with 10% of *Z*-**6** and 5% of the diketone **4**. The anhydrides *E*-**6** and *Z*-**6** were not isolated in pure form. *E*-**6**: $^1H$ NMR ($CDCl_3$) δ 0.26 (s, 9), 2.77 (d, 1, $J$ = 3.6 Hz), 4.06 (d, 1, $J$ = 3.6 Hz), 7.5 (m, 5); $^{13}C$ NMR ($CDCl_3$) δ -3.24, 41.65, 49.99, 126.87, 128.54, 129.54, 136.57, 172.22, 172.41; IR ($CDCl_3$) 1772, 1791 $cm^{-1}$; EIMS *m/z* 248 ($M^+$, 1), 205 ($M^+$-$C_2H_3O$, 6), 176 ($M^+$-$C_2O_3$, 9), 161 ($M^+$-$C_3H_3O_3$, 9), 104 ($PhCHCH_2^+$, 100).

Photolysis as above at 45 °C led to a product containing predominantly *Z*-**6** (85%) with 10% *E*-**6** and 5% of **4**. *Z*-**6**: $^1H$ NMR ($CDCl_3$) δ -0.13 (s, 9), 3.09 (d, 1, $J$ = 10.4 Hz), 4.69 (d, 1, $J$ = 10.4 Hz), 7.1-7.4 (m, 5); $^{13}C$ NMR ($CDCl_3$) δ -1.86, 40.47, 49.69, 128.69, 129.10, 129.15, 133.54, 171.71, 172.33; IR ($CDCl_3$) 1770, 1793 $cm^{-1}$; EIMS *m/z* 248 ($M^+$, 2), 205 ($M^+$-$C_2H_3O$, 3), 176 ($M^+$-$C_2O_3$, 10), 161 ($M^+$-$C_3H_3O_3$, 6), 104 ($PhCHCH_2^+$, 100).

**N,N'-Dimethyl-N,N'-diphenyl-2-trimethylsilyl-3-phenylsuccinamide (10).** The diketone **4** (23.2 mg, 0.101 mmol) in 0.5 mL $CDCl_3$ in an NMR tube was photolysed 1.5 hours with 350 nm light at room temperature. N-Methyl aniline (10 μL, 0.924 mmol) was added with shaking and the sample was left at 0 °C for 10 hours. The solvent was evaporated and the residue purified by radial chromatography to give diamide **10** (13.5 mg, 0.03 mmol, yield 30%): mp 121.5-123.5 °C; $^1$H NMR (acetone-$d_6$) δ 0.03 (s, 9), 2.60 (d, 1, J = 11.4 Hz), 2.83 (s, 3), 3.08 (s, 3), 4.04 (d, 1, J = 11.4 Hz), 6.20-7.50 (m, 15); $^{13}$C NMR (acetone-$d_6$) δ -0.31, 36.77, 37.83, 41.97, 51.20, 127.45, 128.10, 128.17, 128.51, 128.65, 129.37, 129.50, 130.01, 130.07, 142.07, 144.24, 145.17, 172.63, 173.42; IR (film) 1651 (s), 1635 (s) cm$^{-1}$; EIMS *m/z* 444 ($M^+$, 3), 429 ($M^+$ -Me, 11), 338 ($M^+$ -MeNPh, 100), 310 ($M^+$ -CON(Me)Ph, 32), 107 ( $(MeNHPh)^+$, 21), 106 ($(MeNPh)^+$, 21); HRMS *m/z* calcd for $C_{27}H_{32}SiN_2O_2$ 444.2233, found 444.2235.

**2-Phenyl-3-trimethylsilylmaleic anhydride (11).** A solution of the cyclobutenedione **4** (21.1 mg, 0.092 mmol) in 0.5 mL $CDCl_3$ was photolyzed 1 hour with 350 nm light, giving a 93% conversion to the bisketene **5** as measured by $^1$H NMR. Air was then bubbled in for 1.5 hours at room temperature. The solvent was evaporated and the crude product was purified by radial chromatography (5% EtOAc/hexane on silica gel) to give the anhydride **11** (13.6 mg, 0.055 mmol, 65%) as a colorless solid, mp 80-82 °C; $^1$H NMR ($CDCl_3$) δ 0.24 (s, 9), 7.44-7.52 (m, 5); $^{13}$C NMR ($CDCl_3$) δ -0.92, 128.37, 128.84, 129.48, 131.01, 144.39, 155.61, 165.59, 167.3; IR ($CDCl_3$) 1754 cm$^{-1}$; EIMS *m/z* 246 ($M^+$, 17), 231 ($M^+$-$CH_3$, 17), 174 ($M^+$-$C_2O_3$, 37), 159

($M^+$-$C_2O_3$,$CH_3$, 100); HRMS *m/z* calcd for $C_{13}H_{14}O_3$ 246.0712, found 246.0711.

**Reaction of 12 with aniline.** The bisketene 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione **12** (79.8 mg, 0.353 mmol) was dissolved in $CDCl_3$ (0.5 mL) in an NMR tube, and then cooled in liquid nitrogen, and aniline (32.8 mg, 0.352 mmol) was added. The reaction mixture was warmed up to room temperature, and then left in a refrigerator overnight. The $^1H$ NMR spectrum indicated the formation of monoketene product N-phenyl 2,3-bis(trimethylsilyl)-4-oxobut-3-enamide **13** (60%). The crude product mixture was purified using thin layer chromatography (35% EtOAc/hexane on silica gel), but only the N-phenyl succinic acid monoamide[24] **14** was separated (yield not determined). In another case, the major product separated was **15** (yield not determined). N-Phenyl 2,3-bis(trimethylsilyl)-4-oxobut-3-enamide **13**: $^1H$ NMR ($CDCl_3$) δ 0.14 (s, 9), 0.15 (s, 9), 2.07 (s,1), 6.95-7.50 (m, 5), 7.60 (s, 1); $^{13}C$ NMR ($CDCl_3$) δ -2.26, -1.22, 10.69, 33.31, 120.11, 124.35, 129.11, 137.94, 170.01, 179.72; IR ($CDCl_3$) 2087 (vs), 1693 (s) $cm^{-1}$. N-Phenyl succinic acid monoamide[24] **14**: mp 147-148 °C (lit[24] mp 148.5 °C); $^1H$ NMR (DMSO) δ 3.40 (m, 4), 6.90-7.10 (m, 1), 7.20-7.40 (m, 2), 7.50-7.70 (m, 2), 9.98 (s, 1), 12.20 (s, 1); $^{13}C$ NMR (DMSO) 29.05, 31.28, 119.19, 123.18, 128.93, 139.58, 170.35, 174.11. Methyl 3 or 2-trimethylsilyl-4-oxo-4-(phenylamino) butanate **(15a)** or **(15b)**: $^1H$ NMR ($CDCl_3$) δ 0.10 (s, 9), 2.38 (dd, $J_{1,2}$ = 14.1, 2.0 Hz), 2.61-2.70 (dd. $J_{1,2}$ = 11.7, 2.0 Hz), 2.72-2.87 (dd. $J_{1,2}$ = 14.1, 11.7 Hz), 3.63 (s, 3); 6.95-7.10 (m, 1), 7.20-7.30 (m, 2), 7.40-7.50 (m, 2), 7.72 (s, 1); $^{13}C$ NMR ($CDCl_3$) δ -2.64, 33.52, 34.44, 51.42, 119.73, 124.07, 128.92, 138.04, 170.56,

175.95; IR ($CDCl_3$) 1724 (s), 1661 (s) $cm^{-1}$; EIMS *m/z* 279 ($M^+$, 25), 264 ($M^+$-Me, 17), 248 ($M^+$-MeO, 11), 187 ($M^+$-PhNH, 83), (93, $PhNH_2^+$, 69), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{14}H_{21}NO_3Si$ 279.1291, found 279.1301.

**Dimethyl 2-trimethylsilyl-3-ethoxysuccinate (18).** 3-Trimethylsilyl-4-ethoxycyclobutenedione **16** (10.2 mg, 0.052 mmol) was dissolved in CDCl3 (0.5 mL), and methanol (20 μL, 16mg, 0.50 mmol) was injected by using a syringe and then the solution was photolysed by 350 nm lamps for 2 h at 6 °C. The reaction was monitored by $^1H$ NMR and showed the two isomeric diesters **18** in a ratio of 7.2/1.0. The solvent was removed by a rotary evaporator to give the crude product which was further purified by thin layer chromatography (on silica gel eluted using 3% ethyl acetate in hexane). One of the diesters **18** was isolated as a colorless oil (8.1 mg, 0.031 mmol, 60%). $^1H$ NMR (CDCl3) δ 0.10 (s, 9), 1.16 (t, 3, $J_{1,2}$ = 7.0 Hz), 2.66 (d, 1, $J_{1,2}$ = 9.8 Hz), 3.42 (m, 2), 3.67 (s, 3), 3.75 (s, 3), 4.16 (d, 1, $J_{1,2}$ = 9.8 Hz); $^{13}C$ NMR (CDCl3) δ -2.12, 15.08, 42.52, 51.27, 51.89, 66.68, 78.26, 172.32, 172.92; IR ($CDCl_3$) 1718 (bvs) $cm^{-1}$; EIMS *m/z* 247 ($M^+$-$CH_3$, 1.8), 217 ($M^+$-$CH_3CH_2O$,10.9), 203 ($M^+$-COOMe, 35.5), 113 ($MeOOCCHCHCO^+$, 68.0), 99 ($TMSCHCH^+$, 100), 73 ($TMS^+$, 45.0); HRMS calcd for $C_{10}H_{19}O_5Si$ ($M^+$-Me) 247.1001, found 247.0999.

**Dimethyl *d,l*-2,3-di-*tert*-butylsuccinate (21).**[25] 2,3-Di-*tert*-butyl cyclobutenedione **19** (52.0 mg, 0.268 mmol) was dissolved in CDCl3 (0.5 mL), and methanol (50 μL, 40 mg, 1.25 mmol) was injected by using a syringe and

then the solution was photolysed using 350 nm lamps for 12 h at 6 °C. The solvent was removed by a rotary evaporator to give the diester **21** as a colorless oil as the sole product (69.2 mg, 0.268 mmol, 100%). $^{1}$H NMR ($CDCl_3$) δ 1.02 (s, 19), 2.50(s, 2), 3.63 (s, 6); $^{13}$C NMR ($CDCl_3$) δ 28.0, 34.3, 51.1, 54.0, 174.2; IR ($CDCl_3$) 1733 (vs), 1721 (vs) $cm^{-1}$; EIMS *m/z* 227 ($M^+$-MeO, 14), 183 (16), 145 (90), 131 (58), 113 (65), 57 (*t*-$Bu^+$, 100).

A sample of bisketene **20** along with dione **19** in 0.5 mL $CDCl_3$ (see Chapter 3) was mixed with methanol (0.5 mL), and the reaction mixture was left at room temperature for 6 hr, and then the solvent was removed by a rotary evaporator at room temperature and the residue was redissolved in $CDCl_3$. The $^{1}$H NMR of the residue showed the presence of the diester **21** (ca. 8%) along with dione **19** and other impurities. Diester **21**: $^{1}$H NMR ($CDCl_3$) δ 1.02 (s, 18), 2.50(s, 2), 3.63 (s, 6).

***cis*-2,3-Di-*tert*-butylsuccinic anhydride (22).** 2,3-Di-*tert*-butyl-cyclobutenedione (**19**) (28.0 mg, 0.144 mmol) was dissolved in $CDCl_3$ (0.5 mL), and water (20 μL) was injected by using a syringe and then the solution was photolysed by 350 nm lamps for 20 h at 6 °C. The solvent was removed by a rotary evaporator to give the crude product which was purified by recrystallization from THF/hexane to give the anhydride **22** (24.2 mg, 0.114 mmol, 79%). $^{1}$H NMR ($CDCl_3$) δ 1.05 (s, 18), 2.60 (s, 2); EIMS *m/z* 213 ($M^+$+1, 2), 156 ($M^+$ - $CH_2$=$C(CH_3)_2$, 20), 125 (*t*-BuCH=CHBu-*t*)$^+$ - $CH_3$, 36), 100 (60), 57 (*t*-$Bu^+$, 100).

## 4.4 References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23. The authentic cis anhydride **22** was provided by A. D. Allen in this laboratory; Eberson, L. *Acta Chem. Scand.* **1959**, *13*, 40-49.
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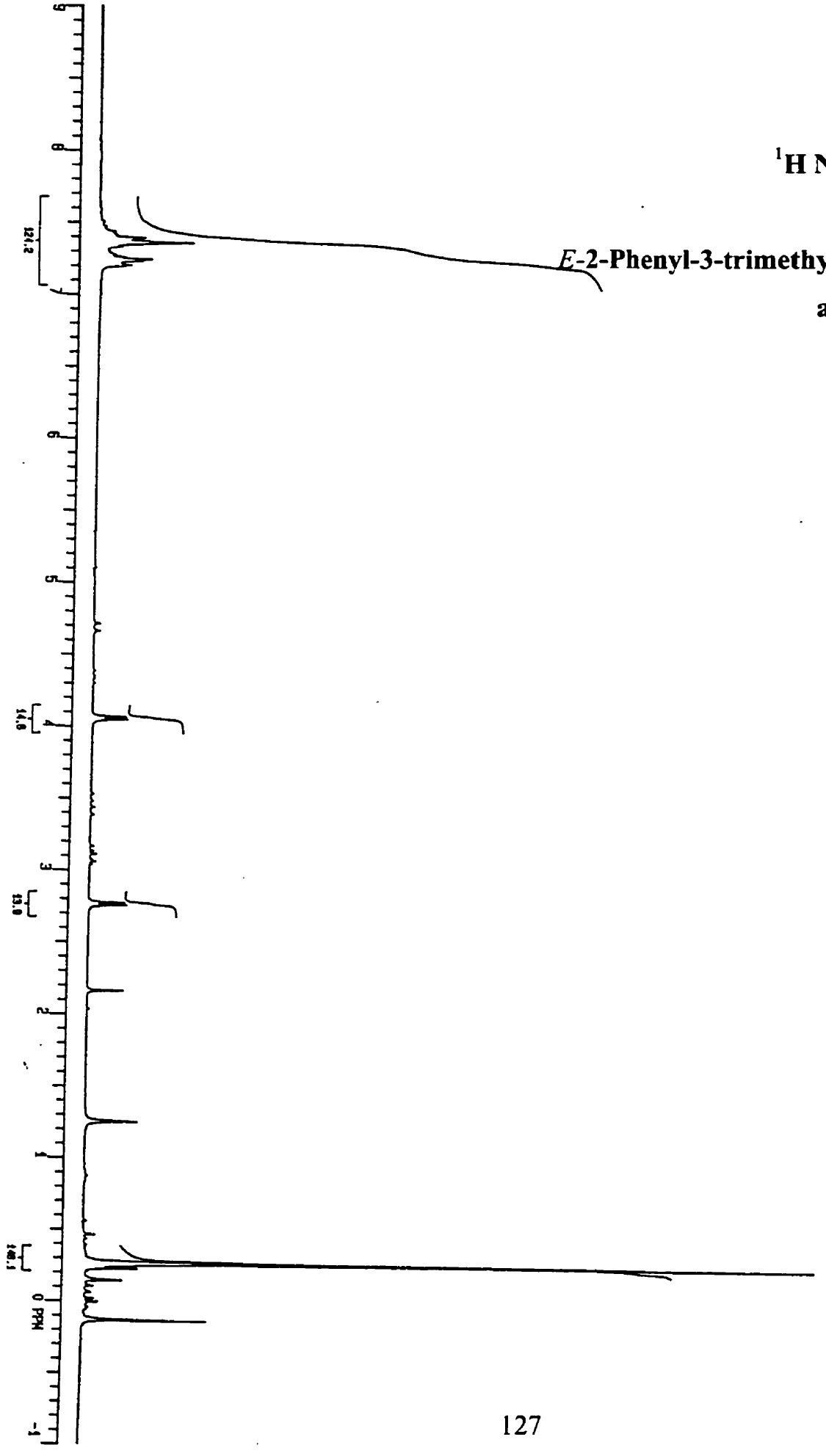
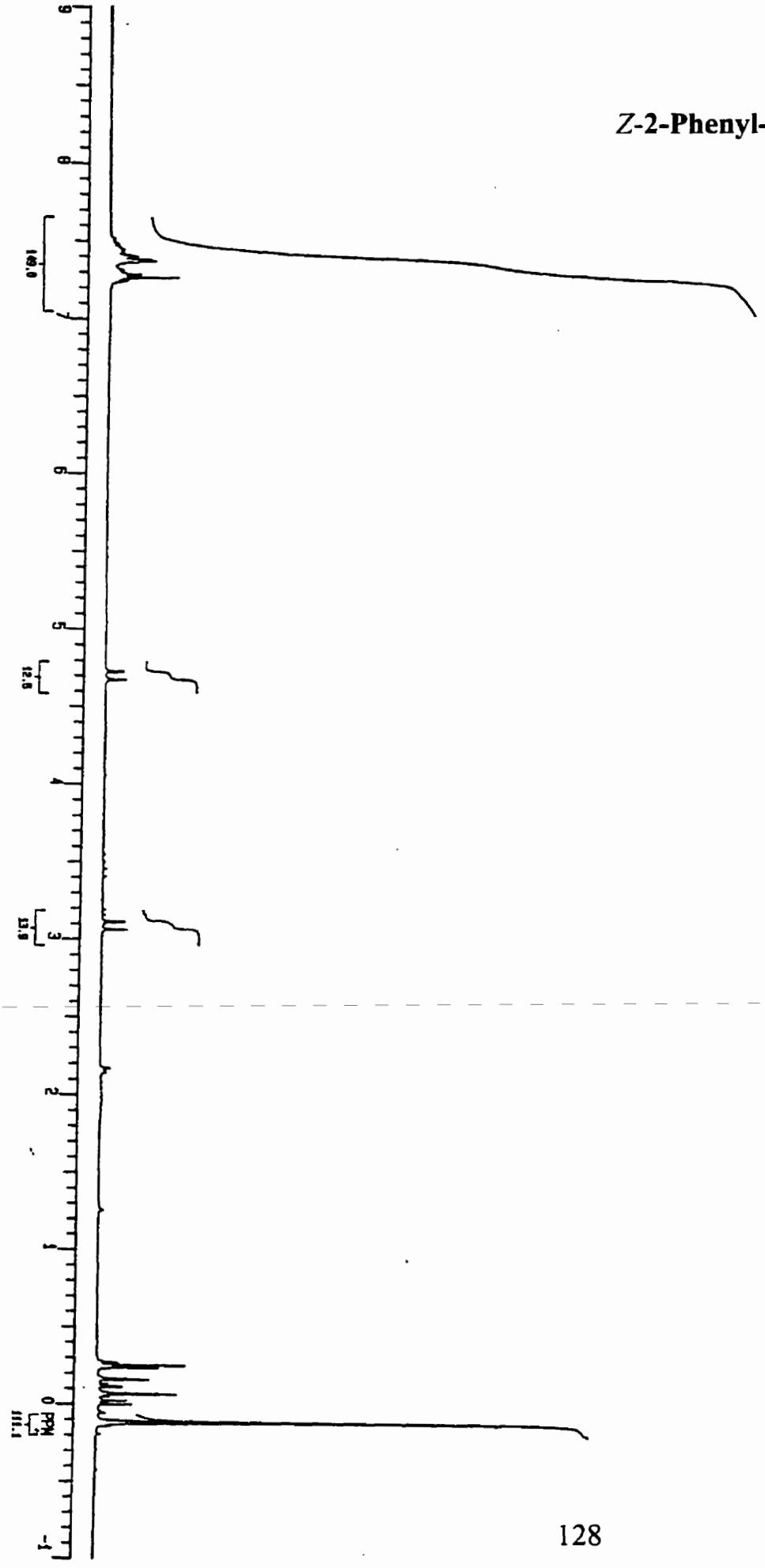
**Appendix 1**

**$^{1}$H NMR Spectra**

*E*-2-Phenyl-3-trimethylsilylsuccinic anhydride (6)

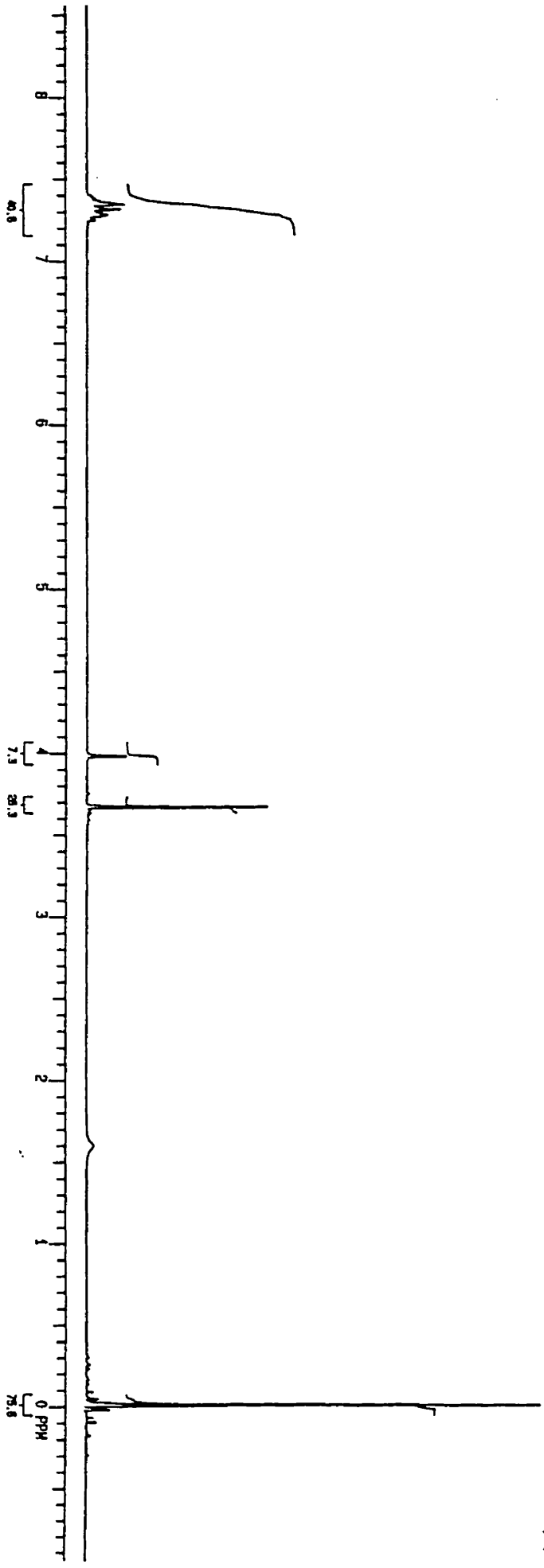


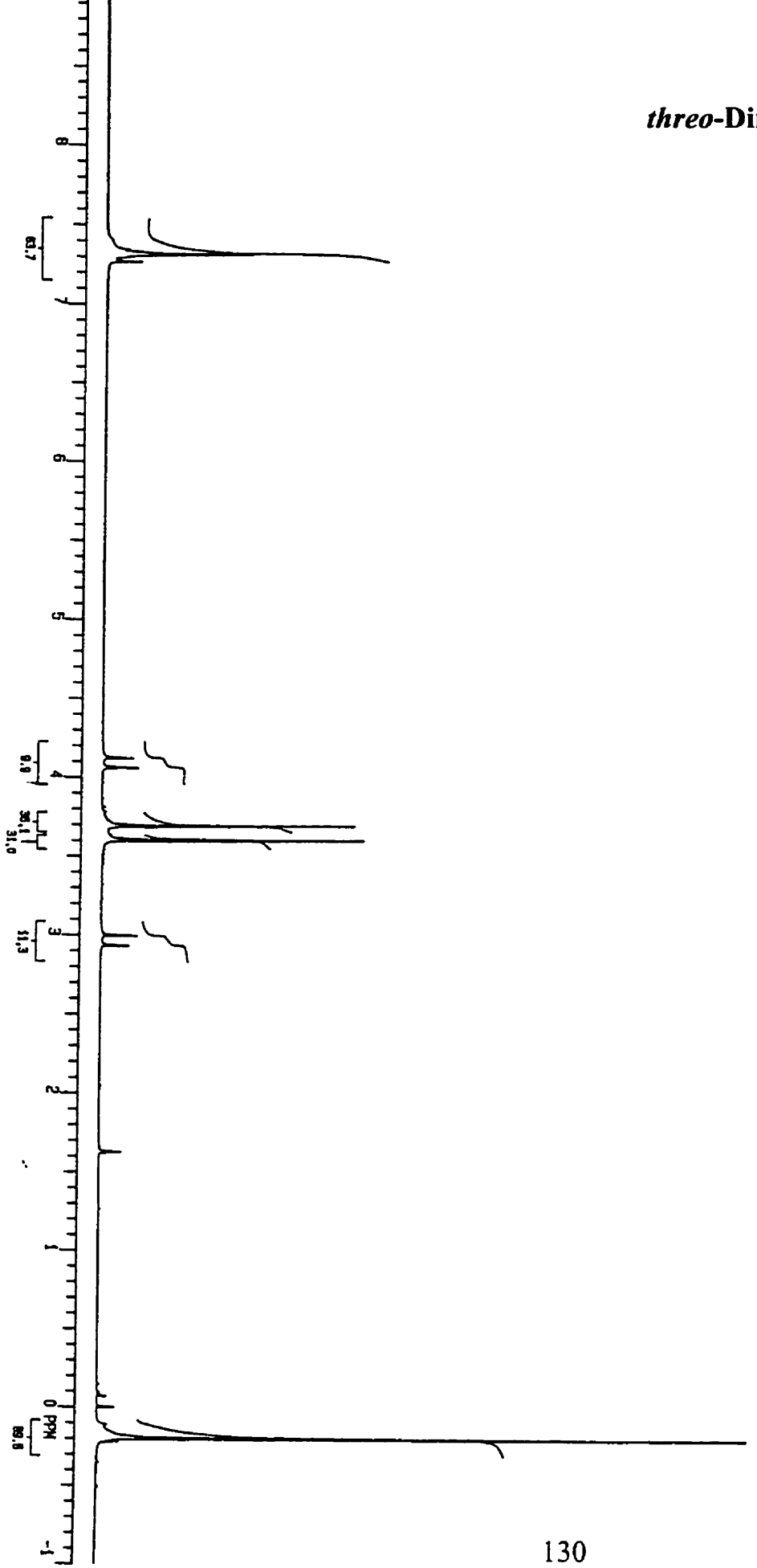
**Z-2-Phenyl-3-trimethylsilylsuccinic anhydride (6)**



**2-Trimethylsilyl-3-carbomethoxy-**

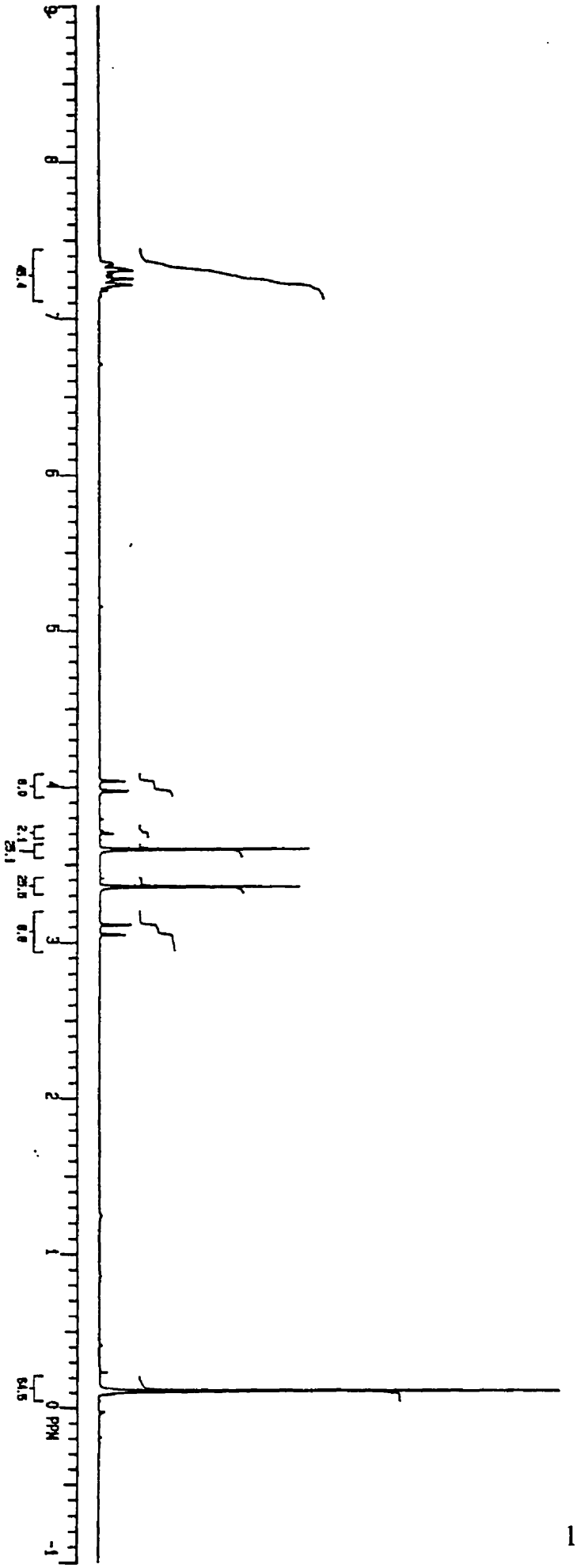
**3-phenylprop-1-ene-1-one (7)**



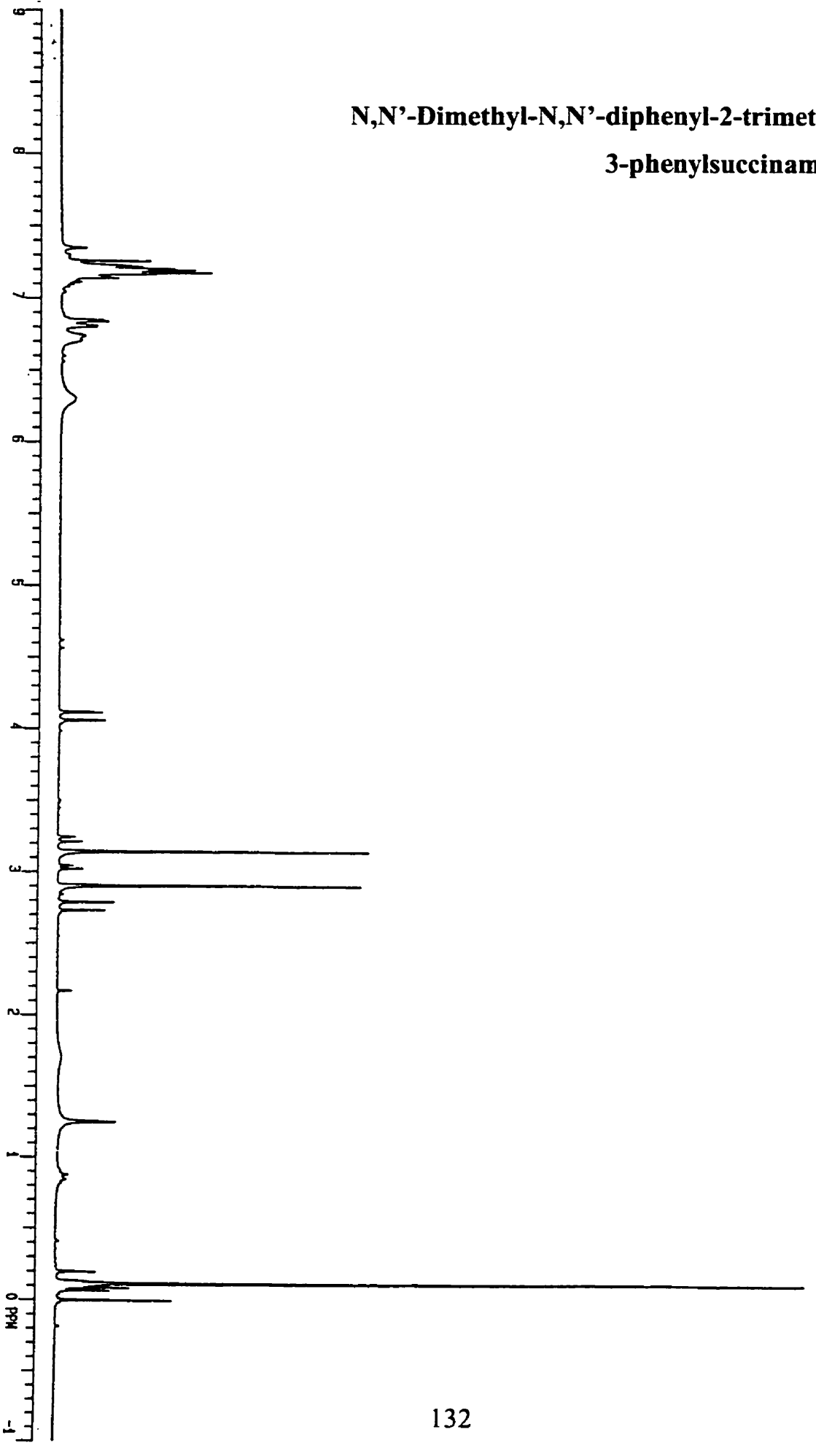


***threo*-Dimethyl 2-trimethylsilyl-3-phenylsuccinate (8)**

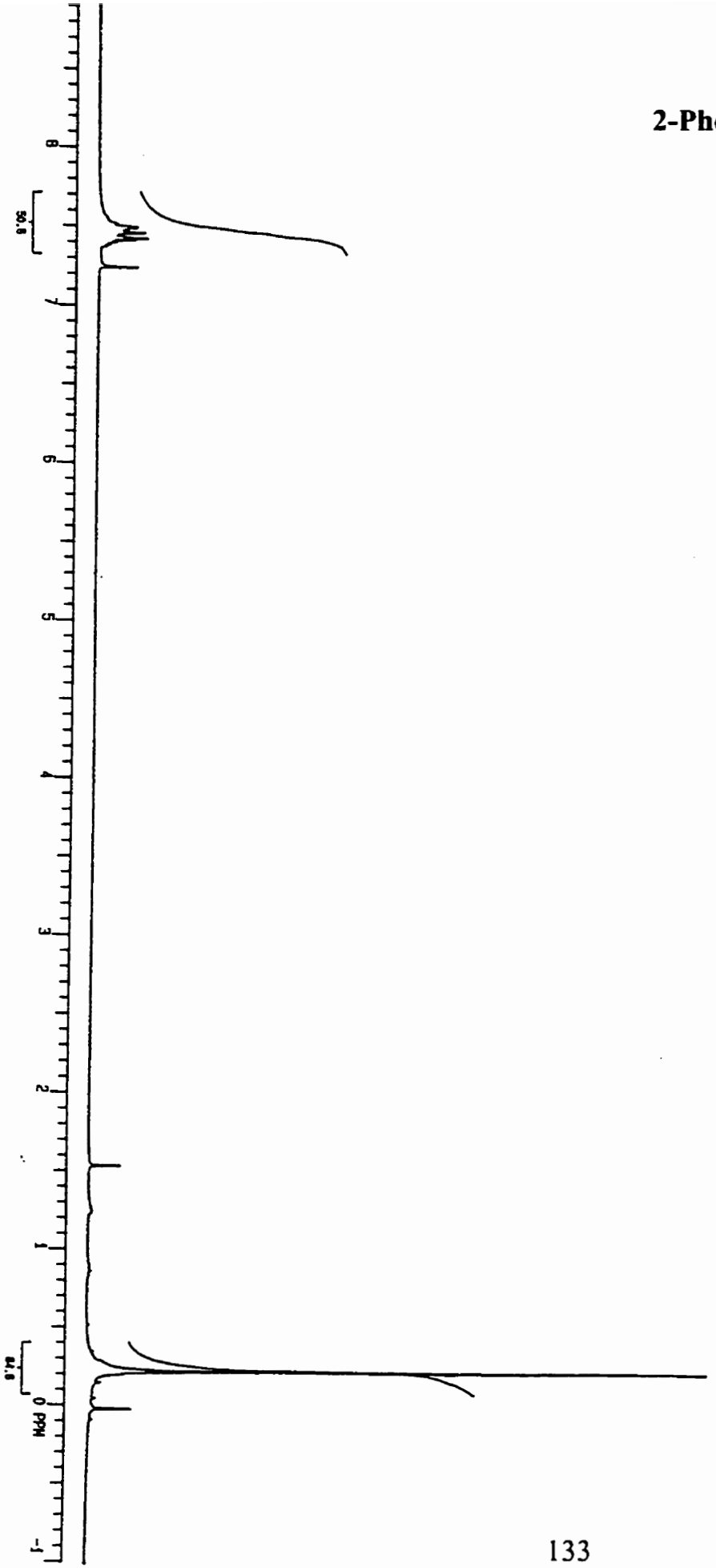
*erythro*-Dimethyl 2-trimethylsilyl-3-phenylsuccinate (8)



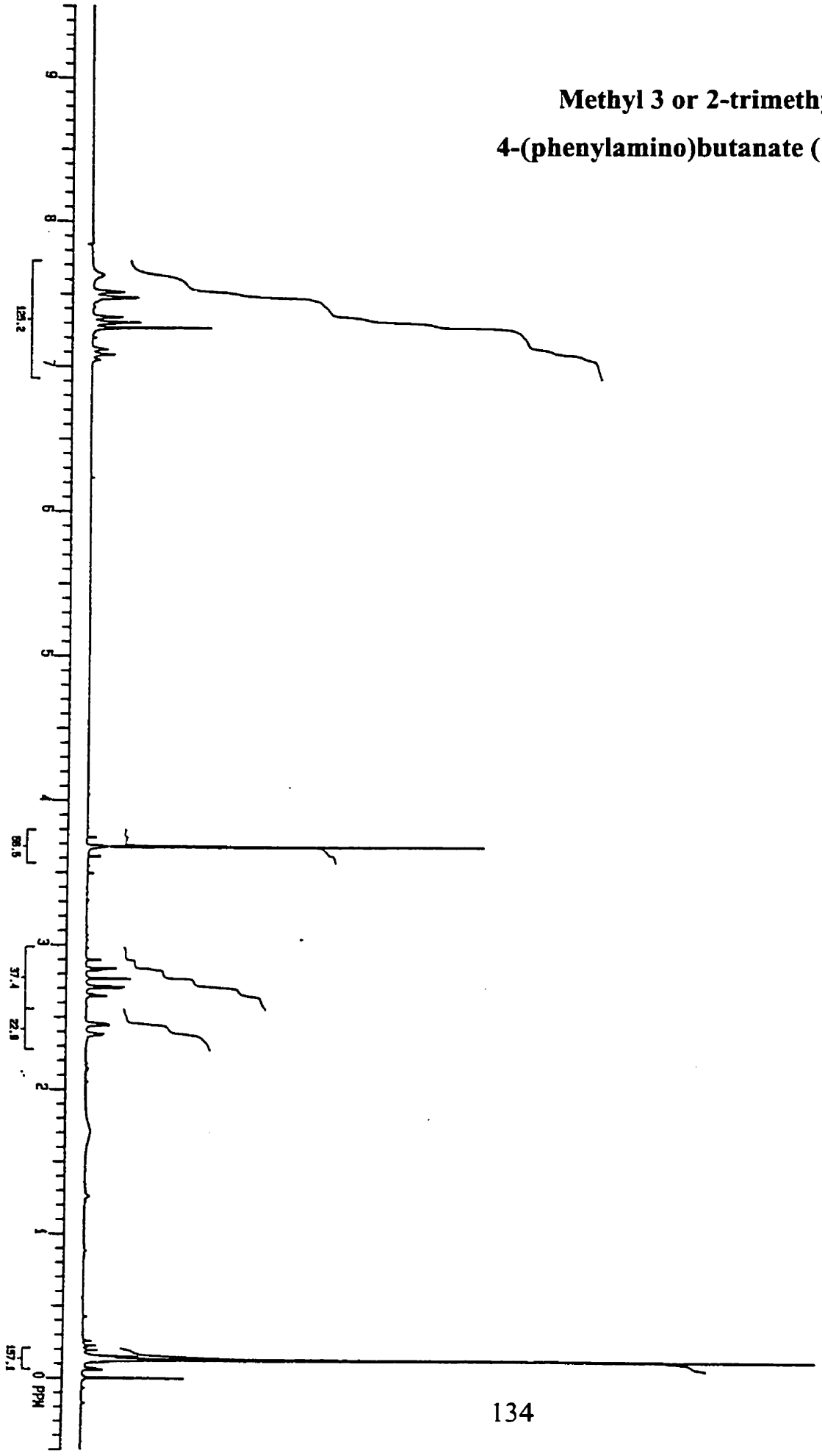
**N,N'-Dimethyl-N,N'-diphenyl-2-trimethylsilyl-3-phenylsuccinamide (10)**



**2-Phenyl-3-trimethylsilylmaleic anhydride (11)**

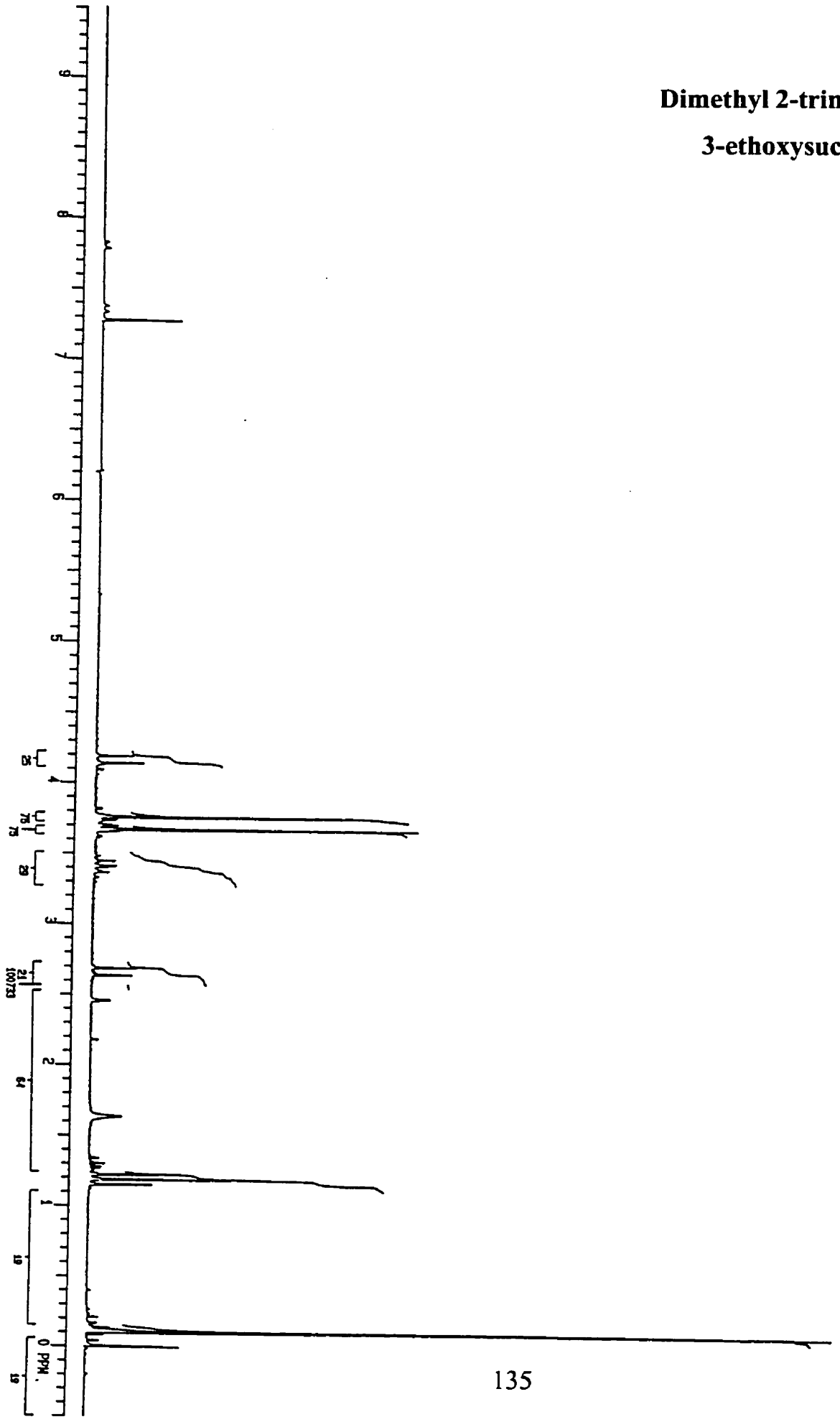


**Methyl 3 or 2-trimethylsilyl-4-oxo-4-(phenylamino)butanate (15a) or (15b)**

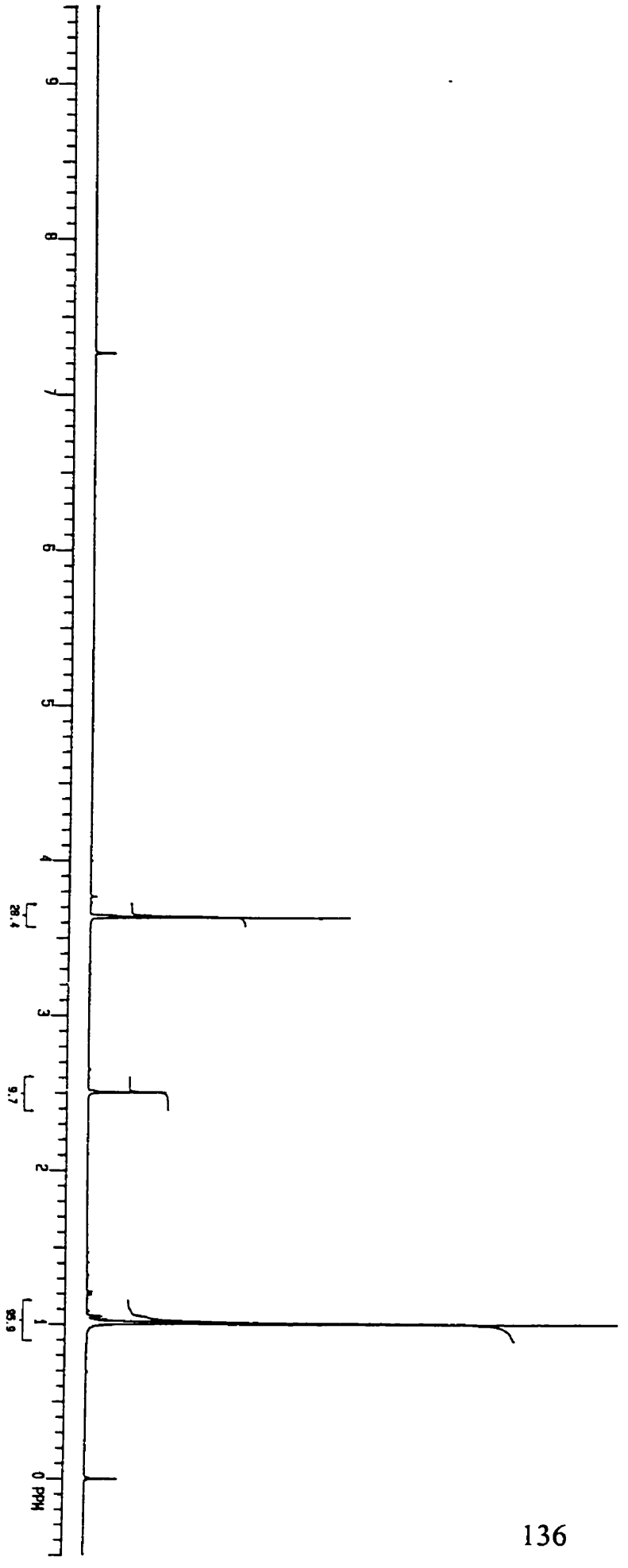


**Dimethyl 2-trimethylsilyl-**

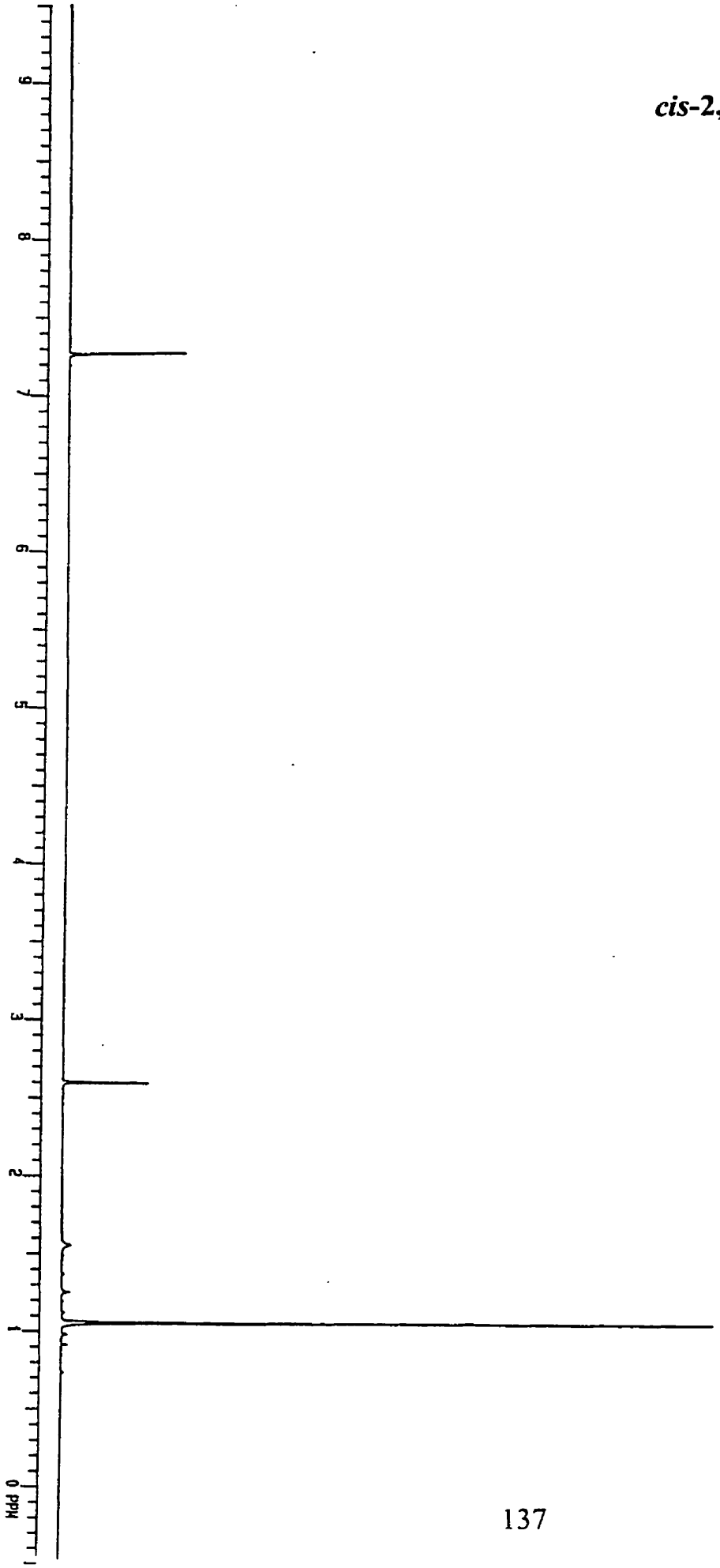
**3-ethoxysuccinate (18)**



**Dimethyl *d,l*-2,3-di-*tert*-butylsuccinate (21)**



**_cis_-2,3-Di-_tert_-butylsuccinic anhydride (22)**



# *Chapter 5*

# Electrophilic Reactions of Bisketenes

## 5.1 Introduction

Electrophilic reactions of ketenes have not been thoroughly studied, partially because the instability of the ketenes renders such study difficult, and perhaps also because electrophilic reaction of alkenes are well understood and electrophilic reactions of ketenes were considered similar to the reactions of alkenes and of little interest.

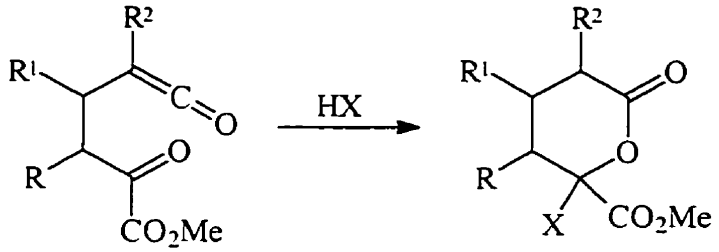
There have been some mechanistic studies of protonation reactions of ketenes, and these have been interpreted as occurring by rate limiting electrophilic attack at Cβ of the ketene giving an acylium ion which is then trapped by a nucleophile (Eq. 1). A detailed discussion was given in Chapter 4.

$$RHC{=}C{=}O \xrightarrow{H^+} RCH_2C^+{=}O \xrightarrow{X^-} RCH_2COX \qquad (1)$$

The rate ratio $k_{H+}/k_{H2O}$ ($M^{-1}$) of trimethylsilylketene has the value of $1.7\times10^5$ (Eq. 2). This larger effect than normal was interpreted as being due to the presence of the β-silicon substituent which stabilized the forming carbocation.[17]

$$Me_3SiHC{=}C{=}O \xrightarrow{H^+} Me_3SiCH_2C^+{=}O \xrightarrow{H_2O} Me_3SiCH_2CO_2H \qquad (2)$$

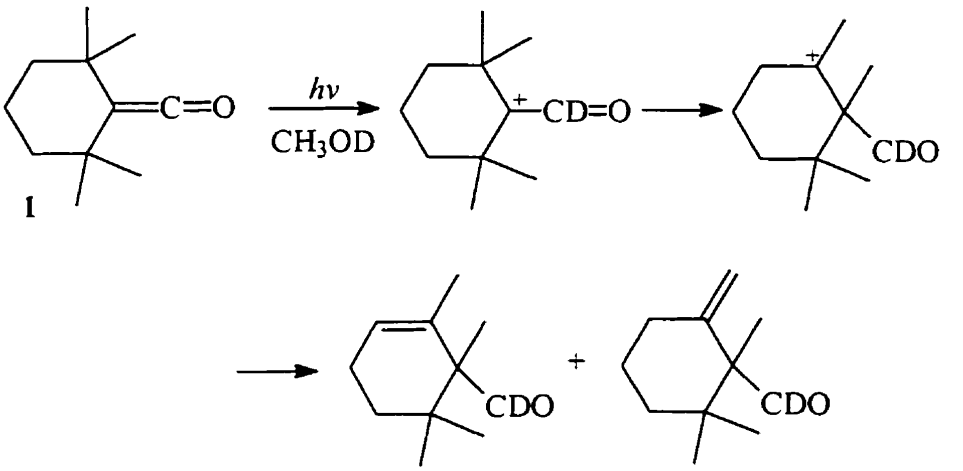
The reactions of ketenes with hydrogen halides yield acyl halides.[18, 19] The reaction of γ-acylketenes with HCl or $CF_3CO_2H$ leads to lactones in a process involving protonation at $C_\beta$ (Eq. 3).[20]




X = Cl, $O_2CCF_3$ (3)

Attack at $C_\beta$ to produce an acylium ion is the exclusive pathway observed in all previous theoretical and experimental studies of electrophilic attack on carbon in ground state reactions of simple ketenes.[17-20] Initial attack on oxygen can also occur. This is understandable because of the large coefficients of the HOMO of ketenes at $C_\beta$ and oxygen, whereas the largest coefficient of the LUMO, and the site of nucleophilic attack, is at $C_\alpha$.[21]

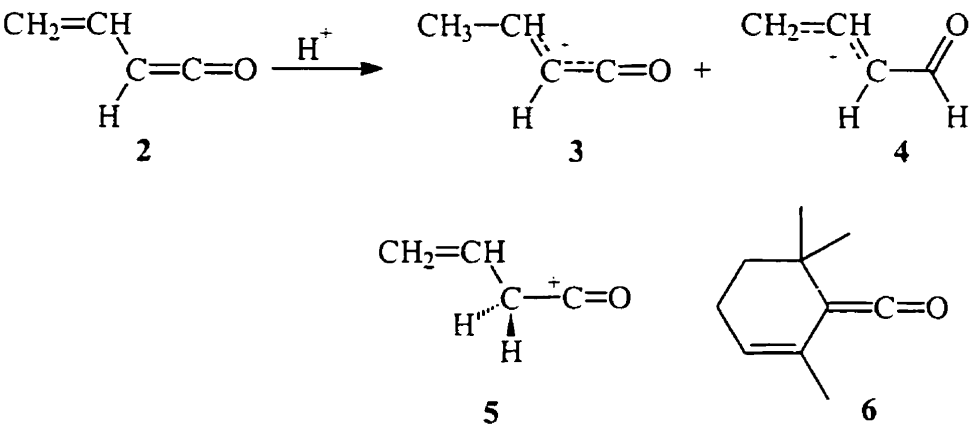
In the case of photoreactions of certain crowded ketenes evidence for protonation at $C_\alpha$ was obtained, as for example in the photolysis of **1** in $CH_3OD$ (Eq. 4). This was attributed to the presence of significant charge density at $C_\alpha$ in the first excited state of ketenes.[22]




1

(4)

Calculation at the 6-31G*//3-21G level of the protonation of vinylketene **2**,[23a] indicated that protonation at $C_\delta$ forming **3** was 38.1 and 15.8 kcal/mol more favorable than protonation at $C_\alpha$ and $C_\beta$, forming **4** and **5**, respectively (Eq. 5). This prediction of protonation at the δ-carbon was confirmed experimentally in the study of **6**.[23b]




**2** **3** **4**

**5** **6**

(5)

Other electrophilic reactions of ketenes such as bromination are much less well studied, even though the electrophilic addition of $Br_2$ to alkenes is certainly one of the best known organic reactions, and its mechanism has been extensively studied.[1] It is perhaps surprising that there is still some ground

work to be done in this field, as has been demonstrated by recent synthetic, spectroscopic, and theoretical works.[2]

As early as 1937, Roberts and Kimball[3] explained the *anti* selectivity of the bromination of olefins by proposing an intermediate bridged bromonium ion. Thirty years later, such intermediates were detected under "stable ion conditions" by NMR spectroscopy.[4-7] The halonium ions of chlorine,[5] bromine,[6] and iodine[7] with adamantylideneadamantane are even isolable as stable salts, because the subsequent nucleophilic attack of the counterion is prevented by steric hindrance in the substrate. It is generally accepted that $\pi$ complexes proceed formation of such halonium ions,[1] and there is evidence that strongly cation stabilizing substituents (e.g., phenyl) on the olefin lead to unsymmetrically bridged or even nonbridged cations.[1]

The generally accepted mechanism[1,8] for addition of $Br_2$ to alkenes is given in Fig. 1. In protic solvents at low [$Br_2$], the reaction is first order in [$Br_2$], and proceeds via a 1:1 charge-transfer complex (CTC). In low-polarity solvents, the reaction is second order in [$Br_2$] and is interpreted in terms of $Br_2$-assisted ionization of the 1:1 CTC.

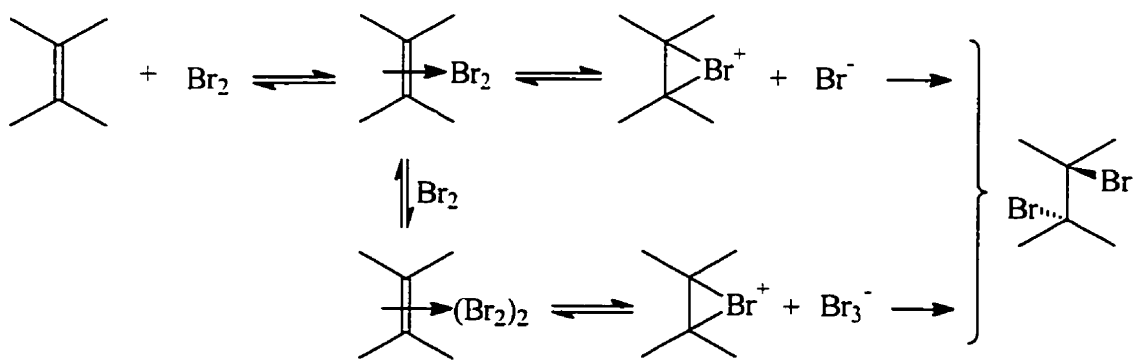
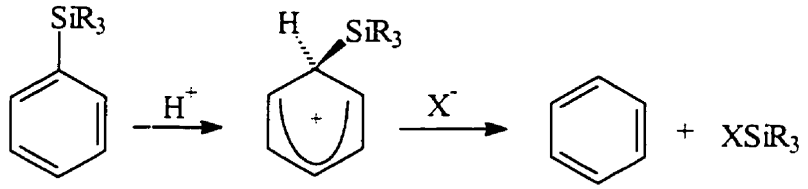


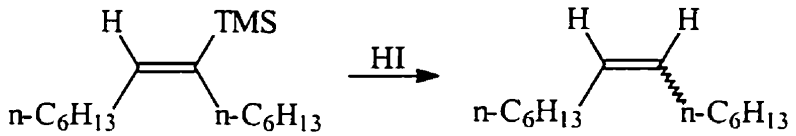

**Figure 1**

Electrophilic addition reactions of vinylsilanes are widely used reactions in organic synthesis. The electrophilic addition of a vinylsilane was reported in 1954.[9] Since then there has been extensive study of this reaction. The influence of silyl substituents on the electrophilic reactions of alkenes is unique. The trimethylsilyl group is suggested to be a weak σ donor and a weak π acceptor ($\sigma^{o}_{R}$ = +0.07; $\sigma^{o}_{I}$ = - 0.09).[10] In consequence, its effect on the ground state of a carbon-carbon double bond to which it is directly attached is uncertain, but some calculations suggest that it is overall a mild donor.[11] Quantitative work has been reported on the reactivity of arylsilanes, where it is well known that a silyl group activates the benzene ring to electrophilic attack *ipso* to the silyl group (Eq. 6). This activation is high for protodesilylation (a factor of about $10^4$) and for bromodesilylation.[31]

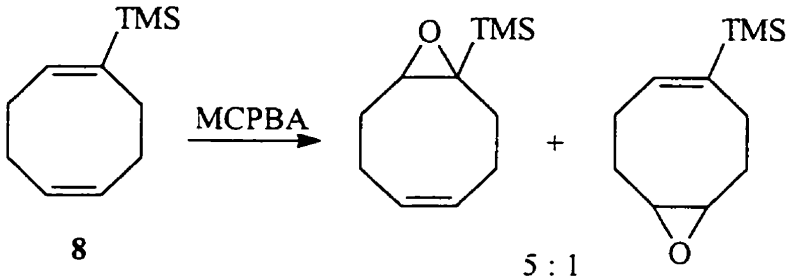



(6)

The protodesilylation of (*E* )-vinylsilanes **7** takes place cleanly when a proper acid is used (Eq. 7).[12] This implies that the protonation of the vinylsilane is significantly faster than the protonation of the product. The protonation of the product would have caused stereochemical equilibration and double bond shifts. Another example of the greater reactivity of vinylsilanes is the epoxidation of the diene **8**, where the silylsubstituted double bond is epoxidized about five times faster than the unsubstituted double bond (Eq. 8).[13]




7 *Z:E* 94:6 (7)




**8** 5 : 1 (8)

The regioselectivity of attack by electrophiles is determined by two factors. The first factor is the relative stability of the cations produced by attack at each end of the double bond. The second is the ground state polarization of the C=C double bond HOMO. Hydroboration does not take place by way of a cationic intermediate, and the regioselectivity of attack is therefore likely to be affected more by the ground-state polarization of the HOMO than by product stability.[14] The arrows on the structures show the relative proportions of attack by boron at the two sites in the hydroboration of some vinylsilanes with diborane (Fig. 2).[14] These results may still indicate the effect of the ground state polarization and/or the polarized transition state. Therefore the extent of the effect of ground state-polarization is still uncertain.

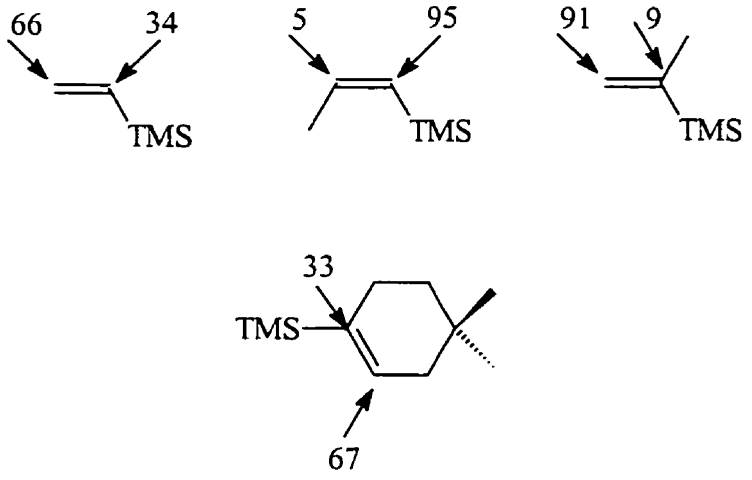
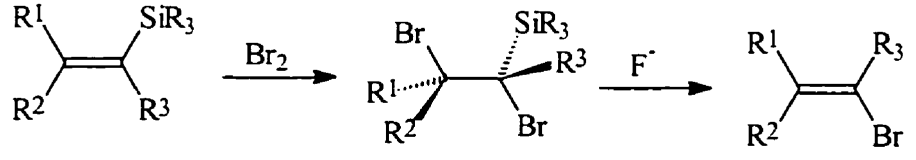



**Figure 2**

The reaction of bromine or chlorine with vinylsilanes occurs by normal 1,2-addition (Eq. 9). 1,2-Addition is almost always the first step, and these addition products can be isolated, but it is usual to add fluoride ion or sodium methoxide to give the electrophilic substitution products.[15]




(9)

## 5.2 Results and discussion

Because of the lack of study of the reactions of electrophiles such as $Br_2$ with ketenes,[32] it was of particular interest to study the bromination reactions of silylated 1,2-bisketenes.

To evaluate the possible course of electrophilic attack on bisketenes the structures and energies of the isomeric ions **10** and **11** resulting from protonation of the parent **9**, and isomeric ions **12** and **13** resulting from addition of chloronium ion ($Cl^+$) to **9**, were calculated by McAllister at various levels of *ab initio* theory. Calculated relative energies (kcal/mol) are given in parentheses in Fig. 3.[24]

Protonation at $C_\beta$ of **9** produces three isomeric ions **10a-c** that are energy minima and of these **10c** with a twisted conformation is the most stable, by 6.9 kcal/mol relative to the next most stable conformer **10a**. The structure **10c** resembles the most stable conformer of the bisketene **9**, which is also twisted as discussed in Chapter 3. This conformation of **9** and **10c** minimizes the unfavorable interactions between the dipoles in both species.

Protonation at $C_\alpha$ produces four minimum energy isomeric structures, and of these the *s-**Z*** conformer **11d** is most stable, by 4.6 kcal/mol relative to **11b**, the next most stable product of α-protonation, and **11d** is also more stable by 3.3 kcal/mol relative to **10c**, the most stable product of β-protonation. The preference for the syn conformation **11d** evidently arises from a favorable dipole interaction between the aldehydic oxygen and the delocalized positive charge, as reflected in the short O(2)-C(2) distance. Cyclization to the ion **11e** is endothermic by 1.6 kcal/mol.

Protonation at $C_\alpha$ in **9** is favored relative to this process in other ketenes because of the allylic nature of the resulting ketenyl carbocation, and parallels electrophilic attack on other 1,3-dienes, which also preferentially occurs at the

terminal carbon.[25] The ions **11a-d** also have acylium ion character, just as for **10a-c**. Formation of acylium ions is one of the driving forces for protonation at $C_\beta$ in other ketenes. The protonation at $C_\alpha$ of **9** also corresponds to protonation of $C_\delta$ of **2** to produce **3**, as the same type of vinyl acylium ion is formed.[23a] Protonation at $C_\beta$ in **9** is also disfavored because of the presence of the electron-withdrawing ketenyl group. This corresponds to the rate -retarding effect noted in ordinary alkenes for protonation at a vinyl or phenyl substituted carbon.[23b]

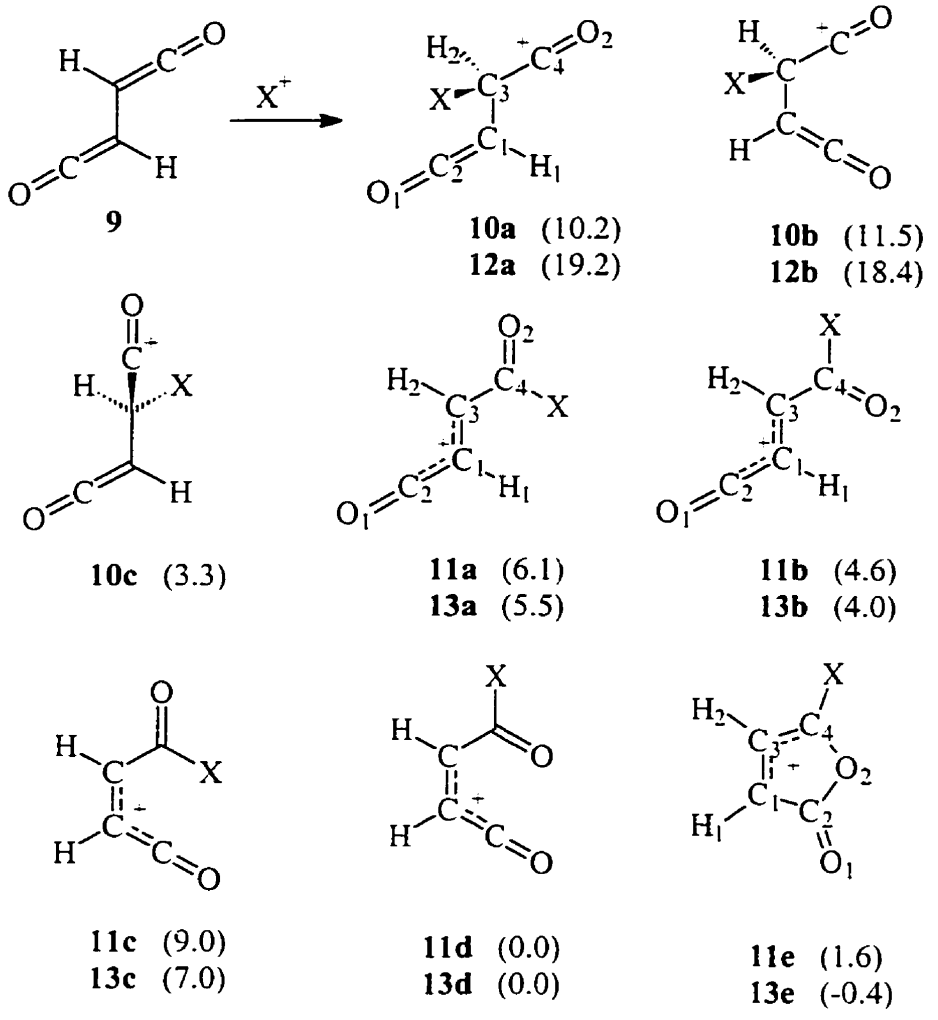
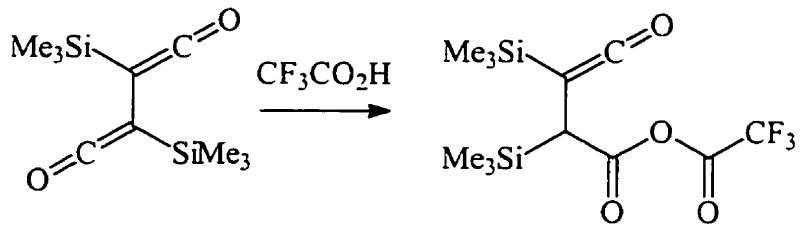



**Figure 3.** Relative calculated (6-31G*//6-31G*) energies (kcal/mol) of the ions from proton and chloronium ion addition to 2,3-butadiene-1,4-dione (**11**)[24] (**10**, **11**; X = H; **12**, **13**, X = Cl)

The structure and energy of the isomeric products of addition of $Cl^+$ were examined computationally as shown in Fig. 3. The products **12a** and **12b** of chlorine addition to $C_\beta$ are much less stable than any of the products of attack at $C_\alpha$, by a minimum of 11.4 kcal/mol. This is understandable in terms of the expected inductive destabilization by the β-chlorine of the acylium ion. The

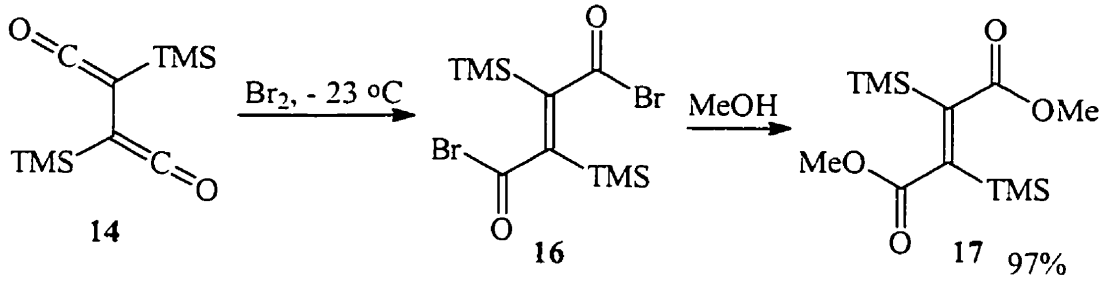
most stable product conformer resulting from chloronium attack at $C_\alpha$ is **13d**, which corresponds to the most favorable product of proton addition. The cyclized form **13e** is barely more stable than **13d**, by -0.4 kcal/mol, whereas the cyclized ion **11e** from proton addition is less stable than **11d** by 1.6 kcal/mol. Some stabilization of **13e** due to the π-donor ability of chlorine is expected, and this counterbalances the inductive electron withdrawing effect of the chlorine. A destabilizing effect of -15.5 kcal/mol has been calculated for a β-chlorine on an ethyl cation when the chlorine is prevented from bridging, whereas $ClCH_2^+$ is calculated to be stabilized by 13.2 kcal/mol relative to $CH_3^+$.[26]

Experimentally the reaction of bisketene **14** with trifluoroacetic acid in $CDCl_3$ led to formation of the ketenyl mixed anhydride **15** as the only observed product by NMR at 0 °C (Eq. 10), as identified by its spectral properties, especially the distinctive ketene IR band at 2095 $cm^{-1}$, and the ketenyl carbon at δ 9.93. Thus the product was the result from protonation of **14** at $C_\beta$. This result indicates a kinetically controlled process has occurred despite the possible protonation reaction at $C_\alpha$ which would give the thermodynamically stable product. This could be explained by considering that attack occurs preferentially at the HOMO orbital of one of the two ketene moieties in the bisketene molecule, which has a large coefficient at $C_\beta$, and that migration of hydrogen via a bridged protonium species leading to the formation of the thermodynamically more stable ions **11a-e** does not compete with capture of the acylium ion.

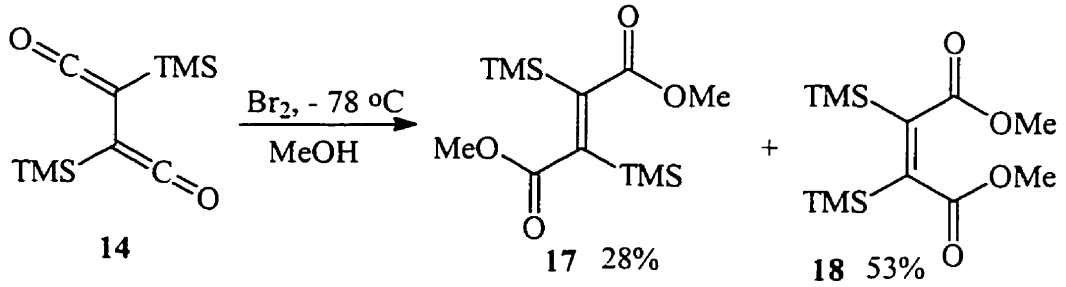



**14** **15** (10)

The reaction of the bisketene 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione **14** with bromine in $CHCl_3$ at - 23 °C gave fumaryl bromide **16** as the only observed product, which reacted with methanol at low temperature (-77 °C) to afford methyl fumarate **17** (Eq. 11). However, when the bromination reaction was carried out in methanol, dimethyl 2,3-bis(trimethylsilyl)maleate **18** was the major product (53%), and dimethyl 2,3-bis(trimethylsilyl)fumarate **17** was the minor product (28%) (Eq. 12).




**14** **16** **17** 97% (11)




**14** **17** 28% **18** 53% (12)

The structures of **16** and **17** were proven by X-ray structure analysis (Fig. 4, 5). The X-ray structure of **17** was previously reported by Maas, et al.[29] The structure of **18** was assigned by comparison with the spectra of **17**. It is of interest to notice that the acyl bromide groups are twisted relative to the plane of the C=C double bond by 76.7 degree.

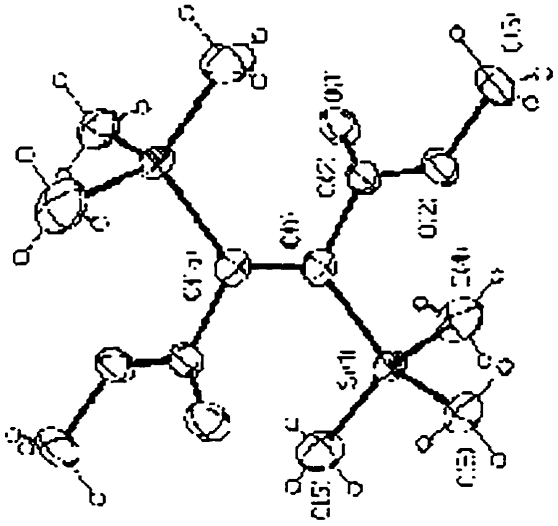


**Figure 4:** X-ray structure of **17.**

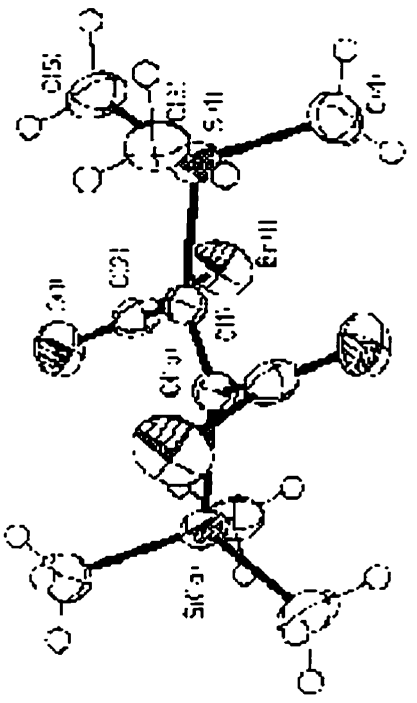
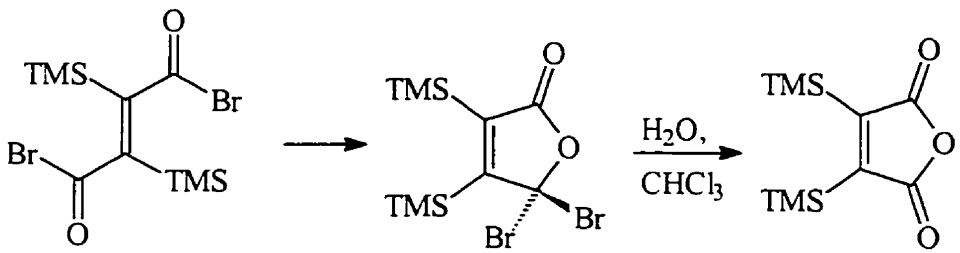


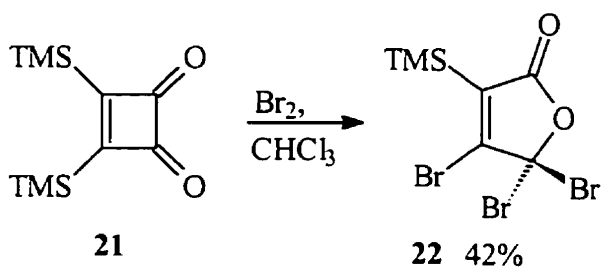
**Figure 5:** X-ray structure of **16**.

2,3-Bis(trimethylsilyl)fumaryl bromide **16** was not stable at room temperature in $CDCl_3$ and cyclized to 5,5-dibromo-3,4-bis(trimethylsilyl)-2(5H)-furanone **19** (Eq. 13), which was characterized by its spectral properties. Addition of water to the solution of **16** in $CDCl_3$ resulted in the formation of maleic anhydride **20**, probably through the intermediate **19** (Eq. 13). A similar reaction to the formation of **19** was observed when $Br_2$ was reacted with the dione **21** at room temperature, and 4,5,5,-tribromo-3-trimethylsilyl-2(5H)-furanone **22** was obtained in 42% yield (Eq. 14). The formation of **22** might result from the reaction of $Br_2$ with the intermediate **19**. The structures of **19** and **22** were established by their spectroscopic properties and chemical behavior. The presence of the lactone moieties of **19** and **22** was proven by their $^{13}C$ NMR absorptions at δ 183.4 and 165.4 of the carbonyl carbon,

respectively, and were confirmed by their infrared absorptions at 1792 or 1795 $cm^{-1}$, respectively. The presence of the conjugated C=C double bond was indicated by the $^{13}C$ NMR absorptions at δ 165.8 and 137.8, and 161.6 and 130.3, respectively, and was also confirmed by the UV absorption maximum of **19** at 252 nm. The assignment of the bromo substituent at C-4 in **22** was supported by comparing the $^{13}C$ NMR of the carbonyl group with that of **19**, in which the former is shifted upfield 18 ppm due to a conjugative effect. This assignment was also confirmed by comparing with the $^{13}C$ NMR spectrum of 2,3,4,4-tetrabromobut-2-en-4-olide[33] which showed signals at δ 159.18, 152.91, 115.38, and 73.79.



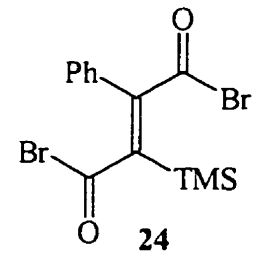

(13)



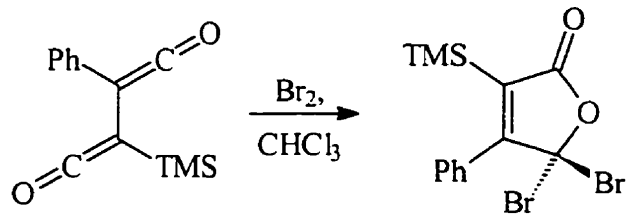

(14)

The reaction of $Br_2$ with the 2-phenyl-3-trimethylsilyl bisketene **23** at -23 °C in $CHCl_3$ resulted in the formation of **25** as the only observed product,

without the observation of any detectable amount of the fumaryl bromide **24** (Eq. 15). The structure of **25** was established by its spectroscopic properties. The presence of the lactone moiety of **25** was indicated by the $^{13}C$ NMR absorption at δ 176.6 of the carbonyl carbon, and was confirmed by the infrared absorption at 1782 $cm^{-1}$. The presence of the conjugated C=C double bond was indicated by the $^{13}C$ NMR absorption at δ 167.5 and 130.7. The assignment of the phenyl substituent at C-4 in **25** was indicated by comparing the $^{13}C$ NMR of the carbonyl group with that of **19**, and the former is shifted upfield 6.8 ppm due to the conjugative effect.




**24**




**23** **25** 86% (15)

Thus the reaction of bromine with bisketenes gives products from attack at $C_\alpha$ exclusively. All these results can be explained by the formation of the thermodynamically stable intermediate ions as predicted by the calculational results shown in Fig. 3. The difference with the protonation reaction is that the

formation of bridged bromonium ions can lead to the more stable ions and result in the formation of the stable products as observed. To explain these results, the mechanism shown in Fig. 6 is suggested. The bisketene reacts with $Br_2$ to form the CTC (charge transfer complex) **26** (note, such complexes are feasible for ketenes, which give $1e^-$ oxidation as shown in Eq. 16[27]), which gives the bridged bromonium ion **27** after loss of the bromide anion. As the trimethylsilylketenyl group in **27** can rotate relatively freely around the carbon-carbon single bond, both *cis*-**28a** and *trans*-**32a** could be formed after the opening of the bridged bromonium ion **27**. The acylium ion character shown by the resonance structures *cis*-**28b** and *trans*-**32b** would stabilize these structures.

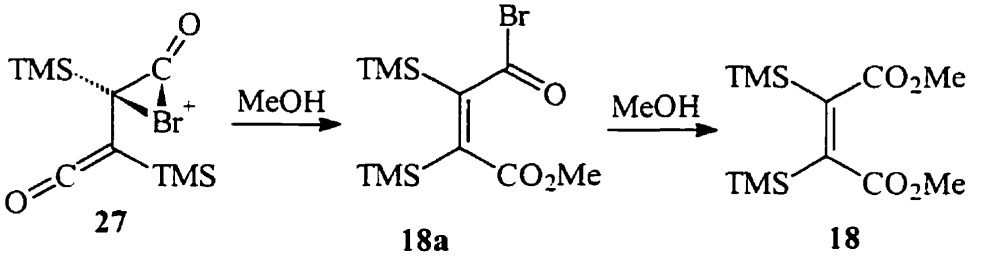
$$RCH{=}C{=}O \xrightarrow{-e^-} R\dot{C}H\text{-}\bar{C}{=}O \qquad (16)$$

At - 23 °C the primary product observed is **16**, which forms by reaction of *trans*-**32b** with bromide. Formation of the intermediate *trans*-**32b** is expected to be favored over *cis*-**28b**, which is less stable because of the two adjacent bulky trimethylsilyl groups. At room temperature, the bisacyl bromide **16** could reversibly form *trans*-**32b** and then rearrange through *cis*-**28b** to the more stable cation **29**, which is captured by bromide to give the thermodynamically stable product **19**.

It is possible that *cis*-**28b** could give a 1,4-bridged bromonium ion *cis*-**30** (a similar intermediate has been used by Ehlinger and Magnus to explain experimental results[16]). Trapping of *cis*-**30** with bromide could give **31**, which could rearrange to **19** via **29**.

When the reaction was carried out in methanol the esters **17** and **18** were formed in 28 and 53% yields, respectively. The formation of the maleate

product **18** could occur by trapping by MeOH of the initially formed **27** to give **18a**, which reacts further with MeOH to give **18** (Eq. 17).




**27** **18a** **18** (17)

The silyl group could enhance bromide loss from **16** due to β-silyl stabilization of the acylium ion structure *trans*-**32b**. Thus **16** can readily revert to **27**, and simple rotation around the carbon-carbon single bond and ring opening would give the needed syn-conformation *cis*-**28a**.

In the intermediates **28** and **32** the acyl bromide group could be twisted out of the plane, as is observed in the crystal structure of **16**, so that the acyl bromide moiety acts as a simple electron withdrawing group. Furthermore, the carbon-bromine bonds in such twisted acyl bromide groups would be in an almost paralled conformations with the p-orbitals of the α-carbocation centers so that they could easily form the bridged bromonium ion to reform **27**.

The mechanism of the formation of **25** from the reaction of $Br_2$ with the bisketene **23** is shown in Figs. 7 and 8. As bisketene **23** is unsymmetrical, the bromination reaction could occur at either ketenyl moiety. As mentioned before the silyl group behaves as a slightly activating group to electrophilic attack by protons on the directly connected double bond compared to the alkene without the silyl group. Figure 8 shows the initial bromination occurring at the trimethylsilylketene moiety. The reaction of $Br_2$ with bisketene **23** results in the CTC **38**, which gives the bromonium ion **39** after loss of the bromide. However **39** is a relatively unstable intermediate as it does not have the silyl-

stabilization of the ketene moiety. On the other hand, the reaction of $Br_2$ with the phenylketene moiety via the CTC **33** gives the bromonium ion **34** as shown in Fig. 7. Ion **34** is a more stable intermediate than **39**, as the silyl group stabilizes the ketene moiety. Rearrangement of **34** to *cis*-**35a** would be highly favorable, as the latter intermediate has stabilization of the carbocation center by both the β-silyl and the α-phenyl groups. This intermediate then leads to **25** as the only observed product, and this is expected to be the most stable product because of the stable lactone structure with the phenyl conjugated in the unsaturated lactone structure. The intermediate *trans*-**37** is also highly stabilized and the fumaryl bromide **24** could be formed as an observed product by this route. However the phenyl group promotes reionization of **24** to form **37** so that even at low temperature the only observed product is **25**.

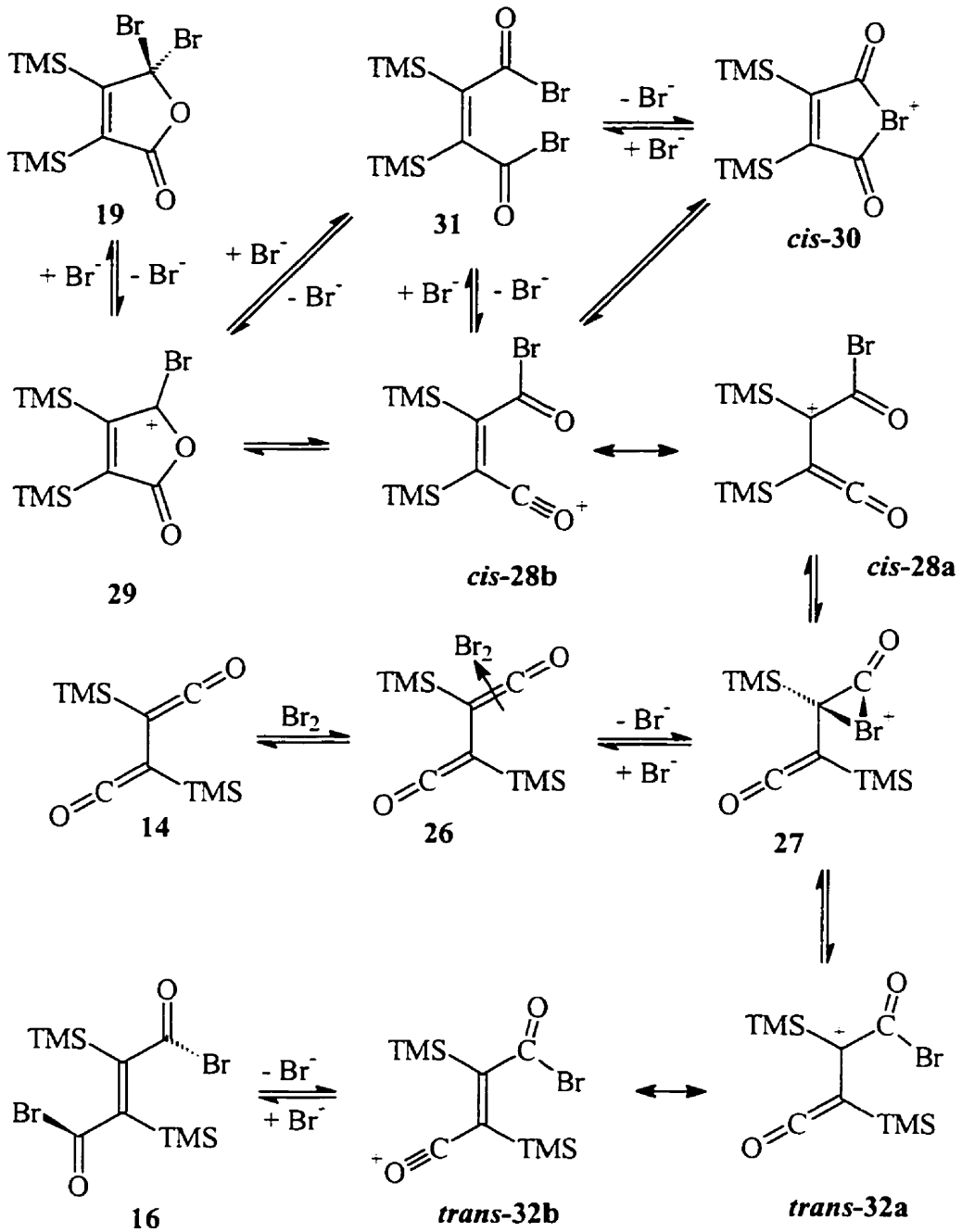
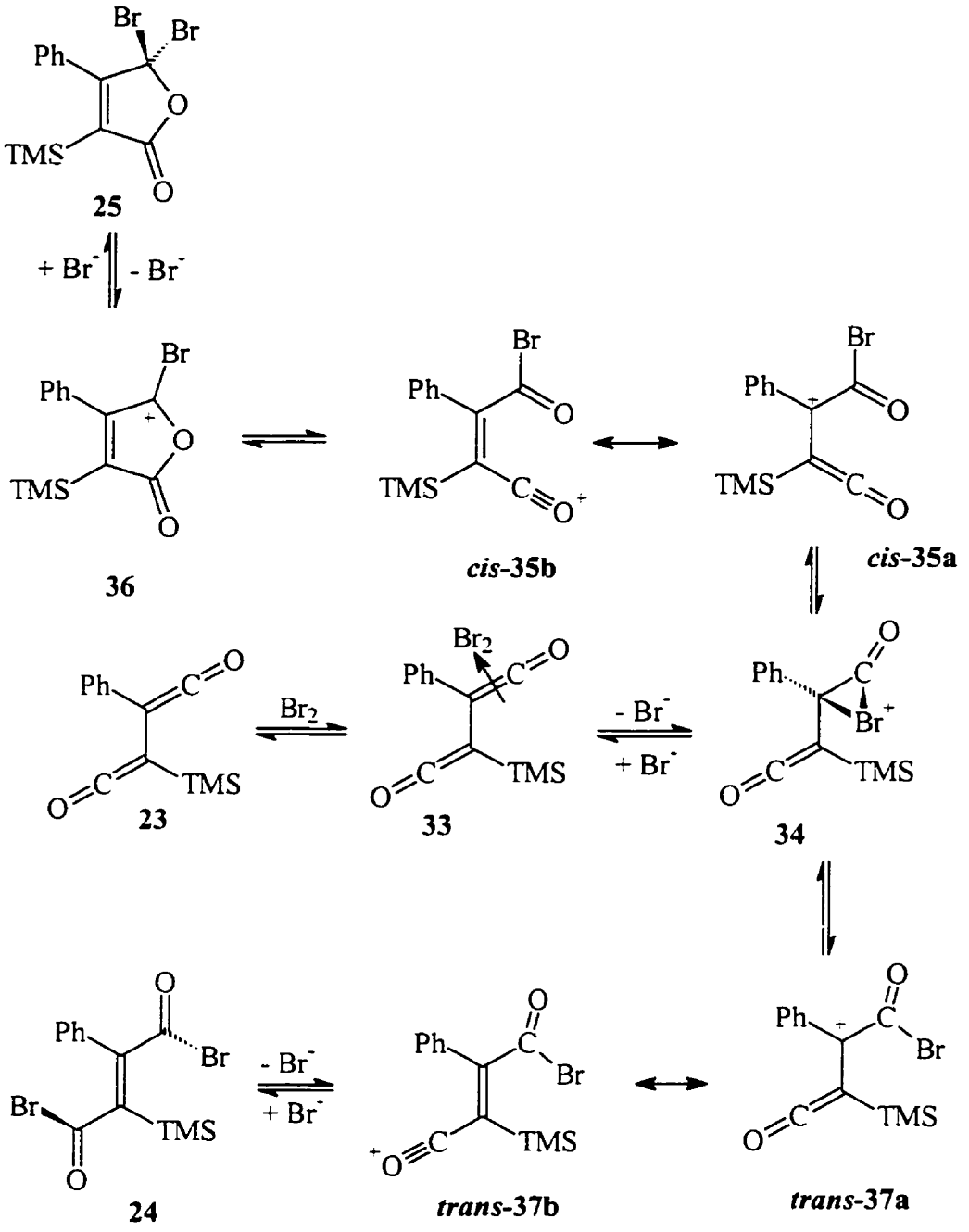



**Figure 6**


Br
Br
Ph
O
TMS
O
25
+ Br⁻
- Br⁻
Br
Ph
O
TMS
O
36
Br
Ph
O
TMS
C
O⁺
cis-35b
Br
Ph
O
TMS
C
O
cis-35a
Ph
C
O
TMS
O
23
Br₂
Br₂
Ph
C
O
TMS
O
33
- Br⁻
+ Br⁻
Ph
C
O
Br⁺
TMS
O
34
Ph
Br
Br
TMS
O
24
- Br⁻
+ Br⁻
Ph
O
C
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O
C
trans-37a

**Figure 7**

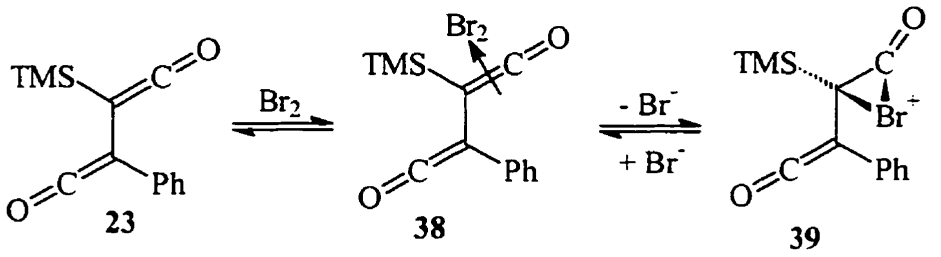


**Figure 8**

Treatment of the bisketene **14** with *t* -BuCl and a catalytic amount of AlCl3 (10 mol%) at - 78 °C gave the *t*-Bu substituted bisketene **40** (Fig. 9). This structural assignment was supported by the $^{1}$H NMR spectrum, and by the IR absorption at 2091 cm$^{-1}$, and was further verified by the reaction of **40** in situ with Br2 followed by methanol to yield the dimethyl fumarate **41**. The bisketene has also been generated in this laboratory by photolysis of 3-trimethylsilyl-4-*tert*-butyl-1,2-cyclobutenedione.[30] The $^{1}$H NMR of **40** generated by photolysis shows absorptions at δ 0.20 and 1.12 which are comparable with the signals of **40** at 0.23 and 1.10, respectively. The small difference could be the result of the concentration and the presence of $AlCl_3$ in the sample. The structure of **41** was established by its spectroscopic properties. The presence of the ester moieties of **41** was shown by its $^{13}$C NMR absorption at δ 172.3 and 169.9 of the carbonyl carbons, which are comparable to the $^{13}$C NMR of **17** at δ 172.1, and was confirmed by the infrared absorption at 1726 cm$^{-1}$. The presence of the conjugated C=C double bond was shown by the $^{13}$C NMR absorptions at δ 153.9 and 135.1, which are comparable to the $^{13}$C NMR shift of **17** at δ 153.5. The stereochemistry of **41** was determined by an nOe

study, which showed no nOe between the trimethylsilyl group and the tert-butyl group.

The preferred formation of **41** upon bromination and methanolysis of **40** is presumably mainly due to steric factors, as the bulky *t*-Bu group will strongly prefer to be *trans* to the TMS group. Bisketene **40** was not stable under the reaction conditions at higher temperatures, as when the reaction mixture was allowed to warm up to room temperature it afforded TMSCl and other unidentified products as shown by $^1$H NMR spectroscopy.

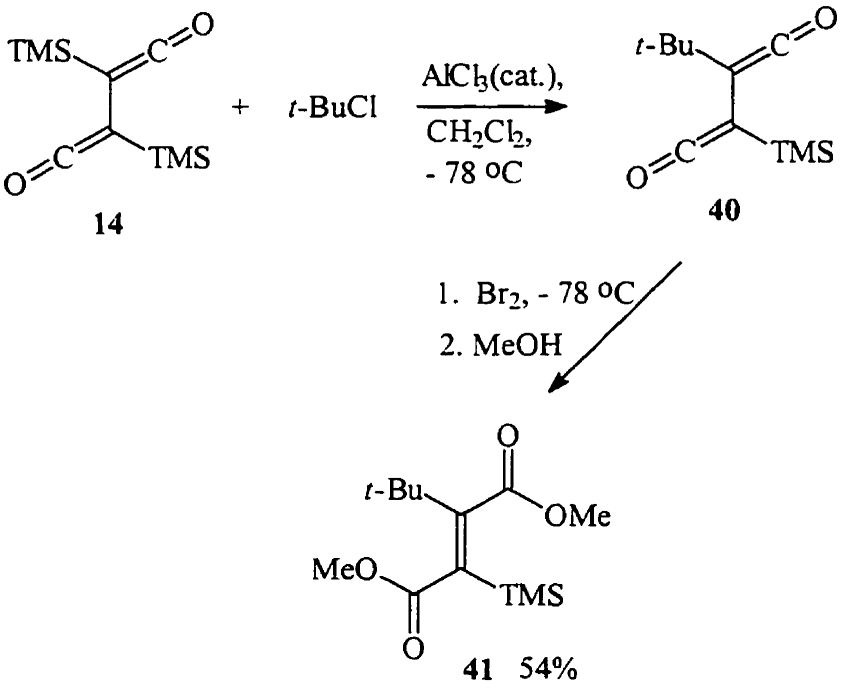


**Figure 9**

In conclusion, ab initio calculations carried out by Mike McAllister predict that electrophilic attack on 1,2-bisketenes gives more stable products by

attack at $C_\alpha$ rather than $C_\beta$. Experimentally, small electrophiles like $H^+$ ( as in $CF_3CO_2H$) gave exclusively attack at $C_\beta$ and resulted in 1,2-addition to gave a kinetically controlled ketenyl anhydride product. However the large electrophile $Br_2$ gave product from exclusive attack at $C_\alpha$, forming 1,4-addition products, and this was explained by the formation of the bridged bromonium ion which led to the thermodynamically stable product. The bis(trimethylsilyl) 1,2-bisketene was also found to react with the carbon electrophile t-BuCl with substitution of one of the silyl groups in the bisketene.

In future work, further study of the electrophilic reaction of these species may be considered. As indicated in this work, reaction of carbon electrophiles with silylketenes is possible, and these reactions involve formation of a new C-C bond, and therefore the scope of this reaction should be further explored.

## 5.3 Experimental

The general procedures are given in Chapter 2. X-ray structures were determined by Dr. Alan Lough.

**2,3-Bis(trimethylsilyl)-4-(trifluoroacetoxy)but-1-ene-1,4-dione (15).** To the bis(trimethylsilyl)bisketene **14** (28.0 mg, 0.124 mmol) in $CDCl_3$ (0.5 mL) in an NMR tube at room temperature was added $CF_3CO_2H$ (14.1 mg, 0.124 mmol). The NMR spectra revealed the formation of the sole product **15**: $^1H$ NMR ($CDCl_3$) δ 0.19 (s, 9), 0.24 (s, 9), 2.21 (s, 1); $^{13}C$ NMR ($CDCl_3$) δ -2.31, -1.14, 9.93, 32.14, 113.80 (q, $J^{13}C\text{-}^{19}F$ = 286.2 Hz), 167.22, 174.16 (q, $J^{13}C\text{-}^{19}F$ = 63.3 Hz), 179.46; IR ($CDCl_3$) $cm^{-1}$ 2095 (vs), 1837 (s), 1767 (s); EIMS *m/z* 340 ($M^+$, 1), 226 ($M^+$-$CF_3COOH$, 40), 155 ($TMSCCSiMe_2^+$, 99), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{12}H_{19}F_3Si_2O_4$ 340.0774, found

340.0761. (The mass spectra were determined using a concentrated sample in $CDCl_3$)

**2,3-Bis(trimethylsilyl)fumaryl bromide (16).** The bistrimethylsilyl-bisketene **14** (46.0 mg, 0.204 mmol) in $CDCl_3$ (0.5 mL) in an NMR tube was cooled to - 23 °C and bromine (32.6 mg, 0.204 mmol) in $CDCl_3$ (0.2 mL) was added in 5 min, with instantaneous disappearance of the bromine red color. The product was warmed to room temperature and immediate examination of the $^1H$ NMR spectrum showed 2,3-bis(trimethylsilyl)fumaryl bromide as the only compound visible. **16**: $^1H$ NMR ($CDCl_3$) δ 0.42 (s, 18); $^{13}C$ NMR (CDCl3) δ 0.1, 154.7, 165.8; IR ($CDCl_3$) 1795 (s) $cm^{-1}$. The solvent was immediately removed by a rotary evaporator to give the colorless solid product, which was redissolved in anhydrous ether (0.2 mL) and left in a refrigerator (- 25 °C) for 2 days. The 2,3-bis(trimethylsilyl)fumaryl bromide crystal was formed and the solvent was removed with a pipette. The crystal was submitted to an X-ray analysis immediately.

**3,4-Bis(trimethylsilyl)-5,5-dibromo-2(5H)-furanone (19).** Upon standing for 3 days at 4 °C a sample of 2,3-bis(trimethylsilyl)fumaryl bromide prepared as above showed by $^1H$ NMR conversion to the extent of 90% to 3,4-bis(trimethylsilyl)-5,5-dibromo-2(5H)-furanone (**19**). The solvent was removed by a rotary evaporator to give the crude product as a colorless oil, which was purified by radial thin layer chromatography (eluted by 5% ethyl acetate in hexane) to give the colorless oil **19** (78.0 mg, 80%): $^1H$ NMR (CDCl3) δ 0.37 (s, 9), 0.53 (s, 9); $^{13}C$ NMR (CDCl3) δ 0.095, 1.409, 79.7, 137.8, 165.8, 183.4; IR (CDCl3) 1792 (s) $cm^{-1}$; EIMS *m/z* 386 ($M^+$, 1), 279 and 277 ($M^+$ - Br, CO,

18, 16), 155 (TMSCCTMS$^+$ - $CH_3$, 88) 73 (TMS$^+$, 100); HRMS *m/z* calcd for $C_{10}H_{18}Br_2O_2Si_2$ 383.9212, found 383.9207; UV $\lambda_{max}$ ($CDCl_3$) 252 nm ($\varepsilon = 5.6\times10^4$).

**3-Trimethylsilyl-4,5,5-tribromo-2(5H)-furanone (22).** Bromine (0.73g, 4.58 mmol) was added over 10 min at 25 °C to a solution of 3,4-bis(trimethylsilyl)cyclobutane-1,2-dione **21** (0.513 g, 2.29 mmol) in chloroform (9 mL). The solution was stirred 16 h, the solvent was evaporated, and the product was purified by radial thin layer chromatography (eluted with 10% ethyl acetate in hexane) to give **22** (0.415 g, 1.06 mmol, 42%): mp 70.5-71.0 °C; $^1$H NMR ($CDCl_3$) $\delta$ 0.39 (s, 9); $^{13}$C NMR ($CDCl^3$) $\delta$ - 1.887, 76.73, 130.3, 161.6, 165.4; IR ($CDCl_3$) 1795(s), 1570 (w) cm$^{-1}$; EIMS *m/z* 377 (M$^+$-$CH_3$, 5), 340 (M$^+$-$CH_3$, CO, 2), 313 (M$^+$-Br, 29), 285 (M$^+$-Br, CO, 9), 234 (M$^+$-2Br, 8), 73(TMS$^+$, 100); HRMS *m/z* calcd for $C_6H_6Br_3O_2Si$ (M$^+$-$CH_3$) 374.7687, found 374.7696. When the reaction was monitored by $^1$H NMR peaks attributed to 2,3-bis(trimethylsilyl)fumaryl bromide **16** and 3,4-bis(trimethylsilyl)-5,5-dibromo-2(5H)-furanone **19** were observed during the course of the reaction.

**Hydration of 2,3-bis(trimethylsilyl)fumaryl bromide (16).** To a solution of 2,3-bis(trimethylsilyl)fumaryl bromide **16** (25.2 mg, 0.065 mmol) prepared as above in $CDCl_3$ (0.5 mL) was added water (10 mg, 0.54 mmol) at 4 °C and the solution was shaken and monitored with time. Signals attributed to 3,4-bis(trimethylsilyl)-5,5-dibromo-2(5H)-furanone were observed, and after 3 days the $^1$H NMR spectrum indicated the formation of the 3,4-bis(trimethylsilyl)maleic anhydride. Purification by radial thin layer chromatography (on silica gel eluted with 15% ethyl acetate in hexane) gave

colorless solid 3,4-bis(trimethylsilyl)maleic anhydride **20** (12.7 mg, 0.052 mmol, 80%): $^{1}$H NMR ($CDCl_3$) δ 0.39 (s, 18); $^{13}$C NMR ($CDCl_3$) δ 0.11, 161.6, 168.4, identified by comparison of the spectra to those of authentic material.[28]

**Dimethyl 2,3-bis(trimethylsilyl)fumarate (17).** The bisketene 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione (**14**) (21.6 mg, 0.096 mmol) was dissolved in carbon tetrachloride (2 mL), and cooled to -23 °C ($CCl_4/CO_2$) and one equivalent of bromine (15.4 mg, 0.096 mmol) was dropped in over 5 min with stirring until the red bromine color did not disappear. The reaction mixture was cooled to -77 °C ($CO_2$/acetone), and methanol (4 mL) was dropped in . The solvent was removed by a rotary evaporator at room temperature to give a crude solid product which was purified by thin layer chromatography (on silica gel eluted with 3% ethyl acetate in hexane) to give the colorless solid **17** (26.8 mg, 0.093 mmol, 97%): mp 128.0-128.5 °C; $^{1}$H NMR ($CDCl_3$) δ 0.15 (s, 18), 3.72 (s, 6); $^{13}$C NMR ($CDCl_3$) δ -1.21, 51.38, 154.22, 171.91; IR ($CCl_4$) 1723 (s), 1550 (m) cm$^{-1}$; EIMS *m/z* 288 ($M^+$, 3), 273 ($M^+$-Me, 75), 229 $M^+$-Me, $CO_2$, 41), 155 ($TMSCCTMS^+$- Me, 60), 125 ($TMSCCCO^+$, 100), 73 ($TMS^+$, 64); HRMS *m/z* calcd for $C_{12}H_{24}O_4Si_2$ 288.1213, found 288.1212. The structure and stereochemistry of **17** were established by x-ray crystallography.

**Dimethyl 2,3-bis(trimethylsilyl)maleate (18) and fumarate (17).** The bisketene 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione **14** (41.0 mg, 0.181 mmol) was dissolved in anhydrous ether (2 mL) and then methanol (4 mL) was added at -77 °C ($CO_2$/acetone). One equivalent of bromine (29.0 mg, 0.181

mmol) in chloroform (0.2 mL) was dropped in over 5 min until the red bromine color persisted. The solvent was removed by a rotary evaporator at room temperature and the crude solid product was purified by thin layer chromatography (on silica gel eluted with 3% ethyl acetate in hexane) to give **17** (14.4 mg, 0.050 mmol, yield 28%), mp 128.0-128.5 °C, $R_f$ 0.36 (10% ethyl acetate in hexane) , and **18** (27.8 mg, 0.097 mmol, 53%), mp 91.5-92.5 °C, $R_f$ 0.10 (10% ethyl acetate in hexane). **18**: $^1$H NMR ($CDCl_3$) δ 0.27 (s, 18), 3.71 (s, 6); $^{13}$C NMR ($CDCl_3$) δ 0.21, 51.69, 153.45, 172.13; IR ($CCl_4$) 1715 (s), 1549 (m) cm$^{-1}$; EIMS *m/z* 288 ($M^+$, 4), 273 ($M^+$-Me, 58), 229 ($M^+$-Me, CO2, 50), 155 (TMSCCTMS-Me, 10), 125 ($TMSCCCO^+$, 100), 73 ($TMS^+$, 56); HRMS calcd for $C_{12}H_{24}O_4Si_2$ 288.1213, found 288.1207.

**5,5-Dibromo-4-phenyl-3-trimethylsilyl-2(5H)-furanone (25).** 3-Phenyl-4-trimethylsilylcyclobutene-1,2-dione (46.0 mg, 0.2 mmol) was dissolved in $CDCl_3$ (0.5 mL) in a NMR tube. The reaction mixture was irradiated with 350 nm lamps for 1 h at 6 °C, and gave the bisketene **23** in 83% yield as shown by the $^1$H NMR spectrum. Bromine (27.0 mg, 0.17 mmol, in $CDCl_3$ (0.2 mL) was added to the reaction mixture in 5 min. at - 23 °C ($CCl_4/CO_2$). The solvent was removed and yielded the crude product mixture, which was purified by radial thin layer chromatography to give the colorless oil **25** (54.0 mg, 0.14 mmol, 86% based on the bisketene): $^1$H NMR ($CDCl_3$) δ 0.04 (s. 9), 7.40-7.65 (m, 5); $^{13}$C NMR ($CDCl_3$) δ -1.64, 77.79, 128.08, 128.81, 129.60, 130.18, 130.78, 167.50, 176.57; IR ($CDCl_3$) 1782 (v.s) cm$^{-1}$; EIMS *m/z* 390 ($M^+$, 2), 311 ($M^+$-Br, 26), 283 ($M^+$-Br, 29), 283 ($M^+$-Br, CO, 24), 230 ($M^+$-2Br, 35), 174 ($PhCCTMS^+$, 46); 159 ($PhCCTMS^+$-$CH_3$, 100); HRMS *m/z* calcd for $C_{13}H_{14}Br_2O_2Si$ 389.9109, found 389.9102.

**2-*tert*-Butyl-3-trimethylsilyl-1,3-butadiene-1,4-dione (40).** The bisketene 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione **14** (102.5 mg, 0.454 mmol) was dissolved in $CH_2Cl_2$ (7 mL) under nitrogen, and then *t*-BuCl (88.1 mg, 0.952 mmol) was added and the reaction mixture was cooled to -78 °C ($CO_2$/acetone). Anhydrous $AlCl_3$ (6.1 mg, 0.045 mmol) was added in one portion with stirring. After 20 min, the reaction was monitored by $^1H$ NMR and by IR, and showed the formation of **40**: $^1H$ NMR ($CDCl_3$) δ 0.23 (s, 9), 1.10 (s, 9); IR ($CH_2Cl_2$) 2091 (vs) $cm^{-1}$.

The $^1H$ NMR spectra of **40** was measured by taking 50 μL of the reaction mixture and then dissolved in 0.5 mL $CDCl_3$.

**Dimethyl 2-*tert*-butyl-3-trimethylsilylfumarate (41).** Bromine (72.6 mg, 0.454 mmol, in $CH_2Cl_2$ (1 mL)) was added into the above reaction mixture at -78 °C, followed the addition of methanol (2 mL) in one portion, and then the solvent was evaporated at room temperature to give a solid crude product. This was redissolved in 20% ethyl acetate in hexane (5 mL), and directly passed through a short column of neutral alumina, with elution with 20% ethyl acetate in hexane. The solvent was removed and gave the solid crude product, which was further purified with radial thin layer chromatography (eluted with 5% ethyl acetate in hexane) to yield the colorless solid **41** (66.7 mg, 0.245 mmol, 54%): $^1H$ NMR ($CDCl_3$) δ 0.20 (s, 9), 1.18 (s, 9), 3.71 (s, 3), 3.73 (s, 3); $^{13}C$ NMR ($CDCl_3$) δ -1.29, 29.39, 37.41, 51.17, 51.24, 135.12, 153.89, 169.92, 172.29; IR ($CDCl_3$) 1726 (b.v.s) $cm^{-1}$; EIMS *m/z* 272 ($M^+$, 8), 257 ($M^+$-Me, 57), 213 ($M^+$-$CO_2Me$, 71), 109 (78), 73 ($TMS^+$, 100), 59 ($CO_2Me^+$, 79), 57 (*t*-$Bu^+$, 25); HRMS calcd for $C_{13}H_{24}O_4Si$ 272.1444, found 272.1444.

**nOe Study of fumarate 41.** When the $(CH_3)_3Si$ protons were saturated no increase was observed at 1.18 ppm $(CH_3)_3C$ protons, and small enhancements 0.5% and 0.4% were observed at 3.71 and 3.73 ppm $CH_3O$ groups protons, respectively. When the $(CH_3)_3C$ protons were saturated no increase was observed at 0.20 ppm $(CH_3)_3Si$ protons, and small enhancements 0.5% and 0.6% were observed at 3.71 and 3.73 ppm $CH_3O$ groups protons, respectively.

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**Appendix 1**

**X-ray Structure Data**

**Table 1. X-ray Structure Data of 2,3-Bis(trimethylsilyl)fumaryl bromide (16)** The molecule has a crystallographic inversion center.

Bond lengths ( $\mathring{A}$ ) and Angles (deg)

| | | | |
|---|---|---|---|
| Br (1)-C (2) | 1.989 (3) | Si (1) -C (5) | 1.856 (4) |
| Si (1) - C (1) | 1.927 (3) | C (1) -C (1) #1 | 1.345 (6) |
| Si (1) -C (4) | 1.854 (4) | Si (1) -C (3) | 1.860 (4) |
| O (1) - C (2) | 1.177 (4) | C (1) -C (2) | 1.479 (4) |
| | | | |
| C (4) -Si (1) -C (5) | 113.0 (2) | C (5) -Si (1) -C (3) | 108.6 (2) |
| C (5) -Si (1) -C (1) | 106.5 (2) | C (1) #1 -C (1) -C(2) | 116.9 (4) |
| C (2) -C (1) -Si (1) | 114.5 (2) | O (1) -C (2) -Br (1) | 118.5 (3) |
| C (4) -Si (1) -C (3) | 111.6 (2) | C (4) -Si (1) -C (1) | 108.2 (2) |
| C (3) -Si (1) -C (1) | 108.7 (2) | C (1) #1 -C (1) -Si (1) | 128.5 (3) |
| O (1) -C (2) -C (1) | 129.9 (3) | C (1) -C (2) -Br (1) | 111.6 (2) |
| | | | |
| C (4) -Si (1) -C (1) -C (1) #1 | 81.59 | C (5) -Si (1) - C (1) -C (1) #1 | -156.54 |
| C (3) -Si (1) -C (1) -C (1) #1 | -39.73 | C (4) -Si (1) -C (1) -C (2) | -101.57 |
| C (5) -Si (1) -C (1) -C (2) | 20.20 | C (3) -Si (1) -C (1) -C (2) | 137.10 |
| C (1) #1 -C (1) -C (2) -O (1) | 68.21 | Si (1) -C (1) -C (2) - O (1) | - 109.02 |
| C (1)#1 -C (1) -C (2) -Br (1) | -113.37 | Si (1) -C (1) -C (2) -Br (1) | 69.40 |

**Table 2. X-ray Structure Data of Dimethyl 2,3-bis(trimethylsilyl)fumarate (17)** The molecule has a crystallographic inversion center.

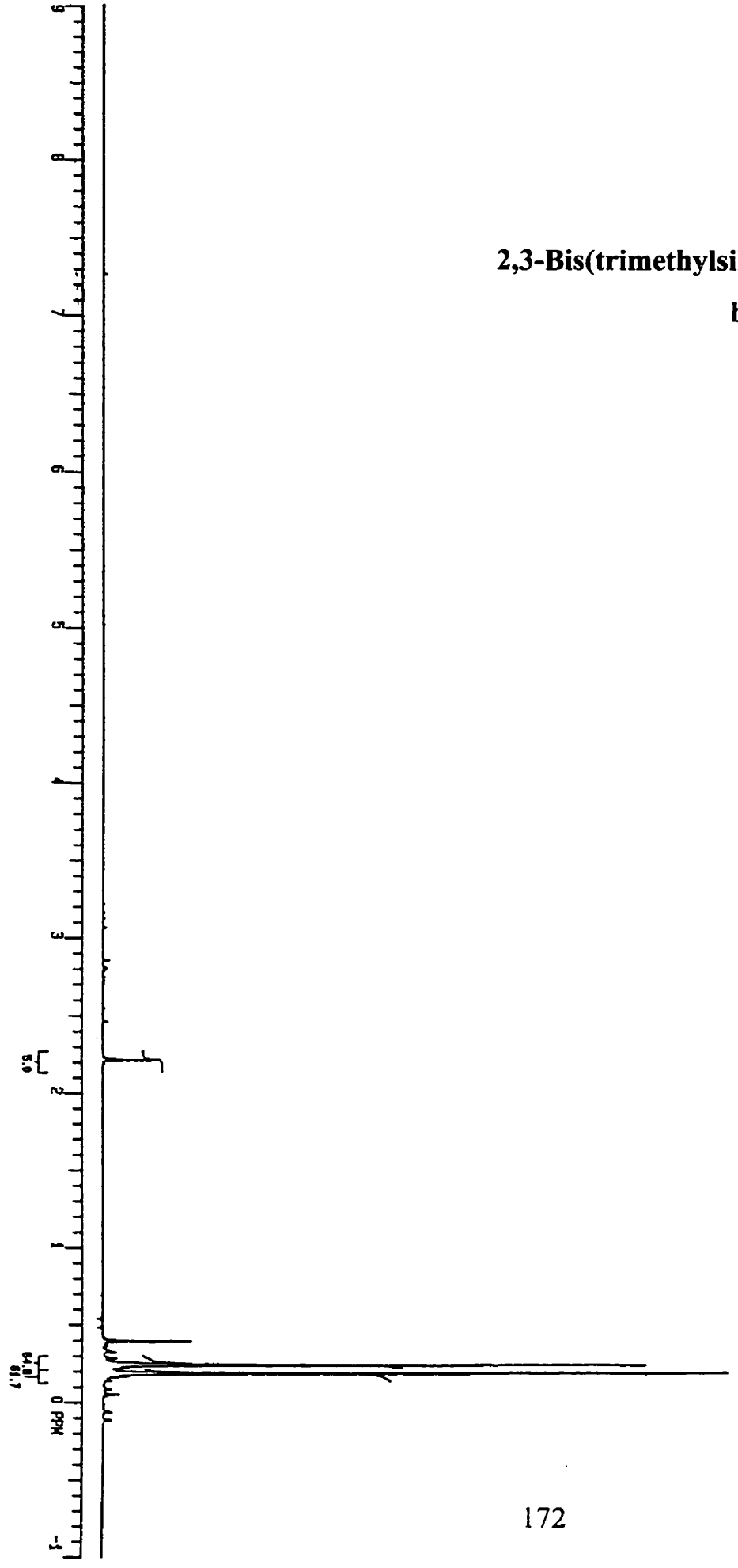
Bond lengths ( $\mathring{A}$ ) and Angles (deg)

| | | | |
|---|---|---|---|
| Si (1) - C (6) | 1.846 (3) | Si (1) - C (5) | 1.855 (4) |
| Si (1) - C (4) | 1.858 (4) | Si (1) - C (1) | 1.912 (3) |
| O (1) - C (2) | 1.193 (3) | O (2) - C (2) | 1.325 (3) |
| O (2) - C (3) | 1.456 (4) | C (1) - C (1) #1 | 1.329 (5) |
| C (1) - C (2) | 1.508 (3) | | |
| | | | |
| C (6) - Si (1) - C (5) | 111.0 (2) | C (6) - Si (1) - C (4) | 110.6 (3) |
| C (5) - Si (1) - C (4) | 108.8 (3) | C (6) - Si (1) - C (1) | 109.0 (2) |
| C (5) - Si (1) - C (1) | 112.4 (2) | C (4) - Si (1) - C (1) | 104.8 (2) |
| C (2) - O (2) - C (3) | 115.9 (3) | C (1) #1 - C (1) - C (2) | 116.7 (3) |
| C (1) #1 - C (1) - Si (1) | 128.3 (3) | C (2) - C (1) - Si (1) | 114.9 (2) |
| O (1) - C (2) - O (2) | 124.2 (2) | O (1) - C (2) - C (1) | 126.0 (2) |
| O (2) - C (2) - C (1) | 109.8 (2) | | |

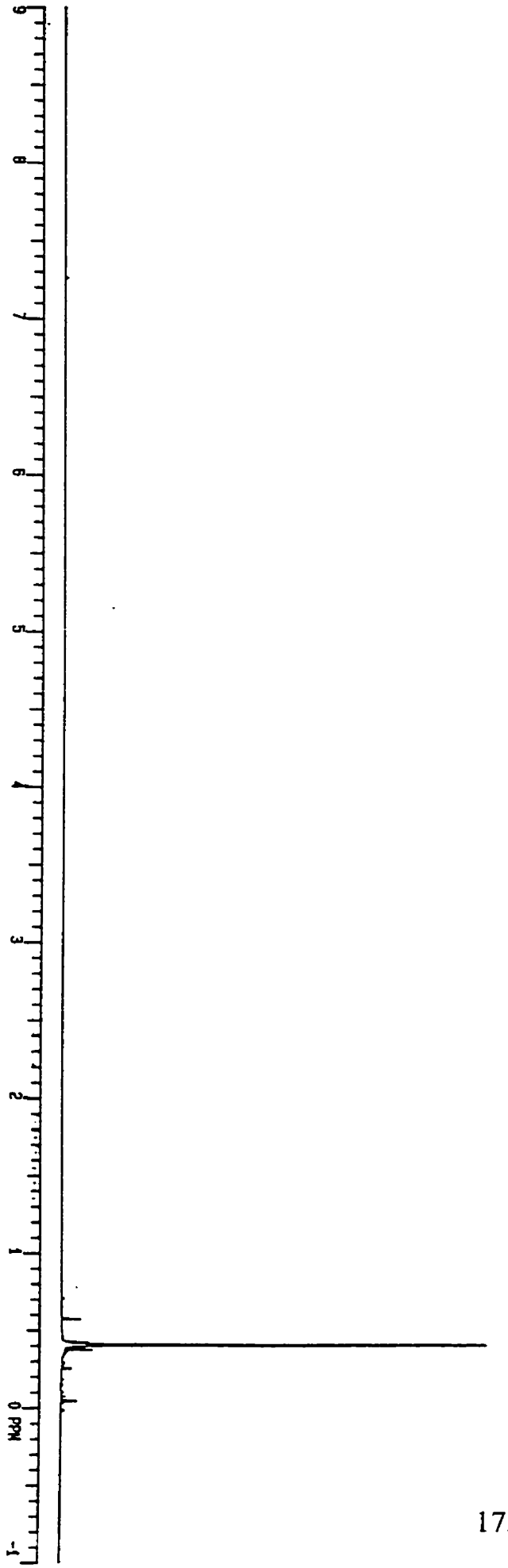
## Appendix 2

## $^1$H NMR Spectra

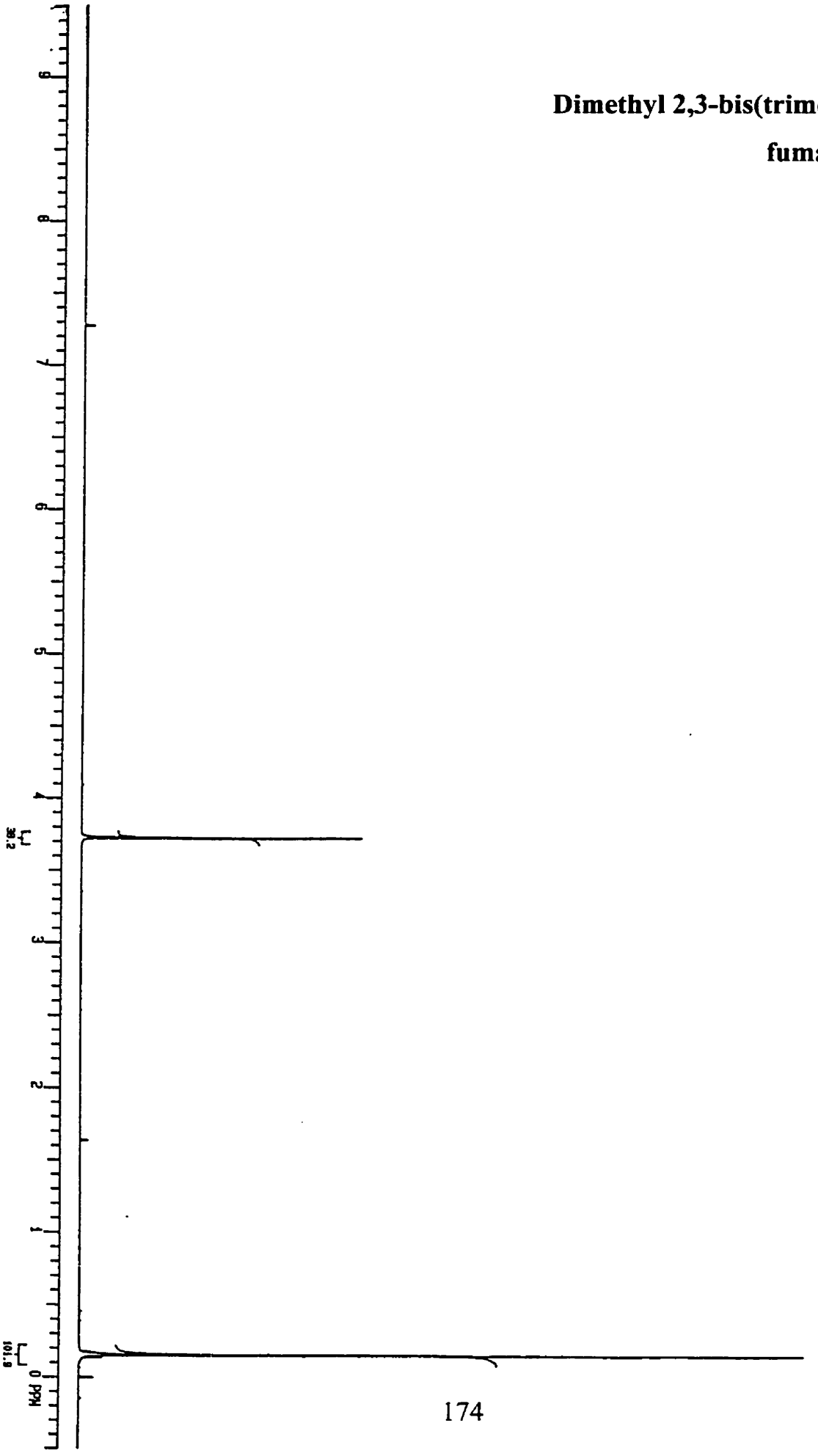
### 2,3-Bis(trimethylsilyl)-4-(trifluoroacetoxy) but-1-ene-1,4-dione (15)



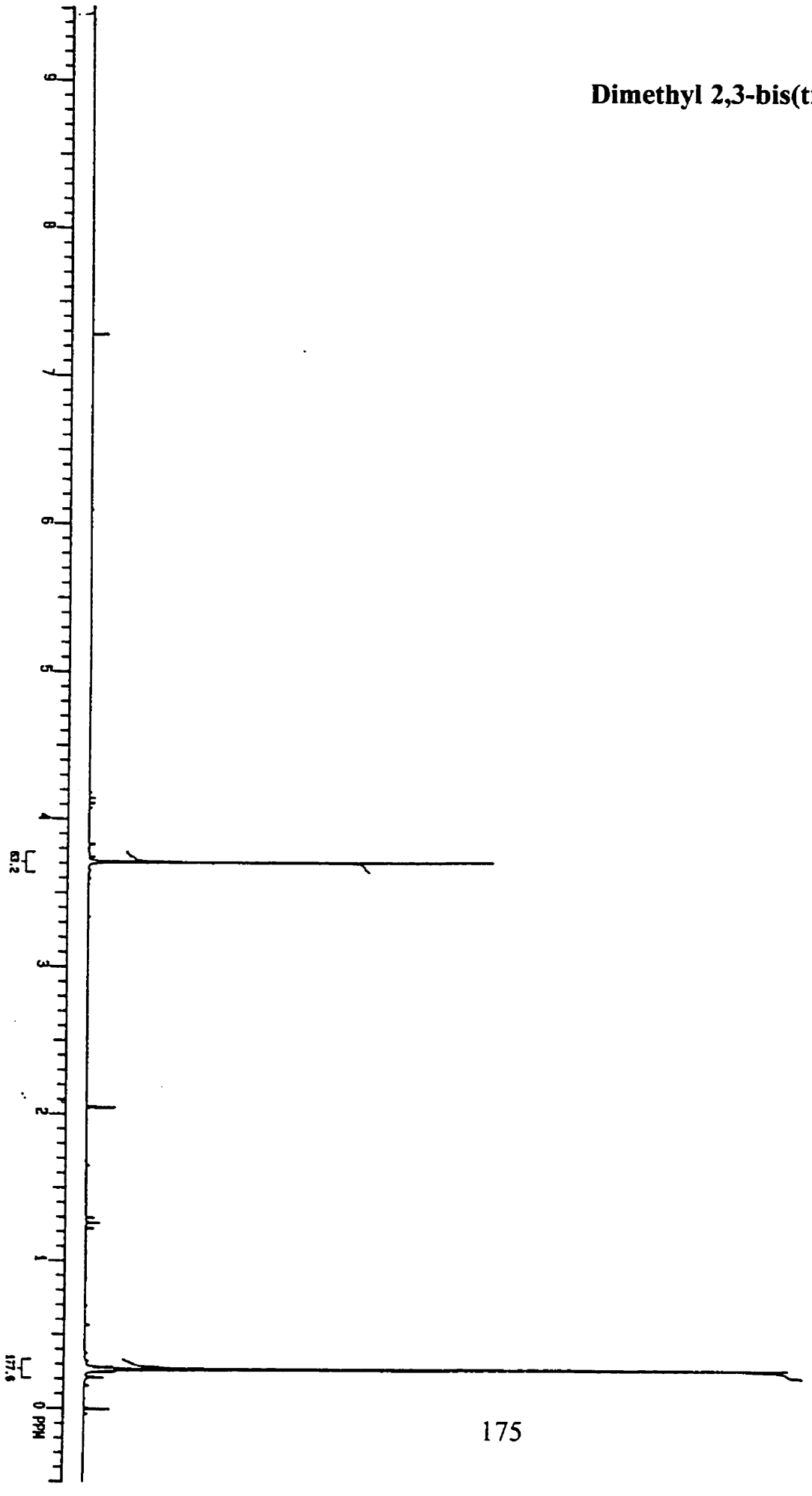
**2,3-Bis(trimethylsilyl)fumaryl bromide (16)**



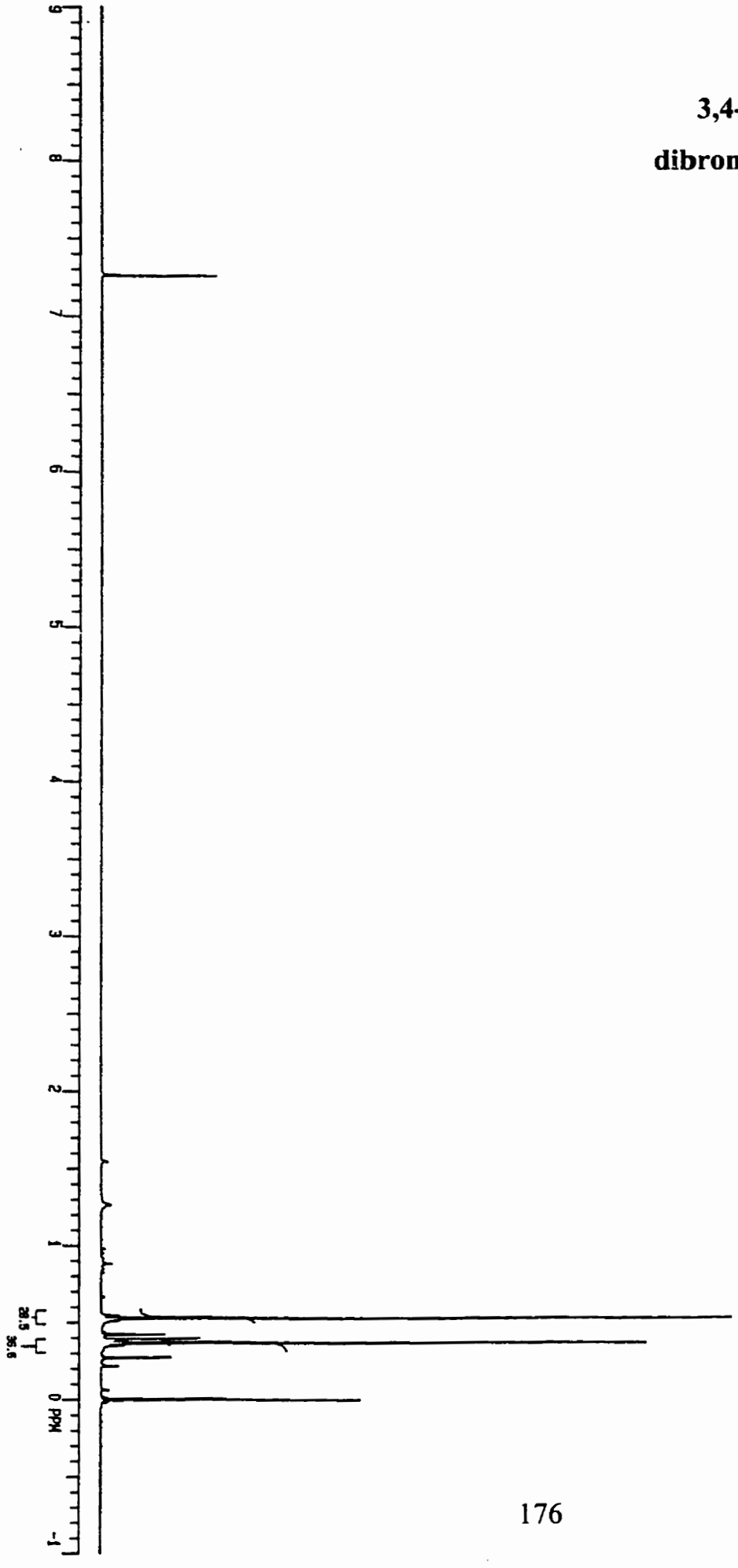
**Dimethyl 2,3-bis(trimethylsilyl) fumarate (17)**



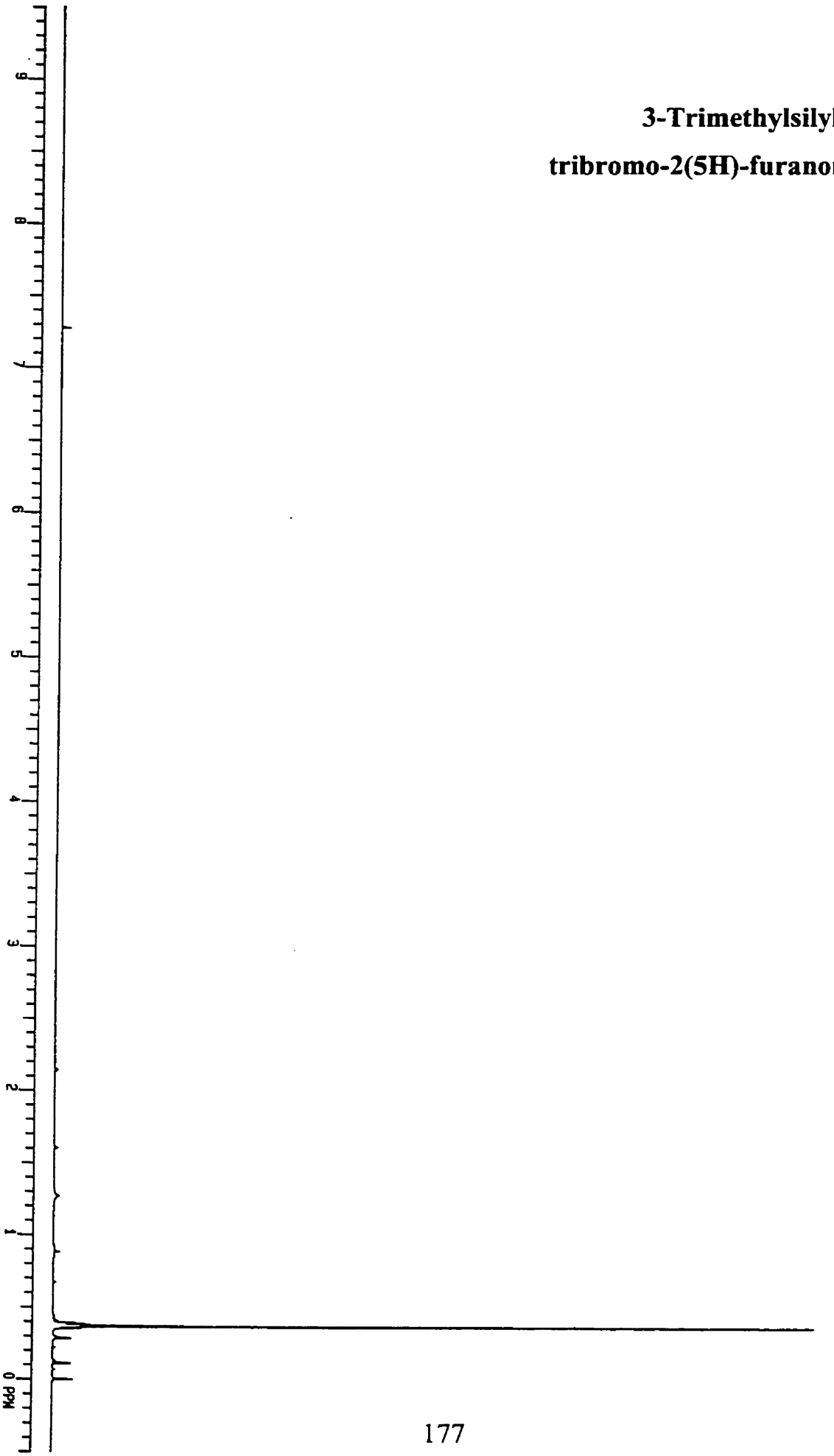
**Dimethyl 2,3-bis(trimethylsilyl) maleate (18)**



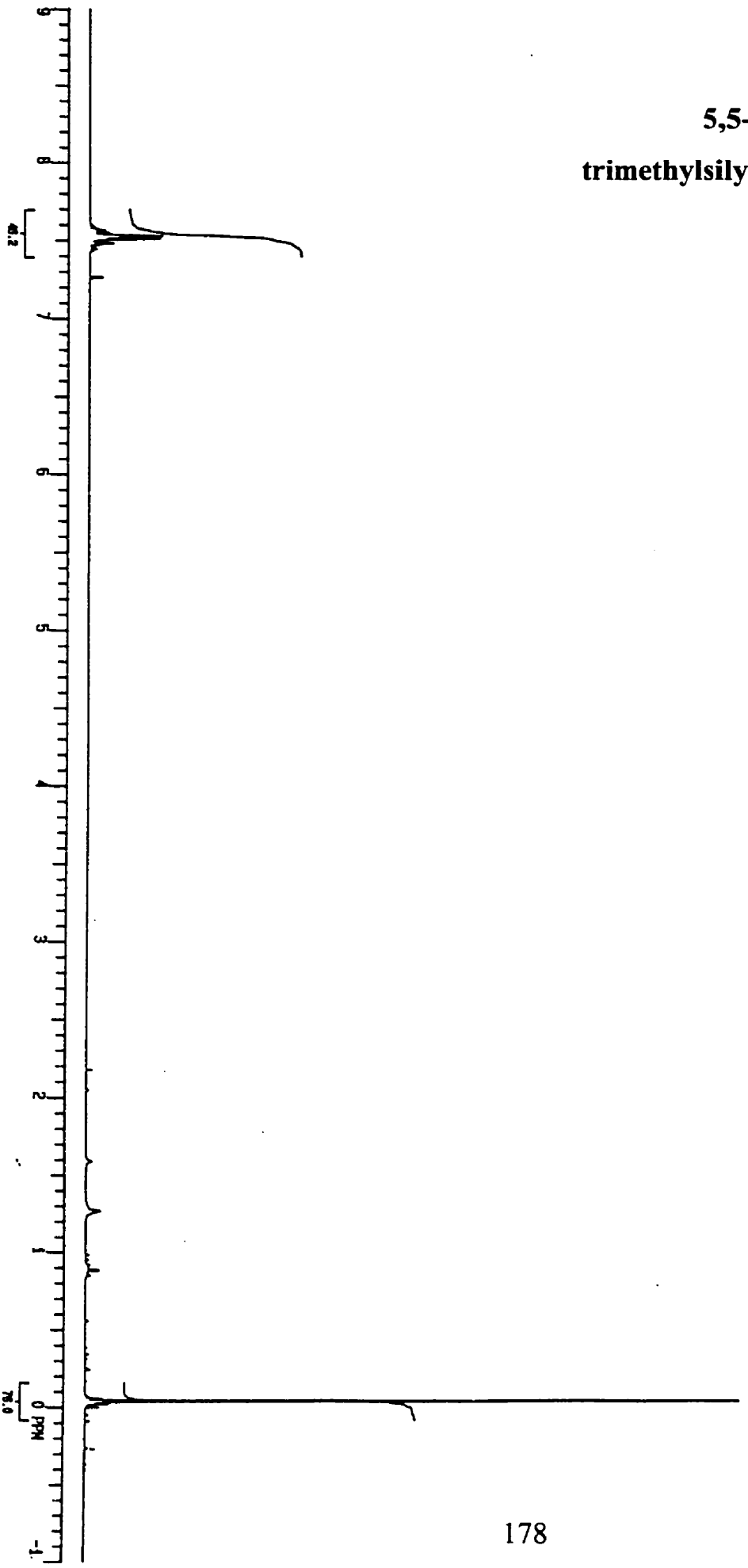
**3,4-Bis(trimethylsilyl)-5,5-dibromo-2(5H)-furanone (19)**



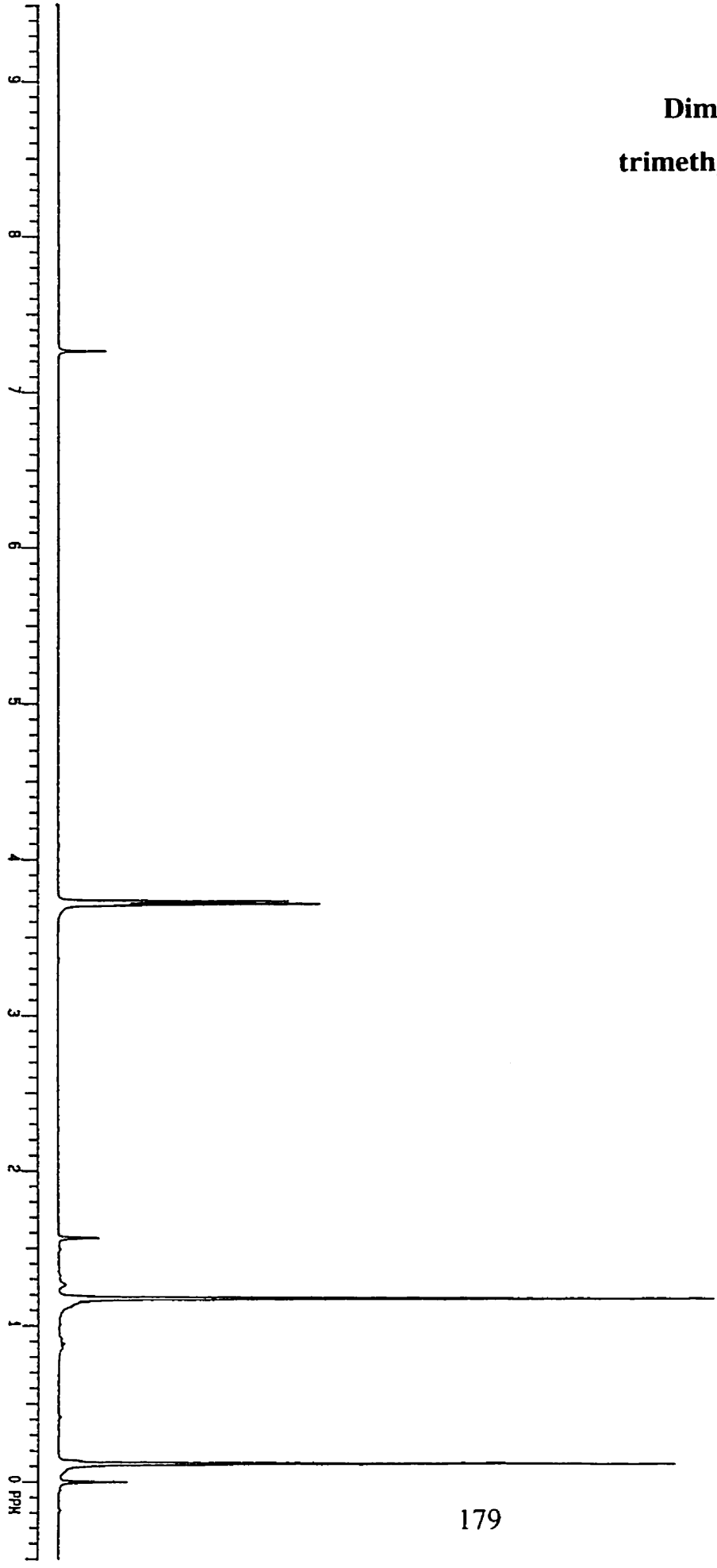
**3-Trimethylsilyl-4,5,5-tribromo-2(5H)-furanone (22)**



**5,5-Dibromo-4-phenyl-3-trimethylsilyl-2(5H)-furanone (25)**



**Dimethyl 2-*tert*-butyl-3-trimethylsilylfumarate (41)**



# *Chapter 6*

# Cycloaddition Reactions of Bisketenes

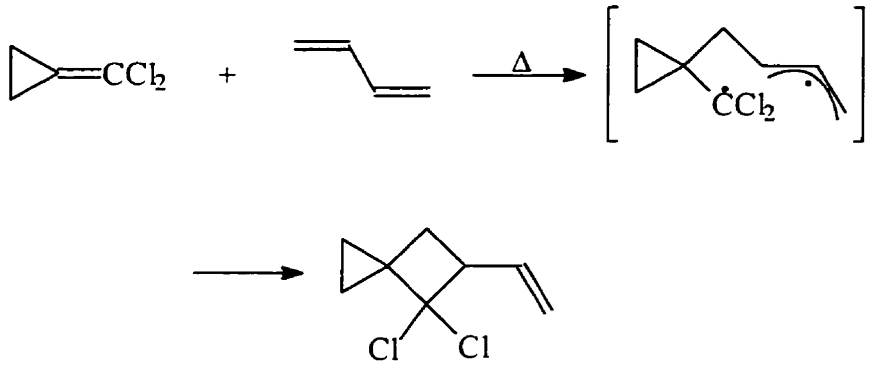
## 6.1 Introduction

Among the principal reactions of ketenes are nucleophilic addition, electrophilic addition, cycloaddition, and polymerization.[1] Of these, the most synthetically useful reaction is the [2+2] cycloaddition to yield versatile four-membered ring compounds.[2] Ketenes undergo this cycloaddition with a wide variety of unsaturated compounds, and these processes include dimerization and reactions with alkenes, acetylenes, imines, and aldehydes giving cyclobutanones,[2] cyclobutenones,[2] β-lactams,[3] and 2-oxetanones (β-lactones),[4] respectively.

### 6.1.1 [2+2] Cycloaddition with alkenes

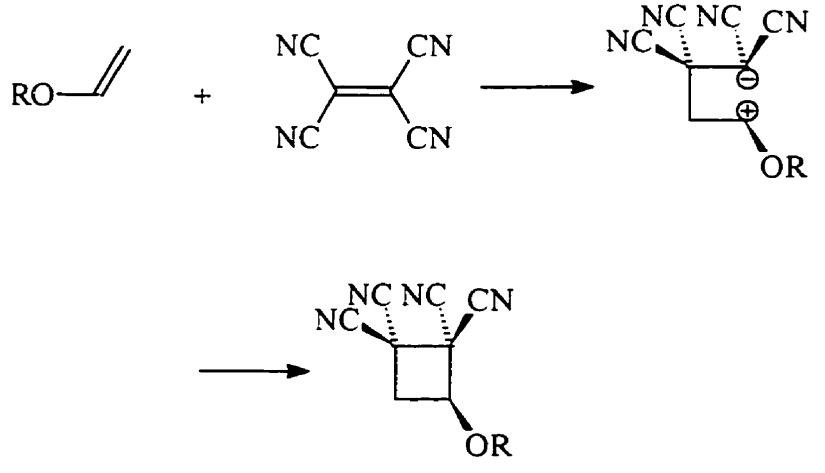
One of the most synthetically important [2+2] cycloaddition reactions of ketenes is the reaction with the carbon-carbon double bond of alkenes to give cyclobutanones.[2] The reactivity of alkenes in this reaction parallels the nucleophilicity of the alkenes. Electron deficient alkenes normally do not undergo this reaction, while electron rich alkenes react readily. This reaction has been periodically reviewed,[1,2] and here is given just a brief discussion of the mechanism, regioselectivity and stereoselectivity of this reaction.

Most simple alkenes can not be induced to undergo [2+2] addition reactions with other alkenes thermally, but those in which the double bond is substituted by fluorine and chlorine atoms undergo thermal [2+2] cycloaddition under relatively mild conditions.[27] In this case, it is known through work of Bartlett and his coworkers that the addition reaction is stepwise by way of a biradical intermediate (Eq. 1).[27]




(1)

Also known are [2+2] cycloadditions proceeding by way of zwitterionic intermediates (Eq. 2).[28] Tetracyanoethylene adds by this mechanism to *p*-methoxyphenyl-,[29] alkoxyl-,[30] and cyclopropyl-[31] substituted alkenes.




(2)

Ketenes usually add to alkenes with retention of the *cis-trans* geometry of the alkene component and with the stereochemistry that yields the sterically most hindered products. Thus in additions to cyclopentadiene the large substituent $\mathbf{R_L}$ assumes the more crowded *endo* position,[32] and additions to *cis* alkenes yield the *syn* product (Fig. 1).

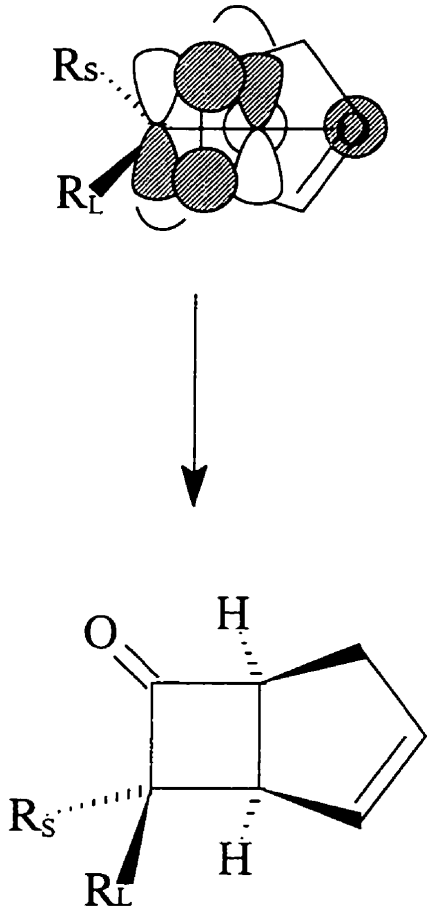



**Figure 1.** $[\pi 2_s + \pi 2_a]$ Transition state

The reaction has been described.[45] "The suprafacial-antarafacial [$\pi 2_S$ + $\pi 2_a$] transition state was proposed by Woodward and Hoffmann to account for the characteristics of the reaction.[33] The least hindered approach of reactants leads to the most hindered product. The p orbital of the electron deficient carbonyl carbon (perpendicular to the page in Figure 1) impinges directly on the alkene $\pi$ bond in the [$\pi 2_S$ + $\pi 2_a$] approach. This interaction is considered to provide a key stabilizing influence." [45] Houk[46] calculated the geometry and energy of the transition state for the [2+2] cycloaddition of ketene and ethylene at the MP2/6-31G* level and found a highly asymmetric geometry as shown in Figure 2. This geometry may give us a more clear picture of the approach of the ketene toward the alkene.

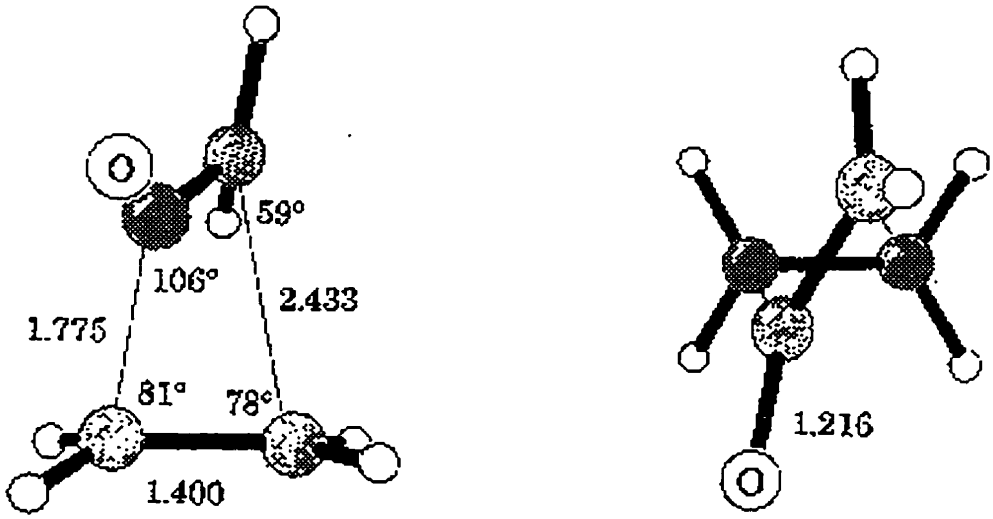



**Figure 2.** Calculated MP2/6-31G* Transition State for [2+2] Cycloaddition of Ketene and Ethylene[46]

An alternative approach has been proposed for the alkene-ketene addition (Fig. 3).[34] One end of the alkene double bond interacts with the ketene C=C $\pi$ bond, but the other end interacts with the perpendicular C=O $\pi$

bond of the carbonyl carbon. The reaction is described as a thermal [$\pi 2_S$ + ($\pi 2_S$ + $\pi 2_S$)] process. The predicted stereochemistry is the same as that for [$\pi 2_S$ + $\pi 2_a$] cycloaddition. No experimental distinction has been made between the two alternative routes.

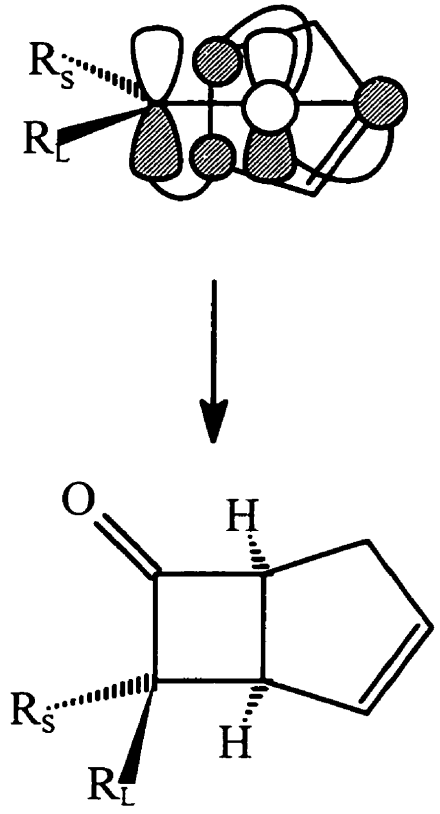



**Figure 3.** [$\pi 2_S$ + ($\pi 2_S$ + $\pi 2_S$)] Transition state

The most recent theoretical calculations for the ketene-cyclopentadiene reaction propose a more sophisticated electronic arrangement for this transition state, with the characteristics of an initial [4+2] cycloaddition[35].

The most distinguishing feature of the electronic structure of ketene is the presence of the highest occupied orbital (HOMO) perpendicular to the ketene plane (CC $\pi$ bond), and the lowest unoccupied orbital (LUMO) in the ketene plane (CO $\pi$ bond).[38] Analysis of the frontier molecular orbital (FMO)

interactions in the ketene-alkene cycloaddition shows that the [$\pi 2_S$ + ($\pi 2_S$ + $\pi 2_S$)] process is the right choice. Since the HOMO and LUMO of ketene expand orthogonally, their FMO interactions can be regarded as involving two one-center orbital interactions, so that the reactions are not concerned with [2+2] or [4+2] orbital symmetries. In some cases, one of two interactions becomes extremely important, leading to the zwitterionic intermediate.[35]

Analysis of the ketene resonance structures (Fig. 4) indicates that a substantial negative charge is placed on oxygen and on $C_\beta$ and that the positive charge is placed on $C_\alpha$, and shows that nucleophiles are expected to attack ketene perpendicular to the molecular plane at the $C_\alpha$, while electrophiles will approach in the plane at $C_\beta$.

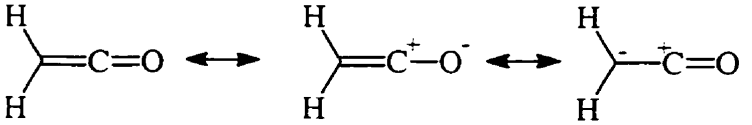


**Figure 4.** Resonance structures of ketene

Based on all the available evidence, there is support that many ketene cycloadditions proceed by a two-step process with initial formation of a bond between the ketene carbonyl carbon and the more nucleophilic alkene carbon to give a zwitterionic intermediate (Fig. 5).[1c] In some cases such zwitterions may be trapped depending on the lifetime of this intermediate. The advantage of this mechanism is that it can convincingly explain all the [2+2] cycloaddition process of ketene-alkene addition. The predicted stereochemistry is the same as that for concerted [$\pi 2_S$ + $\pi 2_a$] or [$\pi 2_S$ + ($\pi 2_S$ + $\pi 2_S$)] cycloadditions. It can easily predict the regioselectivity based on the stability of the forming zwitterionic intermediate. More important is the ability of the stepwise process

to rationalize failed [2+2] cycloadditions and other proven stepwise [2+2] cycloaddition processes. These include cases where the stereochemistry of the alkene is not preserved.

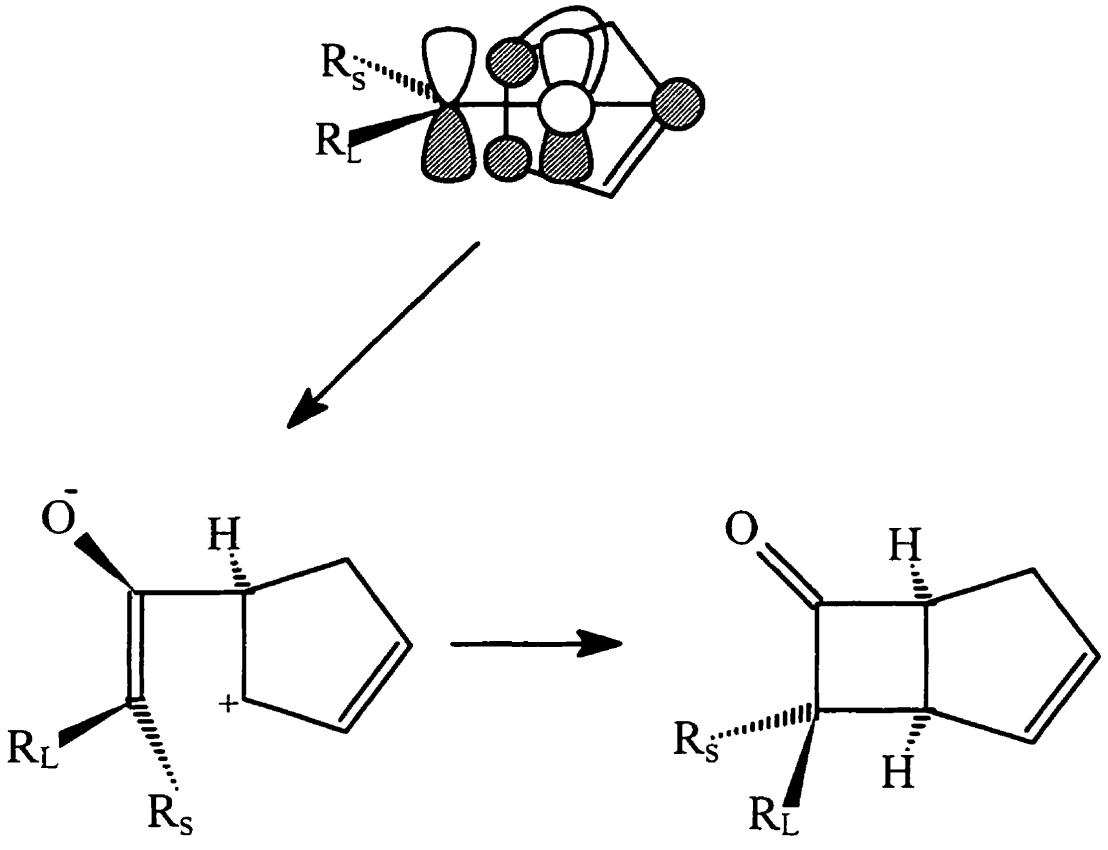


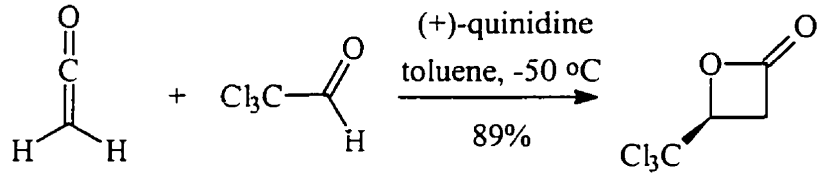

**Figure 5.** [2+2] Stepwise mechanism

Although only the mechanism of [2+2] addition between ketenes and alkenes has been discussed, the same argument can be used in all other ketene [2+2] cycloaddition process. In this thesis, we will use the stepwise mechanism to explain our results. As will be seen, it gives convincing explanations.

### 6.1.2 [2+2] Cycloaddition with aldehydes and ketones

The reaction of ketenes with aldehydes and ketones gives 2-oxetanones (β-lactones)[4] which are versatile and useful synthetic intermediates in the preparation of alkenes,[5] allenes,[6] carboxylic acid derivatives[7] including amino acids,[7k] and polymers.[8] Only systems bearing strongly electronegative substituents, such as carbonyl cyanide or perfluoroketones, react readily with simple ketenes in the absence of catalysts.[18] Catalysis is an important factor in most cycloadditions of ketenes to carbonyl compounds. Boron trifluoride etherate, aluminum chloride, and zinc chloride are generally useful.

A remarkable result was reported by Wynberg and Staring (Eq. 3),[36,37] namely the asymmetric cycloaddition between ketene and chloral in the presence of (+) - quinidine at - 50 °C in toluene yielding the corresponding β-lactone, with 98% *ee*.




(3)

Brady and Saidi[10a] reported that boron trifluoride etherate promoted cycloaddition of trimethylsilylketene[9] with saturated aldehydes gave rise to a mixture of *cis* - and *trans* -2-oxetanones without any stereoselectivity.[10] Yamamoto recently reported a new method for effecting such cyclization in a highly stereoselective manner under the influence of the exceptionally bulky methylaluminum bis(4-bromo-2,6-di-tert-butylphenoxide) as a promising Lewis acid (Fig. 6).[11]

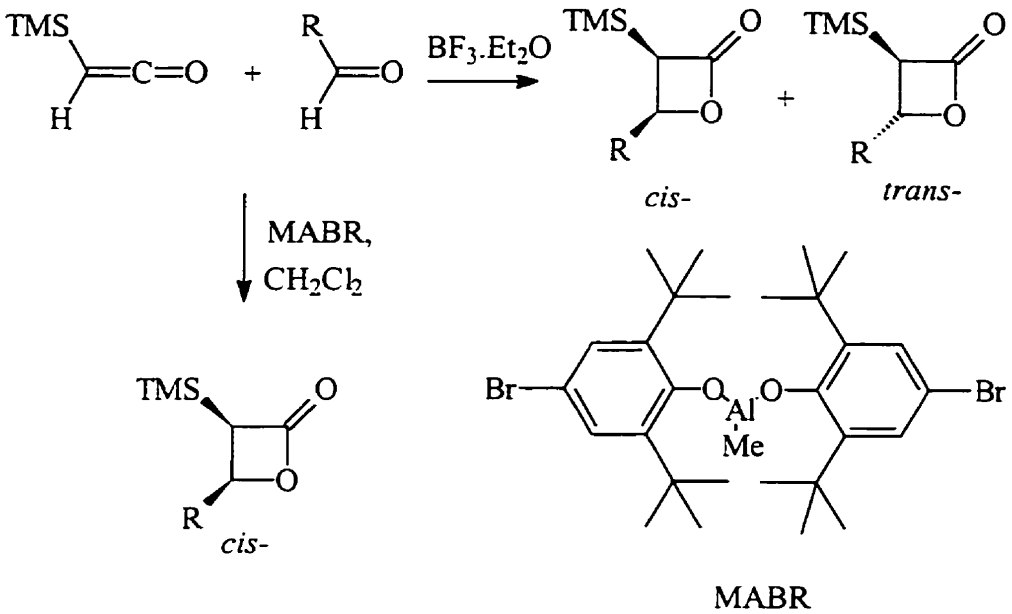



**Figure 6.** [2+2] Cycloaddition with aldehydes

It has been suggested that in the [2+2] cycloaddition of ketenes and aldehydes, the ketene behaves as a nucleophile.[12] Thus, the reaction occurs *via* the highest occupied molecular orbital (HOMO) of the ketene (CC $\pi$ bond) and the lowest unoccupied molecular orbital (LUMO) of the aldehyde. The use of a Lewis acid, upon complexation with the aldehyde, will induce a decrease in the activation energy of the reaction, and the Lewis acid may coordinate to the aldehyde using the lone pair *anti* with respect to the substituent R. The [2+2] cycloaddition leads in general to a mixture of *cis* - and *trans* - 3, 4-disubstituted 2-oxetanones with a preference for the *cis* -isomers.[12c]

The thermal decomposition of β-lactones results in a stereospecific *cis* - elimination.[23] The rate of decarboxylation is higher for the *trans* -derivatives than for the cis -derivatives[24] and is highly dependent on the nature of the substituent at the $C_4$ position of the 2-oxetanone; electron-donor groups

facilitate the decarboxylation while electron-withdrawing groups slow the rate of the reaction.[19a] As for the mechanism, it is still under investigation; and was formerly believed to be concerted[25a] until, in 1979-1980, Nishida and Imai[25b,c] and Mulzer[25d,e] independently argued, on the basis of kinetic studies, in favor of a mechanism involving a stepwise fragmentation through a zwitterionic intermediate (Fig. 7).

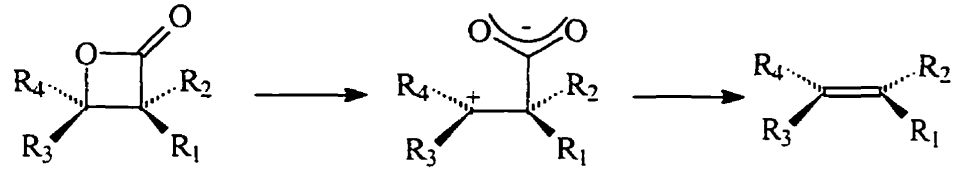


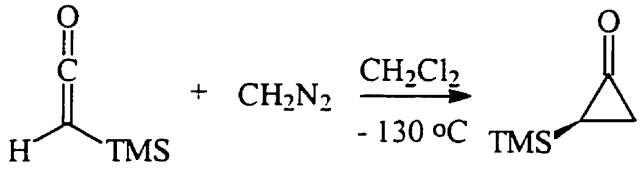

**Figure 7.** Mechanism of β-Lactone Decarboxylation

### 6.1.3 [3+2] Cycloadditions

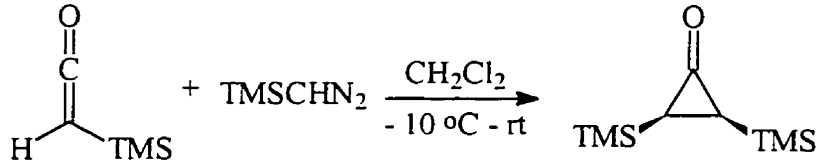
Both the carbonyl and the carbon-carbon double bonds of ketenes react by 1,3-dipolar pathways with 4-electron, 3-center bonds, including the reactions with azomethine ylides,[13] alkyl- and arylnitrones,[14] nitrile oxides,[15] diazomethane,[16] α-diazoketones,[19] azides,[20] ozone,[21] and other polar reactants like 3-oxidopyridinium betaine.[22]

An interesting reaction is that with diazomethane or its derivatives to give cyclopropanones. It is a useful way for making cyclopropanones. This reaction was first explored by Turro and Hammond[16c] and by de Boer and coworkers.[16d] In general the cyclopropanones which have been prepared in this way are too unstable to be isolated, and are trapped by alcohols, water, amines or as other carbonyl addition products. An example of stable species is the preparation of silylated or germylated cyclopropanones that has been provided

by Zaitseva and his coworkers,[16f,g] who added diazomethane in ether or methylene chloride at -130 °C to equimolar amounts of trimethylsilyl or trimethylgermylketene (Eq. 4). The cyclopropanones made this way were purified by vacuum distillation and were relatively stable at 5 °C. More recently these authors[16j,k] prepared the more stable bis(trimethylsilyl)cyclopropanone by adding trimethylsilyldiazomethane to one equivalent of trimethylsilylketene at - 10 °C, and subsequently warming the reaction mixture to room temperature (Eq. 5). The product bis(trimethylsilyl)cyclopropanone could be purified by fractional distillation without polymerization.



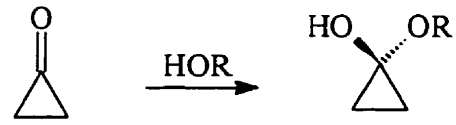

(4)



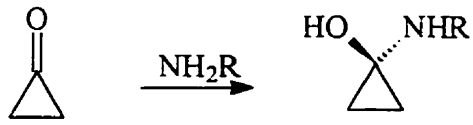

(5)

The reaction of α-diazoketones with ketenes gives furanone derivatives, in a synthetically useful reaction catalyzed by Cu (II).[19]

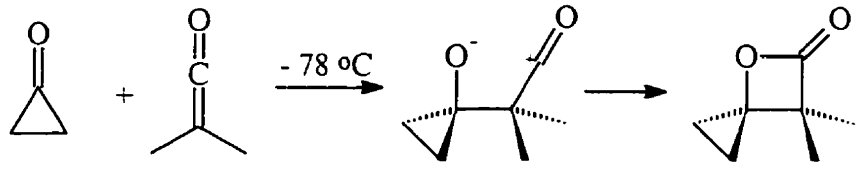
Two of the typical reactions of cyclopropanones, namely the addition of nucleophiles (Eq. 6,7), and the cycloaddition with ketenes (Eq. 8) are helpful to understand the reactions we have studied.




(6)




(7)




(8)

First, the carbonyl carbon of cyclopropanone is very reactive toward nucleophiles. In other words cyclopropanones are very good electrophiles, and they react with water, alcohol, and amines very easily to give the carbonyl adducts. An interesting example of these reactions is the reaction with ketenes. Turro and his coworkers[17] reported that dimethylketene and 2,2-dimethylcyclopropanone, upon mixing at - 78 °C, gave quantitatively the [2+2] cycloaddition product. As discussed above usually only carbonyl groups bearing strongly electronegative substituents, such as carbonyl cyanide or perfluoroketones, react readily with simple ketenes in the absence of catalysts.[18] As cyclopropanones are known to be good electrophiles, it is relatively easy for them to react with a ketene to generate the zwitterion and then cyclize to the product (Eq. 8) or to react by a concerted reaction with dipolar character represented by the zwitterion in Eq. 8.

All these reactions may be understood by considering the highly strained carbonyl group in cyclopropanones. In a normal ketone molecule, the two

carbon substituents are separated by an angle of about 120°, consistent with an $sp^2$ hybridized carbonyl carbon. This angle has been limited to a value near 60° by the cyclopropane ring in cyclopropanones and therefore the molecule is highly strained. To reduce this strain there is a longer C(2)-C(3) bond in the cyclopropanone than that in normal cyclopropanes, which means the tautomers **b** and **c** as shown in Fig. 8 have some contribution to the structure of cyclopropanones. All the reactions discussed above could be explained as proceeding to release this strain and transform an $sp^2$ carbonyl carbon to a saturated $sp^3$ carbon. Cyclopropanones also react as 1,3-dipolar reagents which release the strain by opening the cyclopropane ring. Lengthening the C-C bond releases strain, giving zwitterionic character as shown in **c**.

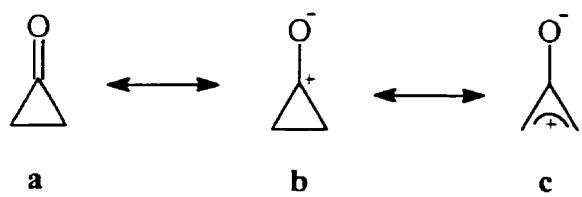
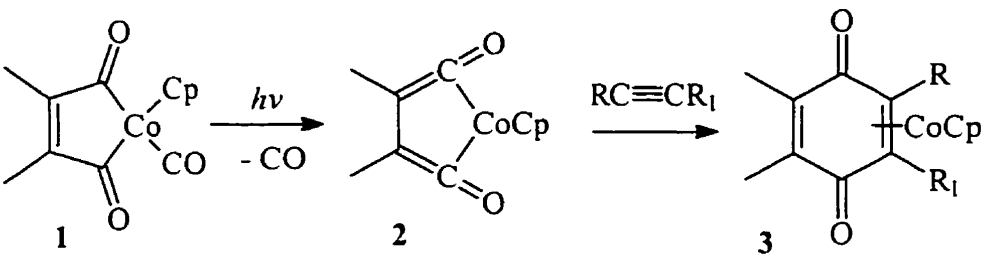



**Figure 8.** Resonance structures of cyclopropanone

### 6.1.4 Cycloaddition reactions of bisketenes

Bisketenes have been rare species and only a few cycloaddition reactions of this family have been studied (see Chapter 1). The metal complex **2** reacts by a net [4+2] cycloaddition to form quinone complexes **3** (Eq. 9).[39a]




Cp = cyclopentadienyl (9)

Photolyses of cyclobutene-1,2-diones such as **4** in the presence of cyclopentadiene were proposed to give bisketene **6** which reacted by [2+2] cycloaddition to form the unobserved ketenes **7** which rearranged to the spirocyclopropyl $\Delta^{\alpha,\beta}$-butenolide adducts **8** (Fig. 9).[39b] Two possible mechanisms for the formation of **8** are shown, as previously discussed in Chapter 1, Figure 7.

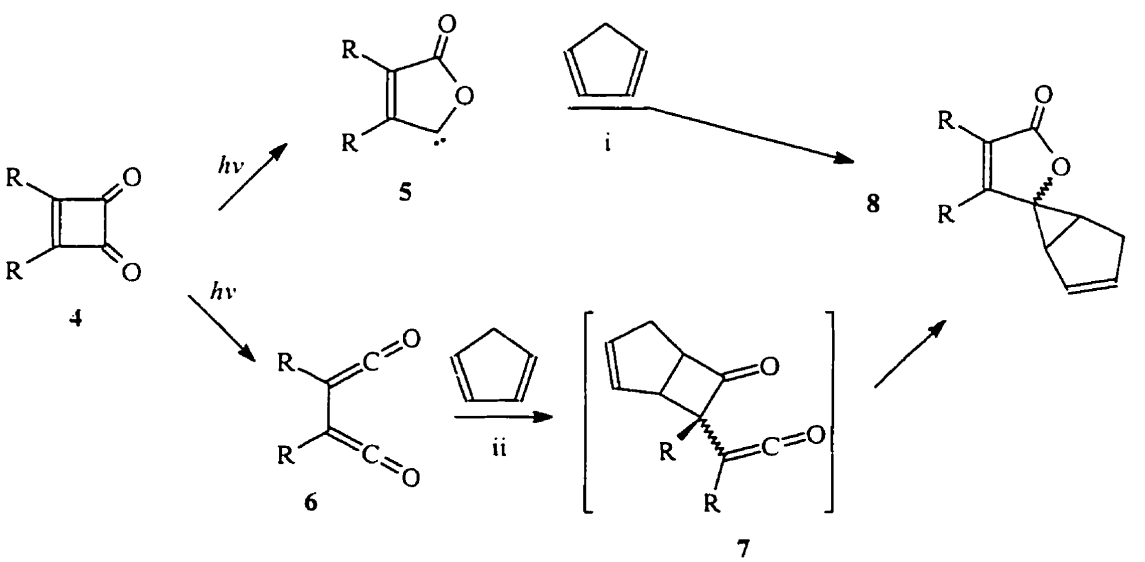
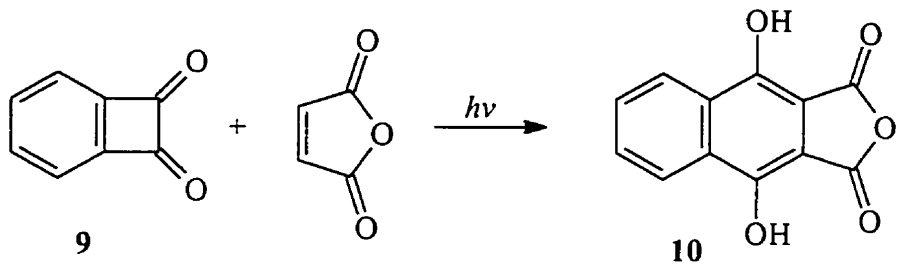
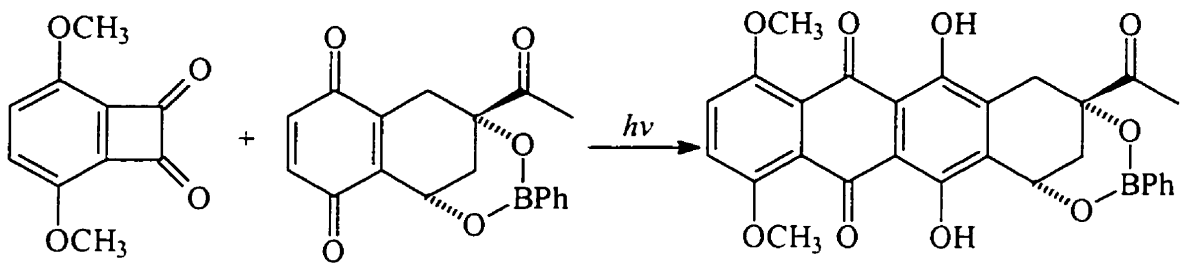



**Figure 9.** Mechanisms of cycloaddition reaction between bisketene and cyclopentadiene

The dione **9** was reported to form a bisketene on photolysis which gives a [4+2] cycloaddition with maleic anhydride (Eq. 10),[39c-e] and the similar reaction of **11** with substituted benzoquinones[39f] has been utilized in the synthesis of daunomycinones (Eq. 11).

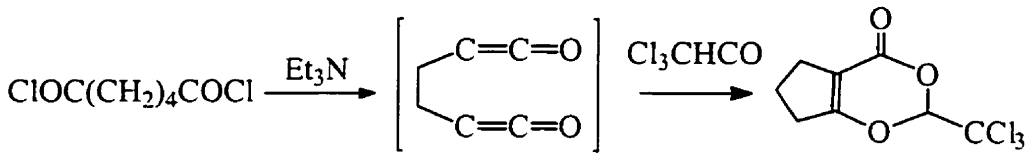



**9** **10** (10)




**11** **12** 72% (11)

Reaction of adipyl chloride with triethylamine in the presence of chloral gave **14**, and this could have involved reaction of the bisketene **13**, but as simple acyclic 1,4-bisketenes such as **13** are unknown stepwise routes are more likely (Eq. 12).[39g]

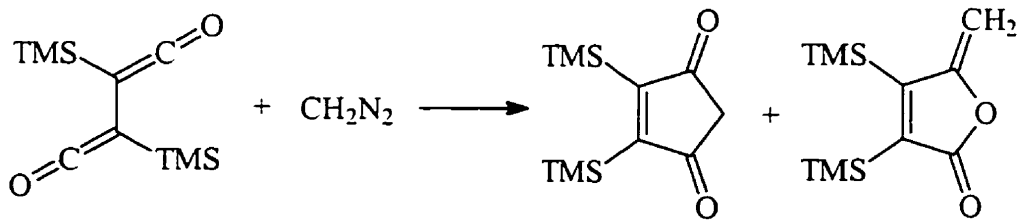



13 14 (12)

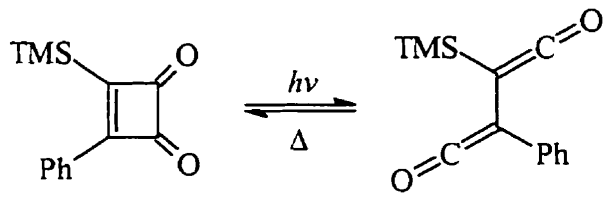
## 6.2 Results and discussion

### 6.2.1 [4+1] Cycloaddition Reaction of Bisketenes with Diazo Compounds

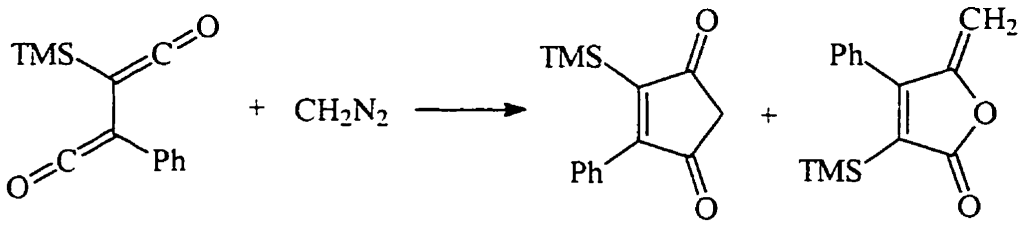
Reaction of diazomethane with the stable bisketene 2,3-bis(trimethylsilyl)-1,3-butadiene-1,4-dione (**15**) and with the bisketene 2-trimethylsilyl-3-phenyl-1,3-butadiene-1,4-dione (**19**) formed from photolysis of the dione **18** (Eq. 14), gave 4-cyclopentene-1,3-dione (**16** and **20**) and 5-methylene-2(5H)-furanone (**17** and **21**) derivatives, respectively (Eq. 13,15).




15 16 22% 17 63% (13)




**18** **19** (14)



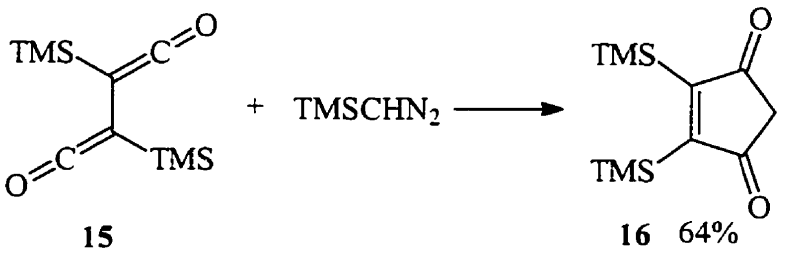

**19** **20** 56% **21** 18% (15)

The structures of these compounds were assigned by their spectroscopic properties. The $^{13}C$ NMR spectrum of the dione **16** clearly indicated the carbonyl groups at δ 205.80, and the conjugated C=C double bond carbon signal at 175.48. The presence of carbonyl groups was confirmed by the infrared absorption at 1730 and 1690 $cm^{-1}$. The dione **20** has similar spectra to those of the dione **16**. The $^{13}C$ NMR spectrum of the dione **20** indicated the carbonyl groups at δ 200.73 and 203.96, and the C=C double bond at δ 161.48 and 168.44. The infrared spectrum also showed the absorption of the carbonyl groups at 1733 and 1696 $cm^{-1}$. The presence of the phenyl group has shifted the carbonyl and the C=C double bond carbon absorptions upfield and the infrared absorption to higher frequency. The $^{13}C$ NMR spectrum of **17** clearly indicated the presence of the lactone carbonyl at δ 173.01 and the C=C double bond carbons at δ 97.04, 144.22, 159.63, and 165.82. The presence of the lactone carbonyl was confirmed by the infrared absorption at 1744 $cm^{-1}$. The

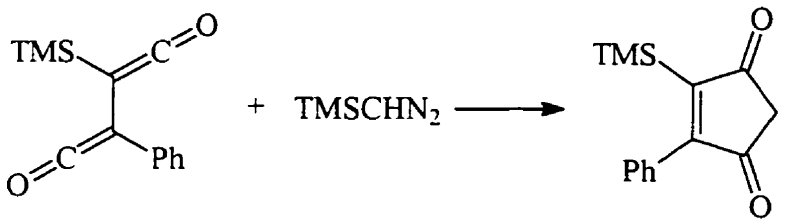
$^1$H NMR showed the typical coupling pattern of a terminal methylene group with a coupling constant of 2.50 Hz. The $^{13}$C NMR spectrum of **21** clearly indicated the presence of the lactone carbonyl at δ 169.44 and the C=C double bond carbons at δ 98.20, 131.39, 142.85, and 157.63. The presence of the lactone carbonyl was also confirmed by the infrared absorption at 1746 cm$^{-1}$. The $^1$H NMR also showed the typical coupling pattern of the methylene group with a coupling constant of 2.56 Hz. The position of the exocyclic methylene group in **21** was expected to be on the same side as the phenyl group based on the expected reaction pathway (see below) and was also confirmed by comparing the carbonyl carbon $^{13}$C NMR shifts of **17** and **21** which show an upfield shift of 3.57 ppm by the phenyl group conjugative effect without much effect on the methylene carbons at δ 97.04 and 98.20, respectively.

Attempted reaction of the bisketene **15** with $CH_2I_2$ and Zn activated by flame drying or sonication was not successful, as no reaction was observed. In the reaction with $(CH_3)_2S^+CH_2^-$ generated from the reaction of $(CH_3)_3SI$ with KH (generation of the reagent was confirmed by the reaction with benzaldehyde giving the product styrene oxide), a complex product mixture was formed, from which no stable products could be isolated. Reactions with the more stable diazo compounds $TMSCHN_2$ and $PhCHN_2$ were much more simple, with only the 4-cyclopentene-1,3-dione derivatives **16**, **20**, and **22** being isolated (Eq. 16-18) (Note the products **16** and **20** were obtained after loss of the TMS group during the course of the reaction and work up). However no reaction was observed with the much less reactive $N_2CHCOOEt$, even upon refluxing in chloroform. Metal catalysis of the process was not examined. For the more reactive diazohexane (n-$C_5H_{11}CHN_2$), high

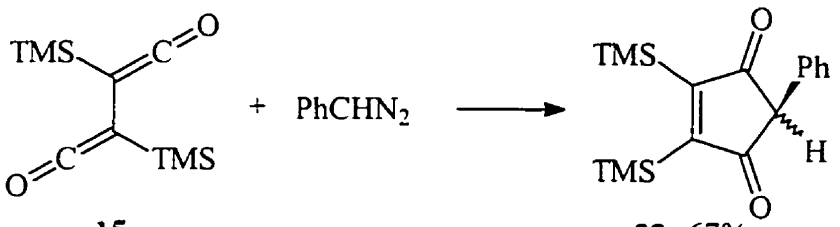
molecular weight unidentified products were obtained when excess diazohexane was used.




**15** **16** 64% (16)




**19** **20** 69% (17)




**15** **22** 67% (18)

The formation of these products may be explained by a process involving initial attack of the diazomethane on the more activated of the ketenyl groups (Fig. 10), which is the phenyl substituted moiety for **19** (R=Ph), to form the stereoisomeric zwitterions **A** or **B**, depending upon whether the diazomethyl attacks the ketenyl group *anti* or *syn* to the substituent R, respectively. In previous studies it has been concluded that nucleophilic additions to ketenes occur *syn* to the smaller group.[41] In the present case

inspection of the structures suggests that approach of the nucleophilic diazoalkane may be more facile *syn* to the ketenyl group $Me_3SiC{=}C{=}O$. Ring closure of the zwitterions **A** and **B** after loss of nitrogen would lead to the cyclopentenediones or the methylenefuranones, respectively. When the diazomethane bears a bulky $Me_3Si$ or Ph substituent the size of the reagent evidently permits only attack *anti* to the large group R ($Me_3Si$ or Ph), so that the less hindered approach is syn to the $Me_3SiC{=}C{=}O$ substituent. Only for $CH_2N_2$ is some attack *syn* to the R groups feasible, leading to some formation of methylenefuranones. Consistent with this interpretation, it has been previously proposed[39b] that attack on **6** occurs preferentially from the side of the RC=C=O group.

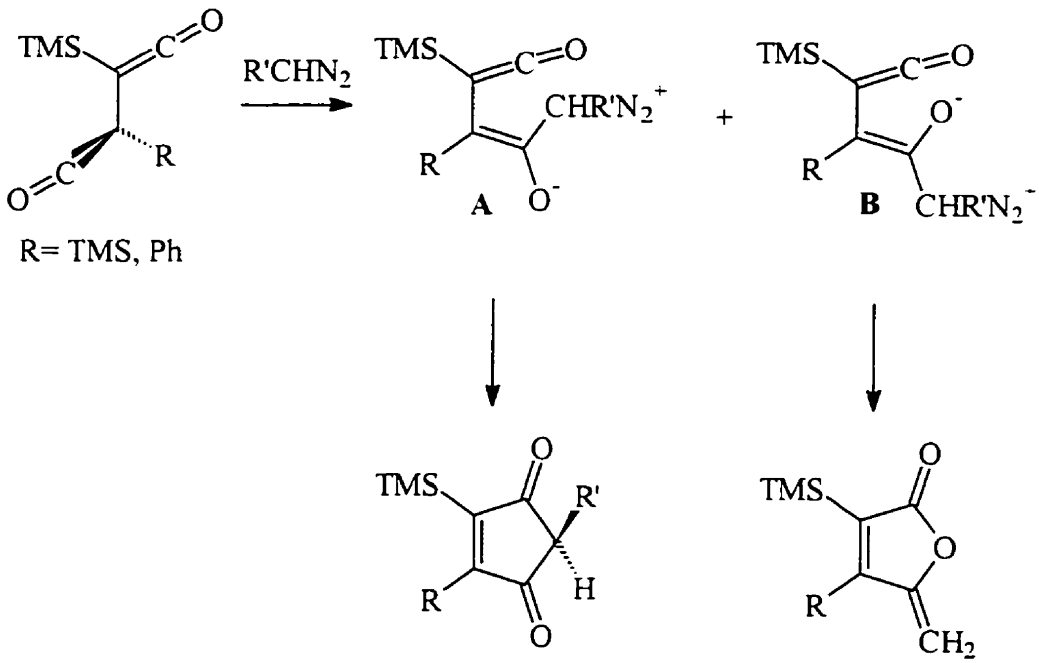



**Figure 10**

The formation of the very reactive ketenyl cyclopropanone intermediates (Fig. 11) from **A** and **B** can not be excluded although their formation appears highly unlikely. No direct evidence for the existence of such intermediates was

obtained and the formation of such molecules would result in a highly strained cyclopropanone bearing a reactive ketenyl group, especially in the cases where R' is a TMS or Ph group. The carbonyl oxygen of such cyclopropanones could attack the ketene group at $C_\alpha$ forming the zwitterion (path 1, Fig 11) and then rearrange to the final product. As mentioned before, the cyclopropanone could also give a ring opened 1,3-dipolar species (path 2, Fig 11) which would be stabilized by the phenyl substituent, and this route could give cyclization with the ketene C=C double bond to give the cyclopentenedione derivatives.

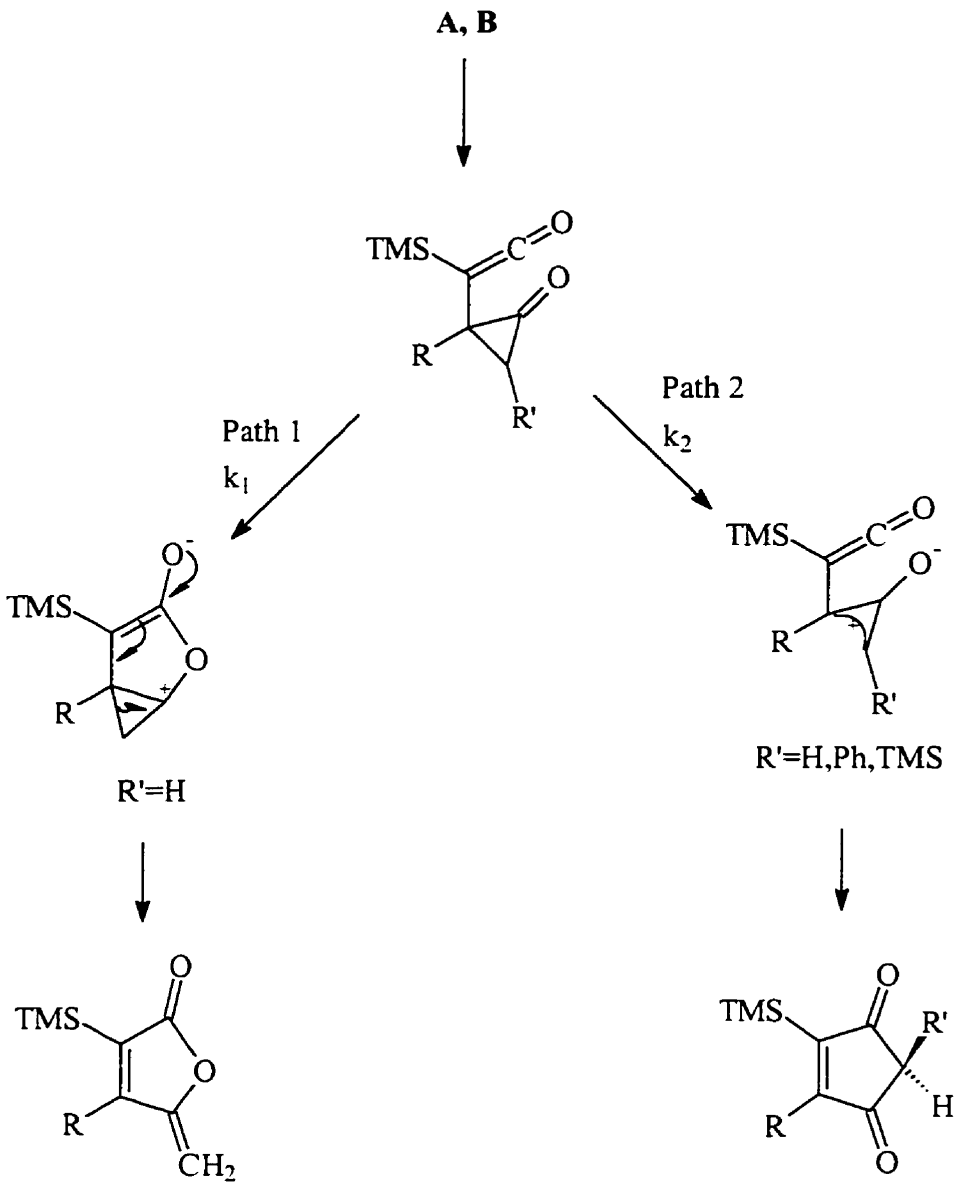



**Figure 11**

### 6.2.2 [2+2] Cycloaddition reactions of bisketenes with aldehydes

To test whether the bisketene **15** might have the property of a 1,3-butadiene in [4+2] cycloaddition reactions, the reaction with dienophiles, such as $MeO_2CCCCO_2Me$, $CH_2$=CHOEt, TMSCCTMS, $CH_3CH$=O, and

PhCH=NPh (Fig. 12), was examined, but no new products were observed on heating to 150 °C.

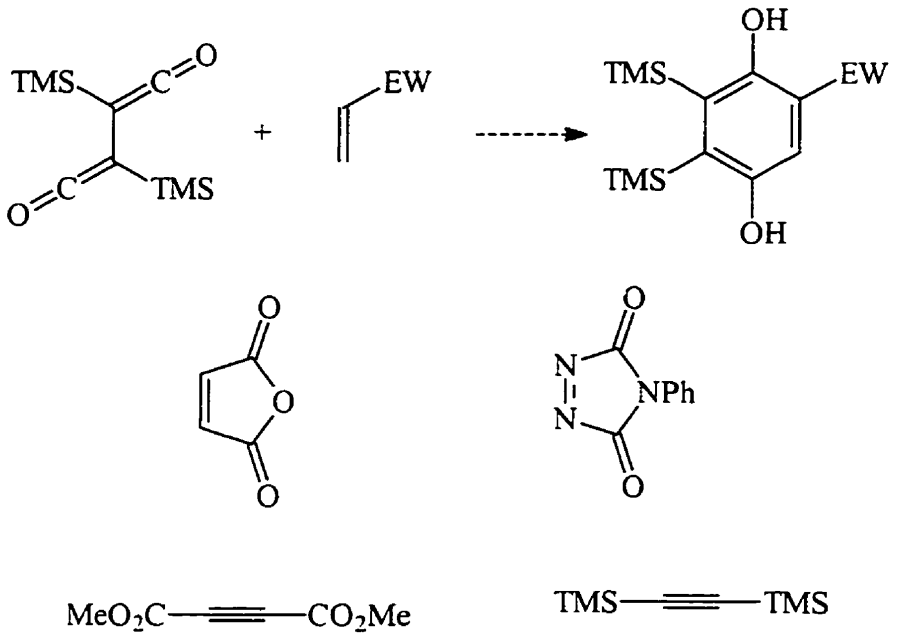
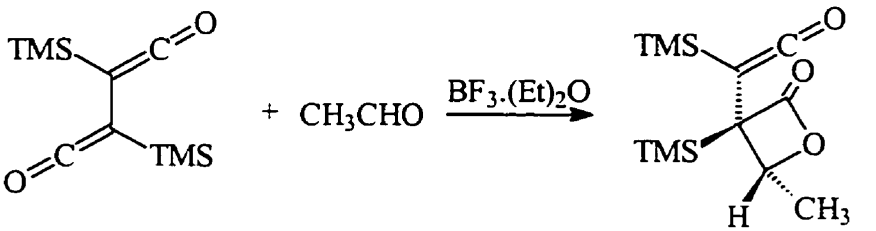


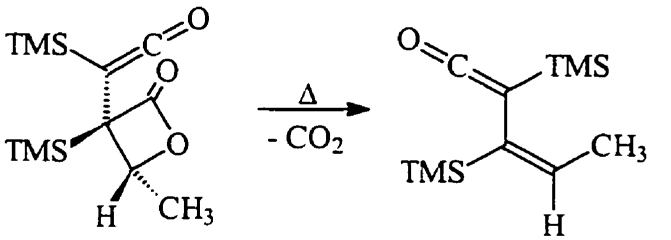

**Figure 12**

However bisketene **15** was observed to react with acetaldehyde with boron trifluoride etherate complex as a catalyst at room temperature. The [2+2] product (**23**) was the only observed product, and was isolated from the reaction mixture in good yield (82%) after recrystallization (Eq. 19). The product **23** is not stable when heated to reflux in chloroform and during attempted purification by gas chromatography, it lost $CO_2$ to give the vinyl monoketene **24** (Eq. 20). The structures of **23** and **24** were established by their spectroscopic properties and chemical behavior. The presence of the ketene moieties of **23** and **24** was proven by their $^{13}C$ NMR absorption at δ 11.38 or 17.21 for the β-carbon and at δ 178.60 or 176.61 for the carbonyl carbon, respectively, and was confirmed by the infrared absorption at 2084 or 2080 $cm^{-1}$, respectively. The presence of the β-lactone of **23** was proven by the $^{13}C$

NMR at δ 171.38 of the carbonyl carbon and was also confirmed by infrared absorption at 1796 $cm^{-1}$. The stereochemistry of **23** was determined by an nOe experiment in which irradiation of the ketenyl TMS group resulted in 0.95% and 0.63% enhancement of the Me and CH resonances, respectively, while irradiation of the lactone TMS group resulted in 1.01% and 13.6% enhancement of the Me and CH resonances, respectively. It was found that monoketene **24** did not react with $TMSCHN_2$ at room temperature. The lower reactivity of **24** compared to **15** is consistent with the known reactivity of **15** with nucleophiles, in which the reactivity of the first ketenyl group is about $10^3$ greater than the second.[40] Also vinylketenes are stabilized relative to other ketenes, whereas 1,2-bisketenes are destabilized relative to other monoketenes.[1c] The monoadducts are also more crowded, further reducing their reactivity. However, α-$Me_3Si$ vinylketenes do give [4+2] cycloaddition reactions with dienophiles.[44] The major reason bisketenes do not give [4+2] cycloaddition reactions may be because the bisketenes have nonplanar conformations as discussed in Chapter 3, resulting in the difficulty for their forming a coplanar transition state. The second reason is the LUMO orbital at $C_\alpha$ is in the bisketene plane, and therefore is not oriented properly for [4+2] reaction with nucleophilic dienophiles, and the HOMO orbital is concentrated at $C_\beta$, and does not promote [4+2] cycloadditions with electrophilic dienophiles (Fig. 13).




**15** **23** 82% (19)




**23** **24** 35% (20)

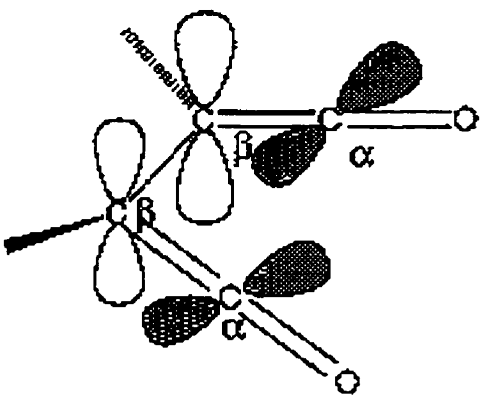
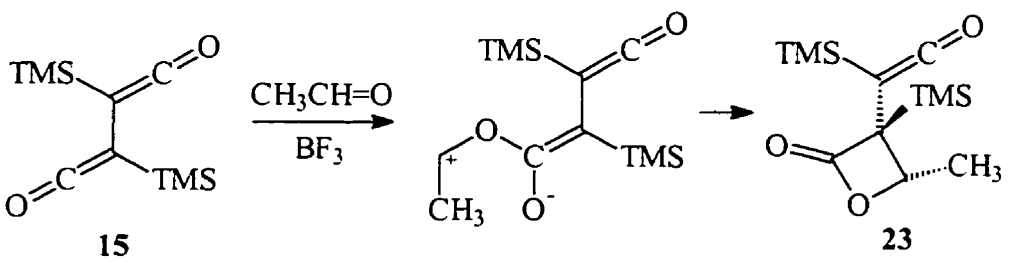



**Figure 13.** HOMO and LUMO orbitals of bisketenes

The formation of **23** could take place *via* an initial nucleophilic attack on the bisketene catalyzed by $BF_3.Et_2O$ giving an intermediate zwitterion (Fig 14), consistent with the known reactivity of the bisketene **15** with nucleophiles.[40] Formation of the intermediate zwitterion by attack anti to the TMS group is favored sterically as discussed above. This zwitterion could collapse to **23** to avoid the steric interaction between methyl group and the bulky $Me_3Si$ group. This stereoselectivity can also be rationalized as resulting from the more favorable of the four possible stereochemistries of approach **C**, **D**, **E** and **F** (Fig 15). In the transition states **E** and **F**, there are serious steric interactions between the BF3 group and the trimethylsilylketenyl group or $CH_3$ group and the trimethylsilyl-ketenyl group which would lead to the disfavored *cis-* product, based on the twisted conformation of the bisketene. The transition states **C** and **D** are expected to be favored as they appear to have less steric interaction, and would give the observed *trans-* product. The resulting product is more crowded than the reactant, contributing to the absence of further reaction under the reaction conditions.




15 23

**Figure 14**

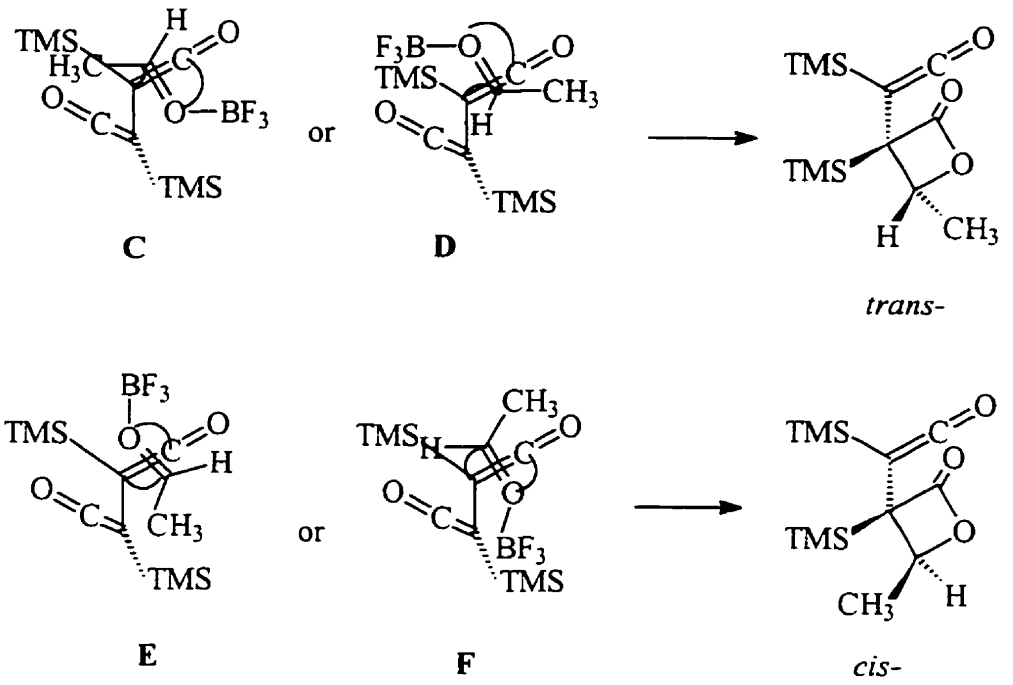
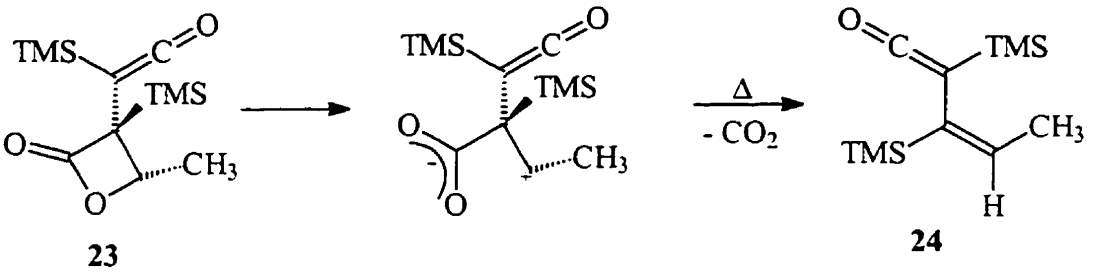



**Figure 15**

The ketenyl-β-lactone **23** was easily decarboxylated to give the vinylketene, and this reaction may proceed by a zwiterionic intermediate which is stabilized by the β-trimethylsilyl group (Fig 16). The resulting vinylketene has promise as a versatile synthetic intermediate, and would be difficult to make by other methods. These results demonstrate that introducing a silyl group into the 2 position of the β-lactone ring could facilitate the formation of carbon dioxide and alkene products which could open a potentially useful new synthesis beginning with bisketenes.




23 24

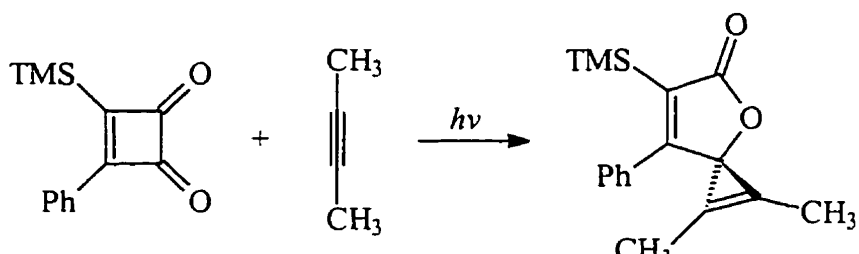
**Figure 16**

The attempted use of boron trifluoride etherate complex as a catalyst for the bisketene reaction with the imine PhCH=NPh was not successful, as the bisketene was consumed, but gave a complex mixture of products from which no pure materials were isolated by chromatography. It is worth mentioning here that the bisketene reacted with DMSO used as solvent in other attempted reactions and gave uncharacterized products.

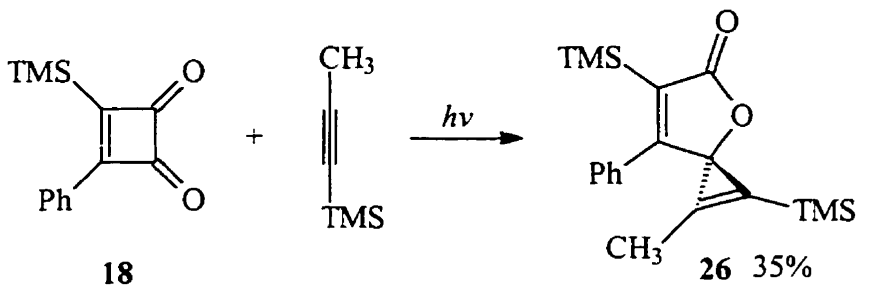
### 6.2.3 Cycloaddition reactions of bisketenes with alkynes

2-Phenyl-3-trimethylsilylbisketene **19** generated from the dione by photolysis (Eq. 14) was found to react with acetylenes to give the spiro(cyclopropenyl) furanone derivatives **25**, **26** and **27** (Eq. 21-23). The reaction was carried out by photolysis of the dione **20** with an excess of an alkyne at 6 °C. Continuous photolysis was used to maintain the concentration of the bisketene **19** during the reaction in order to avoid reformation of the dione **20**. The products could result from a first formed ketenyl cyclobutenone by [2+2] cycloaddition, followed a ketenyl ketone rearrangement (Fig. 9), or by formation of a zwitterion which undergoes cyclization, as illustrated below (Fig. 17). The structures of these compounds were assigned according to their spectroscopic properties. The presence of the lactone carbonyl groups of **25**,

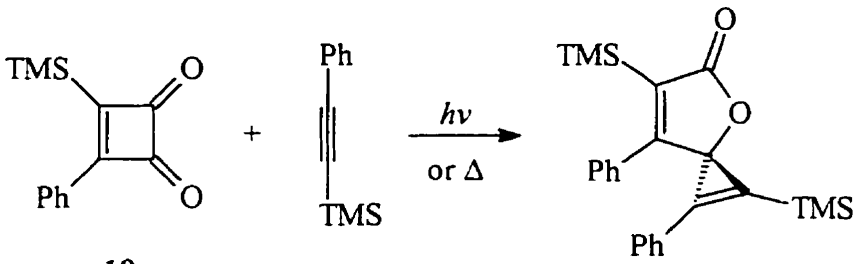
**26** and **27** was proved by their $^{13}C$ NMR which showed absorption at δ 176.98, 178.38, 177.68, respectively, and was confirmed by their infrared absorptions at 1728, 1730, and 1730 $cm^{-1}$, respectively. The presence of the β-carbons of the conjugated C=C double bond was proved by their $^{13}C$ NMR signals at δ 174.58, 174.56, and 174.45, respectively and was also confirmed by the UV absorption of **25** at $\lambda_{max}$ 248 nm. The tertiary carbon $^{13}C$ NMR signals of **25**, **26** and **27** were not detected. This could be because the highly strained structure resulted in long relaxation times. The location of the spirocyclopropenyl group on the same side as the phenyl group was assigned based on mechanistic considerations, with initial reaction of the more reactive phenyl substituted ketene with the alkynes (see Fig. 17) and was also confirmed by comparing with the spectra of 3-trimethylsilyl-4-phenyl-5,5-dibromo-2(5H)-furanone in Chapter 5. The product **27** was also generated by heating the dione with the phenyl trimethylsilylacetylene in a sealed vial at 120 $^0C$, confirming that in this case the cycloaddition can occur by a thermal reaction. It may also be inferred that the formation of **25** and **26** also occurs by thermal reactions of the bisketene **19** formed photochemically, but this is not proven. Furthermore bis(trimethylsilyl)bisketene **15** was found not to react with alkynes under these reaction conditions.




**18** **25** 43% (21)

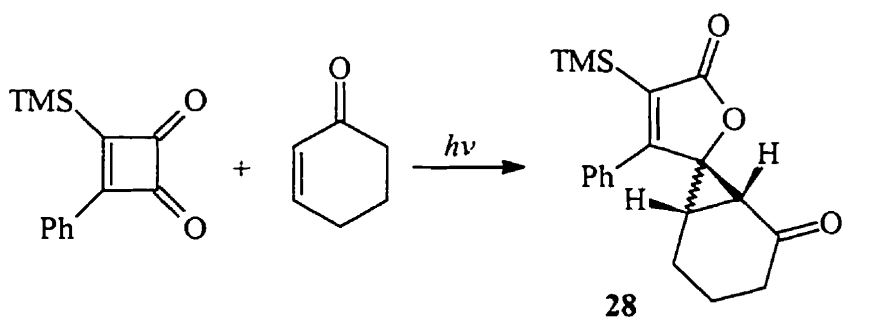



**18** **26** 35% (22)



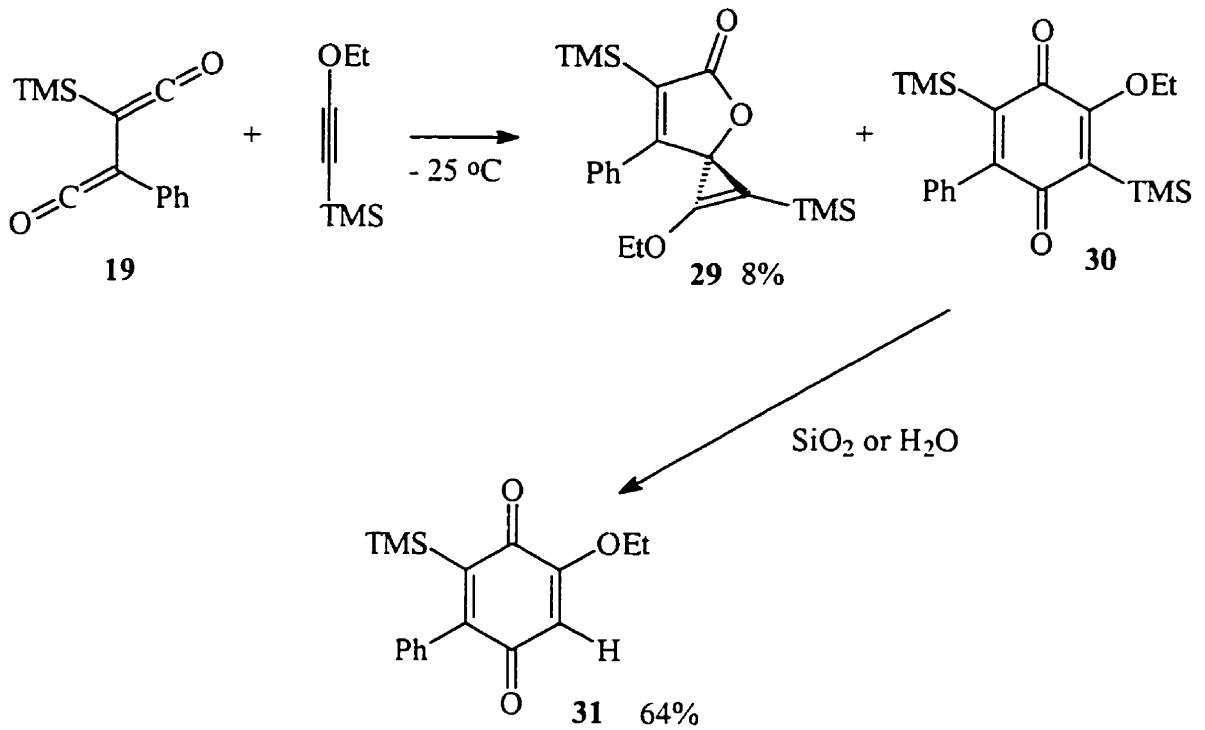

**18** **27** 37%, 42% (23)

The bisketene **19** generated photochemically reacted with cyclohexenone to give **28**, of undetermined stereochemistry, in 11% yield (Eq. 24). This process is unusual in that it involves reaction of an electrophilic alkene with a ketene. The intramolecular reaction of ketenes with conjugated ketones is known from the work of Agosta[42b] and Becker[42a], and these results were explained as photoreactions of the conjugated ketones, with the ketenes simply providing the C=C π bond needed for these reactions.




**28** (24)

The bisketene generated from the dione was found to react with a more active acetylene at - 25 °C. The reaction was carried out by first generating the bisketene **19** photochemically and then adding the reactant ethoxy trimethylsilyl acetylene at - 25 °C. After reaction overnight, the two products **29** and **30** were observed by $^{1}H$ NMR with the quinone **30** as the major product (Eq. 25). These products were quite sensitive and the reaction was not consistently reproducible. In one case quinone **30** was separated chromatographically and characterized but this compound was very unstable and could only be stored at low temperature in solution for a few days. On other attempts at chromatography on silica gel only the desilylated quinone **31** was obtained (Eq. 25). Quinone **31,** which could only be stored in solution for about one week at low temperature, also decomposed to other unidentified products when kept neat at room temperature. The structures of **30** and **31** were assigned based on their spectroscopic properties. The $^{13}C$ NMR spectra of **30** and **31** each showed two carbonyl carbon signals, at δ 191.47 and 203.99, and 187.28 and 199.99, respectively. The presence of the carbonyl groups was further confirmed by the mass spectra which showed typical peaks for losing two carbonyls for **30** at *m/z* 344 ($M^{+}$-CO, 33) and 316 ($M^{+}$-2CO, 40), and for **31** at *m/z* 272 ($M^{+}$-CO, 95) and 244 ($M^{+}$-2CO, 40). The structure of **31** was further confirmed by an nOe study which showed strong nOe between $CH_2$ of the ethyl group with the single ring proton, and between 2 H of the phenyl group with the TMS group. The regiochemistry of this compound also follows based on the expected reactivity of the phenylketene moiety with the alkyne (Fig. 17).




(25)

The mechanism for this reaction could involve an initial stepwise ketene [2+2] reaction resulting in a ketenylcyclobutenone which undergoes a ketenyl ketone rearrangement (see Fig 9) to give either the spirocyclopropenyl furanone derivative or the quinone product. Alternatively reaction of **19** could lead to the stereoisomeric zwitterions **G** and **H**, which could cyclize to **29** and **30**, respectively (Fig. 17).

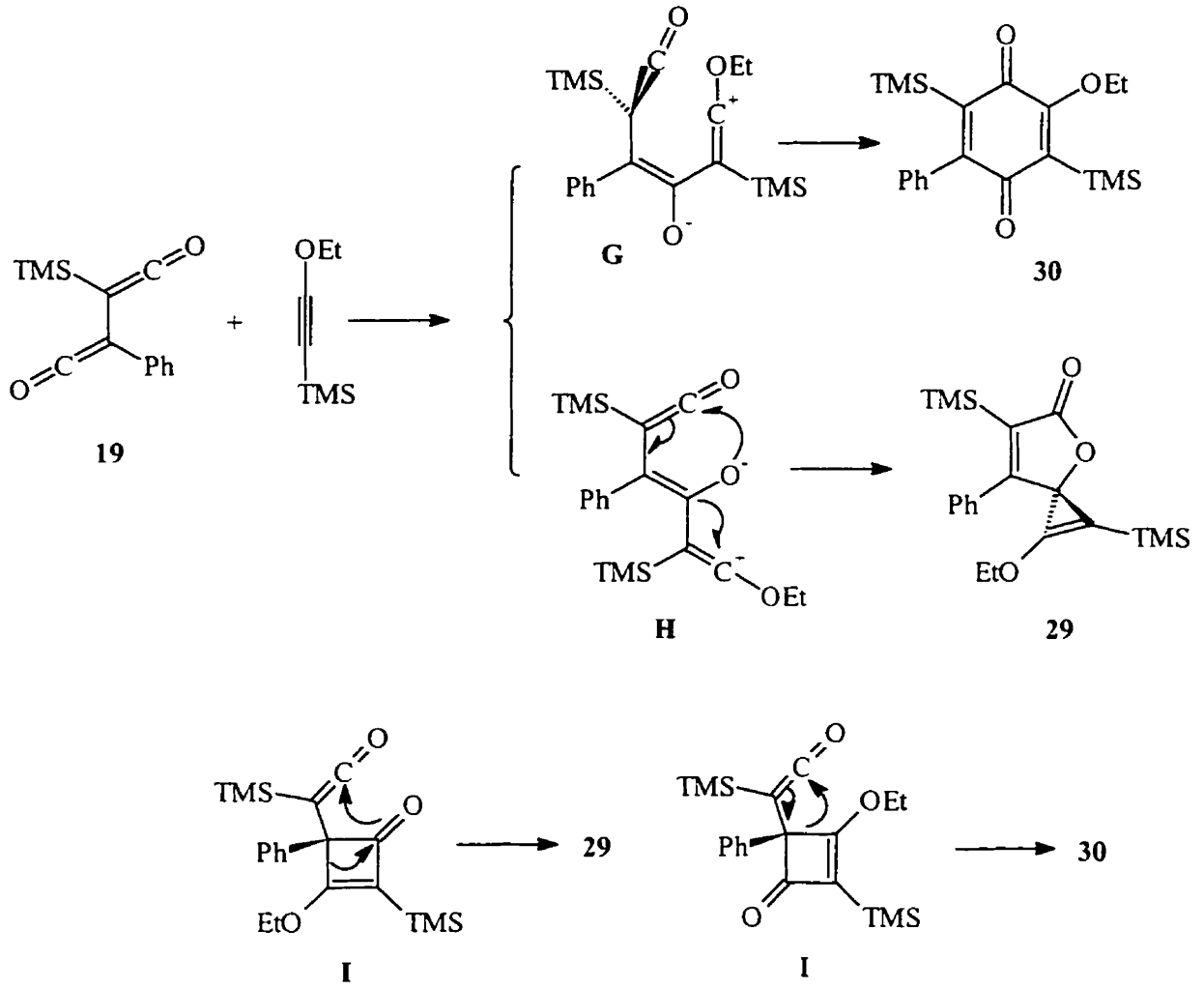



**Figure 17**

The quinone **30** is very sensitive to water, and this can be explained by protonation with the formation of a carbocation stabilized by the EtO group and by the β-$Me_3Si$, followed by loss of the silyl group to give the observed quinone **31** as the product (Fig 18).

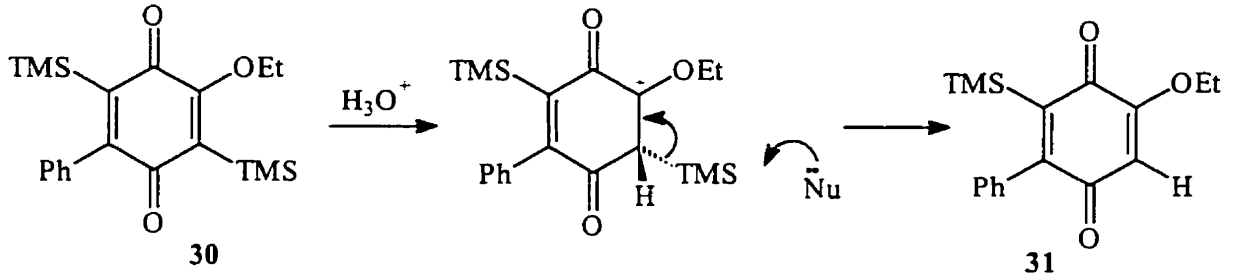



**Figure 18**

In conclusion, bisketenes were found to react with diazo compounds to give furanone and cyclopentenedione derivatives. These reactions could be explained by a stepwise mechanism or by the formation of highly reactive intermediate ketenyl cyclopropanones.

Bisketenes were found not to give Diels-Alder reactions with various dienophiles, and this may be because the twist conformation of the bisketenes and the low coefficient of the HOMO at $C_\alpha$ render such processes difficult. However, the bis(trimethylsilyl)-1,2- bisketene was found to react with acetaldehyde to give a ketenyl lactone which upon heating gave a vinyl ketene after loss of $CO_2$, and this reaction occurred in a highly stereoselective manner.

The more reactive phenyl trimethylsilyl 1,2-bisketene was found to react with electron-rich alkynes to give spiro-cyclopropenyl furanones under photolysis conditions or heating. With the reactive ethoxytrimethylsilylethyne, this reaction proceeded at low temperature (-25 °C), and quinones were obtained as the major product.

In future work, the cycloaddition reactions of bisketene are very interesting both theoretically and practically. To further understand the electronic properties of bisketenes in these reactions other cycloaddition processes should be examined, such as using electron rich alkenes like $(CH_3O)_2C{=}C(OCH_3)_2$ with phenyl trimethylsilyl bisketene. Metal complexes

of bisketenes and their cycloaddition reactions remain unexplored. The scope of the generation of vinyl ketenes from bisketenes should also be explored, considering the vast utility of vinyl ketenes.

## 6.3 Experimental

General procedures are described in Chapter 2.

The nOe spectral study was carried out on a Varian Gemini 400 spectrometer. Trimethylsilyldiazomethane was obtained from Aldrich. Diazomethane was prepared according to a standard method.[43] Diazohexane and phenyldiazomathane were prepared according to literature methods.[26]

**4,5-Bis(trimethylsilyl)-4-cyclopentene-1,3-dione (16).** The bisketene 2,3- bis(trimethylsilyl)-1,3-butadiene-1,4-dione **15** (20.5 mg, 0.091 mmol) was dissolved in anhydrous ether (3 mL), and then trimethylsilyldiazomethane in hexane (55 μL, 2 M) was dropped in with stirring at room temperature. The reaction was kept overnight under nitrogen protection, and then the solvent was removed by a rotary evaporator to give a crude yellow solid product, which was further purified using thin layer chromatography (eluted using 3% ethyl acetate in hexane), to give the yellow solid product **16** (14.0 mg, 0.058 mmol, 64%), mp 38.0-38.5 °C. $^1$H-NMR ($CDCl_3$) δ 0.34 (s, 18), 2.76 (s, 2); $^{13}$C NMR δ 0.51, 41.18, 175.48, 205.80; IR 1730 (s), 1690 (vs) cm$^{-1}$; EIMS *m/z* 240 ($M^+$, 22), 225 ($M^+$-$CH_3$, 47), 197 ($M^+$-$CH_3$, CO, 49), 155 (TMSCCTMS$^+$-$CH_3$, 100), 73 ($TMS^+$, 57); HRMS *m/z* calcd for $C_{11}H_{20}O_2Si_2$ ($M^+$) 240.1002, found 240.1000.

**4,5-Bis(trimethylsilyl)-4-cyclopentene-1,3-dione (16) and 3,4-bistrimethylsilyl-5-methylene-2(5H)-furanone (17).** The bisketene **15** (27.8 mg, 0.123 mmol) was dissolved in anhydrous ether (2 mL) and then diazomethane (0.63 mmol in 5 mL ether) was added and the solution was stirred at room temperature under nitrogen protection for 2 h. Then the solvent was removed by a rotary evaporator to give the crude product which was further purified by thin layer chromatography (on silica gel eluted by 3% ethyl acetate in hexane) to give the yellow solid product **16** (6.5 mg, 0.027 mmol, 22%), and the colorless oil **17** (18.5 mg, 0.077 mmol, 63%). **17** $^{1}H$ NMR ($CDCl_3$) δ 0.35 (s, 9), 0.39 (s, 9), 4.98 (d, $J_{1,2}$=2.5 Hz, 1), 5.19 (d, $J_{1,2}$=2.5 Hz, 1); $^{13}C$ NMR ($CDCl_3$) δ 0.53, 1.60, 97.04, 144.22, 159.63, 165.82, 173.01; IR ($CDCl_3$) 1744 (vs), 1628 (s) $cm^{-1}$; EIMS *m/z* 240 ($M^+$, 22), 225 ($M^+$-$CH_3$, 65), 197 ($M^+$-$CH_3$, CO, 46), 181 ($M^+$-Me, $CO_2$, 54), 155 (TMSCCTMS$^+$-Me, 100), 73 ($TMS^+$, 60); HRMS *m/z* calcd for $C_{11}H_{20}O_2Si_2$ 240.10018, found 240.09995.

**4-Trimethylsilyl-5-phenyl-4-cyclopentene-1,3-dione (20).** 3-Trimethylsilyl-4-phenyl-3-cyclobutene-1,2-dione **18** (17.2 mg, 0.075 mmol) was dissolved in $CDCl_3$ (0.5 mL) and the solution was photolysed for 2 h using 350 nm lamps at 6 °C, to give the bisketene 2-trimethylsilyl-3-phenyl-1,3-butadiene-1,4-dione ( **19** ) in 99% yield as measured by $^{1}H$ NMR. Then the bisketene was added to $TMSCHN_2$ (15 mg, 0.132 mmol) in hexane (2 mL) and stirred under nitrogen for 16 hour at room temperature. The solvent was removed by a rotary evaporator to give a crude solid product, which was further purified by thin layer chromatography (on silica gel eluted by 5% ethyl acetate in hexane) to give **20** as a yellow green solid product ( 12.6 mg, 0.052 mmol, 69%), mp 98.5-99.0 °C. **20**: $^{1}H$ NMR ($CDCl_3$) δ 0.12 (s, 9), 3.02 (s, 2),

7.20-7.30 (m, 2), 7.40-7.50 (m, 3); $^{13}C$ NMR ($CDCl_3$) δ -0.72, 41.96, 128.08, 128.96, 129.80, 131.00, 161.48, 168.44, 200.73, 203.96; IR ($CDCl_3$) 1733 (s), 1696 (s) $cm^{-1}$; EIMS *m/z* 244 ($M^+$, 53), 229 ($M^+$-$CH_3$, 58), 201 ( M+-$CH_3$, CO, 23), 159 ($PHCCTMS^+$-$CH_3$, 100), 73 ( $TMS^+$, 7); HRMS calcd for $C_{14}H_{16}O_2Si$ 244.0919, found 244.0915.

**3-Trimethylsilyl-4-phenyl-5-methylene-2(5H)-furanone (21) and 4-trimethylsilyl-5-phenyl-4-cyclopentene-1,3-dione (20).** 3-Trimethylsilyl-4-phenyl-3-cyclobutene-1,2-dione **18** (51.0 mg, 0.222 mmol) was dissolved in anhydrous $CDCl_3$ (1 mL), and was photolysed for 1.5 h to give the bisketene 2-trimethylsilyl-3-phenyl-1,3-butadiene-1,4-dione **19** (87%, monitored by $^1H$ NMR). The solution was cooled to 0 °C and diazomethane (0.266 mmol) in ether (1.1 mL) was added over 5 min, and the solution was kept at 0 °C for 1 h and then at room temperature overnight under nitrogen protection. The solvent was removed by a rotary evaporator to give a crude product oil. which was further purified by a thin layer chromatography (on silica gel eluted using 5% ethyl acetate in hexane) to give **20** as a yellow green solid (26.5 mg, 0.11 mmol, 49%, 56% based on bisketene), and **21** as a colorless oil (8.7 mg, 0.036 mmol, 16%, 18% based on bisketene). **21**: $^1H$ NMR ($CDCl_3$) δ 0.17 (s, 9), 5.01 (d, 1, $J_{1,2}$ = 2.56 Hz), 5.31 (d, 1, $J_{1,2}$ = 2.56 Hz), 7.25-7.50 (m, 5); $^{13}C$ NMR ($CDCl_3$) δ 0.22, 98.20, 128.12, 128.41, 129.22, 129.50, 131.39, 142.85, 157.63, 169.44; IR ($CDCl_3$) 1746 (vs), 1630 (s) $cm^{-1}$; EIMS *m/z* 244 ($M^+$, 47), 229 ($M^+$-Me, 26), 201 ($M^+$-$CH_3$, CO, 18), 159 ($PhCCTMS^+$-Me, 100), 73 ($TMS^+$, 15); HRMS calcd for $C_{14}H_{16}O_2Si$ 244.0919, found 244.0916.

**4,5-Bis(trimethylsilyl)-2-phenyl-4-cyclopentene-1,3-dione (22).** The bisketene **15** (32.6 mg, 0.144 mmol) dissolved in anhydrous ether (0.5 mL), was added to 2.5 eq of phenyldiazomethane[26] (43 mg, 0.36 mmol) in

anhydrous ether under nitrogen protection and the reaction was stirred 16 h at room temperature. The solvent was removed by a rotary evaporator to give the crude solid product, which was further purified by thin layer chromatography (on silica gel eluted using 5% ethyl acetate in hexane) to give **22** as a yellow solid (30.5 mg, 0.097 mmol, 67%), mp 87.6-88.0 °C. **22**: $^{1}$H NMR ($CDCl_3$) δ 0.38 (s, 18), 3.76 (s, 1), 7.00-7.10 (m, 2), 7.20-7.35 (m, 3); $^{13}$C NMR ($CDCl_3$) δ 0.51, 56.40, 127.35, 128.36, 128.88, 133.50, 175.31, 205.76; IR ($CDCl_3$) 1689 (s) $cm^{-1}$; EIMS *m/z* 316 ($M^+$, 37), 301 ($M^+$-$CH_3$, 6), 183 ($M^+$-118, $CH_3$, 9), 155 (TMSCCTMS$^+$-$CH_3$, 13), 118 ( $PhCHCO^+$, 100), 73 ($TMS^+$, 42); HRMS calcd for $C_{17}H_{24}O_2Si_2$ 316.1315, found 316.1315.

**E-2-Trimethylsilyl-2-(1'-trimethylsilyl-2'-oxoethenyl)-3-methylpropiolactone (23).** Bisketene **15** (156 mg, 0.69 mmol) was dissolved in 1 mL of $CHCl_3$, and acetaldehyde (200 μL, 160 mg, 3.6 mmol) and $BF_3.Et_2O$ (10 μL, 12 mg, 0.08 mmol) were dropped in. The solution was left for 1 h at room temperature and the solvent evaporated, and the residue was recrystallized from ether to give **23** (153 mg, 0.57 mmol, 82%), mp 64.5-65.0 °C: $^{1}$H NMR ($CDCl_3$) δ 0.22 (s, 9), 0.29 (s, 9), 1.51 (d, 3, J = 6.2 Hz), 4.55 (q, 1, J = 6.2 Hz). $^{13}$C NMR ($CDCl_3$) δ -3.66, 0.35, 11.38, 18.09, 48.19, 73.63, 171.38, 178.60; IR ($CDCl_3$) 2084 (s), 1796 (s) $cm^{-1}$; EIMS *m/z* 270 ($M^+$, 31), 255 ($M^+$ -$CH_3$, 22), 227 ($M^+$ -CO, $CH_3$, 33), 199 (30), 171 (44), 155 (46), 147 (68), 73 ($Me_3Si$, 100); HRMS *m/z* calcd for $C_{12}H_{22}O_3Si_2$ 270.1108 found 270.1086; calcd for $C_{11}H_{19}O_3Si_2$ 255.0873, found 255.0863.

**2,3-Bis(trimethylsilyl)-1,3(Z)-pentadiene-1-one (24).** The ketenyl β-lactone **23** (30.0 mg, 0.111 mmol ) dissolved in anhydrous ether (200 μL) was injected into a gas chromatograph ( column O.V.17, injector 250 °C, col. 100 °C, retention time 22 min.), to give the vinyl ketene **24** as a colorless oil ( 8.8

mg, 0.039 mmol, 35 %): $^1$H NMR ($CDCl_3$) δ 0.09 (s, 9), 0.18 (s, 9), 1.74-1.77 (d, 3, $J_{1,2}$ = 6.6 Hz), 6.05 (q, 1, $J_{1,2}$ = 6.6 Hz); $^{13}$C NMR ($CDCl_3$) δ -1.26, 0.15, 17.21, 29.70, 129.30, 139.08, 176.61; IR ($CDCl_3$) 2080 (s) $cm^{-1}$; EIMS *m/z* (relative intensity) 226 ($M^+$, 24), 198 ($M^+$-CO, 12), 171 (36), 110 ($M^+$-TMS, $CH_3$, CO, 77), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{11}H_{22}OSi_2$ 226.1209, found 226.1212.

**Attempted reaction of the vinyl ketene (24) and trimethylsilyl diazomethane.** The vinyl monoketene **24** ( 4.1 mg, 0.018 mmol) was dissolved in $CDCl_3$ (0.5 mL) and then trimethylsilyldiazomethane (0.090 mmol) in hexane (45 uL, 2 M) was dropped in under shaking and nitrogen protection. The reaction was kept at room temperature for 40 hr, and the reaction was monitored by $^1$H NMR. No new product was observed.

**Attempted [2+2] reaction of bisketene 15.** The bisketene **15** (9.6 mg, 0.042 mmol) and bistrimethylsilylacetylene (15.2 mg, 0.089 mmol) were dissolved in $CDCl_3$ (0.5 mL). The solution was photolysed for 8 h using 350 nm lamps. The reaction was monitored by $^1$H NMR, and showed no new product.

**General procedure for photochemical alkyne cycloaddition reactions**

3-Phenyl-4-trimethylsilylcyclobutenedione **18** (46 mg, 0.2 mmol) was dissolved in chloroform (2 mL) and the alkyne (5 eq) was added, and then argon was bubbled through the solution for 0.5 hour and then the solution was photolysed using 350 nm lamps for 7 day at 5 $^oC$. The solvent was removed by a rotary evaporator, and the residue was further purified by thin layer chromatography (on silica gel, eluted with 5% ethyl acetate/hexane) to give a yellow oil. **3-Trimethylsilyl-4-phenyl-5-spiro(1',2'-dimethylcyclopropenyl)-**

**2(5H)-furanone 25** (24.5 mg, 0.086 mmol, 43%): $^1$H NMR ($CDCl_3$) δ 0.05 (s, 9), 2.01 (s, 6), 6.95-7.05 (m, 2), 7.30-7.40 (m, 3); $^{13}$C NMR ($CDCl_3$) δ -0.92, 9.02, 115.52, 127.23, 127.94, 128.47, 131.21, 134.03, 174.58, 176.98.; IR ($CCl_4$) 1728 (vs), 1585 (s) cm $^{-1}$; EIMS m/z 284 ($M^+$, 14), 269 ($M^+$-$CH_3$, 57), 241 ($M^+$-$CH_3$-CO, 60), 174 ($TMSCCPh^+$, 20), 159 ($TMSCCPh^+$-$CH_3$, 93), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{17}H_{20}SiO_2$ 284.1233, found 284.1232; UV ($CH_3CN$) $\lambda_{max}$ 248 nm ($\varepsilon = 8.8x10^3$).

**3-Trimethylsilyl-4-phenyl-5-spiro(1'-methyl-2'-trimethylsilyl-cyclopropenyl)-2(5H)-furanone (26)** (24 mg, 0.07 mmol, 35%): $^1$H NMR ($CDCl_3$) δ 0.064 (s, 9), 0.25 (s, 9), 2.20 (s, 3), 7.25-7.35 (m, 2), 7.40-7.50 (m, 3); $^{13}$C NMR ($CDCl_3$) δ -1.24, -0.75, 11.63, 121.47, 127.76, 127.81, 128.57, 129.98, 133.79, 133.87, 174.76, 178.38. IR ($CCl_4$) 1730 (vs), 1587 (s) cm$^{-1}$; EIMS *m/z* 342 ($M^+$, 6), 327 ($M^+$-$CH_3$), 58) 299 ($M^+$-$CH_3$, CO, 56), 159 ($TMSCCPh^+$-$CH_3$, 88), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{19}H_{26}Si_2O_2$ 342.1471, found 342.1469

**3-Trimethylsilyl-4-phenyl-5-spiro(1'-trimethylsilyl-2'-phenyl-cyclopropenyl)-2(5H)-furanone (27)** (30 mg, 0.074 mmol, 37%): $^1$H NMR ($CDCl_3$) δ 0.12 (s, 9), 0.15 (s, 9), 6.90-7.00 (m, 2), 7.15-7.30 (m, 3), 7.40-7.60 (m, 5); $^{13}$C NMR ($CDCl_3$) δ -0.72, -1.19, 122.02, 126.92, 127.80, 128.00, 128.76, 129.06, 129.55, 130.67, 133.37, 133.66, 136.35, 174.75, 177.68; IR ($CCl_4$) 1730 (vs), 1600(s), 1587 (s) cm$^{-1}$.; EIMS *m/z* 404 (M+, 3) 389 ($M^+$-$CH_3$, 58), 299 ($M^+$-$CH_3$,CO, 56), 174 ($TMSCCPh^+$, 65), 159 ($TMSCCPh^+$-$CH_3$, 94), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{24}H_{28}Si_2O_2$ 404.1628, found 404.1624.

**3-Trimethylsilyl-4-phenyl-5-spiro(3'-oxo-1',2'-cyclohexano-cyclopropenyl)-2(5H)-furanone (28)** (7 mg, 0.022 mmol, 11%): $^1$H NMR

($CDCl_3$) δ -0.07 (s, 9), 1.70-1.90 (m, 1), 2.05-2.15 (m, 5), 2.20-2.40 (m, 1), 2.45-2.65 9 (m, 1), 7.05-7.15 (m, 2), 7.35-7.45 (m, 3); $^{13}C$ NMR ($CDCl_3$) δ -1.36, 17.78, 24.13, 25.97, 31.57, 39.24, 76.19, 127.60, 128.47, 128.97, 129.25, 131.14, 174.09, 175.13, 203.77; IR ($CCl_4$) 1730 (vs), 1721 (vs) $cm^{-1}$; EIMS *m/z* 326 ($M^+$, 20), 311 ($M^+$ -$CH_3$, 18), 270 (43), 174 ($TMSCCPh^+$, 34), 159 ($TMSCCPh^+$ -$CH_3$, 100), 73 ($TMS^+$, 80); HRMS *m/z* calcd for $C_{19}H_{22}SiO_3$ 326.1338, found 326.1334.

**Thermal cycloaddition.** 3-Phenyl-4-trimethylsilyl cyclobutenedione **18** (46 mg, 0.2 mmol) was dissolved in chloroform (2 mL) and phenyl trimethylsilylacetylene (5 eq) was added, and then the reaction mixture was bubbled with argon for 0.5 hour and was sealed in a vial, which then was heated at 120 °C for 24 hr. The solvent was removed by a rotary evaporator, and the resulted crude product was purified by thin layer chromatograph on silica gel eluted by a 5% ethyl acetate/hexane to give **27** (34 mg, 0.084 mmol, 42%).

**3-Trimethylsilyl-4-phenyl-5-spiro(1'-trimethylsilyl-2'-ethoxy-cyclopropenyl)-2(5H)-furanone (29) and quinones (30), (31).** 3-Phenyl-4-trimethylsilyl cyclobutenedione **18** (46 mg, 0.2 mmol) was dissolved in $CDCl_3$ (2 mL), and argon was bubbled through for 0.5 hour, and then the solution was photolysed for 1 hour using 350 nm lamps at 6 °C. The reaction was monitored by $^1H$ NMR and gave the bisketene (88%), and then the reaction mixture was cooled in a refrigerator at -25 °C and ethoxytrimethylsilylacetylene (71 mg, 0.5 mmol) was added in one portion, and the yellow color of the reaction mixture turned immediately to orange. The reaction was left overnight for 16 hr at - 25 °C in a refrigerator. The solvent was removed by a rotary evaporator and the orange liquid residue was purified by thin layer chromatography (on silica gel,

eluted with 5% ethyl acetate in hexane) to give **29** (5.2 mg, 0.014 mmol, 8%, based on bisketene) and **31** (33.8 mg, 0.113 mmol, 64%, based on bisketene).

In one case the quinone **30** was obtained by chromatography as an orange liquid: $^{1}$H NMR ($CDCl_3$) δ 0.07 (s, 9), 0.03 (s, 9), 1.47 (t, $J_{1,2}$ = 7.0 Hz, 3), 4.28 (q, $J_{1,2}$ = 7.0 Hz) 7.10-7.20 (m, 2), 7.25-7.35 (m, 3); $^{13}$C NMR δ 0.28, 2.21, 15.01, 69.22, 93.20, 111.90, 127.50, 128.06, 129.97, 132.75, 148.41, 148.52, 191.47, 203.99; IR ($CDCl_3$) 1690 (bvs), 1594 (vs) $cm^{-1}$; EIMS *m/z* 372 ($M^+$, 13), 344 ($M^+$-CO, 33), 316 ($M^+$-2CO, 40), 271 (53), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{20}H_{28}O_3Si_2$ 372.1577, found 372.1573; UV ($CH_3CN$) $\lambda_{max}$ 239 nm (ε =3.0x10$^5$) $\lambda_{shoulder}$ 292 nm (ε = 5.9x10$^4$), $\lambda_{shoulder}$ 346 nm (ε = 2.0x10$^4$).

**Furanone 29:** $^{1}$H NMR ($CDCl_3$) δ 0.00 (s, 9), 0.09 (s, 9), 1.48 (t, $J_{1,2}$ = 6.83 Hz, 3), 4.15-4.20 (m, 2), 7.05-7.15 (m, 2), 7.30-7.40 (m, 3); $^{13}$C NMR δ -0.95, -0.81, 14.55, 70.25, 84.40, 127.86, 128.29, 128.94, 131.10, 133.60, 146.35, 175.50, 178.00; IR (film) 1809 (vs), 1730 (vs), 1702 (vs) $cm^{-1}$; EIMS *m/z* 372 ($M^+$, 6), 343 ($M^+$-Et, 100), 255 (39), 159 ($PhCCTMS^+$-$CH_3$, 34), 73 ($TMS^+$, 83); HRMS *m/z* calcd for $C_{20}H_{28}O_3Si_2$ 372.1577, found 372.1576

**Quinone 31:** $^{1}$H NMR ($CDCl_3$) δ 0.09 (s, 9), 1.47 (t, 3, J = 6.90 Hz), 4.14 (q, 2, J = 6.90 Hz), 4.69 (s, 1), 7.15-7.25 (m, 2), 7.30-7.40 (m, 3).; $^{13}$C NMR δ 0.65, 14.70, 68.10, 86.71, 128.08, 128.76, 129.20, 130.40, 132.85, 145.71, 146.84, 187.28, 199.99; IR ($CDCl_3$) 1700 (vs), 1650 (w) 1594(vs) $cm^{-1}$; EIMS *m/z* 272 ($M^+$-CO, 95), 244 ($M^+$-2CO, 40), 229 (81), 159 (82), 73 ($TMS^+$, 100); HRMS *m/z* calcd for $C_{16}H_{20}O_2Si$ ($M^+$-CO) 272.1232, found 272.1230; UV ($CH_3CN$) $\lambda_{max}$ 235 nm (ε = 1.3x10$^5$) $\lambda_{shoulder}$ 273 nm (ε = 3.5x10$^4$).

**nOe Study of quinone 31.** When the $CH_2$ protons were saturated a 15.7% increase was observed at the 4.69 ppm single proton, and no other nOe with the phenyl or trimethylsilyl groups was observed. When the single proton at 4.69 ppm was saturated, an nOe of 4.1% with the $CH_2$ group was observed with no nOe of the phenyl and trimethylsilyl groups. When the TMS protons were saturated a strong nOe of 7.2% was observed with the 7.15-7.25 signal of the phenyl group and no nOe was observed with CH and ethyl groups.

## 6.4 References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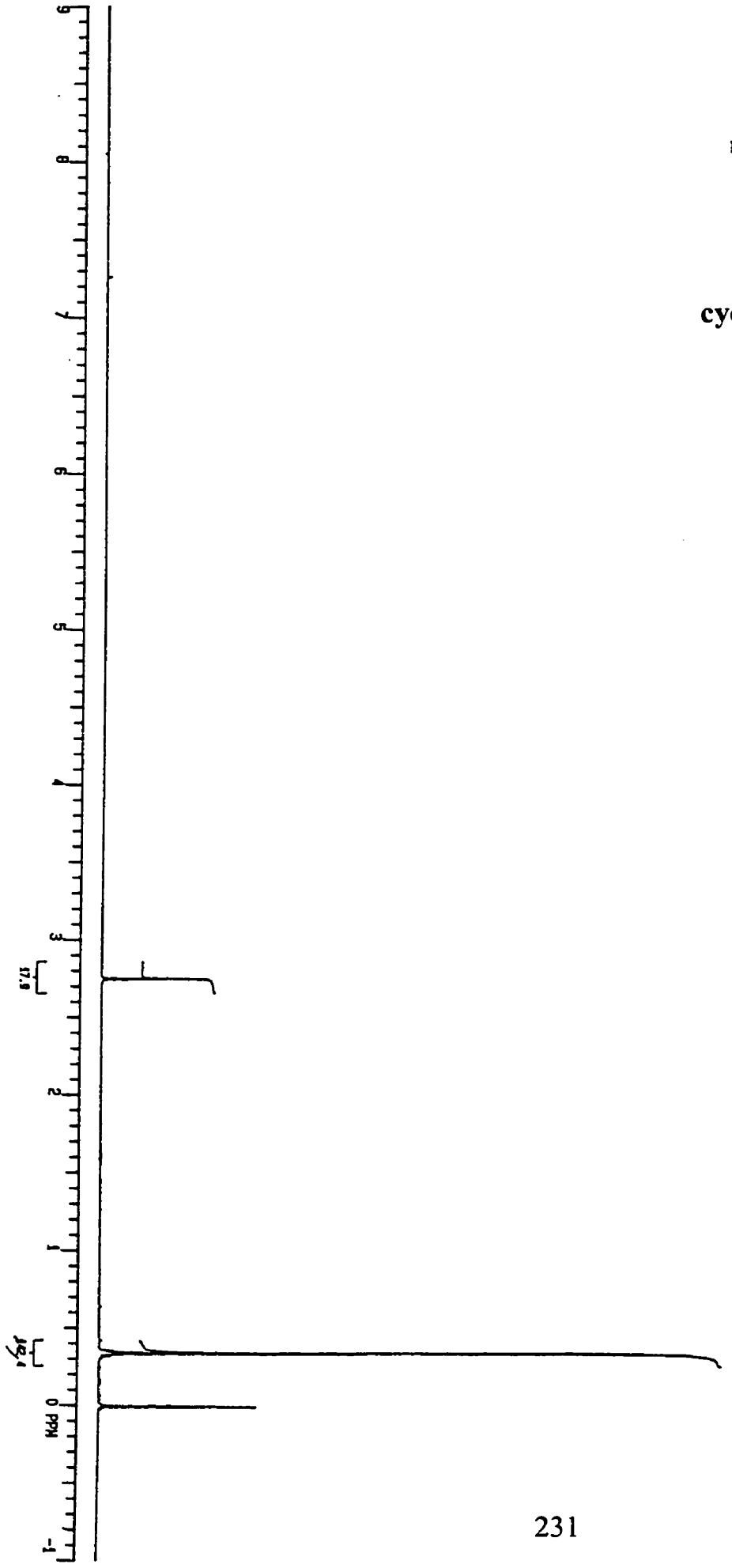
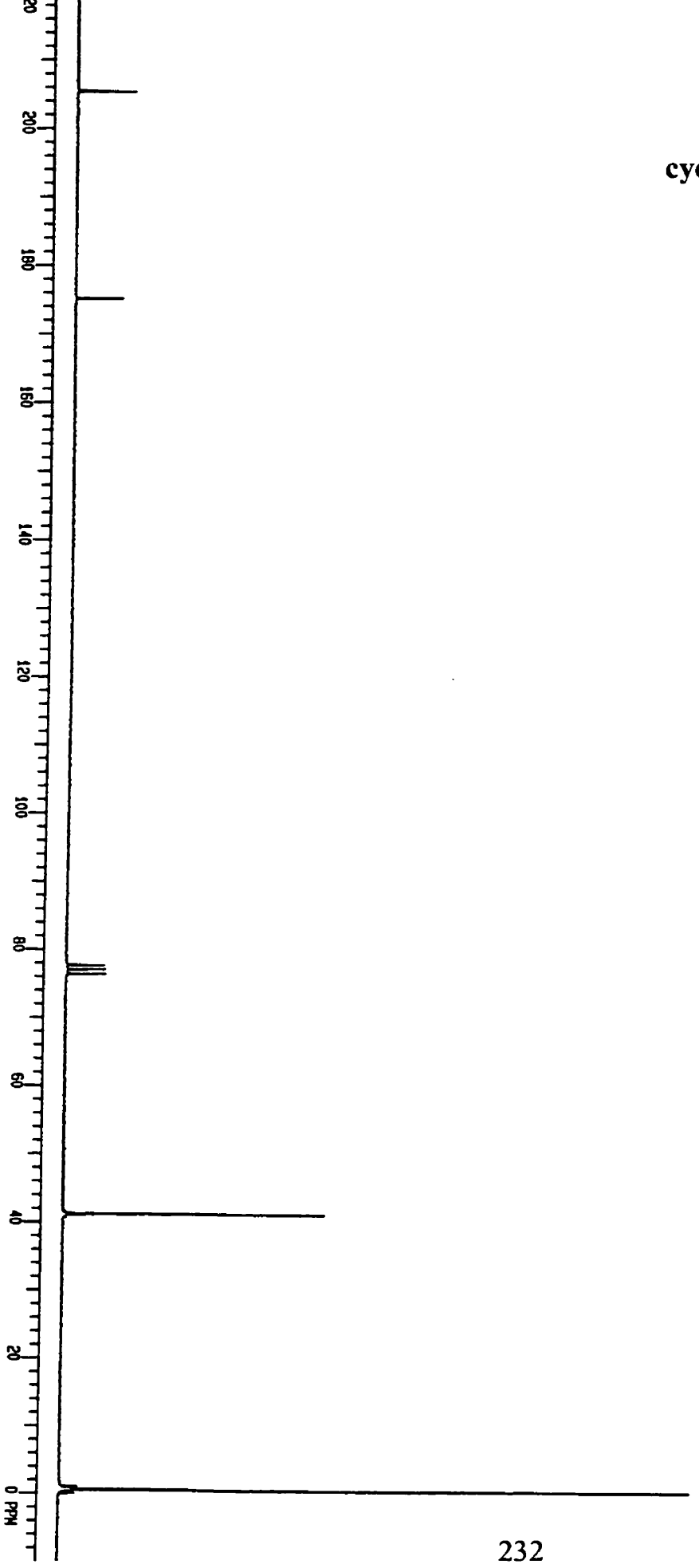
## Appendix 1

## $^{1}H$ and $^{13}C$ NMR Spectra

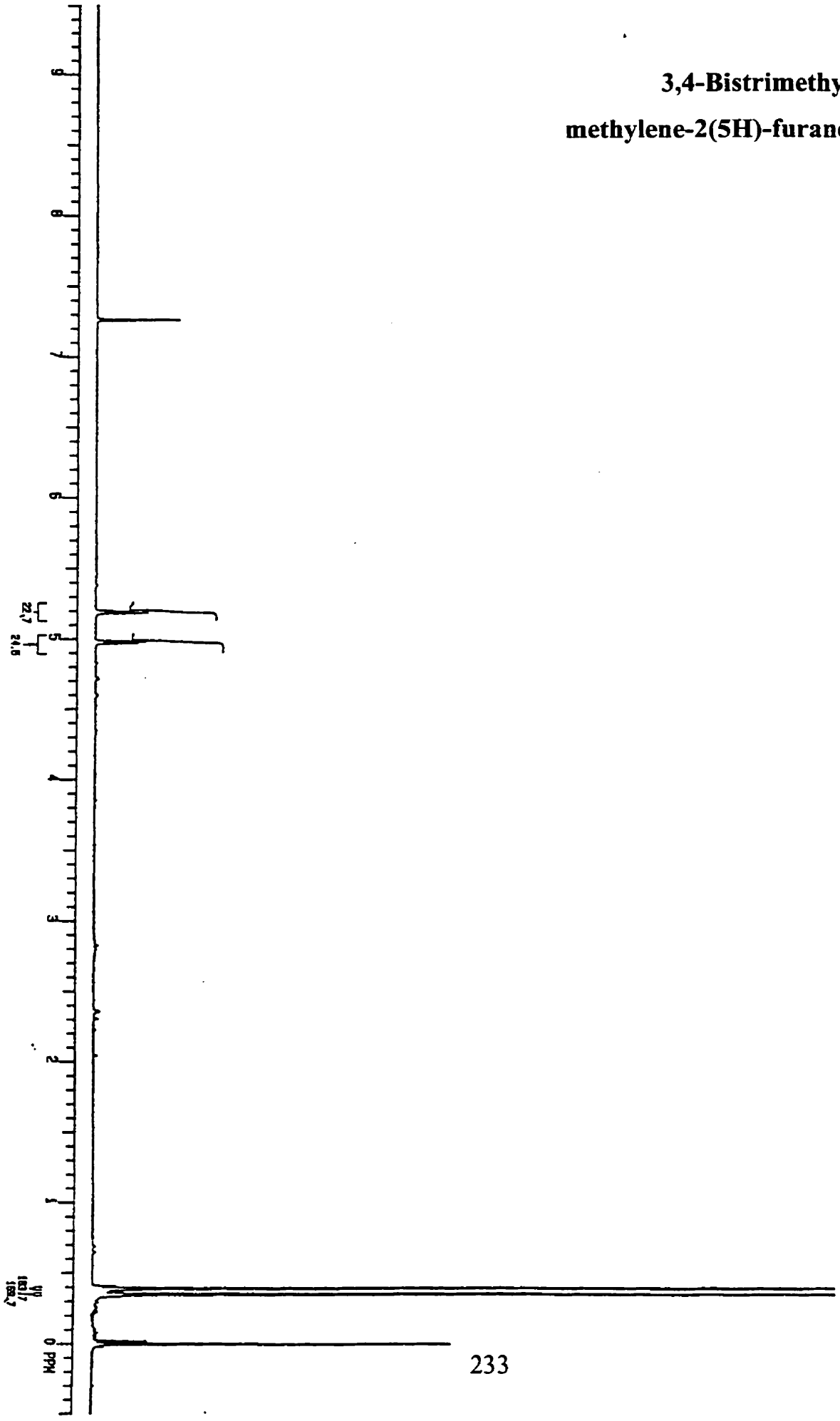
### 4,5-Bis(trimethylsilyl)-4-cyclopentene-1,3-dione (16)



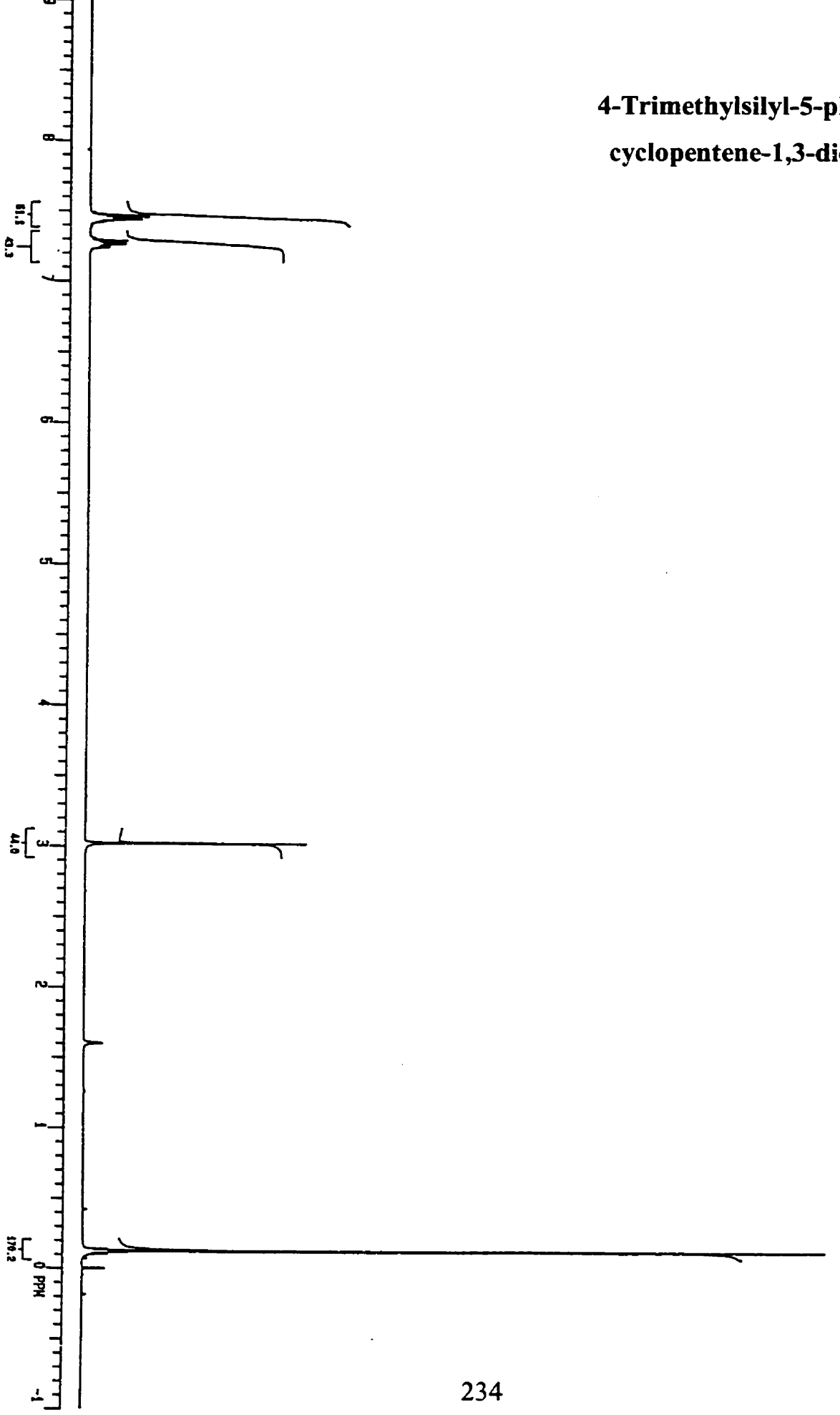
**4,5-Bis(trimethylsilyl)-4-cyclopentene-1,3-dione (16)**



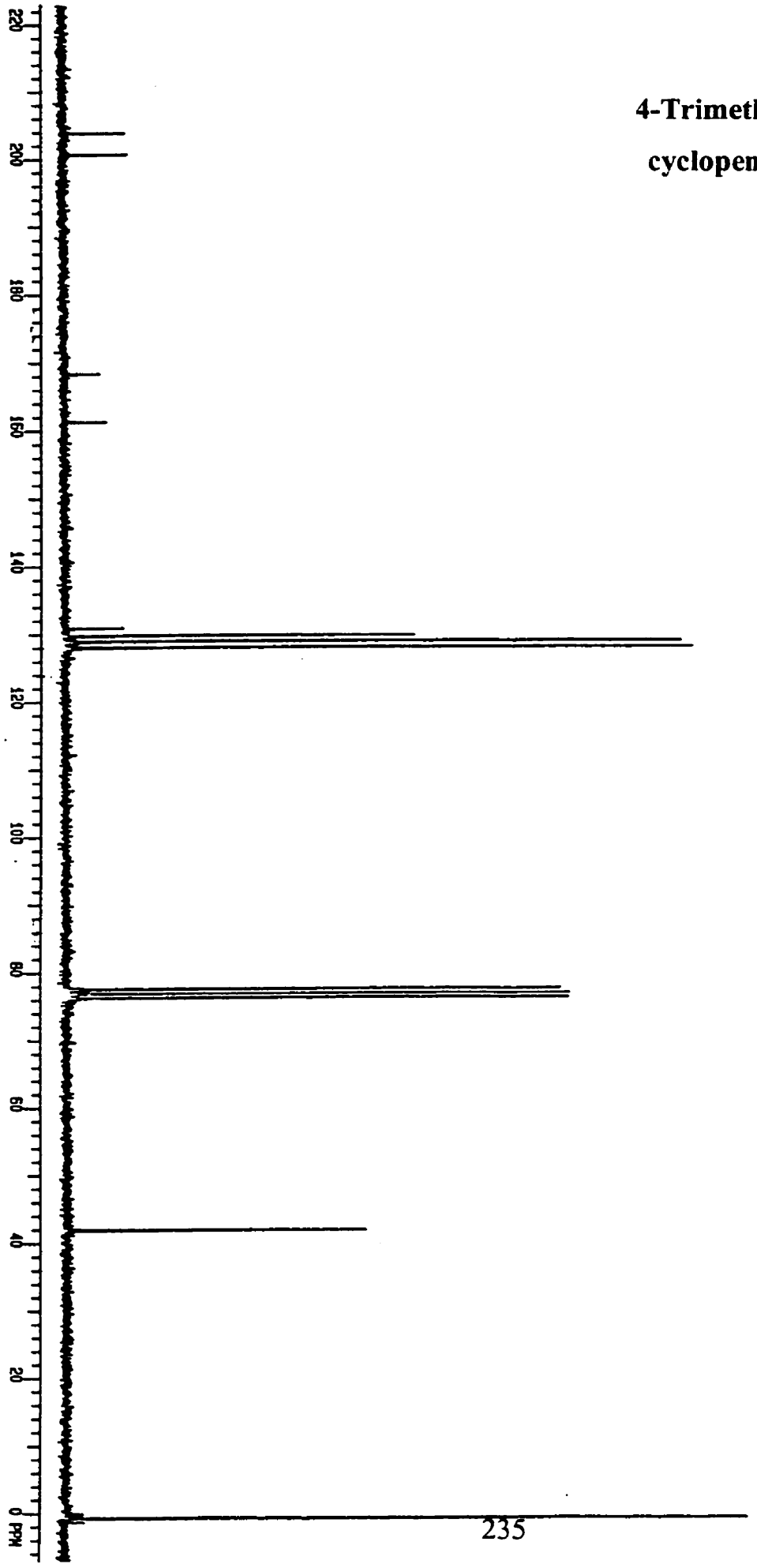
**3,4-Bistrimethylsilyl-5-methylene-2(5H)-furanone (17)**



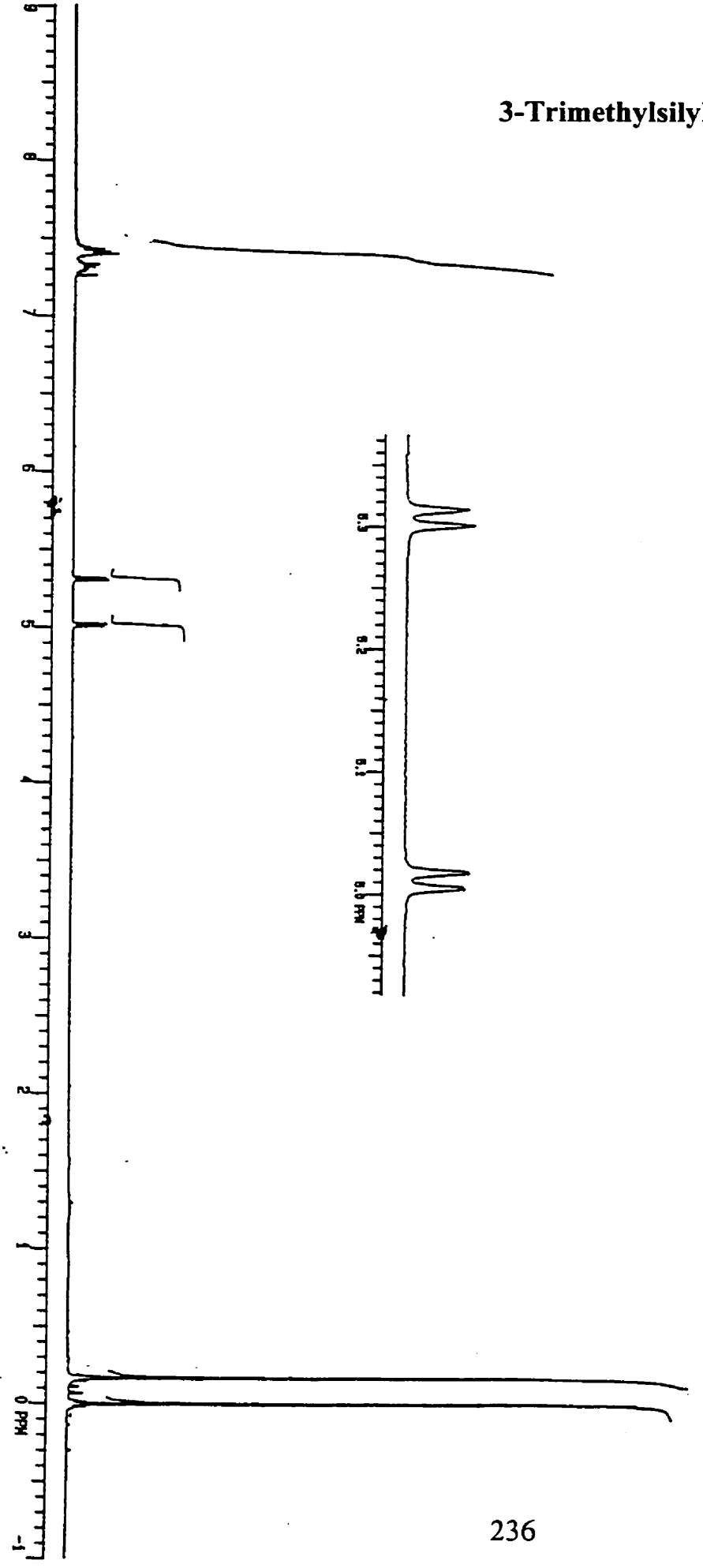
**4-Trimethylsilyl-5-phenyl-4-cyclopentene-1,3-dione (20)**



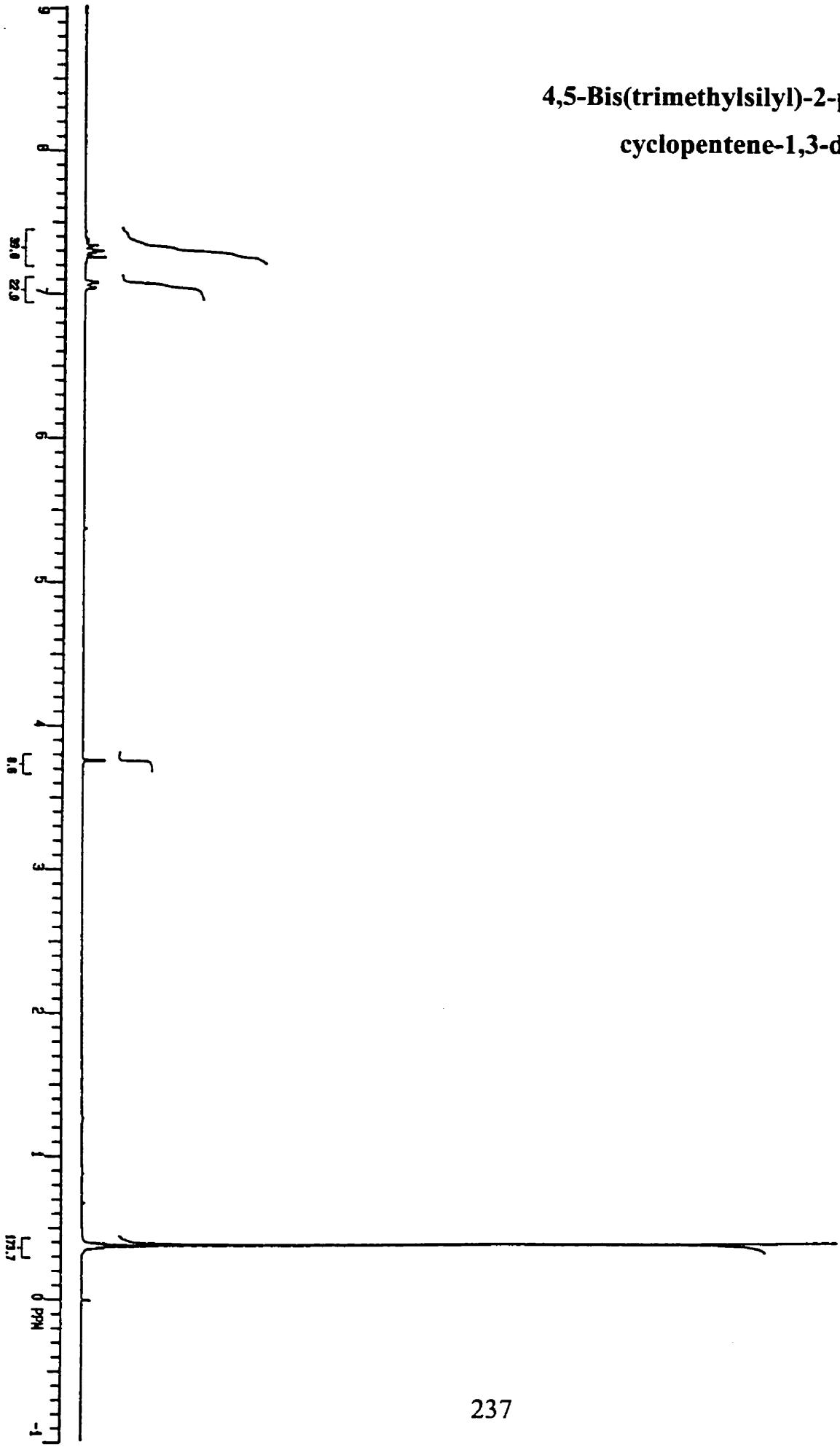
**4-Trimethylsilyl-5-phenyl-4-cyclopentene-1,3-dione (20)**



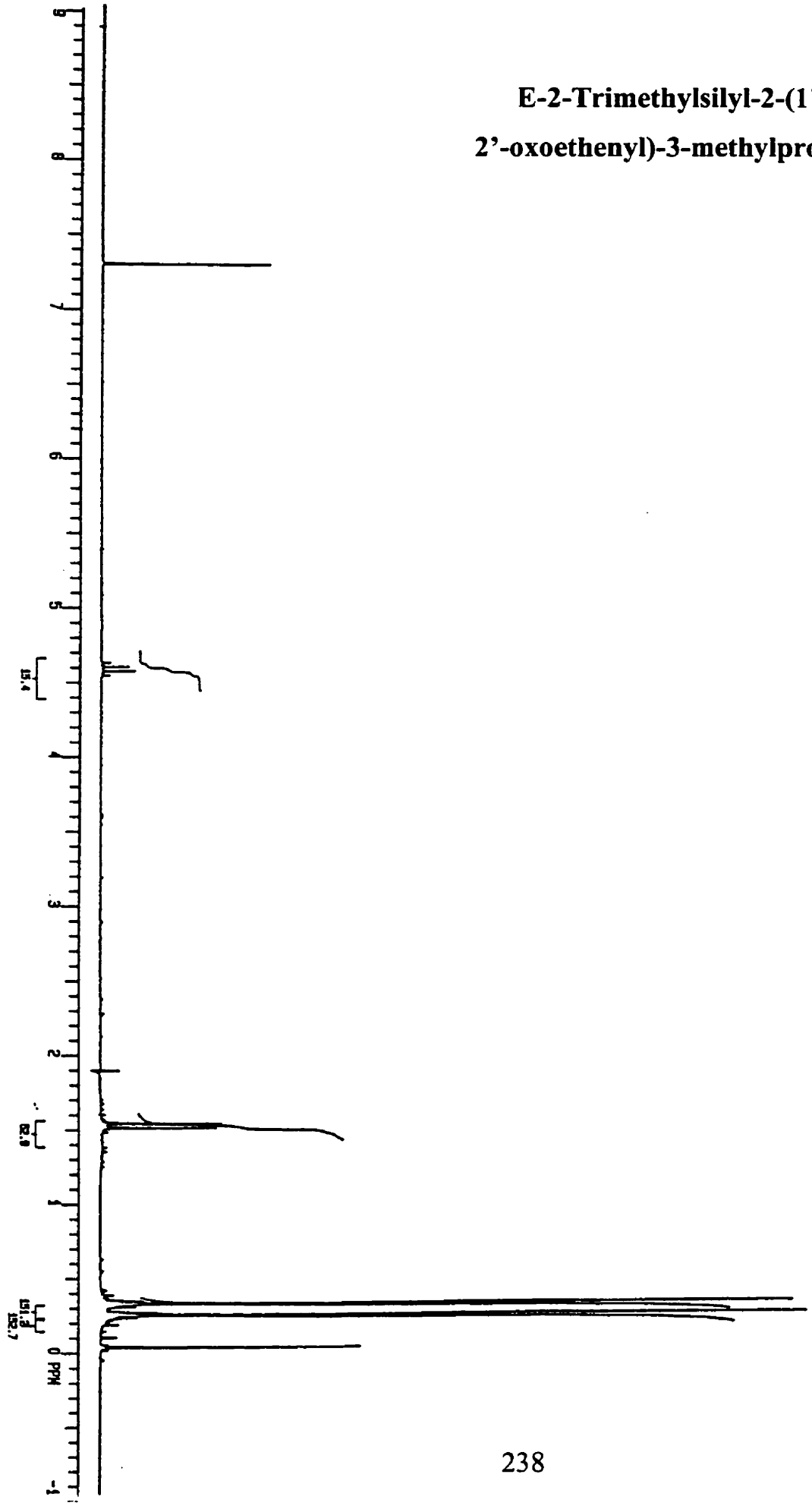
**3-Trimethylsilyl-4-phenyl-5-methylene-2(5H)-furanone (21)**



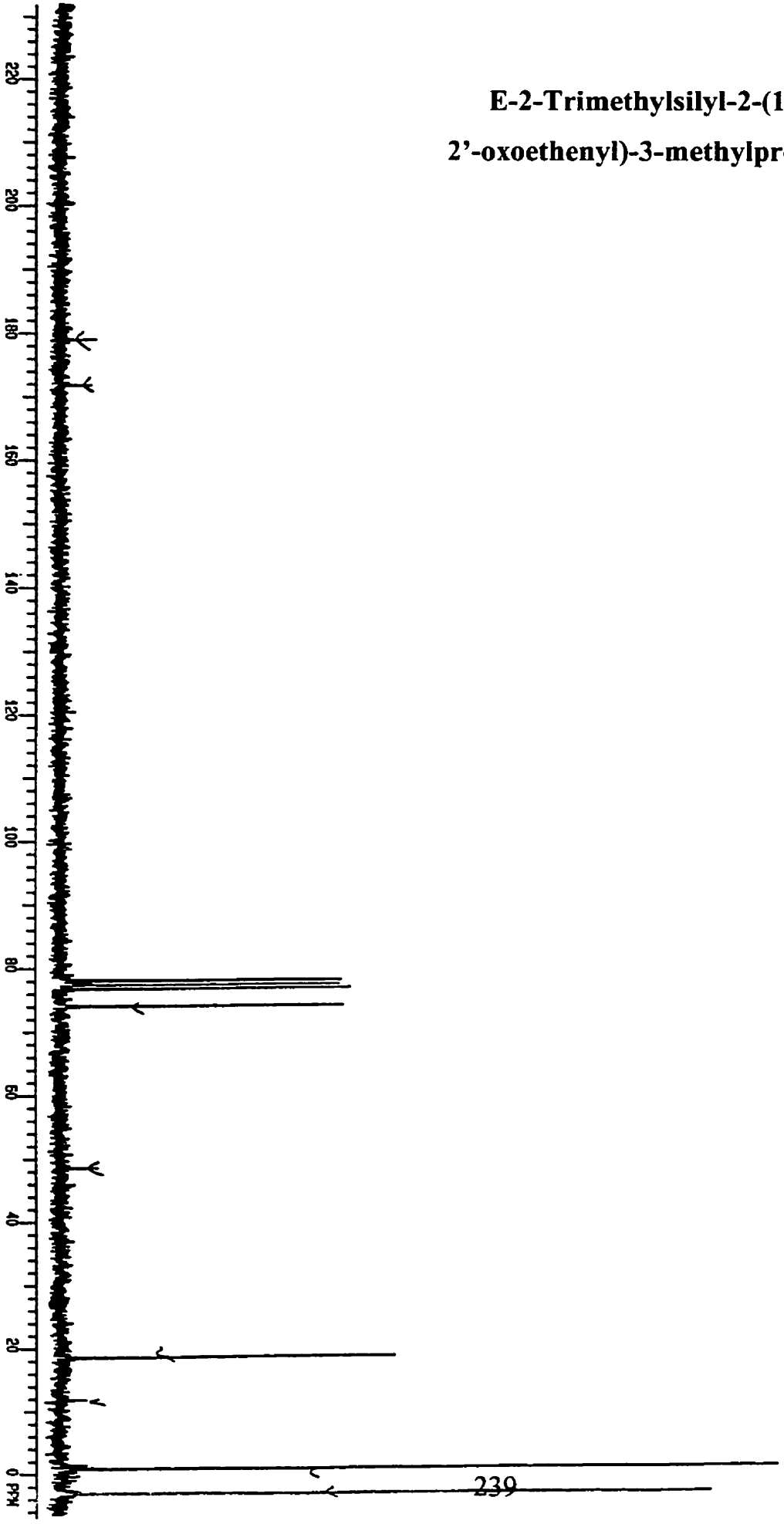
**4,5-Bis(trimethylsilyl)-2-phenyl-4-cyclopentene-1,3-dione (22)**



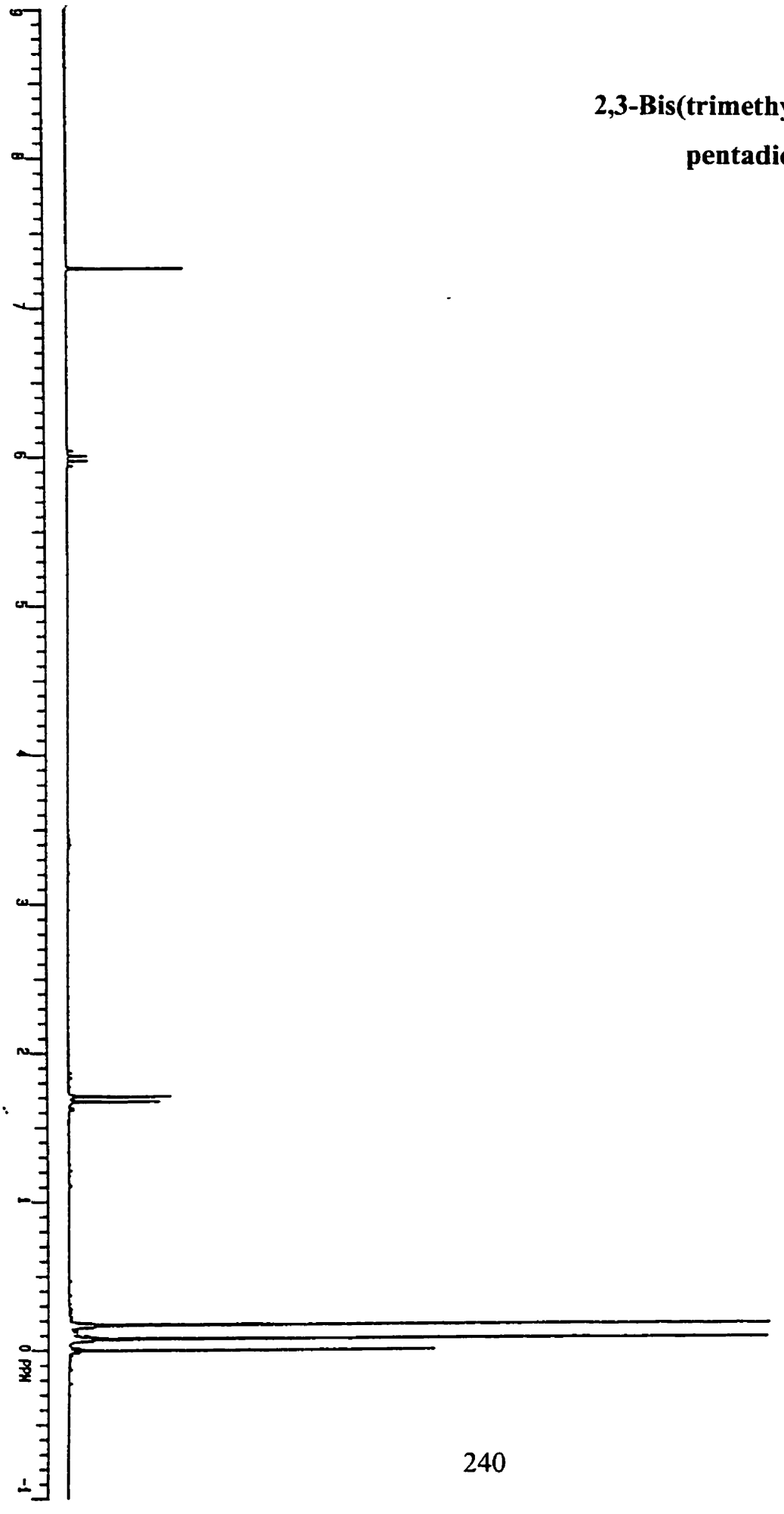
**E-2-Trimethylsilyl-2-(1'-trimethylsilyl-2'-oxoethenyl)-3-methylpropiolactone (23)**



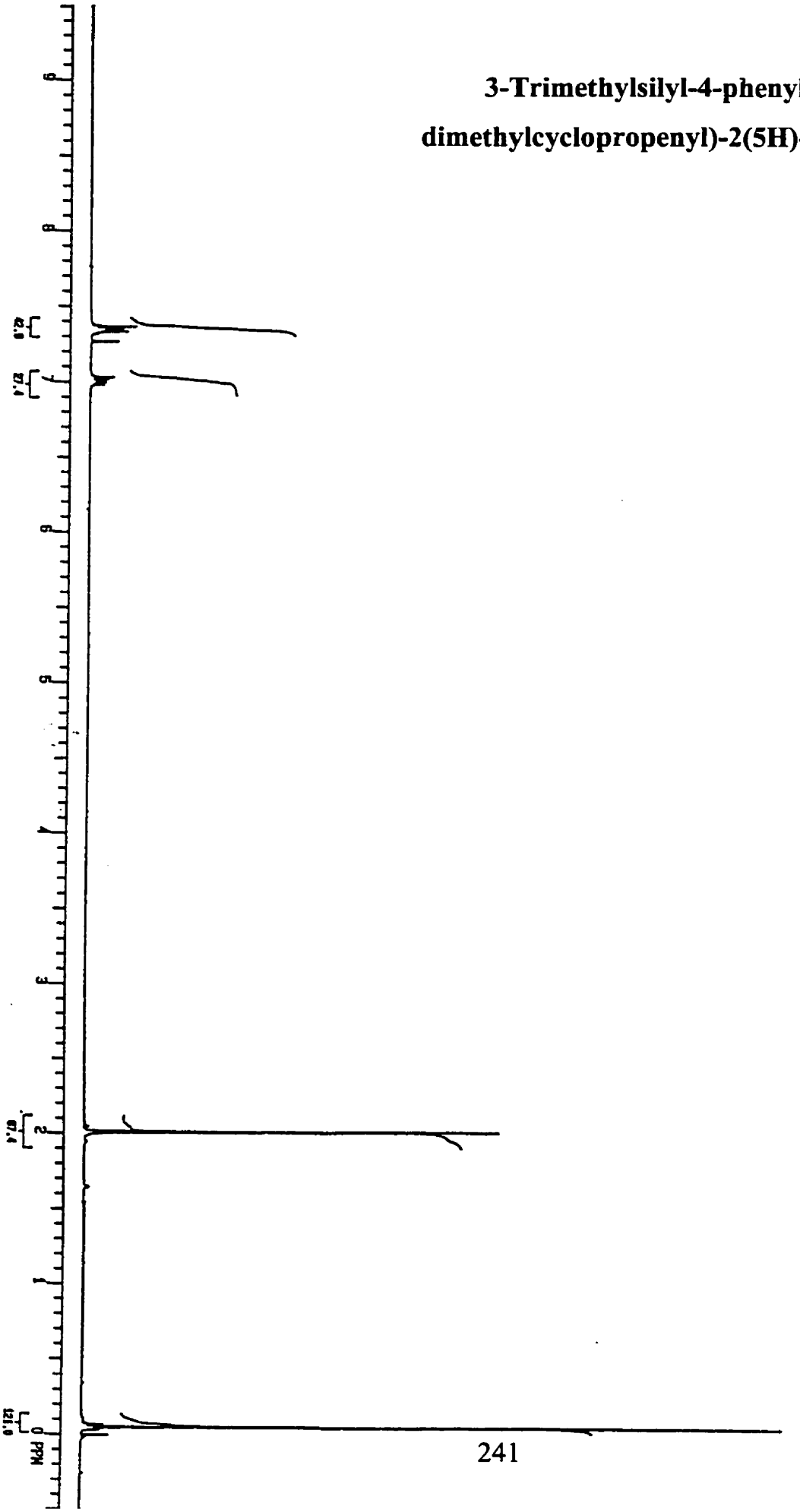
**E-2-Trimethylsilyl-2-(1'-trimethylsilyl-2'-oxoethenyl)-3-methylpropiolactone (23)**



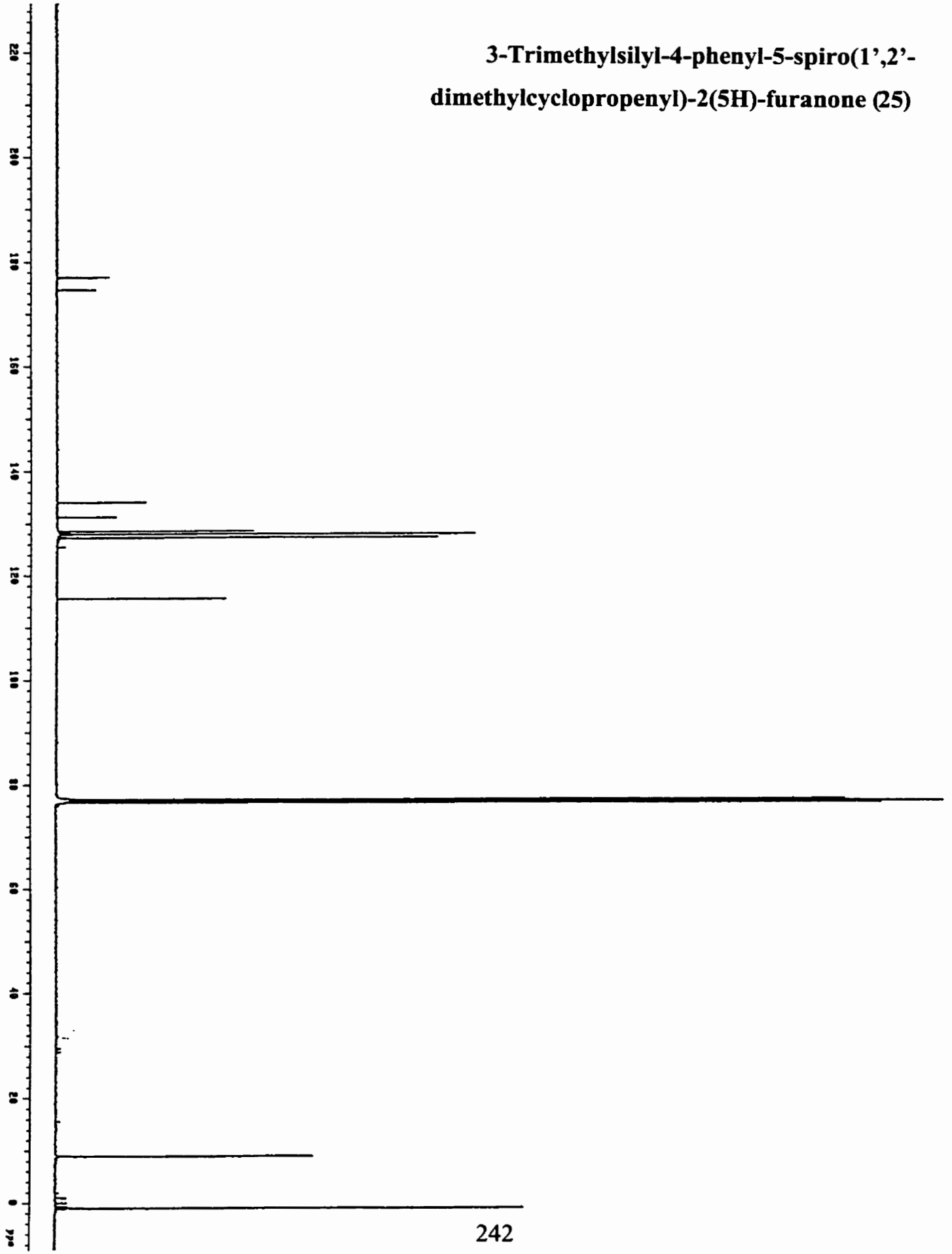
**2,3-Bis(trimethylsilyl)-1,3(Z)-pentadiene-1-one (24)**



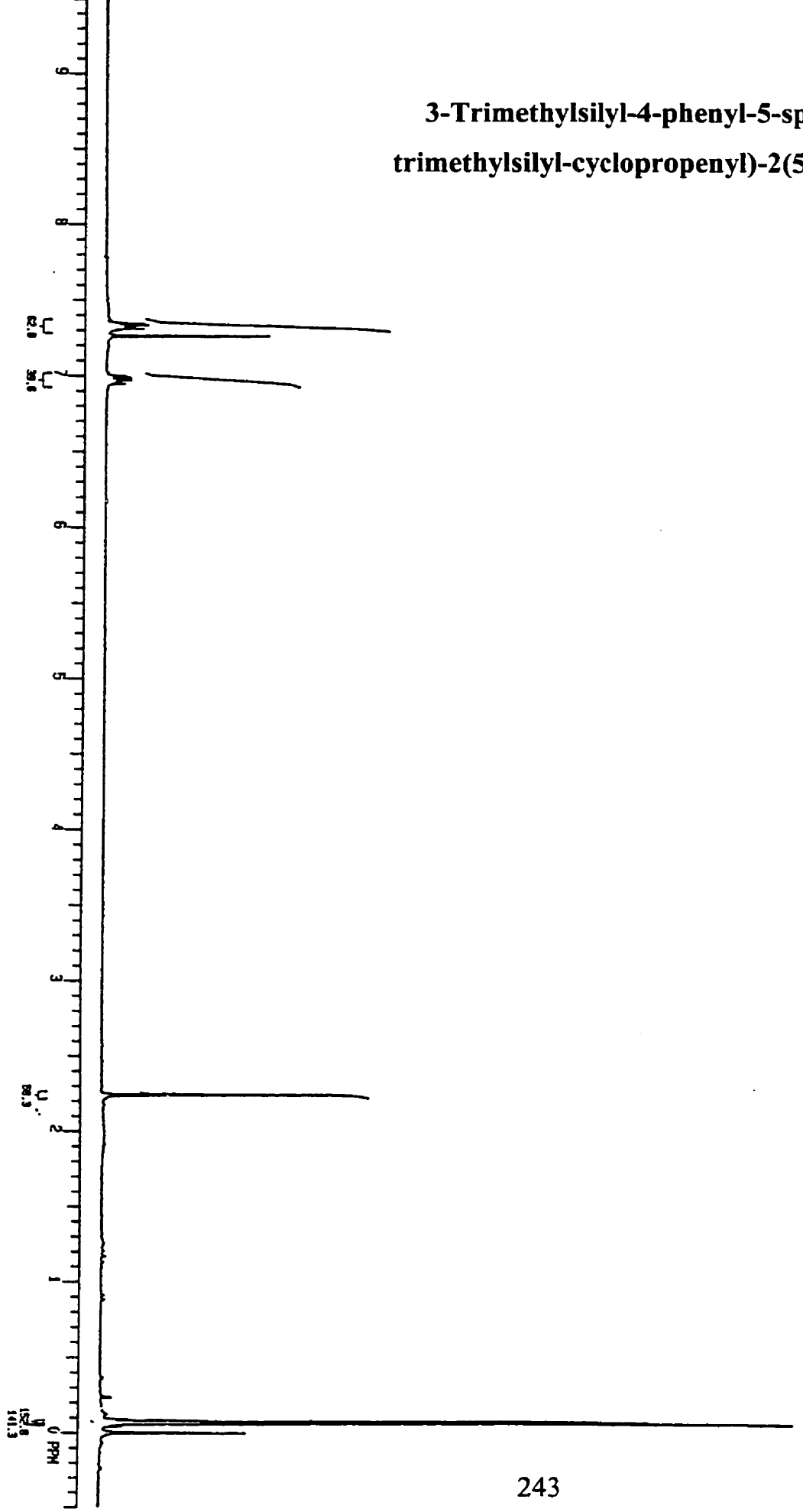
**3-Trimethylsilyl-4-phenyl-5-spiro(1',2'-dimethylcyclopropenyl)-2(5H)-furanone (25)**



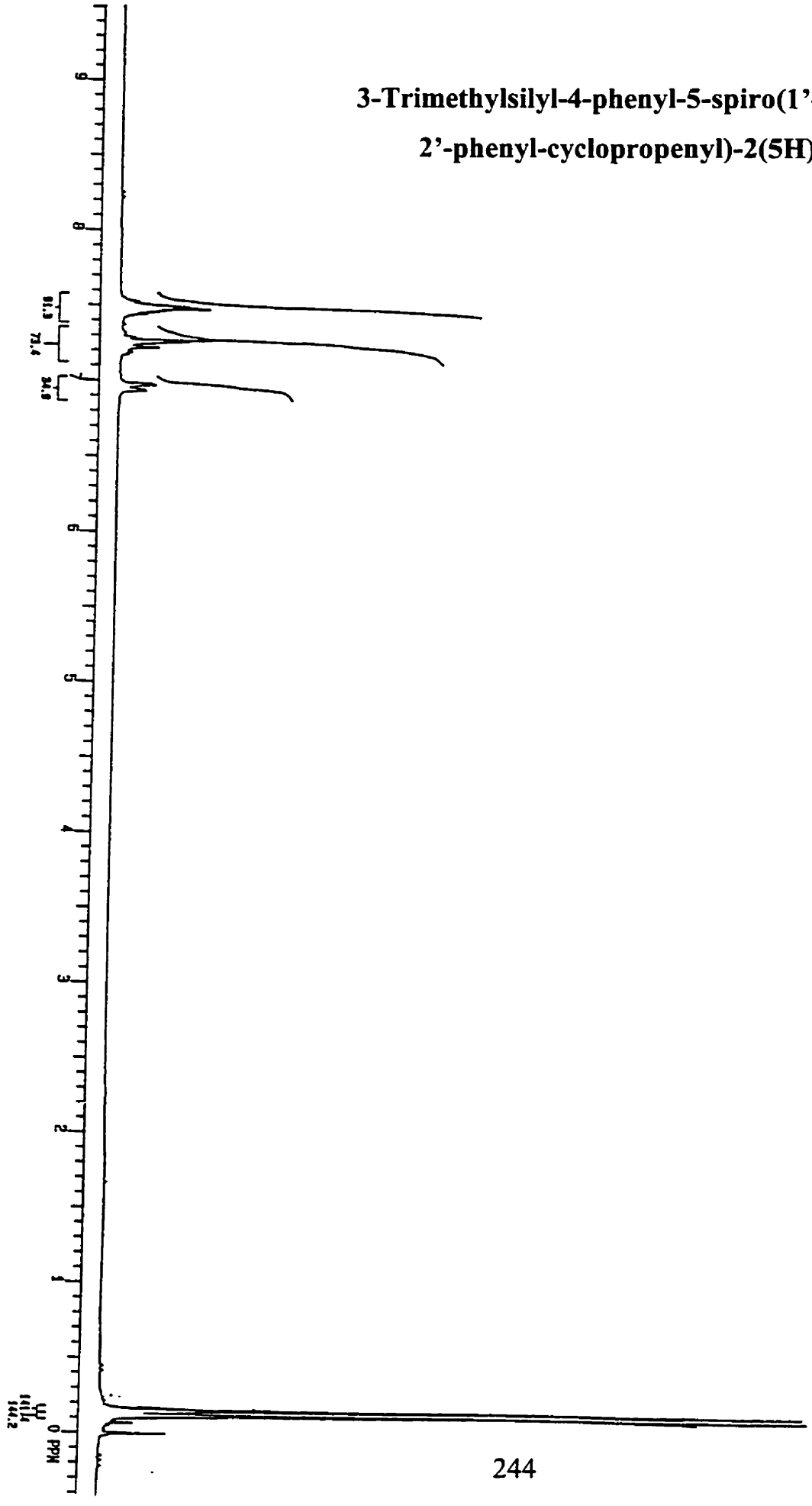
**3-Trimethylsilyl-4-phenyl-5-spiro(1',2'-dimethylcyclopropenyl)-2(5H)-furanone (25)**



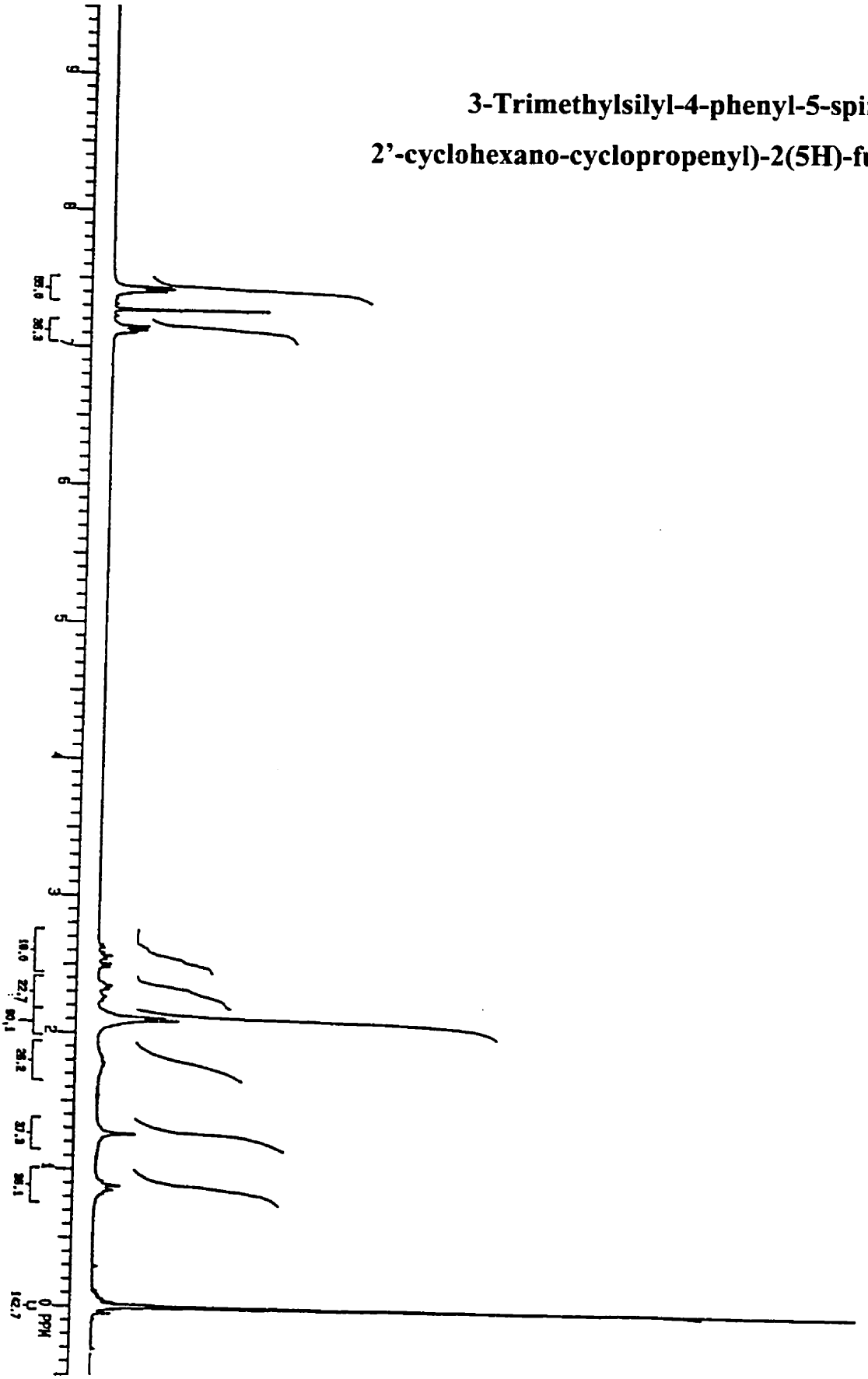
**3-Trimethylsilyl-4-phenyl-5-spiro(1'-methyl-2'-trimethylsilyl-cyclopropenyl)-2(5H)-furanone(26)**

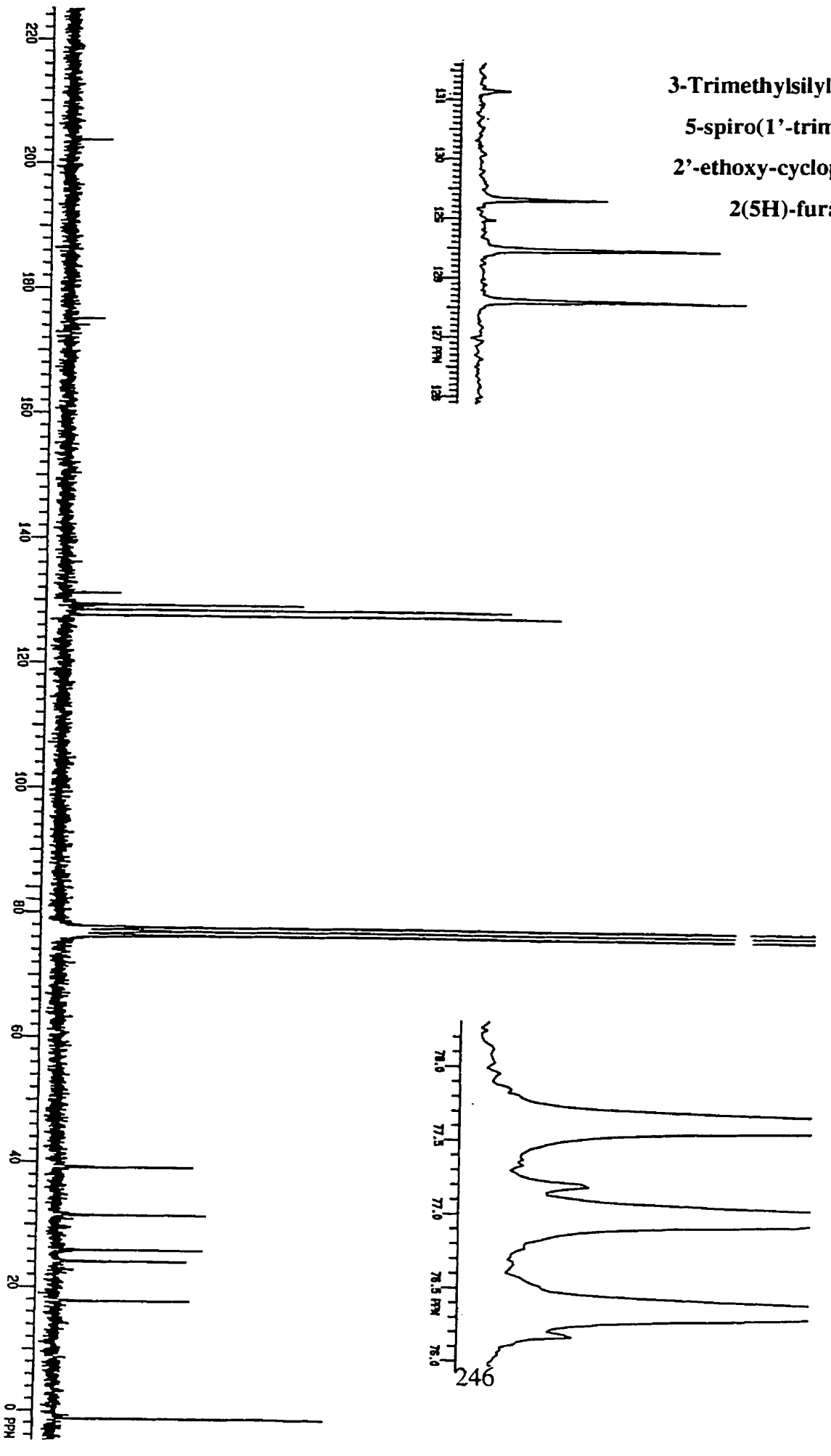


**3-Trimethylsilyl-4-phenyl-5-spiro(1'-trimethylsilyl-2'-phenyl-cyclopropenyl)-2(5H)-furanone (27)**



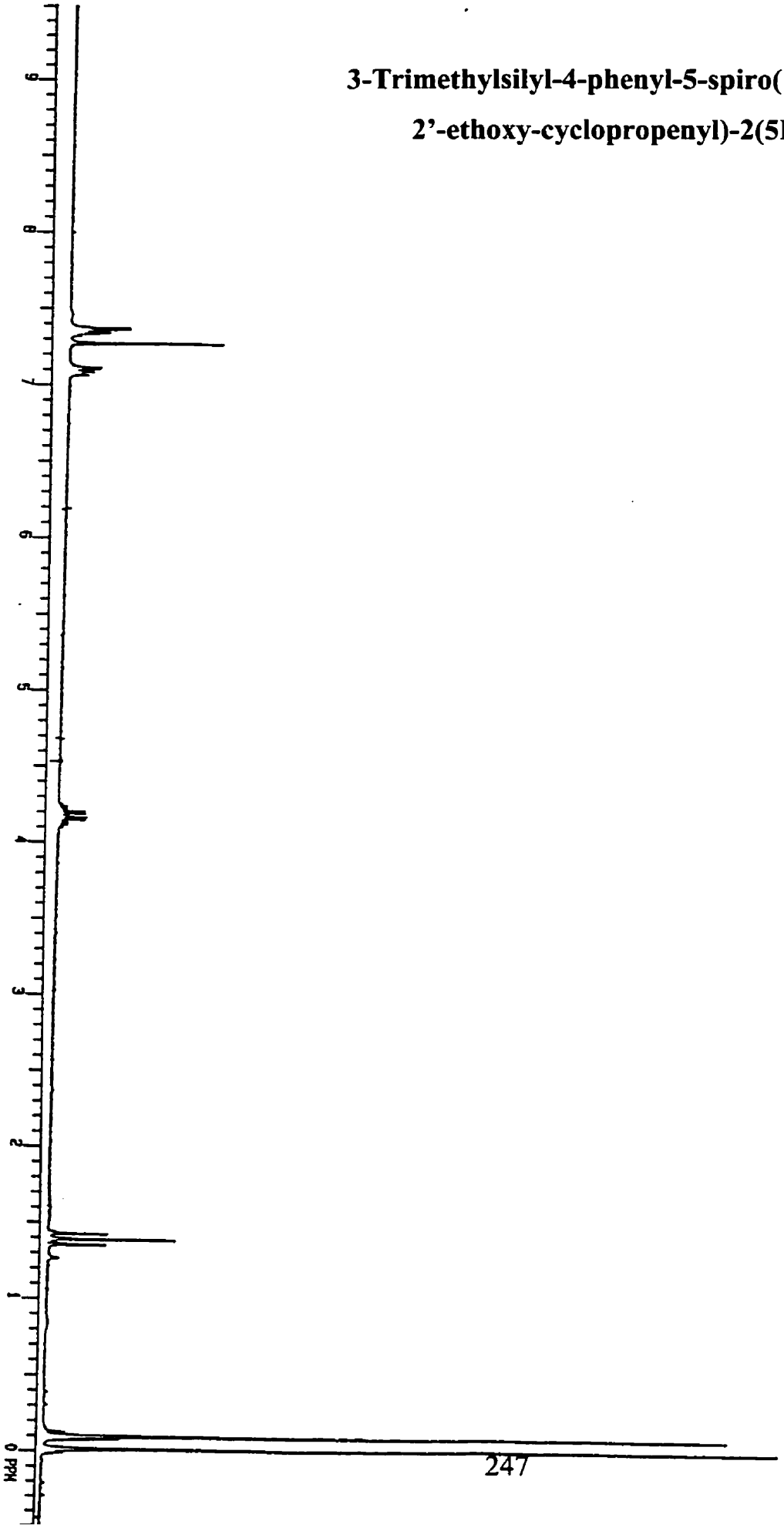
**3-Trimethylsilyl-4-phenyl-5-spiro(3'-oxo-1', 2'-cyclohexano-cyclopropenyl)-2(5H)-furanone (28)**



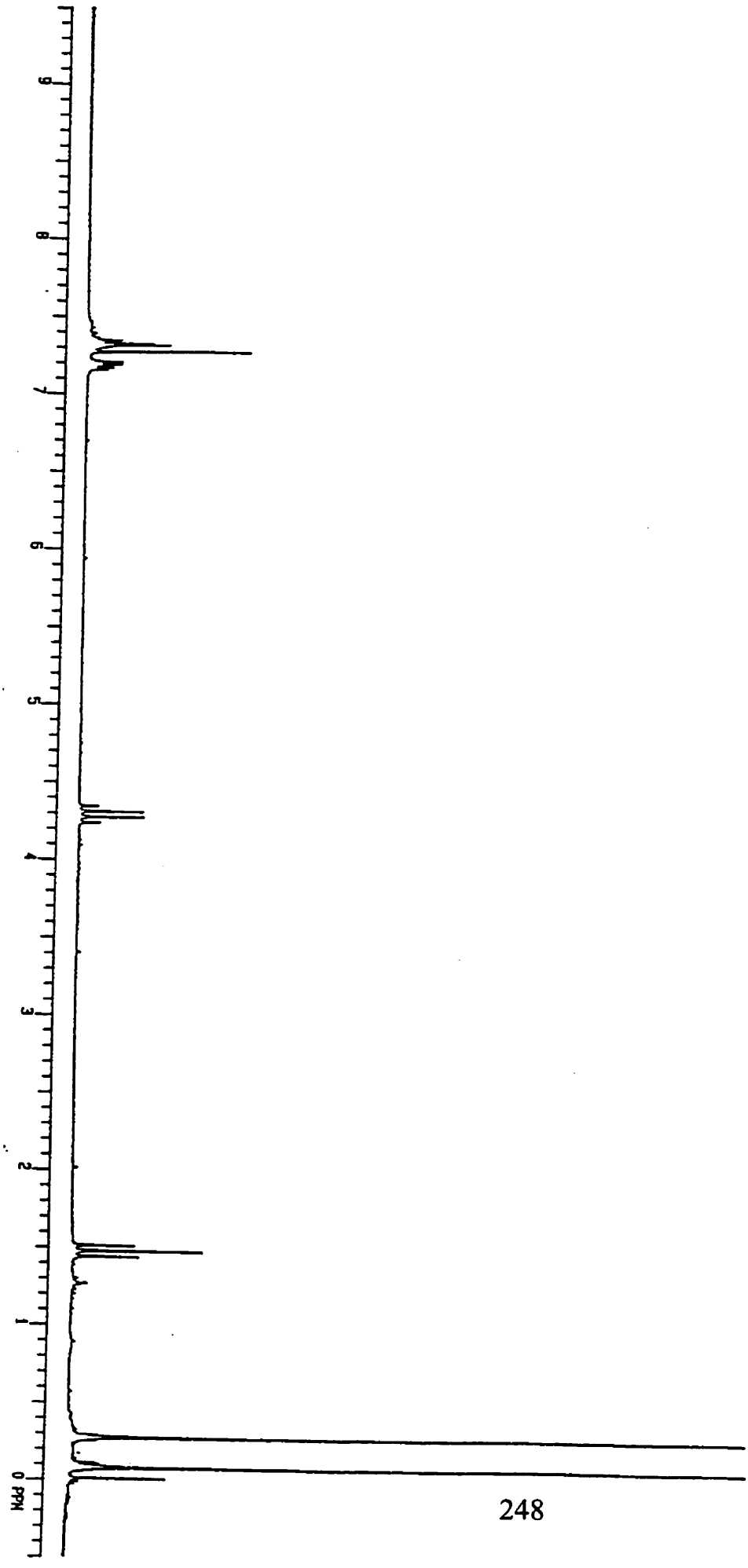


**3-Trimethylsilyl-4-phenyl-5-spiro(1'-trimethylsilyl-2'-ethoxy-cyclopropenyl)-2(5H)-furanone (29)**

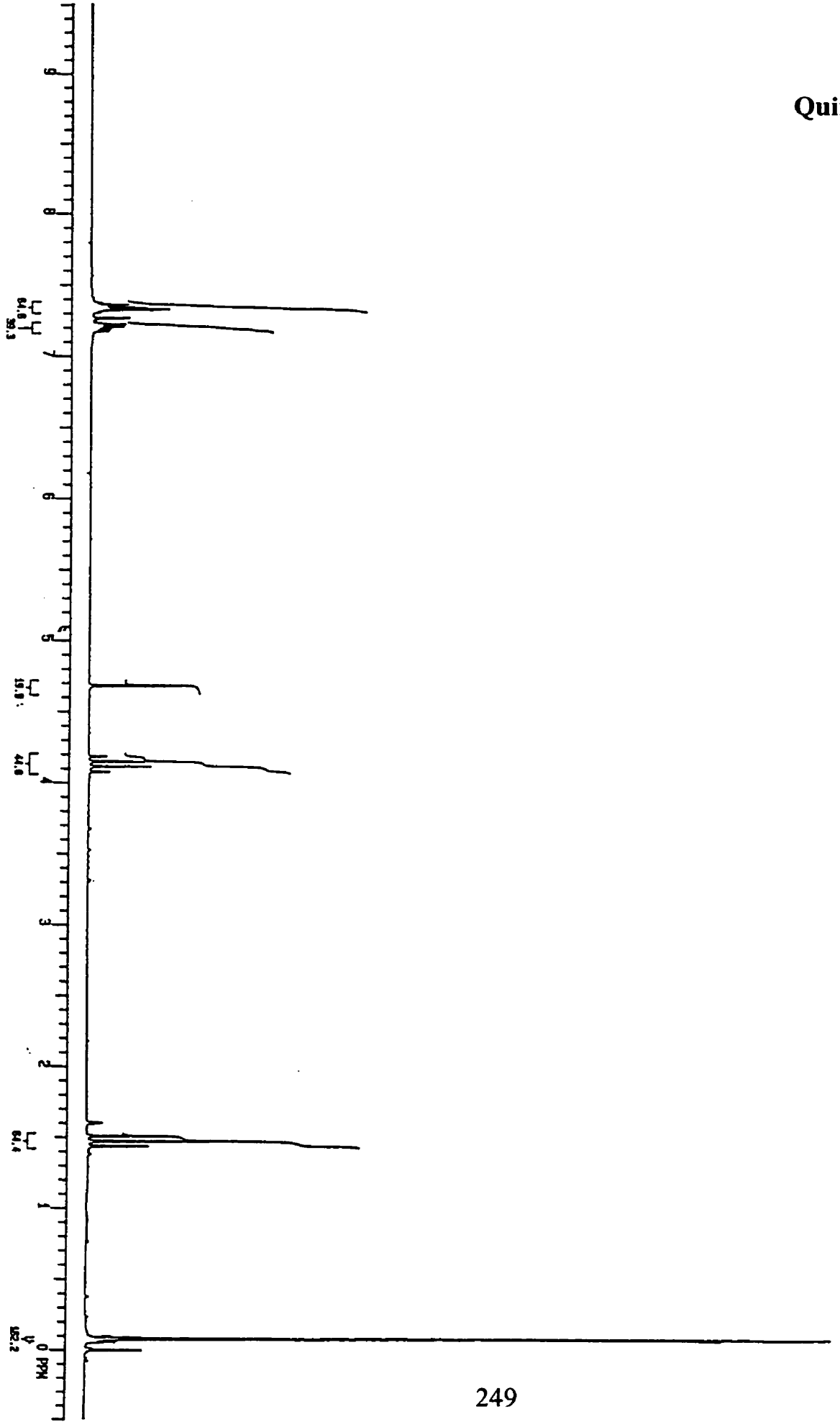
**3-Trimethylsilyl-4-phenyl-5-spiro(1'-trimethylsilyl-2'-ethoxy-cyclopropenyl)-2(5H)-furanone (29)**



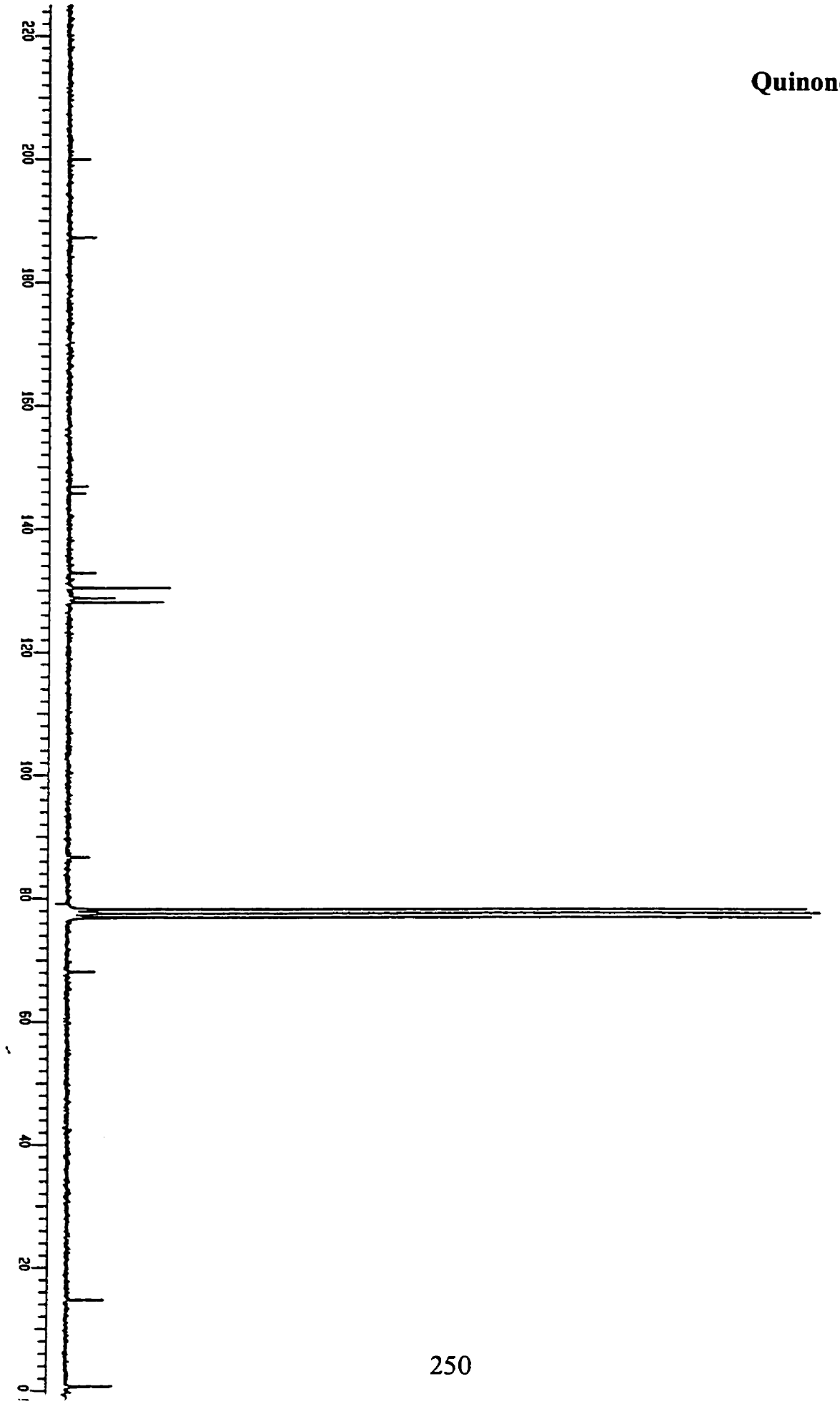
**Quinone (30)**



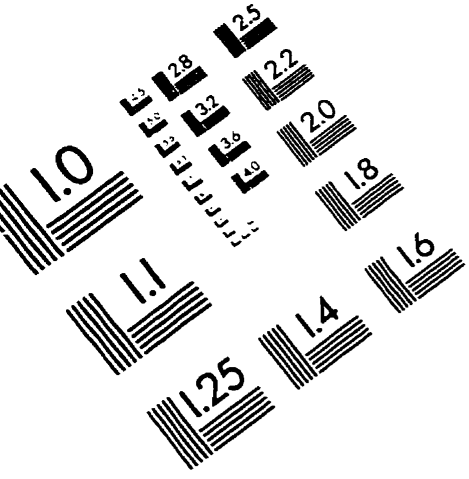
**Quinone (31)**

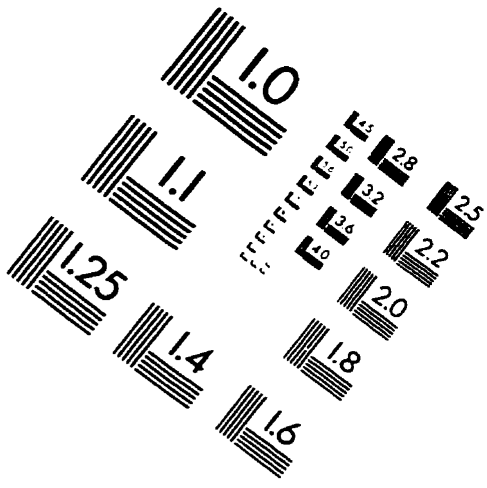


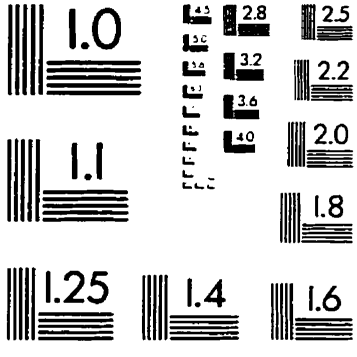
**Quinone (31)**

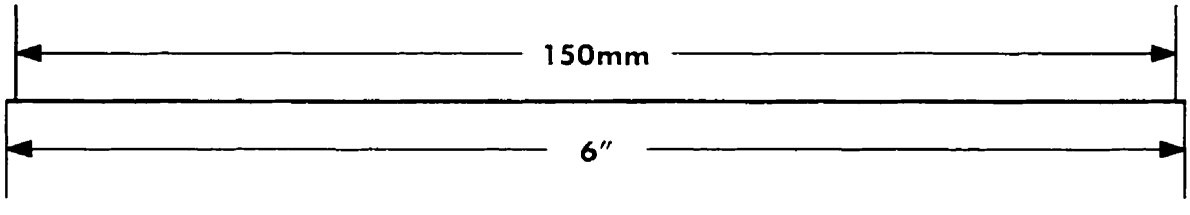


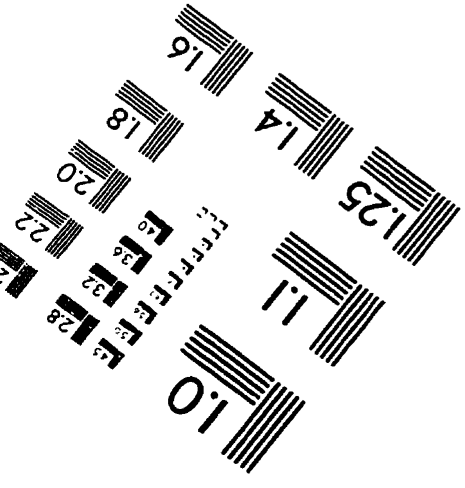
# IMAGE EVALUATION
# TEST TARGET (QA-3)

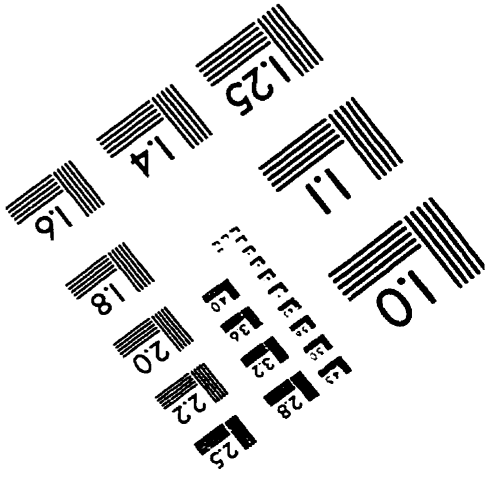
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