Highly Selective Synthesis of Polyfunctionalized Carbo- and Heterocyclic Compounds from Squaric Acid

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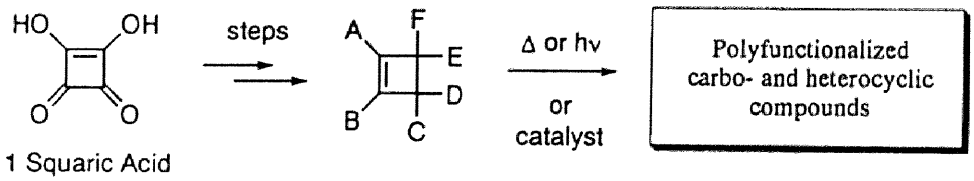
Chapter 1

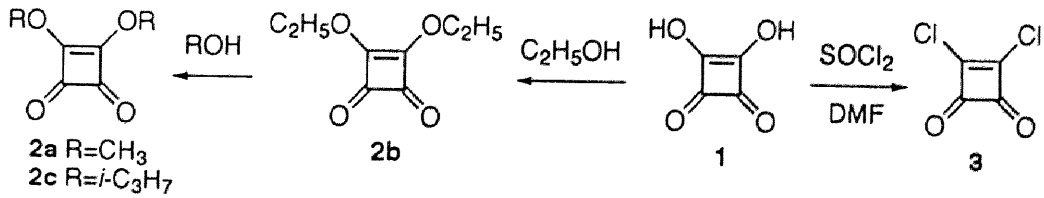
General Introduction

Building block methodologies provided a viable solution for the assembly of highly functionalized molecules that would require lengthy steps using other methods. In this respect, cyclobutenediones and cyclobutenones derived from squaric acid **1**, a commercially available four-membered oxocarbon,[1] have recently been utilized as C_4-synthons for highly substituted cyclic compounds (Figure 1).[2] While squaric acid itself has been studied theoretically and applied as a key component of advanced materials,[3] it also provides a wide variety of cyclobutenediones and cyclobutenones having multiple substitution patterns by virtue of its useful multifunctionality. Hopefully, the modified cyclobutenone rings have many possibilities to be transformed to other ring systems, and these transformations, in principle, are achieved by two sequences: (1) conversion of cyclobutenedione to satisfactory substituted cyclobutene by addition of a carbon nucleophile and (2) regio- and stereoselective rearrangement of the resulted cyclobutene to the final product by thermolysis, photolysis, and catalysis with the aid of relief of ring strain (Scheme 1).



Scheme 1

As mentioned above, this strategy starts from carbon-carbon bond formation on the ring. Based on the cyclobutenedione structure, acidic hydroxy groups are replaced by better leaving groups (*i.e.* chloride and alkoxides: Scheme 2) and then various nucleophiles can be introduced at the carbonyl (*via* 1,2-addition) or olefinic carbon (*via* 1,4-addition) (Figure 2).[4]



Scheme 2

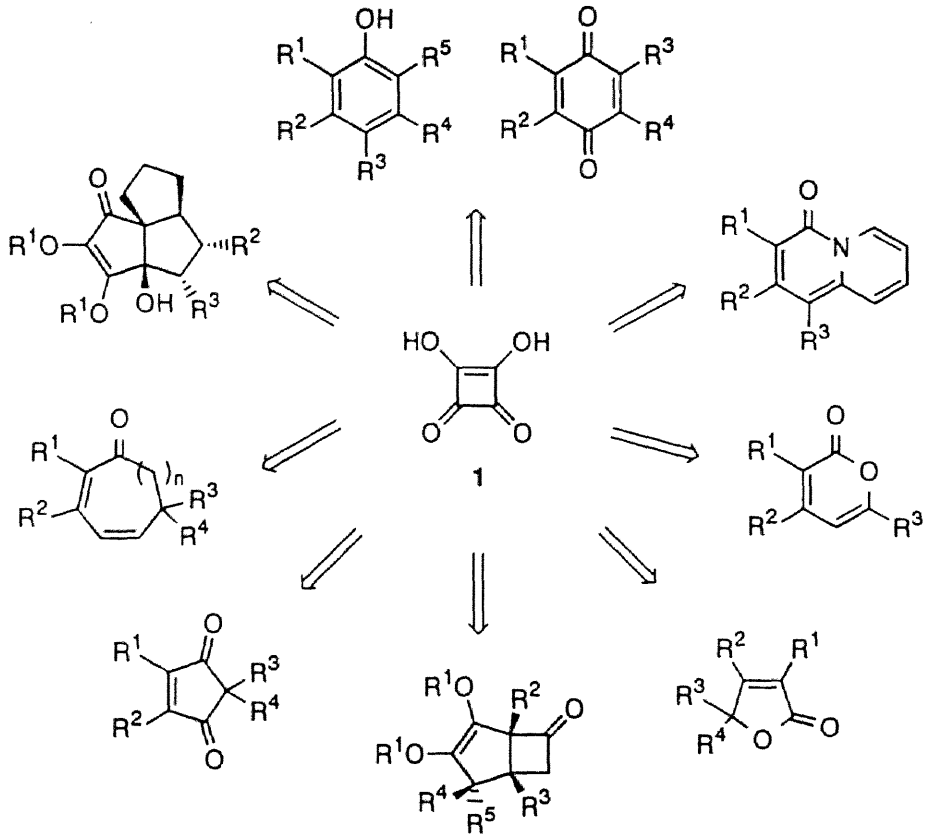


Figure 1. Transformation of Squaric Acid to Various Ring Systems

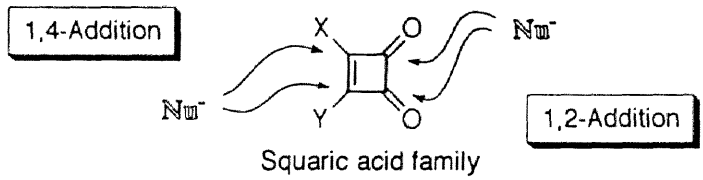
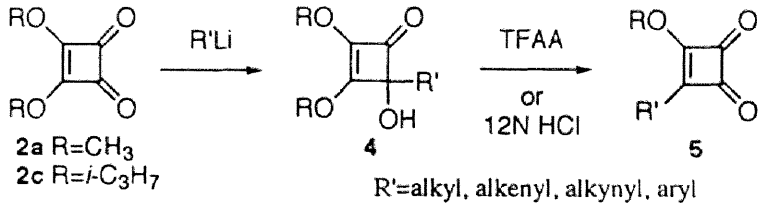


Figure 2. Addition Patterns of Nucleophiles toward Squaric Acid Family

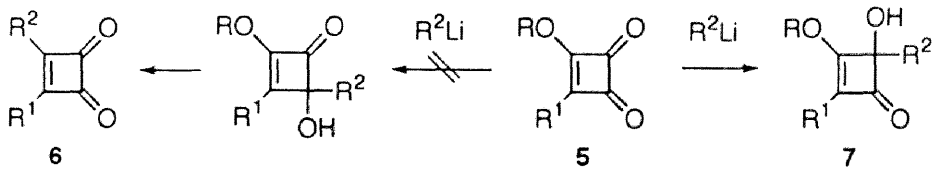
Until now, additions to ring enone moiety have been achieved mainly with organolithiums and -magnesiums. Kraus reported that organolithiums underwent clean 1,2-addition toward dimethyl squarate **2a**, whereas organomagnesiums added in 1,4-fashion.[5] On the contrary, Dehmlow and Schell reported that the yield of reaction of a number of dialkyl squarates with Grignard reagents were variable depending on the alkoxy groups.[6] Moreover, recent report showed allyl Grinard reagents adds to dimethyl squarate and methyl semisquarate

derivatives in 1,2-fashon.[7] Thus, a modified 2-step procedure for the synthesis of 4-substituted-3-alkoxy-3-cyclobutene-1,2-diones was developed by both Moore's group and Liebeskind's group, independently.[8] As outlined in scheme 3, 1,2-addition of an organolithium to diester **2a** or **2c** gave 4-substituted-4-hydroxy-2,3-dialkoxycyclobutenones **4**, which were then hydrolyzed under acidic conditions to produce the cyclobutenediones **5**.



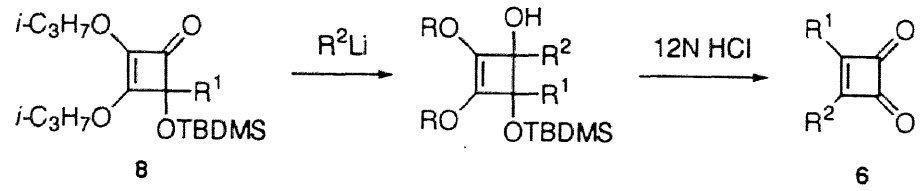
Scheme 3

Direct introduction of the second substituent to cyclobutenediones **5** can not give desired differentially substituted cyclobutenediones **6** because organolithium reagents preferencially add to the more electrophilic enone system without a donor alkoxy group to produce alcohols **7** (Scheme 4). A wide variety of 4-substituted-4-hydroxycyclobutenones have been synthesized based on this exact selectivity.[2b]

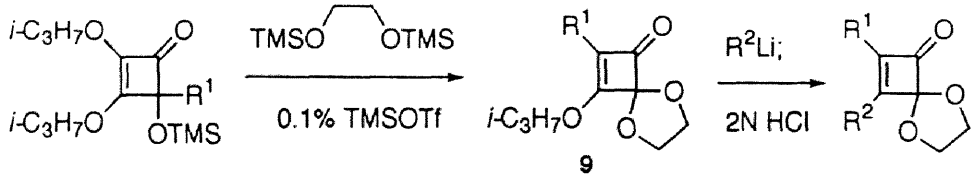


Scheme 4

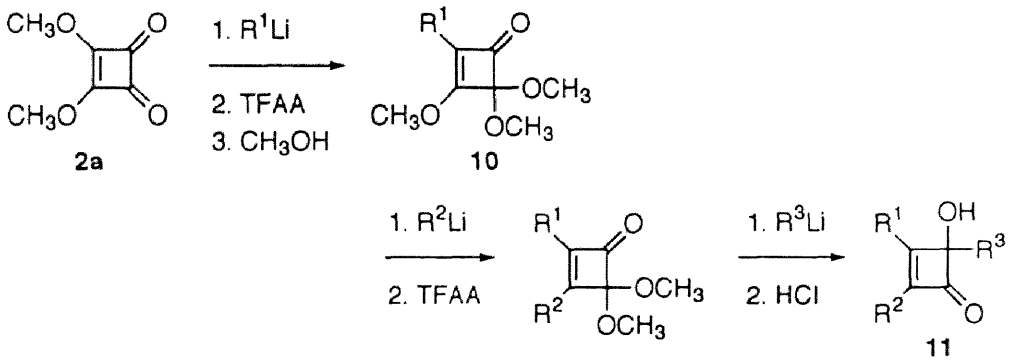
Liebeskind *et al.* demonstrated that protection of the free alcohol of the intermediate 1,2-adduct **4** as a *tert*-butyldimethylsilyl (TBDMS) ether **8** allows addition of a second organolithium reagent, and then acid hydrolysis generates differentially disubstituted cyclobutenediones **6** in good yield (Scheme 5).[8b] Ethylene ketals **9**[9] and dimethyl acetals **10**[10] are another useful intermediates leading to differentially disubstituted cyclobutenediones **6** and 2,3,4-trisubstituted-4-hydroxy-cyclobutenones **11** (Scheme 6 and 7).



Scheme 5

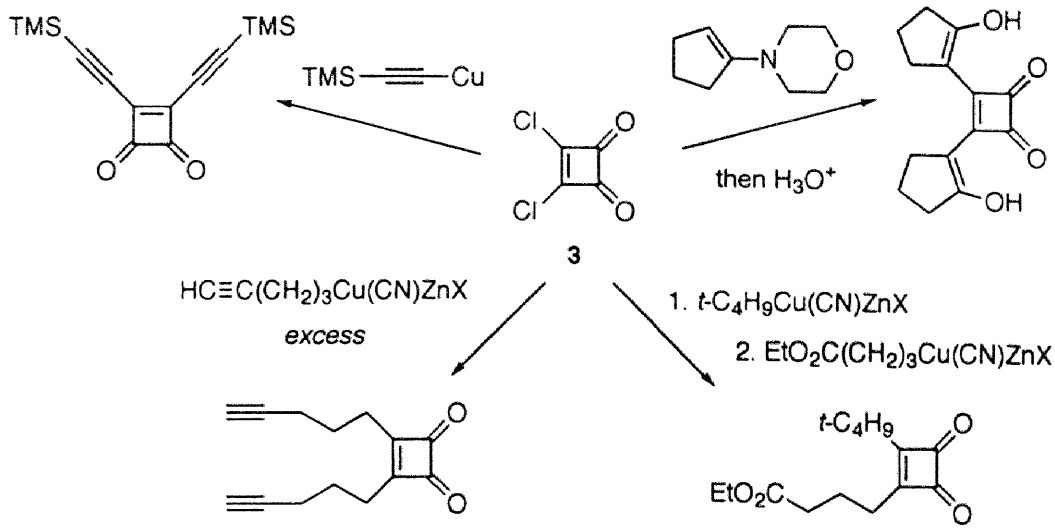


Scheme 6



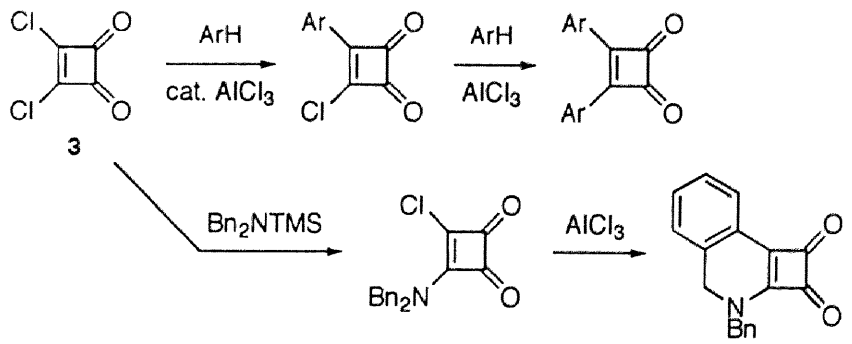
Scheme 7

Straightforward routes to substituted cyclobutenediones have been developed by direct introduction of nucleophiles to the olefinic position. For this purpose, dichloride **3** more reactive than esters **2** was mainly used as an efficient substrate. Enamine has been reported to be useful nucleophile, and mono- and di-substitution products were obtained from diethyl ester **2b** and dichloride **3**, respectively.[11] Reaction of dichloride **3** with alkynylcopper reagents gave enediynes as disubstitution products in moderate yields.[12] Functionalized zinc-copper organometallics developed by Knochel *et al.* selectivelty provided cyclobutenediones having a variety of functionalized substituents at 3- and 4-positions from dichloride **3**.[13] Selected examples are depicted in Scheme 8.



Scheme 8

In contrast to the above nucleophilic reactions, electrophilic reaction has received less attention; for all the auther knows, only arylation of acid chlorides under Friedel-Crafts conditions has been reported (Scheme 9).[14]



Scheme 9

Thus, the auther first attempted to develop electrophilic reaction of squaric acid family with unsaturated organosilanes. The electrophilic C-C bond formation using unsaturated organosilanes have following advantages;

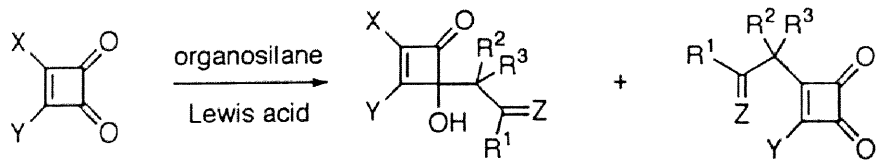
(1) Various substituents having an unsaturated functional group can be introduced with the reaction site on the organosilanes controlled exactly by β-effect of the silyl group.[15]

(2) Reaction site on the cyclobutenedione ring can be controlled by the choice of Lewis acids or other promoters.

(3) If selective activation of the ring is possible, the presence of reactive functional groups in a side chain on the ring or on the employed organosilane itself does not interfere with regioselectivity.[1]

(4) 2π-Aromatic character,[16] if it exists, can work preferably under the electrophilic conditions.

In fact, Lewis acid-catalyzed reaction of squaric acid chlorides **3**,**12**, and **13** and diethyl ester **2a** with allylsilane, silyl enol ether, and silyl ketene acetal gave 4-substituted-4-hydroxycyclobutenones **14** and/or 4-substituted-cyclobutenediones **15** depending on substitution patterns of both substrate cyclobutenediones and silanes, reaction temperature, and employed catalyst (Scheme 10). The obtained adducts were further converted to other cyclic compounds.

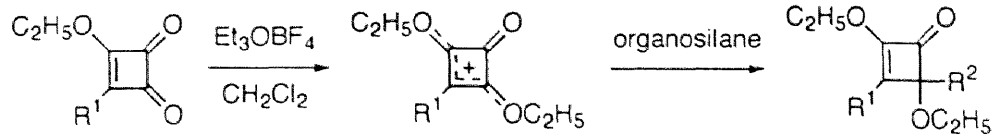


2a X=Y=OC_2H_5
3 X=Y=Cl
12 X=Cl, Y=OMe
13 X=Cl, Y=$N(C_2H_5)_2$

14 **15**

Scheme 10

In continuation of this work, the auther found that Meerwein salt, triethyloxonium tetrafluoroborate (Et_3OBF_4),[16] also promotes the reaction of squaric acid esters **2a** and **16** with silyl cyanide, allylsilane, silyl enol ether, and silyl ketene acetal to afford 4-ethoxy-4-substituted cyclobutenones **18**. In sharp contrast to nucleophilic reactions, the addition occurred in opposite regioselectivity because the thermodynamically more favorable ethoxycarbenium ion **17** should be formed from the β-ethoxy enone under the employed conditions and react with the silanes (Scheme 11).



2a R=OEt
16 R=alkyl, aryl, alkynyl, H

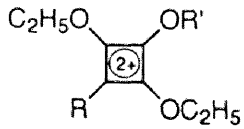
17

18

R^2=CN, allyl, acylmethyl

Scheme 11

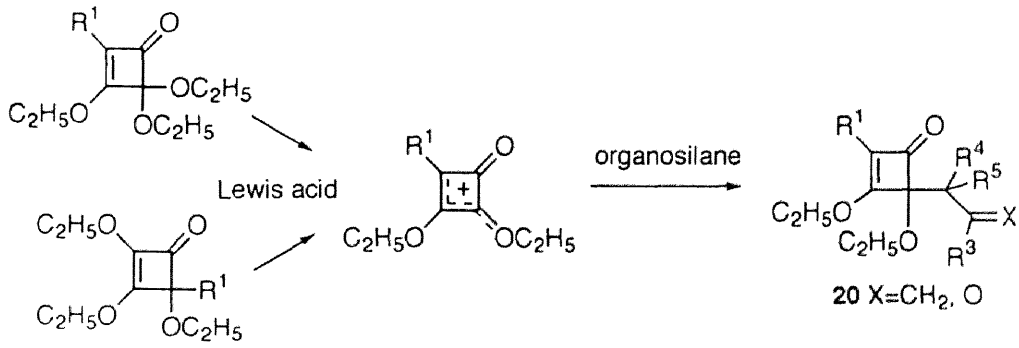
The above reaction was found to be rather specific to squaric acid system, and this seems to be related with possible 2π-aromatic intermediates **19** involved (Figure 3).



19 R'= - or C_2H_5

Figure 3. Possible 2π-Aromatic Intermediates

A similar reaction of cyclobutenedione monoacetals and its vinylogues also gave 2,4-disubstituted cyclobutenones **20**, in which 4-allylcyclobutenones were directly converted to synthetically useful precursor, bicyclo[3.2.0]butenones by refluxing in xylene (Scheme 12).[7] The details of these studies are discribed in the next chapter.

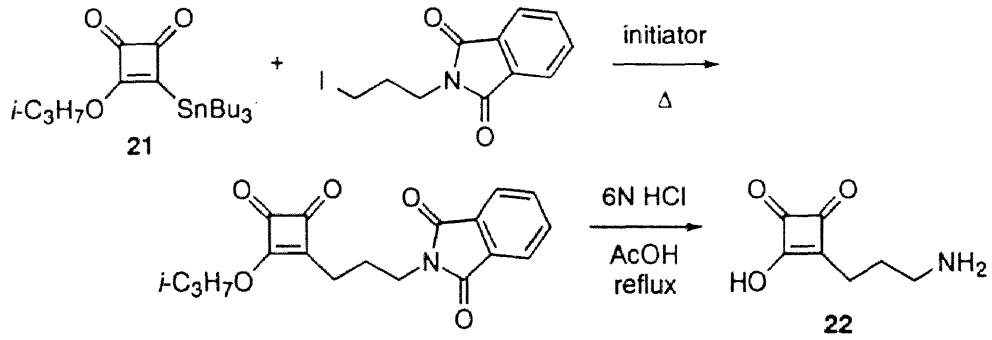


20 X=CH_2, O

Scheme 12

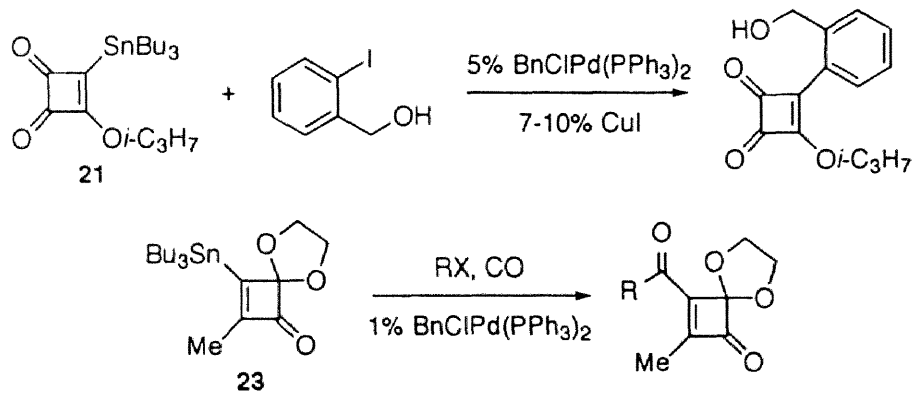
Introduction of functionalized substituents to the cyclobutenedione system has drawn continuous attention because such cyclobutenediones are potent pharmaceuticals; *i.e.* squaric acid was found to be a remarkably strong acid for an enol, having pK_a values close to those for

sulfuric acid, and thus, a 3-hydroxy-3-cyclobutene-1,2-dione moiety can be used as a bioequivalent to a carboxylic acid or tetrazole.[17] From this point of view, semisquaric acid derivatives obtainable from above-mentioned methods are of importance as lead compounds of novel pharmaceuticals. Recently, additional two methods, producing cyclobutenediones having functionalized substituents, were reported. An aminoalkyl-substituted semisquaric acid derivatives **22** (a potential neuroprotective agent) were synthesized by use of free radical reaction of 3-isopropoxy-4-(tri-*n*-butylstannyl)-3-cyclobutene-1,2-dione **21** with a functionalized alkyl halide (Scheme 13).[17d]



Scheme 13

Liebeskind's group have developed palladium/copper-catalyzed cross-coupling of 4-(tri-*n*-butylstannyl)-3-cyclobutene-1,2-dione **21** and 3-(tri-*n*-butylstannyl)cyclobutenedione ethylene acetal **23** with alkenyl, alkynyl, and aryl halides and triflates (Scheme 14).[18]



Scheme 14

As shown in Figure 1, cyclobutenones and cyclobutenediones, readily available from squaric acid **1**, can be transformed to various polyfunctionalized cyclic compounds. Cyclobutenones have been utilized for synthesis of substituted phenol derivatives as precursors of variously substituted vinylketenes (Figure 3) since it is confirmed that cyclobutenone **24** is participated in formation of α-naphthols from the thermal reaction of diphenylketene with alkynes (Scheme 15).[19]

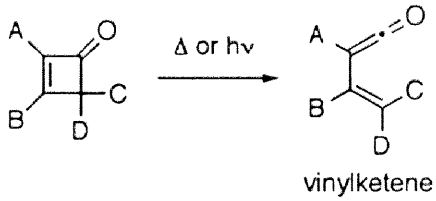
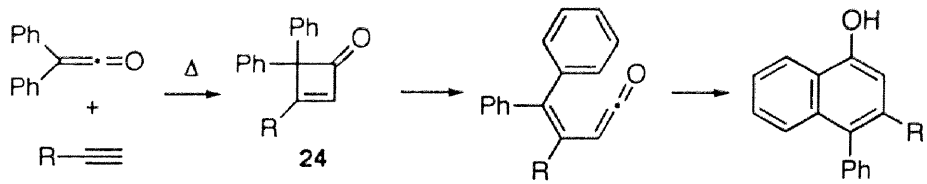
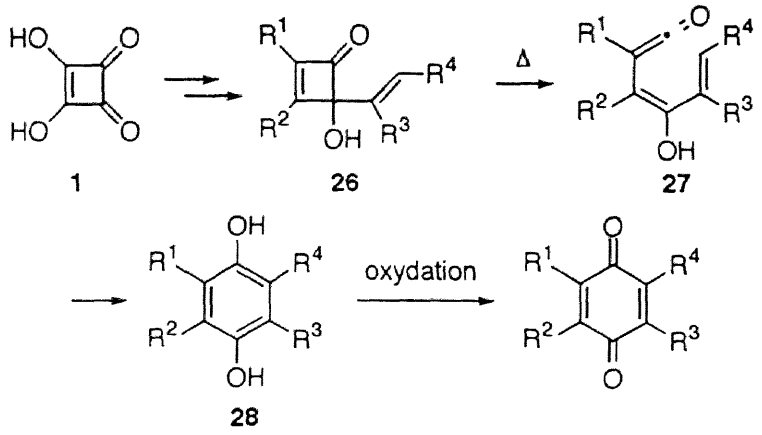


Figure 3



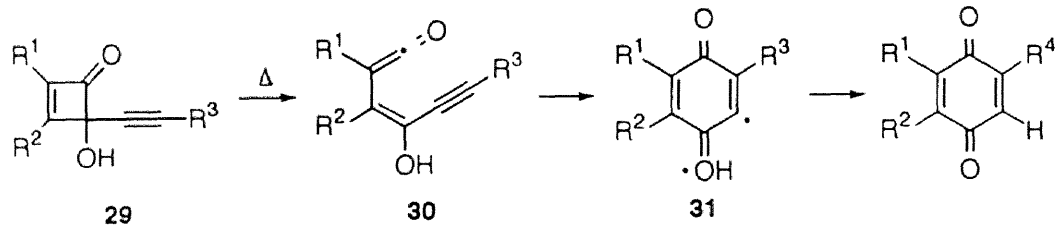
Scheme 15

Many studies for synthetic application of squaric acid focused on application of these reactive intermediates. Moore's group and Liebeskind's group have independently developed the method to construct highly substituted quinones starting from squaric acid **1**.[2] General scheme was given below. Thermal electrocyclic ring opening of 4-hydroxycyclobutenones **25** having an unsatureated substituent, prepared from **1**, followed by 6π-electrocyclization of resulted unsaturated ketene intermediates **26** generates hydroquinones **26**, which are finally oxidized to quinones (Figure 16). This novel entry to quinones were potentially general because cyclobutenones with diverce substituent patterns are now accessible (*vide supra*), and thus applied to the synthesis of various biologically active natural products.



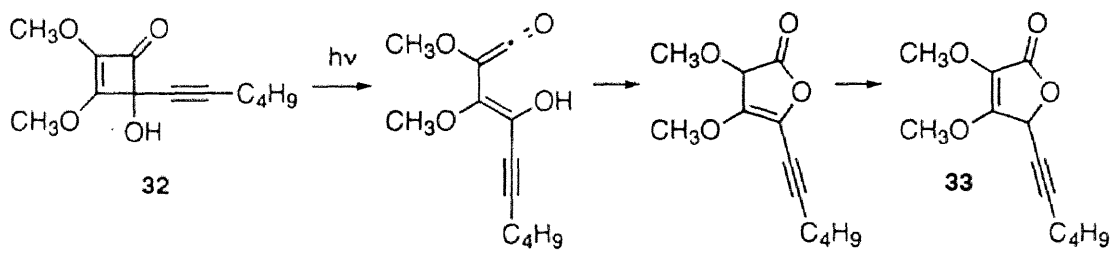
Scheme 16

Moore *et al.* found that 4-alkynyl-4-hydoxycyclobutenones **29** also participate in a similar transformation, but substituted quinones were directly obtained without oxidation (Scheme 17).[20] This rearrangement was reported to proceed through a biradical intermediate **31** produced by the reclosure of an enynylketene **30**, and this mechanism is in close relation to enediyne cyclization (Masamune-Bergman rearrangement).[21]



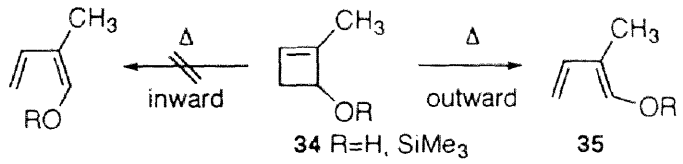
Scheme 17

The success of above-mentioned examples depends on the stereoselectivity of electrocyclic ring opening (torquoselectivity). In fact, photolytic conditions gave different results. Scheme 18 illustrates that the photolysis of 4-alkynyl-4-hydroxycyclobutenone **32** produced a butenolide **33** arising from inward rotation of the hydroxy group.[20a,22]



Scheme 18

The thermal ring opening of 3-hydroxy and 3-trimethylsilyloxy-2-methylcyclobutene **34** were reported to give only products **35** arising from outward rotation of the oxygen substituents even though these products appear to be less stable than those arising from inward rotation (Scheme 19).[23]



34 R=H, $SiMe_3$ **35**

Scheme 19

Supportive calculations showed the stereochemistry in the thermal electrocyclic conrotatory opening of substituted cyclobutene can be rationalized on the basis of electronic effects. Rondan and Houk *et al.* demonstrated computationally that electron donors at C_3 and C_4 preferentially rotate outward in order to maximize the stabilizing two-electron interaction between the donor orbitals on the substituent with the $\sigma^*_{C_3C_4}$ orbital (σ^*-π in Figure 4) and to minimize the repulsive four-electron interaction between the same donor orbitals with the $\sigma_{C_3C_4}$ orbital (σ+π in Figure 4).[24] They also showed that the preference for outward rotations of the substituents increases as the electron-donor ability of the substituents increases. Powerful electron acceptors should have the opposite effect, and consequently, opposite stereochemical results are predicted.[25]

On the contrary, an exception depicted in Scheme 20 was reported by Moore *et al.*.[26a] If the electrocyclization of a ketene intermediate **36** through the outward rotation of the hydroxy group is impossible, the inward rotation of the hydroxy group followed by lactonization consequently gave a mixture of butenolides. Similar unusual results were reported by Liebeskind's group[26b] and the auther. Adducts **37** obtained from the reaction of methyl ester chloride and silyl enol ethers or silyl ketene acetals afforded (*Z*)-5-acylmethylenetetronates **38** *via* an similar lactonization and subsequent dehydrochlorination (Scheme 21). This thermal lactone formation was applied to the synthesis of naturally occuring aminobutenolide basidalin. Detailed informations were given in the next chapter.

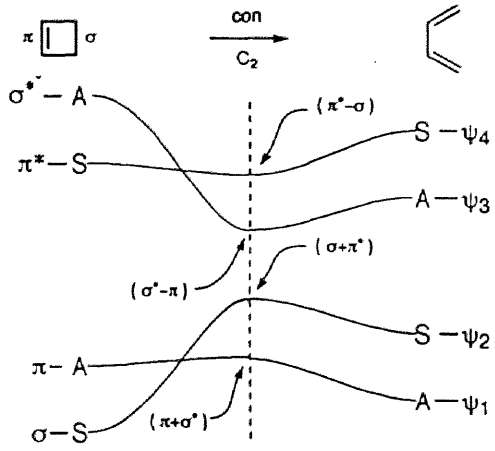
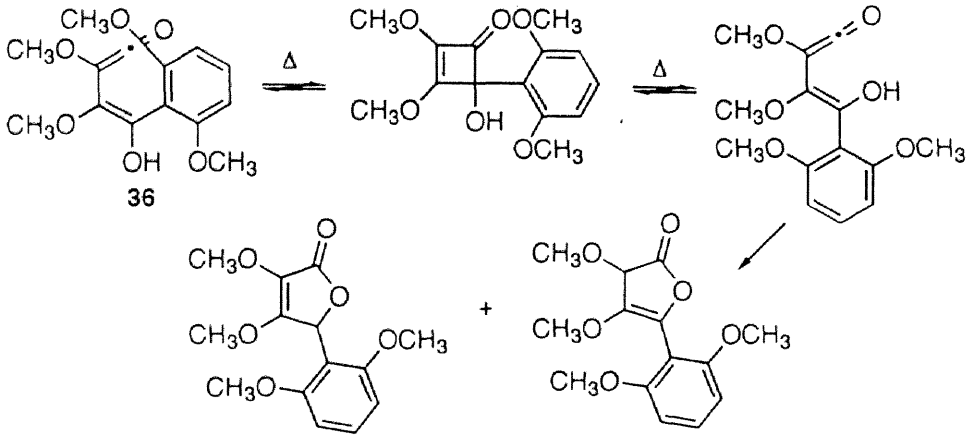
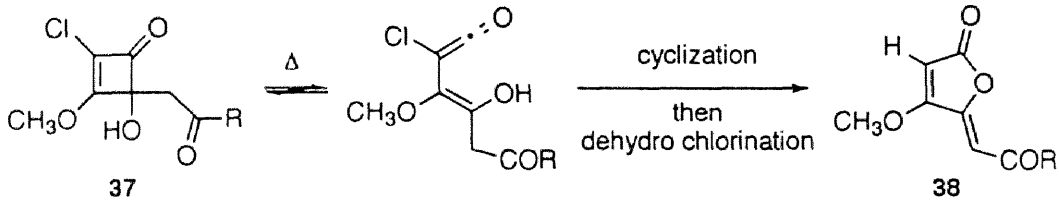


Figure 4. Schematic representation of the behavior of the orbitals involved in bonding changes in the conrotatory electrocyclization of cyclobutene.
(N. G. Rondan and K. N. Houk, *J. Am. Chem. Soc.*, **107**, 2099 (1985).



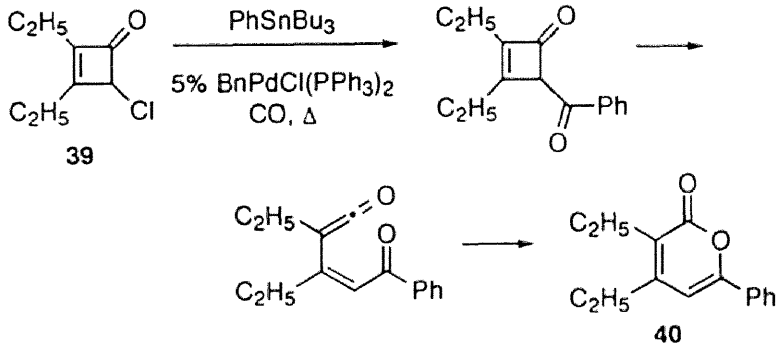
Scheme 20



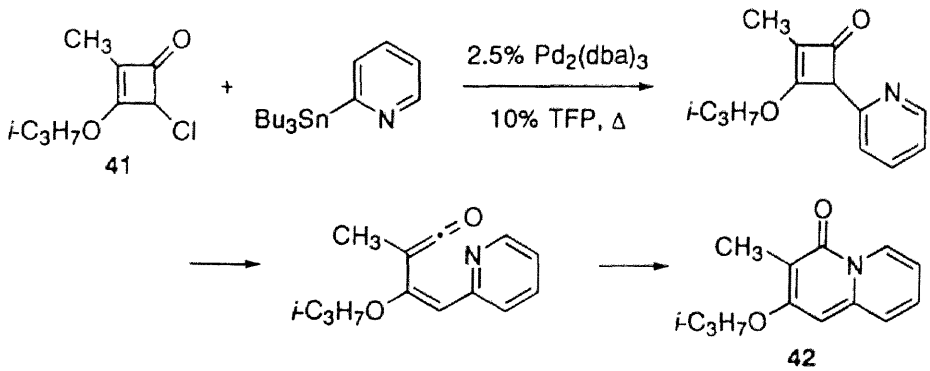
Scheme 21

Liebeskind *et al.* reported that the cross-coupling of 4-chlorocyclobutenone and alkenylzirconiums and stannanes produced 4-alkenylcyclobutenones in a regiocontroled way.

which were converted to highly substituted phenol derivatives under employed conditions.[27] A carbonylated cross-coupling of 4-chlorocyclobutenone **39** directly produced a rearranged pyrone **40** (Scheme 22).[28] In a palladium-catalyzed cross-coupling of **41** and 2-stannylpyridine, 6π-electrocyclization involving a carbon-nitrogen double bond proceeded to furnish quinolizinone derivatives **42** (Scheme 23).[26b] This result showed a preference of carbon-nitrogen double bond over carbon-carbon double bond in the present cyclization.



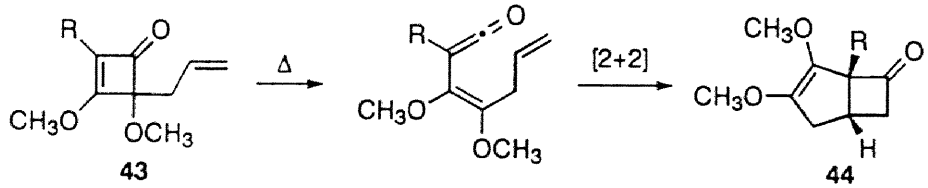
Scheme 22



Scheme 23

Intramolecular [2+2] cyclization of ketenes with an alkene provides a viable route for bicyclic cyclobutanones,[29] which have been utilized as precursors for the synthesis of various bicyclic compounds.[30] Recently, Moore and co-workers reported that the thermolysis of 4-allylcyclobutenones **43** gave bicyclo[3.2.0]heptenones **44** *via* stereoselective thermal ring

opening and subsequent intramolecular [2+2] cycloaddition of resultant vinylketenes (Scheme 24).[7]

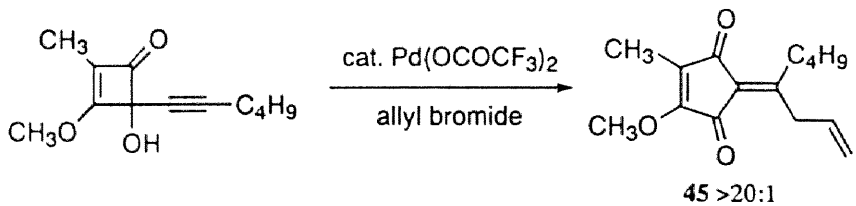


43 44

Scheme 24

In this example, 4-Allyl-4-hydroxycyclobutenones were obtained by the 1,2-addition of allylmagnesium bromide to dimethyl squarate in good yield. However, the extension of this method to obtain 4-allyl-4-hydroxycyclobutenones having a variety of substituents at 2-position was less effective. The addition of allyllithium was also reported to be unsuccessful. Therefore, the auther attempted the reaction of cyclobutenedione monoacetals with various allylsilane. As a result, 4-allyl-4-alkoxycyclobutenones were synthesized directly in good yields, and the adducts were converted highly substituted bicyclo[3.2.0]heptenones (*vide supra*).

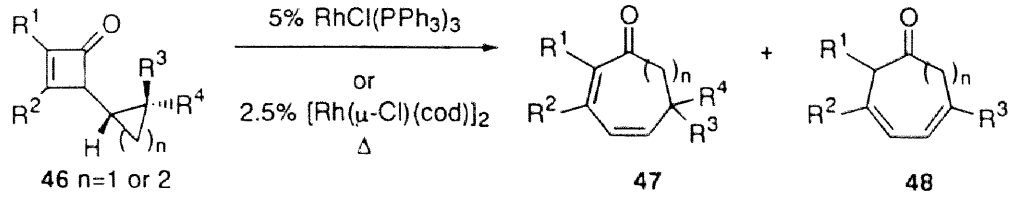
Above examples showed that previous studies principally focused on the electrocyclic ring opening of cyclobutenones and successive ring closure of the resulting vinylketene intermediates. Nevertheless, some examples do not fall into this category. For example, a $Pd(OCOCF_3)_2$-catalyzed ring enlargement of 4-alkynylcyclobutenone to alkylidenecyclopentenedione **45** was reported by Liebeskind and co-workers (Scheme 25).[31] In this reaction, the stereochemistry of the resulted exo-methylene was effectively controlled. An antiviral compound, called benzoabikoviromycin, was synthesized by use of this tactics. Other related examples were also reported.[32]



45 >20:1

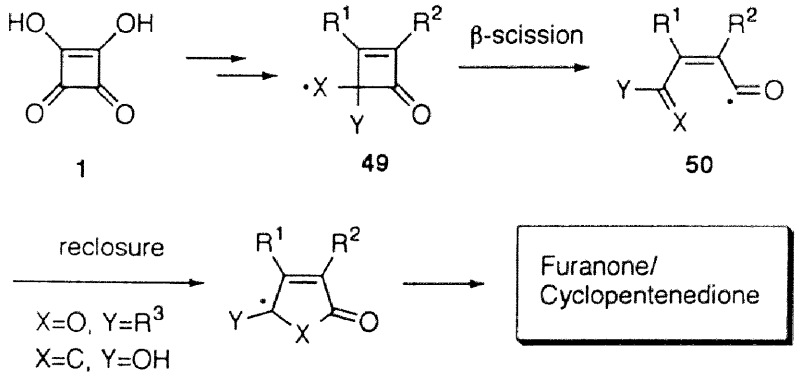
Scheme 25

Liebeskind's group further developed a novel method to synthesize seven- and eight-membered cycloalkenones from 4-cyclopropyl- and 4-cyclobutylcyclobutenones **46**. Rhodium-catalyzed ring enlargement involving both cyclobutenone and cyclopropane or cyclobutane ring gave rise to cycloheptadienones **47** and cyclooctadienones **48** (Scheme 26).[33]



Scheme 26

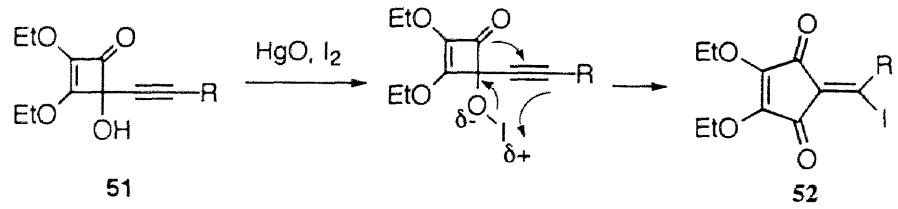
Encouraged by these reports, the auther developed a novel ring transfroming method by use of radical intermediates. In this method, ring opening was effected by β-scission of a radical generated at the position adjacent to the cyclobutene ring. As illustrated in Scheme 27, acyl radical intermediates **50**, which are generated by β-scission from the initial radicals **49** (X=O, C), contribute to subsequent intramolecular reclosur in the 5-*endo* mode to form five-membered ring systems. These unieque 5-*endo* cyclizations of pentadienoyl radical to cyclopentenone radical and its oxa version are discussed by use of computational analyses.



Scheme 27

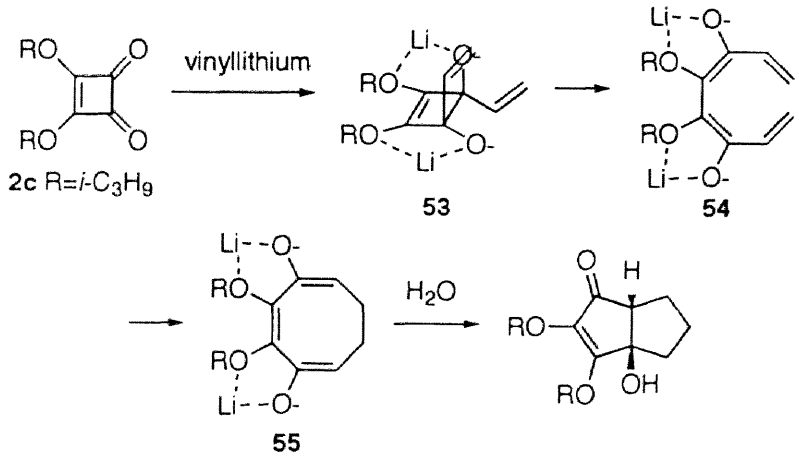
In contrast to theses results, the reaction of 4-alkynyl-4-hydroxycyclobutenones **51** with I_2/HgO, affording iodomethylenecyclopentenediones **52** as a sole rearranged product, was found to proceed without light or heating, and thus can be best explained by an ionic

mechanism depicted in Scheme 28. Detailed results of these new ring transforming methods are described in Chapter 3.



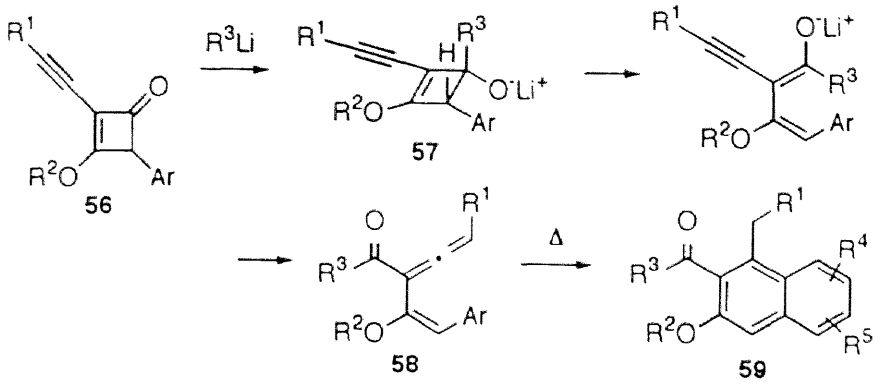
Scheme 28

Very recently, Paquette *et al.* showed that 2-fold addition of vinyllithiums to dialkyl squarate dilectly produced complex polyquinanes.[34] In this reaction, an initially formed trans adduct **53** underwent facile conrotatory ring opening to produce an octatetraene **54**, and subsequent electrocyclization of **54** followed by intramolecular aldolization of resulted cyclooctatriene **55** gave the final product.



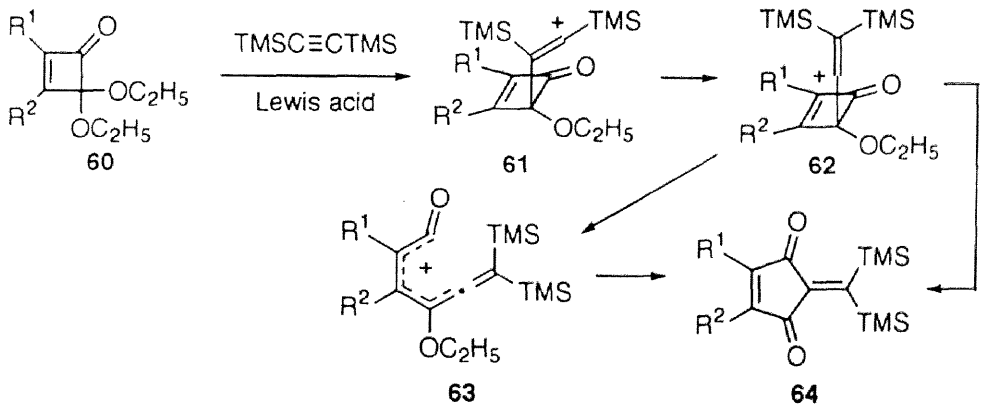
Scheme 29

Oxyanion accelated ring opening of cyclobutene was also documented in a following example (Scheme 30). Addition of an alkyllithium or aryllithium to 2-alkynyl-4-arylcyclobutenones **56** produced ring opening products **58** via conrotatory ring opening of **57**. Thermal electrocyclization of **58** gave highly substituted naphthalenes **59**.[35]



Scheme 30

Finally, the auther found that Lewis acid-catalyzed rection of cyclobutenedione monoacetals **60** with bis(trimethylsilyl)acetylene gave ring expanded products (Scheme 31). Bis(trimehylsilyl)methylenecyclopentenedione **64** was considered to be produced by direct ring expansion of **62**, which was formed by 1,2-silyl migration of **61**. As an alternative possibility, ring opening of **62** and subsequent Nazarov type cyclization of resulted intermediate **63** might produce **64**. The final chapter is devoted to this fomal [4+1] reaction.



Scheme 31

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Chapter 2

Regiocontrolled Derivatization of Squaric Acid Ring Using Electrophilic Addition of Unsaturated Organosilanes and Application of the Adducts

Chapter 2

Regiocontrolled Derivatization of Squaric Acid Ring Using Electrophilic Addition of Unsaturated Organosilanes and Application of the Adducts

Section 1

Lewis Acid-catalyzed Reaction of Squaric Acid Dichloride, Methyl Ester Chloride, Diethylamide Chloride, and Ethyl Diester with Unsaturated Organosilanes

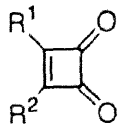
Abstract: The squaric acid chlorides and diester reacted with a variety of unsaturated organosilanes in the presence of a catalyst, typically titanium tetrachloride, at -78 to 0 °C to give addition products and/or substitution products after dechlorosilylation eiyher *via* 1,2- or 1,4-addition. The mode of addition depended on the nature of the acid family and on the substitution pattern of the organosilane. The former product predominated in the reaction of the acid chlorides with all silyl ketene acetals used, and with some allylsilanes and silyl enol ethers unless the reactive site (γ to a silyl group) of these silanes was more crowded, whereas the diester gave rise to the latter product irrespective of the substitution pattern. In some cases, catalyst and reaction temperature also affected the mode of addition.

Squaric acid **1** has long been known as a small ring system having unique characteristics the derivatives of which have wide application.[1] As mentioned in Capter 1, whereas derivatization of **1** has been achieved under nucleophilic conditions,[2] only a few cases employing electrophilic condtions have been reported.[3] Thus, we investigated a novel Lewis acid-catalyzed addition of squaric acid family with unsaturated organosilanes.

The required squaric acid family **2-5** (Figure 1) were prepared according to established procedures. The dichloride **2** was obtained in an acceptable yield by reported $SOCl_2$-dimethylformamide (DMF) method;[4] sublimation was applied for purification, because the sample obtained after only recrystallization (reported) was contaminated with tarry materials. The methyl ester chloride **3**[2b,5] and the diethylamide chloride **4**[3c,5] were synthesized from dichloride **2** by displacement with an appropriate alcohol and amine. The dichloride **2** was reported to be doubly substituted with simple alcohols.[5] In our hands, however, half-ester **3** was prepared by selective monosubstitution of dichloride **2** with methanol under reflux conditions in tetrahydrofurane (THF). This is in accord with the monohydroxylation of dichloride **2** with water under these conditions.[6] The diester **5** can be purchased or simply prepared with ethanol from acid **1** under azeotropic conditions.[7]

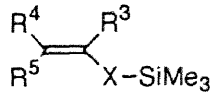
First, the chloride **2**, which is expected to be the most reactive of the derivatives under investigation here, was chosen for the reaction with allylsilanes (Figure 1).[8] Typically, dichloride **2** and allyltrimethylsilane **6a** was treated with titanium tetrachloride at -78 °C in dichloromethane for 5 min, and the reaction mixture was quenched with ice-water. After the usual work-up, products were separated by silica gel chromatography to give 2,3-dichloro-4-hydroxy-4-(-2-propenyl)-2-cyclobutenone **7a** in 54% yield: the product resulted from 1,2-addition (Scheme 1). The yield decreased rapidly at higher temperatures (0% at 0 °C) and more slowly at lower temperatures (34% at -95 °C), and increased slightly for prolonged reaction times (66% after 10 min) (Table 1). Among other Lewis acids examined, tin(IV) chloride was less effective (34%; entry 2), and both zinc chloride (at room temperature) and boron trifluoride-diethyl ether (at -78 °C) were ineffective. The structure was elucidated by spectral

Squaric acid family

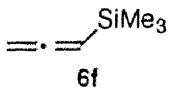


Compound	R^1	R^2
1	OH	OH
2	Cl	Cl
3	Cl	OCH_3
4	Cl	$N(C_2H_5)_2$
5	OC_2H_5	OC_2H_5

Unsaturated organosilanes



	R^3	R^4	R^5	X
a;	H	H	H	CH_2
b;	CH_3	H	H	CH_2
c;	H	H (CH_3)	CH_3 (H)	CH_2
d;	H	CH_3	CH_3	CH_2
e;	H	H	-$(CH_2)_2$CH-	
g;	Ph	H	H	O
h;	Ph	CH_3	H	O
i;	Ph	CH_3	CH_3	O
j;	Ad	H	H	O
k;	-$(CH_2)_4$-		H	O
l;			H	O
m;	H	CH_3	CH_3	O
n;	OPh	H	H	O
o;	OEt	CH_3	H	O
p;	OMe	CH_3	CH_3	O



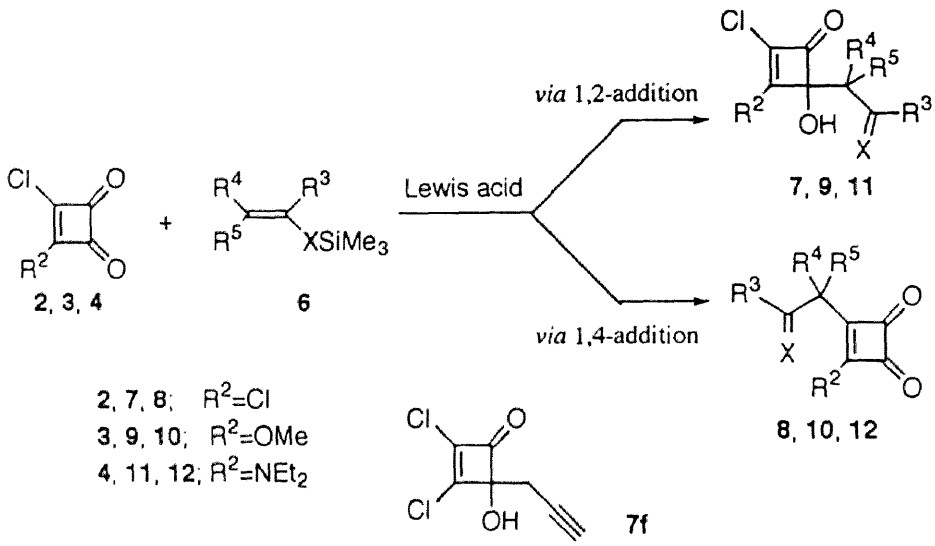
6f

Figure 1. Squaric Acid Family and Unsaturated Organosilanes

inspection; the key signals indicated the presence of hydroxy and strained carbonyl groups (3319 and 1784 cm^{-1} in the IR spectrum), and of a cyclobutenone ring involving three sp^2 and one sp^3 carbons (δ_C 187.7, 170.7, 133.7 and 93.2 in the ^{13}C NMR spectrum), and the presence of both chloride atoms (*m/z* 192, 194, 196; M^+, M^++2, M^++4; 9:6:1 in the mass spectrum). On going to a more substituted allylsilane, the addition mode changed as was demonstrated in the case of trimethylprenylsilane **6d**. The reaction with this silane under the same conditions afforded 3-chloro-4-(1,1-dimethyl-2-propenyl)-3-cyclobutene-1,2-dione **8d** as the predominant product which resulted from 1,4-addition followed by dechlorosilylation. The structure was clearly confirmed by the spectral data; (1) No absorption due to a hydroxy group,

but a couple of absorptions, at 1775 and 1809 cm^{-1}, due to a 1,2-dione moiety (IR), (2) four signals, at δ_c 185.3, 193.0, 195.5 and 206.1, due to ring carbons (^{13}C NMR), and (3) two 3:1 parent peaks at *m/z* 184 and 186 due to their being only one chlorine atom residing on the ring (MS). The reactions using silanes **6b,c** and **e** resulted in the formation of 4-hydroxycyclobutenones **7b,c** and **e** respectively, and thus it was shown that γ-monosubstitution in the allylsilane did not change the mode of reactivity (1,2-addition), where a diastereoisomeric mixture was obtained (entries 4 and 6). Analogously, allenyltrimethylsilane **6f** added to the dichloride **2** to give the propargylated 1,2-addition product **7f** albeit in a low yield. On the other hand, propargyltrimethylsilane reacted but to give a complex mixture, and less nucleophilic ethenyl- and ethynyl-trimethylsilanes did not give any addition products. Next to be attempted was the reaction with silyl enol ethers **6g-m**[9] in the same way as with allylsilanes. In this case the reaction was carried out for 1 min; longer reaction times (10 min) raised the yield as seen in entries 8 and 14, but this is not always the case. As a catalyst, titanium tetrachloride was again better than tin(IV) chloride and zinc chloride with which a complex mixture was formed. A series of silyl enol ethers of phenyl ketones **6g-i** were examined for 1,2- vs 1,4-addition reactivity. As a result, a similar tendency was obserbed for all three; with an increase in the number of methyl substituents on the enol ether (*i.e.* 0 to 2), the mode of addition changed from 1,2 to 1,4 (entries 8, 11 and 12). Although little, if any, 1,4-addition product arose from a silyl enol ether of cyclohexane **6k**, those were considerably accompanied in the reaction with silyl enol ethers **6j** and **l** involving a more bulky group such as an adamantane system in spite of this not being a doubly γ-substituted type. The 1,2- vs. 1,4-mode of addition was therefore influenced by the substitution pattern of the unsaturated organosilanes used (*vide supra*). These results could be explained by a steric factor. The Lewis acid-co-ordinated carbonyl carbon becomes more congested, compared with the olefinic carbon, making the 1,4-addition favorable, if the reactive site of the organosilanes is more crowded. alternatively, this result may be considered in terms of thermodynamics, since the first formed 1,2-addition product possibly isomerizes to the 1,4-addition product.[10] Yet this

seems unlikely because the control experiment (treatment of compound **7a** with titanium tetrachloride) did not show any evidence for isomerization. In the reactions of compound **6g**, interesting temperature and catalyst effects were obserbed. When lower temperatures such as at -95 °C or the presence of trimethylsilyl triflate as a catalyst was employed, 1,4-addition was rather favored (entries 9 and 10). Such a temperature effect was observed also in compound **6k** (entry 15).



Scheme 1

The reaction with a series of silyl ketene acetals **6n-p** was carried out smilarly, and in this case titanium tetrachloride and zinc chloride were both found to be effective. However, these catalysts played a contrasting role. In the titanium tetrachloride-catalyzed reaction, a disubstituted acetal **6p** no longer followed the previous mode of addition even if the reactive site is more crowded. All the ketene acetals **6n-p** underwent the 1,2-addition at -78 °C to give acyloins **7n-p** (entries 17, 20 and 22). On the other hand, zinc chloride catalyzed the 1,4-addition at room temperature to give product **8n-p** (entries 18, 21 and 23). The difference in catalytic action of the Lewis acids led to the formation of either addition products **7n-p** or substitution products **8n-p**.[11] A related example of the dependence of products on a Lewis acid has been reported in silyl ketene acetal chemistry.[12] The temperature effect found for

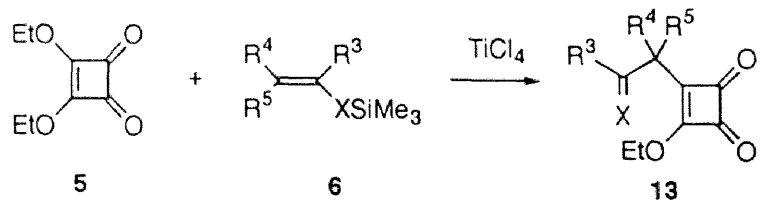
Table 1. Addition reaction of the squaric acid family, *viz.* dichloride **2**, methyl ester chloride **3**, diethylamide chloride **4** and ethyl diester **5** with unsaturated organosilanes **6**

Entry	Acid family	Silane	Reaction conditions[a] Time (*t*/min)	Temp. (*T*/°C)	Catalyst[c]	Products (% yield)[b] *via* 1,2-Addn.	1,4-Addn.
1	2	**6a**	5[10]	-78	T	**7a**(54)[66][d]	
2	2	**6a**	5	-78	S	**7a**(34)	
3	2	**6b**	5	-78	T	**7b**(50)	
4	2	**6c**	5[10]	-78	T	**7c**(26)[55][d]	
5	2	**6d**	5	-78	T	**7d**(8)	**8d**(68)
6	2	**6e**	5	-78	T	**7e**(32)	
7	2	**6f**	30	-50	T	**7f**(19)	
8	2	**6g**	1[10]	-78	T	**7g**(52)[74][d]	
9	2	**6g**	5	-95	T		**8g**(32)
10	2	**6g**	1	r.t.	Tf		**8g**(28)
11	2	**6h**	1	-78	T	**7h**(38)	
12	2	**6i**	1	-78	T	**7i**(7)	**8i**(82)
13	2	**6j**	1	-78	T	**7j**(73)	**8j**(26)
14	2	**6k**	1[10]	-78	T	**7k**(58)[70][d]	
15	2	**6k**	5	-95	T		**8k**(40)
16	2	**6l**	1	-78	T	**7l**(32)	**8l**(40)
17	2	**6n**	10	-78	T	**7n**(86)	
18	2	**6n**	60	r.t.	Z		**8n**(36)
19	2	**6n**	10	-95	T	**7n**(84)	
20	2	**6o**	10	-78	T	**7o**(22)	
21	2	**6o**	60	r.t.	Z		**8o**(56)
22	2	**6p**	10	-78	T	**7p**(46)	
23	2	**6p**	60	r.t.	Z		**8p**(50)
24	3	**6a**	10	-15	T	**9a**(82)	
25	3	**6b**	10	-15	T	**9b**(83)	
26	3	**6c**	10	-15	T	**9c**(37)	
27	3	**6d**	10	-15	T		**10d**(62)
28	3	**6g**	10	-15	T	**9g**(80)	
29	3	**6h**	10	-15	T	**9h**(49)	
30	3	**6i**	10	-15	T		**10i**(77)
31	3	**6k**	10	-15	T	**9k**(74)	
32	3	**6m**	10	-15	T		**10m**(69)
33	3	**6p**	10	-15	T	**9p**(76)	
34	4	**6a**	10	0	T	**11a**(83)	
35	4	**6b**	10	0	T	**11b**(66)	
36	4	**6g**	10	0	T	**11g**(83)	
37	4	**6h**	10	0	T	**11h**(67)	
38	4	**6i**	10	0	T		**12i**(14)
39	4	**6k**	10	0	T	**11k**(21)	
40	4	**6m**	10	0	T		**12m**(54)
41	4	**6p**	10	0	T	**11p**(61)	
42	5	**6g**	10	-15	T		**13g**(42)
43	5	**6h**	10	-15	T		**13h**(57)
44	5	**6k**	10	-15	T		**13k**(63)
45	5	**6p**	10	-15	T		**13p**(83)

[a] Proportions of each reagent (acid family:silane:catalyst) employed were 1:2:1. [b] Isolated yields are given.
[c]Catalyst: T=$TiCl_4$; Tf=TMSOTf; S=$SnCl_4$; Z=$ZnCl_2$. [d] The yield for the reaction time shown in square brackets.

compounds **6g** and **k** was also looked for in acetal **6n**, but no change in the mode of addition was observed (entry 19).

With these results in mind, we have applied the present method to the methyl ester chloride **3**, the diethyl amide chloride **4**, and the ethyl diester **5**. These compounds are expected to have relatively lower reactivity than the dichloride **2**, and in fact this was reflected in the higher reaction temperature and non-reactivity with some organosilanes. In particular, the reaction site was limited to the olefinic carbon in reactions with the diester **5**. As amino and alkoxy substituents on the ring attenuate one of the two carbonyl functionalities (namely, vinylogous ester and amide), the reaction occured preferentially across the alternative chlorine-substituted enone moiety. First, the reaction of the ester chloride **3** was examined from -78 to 0°C in the presence of titanium tetrachloride for 10 min, and the best yield was attained at -15 °C. The diethylamide chloride **4** was in turn less reactive than the ester chloride **3** and the products were obtained in satisfactory yields only at 0 °C, although the yield decreased substantially for the more crowded organosilane **6i** and no product was obtained from compound **6d**. Notably, the mode of addition of substrates **3** and **4** with a series of unsaturated organosilanes resembled that of the dichloride **2**. Compared with the above chlorides **2-4**, diester **5** showed diverse reactivity. Under the catalyzed conditions with titanium tetrachloride at -15 °C, diester **5** reacted with silyl enol ethers **6g**, **h** and **k** and a silyl ketene acetal **6p**, but not with the allylsilane **6a** or the more crowded silyl enol ether **6i**, because of its poor electrophilicity. In these cases, all the products, **13g**, **h**, **k** and **p**, arose from 1,4-addition, irrespective of the substitution pattern of the organosilanes (entries 42-45). Hence, diester **5** has the advantage of selective synthesis for 3-substituted cyclobutene-1,2-dione (Scheme 2).



5 6 13

Scheme 2

The structural determination was based in IR, NMR and mass spectra, and whether the product formed via 1,2- or 1,4-addition could be clearly deduced by spectral analysis as exemplified first in the case of products **7a** and **8d**. the products from γ-monosubstituted silanes **6c,e,h,k,l** and **o** each consisted of a diastereomeric mixture (ratio ~ 1:1 to 1:4) which was analysed without further separation.

In conclusion, the squaric acid family consisting of the dichloride **2**, methyl ester chloride **3**, diethylamide chloride **4**, and ethyl diester **5** were shown to be reactive with unsaturated organosilanes **6** in the presence of a Lewis acid, furnishing 1,2-addition products **7,9** and **11** and/or β-substitution product **8,10,12** and **13** via 1,4-addition followed by dechlorosilylation; (1) The reactivity is in the order **2>3>4**, corresponding to the reaction temperature from -95 to 0 °C. The much lower reactivity of diester **5** is reflected in the limited reaction (*i.e.*, only with a silyl enol ether and silyl ketene acetal). (2) The 1,2- *vs*. 1,4-addition reactivity is controlled primarily by the presence of one substituent on both the squaric acid **1** and the organosilanes **6**; 1,2-addition occurs with the chlorides **2,3** and **4**, and 1,4-addition with the diester **5**. Instead, 1,4-addition prevails over 1,2-addition if allylsilanes and silyl enol ethers are doubly substituted at the reactive site g to a silyl group. (3) This addition mode is changed in some cases by both change in reaction temperature and the presence of a catalyst, *e.g.* from 1,2- to 1,4-addition at -95 °C or by addition of zinc chloride.

Experimental Section

General. IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ solution with $SiMe_4$ as an internal standard. Mass spectra were recorded on a ESCO-EMD-05B mass spectrometer (EI at 20 or 70 eV). Flash chromatography was performed with a silica gel column (Fuji-Davison BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400 elemental analyzer. Dichloromethane was dried over $CaCl_2$, distilled, and stored over 4Å molecular sieves. Silyl enol ethers and silyl ketene acetals were obtained according to the standard methods developed by House and Ainsworth,[13] and allylsilanes were prepared by reactions of the corresponding organometallics with trimethylsilyl chloride;[14] Sakurai's modification[15] was used for crotylsilane **6c** (*E*:*Z* 36:64). Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.

Squaric Acid Family.

Dichloride **2**, methyl ester chloride **3**, diethylamidechloride **4**, and ethyl diester **5** were prepared by following the reported procedures.

3,4-Dichloro-3-cyclobutene-1,2-dione (2). A mixture of acid **1** (1.14 g, 10 mmol), thionyl dichloride (1.8 mL, 20 mmol) and DMF (5 drops) in dry benzene (10 mL) was refluxed for 6 h. The solvent was replaced with hexane (20 mL) and the soluble products were separated from gummy precipitates. Concentration and cooling, followed by filtration under nitrogen, gave yellow crystallines, which were further purified by sublimation (50 °C/20 mmHg) to give chloride **2** (0.82 g, 54%).

3-Chloro-4-methoxy-3-cyclobutene-1,2-dione (3). A solution of dichloride **2** (0.76 g, 5 mmol) in dry THF (10 mL) containing methanol (0.39 mL, 10 mmol) was refluxed for 40 min. After evaporation of the solvent, addition and evaporation of dry diethyl ether (5 mL) were repeated until the residue solidified. Sublimation of the solid (120 °C/0.1 mmHg) gave

methyl ester chloride **3** (0.68 g, 94%) as yellow crystals; mp. 43.5-47.1 °C; IR ($CHCl_3$) 1811, 1767, 1605 cm^{-1}; ^1H NMR δ 4.53 (3 H, s); ^{13}C NMR δ 62.2, 167.0, 189.2, 192.1, 197.4; MS (EI) *m/z* 148 and 146 (M^++2, M^+; 1:3), 120 and 118 (M^++2-CO, M^+-CO; 1:3), 105 and 103 (M^++2-CO-CH_3, M^+-CO-CH_3; 1:3).

4-Diethylamino-3-chloro-3-cyclobutene-1,2-dione (4). To a solution of dichloride **2** (0.91 g, 6 mmol) in dry dichloromethane (8 mL) at below 10 °C was added diethylamino(trimethyl)silane (0.87 g, 6 mmol) dropwise, and the solution was refluxed for 30 min. after evaporation of the solvent, the residue was chromatographed on a silica gel column (elution H-A 2:1) to give diethylamide chloride 4 (0.99 g, 85%) as deep yellow crystals; mp. 49.2-53.3 °C; IR ($CHCl_3$) 1800, 1746, 1622 cm^{-1}; ^1H NMR δ 1.31 and 1.36 (each 3 H, t, *J*=7.2 Hz), 3.67 and 3.81 (each 2 H, q, *J*=7.2 Hz); ^{13}C NMR δ 14.3, 14.4, 44.5, 45.0, 150.7, 178.9, 185.5, 191.5; MS (EI) *m/z* 189 and 187 (M^++2, M^+; 1:3), 161 and 159 (M^++2-CO, M^+-CO; 1:3), 133 and 131 (M^++2-2CO, M^+-2CO; 1:3), 118 and 116 (M^++2-2CO-CH_3, M^+-2CO-CH_3; 1:3).

3,4-Diethoxy-3-cyclobutene-1,2-dione (5). A suspension of acid **1** (1.14 g, 10 mmol) in ethanol (30 mL)-benzene (10 mL) was refluxed for 10 h, using a Dean-Stark apparatus containing 3 Å molecular sieves as a dehydrant. Then the solvent was replaced with diethyl ether, and precipitates were removed by filtration. After evaporation of the solvent, the residual oil was subjected to bulb-to-bulb distillation [95 °C (oven temp.)/0.1 mmHg] to give diester **5** (1.51 g, 89%).

Reaction of Squaric Acid Family with Unsaturated Organosilanes. General Procedure. To a solution of the acid family (0.5 mmol) and an organosilane (1 mmol) in dry dichloromethane (2 mL) was added titanium tetrachloride (0.06 mL, 0.5 mmol) by syringe at the temperature depicted in Table 1 with exclusion of moisture. After an appropriate time, the reaction mixture was poured into cold water and extracted with dichloromethane. The extracts were washed with water, dried (Na_2SO_4) and evaporated to dryness. Flash chromatography of

the residue with the solvent specified gave the products. Unless otherwise noted, this procedure was applied to obtain the following products. Other catalysts employed were trimethylsilyl triflate (entry 10; catalytic amount, 5 mol%), tin(IV) chloride (entry 2) and zinc chloride (entries 18, 21 and 23), ith which the reactions were carried out similarly at -78 °C or room temperature. See Table 1 for reaction conditions and isolated yields for each cases.

2,3-Dichloro-4-hydroxy-4-(2-propenyl)-2-cyclobutenone (7a): *oil* (Elution H-A 15:2); IR ($CHCl_3$) 3319, 1784, 1642, 1579 cm^{-1}; ^1H NMR δ 2.67 (2 H, d, *J*=7.4 Hz), 2.75 (1 H, br s), 5.27 (2 H, m), 5.78 (1 H, m); ^{13}C NMR δ 37.5, 93.2, 122.1, 130.2, 133.7, 170.7, 187.7; MS (EI) *m/z* 196, 194 and 192 (M^++4, M^++2, M^+; 1:6:9), 168, 166 and 162 (M^++4-CO, M^++2-CO, M^+-CO; 1:6:9), 131 and 129 (M^++2-CO-Cl, M^+-CO-Cl; 1:3; base); Anal Calcd for $C_7H_6Cl_2O_2$: C, 43.6; H, 3.1. Found: C, 43.8; H, 3.3.

2,3-Dichloro-4-hydroxy-4-(2-methyl-2-propenyl)-2-cyclobutenone (7b). *oil* (Elution H-A 15:2); IR (neat) 3431, 1780, 1647, 1580 cm^{-1}; ^1H NMR δ 1.85 (3 H, s), 2.56 and 2.70 (each 1 H, dd, *J*=14.0, 0.8 Hz), 3.20 (1 H, br s), 5.01 (2 H, m); ^{13}C NMR δ 23.3, 41.2, 92.5, 118.1, 139.4, 140.9, 170.4, 187.6; MS (EI) *m/z* 210, 208 and 206 (M^++4, M^++2, M^+; 1:6:9), 195, 193 and 191 (M^++4-CH_3, M^++2-CH_3, M^+-CH_3; 1:6:9), 182, 180 and 178 (M^++4-CO, M^++2-CO, M^+-CO; 1:6:9), 145 and 143 (M^++2-CO-Cl, M^+-CO-Cl; 1:3), 107 (base); Anal Calcd for $C_8H_8Cl_2O_2$: C, 46.4; H, 3.9. Found: C, 46.2; H, 4.0.

2,3-Dichloro-4-hydroxy-4-(1-methyl-2-propenyl)-2-cyclobutenone (7c). Obtained as a ~1:1 diastereomeric mixture; *oil* (Elution H-A 15:2); IR (neat) 3451, 1782, 1640, 1580 cm^{-1}; ^1H NMR δ 1.11 and 1.15 (each 1.5 H, d, *J*=7.0 Hz), 2.78 (1 H, m), 2.80 (1 H, br s), 5.28 (2 H, m), 5.85 (1 H, m); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 15.0 and 15.4, 41.8 and 42.2, 95.8 and 95.7, 119.6 and 120.0, 133.8 and 134.1, 136.7 and 137.2, 169.2 and 170.3, 187.4 and 187.5; MS (EI) *m/z* 210, 208 and 206 (M^++4, M^++2, M^+; 1:6:9), 195, 193 and 191 (M^++4-CH_3, M^++2-CH_3, M^+-CH_3; 1:6:9), 182, 180

and 178 (M^++4-CO, M^++2-CO, M^+-CO; 1:6:9), 107 (base); Anal Calcd for $C_8H_8Cl_2O_2$: C, 46.4; H, 3.9. Found: C, 46.2; H, 4.0.

3-Chloro-4-(1,1-dimethyl-2-propenyl)-2-cyclobutenone (8d). Isolated as the first fraction; *oil* (Elution H-A 15:2); IR (neat) 1809, 1775, 1635, 1561 cm^{-1}; ^1H NMR δ 1.54 (6 H, s), 5.18 and 5.23 (each 1 H, d, *J*=17.3 and 10.5 Hz, respectively), 6.07 (1 H, dd, *J*=17.3, 10.5 Hz); ^{13}C NMR δ 24.3, 41.5, 115.4, 140.1, 185.3, 193.0, 195.5, 206.1; MS (EI) *m/z* 186 and 184 (M^++2, M^+; 1:3), 171 and 169 (M^++2-CH_3, M^+-CH_3; 1:3), 158 and 156 (M^++2-CO, M^+-CO; 1:3), 121 (M^+-CO-Cl), 91 (base); Anal Calcd for $C_9H_9ClO_2$: C, 58.6; H, 4.9. Found: C, 58.5; H, 4.9.

The second fraction was the minor product 2,3-dichloro-4-hydroxy-4-(1,1-dimethyl-2-propenyl)-2-cyclobutenone (**7d**); *oil* (Elution H-A 15:2); IR (neat) 3461, 1782, 1635, 1582 cm^{-1}; ^1H NMR δ 1.25 and 1.26 (each 3 H, s), 2.80 (1 H, br s), 5.29 and 5.33 (each 1 H, dd, *J*=17.4, 1.0 and 10.8, 1.0 Hz, respectively), 6.06 (1 H, dd, *J*=17.4, 10.8 Hz); ^{13}C NMR δ 21.9, 22.7, 42.4, 97.9, 116.8, 134.4, 141.9, 169.5, 187.6; MS (EI) *m/z* (no molecular ion) 208, 206 and 204 (M^++4-CH_4, M^++2-CH_4, M^+-CH_4; 1:6:9), 181, 179 and 177 (M^++4-CO-CH_3, M^++2-CO-CH_3, M^+-CO-CH_3; 1:6:9), 92 (base); Anal Calcd for $C_9H_{10}Cl_2O_2$: C, 48.9; H, 4.6. Found: C, 48.9; H, 4.6.

2,3-Dichloro-4-(2-cyclopentenyl)-4-hydroxy-2-cyclobutenone (7e). Obtained as a ~1:2 diastereomeric mixture; *oil* (Elution H-A 15:2); IR ($CHCl_3$) 3470, 1782, 1580 cm^{-1}; ^1H NMR δ 2.00-2.20 (2 H, m), 2,30-2.60 (3 H, m), 3.16-3.35 (1 H, m), 5.67 and 6.04 (each 1 H, m); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 24.2 and 23.9, 32.3, 49.6 and 49.5, 95.4 and 95.2, 127.3 and 127.9, 136.2, 137.1 and 137.0, 171.5 and 170.1, 187.9 and 189.7; MS (EI) *m/z* 222, 220 and 218 (M^++4, M^++2, M^+; 1:6:9), 194, 192 and 190 (M^++4-CO, M^++2-CO, M^+-CO; 1:6:9), 157 and 155 (M^++2-CO-Cl, M^+-CO-Cl; 1:3), 119 (base); Anal Calcd for $C_9H_8Cl_2O_2$: C, 49.3; H, 3.7. Found: C, 49.4; H, 3.7.

2,3-Dichloro-4-hydroxy-4-(2-propynyl)-2-cyclobutenone (7f). *oil* (Elution H-A 15:2); IR (neat) 3426, 3302, 2120, 1779, 1580 cm^{-1}; ^1H NMR δ 2.19 (1 H, t, *J*=2.7 Hz),

2.85 (2 H, d, J=2.7 Hz), 3.15 (1 H, br s); ^{13}C NMR δ 23.1, 74.0, 76.3, 92.6, 135.6, 169.8, 186.4; MS (EI) *m/z* 194, 192 and 190 (M^++4, M^++2, M^+; 1:6:9), 166, 164 and 162 (M^++4-CO, M^++2-CO, M^+-CO; 1:6:9), 129 and 127 (M^++2-CO-Cl, M^+-CO-Cl; 1:3), 91 (base); Anal Calcd for $C_7H_4Cl_2O_2$: C, 44.0; H, 2.1. Found: C, 43.9; H, 2.1.

2,3-Dichloro-4-hydroxy-4-phenacyl-2-cyclobutenone (7g). *oil* (Elution H-A 5:1); IR (neat) 3432, 1784, 1684, 1582 cm^{-1}; ^{1}H NMR δ 3.49 and 3.63 (each 1 H, d, J=17.8 Hz), 5.20 (1 H, br s), 7.48-7.98 (5 H, m); ^{13}C NMR δ 39.0, 92.4, 128.8, 129.3, 134.5, 135.0, 136.0, 169.8, 185.5, 199.1; MS (EI) *m/z* 274, 272 and 270 (M^++4, M^++2, M^+; 1:6:9), 236 and 234 (M^++2-HCl, M^+-HCl; 1:3), 209 and 207 (M^++2-CO-Cl, M^+-CO-Cl; 1:3), 105 (base); Anal Calcd for $C_{12}H_8Cl_2O_3$: C, 53.2; H, 3.0. Found: C, 53.0; H, 3.1.

3-Chloro-4-phenacyl-3-cyclobutene-1,2-dione (8g). Obtained as *crystals* (Elution H-A 15:2) when the reaction was conducted at -95 °C or with 5 mol% trimethylsilyl triflate as a catalyst; mp. 138-141 °C; IR (KBr) 3432, 1784, 1724, 1564 cm^{-1}; ^{1}H NMR δ 6.21 (1 H, s), 7.45-7.59 (5 H, m), 11.00 (1 H, s); ^{13}C NMR δ 88.7, 128.2, 133.2, 133.3, 172.4, 175.1, 188.4, 187.0, 202.7; MS (EI) *m/z* 236 and 234 (M^++2, M^+; 1:3), 208 and 206 (M^++2-CO, M^+-CO; 1:3), 199 (M^+-Cl), 92 (base); Anal Calcd for $C_{12}H_7ClO_3$: C, 61.4; H, 3.0. Found: C, 61.3; H, 3.1.

4-(1-Benzoylethyl)-2,3-dichloro-4-hydroxy-2-cyclobutenone (7h). Obtained as a ~1:1 diastereomeric mixture; *oil* (Elution H-A 5:1); IR (neat) 3420, 1782, 1678, 1580 cm^{-1}; ^{1}H NMR δ 1.65 and 1.72 (each 1.5 H, d, J=7.2 Hz), 4.06 and 4.14 (each 0.5 H, q, J=7.2 Hz (2 H, m), 5.35 and 5.60 (each 0.5 H, br s), 7.62-8.13 (5 H, m); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 13.8 and 14.8, 42.4 and 42.8, 95.0 and 95.1, 126.3 and 127.9, 128.7 and 128.8, 129.1 and 129.2, 129.4 and 129.5, 134.8 and 135.0, 168.8 and 171.3, 184.8 and 186.5, 203.5 and 204.3; MS (EI) *m/z* 288, 286 and 284 (M^++4, M^++2, M^+; 1:6:9), 273, 271 and 269 (M^++4-CH_3, M^++2-CH_3, M^+-CH_3; 1:6:9), 222 and 220 (M^++2-CO-HCl, M^+-CO-HCl; 1:3), 91 (base); Anal Calcd for $C_{13}H_{10}Cl_2O_3$: C, 54.8; H, 3.5. Found: C, 54.9; H, 3.4.

3-Chloro-4-(1-benzoyl-1-methylethyl)-3-cyclobutene-1,2-dione (8i). *oil* (Elution H-A 15:2); IR (neat) 1813, 1786, 1687, 1557 cm^{-1}; ^1H NMR δ 1.81 (6 H, s), 7.39-7.77 (5 H, m); ^{13}C NMR δ 24.0, 49.9, 128.8, 129.4, 133.9, 134.0, 135.2, 186.7, 192.0, 195.1, 197.8, 204.1; MS (EI) *m/z* 264 and 262 (M^++2, M^+; 1:6:9), 236 and 234 (M^++2-CO, M^+-CO; 1:3), 226 (M^+-HCl), 91 (base); Anal Calcd for $C_{14}H_{11}ClO_3$: C, 64.0; H, 4.2. Found: C, 63.8; H, 4.4.

4-[(1-Adamantyl)carbonylmethyl]-2,3-dichloro-4-hydroxy-2-cyclobutenone (7j). Isolated as the second fraction; *oil* (Elution H-A 15:2); IR ($CHCl_3$) 3389, 1786, 1684, 1584 cm^{-1}; ^1H NMR δ 1.60-2.16 (15 H, m), 2.83 and 3.30 (each 1 H, d, *J*=17.8 Hz), 4.98 (1 H, br s); ^{13}C NMR δ 27.9, 36.5, 38.0, 38.4, 91.1, 135.1, 177.8, 187.8, 196.0; MS (EI) *m/z* 333, 331 and 329 (M^++4, M^++2, M^+; 1:6:9), 295 and 293 (M^++2-HCl, M^+-HCl; 1:3), 267 and 265 (M^++2-CO-HCl, M^+-CO-HCl; 1:3), 135 (base); Anal Calcd for $C_{16}H_{18}Cl_2O_3$: C, 58.4; H, 5.5. Found: C, 58.6; H, 5.4.

The first fraction was the minor product 4-[(1-adamantyl)carbonylmethyl]-3-chloro-3-cyclobutene-1,2-dione (**8j**); *crystals* (H-A 15:2); mp. 134-137 °C; IR (KBr) 3449, 1788, 1736, 1559 cm^{-1}; ^1H NMR δ 1.75-2.18 (15 H, m), 5.52 (1 H, d, *J*=0.6 Hz), 10.77 (1 H, d, *J*=0.6 Hz); ^{13}C NMR δ 28.0, 36.4, 39.8, 40.4, 87.2, 174.4, 184.6, 188.4, 202.7; MS (EI) *m/z* 294 and 292 (M^++2, M^+; 1:3), 266 and 264 (M^++2-CO, M^+-CO; 1:3), 257 (M^+-Cl), 135 (base); Anal Calcd for $C_{12}H_7ClO_3$: C, 61.4; H, 3.0. Found: C, 61.3; H, 3.1.

2-(2,3-Dichloro-1-hydroxy-4-oxo-2-cyclobutenyl)cyclohexanone (7k). Obtained as a ~1:4 diastereomeric mixture; *oil* (Elution H-A 5:1); IR ($CHCl_3$) 3470, 1788, 1700, 1578 cm^{-1}; ^1H NMR δ 1.25-3.10 (8 H, m), 2.89 and 3.04 (0.2 and 0.8 H respectively, ddd, *J*=13.0, 5.6, 1.0 Hz), 5.00 (1 H, br s); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 24.3 and 24.4, 26.9 and 26.8, 29.7 and 29.5, 42.5 and 42.3, 51.0 and 51.5, 95.6 and 95.3, 134.9 and 134.8, 169.9 and 167.9, 184.9 and 185.3, 213.6 and 213.1; MS (EI) *m/z* (no molecular ion) 215 and 213 (M^++2-Cl, M^+-Cl; 1:3), 108 (base); Anal Calcd for $C_{10}H_{10}Cl_2O_3$: C, 48.2; H, 4.1. Found: C, 48.2; H, 4.1.

3-Chloro-4-(2-oxocyclohexyl)-3-cyclobutene-1,2-dione (8k). Obtained when the reaction was conducted at -95 °C; *crystals* (H-A 15:2); mp. 78.5-80.2 °C; IR ($CHCl_3$) 3000, 1786, 1734, 1560 cm^{-1}; ^1H NMR δ 1.40-2.70 (8 H, m), 10.96 (1 H, s); ^{13}C NMR δ 21.1, 21.8, 24.3, 31.1, 102.0, 173.8, 176.1, 185.0, 187.4, 202.0; MS (EI) *m/z* 214 and 212 (M^++2, M^+; 1:3), 186 and 184 (M^++2-CO, M^+-CO; 1:3), 177 (M^+-Cl), 113 (base); Anal Calcd for $C_{10}H_9ClO_3$: C, 56.5; H, 4.3. Found: C, 56.3; H, 4.5.

3-Chloro-4-(5-oxo-4-homoadamantyl)-3-cyclobutene-1,2-dione (8l). Isolated as the first fraction; *crystals* (H-A 15:2); mp. 133-136 °C; IR (KBr) 3410, 2918, 1780, 1718, 1543 cm^{-1}; ^1H NMR δ 1.78-3.37 (14 H, m), 11.54 (1 H, s); ^{13}C NMR δ 27.7, 32.1, 34.7, 35.0, 35.1, 39.7, 41.9, 49.1, 57.1, 112.2, 171.1, 183.9, 185.9, 189.9, 203.1; MS (EI) *m/z* 280 and 278 (M^++2, M^+; 1:3), 252 and 250 (M^++2-CO, M^+-CO; 1:3), 243 (M^+-Cl), 92 (base); Anal Calcd for $C_{15}H_{15}ClO_3$: C, 64.6; H, 5.4. Found: C, 64.5; H, 5.6.

The second fraction was the minor product 3-(2,3-Dichloro-1-hydroxy-4-oxo-2-cyclobutenyl)tricyclo[4.3.$1^{1,6}$.1]undecan-2-one (**7l**) consisting of a ~1:1 diastereomeric mixture. This product was not stable enough for microanalysis (it partly decomposed during drying), and structure was assigned only by spectral data; *oil* (H-A 15:2); IR (neat) 3389, 2916, 1786, 1670, 1580 cm^{-1}; ^1H NMR δ 1.60-2.90 (14 H, m), 3.03 and 3.25 (each 0.5 H, s), 5.20 (1 H, br s); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 26.6 and 26.5, 29.0 and 29.3, 30.9 and 30.5, 32.0, 33.0 and 34.0, 35.0, 40.5 and 40.7, 49.3 and 49.2, 57.9, 97.1 and 96.8, 135.6 and 135.1, 167.7 and 169.9, 184.8 and 186.6, 219.8 and 220.6; MS (EI) *m/z* (no molecular ion), 281 and 279 (M^++2-Cl, M^+-Cl; 1:3), 210 (base).

Phenyl (2,3-Dichloro-1-hydroxy-4-oxo-2-cyclobutenyl)acetate (7n). *oil* (Elution H-A 15:2); IR (neat) 3449, 1788, 1759, 1582 cm^{-1}; ^1H NMR δ 3.16 (2 H, s), 4.15 (1 H, br s), 7.09-7.46 (5 H, m); ^{13}C NMR δ 36.6, 91.3, 121.6, 127.0, 130.0, 135.0, 150.3, 169.1, 169.4, 185.1; MS (EI) *m/z* (no molecular ion) 252 and 250 (M^++2-Cl, M^+-Cl; 1:3), 158 (base); Anal Calcd for $C_{12}H_8Cl_2O_4$: C, 50.2; H, 2.8. Found: C, 50.0; H, 2.9.

Phenyl (2-Chloro-3,4-dioxo-1-cyclobutenyl)acetate (8n). Obtained when the reaction was conducted with zinc chloride; *oil* (H-A 15:2); IR ($CHCl_3$) 1811, 1790, 1765, 1589 cm^{-1}; ^1H NMR δ 4.09 (2 H, s), 7.12-7.46 (5 H, m); ^{13}C NMR δ 31.5, 121.5, 127.0, 130.1, 150.5, 164.2, 190.2, 191.7, 193.5, 194.5; MS (EI) *m/z* (no molecular ion) 224 and 222 (M^++2-CO, M^+-CO; 1:3), 187 (M^+-CO-Cl), 92 (base); Anal Calcd for $C_{12}H_7ClO_4$: C, 57.5; H, 2.8. Found: C, 57.4; H, 2.9.

Ethyl 2-(2,3-Dichloro-1-hydroxy-4-oxo-2-cyclobutenyl)propanoate (7o). Obtained as a ~1:2 diastereomeric mixture; *oil* (Elution H-A 15:2); IR (neat) 3430, 1794, 1734, 1582 cm^{-1}; ^1H NMR δ 1.32 (3 H, t, *J*=7.2 Hz), 1.30 and 1.35 (each 2 H and 1 H respectively, t, *J*=7.2 Hz), 2.96 and 3.05 (each 0.6' H and 0.3' H respectively, t, *J*=7.2 Hz), 4.26 (2 H, q, *J*=7.2 Hz), 4.81 (1 H, br s); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 12.9 and 12.4, 14.0 and 14.2, 41.8 and 41.5, 62.2, 94.6 and 94.7, 134.5 and 135.0, 169.2 and 168.6, 174.2 and 174.1, 185.0 and 185.5; MS (EI) *m/z* (no molecular ion) 219 and 217 (M^++2-Cl, M^+-Cl; 1:3), 191 and 189 (M^++2-CO-Cl, M^+-CO-Cl; 1:3), 102 (base); Anal Calcd for $C_9H_{10}Cl_2O_4$: C, 42.7; H, 4.0. Found: C, 42.7; H, 4.0.

Ethyl 2-(2-Chloro-3,4-dioxo-1-cyclobutenyl)propanoate (8o). Obtained when the reaction was conducted with zinc chloride; *oil* (Elution H-A 15:2); IR ($CHCl_3$) 1813, 1785, 1742, 1578 cm^{-1}; ^1H NMR δ 1.29 (3 H, t, *J*=7.0 Hz), 1.63 (3 H, d, *J*=7.4 Hz), 4.02 (1 H, q, *J*=7.4 Hz), 4.25 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 13.8, 14.0, 38.2, 62.5, 169.0, 187.9, 192.2, 194.6, 199.0; MS (EI) *m/z* 218 and 216 (M^++2, M^+; 1:3), 189 and 187 (M^++2-CO-H, M^+-CO-H; 1:3), 161 and 159 (M^++2-CO-Et, M^+-CO-Et; 1:3, base); Anal Calcd for $C_9H_9ClO_4$: C, 49.9; H, 4.2. Found: C, 49.9; H, 4.2.

Mthyl 2-(2,3-Dichloro-1-hydroxy-4-oxo-2-cyclobutenyl)-2-methylpropanoate (7p). *oil* (Elution H-A 5:1); IR (neat) 3436, 1794, 1736, 1578 cm^{-1}; ^1H NMR δ 1.33 and 1.44 (each 3 H, s), 3.80 (3 H, s), 5.14 (1 H, br s); ^{13}C NMR δ 21.5, 21.7, 45.0, 53.1, 97.6, 134.9, 168.5, 176.9, 185.4; MS (EI) *m/z* 256, 254 and 252 (M^++4 ,M^++2, M^+; 1:6:9), 219

and 217 (M^++2-Cl, M^+-Cl; 1:3), 191 (base); Anal Calcd for $C_9H_{10}Cl_2O_4$: C, 42.7; H, 4.0. Found: C, 42.5; H, 4.1.

Methyl 2-(2-Chloro-3,4-dioxo-1-cyclobutenyl)-2-methylpropanoate (8p). Obtained when the reaction was conducted with zinc chloride; *oil* (Elution H-A 15:2); IR ($CHCl_3$) 1815, 1785, 1744, 1568 cm^{-1}; ^1H NMR δ 1.68 (6 H, s), 3.79 (3 H, s); ^{13}C NMR δ 22.8, 45.1, 53.3, 172.3, 186.1, 192.4, 194.4, 202.1; MS (EI) *m/z* 218 and 216 (M^++2, M^+; 1:3), 189 and 187 (M^++2-CO-H, M^+-CO-H; 1:3, base); Anal Calcd for $C_9H_9ClO_4$: C, 49.9; H, 4.2. Found: C, 49.9; H, 4.1.

2-Chloro-4-hydroxy-3-methoxy-4-(2-propenyl)-2-cyclobutenone (9a). *oil* (Elution H-A 5:1); IR (neat) 3380, 1779, 1607 cm^{-1}; ^1H NMR δ 2.61 and 2.68 (each 1 H, dd, *J*=15.2, 7.2 Hz), 3.55 (1 H, br s), 4.34 (3 H, s), 5.16-5.31 (2 H, m), 5.68-5.89 (1 H, m); ^{13}C NMR δ 37.5, 61.0, 89.3, 104.5, 120.8, 131.3, 183.8, 188.1; MS (EI) *m/z* 190 and 188 (M^++2, M^+; 1:3), 175 and 173 (M^++2-CH_3, M^+-CH_3; 1:3), 162 and 160 (M^++2-CO, M^+-CO; 1:3), 153 (M^+-Cl), 103 (base); Anal Calcd for $C_8H_9ClO_3$: C, 51.0; H, 4.8. Found: C, 51.0; H, 4.9.

2-Chloro-4-hydroxy-3-methoxy-4-(2-methyl-2-propenyl)-2-cyclobutenone (9b). *oil* (Elution H-A 5:1); IR (neat) 3387, 1779, 1607 cm^{-1}; ^1H NMR δ 1.81 (3 H, dd, *J*=0.8, 0.6 Hz), 2.57 and 2.66 (each 1 H, dd, *J*=13.7, 0.8 Hz), 3.55 (1 H, br s), 4.53 (3 H, s), 4.96 5.00 (each 1 H, m); ^{13}C NMR δ 23.1, 41.2, 61.0, 88.6, 104.6, 117.1, 140.1, 183.2, 187.7; MS (EI) *m/z* 204 and 202 (M^++2, M^+; 1:3), 189 and 187 (M^++2-CH_3, M^+-CH_3; 1:3), 176 and 174 (M^++2-CO, M^+-CO; 1:3), 166 (M^+-HCl), 123 (base); Anal Calcd for $C_9H_{11}ClO_3$: C, 53.4; H, 5.5. Found: C, 53.2; H, 5.6.

2-Chloro-4-hydroxy-3-methoxy-4-(1-methyl-2-propenyl)-2-cyclobutenone (9c). Obtained as a ~1:2 diastereomeric mixture; *oil* (Elution H-A 5:1); IR (neat) 3412, 1773, 1605 cm^{-1}; ^1H NMR δ 1.12 and 1.13 (2 H and 1 H respectively, d, *J*=7.0 Hz), 2.64-2.82 (1 H, m), 3.29 (1 H, br s), 4.35 and 4.53 (2 H and 1 H respectively, s), 5.16-5.27 (2 H, m), 5.72-5.97 (1 H, m); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 15.1 and

15.3, 41.5 and 42.0, 61.1 and 61.0, 91.7 and 91.8, 104.5 and 104.7, 118.2 and 118.6, 137.9 and 137.8, 183.4 and 182.5, 187.4 and 189.2; MS (EI) *m/z* 204 and 202 (M^++2, M^+; 1:3), 189 and 187 (M^++2-CH_3, M^+-CH_3; 1:3), 176 and 174 (M^++2-CO, M^+-CO; 1:3), 103 (base); Anal Calcd for $C_9H_{11}ClO_3$: C, 53.4; H, 5.5. Found: C, 53.4; H, 5.5.

3-(1,1-Dimethyl-2-propenyl)-4-methoxy-2-cyclobutenone (10d). *oil* (Elution H-A 5:1); IR (neat) 1792, 1765, 1589 cm^{-1}; ^1H NMR δ 1.43 (6 H, s), 4.44 (3 H, s), 5.10 and 5.11 (each 1 H and 1 H, dd, *J*=17.5, 0.6 and 10.3, 0.6 Hz respectively), 6.05 (1 H, dd, *J*=17.5, 10.3 Hz); ^{13}C NMR δ 24.5, 40.4, 61.4, 133.8, 141.6, 188.6, 194.4, 195.2, 197.6; MS (EI) *m/z* 180 (M^+), 165 (M^+-CH_3), 152 (M^+-CO), 137 (M^+-CO-CH_3), 109 (base); Anal Calcd for $C_{10}H_{12}O_3$: C, 66.7; H, 6.7. Found: C, 66.5; H, 6.8.

2-Chloro-4-hydroxy-3-methoxy-4-phenacyl-2-cyclobutenone (9g). *oil* (Elution H-A 3:1); IR (neat) 3399, 1782, 1684, 1611 cm^{-1}; ^1H NMR δ 3.38 and 3.59 (each 1 H, d, *J*=17.5 Hz), 4.35 (3 H, s), 5.15 (1 H, br s), 7.45-7.69 (5 H, m); ^{13}C NMR δ 39.3, 61.3, 88.1, 105.0, 128.8, 129.3, 134.8, 136.3, 182.7, 185.2, 199.5; MS (EI) *m/z* 268 and 266 (M^++2, M^+; 1:3), 230 (M^+-HCl), 203 (M^+-CO-Cl), 105 (base); Anal Calcd for $C_{13}H_{11}ClO_4$: C, 58.6; H, 4.2. Found: C, 58.4; H, 4.3.

4-(1-Benzoylethyl)-2-chloro-4-hydroxy-3-methoxy-2-cyclobutenone (9h). Obtained as a ~1:2 diastereomeric mixture; *oil* (Elution H-A 3:1); IR (neat) 3412, 1784, 1680, 1615 cm^{-1}; ^1H NMR δ 1.43 and 1.56 (1 H and 2 H respectively, d, *J*=7.2 Hz), 3.89 (1 H, q, *J*=7.2 Hz), 4.24 and 4.40 (2 H and 1 H respectively, s), 5.02 and 5.09 (0.3' H and 0.6' H respectively, br s), 7.45-7.99 (5 H, m); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 14.4 and 14.2, 42.9 and 42.2, 61.3, 90.2 and 91.0, 104.4 and 105.2, 129.1 and 129.2, 129.4 and 129.3, 134.7 and 134.5, 135.2 and 135.5, 183.6 and 181.9, 184.7 and 186.3, 204.5 and 204.1; MS (EI) *m/z* 282 and 280 (M^++2, M^+; 1:3), 267 and 265 (M^++2-CH_3, M^+-CH_3; 1:3), 244 (M^+-HCl), 105 (base); Anal Calcd for $C_{14}H_{13}ClO_4$: C, 59.9; H, 4.7. Found: C, 59.7; H, 4.8.

3-(1-Benzoyl-1-methylethyl)-4-methoxy-3-cyclobutene-1,2-dione (10i). *oil* (Elution H-A 3:1); IR (neat) 1792, 1761, 1682, 1589 cm^{-1}; ^1H NMR δ 1.71 (6 H, s), 4.33 (3 H, s), 7.37-7.85 (5 H, m); ^{13}C NMR δ 24.0, 48.9, 61.7, 128.8, 128.9, 133.4, 135.4, 185.8, 193.5, 194.3, 198.0, 199.3; MS (EI) *m/z* 258 (M^+), 230 (M^+-CO), 215 (M^+-CO-CH_3), 105 (base); Anal Calcd for $C_{15}H_{14}O_4$: C, 69.8; H, 5.5. Found: C, 69.7; H, 5.5.

2-(3-Chloro-1-hydroxy-2-methoxy-4-oxo-2-cyclobutenyl)cyclohexanone (9k). Obtained as a ~1:4 diastereomeric mixture; *oil* (Elution H-A 5:1); IR (neat) 3414, 1784, 1709, 1613 cm^{-1}; ^1H NMR δ 1.60-2.60 (8 H, m), 2.85 and 2.95 (0.2 and 0.8 H respectively, ddd, *J*=13.0, 5.8, 1.2 Hz), 4.34 and 4.36 (0.6 H and 2.4 H respectively, s), 4.92 (1 H, br s); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 24.4, 27.0 and 26.8, 29.8 and 29.6, 42.5 and 42.4, 51.0 and 51.8, 61.3 and 61.1, 91.0, 105.4, 182.3 and 180.8, 184.4 and 184.9, 214.1 and 213.3; MS (EI) *m/z* 246 and 244 (M^++2, M^+; 1:3), 217 and 215 (M^++2-CO-H, M^+-CO-H; 1:3), 181 (M^+-CO-Cl), 105 (base); Anal Calcd for $C_{11}H_{13}ClO_4$: C, 54.0; H, 5.3. Found: C, 54.0; H, 5.3.

2-(2-Methoxy-3,4-dioxo-1-cyclobutenyl)-2-methylpropanal (10m). *oil* (Elution H-A 3:1); IR (neat) 1794, 1765, 1734, 1591 cm^{-1}; ^1H NMR δ 1.50 (6 H, s), 4.47 (3 H, s), 9.61 (1 H, s); ^{13}C NMR δ 19.6, 61.8, 103.8, 181.8, 193.7, 194.3, 198.1, 199.1; MS (EI) *m/z* 182 (M^+), 153 (M^+-CHO), 138 (M^+-CHO-CH_3, base); Anal Calcd for $C_9H_{10}O_4$: C, 59.3; H, 5.5. Found: C, 59.1; H, 5.6.

Methyl 2-(3-Chloro-1-hydroxy-2-methoxy-4-oxo-2-cyclobutenyl)-2-methylpropanoate (9p). *oil* (Elution H-A 3:1); IR (neat) 3437, 1784, 1732, 1615 cm^{-1}; ^1H NMR δ 1.32 and 1.37 (each 3 H, s), 3.77 (3 H, s), 4.36 (3 H, s), 4.90 (1 H, br s); ^{13}C NMR δ 21.7, 44.7, 52.9, 61.3, 93.3, 105.4, 177.4, 181.1, 184.9; MS (EI) *m/z* 250 and 248 (M^++2, M^+; 1:3), 235 and 233 (M^++2-CH_3, M^+-CH_3; 1:3), 213 (M^+-Cl), 190 and 188 (M^++2-CO_2Me-H, M^+-CO_2Me-H; 1:3, base); Anal Calcd for $C_{10}H_{13}ClO_5$: C, 48.3; H, 5.3. Found: C, 48.2; H, 5.4.

2-Chloro-3-diethylamino-4-hydroxy-4-(2-propenyl)-2-cyclobutenone (11a). *crystals* ; mp. 97-100 °C; (Elution H-A 2:1); IR (KBr) 3316, 1761, 1595 cm^{-1}; ^1H NMR δ 1.30 (6 H, t, *J*=7.2 Hz), 2.56 and 2.85 (each 1 H, ddt, *J*=14.4, 7.6, 1.0 and 14.4, 7.0, 1.2 Hz respectively), 3.40-3.76 (4 H, m), 5.05-5.18 (2 H, m), 5.25 (1 H, br s), 5.58-5.79 (1 H, m); ^{13}C NMR δ 13.7, 14.4, 38.4, 43.4, 45.5, 88.6, 93.6, 119.2, 132.2, 171.0, 185.9; MS (EI) *m/z* 231 and 229 (M^++2, M^+; 1:3), 216 and 214 (M^++2-CH_3, M^+-CH_3; 1:3), 203 and 201 (M^++2-CO, M^+-CO; 1:3), 142 (M^+-Cl), 103 (base); Anal Calcd for $C_{11}H_{16}ClNO_2$: C, 57.5; H, 7.0; N, 6.0. Found: C, 57.6; H, 7.0; N, 6.0.

2-Chloro-3-diethylamino-4-hydroxy-4-(2-methyl-2-propenyl)-2-cyclobutenone (11b). *crystals* ; mp. 90-93 °C; (Elution H-A 2:1); IR (KBr) 3218, 1763, 1589 cm^{-1}; ^1H NMR δ 1.29 and 1.32 (each 3 H, t, *J*=7.2 Hz), 1.75 (3 H, dd, *J*=14.0, 0.8 Hz), 2.55 and 2.82 (each 1 H, dd, *J*=13.8, 0.6 Hz), 3.37-3.83 (4 H, m), 4.78 and 4.87 (each 1 H, m), 4.97 (1 H, br s); ^{13}C NMR δ 13.4, 14.2, 23.4, 42.4, 43.2, 45.5, 88.6, 93.9, 115.8, 140.7, 170.6, 185.7; MS (EI) *m/z* 245 and 243 (M^++2, M^+; 1:3), 230 and 228 (M^++2-CH_3, M^+-CH_3; 1:3), 217 and 215 (M^++2-CO, M^+-CO; 1:3), 188 and 186 (M^++2-CO-C_2H_5, M^+-CO-C_2H_5; 1:3, base); Anal Calcd for $C_{12}H_{18}ClNO_2$: C, 59.1; H, 7.4; N, 5.8. Found: C, 59.1; H, 7.4; N, 5.9.

2-Chloro-3-diethylamino-4-hydroxy-4-phenacyl-2-cyclobutenone (11g). *crystals* ; mp. 135-138 °C; (Elution H-A 1:1); IR (KBr) 3208, 1769, 1676, 1597 cm^{-1}; ^1H NMR δ 1.27 and 1.35 (each 3 H, t, *J*=7.2 Hz), 3.41 and 3.71 (each 1 H, d, *J*=16.0 Hz), 3.50-3.72 (4 H, m), 5.62 (1 H, br s), 7.42-7.99 (5 H, m); ^{13}C NMR δ 13.4, 14.2, 41.1, 43.4, 45.7, 87.1, 94.6, 128.9, 129.0, 134.1, 136.9, 170.2, 183.7, 198.6; MS (EI) *m/z* 309 and 307 (M^++2, M^+; 1:3), 281 and 279 (M^++2-CO, M^+-CO; 1:3), 204 and 202 (M^++2-PhCO, M^+-PhCO; 1:3), 104 (base); Anal Calcd for $C_{16}H_{18}ClNO_3$: C, 62.4; H, 5.9; N, 4.6. Found: C, 62.5; H, 5.9; N, 4.5.

4-(1-Benzoylethyl)-2-chloro-3-diethylamino-4-hydroxy-2-cyclobutenone (11h). Obtained as a ~2:3 diastereomeric mixture; *oil*; (Elution H-A 1:1); IR (neat) 3302,

1763, 1680, 1593 cm^{-1}; ^1H NMR δ 1.18 and 1.21 (each 1.8 H, t, *J*=7.2 Hz), 1.29 and 1.31 (each 1.2 H, d, *J*=7.0 Hz), 1.27 and 1.39 (1.8 H and 1.2 H respectively, d, *J*=7.4 Hz), 3.21-3.78 (4 H, m), 3.59 (1 H, br s), 4.09 and 4.19 (0.6 H and 0.4 H respectively, q, *J*=7.4 Hz), 7.41-8.03 (5 H, m); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 13.5 and 13.2, 14.2 and 14.1, 14.4 and 14.3, 43.4 and 43.1, 46.0 and 46.2, 90.4 and 90.5, 94.9 and 95.3, 128.9 and 129.0, 133.7 and 133.6, 137.0 137.8, 170.0 and 169.8, 182.6 and 184.1, 202.7 and 202.6; MS (EI) *m/z* 323 and 321 (M^++2, M^+; 1:3), 293 and 291 (M^++2-CO, M^+-CO; 1:3), 104 (base); Anal Calcd for $C_{17}H_{20}ClNO_3$: C, 63.5; H, 6.3; N, 4.4. Found: C, 63.6; H, 6.4; N, 4.3.

3-(1-Benzoyl-1-methylethyl)-4-diethylamino-3-cyclobutene-1,2-one (12i). *crystals* ; mp. 125-128 °C; (Elution H-A 1:1); IR (KBr) 1777, 1732, 1676, 1593 cm^{-1}; ^1H NMR δ 0.87 and 1.03 (each 3 H, t, *J*=7.4 and 7.2 Hz respectively), 1.80 (6 H, s), 3.09 and 3.70 (each 2 H, q, *J*=7.2 and 7.4 Hz respectively), 7.39-8.03 (5 H, m); ^{13}C NMR δ 13.1, 14.4, 26.1, 42.9, 45.8, 49.4, 129.1, 129.7, 133.9, 134.7, 171.4, 181.0, 189.7, 194.2, 201.4; MS (EI) *m/z* 299 (M^+), 271 (M^+-CO), 256 (M^+-CO-CH_3), 243 (M^+-2CO), 138 (base); Anal Calcd for $C_{18}H_{21}NO_3$: C, 72.2; H, 7.1; N, 4.7. Found: C, 72.0; H, 7.2; N, 4.8.

2-(3-Chloro-2-diethylamino-1-hydroxy-4-oxo-2-cyclobutenyl)cyclohexanone (11k). Obtained as a ~1:2 diastereomeric mixture; *crystals* ; mp. 150-153 °C; (Elution H-A 1:1); IR (KBr) 3254, 1759, 1711, 1582 cm^{-1}; ^1H NMR δ 1.23 and 1.32 (each 3 H, t, *J*=7.2 Hz), 1.50-2.50 (8 H, m), 2.73 and 3.03 (0.3' H and 0.6' H respectively, dd, *J*=10.4, 6.0 Hz), 3.30-3.78 (4 H, m), 5.38 (1 H, br s); ^{13}C NMR paring signals due to a diastereoisomeric mixture: δ 14.2 and 13.8, 14.8 and 14.6, 24.4 and 24.6, 25.6 and 26.9, 29.0 and 29.4, 42.1 and 42.9, 43.9, 45.6 and 46.2, 52.1 and 51.1, 91.6 and 90.8, 95.7 and 96.0, 166.8 and 171.2, 182.4 and 182.1, 213.0 and 215.7; MS (EI) *m/z* 287 and 285 (M^++2, M^+; 1:3), 258 and 256 (M^++2-CO-H, M^+-CO-H; 1:3), 116 (base); Anal Calcd for $C_{14}H_{20}ClNO_3$: C, 58.8; H, 7.1; N, 4.9. Found: C, 58.9; H, 7.1; N, 4.8.

2-(2-Diethylamino-3,4-dioxo-1-cyclobutenyl)-2-methylpropanal (12m). *oil*; (Elution H-A 1:1); IR (neat) 1778, 1732, 1595 cm^{-1}; ^1H NMR δ 1.23 and 1.26 (each 3 H, t, *J*=7.2 Hz), 1.60 (6 H, s), 3.26 and 3.85 (each 2 H, q, *J*=7.2 Hz), 9.58 (1 H, s); ^{13}C NMR δ 13.0, 14.6, 21.4, 43.4, 46.1, 49.5, 165.7, 181.4, 190.5, 194.4, 200.4; MS (EI) *m/z* 223 (M^+), 195 (M^+-CO), 167 (M^+-2CO), 138 (base); Anal Calcd for $C_{12}H_{17}NO_3$: C, 64.6; H, 7.7; N, 6.3. Found: C, 64.4; H, 7.8; N, 6.2.

Methyl 2-(3-Chloro-2-diethylamino-1-hydroxy-4-oxo-2-cyclobutenyl)-2-methylpropanoate (11p). *oil*; (Elution H-A 1:1); IR (neat) 3318, 1761, 1730, 1597 cm^{-1}; ^1H NMR δ 1.24 and 1.31 (each 3 H, t, *J*=7.2 Hz), 1.34 and 1.42 (each 3 H, s), 3.29-3.74 (4 H, m), 3.77 (3 H, m), 5.15 (1 H, br s); ^{13}C NMR δ 13.4, 14.3, 22.2, 22.6, 43.2, 45.9, 46.3, 52.8, 93.2, 95.8, 168.8, 178.1, 182.0; MS (EI) *m/z* 291 and 289 (M^++2, M^+; 1:3), 276 and 274 (M^++2-CH_3, M^+-CH_3; 1:3), 254 (M^+-Cl), 232 and 230 (M^++2-CO_2Me, M^+-CO_2Me; 1:3), 124 (base); Anal Calcd for $C_{13}H_{20}ClNO_4$: C, 53.9; H, 6.9; N, 4.8. Found: C, 53.7; H, 6.9; N, 4.9.

3-Ethoxy-4-phenacyl-3-cyclobutene-1,2-dione (13g). *crystals* ; mp. 99-102 °C; (Elution H-A 6:1); IR (KBr) 3449, 1782, 1717, 1561 cm^{-1}; ^1H NMR δ 1.54 (3 H, t, *J*=7.0 Hz), 4.90 (2 H, q, *J*=7.0 Hz), 5.98 (1 H, d, *J*=0.6 Hz), 7.39-7.88 (5 H, m), 11.25 (1 H, d, *J*=0.6 Hz); ^{13}C NMR δ 15.8, 71.5, 88.0, 127.4, 129.0, 131.9, 134.2, 168.7, 173.9, 184.4, 191.1, 199.0; MS (EI) *m/z* 244 (M^+), 216 (M^+-CO), 187 (M^+-CO-C_2H_5), 105 (base); Anal Calcd for $C_{14}H_{12}O_4$: C, 68.9; H, 4.9. Found: C, 69.0; H, 4.8.

3-(Benzoylethyl)-4-ethoxy-3-cyclobutene-1,2-dione (13h). *oil* (Elution H-A 6:1); IR (neat) 1796, 1755, 1690, 1597 cm^{-1}; ^1H NMR δ 1.48 (3 H, t, *J*=7.2 Hz), 1.60 (3 H, d, *J*=7.0 Hz), 4.74 (2 H, q, *J*=7.2 Hz), 4.77 (1 H, q, *J*=7.0 Hz), 7.41-8.01 (5 H, m); ^{13}C NMR δ 14.0, 15.6, 39.5, 70.1, 128.9, 129.3, 134.3, 135.5, 180.7, 184.8, 189.8, 196.0, 199.2; MS (EI) *m/z* 258 (M^+), 230 (M^+-CO), 105 (base); Anal Calcd for $C_{15}H_{14}O_4$: C, 69.8; H, 5.5. Found: C, 70.0; H, 5.4.

3-Ethoxy-4-(2-oxocyclohexyl)-3-cyclobutene-1,2-dione (13k). *crystals* ; mp. 129-130 °C (lit.,[2c] 128 °C); (Elution H-A 6:1); IR (KBr) 3449, 1774, 1707, 1580 cm^{-1}; ^1H NMR δ 1.49 (3 H, t, *J*=7.2 Hz), 1.41-1.76 (8 H, m), 4.85 (2 H, q, *J*=7.2 Hz), 10.92 (1 H, s).

Methyl 2-(2-ethoxy-3,4-dioxo-1-cyclobutenyl)-2-methylpropanoate (13p). *oil* (Elution H-A 6:1); IR (neat) 1796, 1755, 1740, 1597 cm^{-1}; ^1H NMR δ 1.48 (3 H, t, *J*=7.0 Hz), 1.59 (6 H, s), 3.75 (3 H, s), 4.82 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 15.7, 23.0, 44.0, 52.9, 71.3, 173.5, 184.2, 193.4, 195.0, 197.3; MS (EI) *m/z* 226 (M^+), 197 (M^+-C_2H_5), 140 (base); Anal Calcd for $C_{11}H_{14}O_5$: C, 58.4; H, 6.2. Found: C, 58.3; H, 6.3.

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11 Competitive formation of a titanate intermediate, prior to addition, may change the course of reaction to the 1,2-addition mode. Indeed, when initial mixing of silyl ketene acetal **6p** and titanium tetrachloride to form a titanium enolate was followed by addition of compound **2**, the product **7p** could be produced also. Similarly, with the silyl enol ether **6i**, the product was **7i** rather than **8i** if the reagents were mixed in this way. The problem on the order of mixing these reagents is discussed [S. Cardani, C. D. Toma, C. gennari and C. Scolastico, *Tetrahedron*, **48**, 5557 (1992)].

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Chapter 2

Regiocontrolled Derivatization of Squaric Acid Ring Using Electrophilic Addition of Unsaturated Organosilanes and Application of the Adducts

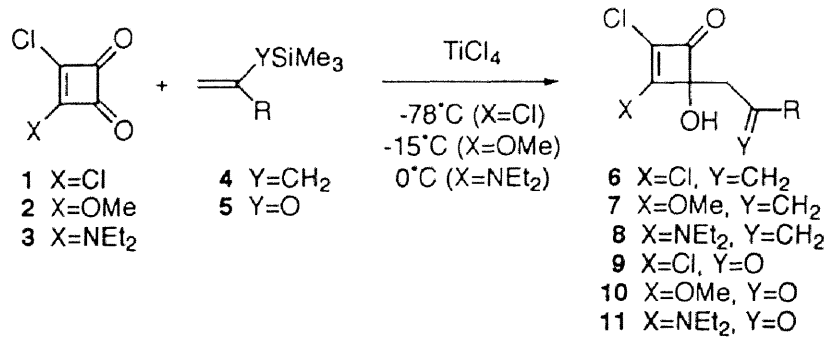
Section 2

Ring Transformation of 4-Acylmethyl- and 4-Allyl-2-chloro-4-hydroxy-2-cyclobutenones

Abstract: 4-Allyl-2-chloro-4-hydroxycyclobutenones prepared from the $TiCl_4$-catalyzed addition of an allylsilane to squaric acid dichloride and ester chloride were subjected to thermolysis (reflux in an aromatic solvent) after acetylation of 4-hydroxy group, and bicyclo[3.2.0]heptenones were obtained *via* an α,β-unsaturated chloroketene intermediate. In contrast, γ-acylmethylenetetronates were produced stereoselectively with (*Z*)-geometry from corresponding 4-acylmethyl-4-hydroxycyclobutenones. The mechanism, application of this novel rearrangement to synthesis of basidalin and related photolysis were described.

As described in the preceding section, we have developed a novel Lewis acid-catalyzed reaction of squaric acid family with unsaturated organosilanes. In contiunation of this study, thermal rearrangement of 4-acylmethyl- and 4-allyl-2-chloro-4-hydroxycyclobutenones, obtained from the above method, were then investigated. The detailed results and an application to a natural product synthesis are reported here.

The ring transformation starts from the reaction of squaric acid families, dichloride **1** (3,4-dichloro-3-cyclobutene-1,2-dione), ester chloride **2** (3-chloro-4-methoxy-3-cyclobutene-1,2-dione), and amide chloride **3** (3-chloro-4-diethylamino-3-cyclobutene-1,2-dione) with unsaturated organosilanes. Thus, $TiCl_4$-catalyzed addition of allylsilanes **4** and silyl enol ethers **5** to these chlorides **1**, **2** and **3** proceeded smoothly at -78 °C, -15 °C and 0 °C, respectively, to give 4-allyl- and 4-acylmethyl-4-hydroxycyclobutenones **6-11** (Scheme 1).



1 X=Cl
2 X=OMe
3 X=NEt_2

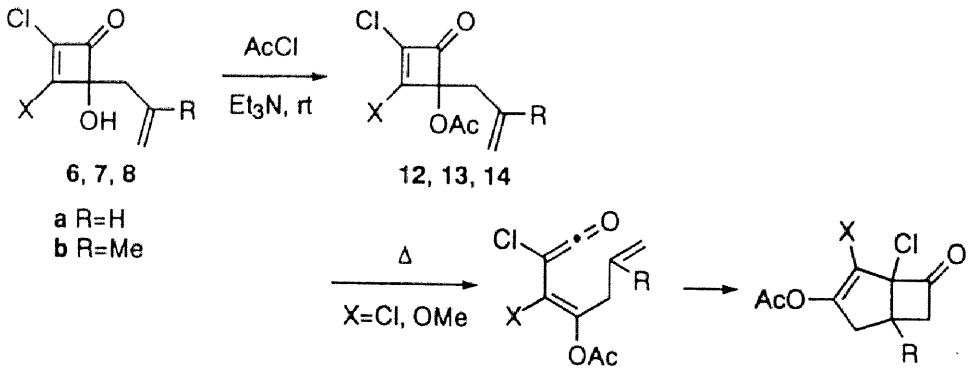
4 Y=CH_2
5 Y=O

6 X=Cl, Y=CH_2
7 X=OMe, Y=CH_2
8 X=NEt_2, Y=CH_2
9 X=Cl, Y=O
10 X=OMe, Y=O
11 X=NEt_2, Y=O

Scheme 1

Cyclobutenones undergo thermal ring-opening to α,β-unsaturated ketenes with high torquoselectivity.[1] Then the ring transformation is achieved by efficient trapping of these intermediates. When an allylic group lies at C_4 in the ring, facile intramolecular [2+2]cycloaddition gives rise to bicyclo[3.2.0]heptenones *via* the preferred inward rotation of the substituent, as demonstrated in the Moore's work.[2] In our case, the chloroketenes from squaric acid dichloride-allylsilane adducts **6a**, **b** were so reactive that the expected products were obtained more easily in higher yields than in the reported cases;[2] thermolysis of *O*-acetylated cyclobutenones **12a**, **b** in refluxing xylene for 1 h afforded the bicyclo[3.2.0]heptenones **15a**, **b** in more than 90 % yield (Scheme 2). Here, acylation of the

4-hydroxyl group was requisite since this reaction failed in an unprotected form (*i.e.*, **6**), which may cause decomposition of the product. Also protection with a trimethylsilyl group was not successful for the rearrangement. The structure of **15a** was assigned on the basis of following spectral data. In addition to the satisfactory MS measurement, the IR spectrum showed an absorption due to cyclobutanone at 1790 cm^{-1}, and the ^1H NMR spectrum indicated the presence of a couple of unequivalent methylene protons (δ 2.76 and 3.10, and 3.29 and 3.52 ppm) and a bridgehead proton (δ 3.02 ppm). The ^{13}C NMR signals were compatible with the assigned structure. In a similar fashion, the 3-methoxy-4-acetoxycyclobutenones **13a**, **b** were transformed in refluxing toluene to **16a**, **b** also in good yields. While the reaction of **13** (C_3-OMe) occurred at lower temperature than that of **12** (C_3-Cl), **14** (C_3-NEt_2) was found to be intact even at higher temperature (reflux in mesitylene) as shown in Table 1. These facts indicate that the above ring-opening reactivity depends on a C_3-substituent, although further studies are awaited for the reasonable explanation. Previously, it has been established that the electrocyclic ring opening of cyclobutene is influenced to great extent by a C_4-substituent.[1]



Scheme 2

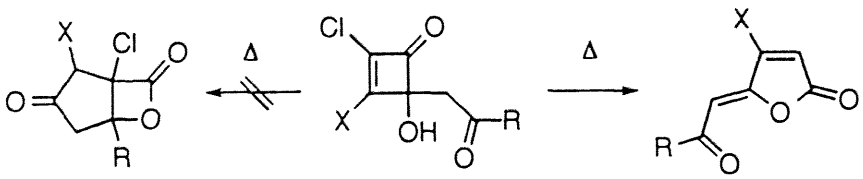
In connection with the ring transformation described above, the thermal behavior of 4-acylmethyl-substituted cyclobutenones **9-11** next attracted our attention. As depicted in Scheme 3, a cyclopentane-fused β-lactone **17** (or its decarboxylated product)[3] was expected to be produced *via* the cycloaddition reaction similar to the transformation of **12** to **15**. In this regard, the thermal rearrangement of 4-phenacylcyclobutenone **9** occurred smoothly in

Table 1. Rearrangement of 4-Allyl-4-acetoxycyclobutenones **12**, **13**, **14** to Bicyclo[3.2.0]heptenones **15**, **16**

entry	X	R	cyclobutenone (Yield %)	solvent	time (h)	bicycloheptenone (Yield %)
1	Cl	H	**12a** (61)	xylene	1	**15a** (91)
2	Cl	Me	**12b** (59)	xylene	1	**15b** (90)
3	OMe	H	**13a** (67)	toluene	1	**16a** (93)
4	OMe	Me	**13b** (85)	toluene	1	**16b** (84)
5	NEt_2	H	**14a** (67)	mesitylene	3	no reaction

refluxing benzene for 2 h, but unexpected γ-phenacylidene-2(*5H*)-furanone **18** was obtained in 37 % yield after chromatographic separation. The structure was elucidated by spectral inspections; the mass spectral and elemental analyses indicated loss of HCl from the molecule, and the IR absorptions at 1795 and 1661 cm^{-1} suggested the existence of a furanone moiety. The ^{13}C NMR signals appeared all at lower field (δ 106.3, 128.7, 129.3, 132.0, 134.3, 136.6, 138.1, 157.8, 163.4 and 189.3 ppm), showing all the carbons to be sp^2 hybridized. Particularly, the ^1H NMR spectrum revealed that two vinylic protons (δ 7.03 and 8.36 ppm) had a long-range coupling (*J*=0.6 Hz). The observed spectral patterns were closely related to those reported for a γ-methylenefuranone[4] and supported *Z*-stereochemistry at the acylmethylene moiety by the observed long-range coupling.[5] In the same manner the 3-methoxy-substituted analogue **10a** produced γ-phenacylidenetetronate **19a** upon heating in xylene for 2 h. Again, the spectral data of **19a** were consistent with the tetronate structure. In this case, the yield was low (15 %), probably because the liberated HCl damaged the product. To this end, the reaction was carried out in the presence of a base; pyridine was more effective than 4-diethylaminopyridine, triethylamine and *N*,*N*-diethylaniline and the yield was raised to 64 %. The other γ-acylmethylenetetronates **19b-i** were thus produced in 54-63 % yields under these conditions from the adducts **10b-i** of ester chloride **2** which were obtained from the reaction with silyl enol ethers **5b-h** of alkyl, alkenyl, aryl and trimethylsilyl ketones and a silyl ketene acetal **5i**. These results are summarized in Table 2. In contrast to the above successful results for **9** and **10**, the attempted reaction using the 3-diethylamino-substituted analogue **11**

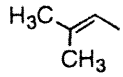
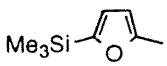
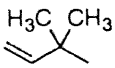
did not afford the corresponding aminofuranone but resulted in the formation of a complex mixture; disubstitution on the amino group might sterically suppress the smooth ring-opening reactivity (for an unsubstituted case, see the basidalin synthesis described below).



17 **9** X=Cl, R=Ph; **10** X=OMe; **18** X=Cl, R=Ph; **19** X=OMe

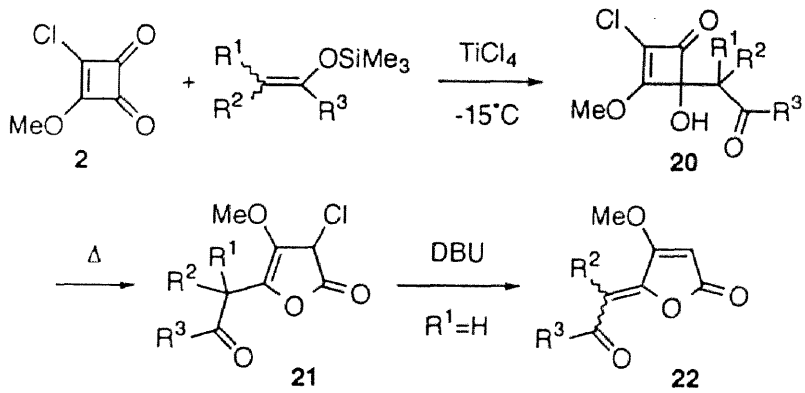
Scheme 3

Table 2. Formation of Tetronates **19** from Ester Chloride **2** and Silyl Enol Ethers **5**

entry	R	**5**	**10** (Yield %)	**19** (Yield %)	mp (°C)
1	Ph	**5a**	**10a** (80)	**19a** (64)	159-162
2	CH_3	**5b**	**10b** (72)	**19b** (56)	80-83
3	$CH_3(CH_2)_4$-	**5c**	**10c** (61)	**19c** (63)	oil
4		**5d**	**10d** (45)	**19d** (61)	74-78
5		**5e**	**10e** (73)	**19e** (61)	77-80
6		**5f**	**10f** (82)	**19f** (54)	131-133
7		**5g**	**10g** (66)	**19g** (61)	84-88
8	Me_3Si	**5h**	**10h** (80)	**19h** (60)	77-80
9	PhO	**5i**	**10i** (83)	**19t** (61)	136-139

The other 4-acylmethylcyclobutenones **20** having substituents on their acylmethyl side chain showed different chemical behavior. These were prepared by the reaction of ester chloride **2** with a methyl-substituted silyl enol ether, silyl ketene acetal, and dimethyl-substituted silyl ketene acetal. When **20a-c** were heated in xylene, thermal rearrangement occurred without liberation of HCl, affording 2(3*H*)-furanones **21a-c** in good yields. Here, relatively longer reaction time was required than that for **10** (Scheme 4). The 2(3*H*)-furanone

structures were determined as follows. Primarily, their mass spectral and elemental analyses indicated the presence of a chlorine atom. The IR spectra showed a non-conjugated carbonyl absorption near 1800 cm^{-1} and the ^1H NMR spectra of **21a, b** had two signals due to methine protons on the ring and side chain. Finally, **21a, b** were further converted to γ-acylmethylenetetronates **22a, b** by treatment with DBU in THF at ambient temperature. In these cases, corresponding tetronate **22a** was obtained as a pure *Z*-isomer in 95 % yield and **22b** as a 3:1 mixture of *Z*- and *E*-isomers in 72 % yield (Table 3). The stereochemistry was deduced from the relative chemical shifts of the methyl protons on the γ-methylene moiety in the ^1H NMR of **22b**; the methyl proton of the *E*-isomer (δ 2.21 ppm) was more deshielded by virtue of its *cis*-relationship to the butenolide oxygen than that of the *Z*-isomer (δ 2.12 ppm).[6] On the analogy of **19a** and **22b**, **22a** is believed to have *Z*-stereochemistry. The observed stereorandomness in the reaction of **21b** to **22b** was informative for the reaction pathway of the present ring transformation (*vide infra*).

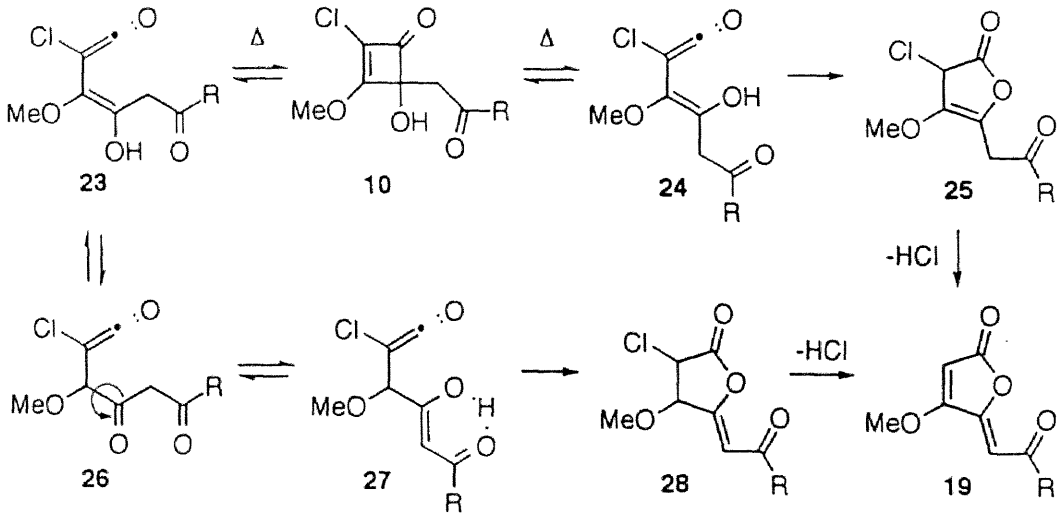


Scheme 4

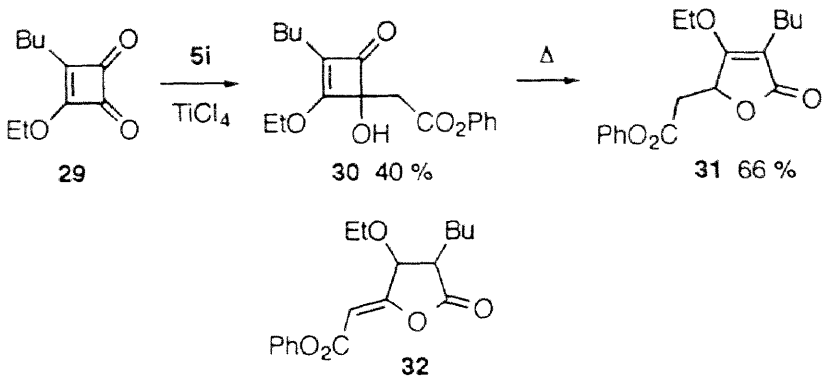
Table 3. Formation of 2(3*H*)-Furanones **21** and Tetromates **22** from Ester Chloride **2**

entry	R^1	R^2	R^3	**20** (Yield %)	reflaux time (h)	**21** (Yield %)	**22** (Yield %)
1	H	Me	Ph	**20a** (49)	2	**21a** (77)	**22a** (95)
2	H	Me	OEt	**20b** (64)	6	**21b** (86)	**22b** (72)
3	Me	Me	OMe	**20c** (76)	12	**21c** (76)	-

Scheme 5 illustrates the plausible mechanisms for the stereoselective formation of the tetronate **19**. The 4-hydroxycyclobutenone **10** undergoes thermally allowed conrotatory electrocyclic ring-opening to generate a kinetically favored enol ketene **23** and a minor stereoisomer **24**, which are in equilibrium under thermal conditions. Although the torquoselectivity orients a hydroxyl group outwardly, the equilibrium allows the reaction to shift to 2(3*H*)-furanone **25** as a result of lactonizaton of **24**. Finally, stereoselective dehydrochlorination of **25** produces thermodynamically more stable tetronate **19**.[6] This stereoselectivity might be explained by the other mechanism. Isomerization of the enol moiety in the ketene intermediate **23** leads to **27** *via* a 1,3-diketone **26** and following recyclization gives a γ-lactone **28**.[7] Subsequent dehydrochlorination affords the tetronate **19**, in which the stereoselectivity originates from intramolecular hydrogen-bonding in **27**. However, involvement of **27** is incompatible with the formation of a *Z*- and *E*-isomeric mixture from **21b**. Furthermore, the latter mechanism was not supported by the reaction using **30** (Scheme 6). Because a chlorine atom is absent in this molecule, a primary product **32** should be formed. Actually, the product derived therefrom was 2(5*H*)-furanone **31**. Consequently, the reaction pathway *via* **24**→**25**→**19** is likely for the ring transformation of squaric acid ester chloride-silyl enol ether adducts to tetronates.

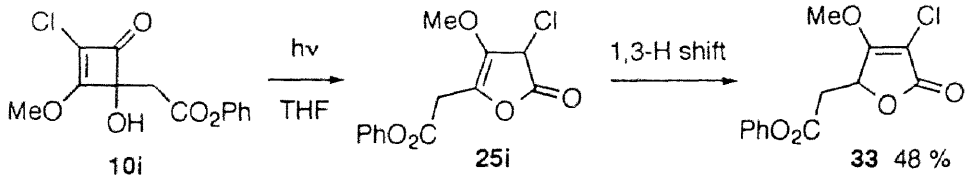


Scheme 5



Scheme 6

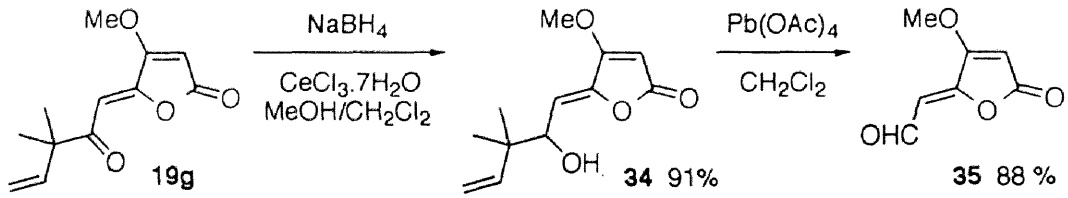
Associated with the thermolysis, photolysis of a 4-acylmethyl-substituted cyclobutenone was also undertaken (Scheme 7). The photorearrangement of cyclobutenone **10i** was carried out in THF at ambient temperature using a high-pressure mercury lamp with a quartz immersion well. The reaction was completed within 5 h to give the α-chlorotetronate **33** in 48 % yield, where 1,3-hydrogen shift took place in preference to dehydrochlorination of the 2(3*H*)-furanone intermediate **25i**. The structural determination was based on the spectral inspections: MS M^+ peak at m/z 282, IR absorption due to a conjugated carbonyl group at 1771 cm^{-1}, and ^1H NMR ABX signals at δ 2.91, 3.16 and 5.22 ppm. Thus, photolysis of **10i** provides a method for construction of chlorinated tetronate derivatives.[8]



Scheme 7

A wide variety of compounds containing the 5-ylidene-2(5*H*)-furanone structure are found in nature,[9] and some of them display useful biological properties (*e.g.* protoanemonine, fimbrolide, agglomerin and rubrolide).[10] Thus, new synthetic methods to construct this ring system have drawn considerable attention. We have now applied the present ring transformation to the total synthesis of basidalin **41**, isolated from *Leucoagaricus naucina*, a simple enamine derivative of tetronic acid (both *E*- and *Z*-forms are known),

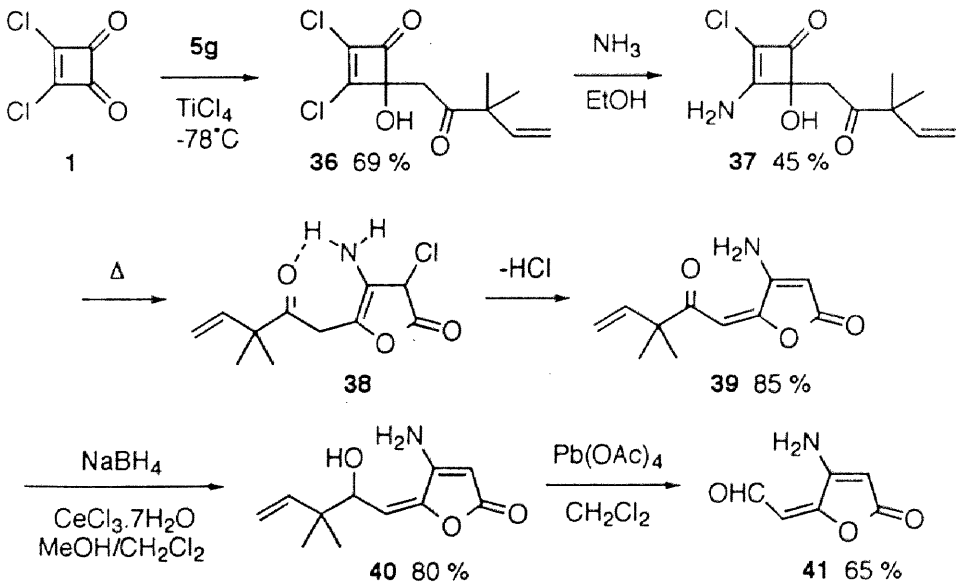
exhibiting antibacterial and antitumor activities.[11] At the outset, synthesis of the related compound **35** (an amino group is replaced by a methoxy group) was attempted for the aim to find out an efficient method for introducing a γ-formylmethylene moiety. At first straightforward addition of a silyl enol ether of acetaldehyde to ester chloride **2** was envisaged but in vain because of polymerization of the reagent. Such polymerization was depressed by using an analogous silane **5h**, however desilylation for both products **10h** and **19h** under various conditions (*e.g.* tetrabutylammonium fluoride / aq. THF, K_2CO_3 / MeOH and tetrabutylammonium hydroxide / CH_3CN) failed. These discouragements were surmounted by employing an alternative silane **5g**. (*Z*)-γ-Acylmethylenetetronate **19g**, obtainable from **5g** as indicated in entry 7 (Table 2), was followed by reduction/oxidation procedures;[12] selective reduction of **19g** to alcohol **34** with $NaBH_4/CeCl_3$ and subsequent oxidation of **34** with $Pb(OAc)_4$ gave rise to desired **35** fruitfully. The structure of **35** was clarified by the IR absorptions at 1820 and 1674 cm^{-1}, and the ^1H NMR signals at δ 5.45 (d, *J*=0.6 Hz), 5.76 (dd, *J*=0.6, 8 Hz) and 10.17 (d, *J*=8 Hz) ppm. The coupling constant of vinyl protons (*J*=0.6 Hz) confirmed the *Z*-stereochemistry of **35** (Scheme 8).



Scheme 8

With these results in hand, the total synthesis of basidalin was carried out as outlined in Scheme 9. In the beginning, required 4-hydroxycyclobutenone **36** was obtained by the $TiCl_4$-catalyzed addition of the silane **5g** to squaric acid dichloride **1**. This was converted to amide chloride **37** with ethanolic NH_3. Thus prepared aminocyclobutenone **37** was transformed to a (*E*)-5-acylmethylene-4-amino-2(5*H*)-furanone **39** upon heating in xylene for 2 h in the presence of pyridine. The *E*-configuration of the product was indicated by the long-range

coupling (J=1.4 Hz) in the ^{1}H NMR spectrum. The observed stereospecific dehydrochlorination to only *E*-isomer deserves to be mentioned; in contrast to the formation of the *Z*-isomer **19g** (*vide supra*), the *E*-isomer **39** was formed as a result of the different substitution at C3 (*i.e.*, MeO *vs* NH_2). This is ascribable to hydrogen-bonding between amino and carbonyl groups prior to 1,4-elimination as shown in the 2(3*H*)-furanone intermediate **38**. This phenomenon seems to be, in some sense, mimic to the biogenetic route of naturally occurring 5-ylidene-2(5*H*)-furanones, in which the covalent bond plays a role to fix the *E*-geometry.[13] Furthermore it is of interest that, in spite of lack of ring-opening reactivity of 3-diethylaminocyclobutenone **8** (entry 5 in Table 1), the rearrangement of **37** having an amino function was accomplished (85 % yield). Finally, **39** was subjected to the reduction/oxidation procedures as employed for **19g**, affording (*E*)-basidalin (**41**). Synthesized basidalin showed the physical and spectral properties identical with those reported for the natural product.[11]



Scheme 9

In conclusion, thermal rearrangement of 4-acylmethyl-2-chloro-4-hydroxy-2-cyclobutenones prepared from squaric acid ester chloride and a silyl enol ether provided the novel entry to γ-acylmethylenetetronates in which an acyl group was introduced

stereoselectively (*Z*-geometry). As for C_3-substituent on the cyclobutene ring, replacement of a methoxy group with an amino group reversed the stereochemistry of the product (*E*-geometry). This merit of preparation overcomes the nonstereoselective condensation reaction of maleic anhydride with an ylide,[6] and was successfully applied to the total synthesis of (*E*)-basidalin. In contrast, photolysis of the 4-acylmethyl-2-chloro-4-hydroxycyclobutenone produced the γ-acylmethyl-α-chlorotetoronate.

Experimental Section

General. IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ or DMSO-d_6 with $SiMe_4$ as internal standard. Mass spectra were recorded on a JEOL JMS-AX 505 HA mass spectrometer. Flash chromatography was performed with a silica gel column (Fuji-Davison BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400S CHN elemental analyzer. THF was freshly distilled over Na and benzophenone. Benzene, toluene, xylene and mesitylene were dried over Na. Dichloromethane was dried over $CaCl_2$, distilled, and stored over 4Å molecular sieves. Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.. Its derivatives, dichloride **1** and methyl ester chloride **2**, were prepared by our methods and diethylamide chloride **3** was prepared by the established procedure (see, Section 1). The cyclobutenones **6-9** and **11** were obtained according to the methods described in Section 1.

Synthesis of 4-Hydroxycyclobutenones 10. General Procedure. To a solution of **1** (0.5 mmol) and **5** (1 mmol) in dry dichlroromethane (2 mL) was added $TiCl_4$ (0.06 mL, 0.5 mmol) by syringe at -78°C under exclusion of moisture, and the solution was stirred for 10 min. The reaction mixture was poured into cold water, extracted with dichloromethane, dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue with the solvent specified gave the product. The yields are listed in Table 2. The compound **10a** was reported in Section 1.

2-Chloro-4-hydroxy-3-methoxy-4-(2-oxopropyl)-2-cyclobutenone (10b). *oil* (Elution H-A 3:1); IR (neat) 3399, 1782, 1713, 1613 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.28 (3 H, s), 2.95 and 3.05 (each 1 H, d, J=17.4 Hz), 4.35 (3 H, s), 4.98 (1 H, br s); ^{13}C NMR ($CDCl_3$) δ 31.2, 44.0, 61.2, 87.5, 105.5, 182.7, 185.8, 208.4; MS (EI) *m/z* (rel. intensity) 204 (M^+, 43), 168 (43), 161 (100), 153 (59); Anal Calcd for $C_8H_9ClO_4$: C, 46.96; H, 4.43. Found: C, 46.83; H, 4.66.

2-Chloro-4-hydroxy-3-methoxy-4-(2-oxoheptyl)-2-cyclobutenone (10c). *oil* (Elution H-A 3:1); IR (neat) 3395, 2957, 1784, 1711, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (3 H, t, *J*=6.6 Hz), 1.22-1.59 (6 H, m), 2.52 (2 H, m), 2.90 and 3.00 (each 1 H, d, *J* =17.0 Hz), 4.35 (3 H, s), 4.98 (1 H, br s); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.4, 23.0, 31.1, 42.9, 44.1, 61.2, 87.7, 105.0, 182.6, 185.7, 211.2; MS (EI) *m/z* (rel. intensity) 260 (M^+, 11), 225 (14), 203 (21), 189 (30), 168 (71), 161 (91), 153 (100); Anal Calcd for $C_{12}H_{17}ClO_4$: C, 55.28; H, 6.57. Found: C, 55.20; H, 6.64.

4-[(1-Adamantyl)carbonylmethyl]-2-chloro-4-hydroxy-3-methoxy-2-cyclobutenone (10d). *oil* (Elution H-A 3:1); IR (neat) 3399, 2908, 1786, 1700, 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.64-2.07 (15 H, m), 2.91 and 3.04 (each 1 H, d, *J*=17.4 Hz), 4.33 (3 H, s), 5.41 (1 H, br s); ^{13}C NMR ($CDCl_3$) δ 27.7, 36.3, 36.5, 37.6, 47.4, 61.1, 88.2, 104.8, 182.7, 185.6, 216.3; MS (EI) *m/z* (rel. intensity) (no molecular ion), 288 (79), 260 (91), 161 (57), 107 (100); Anal Calcd for $C_{17}H_{21}ClO_4$: C, 62.86; H, 6.52. Found: C, 62.73; H, 6.64.

2-Chloro-4-hydroxy-3-methoxy-4-(4-methyl-2-oxo-3-pentenyl)-2-cyclobutenone (10e). *oil* (Elution H-A 3:1); IR (neat) 3393, 2955, 1786, 1680, 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.94 (3 H, d, *J*=1.2 Hz), 2.19 (3 H, d, *J*=1.0 Hz), 2.90 and 3.00 (each 1 H, d, *J* =17.0 Hz), 4.33 (3 H, s), 5.49 (1 H, br s), 6.08 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 21.4, 28.1, 43.7, 61.1, 88.3, 104.7, 123.6, 160.9, 182.9, 185.8, 199.5; MS (EI) *m/z* (rel. intensity) 244 (M^+, 21), 229 (43), 212 (93), 208 (63), 193 (43), 161 (100); Anal Calcd for $C_{11}H_{13}ClO_4$: C, 54.00; H, 5.36. Found: C, 53.75; H, 5.51.

2-Chloro-4-hydroxy-3-methoxy-4-[(5-trimethylsilyl-2-furoyl)methyl]-2-cyclobutenone (10f). *oil* (Elution H-A 3:1); IR (neat) 3389, 2959, 1786, 1667, 1615, 1252, 854 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.33 (9 H, s), 3.37 and 3.46 (each 1 H, d, *J* =16.2 Hz), 4.35 (3 H, s), 5.22 (1 H, br s), 6.74 (1 H, d, *J*=3.7 Hz); ^{13}C NMR ($CDCl_3$) δ -2.0, 39.2, 61.2, 88.1, 105.0, 119.4, 122.1, 155.7, 169.1, 182.8, 185.4, 187.5; MS (EI) *m/z* (rel.

intensity) 328 (M^+, 52), 313 (77), 292 (65), 284 (36), 277 (46), 167 (100); Anal Calcd for $C_{14}H_{17}ClO_5Si$: C, 51.14; H, 5.21. Found: C, 51.09; H, 5.25.

2-Chloro-4-(3,3-dimethyl-2-oxo-4-pentenyl)-4-hydroxy-3-methoxy-2-cyclobutenone (10g). *oil* (Elution H-A 4:1); IR (neat) 3407, 1788, 1711, 1613 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 and 1.25 (each 3 H, s), 2.93 and 3.05 (each 1 H, d, *J* =17.6 Hz), 4.33 (3 H, s), 5.18 (1 H, br s), 5.21 (1 H, dd, *J*=17.2, 0.8 Hz), 5.23 (1 H, dd, *J*=11.0, 0.8 Hz), 5.86 (1 H, dd, *J*=17.2, 11.0 Hz); ^{13}C NMR ($CDCl_3$) δ 23.0, 23.1, 38.1, 51.7, 61.1, 88.1, 104.9, 116.2, 141.3, 182.5, 185.4, 213.6; MS (EI) *m/z* (rel. intensity) (no molecular ion) 243 (4), 189 (4), 161 (61), 153 (37), 147 (23), 133 (13), 119 (8), 98 (100); (CI) *m/z* (rel. intensity) 259 (MH^+, 100), 223 (41); Anal Calcd for $C_{12}H_{15}ClO_4$: C, 55.71; H, 5.84. Found: C, 55.85; H, 5.70.

2-Chloro-4-hydroxy-3-methoxy-4-[(trimethylsilyl)carbonylmethyl]-2-cyclobutenone (10h). *oil* (Elution H-A 4:1); IR (neat) 3397, 1784, 1613, 1252, 849 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.24 (9 H, s), 3.04 and 3.18 (each 1 H, d, *J* =17.4 Hz), 4.33 (3 H, s), 5.02 (1 H, br s); ^{13}C NMR ($CDCl_3$) δ -3.6, 46.8, 61.1, 88.4, 112.7, 182.6, 185.6, 250.1; MS (EI) m/z (rel. intensity) (no molecular ion) 234 (7), 211 (5), 199 (3), 183 (5), 144 (3), 73 (100); (CI) *m/z* (rel. intensity) 263 (MH^+, 100), 227 (48); Anal Calcd for $C_{10}H_{15}ClO_4Si$: C, 45.72; H, 5.76. Found: C, 45.78; H, 5.70.

Phenyl (3-Chloro-1-hydroxy-2-methoxy-4-oxo-2-cyclobutenyl)acetate (10i). *oil* (Elution H-A 3:1); IR (neat) 3410, 1784, 1757, 1610 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.11 and 3.18 (each 1 H, d, *J* =14.0 Hz), 4.37 (3 H, s), 4.47 (1 H, br s), 7.01-7.43 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 37.1, 61.3, 87.2, 105.4, 121.7, 126.7, 129.9, 150.4, 169.3, 182.3, 185.4; MS (EI) *m/z* (rel. intensity) 282 (M^+, 10), 246 (9), 189 (13), 161 (54), 153 (100); Anal Calcd for $C_{13}H_{11}ClO_5$: C, 55.24; H, 3.92. Found: C, 55.17; H, 4.08.

Synthesis of Bicyclo[3.2.0]heptenones 15 and 16. General Procedure. Acetylation of **6**, **7** and **8** was performed as follows. To a solution of 4-allyl-4-

hydroxycyclobutenone (0.3 mmol) and acetyl chloride (47 mg, 0.6 mmol) in dry ether (2mL) was added triethylamine (61 mg, 0.6 mmol) by syringe. After being stirred overnight at ambient temperature, the reaction mixture was diluted with dichloromethane and washed with water. The organic layer was dried (Na_2SO_4) and evaporated to dryness. Flash chromatography of the residue (H-A 5:1) gave the product. The yields are listed in Table 1.

4-Acetoxy-2,3-dichloro-4-(2-propenyl)-2-cyclobutenone (12a). *oil* ; IR (neat) 1796, 1761, 1645, 1589 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.08 (3 H, s), 2.72-2.79 (2 H, m), 5.13-5.26 (2 H, m), 5.58-5.80 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 20.9, 35.7, 96.3, 121.6, 129.3, 135.5, 165.3, 169.8, 182.7; MS (EI) m/z (rel. intensity) (no molecular ion), 198 (100), 164 (46), 157 (45); (CI) *m/z* 235 (MH^+, 100); Anal Calcd for $C_9H_8Cl_2O_3$: C, 45.99; H, 3.43. Found: C, 45.76; H, 3.56.

4-Acetoxy-2,3-dichloro-4-(2-methyl-2-propenyl)-2-cyclobutenone (12b). *oil* ; IR (neat) 1796, 1759, 1649, 1589 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.73, (3 H, dd, *J*=1.4, 0.8 Hz), 2.09 (3 H, s), 2.67 and 2.82 (each 1 H, dd, *J*=14.4, 0.8 Hz), 4.87 and 4.98 (each 1 H, m); ^{13}C NMR ($CDCl_3$) δ 21.0, 23.5, 39.4, 96.5, 117.9, 135.4, 138.0, 165.5, 169.7, 182.6; MS (EI) *m/z* (rel. intensity) (no molecular ion), 206 (36), 191 (47), 171 (100); Anal Calcd for $C_{10}H_{10}Cl_2O_3$: C, 48.22; H, 4.05. Found: C, 48.25; H, 4.02.

4-Acetoxy-2-chloro-3-methoxy-4-(2-propenyl)-2-cyclobutenone (13a). *oil* ; IR (neat) 1796, 1750, 1622 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.07 (3 H, s), 2.72-2.78 (2 H, m), 4.35 (3 H, s), 5.14-5.24 (2 H, m), 5.63-5.84 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 21.0, 35.5, 61.0, 92.6, 105.6, 120.5, 130.3, 169.7, 180.0, 182.4; MS (EI) m/z (rel. intensity) (no molecular ion), 188 (100), 173 (4), 160 (4), 153 (21); (CI) *m/z* 231 (MH^+, 100); Anal Calcd for $C_{10}H_{11}ClO_4$: C, 52.07; H, 4.81. Found: C, 52.04; H, 4.87.

4-Acetoxy-2-chloro-3-methoxy-4-(2-methyl-2-propenyl)-2-cyclobutenone (13b). *oil* ; IR (neat) 1796, 1755, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77, (3 H, dd, *J*=1.4, 1.0 Hz), 2.06 (3 H, s), 2.67 and 2.77 (each 1 H, dd, *J*=14.0, 0.8 Hz), 4.35 (3 H, s), 4.84 and 4.94 (each 1 H, m); ^{13}C NMR ($CDCl_3$) δ 21.1, 23.2, 39.1, 61.0, 92.9, 105.7, 116.9, 138.8,

169.7, 179.8, 182.5; MS (EI) *m/z* (rel. intensity) (no molecular ion), 202 (100), 187 (19), 167 (10), 161 (44); (CI) m/z 245 (MH^+, 100); Anal Calcd for $C_{11}H_{13}ClO_4$: C, 54.00; H, 5.36. Found: C, 53.97; H, 5.43.

4-Acetoxy-2-chloro-3-diethylamino-4-(2-propenyl)-2-cyclobutenone (14a). *crystals*, mp 65-66°C; IR (KBr) 1782, 1763, 1611 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, *J*=7.2 Hz), 1.29 (3 H, t, *J*=7.2 Hz), 2.06 (3 H, s), 2.55 and 2.98 (each 1 H, ddt, *J*=14.5, 7.8, 1.0 Hz), 3.39 (2 H, q, *J*=7.2 Hz), 3.60 and 3.63 (each 1 H, dq, *J*=8.4, 7.2 Hz), 5.11-5.23 (2 H, m), 5.60-5.81 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 13.6, 14.1, 21.4, 37.3, 43.2, 45.4, 92.3, 95.3, 120.0, 130.7, 167.3, 169.5, 179.3; MS (EI) *m/z* (rel. intensity) 271 (M^+, 26), 229 (100), 214 (39), 194 (82); (CI) *m/z* 231 (MH^+, 100); Anal Calcd for $C_{13}H_{18}ClNO_3$: C, 57.46; H, 6.62; N, 5.15. Found: C, 57.32; H, 6.75; N, 5.16.

Thermal rearrangement of **12** and **13** was performed as follows. A solution of **12** (or **13**) (0.45 mmol) in dry xylene (or in dry toluene) (15 mL) was refluxed for 1 h. The obtained colorless solution was cooled to ambient temperature and the solvent was removed under reduced pressure. The residue was chromatographed (H-A 5:1) to afford the product. The yields are listed in Table 1.

3-Acetoxy-1,2-dichlorobicyclo[3.2.0]hept-2-en-7-one (15a). *oil* ; IR (neat) 1790, 1779, 1651, 1186 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.26 (3 H, s), 2.76 (1 H, d, *J*=17.4 Hz), 3.02 (1 H, m), 3.10 (1 H, dd, *J*=17.4, 6.2 Hz), 3.29 (1 H, dd, *J*=17.4, 7.0 Hz), 3.52 (1 H, dd, *J*=17.4, 9.2 Hz); ^{13}C NMR ($CDCl_3$) δ 20.7, 34.6, 35.9, 50.5, 84.5, 114.4, 150.3, 167.4, 196.1; MS (EI) *m/z* (rel. intensity) 234 (M^+, 6), 199 (27), 192 (100); Anal Calcd for $C_9H_8Cl_2O_3$: C, 45.99; H, 3.43. Found: C, 45.90; H, 3.52.

3-Acetoxy-1,2-dichloro-5-methylbicyclo[3.2.0]hept-2-en-7-one (15b). *oil* ; IR (neat) 1796, 1784, 1655, 1173 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (3 H, s), 2.25 (3 H, s), 2.94 (2 H, s), 3.02 (1 H, d, *J*=17.8 Hz), 3.18 (1 H, d, *J*=17.8 Hz); ^{13}C NMR ($CDCl_3$) δ 20.7, 21.1, 38.7, 42.8, 56.9, 87.2, 115.1, 149.8, 167.5, 196.9; MS (EI) *m/z* (rel. intensity) (no

molecular ion) 206 (41), 164 (100), 129 (19); Anal Calcd for $C_{10}H_{10}Cl_2O_3$: C, 48.22; H, 4.05. Found: C, 48.16; H, 4.11.

3-Acetoxy-1-chloro-2-methoxybicyclo[3.2.0]hept-2-en-7-one (16a). *oil* ; IR (neat) 1792, 1769, 1682, 1198 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (3 H, s), 2.55 (1 H, d, *J*=16.4 Hz), 2.80 (1 H, m), 3.11 (1 H, dd, *J*=16.4, 7.4 Hz), 3.12 (1 H, dd, *J*=18.2, 6.8 Hz), 3.46 (1 H, dd, *J*=18.2, 9.6 Hz), 3.77 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 20.7, 32.7, 33.3, 50.6, 58.6, 82.6, 131.8, 137.4, 168.4, 197.7; MS (EI) *m/z* (rel. intensity) 230 (M^+, 2), 187 (60), 160 (80), 146 (100); Anal Calcd for $C_{10}H_{11}ClO_4$: C, 52.07; H, 4.81. Found: C, 51.91; H, 4.97.

3-Acetoxy-1-chloro-2-methoxy-5-methylbicyclo[3.2.0]hept-2-en-7-one (16b). *oil* ; IR (neat) 1794, 1767, 1686, 1198 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (3 H, s), 2.20 (3 H, s), 2.75 (2 H, s), 2.96 (1 H, d, *J*=17.6 Hz), 3.37 (1 H, d, *J*=17.6 Hz), 3.76 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 20.6, 20.7, 35.8, 40.6, 56.8, 58.5, 85.3, 131.5, 138.0, 168.4, 198.5; MS (EI) *m/z* (rel. intensity) 244 (M^+, 3), 210 (8), 201 (63), 173 (38), 159 (100); Anal Calcd for $C_{11}H_{13}ClO_4$: C, 54.00; H, 5.36. Found: C, 53.99; H, 5.37.

Synthesis of (*Z*)-4-Chloro-5-phenacylidene-2(5*H*)-furanone (18). A solution of **9** (191 mg, 0.70 mmol) in dry benzene (30 mL) was refluxed for 2 h. The resulting dark brown solution was cooled to ambient temperature and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (H-A 10:1) to afford **18** (62 mg, 37 %) as yellow crystals: mp 97-100°C; IR (KBr) 1796, 1661, 1603, 986 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.03 (1 H, d, *J*=0.8 Hz), 7.48-8.00 (5 H, m), 8.36 (1 H, d, *J*=0.8 Hz); ^{13}C NMR ($CDCl_3$) δ 106.3, 128.7, 129.3, 132.0, 134.3, 136.6, 138.1, 157.8, 163.4, 189.3; MS (EI) *m/z* (rel. intensity) 234 (M^+, 7), 206 (8), 157 (11), 105 (100); Anal Calcd for $C_{12}H_7ClO_3$: C, 61.43 ; H, 3.01. Found: C, 61.26 ; H, 3.28.

Synthesis of γ-Acylmethylenetetronates 19. General Procedure. A solution of **10** (0.3 mmol) and pyridine (26 mg, 0.33 mmol) in dry xylene (10 mL) was refluxed for 2 h. The

resulting dark brown solution was cooled to ambient temperature and the solvent was removed under reduced pressure. The residue was purified by flash chromatography [H-A 3:1 except for **19h** (H-A 4:1)] to afford the product. The yield and physical data were listed in Table 2.

(*Z*)-4-Methoxy-5-phenacylidene-2(5*H*)-furanone (19a). IR (KBr) 1803, 1680, 1624, 961, 833 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.03 (3 H, s), 5.44 (1 H, d, *J*=0.6 Hz), 6.55 (1 H, d, *J*=0.6 Hz), 7.44-8.00 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 59.9, 91.4, 100.2, 128.9, 129.0, 133.8, 138.0, 151.0, 167.6, 171.0, 188.5; MS (EI) *m/z* (rel. intensity) 230 (M^+, 10), 170 (36), 105 (100); Anal Calcd for $C_{13}H_{10}O_4$: C, 67.82 ; H, 4.38. Found: C, 67.57 ; H, 4.43.

(*Z*)-5-(Acetylmethylene)-4-methoxy-2(5*H*)-furanone (19b). IR (KBr) 1796, 1769, 1665, 1645, 1613, 976, 847 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.53 (3 H, s), 4.02 (3 H, s), 5.43 (1 H, d, *J*=0.6 Hz), 6.75 (1 H, d, *J*=0.6 Hz); ^{13}C NMR ($CDCl_3$) δ 31.2, 60.0, 91.0, 105.3, 150.8, 166.8, 171.4, 196.8; MS (EI) *m/z* (rel. intensity) 168 (M^+, 26), 153 (100), 137 (84), 125 (42), 111 (39); Anal Calcd for $C_8H_8O_4$: C, 57.14 ; H, 4.80. Found: C, 57.03 ; H, 4.91.

(*Z*)-5-(Hexanoylmethylene)-4-methoxy-2(5*H*)-furanone (19c). IR (neat) 2934, 1796, 1680, 1624, 961, 833 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (3 H, t, *J*=6.6 Hz), 1.32-1.63 (6 H, m), 2.84 (2 H, t, *J*=7.2 Hz), 4.01 (3 H, s), 5.42 (1 H, d, *J*=0.8 Hz), 5.75 (1 H, d, *J*=0.8 Hz); ^{13}C NMR ($CDCl_3$) δ 13.9, 22.5, 23.5, 31.3, 43.5, 59.9, 90.9, 104.8, 150.1, 167.0, 171.5, 199.4; MS (EI) *m/z* (rel. intensity) 224 (M^+, 11), 168 (79), 153 (100), 125 (84), 111 (35); Anal Calcd for $C_{12}H_{16}O_4$: C, 64.27 ; H, 7.19. Found: C, 64.26 ; H, 7.19.

(*Z*)-5-[(1-Adamantyl)carbonylmethylene]-4-methoxy-2(5*H*)-furanone (19d). IR (KBr) 2903, 1802, 1701, 1680, 1628, 959, 829 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.73-2.08 (15 H, m), 4.00 (3 H, s), 5.40 (1 H, d, *J*=0.8 Hz), 6.20 (1 H, d, *J*=0.8 Hz); ^{13}C NMR ($CDCl_3$) δ 27.9, 36.5, 37.9, 46.7, 59.8, 91.3, 98.6, 150.8, 168.0, 171.0, 202.5; MS (EI) *m/z* (rel. intensity) 288 (M^+, 8), 260 (22), 188 (100); Anal Calcd for $C_{17}H_{20}O_4$: C, 70.81 ; H, 6.99. Found: C, 70.69 ; H, 7.10.

(*Z*)-4-Methoxy-5-[(3-methyl-2-butenoyl)methylene]-2(5*H*)-furanone (19e). IR (KBr) 1796, 1660, 1649, 1613, 974 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 and 2.20 (each 3 H, d,

J=1.2 Hz), 4.00 (3 H, s), 5.39 (1 H, d, *J*=0.6 Hz), 5.79 (1 H, d, *J*=0.6 Hz), 6.64 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 21.4, 28.1, 59.8, 90.7, 106.9, 124.5, 148.5, 158.8, 167.4, 171.5, 188.1; MS (EI) *m/z* (rel. intensity) 208 (M^+, 41), 193 (25), 180 (38), 153 (100), 125 (48), 111 (73); Anal Calcd for $C_{11}H_{12}O_4$: C, 63.45 ; H, 5.81. Found: C, 63.20 ; H, 6.01.

(*Z*)-4-Methoxy-5-[(5-trimethylsilyl-2-furoyl)methylene]-2(5*H*)-furanone (19f). IR (KBr) 1794, 1678, 1618, 972, 841 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.30 (9 H, s), 4.03 (3 H, s), 5.43 (1 H, d, *J*=0.6 Hz), 6.51 (1 H, d, *J*=0.6 Hz), 6.72 (1 H, d, *J*=3.6 Hz), 7.24 (1 H, d, *J*=3.6 Hz); ^{13}C NMR ($CDCl_3$) δ −1.9, 59.7, 91.3, 99.6, 118.3, 122.1, 151.2, 157.5, 167.7, 167.8, 171.1, 175.8; MS (EI) *m/z* (rel. intensity) 292 (M^+, 57), 277 (70), 264 (22), 193 (26), 164 (100); Anal Calcd for $C_{14}H_{16}O_5Si$: C, 57.51 ; H, 5.52. Found: C, 57.50 ; H, 5.52.

(*Z*)-5-[(2,2-Dimethyl-3-butenoyl)methylene]-4-methoxy-2(5*H*)-furanone (19g). IR (KBr) 1802, 1701, 1626 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (6 H, s), 3.99 (3 H, s), 5.22 (1 H, dd, *J*=17.6, 0.8 Hz), 5.23 (1 H, dd, *J*=10.6, 0.8 Hz), 5.40 (1 H, d, *J*=0.6 Hz), 5.93 (1 H, dd, *J*=17.6, 10.6 Hz), 6.12 (1 H, d, *J*=0.6 Hz); ^{13}C NMR ($CDCl_3$) δ 23.3, 51.1, 59.8, 91.4, 99.3, 115.7, 142.2, 150.9, 167.9, 171.0, 199.5; MS (EI) *m/z* (rel. intensity) 222 (M^+, 1), 153 (100), 125 (9); Anal Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.97; H, 6.23.

(*Z*)-4-Methoxy-5-[(trimethylsilyl)carbonylmethylene]-2(5*H*)-furanone (19h). IR (KBr) 1792, 1657, 1613, 1584, 1250, 845 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.29 (9 H, s), 4.00 (3 H, s), 5.39 (1 H, d, *J*=0.6 Hz), 5.79 (1 H, d, *J*=0.6 Hz); ^{13}C NMR ($CDCl_3$) δ -2.9, 59.9, 90.8, 108.2, 149.4, 167.0, 171.7, 236.4; MS (EI) *m/z* (rel. intensity) 226 (M^+, 11), 211 (2), 198 (16), 183 (31), 169 (7), 125 (2), 89 (38), 73 (100); Anal Calcd for $C_{10}H_{14}O_4Si$: C, 53.08; H, 6.24. Found: C, 52.97; H, 6.35.

(*Z*)-4-Methoxy-5-[(phenoxycarbonyl)methylene]-2(5*H*)-furanone (19i). IR (KBr) 1813, 1728, 1678, 1626, 961, 837 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 4.01 (3 H, s), 5.44 (1 H, d, *J*=0.6 Hz), 5.83 (1 H, d, *J*=0.6 Hz), 7.14-7.45 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 60.0, 91.6, 95.8, 121.8, 126.4, 129.8, 150.8, 153.4, 162.0, 167.0, 170.6; MS (EI) *m/z* (rel. intensity)

246 (M^+, 9), 153 (100), 125 (37); Anal Calcd for $C_{13}H_{10}O_5$: C, 63.42 ; H, 4.09. Found: C, 63.20 ; H, 4.09.

Synthesis of 2(3*H*)-furanones 21. General Procedure. The cyclobutenones **20a** and **20c** were reported in Section 1. The cyclobutenone **20b** was prepared as a *ca.* 1:2 diastereomeric mixture following the same procedures as described in the first part. The yields are listed in Table 3.

Ethyl 2-(3-Chloro-1-hydroxy-2-methoxy-4-oxo-2-cyclobutenyl)propanoate (20b). *oil* (Elution H-A 3:1); IR (neat) 3422, 1786, 1732, 1613 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (3 H, t, *J*=7.2 Hz), 1.29 and 1.34 (2 H and 1 H, respectively, t, *J*=7.4 Hz), 2.96 and 2.97 (2/3 H and 1/3 H, respectively, q, *J*=7.4 Hz), 4.23 (2 H, q, *J*=7.2 Hz), 4.35 and 4.36 (2 H and 1 H, respectively, s), 4.65 (1 H, br s); ^{13}C NMR ($CDCl_3$) pairing signals due to a diastereomeric mixture: δ 12.8 and 12.6, 14.0, 41.9 and 41.6, 61.8 and 61.2, 90.2 and 90.5, 105.1 and 105.2, 174.4, 181.9 and 181.6, 184.7 and 185.3; MS (EI) *m/z* (rel. intensity) 248 (M^+, 21), 212 (23), 189 (19), 174 (100); Anal Calcd for $C_{10}H_{13}ClO_5$: C, 48.30; H, 5.27. Found: C, 48.14; H, 5.43.

The thermal rearrangement of **20** was carried out by refluxing **20** (0.39 mmol) in dry xylene (15 mL) for the specified time in Table 3. The work-up as above and flash chromatography (H-A 3:1) afforded the product. The yields are listed in Table 3.

5-[(1-Benzoyl)ethyl]-3-chloro-4-methoxy-2(3*H*)-furanone (21a). *oil* (*ca.* 7:1 mixture of diastereomers); IR (neat) 1798, 1775, 1684, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.64 and 1.46 (21/8 H and 3/8 H, respectively, d, *J*=7.2 Hz), 3.75 and 4.04 (21/8 H and 3/8 H, respectively, s), 4.21 and 4.47 (7/8 H and 1/8 H, respectively, q, *J*=7.2 Hz), 5.16 and 5.31 (7/8 H and 1/8 H, respectively, s), 7.45-7.96 (5 H, m); ^{13}C NMR ($CDCl_3$) pairing signals due to a diastereomeric mixture: δ 13.2 and 14.2, 47.6 and 49.4, 60.1 and 60.4, 89.3 and 88.9, 98.3, 128.6 and 128.8, 129.2 and 129.4, 134.1 and 134.2, 135.9 and 136.2, 168.3 and 169.5, 179.7 and 181.5, 197.8 and 198.2; MS (EI) *m/z* (rel. intensity) 280 (M^+, 1), 244 (8),

216 (1), 140 (27), 105 (100); Anal Calcd for $C_{14}H_{13}ClO_4$: C, 59.90 ; H, 4.67. Found: C, 59.75 ; H, 4.82.

3-Chloro-5-[1-(ethoxycarbonyl)ethyl]-4-methoxy-2(3*H*)-furanone (21b). *oil* (*ca.* 5:1 mixture of diastereomers) IR (neat) 1800, 1778, 1738, 1645 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 and 1.28 (15/6 H and 3/6 H, respectively, t, *J*=7.2 Hz), 1.58 and 1.35 (15/6 H and 3/6 H, rspectively, d, *J*=7.2 Hz), 3.22 and 3.32 (5/6 H and 1/6 H, respectively, q, *J*=7.2 Hz), 4.00 and 4.01 (15/6 H and 3/6 H, respectively, s), 4.02-4.28 (2 H, m), 5.16 and 5.21 (5/6 H and 1/6 H, respectively, s); ^{13}C NMR ($CDCl_3$) pairing signals due to a diastereomeric mixture: δ 12.1 and 13.2, 14.0 and 14.1, 47.5 and 49.1, 60.3 and 60.4, 61.6 and 61.4, 88.4 and 89.2, 97.8 and 97.0, 168.5 and 168.4, 169.7 and 169.6, 180.8 and 180.3; MS (EI) *m/z* (rel. intensity) 248 (M^+, 11), 213 (100), 203 (22), 174 (26), 167 (20), 147 (56), 141 (100), 119 (65); Anal Calcd for $C_{10}H_{13}ClO_5$: C, 48.30 ; H, 5.27. Found: C, 48.31 ; H, 5.25.

3-Chloro-4-methoxy-5-[1-(methoxycarbonyl)-1-methylethyl]-2(3*H*)-furanone (21c). *oil*; IR (neat) 1798, 1736, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 and 1.52 (each 3 H, s), 3.67 (3 H, s), 4.00 (3 H, s), 5.16 (1 H, s); ^{13}C NMR ($CDCl_3$) δ 21.2, 22.4, 52.1, 52.6, 60.3, 88.4, 101.0, 168.3, 172.9, 182.1; MS (EI) *m/z* (rel. intensity) 248 (M^+, 10), 213 (100), 188 (15), 169 (13), 147 (61), 119 (46); Anal Calcd for $C_{10}H_{13}ClO_5$: C, 48.30 ; H, 5.27. Found: C, 48.13 ; H, 5.44.

Conversion of 2(3*H*)-Furanones 21 to γ-Acylmethylenetetronates 22. General Procedure. To a solution of **21** (0.14 mmol) in THF (2 mL) was added diazabicyclo[5.4.0]undec-7-ene (23 mg, 0.15 mmol), and the solution was stirred for 1 h at ambient temperature. The reaction mixture was diluted with dichloromethane, washed with water, and dried over Na_2SO_4. After evaporation of the solvent, the residue was subjected to chromatography (H-A 3:1) to afford the product. The yields are listed in Table 3.

(Z)-5-(1-Benzoylethylidene)-4-methoxy-2(5*H*)-furanone (22a). *crystals*, mp 125-127 °C; IR (KBr) 1771, 1738, 1672, 1610, 903 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.19 (3 H, s),

3.60 (3 H, s), 5.25 (1 H, s), 7.46-7.94 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 16.0, 59.5, 90.7, 120.6, 129.2, 129.4, 134.3, 136.1, 141.6, 168.1, 169.4, 195.5; MS (EI) *m/z* (rel. intensity) 244 (M^+, 99), 229 (1), 222 (15), 216 (18), 184 (87), 167 (11), 105 (100); Anal Calcd for $C_{14}H_{12}O_4$: C, 68.85 ; H, 4.95. Found: C, 68.75 ; H, 5.04.

5-[(1-Ethoxycarbonyl)ethylidene]-4-methoxy-2(5*H*)-furanone (22b). *crystals* (*ca.* 3:1 mixture of *Z*- and *E*-isomers), mp 75-77 °C; IR (KBr) 1780, 1721, 1690, 1613, 887 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.33 and 1.35 (9/4 H and 3/4 H, respectively, t, *J*=7.2 Hz), 2.12 and 2.21 (9/4 H and 3/4 H, respectively, s), 3.90 and 3.98 (9/4 H and 3/4 H, respectively, s), 4.27 and 4.31 (6/4 H and 2/4 H, respectively, q, *J*=7.2 Hz), 5.31 and 5.40 (3/4 H and 1/4 H, respectively, s); ^{13}C NMR ($CDCl_3$) paring signals due to a *Z*- and *E*-isomeric mixture δ 14.1, 15.0 and 13.0, 59.6 and 59.8, 61.8, 91.1 and 92.4, 114.6 and 113.5, 143.0 and 144.6, 167.7 and 167.3, 167.8 and 166.9, 169.4 and 172.1; MS (EI) *m/z* (rel. intensity) 212 (M^+, 99), 184 (10), 167 (100), 138 (22); Anal Calcd for $C_{10}H_{12}O_5$: C, 61.22 ; H, 6.16. Found: C, 61.09 ; H, 6.28.

Thermal Rearrangement of 4-Hydroxycyclobutenone 30. The cyclobutenone **30** was prepared as follows. To a solution of **29**[14] (69 mg, 0.38 mmol) and **5i** (158 mg, 0.76 mmol) was added $TiCl_4$ (0.042 mL, 0.38 mmol) by syringe at 0°C under exclusion of moisture, and the solution was stirred for 1 h. The reaction was allowed to warm to ambient temperature and the solution was stirred for further 1 h. The work-up as described in the first part and flash chromatography (H-A 1:1) afforded **30** (52 mg, 42%) as a yellow oil, IR (neat) 3355, 1757, 1611 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, *J*=7.2 Hz), 1.23-1.59 (4 H, m), 1.46 (3 H, t, *J*=7.0 Hz), 2.14 (2 H, t, *J*=7.2 Hz), 3.06 and 3.17 (each 1 H, d, *J* =15.2 Hz), 4.44 and 4.52 (each 1 H, dq, *J*=9.6, 7.0 Hz), 4.48 (1 H, br s), 7.06-7.43 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 13.7, 15.0, 22.4, 22.6, 29.8, 38.2, 69.1, 88.3, 121.7, 126.5, 127.8, 129.8, 150.7, 169.6, 181.6, 191.2; MS (EI) *m/z* (rel. intensity) 318 (M^+, 5), 225 (7), 207

(36), 197 (100), 179 (24), 169 (17), 154 (16), 125 (30); Anal Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.96. Found: C, 67.71; H, 7.15.

Thermal rearrangement of **30** was performed by refluxing a solution of **30** (61 mg, 0.19 mmol) in dry mesitylene (10 mL) for 3 h followed by the same work-up as employed for preparation of **19**. The residue was purified by flash chromatography (H-A 3:1) to afford the tetronate **31** (40 mg, 66%) as a pale-yellow oil, IR (neat) 1759, 1661, 1593 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.92 (3 H, t, *J*=7.0 Hz), 1.27-1.57 (4 H, m), 1.41 (3 H, t, *J*=7.0 Hz), 2.37 (2 H, t, *J*=7.0 Hz), 2.81 (1 H, dd, *J*=16.0, 8.0 Hz), 3.10 (1 H, dd, *J*=16.0, 4.4 Hz), 4.37 and 4.43 (each 1 H, dq, *J*=9.4, 7.0 Hz), 5.12 (1 H, dd, *J*=8.0, 4.4 Hz), 7.07-7.43 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 13.8, 15.3, 22.6, 23.2, 32.3, 37.8, 67.7, 73.9, 103.2, 121.8, 126.4, 129.8, 150.8, 168.2, 171.5, 174.5; MS (EI) *m/z* (rel. intensity) 318 (M^+, 25), 272 (2), 225 (100), 197 (34), 183 (57), 179 (90), 155 (26); Anal Calcd for $C_{18}H_{22}O_5$: C, 67.91 ; H, 6.96. Found: C, 67.81 ; H, 7.05.

Photolysis of 4-Hydroxycyclobutenone 10i. A solution of **10i** (85 mg, 0.30 mmol) in dry THF (10 mL) was irradiated with high-pressure Hg lamp (100 W Ushio UM-102) through a quartz filter under an atomosphere of nitrogen for 5 h. The solvent was evaporated, and the residue was purified by flash chromatography (H-A 3:1) to afford the tetronate **33** (42 mg, 48%) as a pale-yellow oil, IR (neat) 1771, 1653 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.91 (1 H, dd, *J*=16.4, 7.6 Hz), 3.16 (1 H, dd, *J*=16.4, 4.2 Hz), 4.37 (3 H, s), 5.22 (1 H, dd, *J*=7.6, 4.2 Hz), 7.06-7.44 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 37.0, 60.2, 73.3, 94.2, 121.6, 126.6, 129.9, 137.6, 150.6, 167.4, 169.6; MS (EI) *m/z* (rel. intensity) 282 (M^+, 69), 247 (37), 189 (70), 161 (74), 147 (100), 121 (66), 119 (33); Anal Calcd for $C_{13}H_{11}ClO_5$: C, 55.24 ; H, 3.92. Found: C, 55.11 ; H, 4.04.

Synthesis of (*Z*)-5-(Formylmethylene)-4-methoxy-2(5*H*)-furanone (35). A solution of **19g** (310 mg, 1.39 mmol) and $CeCl_3 \cdot 7H_2O$ (673 mg, 1,81 mmol) in 1:1 methanol-

dichloromethane (6 mL) was cooled to -70°C and treated with a solution of $NaBH_4$ (79 mg, 2.09 mmol) in 1:1 methanol-dichloromethane (2 mL). The reaction mixture was allowed to warm slowly to -30°C during 1 h and then quenched with saturated aq. $NaHCO_3$ (5 mL). After filtration of precipitates, the organic layer was separated, washed with water and dried (Na_2SO_4). After evaporation of the solvent the residue was purified by flash chromatography (H-A 4:1) to afford the alcohol **34** (284 mg, 91%) as a colorless oil.

To a solution of $Pb(OAc)_4$ (164 mg, 0.37 mmol) in dry dichloromethane (6 mL) was added a solution of **34** (77 mg, 0.34 mmol) in dry dichloromethane (2 mL) at -78°C under an atomosphere of nitrogen, and the solution was stirred for 2 h and for additional 1.5 h at ambient temperature. The work-up as above and flash chromatography (H-A 3:1) afforded the tetronate **35** (46 mg, 88%) as yellow crystals.

Spectral Data for (*Z*)-5-(2-Hydroxy-3,3-dimethyl-4-pentenylidene)-4-methoxy-2(5*H*)-furanone (34). IR (neat) 3453, 1782, 1765, 1611 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 and 1.07 (each 3 H, s), 2.27 (1 H, br s), 3.94 (3 H, s), 4.45 (1 H, d, *J*=9.4 Hz), 5.10 (1 H, dd, *J*=17.4, 1.4 Hz), 5.15 (1 H, dd, *J*=11.0, 1.4 Hz), 5.25 (1 H, d, *J*=0.6 Hz), 5.45 (1 H, dd, *J*=9.4, 0.6 Hz), 5.90 (1 H, dd, *J*=17.4, 11.0 Hz); ^{13}C NMR ($CDCl_3$) δ 21.7, 23.5, 42.2, 59.4, 72.8, 89.7, 109.2, 114.5, 144.3, 144.8, 168.7, 170.3; MS (EI) *m/z* (rel. intensity) 155 (100), 127 (38); (CI) *m/z* (rel. intensity) 225 (MH^+, 84), 207 (100); Anal Calcd for $C_{12}H_{16}O_4$: C, 64.27 ; H, 7.19. Found: C, 64.58 ; H, 6.88.

Spectral Data for (*Z*)-5-(Formylmethylene)-4-methoxy-2(5*H*)-furanone (35). mp 134-138 °C; IR (neat) 1819, 1674, 1661, 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.04 (3 H, s), 5.45 (1 H, d, *J*=0.6 Hz), 5.76 (1 H, dd, *J*=8.0, 0.6 Hz), 10.17 (1 H, d, *J*=8.0 Hz); ^{13}C NMR ($CDCl_3$) δ 60.1, 91.4, 104.6, 156.5, 166.3, 170.6, 189.0; MS (EI) *m/z* (rel. intensity) 154 (M^+, 33), 126 (100); Anal Calcd for $C_7H_6O_4$: C, 54.55 ; H, 3.92. Found: C, 54.54; H, 3.93.

Synthesis of (*E*)-Basidalin (41). To a solution of **1** (1.132 g, 7.5 mmol) and **5g** (2.765 g, 15 mmol) in dry dichloromethane (12 mL) was added $TiCl_4$ (0.83 mL, 7.5 mmol) at -78°C

under exclusion of moisture, and the solution was stirred for 1 h. After the same work-up as described in the first part, the residue was purified by flash chromatography (H-A 8:1) to afford **36** (1.367 g, 69%) as a yellow-green oil.

To a solution of **36** (695 mg, 2.6 mmol) in ether (5 mL) was added a 7.0 M solution of NH_3 in ethanol (1.1 mL, 7.8 mmol) at -30°C, and the solution was stirred for 1 h. The reaction mixture was washed with water, extracted with dichloromethane, dried (Na_2SO_4) and evaporated to dryness. The residue was purified by recrystallization from hot acetone to give the amide **37** (288 mg, 45%) as colorless needles.

A solution of **37** (210 mg, 0.86 mmol) and pyridine (75 mg, 0.95 mmol) was refluxed in dry xylene (100 mL) for 2 h. The work-up as described for the synthesis of **19** and flash chlomatography (H-A 5:1) afforded the aminofuranone **39** (151 mg, 85%) as yellow crystals.

Following the same procedures for the conversion of **19g** to **35**, **39** (126 mg, 0.61 mmol) was reduced and chromatographed (H-A 1:1) to give **40** (102 mg, 80%) as white crystals, and further, **40** (81 mg, 0.39 mmol) was oxidized and chromatographed (H-A 3:1) to give (*E*)-basidalin (**41**) (35 mg, 65%) as yellow crystals.

Spectral Data for 2,3-Dichloro-4-(3,3-dimethyl-2-oxo-4-pentenyl)-4-hydroxy-2-cyclobuten-one (36). IR (neat) 3422, 1786, 1709, 1636, 1586 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (6 H, s), 2.93 and 3.10 (each 1 H, d, *J* =17.8 Hz), 5.23 (1 H, dd, *J*=17.2, 0.6 Hz), 5.25 (1 H, dd, *J*=11.0, 0.6 Hz), 5.28 (1 H, br s), 5.86 (1 H, dd, *J*=17.2, 11.0 Hz); ^{13}C NMR ($CDCl_3$) δ 23.0, 23.1, 37.8, 51.8, 92.5, 116.7, 134.4, 141.1, 169.5, 185.7, 213.5; MS (EI) *m/z* (rel. intensity) 247 (5), 230 (2), 212 (1), 193 (4), 179 (5), 165 (57), 151 (22), 137 (15), 112 (100); (CI) *m/z* (rel. intensity) 263 (MH^+, 100); Anal Calcd for $C_{11}H_{12}Cl_2O_3$: C, 50.21; H, 4.60. Found: C, 50.15; H, 4.66.

Spectral Data for 3-Amino-2-chloro-4-(3,3-dimethyl-2-oxo-4-pentenyl)-4-hydroxy-2-cyclo-butenone (37). mp 198-200°C; IR (KBr) 2800-3600 (broad), 1771, 1709, 1622, 1543 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.13 (6 H, s), 2.70 and 3.17 (each 1 H, d, *J* =17.4 Hz), 5.14 (1 H, dd, *J*=10.6, 1.2 Hz), 5.15 (1 H, dd, *J*=17.6, 1.2 Hz), 5.93 (1 H, dd,

J=17.6, 10.6 Hz), 5.99 (1 H, br s), 7.77 and 8.35 (each 1 H, br s); ^{13}C NMR (DMSO-d$_6$) δ 23.1, 40.2, 50.8, 86.2, 92.9, 114.8, 142.5, 174.7, 184.2, 210.3; MS (EI) *m/z* (rel. intensity) 243 (M^+, 4), 228 (1), 208 (2), 174 (2), 156 (1), 146 (100), 132 (7), 128 (7), 111 (3), 98 (14), 69 (19); Anal Calcd for $C_{11}H_{14}ClNO_3$: C, 54.22; H, 5.79; N, 5.74. Found: C, 54.09; H, 5.87; N, 5.80.

Spectral Data for (*E*)-4-Amino-5-(3,3-dimethyl-2-oxo-4-pentenylidene)-2(5*H*)-furanone (39). mp 135-137°C; IR (KBr) 3349, 1777, 1748, 1678, 1628, 1599 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 1.23 (6 H, s), 5.00 (1 H, d, *J* =1.4 Hz), 5.22 (1 H, dd, *J*=10.4, 1.0 Hz), 5.23 (1 H, dd, *J*=17.4, 1.0 Hz), 6.01 (1 H, dd, *J*=17.4, 10.4 Hz), 6.63 (1 H, d, *J*=1.4 Hz), 8.25 and 8.65 (each 1 H, br s); ^{13}C NMR (DMSO-d$_6$) δ 23.3, 51.0, 83.4, 105.9, 116.0, 142.0, 158.3, 158.5, 168.8, 204.2; MS (EI) *m/z* (rel. intensity) 207 (M^+, 11), 138 (100), 110 (10), 69 (14); Anal Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N, 6.76. Found: C, 64.02; H, 6.28; N, 6.53.

Spectral Data for (*E*)-4-Amino-5-(2-hydroxy-3,3-dimethyl-4-pentenylidene)-2(5*H*)-furanone (40). mp 136-137°C; IR (KBr) 3360, 1721, 1699, 1636, 1574 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 0.99 (6 H, s), 4.23 (1 H, t, *J*=6.6 Hz), 4.80 (1 H, d, *J* =1.4 Hz), 5.01 (1 H, dd, *J*=18.0, 1.4 Hz), 5.02 (1 H, dd, *J*=10.4, 1.4 Hz), 5.62 (1 H, dd, *J*=6.6, 1.4 Hz), 5.91 (1 H, dd, *J*=18.0, 10.4 Hz), 6.04 (1 H, d, *J*=6.6 Hz), 7.43 (2 H, br s); ^{13}C NMR (DMSO-d$_6$) δ 21.9, 23.3, 42.4, 72.3, 84.2, 113.2, 113.7, 144.9, 146.7, 159.0, 167.0; MS (EI) *m/z* (rel. intensity) 209 (M^+, 1), 140 (100), 112 (79), 69 (9); Anal Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23; N, 6.69. Found: C, 63.43; H, 7.19; N, 6.43.

Spectral Data for (*E*)-Basidalin (41). mp. 115-120°C [lit. mp. 116-124 °C][11]; IR (KBr) 3347, 3185, 1748, 1684, 1655, 1579 cm^{-1}; ^{1}H NMR (DMSO-d$_6$) δ 5.10 (1 H, d, *J* =1.4 Hz), 6.33 (1 H, dd, *J*=4.8, 1.4 Hz), 8.10 (2 H, br s), 9.78 (1 H, d, *J*=4.8 Hz); ^{13}C NMR (DMSO-d$_6$) δ 84.7, 108.8, 158.5, 158.8, 168.6, 191.7; MS (EI) *m/z* (rel. intensity) 139 (M^+, 49), 111 (100).

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Chapter 3

Reaction of Alkoxycarbenium Ion Spiecies Generated from Squaric Acid Esters with Unsaturated Organosilanes

Section 1. Triethyloxonium Tetrafluoroborate-Mediated Reaction of Squaric acid Esters with Unsaturated Organosilanes

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Chapter 3

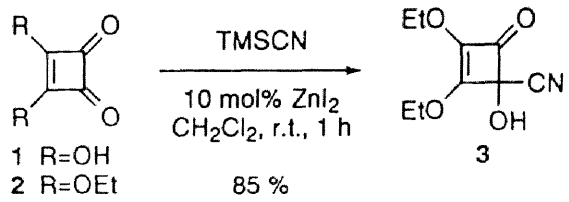
Reaction of Alkoxycarbenium Ion Spiecies Generated from Squaric Acid Esters with Unsaturated Organosilanes

Section 1

Triethyloxonium Tetrafluoroborate-Mediated Reaction of Squaric Acid Esters with Unsaturated Organosilanes

Abstract: Squaric acid esters were treated with triethyloxonium tetrafluoroborate at room temperature to produce ethoxycarbenium ion species, and subsequent addition of trimethylsilyl cyanide to this intermediate at 0 °C afforded *O*-ethyl cyanohydrins in fair to good yields. In the similar manner the ester reacted effectively with silyl enol ether and silyl ketene acetal to give the corresponding *O*-ethylated addition products. On the other hand the reaction with allylsilanes preferred the formation of 1:2 adducts.

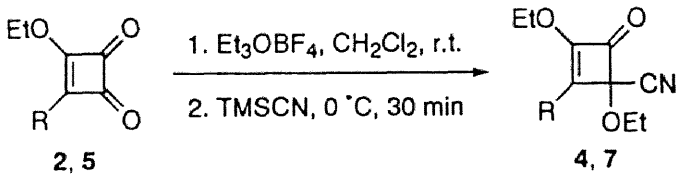
We have recently developed a Lewis acid-catalyzed addition reaction of unsaturated organosilanes to acid families of **1** leading to 4-hydroxy-2-cyclobutenones (Chapter 1, Section 1), which was applied to a new ring transformation to butenolides (Chapter 1, Section 2). In continuation of these works, the auther developed the synthesis of cyanohydrins from squaric acid esters and their ring opening reactions.[1] In this study, cyanohydrin **3** was obtained by the ZnI_2-catalyzed addition reaction of trimethylsilyl cyanide (TMSCN)[2] to diethyl squarate **2** in high yield, but unfortunately it was highly unstable (Scheme 1). In fact, it returned slowly even at -15 °C to starting ester **2** because of a 2π-aromatic character. Thus, appropriate protection of the hydroxy group was needed. After conventional protections of the hydroxyl group were found not to be applicable due to its instability under both acidic and basic conditions, we exploited *O*-alkylative cyanation utilizing a Meerwein's salt; the cyclobutenedione, which was activated with triethyloxonium tetrafluoroborate (Et_3OBF_4), was allowed to react with TMSCN to give the *O*-ethylated cyanohydrin directly. In this section, the detailed results of this novel reaction and extension to other unsaturated organosilanes are described.



Scheme 1

The beginning of these works was established in the *O*-alkylative cyanation of squaric acid ester **2**. In this case, an ethoxycarbenium ion species produced from a squaric acid ester and a Meerwein's salt was envisaged as a promising intermediate.[3] As a matter of fact, a solution of the ester **2** in dry dichloromethane was treated with 1 equivalent of Et_3OBF_4 at room temperature to form the carbenium ion, and thereafter, the addition of TMSCN at 0 °C followed by stirring for 30 min afforded *O*-ethyl cyanohydrin **4** in 22 % yield together with **3** (38 % yield) (Scheme 2). The premixing time seemed to be critical for the formation of this

intermediate; the examinations (Table 1, entries 1-4) revealed that the highest yield was attained after treatment for 5 h. Furthermore the increasing amount of Et_3OBF_4 gave better results. Nearly quantitative yield was achieved with 3 equivalents of Et_3OBF_4 (entry 6). The structure of **4** was elucidated by no hydroxy but a cyano absorption in the IR spectrum and signals due to different three ethoxy groups in the ^1H NMR spectrum.



2, 5 **4, 7**

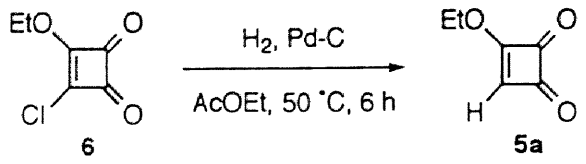
Scheme 2

Table 1. Ethyl Cyanation of Squaric Acid Esters **2** and **5**

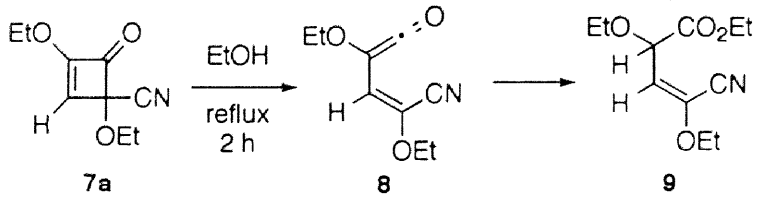
entry	Ester	R	Et_3OBF_4 (equiv)	Et_3OBF_4 [premixing time (h)]	Cyanohydrin (Yield %)
1	**2**	OEt	1	0	**4** (0)[a]
2	**2**	OEt	1	0.5	**4** (22)[b]
3	**2**	OEt	1	5	**4** (56)[b]
4	**2**	OEt	1	12	**4** (22)[b]
5	**2**	OEt	2	5	**4** (80)[b]
6	**2**	OEt	3	5	**4** (99)[b]
7	**5a**	H	3	3	**7a** (44)
8	**5b**	Me	3	3	**7b** (42)
9	**5c**	Bu	3	5	**7c** (18)
10	**5c**	Bu	3	3	**7c** (59)
11	**5d**	$CH=CH_2$	3	2	**7d** (35)
12	**5e**	Ph	3	2	**7e** (43)
13	**5f**	2-furyl	3	1	**7f** (15)
14	**5g**	C≡CPh	3	0.5	**7g** (0)

Then the above ethyl cyanation was applied to monoesters **5a-g**. These were prepared by Liebeskind's procedure[4] except for **5a**. Since preparation of **5a** by the reported 2 step

conversion from **2** using lithium trialkoxyaluminum hydride[4] were less effective (10 % yield), an alternative method was applied. Catalytic hydrogenolysis of ethyl ester chloride **6**, which is readily accessible from squaric acid dichloride and ethanol,[5] afforded **5a** in 79 % yield (Scheme 3). At the outset, butyl-substituted ester **5c** was subjected to premixing with Et_3OBF_4 for 5 h, but it caused darkening of the solution; probably due to partial decomposition of **5c** under the employed conditions, the corresponding adduct **7c** was obtained in unsatisfactory yield (18 %). However, the shorter premixing time (3 h) improved the yield to 59 % (Table 1, entry 10). In this manner, a variety of *O*-ethyl cyanohydrins **7a**, **b**, **d**, and **e** were obtained in 35 - 44 % yields from monoesters **5a**, **b**, **d**, and **e**, respectively. The yield was much lower for furyl-substituted **5f** (15 % even for 1 h premixing) and none of products were obtained from alkynyl-substituted **5g**. These results are summarized in Table 1. The product structure was determined on the analogy of cyanohydrins **3** and **4**; all the spectral data (IR, ^1H and ^{13}C NMR, and MS) were compatible with the assigned structures (Table 3). For the regiochemistry, namely the relative reactivity of the carbonyl carbons at C_1 and C_2, we inferred that the addition occurred across the β-ethoxy enone which should form the thermodynamically more favored ethoxycarbenium ion. This was proved by thermolysis of **7a** in refluxing ethanol; the conrotatory ring-opening of cyclobutenone occurred to afford the ketene intermediate **8**, which was subsequently trapped with ethanol (Scheme 4). The structure of the ketene-ethanol adduct **9** was indicated by MH^+ peak (*m/z* 228, 11 %) in the mass spectrum (CI), and by olefinic and allylic methine signals (δ 5.47 and 4.65, *J*=9.7 Hz) as well as three ethoxy signals in the ^1H NMR spectrum. Here the observed chemical shift and coupling pattern of these protons supported that the cyanohydrin formation was effected at the vinylogous ester functionality. This site-selectivity is worthy to note; usually, cyclobutenediones tend to react with a nucleophile across alkoxy-unsubstituted enone moiety. In contrast, the present nucleophilic addition of a cyano group occurred alternatively across alkoxy-substituted enone moiety by virtue of different mode of activation, *i. e.*, with the Meerwein's salt.

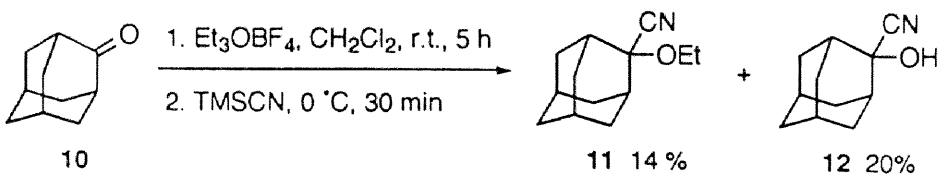


Scheme 3



Scheme 4

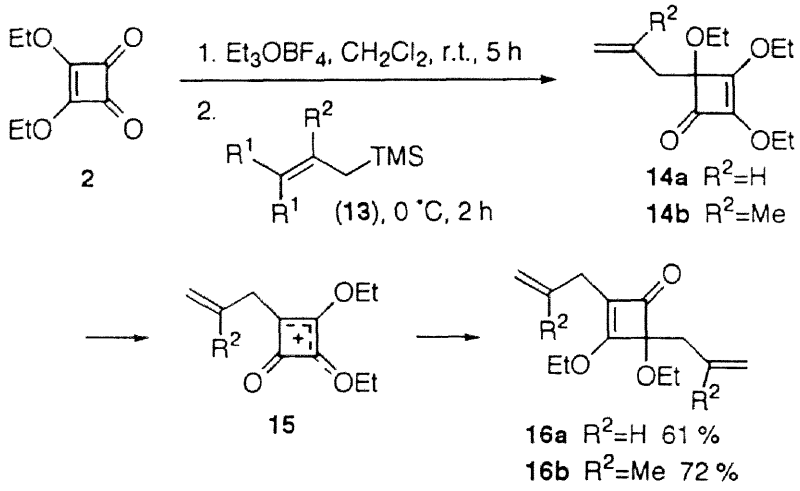
The above *O*-alkylative cyanation is a novel type of addition reaction in organosilicon chemistry. Generally, the nucleophilic addition of organosilanes to carbonyl groups are promoted by a Lewis acid which assists the formation of a cationic site. The different activation of the carbonyl function is now achieved by complexation with the Meerwein's salt, where the product arises as an *O*-alkylated form. Thus, it is interesting and useful if the present method is applicable to other carbonyl compounds. However, attempted ethyl cyanation of cyclohexanone, 3-ethoxycyclohex-2-enone and γ-butyrolactone under these conditions were unsuccessful except for non-enolizable 2-adamantanone **10**, which gave 2-cyano-2-ethoxyadamantane **11** in 14 % yield together with cyanohydrin **12** (Scheme 5). Thus this reaction seemed to be rather specific to squaric acid ester. Presumably the result may be associated with 2π-aromatic character by which the intermediate formed is intrinsically stabilized in this system.



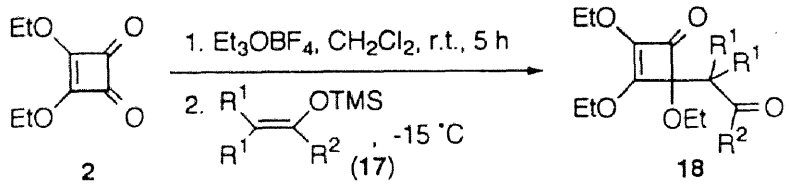
Scheme 5

With these results in hand, addition reactions of other organosilanes such as allylsilane,[6] silyl enol ether[7] and silyl ketene acetal[7] were examined. First, the reaction with allylsilanes was carried out. After the premixing of ester **2** with the Meerwein's salt, 1.1 equivalents of allylsilane **13a** was added at 0 °C and the mixture was stirred for 2 h. In contrast to the straightforward formation of *O*-ethyl cyanohydrin **4**, unexpected 1:2 adduct **16a** was isolated only in 10 % yield instead of the monoadduct **14a**. Nevertheless, the yield was increased to 61 % by employing 5 equivalents of the allylsilane (Table 2, entry 3). The structure of **16a** was characterised by the spectral inspections. In the mass spectrum the required M^+ (*m/z* 236, 20 %) was observed, and the ^1H NMR spectrum indicated the presence of a couple of allyl and ethoxy groups. The mechanism for this double allylation may be explained as depicted in Scheme 6. The addition of one allylsilane to the ethoxy carbenium ion gives the primary monoadduct **14a**, from which the ethoxycarbenium ion **15** was second generated and allowed to react with another allylsilane leading to the final product **16a**. Under these conditions, methallylsilane **13b** gave corresponding adduct **16b** in acceptable yield. On the other hand, prenylsilane **13c**, which has two methyl substituents at the reaction site (γ to the trimethylsilyl group), showed no reactivity. The reaction with silyl enol ethers was performed similarly. In this case, 3 equivalents of silyl enol ether **17a** was employed, and the corresponding monoadduct **18a** was produced selectively in 36 % yield. The lower reaction temperature (-15 °C) raised the yield up to 58 % (Table 2, entry 8). Under these conditions other silyl enol ethers **17b, c** gave monoadducts **18b, c** in 53 and 74 % yields, respectively. Likewise the reaction with silyl ketene acetal **17d** gave the monoadduct **18d** in 52 % yield. Interestingly, the assistance of TBAF increased the yield to 73 % (Table 2, entry 13), as a result of enhanced nucleophilicity by virtue of fluoride anion attack to the trimethylsilyl group.[8] It is remarked here that nucleophilic addition of silyl ketene acetal aided only by TBAF gave **19** and **20** unselectively (Scheme 8). Therefore, the activation with both Meerwein's salt and TBAF realized the site-selective addition. These conditions also effected even the addition of silyl

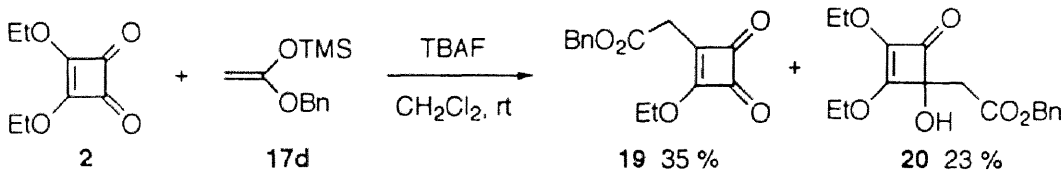
ketene acetal **17e** which has two methyl substituents at the reaction site, giving the corresponding 1:1 adduct **18e** (*vide supra*).



Scheme 6



Scheme 7



Scheme 8

In conclusion, the new type of addition reactions of unsaturated organosilanes to diethyl squarate, namely ethyl cyanation, ethyl allylation and ethyl acylmethylation were accomplished by the use of Meerwein's salt. Further synthetic applications of 4-ethoxycyclobutenones obtained from these reactions are hopeful.

Table 2. Ethyl Allylation and Ethyl Acylmethylation of Squaric Acid Ester **2**

entry	R^1	R^2	Silane (equiv)	Temp. (°C)	Time (h)	Cyclobutenone (Yield %)
	allylsilane					
1	H	H	**13a** (1.1)	0	2	**16a** (10)
2	H	H	**13a** (3)	0	2	**16a** (49)
3	H	H	**13a** (5)	0	2	**16a** (61)
4	H	H	**13a** (5)	-15	2	**16a** (60)
5	H	Me	**13b** (5)	0	2	**16b** (72)
6	Me	H	**13c** (5)	0	2	no reaction
	enol silanes					
7	H	Ph	**17a** (3)	0	1	**18a** (36)
8	H	Ph	**17a** (3)	-15	1	**18a** (58)
9	H	Ph	**17a** (3)	-30	1	**18a** (11)
10	H	Me	**17b** (3)	-15	1	**18b** (53)
11	H	Ad[a]	**17c** (3)	-15	1	**18c** (74)
12	H	OBn[b]	**17d** (3)	-15	1	**18d** (52)
13	H	OBn[b]	**17d** (3)	-15	0.5	**18d** (73)[c]
14	Me	OBn[b]	**17e** (3)	-15	0.5	**18e** (46)[c]

[a] Ad=1-adamantyl. [b] Bn=Benzyl. [c] TBAF was employed as an additive.

Experimental Section

General. IR spectra were recorded on a JASCO FT-IR 5300 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ solution with $SiMe_4$ as internal standard. Mass spectra were recorded on a JEOL JMS-AX505HA mass spectrometer. Flash chromatography was performed on a silica gel column (Fuji BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400 elemental analyzer. Dichloromethane was dried over $CaCl_2$, distilled, and stored over 4 Å molecular sieves. Silyl enol ethers and silyl ketene acetals were obtained according to the standard methods,[9] and allylsilanes were prepared by the reaction of the corresponding organometallics with trimethylsilyl chloride.[10] Triethyloxonium tetrafluoroborate was prepared according to the standard method and stored as ca. 5 M solution in dry dichloromethane.[11] Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.

ZnI_2-Catalyzed Addition of TMSCN to Diethyl Squarate 2.

To a solution of diethyl squarate **2** (85 mg, 0.5 mmol) and ZnI_2 (16 mg, 10 mol %) in CH_2Cl_2 (2 mL) was added TMSCN (0.063 mL, 0.5 mmol) at room temperature. After 1 h stirring, the resultant white suspension was poured into cold water and extracted with CH_2Cl_2. The extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (H-A 3:1) afforded cyanohydrin **3** (168 mg, 85%) as a colorless oil. The obtained sample was so unstable that the precise elemental analysis could not be done, but the following data fully supported the structure.

4-Cyano-2,3-diethoxy-4-hydroxy-2-cyclobutenone (3). IR (neat) 2238, 1750, 1636 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (3 H, t, *J*=7.2 Hz), 1.52 (3 H, t, *J*=7.2 Hz), 2.90 (1 H, br s), 3.84 and 3.89 (each 1 H, dq, *J*=9.2, 7.2 Hz), 4.66 (2 H, q, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 15.1, 15.3, 65.0, 71.6, 81.9, 114.0, 136.4, 161.9, 177.7; MS (EI) *m/z* (rel. intensity) 197 (M^+, 6), 170 (46), 151 (27), 123 (85), 94 (100).

Et_3OBF_4-Mediated Addition of TMSCN to Squaric Acid Esters 2 and 5. General Procedure:

To a solution of squaric acid ester (1 mmol) in dry CH_2Cl_2 (2 mL) was added a 4.9 M solution of Et_3OBF_4 in CH_2Cl_2 (0.61 mL, 3 mmol) at ambient temperature, and the reaction mixture was stirred for the time depicted in Table 1. Then, TMSCN (0.14 mL, 1.1 mmol) was added to this solution at 0 °C, and after 30 min stirring, the reaction mixture was poured into cold water and extracted with CH_2Cl_2. The extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (elution: H-A 3:1 for **4**, 4:1 for **7a**, 6:1 for **7d** and **7f**, 8:1 for **7b**, 10:1 for **7c**, and 12:1 for **7e**) gave the products. The yields are summarized in Tables 1.

4-Cyano-2,3,4-triethoxy-2-cyclobutenone (4). *oil*; IR (neat) 2230, 1790, 1642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (3 H, t, *J*=7.2 Hz), 1.34 (3 H, t, *J*=7.2 Hz), 1.47 (3 H, t, *J*=7.2 Hz), 3.85 and 3.91 (each 1 H, dq, *J*=9.2, 7.2 Hz), 4.36 (2 H, q, *J*=7.2 Hz), 4.53 (2 H, q, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 15.1 (2 C), 15.5, 64.8, 68.1, 70.7, 82.1, 114.6, 137.1, 160.3, 174.4; MS (EI) *m/z* (rel. intensity) 225 (M^+, 17), 197 (49), 180 (90), 169 (32), 152 (19), 140 (49), 124 (37), 112 (100); Anal Calcd for $C_{11}H_{15}NO_4$: C, 58.66; H, 6.71; N. 6.22. Found: C, 58.79; H, 6.95; N, 5.86.

4-Cyano-2,4-diethoxy-2-cyclobutenone (7a). *oil*; IR (neat) 2232, 1798, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (3 H, t, *J*=7.2 Hz), 1.41 (3 H, t, *J*=7.2 Hz), 3.82 and 3.87 (each 1 H, dq, *J*=9.2, 7.2 Hz), 4.19 (2 H, q, *J*=7.2 Hz), 7.11 (1 H, s); ^{13}C NMR ($CDCl_3$) δ 14.2, 15.0, 64.5, 68.3, 83.0, 115.5, 131.5, 163.3, 179.1; MS (EI) *m/z* (rel. intensity) 181 (M^+, 5), 154 (100), 126 (93), 98 (78); Anal Calcd for $C_9H_{11}NO_3$: C, 59.66; H, 6.12; N. 7.76. Found: C, 59.58; H, 6.27; N, 7.67.

4-Cyano-2,4-diethoxy-3-methyl-2-cyclobutenone (7b). *oil*; IR (neat) 2230, 1788, 1647 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, *J*=7.2 Hz), 1.36 (3 H, t, *J*=7.2 Hz), 2.16 (3 H, s), 3.86 (2 H, q, *J*=7.2 Hz), 4.39 (2 H, q, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 10.2, 15.1, 15.3, 64.7, 67.8, 84.9, 115.3, 149.0, 157.3, 178.2; MS (EI) *m/z* (rel. intensity) 195 (M^+, 3), 167

(47), 149 (16), 138 (32), 122 (17), 110 (100); Anal Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N. 7.17. Found: C, 61.55; H, 6.76; N, 7.08.

3-Butyl-4-cyano-2,4-diethoxy-2-cyclobutenone (7c). *oil*; IR (neat) 2230, 1777, 1642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 (3 H, t, *J*=7.4 Hz), 1.25 (3 H, t, *J*=7.2 Hz), 1.35 (3 H, t, *J*=7.2 Hz), 1.30-1.77 (4 H, m), 2.53 (2 H, t, *J*=7.4 Hz), 3.87 (2 H, q, *J*=9.2, 7.2 Hz), 4.39 (2 H, q, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 13.6, 15.2, 15.5, 22.8, 25.7, 28.1, 64.8, 67.9, 84.3, 115.7, 153.5, 157.1, 178.5; MS (EI) *m/z* (rel. intensity) 237 (M^+, 5), 209 (28), 192 (7), 180 (37), 152 (100); Anal Calcd for $C_{13}H_{19}NO_3$: C, 65.80; H, 8.07; N. 5.90. Found: C, 65.53; H, 8.21; N, 6.03.

4-Cyano-3-ethenyl-2,4-diethoxy-2-cyclobutenone (7d). *oil*; IR (neat) 2230, 1769, 1634 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, *J*=7.2 Hz), 1.39 (3 H, t, *J*=7.2 Hz), 3.84 and 3.89 (each 1 H, dq, *J*=8.8, 7.2 Hz), 4.46 (2 H, q, *J*=7.2 Hz), 5.80 (1 H, dd, *J*=10.8, 0.8 Hz), 6.02 (1 H, dd, *J*=17.6, 0.8 Hz), 6.63 (1 H, dd, *J*=17.6, 10.8 Hz); ^{13}C NMR ($CDCl_3$) δ 15.2, 15.4, 64.5, 68.8, 83.3, 115.4, 123.5, 127.1, 145.5, 154.6, 178.5; MS (EI) *m/z* (rel. intensity) 207 (M^+, 17), 179 (28), 162 (39), 151 (61), 135 (53), 124 (100), 96 (52); Anal Calcd for $C_{11}H_{13}NO_3$: C, 63.76; H, 6.32; N. 6.76. Found: C, 63.73; H, 6.56; N, 6.54.

4-Cyano-2,4-diethoxy-3-phenyl-2-cyclobutenone (7e). *oil*; IR (neat) 2230, 1769, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 3.89 and 3.96 (each 1 H, dq, *J*=9.0, 7.0 Hz), 4.57 and 4.63 (each 1 H, dq, *J*=10.2, 7.0 Hz), 7.45-7.81 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 15.2, 15.7, 64.5, 69.1, 83.4, 115.8, 128.5, 128.9, 129.6, 132.0, 146.6, 154.3, 178.0; MS (EI) *m/z* (rel. intensity) 257 (M^+, 24), 229 (48), 212 (4), 200 (39), 184 (9), 172 (93), 144 (100); Anal Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N. 5.44. Found: C, 69.90; H, 6.00; N, 5.44.

4-Cyano-2,4-diethoxy-3-(2-furyl)-2-cyclobutenone (7f). *oil*; IR (neat) 2232, 1771, 1642 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (3 H, t, *J*=7.2 Hz), 1.44 (3 H, t, *J*=7.2 Hz), 3.92 (2 H, q, *J*=7.2 Hz), 4.58 (2 H, q, *J*=7.2 Hz), 6.64 (1 H, dd, *J*=3.6, 1.8 Hz), 7.01 (1 H, dd, *J*=3.6, 0.6 Hz), 7.72 (1 H, dd, *J*=1.8, 0.6 Hz), ; ^{13}C NMR ($CDCl_3$) δ 15.2, 15.6, 64.7, 69.3, 82.7,

113.5, 115.3, 117.5, 135.6, 144.4, 147.5, 151.3, 176.6; MS (EI) *m/z* (rel. intensity) 247 (M^+, 64), 219 (67), 202 (6), 191 (48), 174 (14), 162 (100), 135 (67); Anal Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N. 5.67. Found: C, 62.95; H, 5.49; N, 5.68.

Synthesis of 3-Ethoxy-3-cyclobutene-1,2-dione (5a). A solution of squaric acid dichloride (760 mg, 5 mmol) and dry ethanol (0.59 mL, 10 mmol) in dry THF (10 mL) was refluxed for 40 h. The solution was cooled to ambient temperature and the solvent was removed under reduced pressure to afford crude ethyl ester chloride **6** (710 mg) as a yellow oil. Then a solution of crude **6** (321 mg, 2 mmol) in ethyl acetate (5 mL) was heated at 50 °C with Pd-C (10 % on charcoal, 32 mg, 1 wt %) under an atmosphere of hydrogen for 6 h. After removing insoluble materials through celite filter, the solution was evaporated to dryness, and the residue was purified by chromatography (H-A 2:1) to afford ester **5a** (199 mg, 79 %) as a yellow oil; IR (KBr) 1800, 1775, 1576 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54 (3 H, t, *J*=7.2 Hz), 4.58 (2 H, q, *J*=7.2 Hz), 8.57 (1 H, s); ^{13}C NMR ($CDCl_3$) δ 14.4, 72.2, 163.9, 193.5, 195.3, 201.7; MS (EI) *m/z* (rel. intensity) 126 (M^+, 1), 98 (23), 69 (100); Anal Calcd for $C_6H_6O_3$: C, 57.14; H, 4.80. Found: C, 57.11; H, 4.82.

Thermolysis of 7a. The solution of **7a** (60 mg, 0.33 mL) in dry ethanol (5 mL) was refluxed for 2h. The solution was cooled to ambient temperature and the solvent was removed under reduced pressure. The residue was purified by preparative TLC (H-A 3:1) to afford **9** (90 mg, 40%) as a colorless oil; IR (neat) 2238, 1750, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (3 H, t, *J*=7.0 Hz), 1.31 (3 H, t, *J*=7.0 Hz), 1.36 (3 H, t, *J*=7.0 Hz), 3.57 and 3.63 (each 1 H, dq, *J*=9.2, 7.0 Hz), 3.89 (2 H, q, *J*=7.0 Hz), 4.22 and 4.27 (each 1 H, dq, *J*=10.8, 7.0 Hz), 4.65 (1 H, d, *J*=9.7 Hz), 5.47 (1 H, d, *J*=9.7 Hz); ^{13}C NMR ($CDCl_3$) δ 14.2 (2 C), 15.0, 61.9, 65.7, 66.2, 76.2, 113.1, 113.5, 135.5, 170.2; MS (EI) *m/z* (rel. intensity) 198 (M^+-Et, 1), 182 (2), 170 (10), 154 (100), 126 (38); (CI) 228 (MH^+); Anal Calcd for $C_{11}H_{17}NO_4$: C, 58.14; H, 7.54; N, 6.16. Found: C, 58.17; H, 7.55; N, 6.11.

Ethyl Cyanation of Adamantanone 10. This was carried out using adamantanone **10** (75 mg, 0.5 mmol) according to the procedure described for **4**. Separation by chromatography (H-A 40:1) afforded the product **11** (14 mg, 14%) as the first fraction; *colorless oil*; IR (neat) 2917, 2230 cm^{-1}; ^1H NMR ($CDCl_3$) δ = 1.28 (3 H, t, *J*=7.0 Hz), 1.50-2.28 (14 H, m), 3.65 (2 H, q, *J*=7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 15.4, 26.3, 26.6, 31.0, 34.6, 34.8, 37.1, 59.8, 79.5, 120.8; MS (EI) *m/z* (rel. intensity) 205 (M^+, 52), 190 (44), 178 (19), 159 (100); Anal Calcd for $C_{13}H_{19}NO$: C, 76.06; H, 9.33; N, 6.82. Found: C, 75.85; H, 9.54; N, 6.51.

Cyanohydrin **12** (62 mg, 20%) was obtained as the second fraction, *colorless crystals*; mp. 209-211 °C (sealded tube). [lit. mp. 218-220 °C (sealded tube)][12]; Following spectral properties were identical with those reported in the reference 12; IR (KBr) 3414, 2915, 2241 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.74-2.22 (14 H, m), 2.93 (1 H, br s); ^{13}C NMR ($CDCl_3$) δ 26.2, 26.4, 30.8, 35.0, 37.0, 37.1, 74.2, 122.7; MS (EI) *m/z* (rel. intensity) 150 (M^+-HCN, 100).

Et_3OBF_4-Mediated Addition of Allylsilanes to Diethyl Squarate 2. The premixing of diethyl squarate **2** (85 mg, 0.5 mmol) and Meerwein's salt in dichloromethane as described for **4** was followed by addition of a solution of allylsilane **13** (2.5 mmol) in CH_2Cl_2 (1 mL) at -15 °C. After being stirred for 2 h, the reaction mixture was poured into cold water and extracted with CH_2Cl_2. The extracts were washed with water, dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (elution: H-A 10:1) gave the products. The yields are summarized in Tables 2.

3,4-Diethoxy-2,4-di-(-2-propenyl)-2-cyclobutenone (16a). *oil*; IR (neat) 1761, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (3 H, t, *J*=7.0 Hz), 1.44 (3 H, t, *J*=7.0 Hz), 2.51 and 2.69 (each 1 H, ddt, *J*=14.2, 7.6, 1.4 Hz), 2.86-2.91 (2 H, m), 3.51 and 3.58 (each 1 H, dq, *J*=8.8, 7.0 Hz), 4.37 and 4.43 (each 1 H, dq, *J*=10.4, 7.0 Hz), 5.03-5.18 (4 H, m), 5.63-5.94 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 15.3, 15.4, 26.1, 37.1, 60.7, 68.8, 96.5, 116.6, 118.9, 124.8, 132.6, 133.9, 184.0, 193.0; MS (EI) *m/z* (rel. intensity) 236 (M^+, 20), 207 (100), 179

(8), 161 (11), 151 (9), 133 (15), 109 (70); Anal Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.18; H, 8.50.

3,4-Diethoxy-2,4-di-(2-methyl-2-propenyl)-2-cyclobutenone (16b). *oil*; IR (neat) 1761, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (3 H, t, *J*=7.0 Hz), 1.44 (3 H, t, *J*=7.0 Hz), 2.50 and 2.64 (each 1 H, dd *J*=13.8, 0.8 Hz), 2.79 and 2.88 (each 1 H, d *J*=17.8 Hz), 3.50 and 3.58 (each 1 H, dq, *J*=8.6, 7.0 Hz), 4.42 (2 H, q, *J*=7.0 Hz), 4.74-4.87 (4 H, m); ^{13}C NMR ($CDCl_3$) δ 15.2, 15.4, 22.5, 23.6, 30.1, 40.8, 60.5, 68.8, 96.5, 112.0, 115.7, 125.1, 140.8, 142.3, 183.9, 193.2; MS (EI) *m/z* (rel. intensity) 264 (M^+, 18), 235 (19), 219 (10), 207 (9), 189 (71), 179 (9), 161 (22), 123 (100); Anal Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.62; H, 9.22.

Et_3OBF_4-Mediated Addition of Silyl Enol Ethers and a Silyl Ketene Acetal to Diethyl Squarate 2. This was carried out by the same procedure as above except for using an enol silane (3 equivalents), stirring (1 h), and chromatography (elution: H-A 8:1). The yields are summarized in Tables 2.

2,3,4-Triethoxy-4-phenacyl-2-cyclobutenone (18a). *oil*; IR (neat) 1767, 1690, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.24 (6 H, t, *J*=7.0 Hz), 1.42 (3 H, t, *J*=7.0 Hz), 3.76 and 3.83 (each 2 H, dq, *J*=9.4, 7.0 Hz), 3.78 and 3.88 (each 1 H, d, *J*=19.8 Hz), 4.50 (2 H, q, *J*=7.0 Hz), 7.43-7.64 (3 H, m), 7.97-8.03 (2 H, m); ^{13}C NMR ($CDCl_3$) δ 15.1, 15.4 (2 C), 32.2, 61.8 (2 C), 69.7, 113.6, 123.7, 128.8, 129.1, 134.0, 136.2, 186.2, 192.5, 195.0; MS (EI) *m/z* (rel. intensity) 318 (M^+, 5), 289 (66), 273 (9), 261 (6), 243 (48), 215 (10), 187 (88), 159 (22), 105 (100); Anal Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.96. Found: C, 68.17; H, 6.70.

4-Acetonyl-2,3,4-triethoxy-2-cyclobutenone (18b). *oil*; IR (neat) 1769, 1723, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (3 H, t, *J*=7.0 Hz), 1.26 (3 H, t, *J*=7.0 Hz), 1.44 (3 H, t, *J*=7.2 Hz), 2.22 (3 H, s), 3.22 and 3.26 (each 1 H, d, *J*=17.4 Hz), 3.77 and 3.84 (each 1 H, dq, *J*=9.4, 7.0 Hz), 3.78 and 3.85 (each 1 H, dq, *J*=9.4, 7.0 Hz), 4.43 and 4.50 (each 1 H, dq, *J*=9.6, 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 15.1, 15.4 (2 C), 29.8, 36.6, 61.9 (2 C), 69.7,

113.5, 123.3, 185.9, 192.4, 203.4; MS (EI) *m/z* (rel. intensity) 256 (M^+, 7), 227 (71), 199 (17), 181 (49), 125 (100); Anal Calcd for $C_{13}H_{20}O_5$: C, 60.92; H, 7.87. Found: C, 61.12; H, 7.67.

4-[(1-Adamantyl)carbonylmethyl]-2,3,4-triethoxy-2-cyclobutenone (18c). *oil*; IR (neat) 2907, 1767, 1703, 1628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (6 H, t, *J*=7.0 Hz), 1.42 (3 H, t, *J*=7.2 Hz), 1.71-2.12 (15 H, m), 3.31 (2 H, s), 3.77 and 3.83 (each 1 H, dq, *J*=9.8, 7.0 Hz), 4.46 (2 H, q, *J*=7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 15.1, 15.4 (2 C), 27.9, 29.3, 36.5, 38.2, 46.8, 61.7 (2 C), 69.2, 113.6, 124.6, 186.0, 192.6, 210.3; MS (EI) *m/z* (rel. intensity) 376 (M^+, 3), 347 (28), 331 (2), 319 (3), 301 (28), 273 (2), 245 (5), 217 (2), 135 (100); Anal Calcd for $C_{22}H_{32}O_5$: C, 70.18; H, 8.57. Found: C, 70.33; H, 8.42.

Benzyl (1,2,3-Triethoxy-4-oxo-2-cyclobutenyl)acetate (18d). *oil*; IR (neat) 1773, 1738, 1636 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (3 H, t, *J*=7.0 Hz), 1.28 (3 H, t, *J*=7.0 Hz), 1.36 (3 H, t, *J*=7.0 Hz), 2.87 and 2.96 (each 1 H, d, *J*=14.8 Hz), 3.49 and 3.54 (each 1 H, dq, *J*=9.0, 7.0 Hz), 4.22 and 4.30 (each 1 H, dq, *J*=10.2, 7.0 Hz), 4.35 and 4.42 (each 1 H, dq, *J*=10.2, 7.0 Hz), 5.08 and 5.15 (each 1 H, d, *J*=12.4 Hz), 7.32-7.38 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 15.2, 15.4, 15.6, 37.9, 60.0, 66.6, 67.0, 69.3, 88.9, 128.5, 128.6, 128.8, 134.6, 136.1, 166.4, 169.5, 185.1; MS (EI) *m/z* (rel. intensity) 348 (M^+, 7), 320 (7), 303 (1), 257 (4), 229 (8), 213 (2), 185 (8), 91 (100); Anal Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.52; H, 6.92.

Et_3OBF_4 and TBAF-Assisted Addition of Silyl Ketene Acetals to Diethyl Squarate 2. The premixing of diethyl squarate **2** (85 mg, 0.5 mmol) and Meerwein's salt as described for **4** was followed by successive addition of a solution of silyl ketene acetal **17d** (or **17e**) (1.5 mmol) in CH_2Cl_2 (1 mL) and TBAF (1.5 mL, 1 M solution in THF) at -15 °C. After 30 min stirring, the work-up and chromatography as above gave the products. The yields are summarized in Tables 2.

Methyl [1-Methyl-1-(1,2,3-triethoxy-4-oxo-2-cyclobutenyl)]propionate (18e). *oil*; IR (neat) 1771, 1736, 1632 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.17 (3 H, t, *J*=7.0 Hz), 1.31 (3 H, t, *J*=7.0 Hz), 1.31 and 1.34 (each 3 H, s), 1.43 (3 H, t, *J*=7.0 Hz), 3.44 and 3.50 (each 1 H, dq, *J*=8.8, 7.0 Hz), 3.68 (3 H, s), 4.30 and 4.36 (each 1 H, dq, *J*=10.4, 7.0 Hz), 4.45 and 4.50 (each 1 H, dq, *J*=10.4, 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 15.3, 15.4, 15.7, 21.7, 22.0, 48.2, 51.9, 59.9, 66.9, 69.4, 94.4, 134.9, 166.7, 176.1, 185.8; MS (EI) *m/z* (rel. intensity) 300 (M^+, 14), 271 (90), 241 (23), 213 (31), 201 (100), 171 (33), 155 (31); Anal Calcd for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.84; H, 8.19.

TBAF-Assisted Addition of Silyl Ketene Acetal 17d to Diethyl Squarate 2. A solution of ester **2** (85 mg, 0.5 mmol) and silyl ketene acetal **17d** (335 mg, 1.5 mmol) in dry dichloromethane (2 mL) was treated with TBAF (1.5 mL, 1 M solution in THF) at 0 °C. After being stirred for 15 min, the work-up as above and TLC separation (elution H-A 1:2) gave cyclobutenedione **19** (45 mg, 35%) as a yellow oil (the first fraction); IR (neat) 1802, 1755, 1740, 1605 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.45 (3 H, t, *J*=7.2 Hz), 3.69 (2 H, s), 4.77 (2 H, q, *J*=7.2 Hz), 5.18 (2 H, s), 7.27-7.45 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 15.5, 30.2, 67.9, 71.4, 128.8, 129.0 (1C+2C), 135.3, 166.9, 174.3, 193.9, 194.4; MS (EI) *m/z* (rel. intensity) 274 (M^+, 4), 246 (6), 183 (61), 155 (43), 127 (60), 99 (23), 91 (100); Anal Calcd for $C_{15}H_{14}O_5$: C, 65.69; H, 5.14. Found: C, 65.62; H, 5.21.

Hydroxyccyclobutenone **20** (36 mg, 23%) was also obtained as a colorless oil (the second fraction); IR (neat) 3399, 1773, 1736, 1634 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.29 (3 H, t, *J*=7.0 Hz), 1.37 (3 H, t, *J*=7.0 Hz), 2.84 and 2.92 (each 1 H, d, *J*=16.4 Hz), 4.26 and 4.31 (each 1 H, dq, *J*=10.0, 7.0 Hz), 4.41 (2 H, q, *J*=7.0 Hz), 4.42 (1 H, br s), 5.15 and 5.22 (each 1 H, d, *J*=12.2 Hz), 7.37 (5 H, m); ^{13}C NMR ($CDCl_3$) δ 15.1, 15.6, 37.5, 67.1, 67.3, 69.6, 83.4, 128.8, 128.9, 129.0, 133.2, 135.6, 166.2, 171.7, 184.3; MS (EI) *m/z* (rel. intensity) 320 (M^+, 6), 229 (100), 201 (7), 187 (10), 173 (8), 159 (20); Anal Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.69; H, 6.34.

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Chapter 3

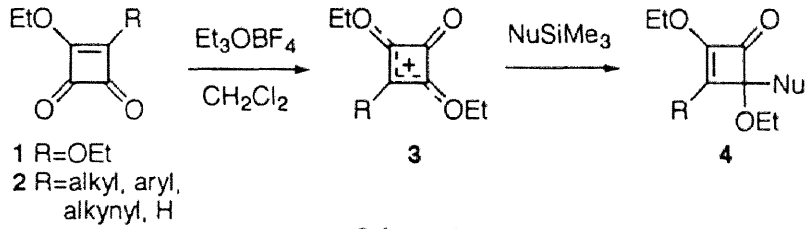
Reaction of Alkoxycarbenium Ion Spiecies Generated from Squaric Acid Esters with Unsaturated Organosilanes

Section 2

BF_3-Catalyzed Reaction of Cyclobutenedione Monoacetal and Its Vinylog with Unsaturated Organosilanes, and Subsequent Ring Transformation of the Adducts

Abstract: Described herein is a novel method for the regio-controlled synthesis of highly substituted cyclobutenones having an unsaturated substituent at 4-position from commercially available squaric acid. BF_3•Et_2O-catalyzed addition of cyclobutenedione monoacetal or its vinylog to allylsilane afforded 4-allyl-4-ethoxycyclobutenones having various substituents at 2-position regioselectively, which were efficiently transformed to highly substituted bicyclo[3.2.0]heptenones by simple refluxing in xylene. The synthetic utility of this process was demonstrated in the construction of tricyclic ring systems. Further extention of the reaction using allenylsilane, silyl enol ether, and silyl ketene acetal also afforded the corresponding 4-substituted products. In contrast to the above 4-allylated product, 4-propargylated and 4-acylmethylated products did not undergo an analogous ring transformation under the same conditions.

In the previous section, the auther demonstrated an interesting reactivity of squaric acid esters **1** and **2** with trimethylsilyl cyanide, in which the addition was promoted by triethyloxonium salt, affording *O*-ethyl cyanides with regiochemistry different from that observed in the addition of organolithiums; compared with the reaction of organolithiums across a β-alkyl (aryl) enone moiety, the cyanide reacted with thermodynamically more favorable ethoxycarbenium ion **3** formed across a β-ethoxy enone moiety (Scheme 1). In the reaction of diethyl ester **1** with allylsilanes, initial mono-adduct **5** was further allylated under the employed conditions to give bis-adduct **7** *via* ethoxycarbenium ion intermediate **6** (Scheme 2). From this result, it is envisaged that acetal **11** or its vinylog **12** should be promising electrophiles readily derivable from squaric acid.

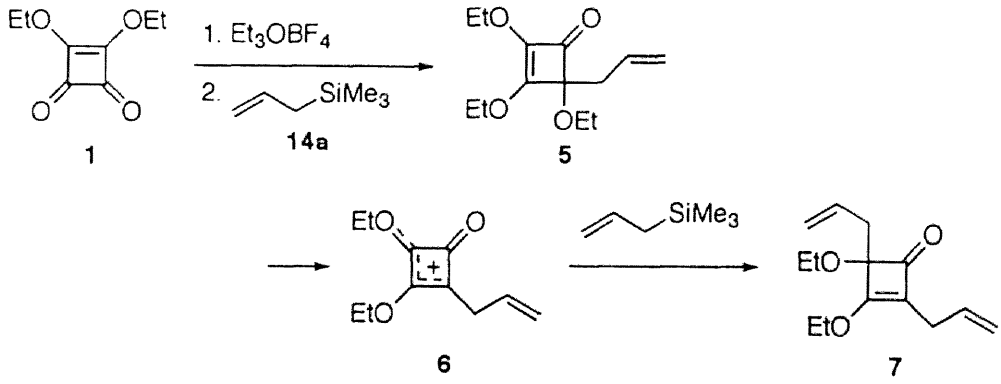


1 R=OEt
2 R=alkyl, aryl, alkynyl, H

3

4

Scheme 1



1

14a

5

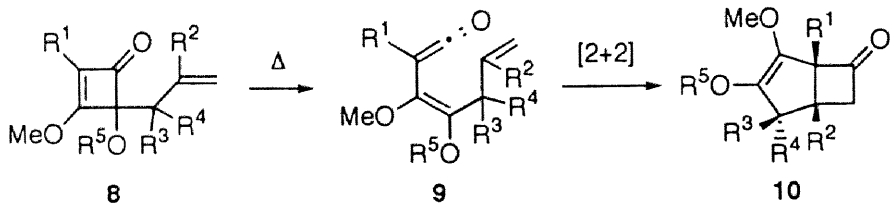
6

7

Scheme 2

Recently, Moore *et al.* reported the thermolysis of 4-allylcyclobutenones to give bicyclo[3.2.0]heptenones *via* tandem electrocyclic ring-opening and intramolecular [2+2]cycloaddition of resulted vinylketenes (Scheme 3).[1] Thus, feasible routes to the 4-allylcyclobutenone having diverse substituents seem to make this reaction more valuable as a

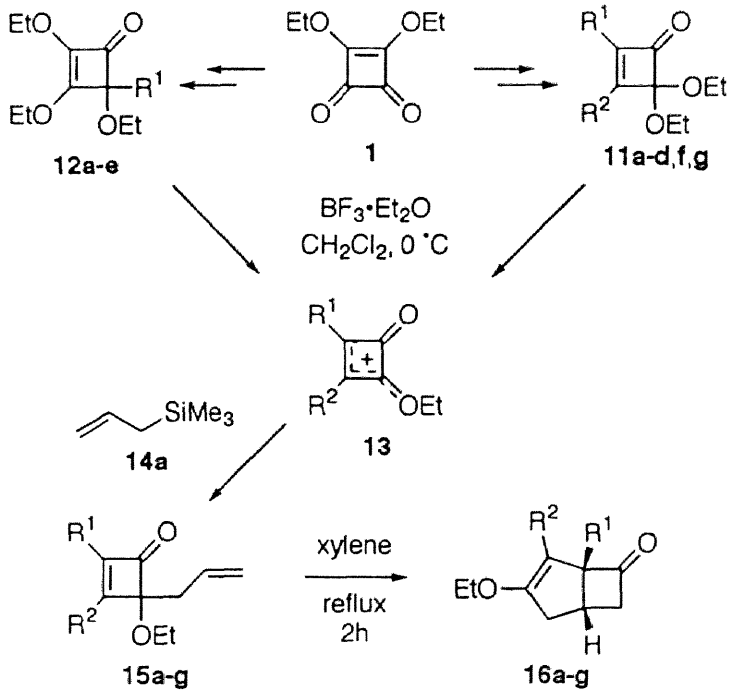
powerful route to various bicycloalkanones. However, these were obtained in some cases inefficiently with allylmagnesium bromide and allyllithium.[1] Moreover, protection of a free hydroxyl group (*e.g.*, R^5=H in **5**, Scheme 3) is preferable for the thermal ring transformation.[1] In these respects, the alternative synthetic method utilizing the addition of allylsilane *via* an ethoxycarbenium ion intermediate (*e.g.* **6**), is expected to solve these problems. In this section described is the full detail of this new allylation method and application to synthesis of highly substituted bi- and tricyclic ring systems. The electrophilic reaction using an acetal of the cyclobutenedione is also shown to be successful with allenylsilane, silyl enol ether, and silyl ketene acetal.



Scheme 3

Scheme 4 illustrates the new route to 4-allylcyclobutenones having a variety of substituents at 2-position from diethyl squarate. The catalytic action of a Lewis acid on monoacetal **11** produced the aforementioned ethoxycarbenium ion species, which reacted with allylsilane **14** regioselectively to afford a desired 4-allyl-4-ethoxycyclobutenone **15**. Typical example is the case of methyl-substituted monoacetal **11a**. Thus, a solution of **11a** and allyltrimethylsilane **14a** (3 equiv.) in dry dichloromethane was allowed to react with BF_3•Et_2O (1.2 equiv.) at 0 °C for 1h and, after standard work-up and chromatographic separation, the expected 4-allyl-4-ethoxycyclobutenone **15a** was obtained in a yield of 79%. The structure was confirmed by comparison with the related known compound, the spectral features of which were in good accordance with those of **15a** (IR, ^{1}H- and ^{13}C-NMR).[1] As shown in Table 1, the similar reaction of phenyl and alkynyl-substituted **11b,c** afforded the corresponding products **15b,c** in 72 and 90% yields, respectively (entry b and c), but the slow reaction of vinyl-substituted **11d** resulted in the formation of the corresponding adduct

15e in a low yield (entry d). 4-Ethoxycyclobutenone **12** is anticipated to be another candidate for the generation of the common ethoxycarbenium ion intermediate **13**. In fact, cyclobutenones **12a-d** were subjected to the above allylation and the same products **15a-c** were obtained in comparable yields. Notably, the reaction of 4-benzyloxycarbonylmethyl-substituted **12e** was effected under these electrophilic conditions to give **15e** in a yield of 66% (entry e). Such chemoselective allylation seems to be rather difficult under related nucleophilic conditions. Furthermore, 2,3-alkyl(aryl)-substituted 4-allylcyclobutenones **15f** and **g** were obtained similarly in 72 and 75% yields, respectively (entry f,g in Table 1). As the route to these compounds, Moore *et al.* also reported the 3-step conversion involving substitution of the 3-alkoxy group of the monoacetal, addition of an organolithium to the carbonyl group and deacetalization.[2] In our method, acetals **11f,g** were allylated directly in one step.



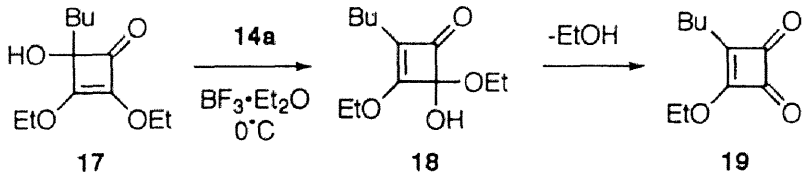
Scheme 4

Table 1. Synthesis and Thermolysis of 4-Allylcyclobutenones **15a-e**.

entry	R^1	R^2	Starting Cyclobutenone	15 Yield, %	16 Yield, %
a	Me	OEt	**11a / 12a**	**15a**, 79[a] (84)[b]	**16a**, 98
b	Ph	OEt	**11b / 12b**	**15b**, 72[a] (75)[b]	**16b**, 73
c	PhC≡C	OEt	**11c / 12c**	**15c**, 90[a] (93)[b]	**16c**, 94
d	H_2C=CH	OEt	**11d / 12d**	**15d**, 15[a] (22)[b]	**16d**, 98
e	BnO_2CCH_2	OEt	**12e**	**15e**, 66[b]	**16e**, 83
f	Me	Ph	**11f**	**15f**, 72[b]	**16f**, 99
g	Ph	Me	**11g**	**15g**, 75[b]	**16g**, 97

[a] Isolated yield from **11**. [b] Isolared yield from **12**.

The above procedure (**12** → **15**) might be more practical if a 1,2-addition product of **1** (*e.g.* **17**) could be used straightforwardly without alkyl-protection for the present allylation. However, BF_3-catalyzed reaction of the hydroxy-form of **17** resulted in the exclusive formation of 4-butyl-3-ethoxy-2-cyclobutene-1,2-dione **19** *via* hemiacetal **18** prior to the desired substitution (Scheme 4). Such a conversion under acidic conditions was exploited in the synthesis of mycotoxin moniliformin derivatives.[3]



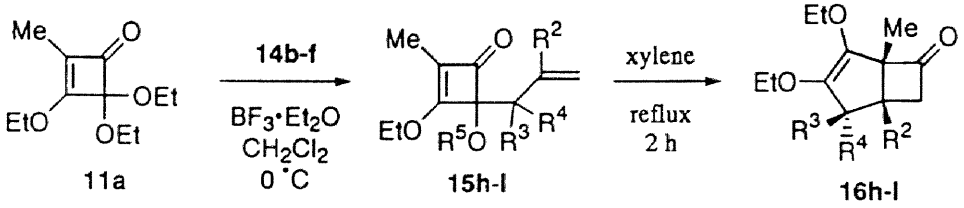
Scheme 5

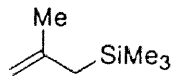
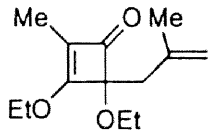
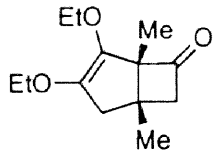
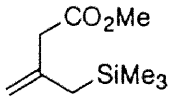
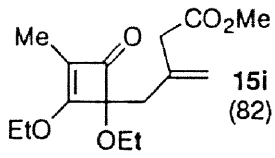
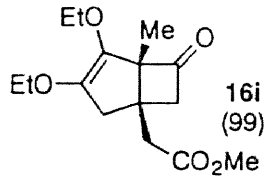
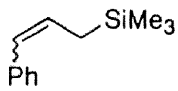
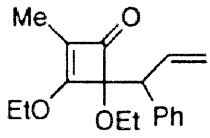
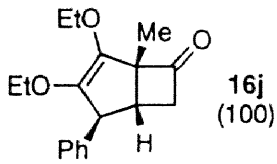
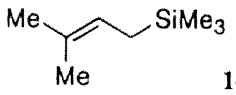
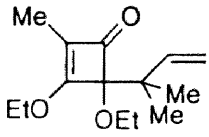
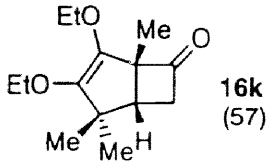
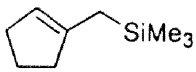
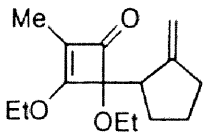
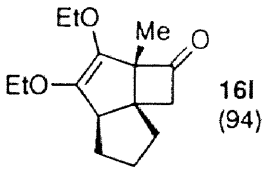
The obtained 4-allylcyclobutenones can be transformed to bicyclo[3.2.0]heptenones *via* an unsaturated ketene intermediate (*i.e.* **9**) as described above (Scheme 3). Thermal rearrangement of an alcohol form (*i.e.* **8**, R^5=H) for this purpose may lead to unsatisfactory results.[1] Advantageously, in our case, the hydroxyl group was already protected by an ethyl group, and therefore, cyclobutenones **15a-g** were converted directly and cleanly into bicycloheptenones **16a-g** in high yields by refluxing in xylene for 2h (Scheme 4, Table 1).

It is well known that allylsilanes react regioselectively (at γ to the silyl group) with electrophiles.[4] Therefore, above reaction sequence using variously substituted allylsilanes provide a method for the regio-controlled synthesis of 4-allyl-4-ethoxycyclobutenones and, in turn, of highly substituted bicyclo[3.2.0]heptenones. Thus, methallylsilane **14b** reacted with monoacetal **11a** under similar catalytic conditions for 5 h to give **15h** in 72% yield. Ester-functionalized allylsilane **14c** afforded cyclobutenyl-enoate **15i** efficiently. The similar reactions of γ-substituted allylsilanes such as cinnamylsilane **14d** and prenylsilane **14e** furnished the corresponding products **15j,k** in 60 and 50% yields, respectively. The 4-allylcyclobutenones **15h-k** obtained here could be also transformed to highly substituted bicyclo[3.2.0]heptenones **16h-k** in the same manner as for **16a**. These results are summarized in Table 2.

Furthermore, synthetic potential of the present method was demonstrated by the construction of tricyclic ring systems. Tricyclo[5.3.0.$0^{1,4}$]decenone **16l**, a possible precursor of angular triquinane,[5] was synthesized in a high yield via a route of our electrophilic allylation and thermal ring expansion (entry e in Table 2); thermolysis of 2-methylenecyclopentyl-substituted cyclobutenone **15l**, which was readily prepared from acetal **11a** and a cyclic allylsilane **14f**, was followed by ring enlargement with *t*-butyl diazoacetate according to the reported procedure[6] to give a triquinane derivative **20** (Scheme 6). When the spiro-annulation of an ω-hydroxy-substituted allylsilane with an acetal[7] was combined with our method, oxaspiro[3.5]nonenone **21** was prepared from acetal **11a** and an appropriate allylsilane **14g** in 73% yield.[8] Then, **21** was converted cleanly into an oxatricyclo[5.4.0.$0^{2,5}$]undecenone derivative **22** as a single diastereomer in 94% yield (Scheme 7). In this case, the stereochemistry of **22** is different from that of phenyl-substituted **16j**. The ^{1}H NMR spectrum of **22** showed that the coupling constant between the allylic proton H_a and the bridgehead proton H_b was 7.4 Hz, whereas the corresponding coupling between H_a and H_b of **16j** was not observed because H_a and H_b were orthogonal in the case of the *exo* orientation of a C_4-substituent (Figure 1). Therefore, the stereochemistry of C_4 in **16j** and C_1 in **22** was

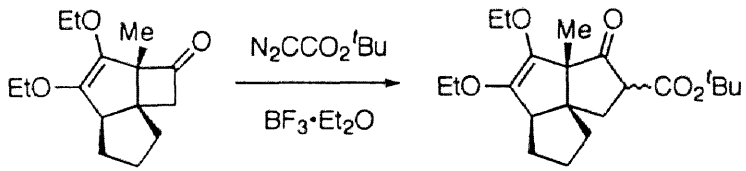
Table 2. Synthesis and Thermolysis of 4-Allylcyclobutenones**15h-l**.



entry	Allylsilane	Reaction Time (h)	4-Allylcyclobutenone (Yield %)	Bicycloheptenone (Yield %)
a	 **14b**	5	 **15h** (72)	 **16h** (94)
b	 **14c**	5	 **15i** (82)	 **16i** (99)
c	 **14d**	5	 **15j** (60)	 **16j** (100)
d	 **14e**	5	 **15k** (50)	 **16k** (57)
e	 **14f**	7	 **15l** (64)	 **16l** (94)

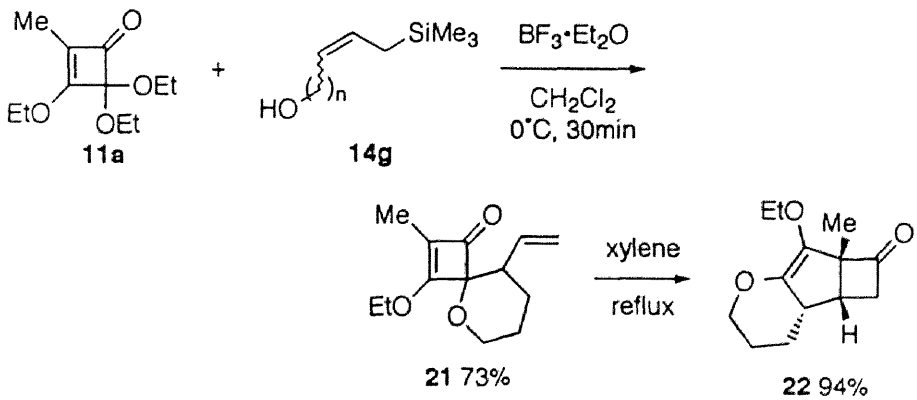
determined to be the *exo*- and *endo*-configurations, respectively. Moore reported the preferential formation of the *exo* isomers in the related rearrangement of 4-(1-methyl-2-propenyl)- and 4-(1-phenyl-2-propenyl)-2,3,4-trimethoxy-2-cyclobutenones.[1] In order to find the origin of the different stereoselectivity in these systems, RHF/PM3 calculations[9] were

performed for 2,3-dimethoxy-1,4-dimethylbicyclo[3.2.0]hept-2-en-7-one **23** and 5-methoxy-4-methyl-8-oxatricyclo[5.4.0.0^{2,5}]undec-6-en-3-one **24**, as models for simplicity. At first, geometries of both *exo*- and *endo*-isomers of **23** was fully optimized by use of the EF routine in the MOPAC package[10] with the keyword PRECISE, and the heat of formation of both isomers were obtained as shown in Figure 1. The *exo*-isomer was found to be slightly favorable in energy (1.0 kcal/mol) than the *endo*-isomer, and this energy difference of the products possibly reflects the predominancy of the *exo*-isomer to the *endo*-isomer. In contrast to this bicyclic system, almost comparable heat of formations were obtained for both isomers of tricyclic **24**. This means that the *exo*-isomer is no longer preferable to the *endo*-isomer. A model study for **23** shows that steric repulsion between the proximate C_4-Me and C_6-H seems to render the *endo*-transition state disadvantageous. In the tricyclic **24**, this steric hindrance (C_{11}-CH_2 and C_3-H) may be less significant at the *endo*-transition state.



16l **20** 54%

Scheme 6



11a **14g** **21** 73% **22** 94%

Scheme 7

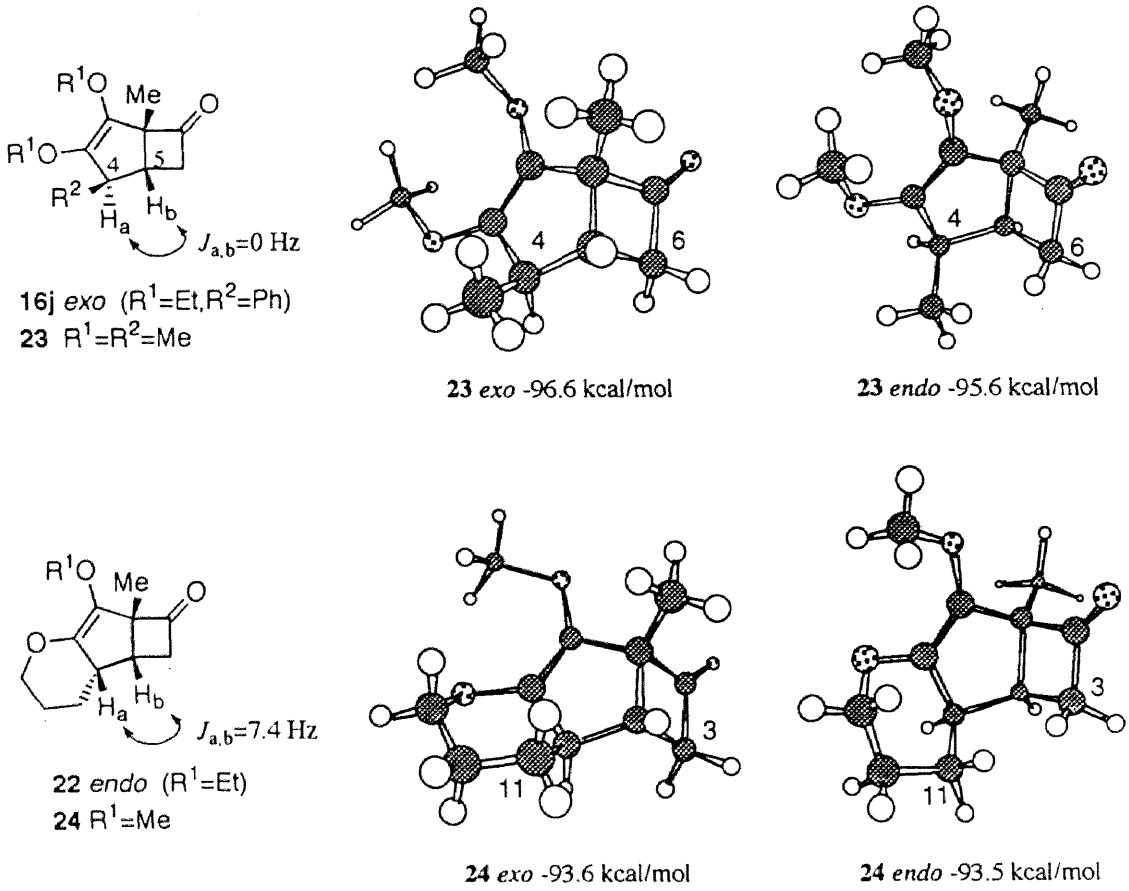
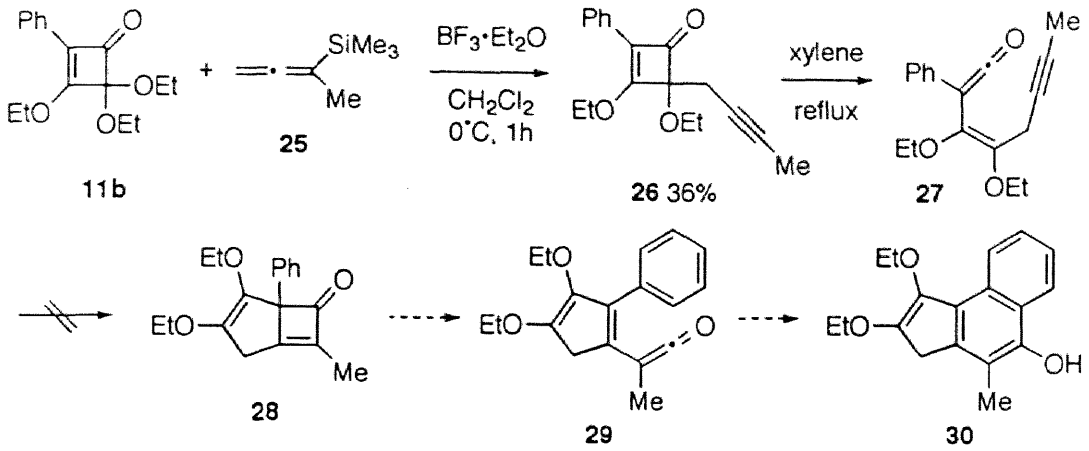


Figure 1. RHF/PM3 Optimized Structures and Calculated Energies.

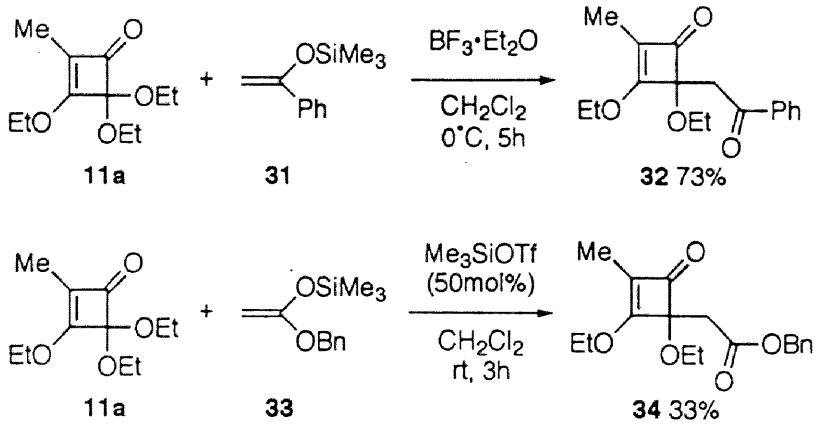
In continuing the reaction with unsaturated organosilanes, we next attempted the propargylation of the monoacetal using an allenylsilane. Under the same conditions employed for the above allylation, a desired propargylated product **26** was obtained from acetal **11b** and allenylsilane **25** in 21 % yield, which was somewhat improved to 36 % by the dropwise addition of **25** to the solution of **11b** and BF_3•Et_2O in dichloromethane at 0 °C. The thermolysis of the 4-propargylcyclobutenone **26** might produce a tricyclic phenol **30** *via* double electrocyclic ring opening/ring reclosure processes as depicted in Scheme 8. However, no sign indicating the conversion of **26** into some products was observed on heating in xylene. It is probably because the intramolecular [2+2] cycloaddition of **27** to a highly strained bicyclo[3.2.0]heptadienone system **28** is disfavored.



Scheme 8

The present method was then extended to the reaction with silyl enol ether and silyl ketene acetal (Scheme 9). A silyl enol ether **31** derived from acetophenone (3 equiv.) was reacted with **11a** in the presence of BF_3•Et_2O (1.2 equiv.) at 0 °C for 5 h to afford 4-acylmethylcyclobutenone **32** in good yield. However, a more reactive silyl ketene acetal **33** produced only a complex reaction mixture under these conditions. Nevertheless, the desired product **34** was obtained in moderate yield, when **11a** and **33** (3 equiv.) were reacted in the presence of 50 mol% of TMSOTf at ambient temperature for 3 h. We previously reported Et_3OBF_4-mediated addition of silyl enol ether and silyl ketene acetal to diethyl squarate, leading to 4-acylmethyl-1,2,4-triethoxycyclobutenones.[11] Thus, these reactions constitute an alternative process for synthesis of such cyclobutenones. The adducts bearing an acylmethyl side chain at 4-position are considered as an oxa-analog of the 4-allylcyclobutenone. Thus, the thermolysis of **32** was attempted to give a bicyclic β-lactone (or its decarboxylated product) *via* the similar type of transformation of **15** → **16**, but **32** remained intact after refluxing in xylene for 1 h.[12]

In conclusion, Regioselective synthesis of 4-allyl-4-ethoxycyclobutenones with alkyl, alkenyl, aryl, and alkynyl substituents at 2-position was achieved by the novel Lewis acid-catalyzed reaction of both 2,4- and 4,4-diethoxycyclobutenones with a variety of allylsilanes. These products were transformed to the corresponding highly substituted bicyclo[3.2.0]-



Scheme 9

heptenones without appreciable side reactions. This method was successfully applied to synthesis of tricyclic compounds. Further extension to other organosilanes such as allenylsilane, silyl enol ether, and silyl ketene acetal gave 4-propargyl- and 4-acylmethyl-substituted cyclobutenone derivatives. The present electrophilic C-C bond formation on the four-membered ring is of considerable value as a method for regio-controlled synthesis of highly substituted cyclobutenones having an unsaturated substituent at 4-position, which could be more practical than synthesis under nucleophilic conditions.

Experimental Section

General. IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ solution with $SiMe_4$ as an internal standard. Mass spectra were recorded on a JEOL JMS-AX 505 HA mass spectrometer. Flash chromatography was performed with a silica gel column (Fuji-Davison BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400S CHN elemental analyzer. Dichloromethane was dried over $CaCl_2$, distilled, and stored over 4Å molecular sieves. Xylene were dried over Na, distilled, and stored over Na. Unsaturated organosilanes used here were synthesized according to reported procedures.[12] Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.

Typical Procedure for Synthesis of Cyclobutenedione Monoacetals 11a-d.

According to the reported procedure,[2] **11a** was synthesized as follows; to a solution of diethyl squarate (510 mg, 3.00 mmol) in dry THF (30 mL) was added methyllithium (3.3 mL, 1 M solution in ether) at -78 °C under a nitrogen atmosphere, and the solution was stirred for 30 min. To this solution was added trifluoroacetic anhydride (0.47 mL, 3.30 mmol). The solution was stirred for 30 min and treated with dry ethanol (12 mL). After stirring for 30 min, the reaction mixture was quenched with 10% $NaHCO_3$ (20mL) and extracted with ether (10 mL × 3). The extracts were washed with brine (20 mL), dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 10:1) gave monoacetal **11a** (792 mg, 74%) as a colorless oil. The other monoacetals **11c-d** were obtained in the same manner with the corresponding organolithiums.

3,4,4-Triethoxy-2-methyl-2-cyclobutenone (11a). IR (neat) 1767, 1628 cm^{-1}; ^{1}H NMR δ 1.24 (6 H, t, *J*=7.0 Hz), 1.45 (3 H, t, *J*=7.2 Hz), 1.74 (3 H, s), 3.75 and 3.81 (each 2 H, dq, *J*=9.4, 7.0 Hz), 4.47 (2 H, q, *J* =7.2 Hz); ^{13}C NMR δ 6.4, 15.1, 15.4 (2C), 61.5 (2C), 69.0, 112.7, 127.1, 183.7, 193.1; MS (EI) *m/z* (rel. intensity) 214 (M^+, 5), 185 (88),

157 (79), 129 (100), 113 (40); Anal Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.79; H, 8.34.

3,4,4-Triethoxy-2-phenyl-2-cyclobutenone (11b). 63%; *oil* (Elution H-A 15:1); IR (neat) 1757, 1634, 1599 cm^{-1}; ^1H NMR δ 1.27 (6 H, t, *J*=7.0 Hz), 1.52 (3 H, t, *J*=7.0 Hz), 3.78 and 3.89 (each 2 H, dq, *J*=9.4, 7.0 Hz), 4.63 (2 H, q, *J* =7.0 Hz), 7.25-7.43 (3H, m), 7.78-7.84 (2H, m); ^{13}C NMR δ 15.5 (3C), 62.1 (3C), 70.0, 114.9, 127.4 (2C), 128.6, 128.8, 128.9 (2C), 182.2, 191.0; MS (EI) *m/z* (rel. intensity) 276 (M^+, 27), 247 (79), 219 (57), 191 (42), 145 (100); Anal Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.67; H, 7.18.

3,4,4-Triethoxy-2-phenylethynyl-2-cyclobutenone (11c). 23%; *oil* (Elution H-A 15:1); IR (neat) 2209, 1773, 1620, 1593 cm^{-1}; ^1H NMR δ 1.26 (6 H, t, *J*=7.0 Hz), 1.56 (3 H, t, *J*=7.0 Hz), 3.84 (4 H, q, *J*=7.0 Hz), 4.77 (2 H, q, *J* =7.0 Hz), 7.30-7.49 (5H, m); ^{13}C NMR δ 15.1, 15.4 (2C), 61.8 (2C), 71.0, 75.7, 95.6, 111.7, 112.4, 128.8 (2C), 129.4 (2C), 132.1, 184.7, 188.3; MS (EI) *m/z* (rel. intensity) 300 (M^+, 75), 271 (78), 243 (57), 215 (71), 187 (100); Anal Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.98; H, 6.63.

2-Ethenyl-3,4,4-triethoxy-2-cyclobutenone (11d). 11%; *oil* (Elution H-A 5:1); IR (neat) 1759, 1642, 1607, 1586 cm^{-1}; ^1H NMR δ 1.25 (6 H, t, *J*=7.0 Hz), 1.47 (3 H, t, *J*=7.0 Hz), 3.76 and 3.83 (each 2 H, dq, *J*=10.2, 7.0 Hz), 4.51 (2 H, q, *J* =7.0 Hz), 5.42 (1 H, dd, *J*=10.6, 2.4 Hz), 5.99 (1 H, dd, *J*=17.6, 2.4 Hz), 6.19 (1 H, dd, *J*=17.6, 10.6 Hz); ^{13}C NMR δ 15.1, 15.4 (2C), 61.7 (2C), 69.7, 113.1, 122.1, 122.4, 127.6, 180.7, 190.6; MS (EI) *m/z* (rel. intensity) 226 (M^+, 17), 197 (52), 169 (30), 141 (46), 113 (100); Anal Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.92; H, 7.80.

Synthesis of Cyclobutenedione Monoketals 11f and g.

According to the reported procedure,[2] **11f** was synthesized as follows; to a solution of **11a** (319 mg, 1.49 mmol) in dry THF (20 mL) was added phenyllithium (4.5 mL, 1 M

solution in cyclohexane-ether) at -78 °C under a nitrogen atmosphere, and the solution was stirred for 30 min. To this solution was added trifluoroacetic anhydride (0.32 mL, 2.23 mmol). After stirring for 30 min, the reaction mixture was quenched with 10% $NaHCO_3$ (10mL) and extracted with ether (10 mL × 3). The extracts were washed with brine (20 mL), dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 40:1) gave monoacetal **11f** (255 mg, 69%) as a colorless oil. Similarly, monoacetal **11g** was obtained from **11b** and methyllithium in 66% yield.

4,4-Diethoxy-2-methyl-3-phenyl-2-cyclobutenone (11f). IR (neat) 1752, 1620, 1574 cm^{-1}; ^1H NMR δ 1.22 (6 H, t, *J*=7.0 Hz), 2.10 (3 H, s), 3.69 and 3.80 (each 2 H, dq, *J*=9.2, 7.0 Hz), 7.45-7.53 (3 H, m), 7.79-7.86 (2 H, m); ^{13}C NMR δ 9.0, 15.6 (2 C), 61.8 (2C), 117.0, 129.1 (2 C), 129.5 (2 C), 130.9, 131.9, 149.6, 174.9, 197.3; MS (EI) *m/z* (rel. intensity) 246 (M^+, 11), 217 (37), 189 (57), 161 (65), 115 (100); Anal Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.18; H, 7.33.

4,4-Diethoxy-3-methyl-2-phenyl-2-cyclobutenone (11g). *oil* (Elution H-A 30:1); IR (neat) 1761, 1636, 1597 cm^{-1}; ^1H NMR δ 1.26 (6 H, t, *J*=7.0 Hz), 2.49 (3 H, s), 3.78 and 3.83 (each 2 H, dq, *J*=9.2, 7.0 Hz), 7.34-7.48 (3 H, m), 7.71-7.77 (2 H, m); ^{13}C NMR δ 13.0, 15.5 (2 C), 61.4 (2C), 115.7, 128.2 (2 C), 129.1 (2 C), 129.4, 130.0, 150.6, 176.3, 193.7; MS (EI) *m/z* (rel. intensity) 246 (M^+, 12), 217 (56), 189 (83), 161 (91), 145 (100), 115 (85); Anal Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.25; H, 7.27.

Typical Procedure for Synthesis of 2,3,4-Triethoxycyclobutenones 12a-d.

According to the reported procedure,[1] **12a** was synthesized as follows; a solution of 2,3-diethoxy-4-hydroxy-4-methyl-2-cyclobutenone (907 mg, 4.87 mmol), iodoethane (3.9 mL, 48.7 mmol) in dry acetonitrile (15 mL) was treated with Ag_2O (4.51g, 19.5 mmol) and K_2CO_3 (3.37g, 24.4 mmol) under a nitrogen atmosphere, and the suspension was stirred overnight. Insoluble materials were filtered off and the filtrate was concentrated under reduced pressure. Flash chromatography of the residue (Elution H-A 15:1) gave cyclobutenone **12a**

(619 mg, 59%) as a colorless oil. In the same manner, **12b-d** were obtained from the corresponding derivatives of 4-hydroxycyclobutenones. Benzyloxycarbonylmethyl-substituted **12e** was reported in the previous section.

2,3,4-Triethoxy-4-methyl-2-cyclobutenone (12a). IR (neat) 1771, 1634 cm^{-1}; ^1H NMR δ 1.20 (3 H, t, *J*=7.0 Hz), 1.31 (3 H, t, *J*=7.0 Hz), 1.43 (3 H, t, *J*=7.0 Hz), 1.47 (3 H, s), 3.50 (2 H, q, *J*=7.0 Hz), 4.28 and 4.33 (each 1 H, dq, *J* =10.2, 7.0 Hz), 4.45 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 15.3, 15.5, 15.6, 18.7, 60.1, 66.8, 69.1, 88.1, 132.7, 169.1, 188.3; MS (EI) *m/z* (rel. intensity) 214 (M^+, 41), 185 (90), 157 (100), 129 (55), 113 (39); Anal Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.86; H, 8.21.

2,3,4-Triethoxy-4-phenyl-2-cyclobutenone (12b). 61%; *oil* (Elution H-A 20:1); IR (neat) 1773, 1634 cm^{-1}; ^1H NMR δ 1.28 (3 H, t, *J*=7.0 Hz), 1.34 (3 H, t, *J*=7.0 Hz), 1.38 (3 H, t, *J*=7.0 Hz), 3.66 (2 H, q, *J*=7.0 Hz), 4.34 and 4.38 (each 1 H, dq, *J* =10.2, 7.0 Hz), 4.37 and 4.44 (each 1 H, dq, *J* =10.2, 7.0 Hz), 7.25-7.41 (3H, m), 7.49-7.56 (2H, m); ^{13}C NMR δ 15.2, 15.5, 15.6, 61.0, 67.1, 69.4, 92.4, 126.6 (2C), 128.5, 128.7 (2C), 135.0, 137.3, 166.0, 184.7; MS (EI) *m/z* (rel. intensity) 276 (M^+, 12), 247 (100), 219 (37), 191 (66), 145 (43); Anal Calcd for $C_{16}H_{20}O_4$: C, 69.55; H, 7.30. Found: C, 69.76; H, 7.10.

2,3,4-Triethoxy-4-phenylethynyl-2-cyclobutenone (12c). 58%; *oil* (Elution H-A 20:1); IR (neat) 2222, 1779, 1642 cm^{-1}; ^1H NMR δ 1.27 (3 H, t, *J*=7.2 Hz), 1.33 (3 H, t, *J*=7.0 Hz), 1.47 (3 H, t, *J*=7.0 Hz), 3.87 and 3.92 (each 1 H, dq, *J*=9.2, 7.0 Hz), 4.34 (2 H, q, *J* =7.2 Hz), 4.52 and 4.58 (each 1 H, dq, *J*=10.2, 7.0 Hz), 7.29-7.36 (3H, m), 7.45-7.51 (2 H, m); ^{13}C NMR δ=15.2, 15.6 (2C), 63.0, 67.3, 69.8, 82.3, 83.8, 89.9, 122.3, 128.6 (2C), 129.2, 132.3 (2C), 135.2, 164.5, 180.7; MS (EI) *m/z* (rel. intensity) 300 (M^+, 14), 271 (41), 243 (100), 215 (91), 187 (59); Anal Calcd for $C_{18}H_{20}O_4$: C, 71.93; H, 6.76. Found: C, 71.98; H, 6.63.

4-Ethenyl-2,3,4-triethoxy-2-cyclobutenone (12d). 44%; *oil* (Elution H-A 20:1); IR (neat) 1773, 1636 cm^{-1}; ^1H NMR δ=1.24 (3 H, t, *J*=7.0 Hz), 1.32 (3 H, t, *J*=7.0 Hz), 1.41 (3 H, t, *J*=7.0 Hz), 3.60 (2 H, q, *J*=7.0 Hz), 4.33 (2 H, q, *J* =7.0 Hz), 4.42 (2 H, q, *J* =7.0

Hz), 5.34 (1 H, dd, *J*=10.6, 1.4 Hz), 5.52 (1 H, dd, *J*=17.4, 1.4 Hz), 5.95 (1 H, dd, *J*=17.4, 10.6 Hz); ^{13}C NMR δ=15.3, 15.4, 15.5, 60.6, 67.0, 69.3, 91.8, 118.5, 134.4, 134.6, 166.8, 185.2; MS (EI) *m/z* (rel. intensity) 226 (M^+, 56), 197 (23), 169 (35), 141 (98), 113 (100); Anal Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.78; H, 7.94.

Typical Procedure for Synthesis of 4-Allylcyclobutenones 15a-g.

To a solution of **11a** (45 mg, 0.21 mmol) and **14a** (72 mg, 0.63mmol) in dry dichloromethane (2 mL) was added BF_3•Et_2O (0.032 mL, 0.25 mmol) at 0 °C under a nitrogen atmosphere. After stirring for 1 h, the reaction mixture was quenched with 10% $NaHCO_3$ (5 mL) and extracted with dichloromethane (5 mL × 3). The extracts were dried (Na_2SO_4) and evaporated to dryness. Flash chromatography of the residue (Elution H-A 5:1) gave 4-allylcyclobutenone **15a** (37 mg, 84%) as a colorless oil. The other allylcyclobutenones **15b-g** were obtained according to the same procedure and isolated yields were shown in Table 1.

3,4-Diethoxy-2-methyl-4-(2-propenyl)-2-cyclobutenone (15a). IR (neat) 1761, 1622 cm^{-1}; ^{1}H NMR δ 1.20 (3 H, t, *J*=7.0 Hz), 1.45 (3 H, t, *J*=7.2 Hz), 1.71 (3 H, s), 2.50 and 2.66 (each 1 H, ddt, *J*=14.2, 7.6, 1.2 Hz), 3.49 and 3.56 (each 1 H, dq, *J* =8.8, 7.0 Hz), 4.39 and 4.45 (each 1 H, dq, *J*=10.0, 7.2 Hz), 5.03-5.17 (2 H, m), 5.62-5.84 (1 H, m); ^{13}C NMR δ 6.3, 15.3, 15.4, 37.0, 60.7, 68.6, 96.2, 118.7, 123.2, 132.7, 183.5, 193.7; MS (EI) *m/z* (rel. intensity) 210 (M^+, 10), 181 (100), 153 (42), 122 (15), 113 (13); Anal Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.80; H, 8.38.

3,4-Diethoxy-2-phenyl-4-(2-propenyl)-2-cyclobutenone (15b). *oil* (Elution H-A 20:1); IR (neat) 1755, 1632, 1599 cm^{-1}; ^{1}H NMR δ 1.24 (3 H, t, *J*=7.0 Hz), 1.53 (3 H, t, *J*=7.0 Hz), 2.61 and 2.88 (each 1 H, ddt, *J*=14.4, 7.6, 1.2 Hz), 3.58 and 3.68 (each 1 H, dq, *J* =9.0, 7.0 Hz), 4.50 and 4.57 (each 1 H, dq, *J* =9.8, 7.0 Hz), 5.05-5.22 (2 H, m), 5.78 (1 H, m), 7.23-7.41 (3H, m), 7.74-7.80 (2H, m); ^{13}C NMR δ 15.4, 15.5, 38.3, 61.1, 69.4, 98.3, 119.1, 125.0, 127.3 (2C), 128.4 (2C), 128.8 (2C), 132.3, 182.1, 190.2; MS (EI) *m/z*

(rel. intensity) 272 (M^+, 46), 243 (100), 215 (28), 145 (91); Anal Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 75.01; H, 7.36.

3,4-Diethoxy-2-phenylethynyl-4-(2-propenyl)-2-cyclobutenone (15c). *oil* (Elution H-A 20:1); IR (neat) 2209, 1769, 1620, 1593 cm^{-1}; ^1H NMR δ 1.23 (3 H, t, *J*=7.0 Hz), 1.55 (3 H, t, *J*=7.0 Hz), 2.56 and 2.67 (each 1 H, ddt, *J*=12.0, 5.4, 1.2 Hz), 3.55 and 3.62 (each 1 H, q, *J* =7.0 Hz), 5.09-5.21 (2 H, m), 5.69-5.89 (1 H, m), 7.30-7.49 (5H, m); ^{13}C NMR δ 15.2, 15.4, 36.7, 61.3, 70.7, 93.3, 96.8, 108.3, 119.3, 122.5, 127.3, 128.7 (2C), 129.3, 131.9, 132.0 (2 C), 185.8, 190.1; MS (EI) *m/z* (rel. intensity) 300 (M^+, 75), 271 (78), 243 (57), 215 (71), 187 (100); Anal Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.98; H, 6.63.

2-Ethenyl-3,4-diethoxy-4-(2-propenyl)-2-cyclobutenone (15d). *oil* (Elution H-A 20:1); IR (neat) 1753, 1642, 1582 cm^{-1}; ^1H NMR δ 1.21 (3 H, t, *J*=7.0 Hz), 1.47 (3 H, t, *J*=7.0 Hz), 2.53 and 2.71 (each 1 H, ddt, *J*=14.4, 7.6, 1.2 Hz), 3.51 and 3.60 (each 1 H, dq, *J*=9.0, 7.0 Hz), 4.43 and 4.48 (each 1 H, dq, *J* =10.0, 7.0 Hz), 5.05-5.18 (2 H, m), 5.37 (1 H, dd, *J*=10.6, 2.4 Hz), 5.75 (1 H, m), 5.95 (1 H, dd, *J*=17.6, 2.4 Hz), 6.13 (1 H, dd, *J*=17.6, 10.6 Hz); ^{13}C NMR δ 15.1, 15.5, 37.4, 61.0, 69.3, 96.9, 118.9, 121.7, 122.1, 124.4, 132.4, 180.8, 191.2; MS (EI) *m/z* (rel. intensity) 222 (M^+, 18), 193 (100), 137 (26), 95 (53), 69 (96); Anal Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.33; H, 8.07.

Benzyl [2,3-Diethoxy-4-oxo-3-(2-propenyl)-1-cyclobutenyl]acetate (15e). *oil* (Elution H-A 8:1); IR (neat) 1767, 1738, 1624 cm^{-1}; ^1H NMR δ 1.15 (3 H, t, *J*=7.0 Hz), 1.40 (3 H, t, *J*=7.0 Hz), 2.50 and 2.68 (each 1 H, ddt, *J*=14.4, 7.6, 1.2 Hz), 3.20 (2 H, s), 3.45 and 3.53 (each 1 H, dq, *J* =9.0, 7.0 Hz), 4.35 and 4.41 (each 1 H, dq, *J*=9.8, 7.0 Hz), 4.99-5.07 (2 H, m), 5.13 (2 H, s), 5.71 (1 H, m), 7.35 (5 H, s); ^{13}C NMR δ 15.1, 15.3, 27.5, 37.2, 60.9, 67.3, 69.1, 96.9, 118.8, 128.7, 128.8 (3 C), 128.9 (2 C), 132.4, 135.7, 169.4, 185.3, 192.1; MS (EI) *m/z* (rel. intensity) 344 (M^+, 5), 253 (100), 225 (12), 179 (51), 151 (34); Anal Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.79; H, 6.98.

4-Ethoxy-2-methyl-3-phenyl-4-(2-propenyl)-2-cyclobutenone (15f). *oil* (Elution H-A 25:1); IR (neat) 1752, 1618, 1572 cm^{-1}; ^1H NMR δ 1.19 (3 H, t, *J*=7.0 Hz), 2.07 (3 H, s), 2.70 and 2.84 (each 1 H, ddt, *J*=14.2, 7.4, 1.2 Hz), 3.43 and 3.53 (each 1 H, dq, *J* =8.8, 7.0 Hz), 4.91-5.04 (2 H, m), 5.66 (1 H, m), 7.47-7.55 (3H, m), 7.71-7.80 (2H, m); ^{13}C NMR δ 8.7, 15.5, 37.9, 60.5, 99.2, 118.7, 128.6 (2C), 129.5 (2C), 131.8, 132.0, 132.9, 145.3, 173.0, 197.3; MS (EI) *m/z* (rel. intensity) 242 (M^+, 7), 213 (100), 171 (30), 157 (36), 129 (33), 115 (75); Anal Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.34; H, 7.45.

4-Ethoxy-3-methyl-2-phenyl-4-(2-propenyl)-2-cyclobutenone (15g). *oil* (Elution H-A 20:1); IR (neat) 1757, 1636, 1597 cm^{-1}; ^1H NMR δ 1.21 (3 H, t, *J*=7.0 Hz), 2.43 (3 H, s), 2.58 and 2.68 (each 1 H, ddt, *J*=14.2, 7.2, 1.2 Hz), 3.46 and 3.56 (each 1 H, dq, *J* =8.8, 7.0 Hz), 5.01-5.18 (2 H, m), 5.78 (1 H, m), 7.32-7.47 (3H, m), 7.70-7.77 (2H, m); ^{13}C NMR δ 13.5, 15.6, 37.6, 60.8, 99.2, 118.6, 128.0 (2C), 129.1 (2C), 129.5, 129.6, 132.9, 147.1, 177.0, 195.0; MS (EI) *m/z* (rel. intensity) 242 (M^+, 3), 213 (100), 171 (7), 157 (18), 129 (15), 115 (24); Anal Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.34; H, 7.46.

Synthesis of 4-Allylcyclobutenones 15h-l.

4-Allylcyclobutenones **15h-l** were obtained from **11a** and **14b-f** in the same manner as described for **15a**. Reaction times and isolated yields are compiled in Table 2.

3,4-Diethoxy-2-methyl-4-(2-methyl-2-propenyl)-2-cyclobutenone (15h). *oil* (Elution H-A 5:1); IR (neat) 1761, 1622 cm^{-1}; ^1H NMR δ 1.20 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 1.72 (3 H, s), 1.73 (3 H, m), 2.47 and 2.62 (each 1 H, dd, *J* =13.8, 0.8 Hz), 3.47 and 3.55 (each 1 H, dq, *J*=8.8, 7.0 Hz), 4.48 (2 H, q, *J*=7.0 Hz), 4.76-4.87 (2 H, m); ^{13}C NMR δ 6.4, 15.2, 15.5, 23.5, 40.8, 60.5, 68.5, 96.3, 115.4, 123.2, 141.0, 183.0, 193.8; MS (EI) *m/z* (rel. intensity) (no molecular ion) 195 (73), 167 (100). (CI) m/z (rel. intensity) 225 (MH^+, 74), 169 (100); Anal Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.76; H, 8.84.

Methyl 3-[(1,2-Diethoxy-3-methyl-4-oxo-2-cyclobuteyl)methyl]-3-butenoate (15i). *oil* (Elution H-A 4:1); IR (neat) 1759, 1740, 1622 cm^{-1}; ^1H NMR δ 1.18 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 1.73 (3 H, s), 2.62 and 2.74 (each 1 H, dd, *J* =14.4, 1.0 Hz), 3.17 (2 H, s), 3.46 and 3.53 (each 1 H, dq, *J*=8.6, 7.0 Hz), 3.68 (3 H, s), 4.44 (2 H, q, *J*=7.0 Hz), 5.00-5.05 (2 H, m); ^{13}C NMR δ 6.6, 15.2, 15.4, 39.3, 41.7, 51.8, 60.6, 68.7, 95.7, 118.6, 123.0, 138.0, 172.5, 183.2, 193.6; MS (EI) *m/z* (rel. intensity) 282 (M^+, 13), 254 (11), 221 (85), 193 (100), 165 (69); Anal Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.82; H, 7.84.

3,4-Diethoxy-2-methyl-4-(1-phenyl-2-propenyl)-2-cyclobutenone (15j). *oil* (Elution H-A 6:1); IR (neat) 1759, 1622 cm^{-1}; ^1H NMR (ca. 1:1 diastereomer mixture) δ 1.19 and 1.13 (each 3/2 H, t, *J*=7.0 Hz), 1.32 and 1.43 (each 3/2 H, t, *J*=7.0 Hz), 1.48 and 1.60 (each 3/2 H, s), 3.42-3.65 (2 H, m), 3.78-3.88 (1 H, m), 4.17 and 4.29 (each 1/2 H, dq, *J* =10.0, 7.0 Hz), 4.35 (1 H, q, *J*=7.0 Hz), 5.21-5.29 (2 H, m), 6.09-6.48 (1 H, m), 7.06-7.20 (5 H, m); ^{13}C NMR δ 6.4 and 6.6, 15.1 and 15.3, 15.4 and 15.5, 53.6 and 54.0, 60.9 and 61.0, 68.5 and 68.6, 98.4 and 98.7, 117.4 and 117.6, 123.7 and 124.1, 126.9 and 127.1, 128.3 and 128.4 (each 1 C), 129.2 and 129.4 (each 1 C), 137.3 and 137.5, 140.2 and 140.3, 181.7 and 181.8, 192.7 and 192.9; MS (EI) *m/z* (rel. intensity) 286 (M^+, 5), 258 (99), 229 (33), 183 (100); Anal Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.45; H, 7.79.

3,4-Diethoxy-2-methyl-4-(1,1-dimethyl-2-propenyl)-2-cyclobutenone (15k). *oil* (Elution H-A 6:1); IR (neat) 1759, 1622 cm^{-1}; ^1H NMR δ 1.12 and 1.14 (each 3 H, s), 1.19 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 1.78 (3 H, s), 3.42 and 3.49 (each 1 H, dq, *J* =9.0, 7.0 Hz), 4.42 (2 H, q, *J*=7.0 Hz), 4.98 (1 H, dd, *J*=10.8, 1.4 Hz), 5.02 (1 H, dd, *J*=17.6, 1.4 Hz), 6.00 (1 H, dd, *J*=17.6, 10.8 Hz); ^{13}C NMR δ 6.9, 15.3, 15.4, 22.7, 23.1, 41.2, 60.6, 68.6, 100.2, 112.3, 123.1, 144.8, 183.0, 194.9; MS (EI) *m/z* (rel. intensity) 238 (M^+, 6), 223 (57), 210 (46), 167 (91), 139 (100); Anal Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.59; H, 9.27.

3,4-Diethoxy-2-methyl-4-(2-methylenecyclopentyl)-2-cyclobutenone (15l). Two diastereometrs of **15l** were separated by flash chromatography (Elution H-A 10:1).

Spectral data of the first eluted diastereomer. 40%; *oil*; IR (neat) 1759, 1622 cm^{-1}; ^1H NMR δ 1.21 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 1.73 (3 H, s), 1.41-1.98 (4 H, m), 2.25 (2 H, m), 2.98 (1 H, m), 3.48 and 3.55 (each 1 H, dq, *J* =8.8, 7.0 Hz), 4.44 (2 H, q, *J*=7.0 Hz), 4.88 and 5.00 (each 1 H, m); ^{13}C NMR δ 6.3, 15.2, 15.4, 24.9, 29.2, 34.7, 46.1, 60.5, 68.3, 98.6, 108.7, 124.0, 152.1, 182.7, 193.6; MS (EI) *m/z* (rel. intensity) 250 (M^+, 4), 222 (100), 193 (52), 177 (17), 165 (39); Anal Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.04; H, 8.78.

Spectral data of the second eluted diastereomer. 24%; *oil*; IR (neat) 1761, 1622 cm^{-1}; ^1H NMR δ 1.21 (3 H, t, *J*=7.0 Hz), 1.45 (3 H, t, *J*=7.0 Hz), 1.75 (3 H, s), 1.41-1.98 (4 H, m), 2.28 (2 H, m), 2.91 (1 H, m), 3.50 and 3.57 (each 1 H, dq, *J* =8.8, 7.0 Hz), 4.44 and 4.45 (each 1 H, dq, *J*=10.0, 7.0 Hz), 5.00 and 5.04 (each 1 H, m); ^{13}C NMR δ 6.5, 15.1, 15.4, 24.8, 29.2, 34.4, 45.6, 60.5, 68.4, 98.4, 108.8, 123.5, 151.4, 182.3, 194.1; MS (EI) *m/z* (rel. intensity) 250 (M^+, 3), 222 (100), 193 (52), 177 (17), 165 (40); Anal Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.07; H, 8.76.

Typical Procedure for Thermal Rearrangement of 4-Allylcyclobutenones 15a-l.

A solution of **15a** (62 mg, 0.29 mmol) in dry xylene (10 mL) was refluxed under a nitrogen atmosphere for 2 h. The solution was cooled to ambient temperature and the solvent was removed under reduced pressure. Flash chromatography of the residue (Elution H-A 10:1) gave bicyclo[3.2.0]heptenone **16a** (61 mg, 98%) as a colorless oil. The other bicycloheptenones **15b-l** were obtained according to the same procedure and isolated yields were indicated in Tables 1 and 2.

2,3-Diethoxy-1-methylbicyclo[3.2.0]hept-2-en-7-one (16a). IR (neat) 1771, 1674 cm^{-1}; ^1H NMR δ 1.21 (3 H, t, *J*=7.0 Hz), 1.27 (3 H, t, *J*=7.0 Hz), 1.29 (3 H, s), 2.22 (1 H, m), 2.29 (1 H, d, *J*=15.8 Hz), 2.84 (1 H, dd, *J* =15.8, 8.2 Hz), 2.92 (1 H, dd, *J* =17.8, 5.8

Hz), 3.22 (1 H, dd, J =17.8, 8.6 Hz), 3.79 and 4.31 (each 1 H, dq, J =9.8, 7.0 Hz), 3.93 and 4.04 (each 1 H, dq, J =9.6, 7.0 Hz); ^{13}C NMR δ 15.3, 15.4, 15.5, 27.7, 33.5, 51.4, 65.3, 66.6, 73.3, 132.5, 137.2, 210.7; MS (EI) *m/z* (rel. intensity) 210 (M^+, 3), 182 (50), 153 (27), 125 (100); Anal Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.68; H, 8.50.

2,3-Diethoxy-1-phenylbicyclo[3.2.0]hept-2-en-7-one (16b). *oil* (Elution H-A 20:1); IR (neat) 1771, 1672, 1601 cm^{-1}; ^{1}H NMR δ 1.07 (3 H, t, J=7.0 Hz), 1.30 (3 H, t, J=7.0 Hz), 2.40 (1 H, d, J=15.8 Hz), 2.63 (1 H, m), 3.01 (1 H, dd, J =15.8, 7.8 Hz), 3.03 (1 H, dd, J =18.2, 5.6 Hz), 3.34 (1 H, dd, J =18.2, 9.2 Hz), 3.72 and 3.89 (each 1 H, dq, J =9.8, 7.0 Hz), 4.01 and 4.11 (each 1 H, dq, J =9.8, 7.0 Hz), 7.20-7.42 (5 H, m); ^{13}C NMR δ 15.3, 15.6, 30.0, 33.7, 51.6, 65.5, 67.0, 80.2, 126.7 (2 C), 127.5, 128.8 (2 C), 132.6, 138.5, 138.7, 207.4; MS (EI) *m/z* (rel. intensity) 272 (M^+, 6), 244 (100), 215 (47), 187 (96), 173 (35); Anal Calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.95; H, 7.42.

2,3-Diethoxy-1-phenylethynylbicyclo[3.2.0]hept-2-en-7-one (16c). *oil* (Elution H-A 10:1); IR (neat) 2226, 1784, 1674, 1597 cm^{-1}; ^{1}H NMR δ 1.27 (3 H, t, J=7.0 Hz), 1.29 (3 H, t, J=7.0 Hz), 2.31 (1 H, d, J=15.6 Hz), 2.75 (1 H, m), 2.98 (1 H, dd, J =15.6, 8.0 Hz), 3.07 (1 H, dd, J =18.4, 5.8 Hz), 3.44 (1 H, dd, J =18.4, 9.2 Hz), 3.96 and 4.13 (each 1 H, dq, J =9.8, 7.0 Hz), 4.03 and 4.17 (each 1 H, dq, J =9.8, 7.0 Hz), 7.26-7.47 (5 H, m); ^{13}C NMR δ 15.4, 15.6, 29.6, 33.8, 52.6, 65.6, 67.2, 69.6, 83.9, 88.5, 123.2, 128.5 (2 C), 128.6, 129.3, 132.1 (2 C), 138.7, 201.5; MS (EI) *m/z* (rel. intensity) 296 (M^+, 12), 268 (63), 239 (55), 211 (100), 197 (39), 183 (45); Anal Calcd for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 77.03; H, 6.77.

1-Ethenyl-2,3-diethoxybicyclo[3.2.0]hept-2-en-7-one (16d). *oil* (Elution H-A 20:1); IR (neat) 1773, 1672, 1632 cm^{-1}; ^{1}H NMR δ 1.20 (3 H, t, J=7.0 Hz), 1.28 (3 H, t, J=7.0 Hz), 2.30 (1 H, d, J=15.8 Hz), 2.49 (1 H, m), 2.87 (1 H, dd, J =15.8, 8.2 Hz), 2.92 (1 H, dd, J =18.2, 5.6 Hz), 3.24 (1 H, dd, J =18.2, 9.0 Hz), 3.79 and 4.00 (each 1 H, dq, J =9.6, 7.0 Hz), 4.02 and 4.07 (each 1 H, dq, J =9.8, 7.0 Hz), 5.22 (1 H, dd, J =10.6, 1.4

Hz), 5.35 (1 H, dd, J =17.4, 1.4 Hz), 5.98 (1 H, dd, J =17.4, 10.6 Hz); ^{13}C NMR δ 15.3, 15.6, 27.7, 33.6, 51.2, 65.4, 66.8, 79.3, 116.9, 131.4, 133.8, 138.2, 207.6; MS (EI) *m/z* (rel. intensity) 222 (M^+, 32), 195 (41), 165 (45), 137 (100); Anal Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.33; H, 8.07.

1-Benzyloxycarbonylmethyl-2,3-diethoxybicyclo[3.2.0]hept-2-en-7-one (16e). *oil* (Elution H-A 10:1); IR (neat) 1777, 1734, 1676 cm^{-1}; ^{1}H NMR δ 1.19 (3 H, t, J=7.0 Hz), 1.25 (3 H, t, J=7.0 Hz), 2.26 (1 H, d, J=15.4 Hz), 2.60 (1 H, m), 2.66 and 3.07 (each 1 H, d, J =17.6 Hz), 2.75 (1 H, dd, J =15.4, 8.0 Hz), 2.85 (1 H, dd, J =17.8, 5.2 Hz), 3.31 (1 H, dd, J =17.8, 8.8 Hz), 3.83 and 3.97 (each 1 H, dq, J =9.8, 7.0 Hz), 3.86 and 4.01 (each 1 H, dd, J =10.6, 1.4 Hz), 5.10 (2 H, s), 7.35 (5 H, s); ^{13}C NMR δ 15.4, 15.5, 25.7, 33.4, 34.7, 52.0, 65.3, 66.8, 67.0, 73.3, 128.7, 128.8 (2 C), 128.9 (2 C), 130.2, 136.0, 138.3, 171.4, 207.9; MS (EI) *m/z* (rel. intensity) 344 (M^+, 8), 316 (100), 302 (58), 225 (19); Anal Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.83; H, 6.94.

3-Ethoxy-1-methyl-2-phenylbicyclo[3.2.0]hept-2-en-7-one (16f). *oil* (Elution H-A 10:1); IR (neat) 1767, 1624, 1601 cm^{-1}; ^{1}H NMR δ 1.31 (3 H, s), 1.34 (3 H, t, J=7.0 Hz), 2.34 (1 H, m), 2.67 (1 H, dd, J=17.0, 0.8 Hz), 2.96 (1 H, dd, J =17.6, 6.2 Hz), 3.18 (1 H, dd, J =17.0, 8.0 Hz), 3.27 (1 H, dd, J =17.6, 8.4 Hz), 4.00 and 4.05 (each 1 H, dq, J =9.6, 7.0 Hz), 7.10-7.36 (3 H, m), 7.69-7.75 (2 H, m); ^{13}C NMR δ 15.6, 17.5, 29.8, 36.8, 51.1, 65.4, 76.3, 114.0, 126.1, 128.2 (2 C), 128.3 (2 C), 134.6, 154.1, 211.8; MS (EI) *m/z* (rel. intensity) 242 (M^+, 3), 214 (100), 198 (84), 185 (53), 171 (56), 157 (46); Anal Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.30; H, 7.50.

3-Ethoxy-2-methyl-1-phenylbicyclo[3.2.0]hept-2-en-7-one (16g). *oil* (Elution H-A 15:1); IR (neat) 1767, 1672, 1601 cm^{-1}; ^{1}H NMR δ 1.30 (3 H, t, J=7.0 Hz), 1.44 (3 H, dd, J=2.2, 1.7 Hz), 2.53 (1 H, m), 2.74 (1 H, m), 2.89 (1 H, dd, J=17.8, 5.2 Hz), 3.11 (1 H, ddq, J =16.2, 7.4, 2.2 Hz), 3.31 (1 H, dd, J =17.8, 9.2 Hz), 3.93 and 3.96 (each 1 H, dq, J =9.8, 7.0 Hz), 7.18-7.37 (5 H, m); ^{13}C NMR δ 8.8, 15.6, 31.9, 36.1, 51.2, 65.0, 83.4, 112.4, 126.4 (2 C), 127.2, 128.8 (2 C), 139.4, 152.6, 208.0; MS (EI) *m/z* (rel.

intensity) 242 (M^+, 2), 214 (100), 185 (59), 171 (30), 157 (24); Anal Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.30; H, 7.50.

2,3-Diethoxy-1,5-dimethylbicyclo[3.2.0]hept-2-en-7-one (16h). *oil* (Elution H-A 15:1); IR (neat) 1771, 1678 cm^{-1}; ^1H NMR δ 1.13 (3 H, s), 1.16 (3 H, s), 1.21 (3 H, t, *J*=7.0 Hz), 1.27 (3 H, t, *J*=7.0 Hz), 2.50 (2 H, s), 2.75 (1 H, d, *J*=17.4 Hz), 3.20 (1 H, d, *J* =17.4 Hz), 3.78 and 3.99 (each 1 H, dq, *J* =9.8, 7.0 Hz), 3.92 and 4.02 (each 1 H, dq, *J* =9.8, 7.0 Hz); ^{13}C NMR δ 11.5, 15.3, 15.5, 20.7, 31.4, 41.2, 58.4, 65.3, 66.5, 73.5, 133.0, 137.1, 211.2; MS (EI) *m/z* (rel. intensity) 224 (M^+, 9), 196 (80), 167 (28), 139 (100); Anal Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.68; H, 8.92.

2,3-Diethoxy-5-methoxycarbonylmethyl-1-dimethylbicyclo[3.2.0]hept-2-en-7-one (16i). *oil* (Elution H-A 10:1); IR (neat) 1773, 1738, 1680 cm^{-1}; ^1H NMR δ 1.16 (3 H, s), 1.21 (3 H, t, *J*=7.0 Hz), 1.27 (3 H, t, *J*=7.0 Hz), 2.48 (2 H, s), 2.66 (2 H, s), 3.08 and 3.27 (each 1 H, d, *J*=18.0 Hz), 3.70 (3 H, s), 3.83 and 4.01 (each 1 H, dq, *J* =9.8, 7.0 Hz), 3.90 and 4.01 (each 1 H, dq, *J* =9.8, 7.0 Hz); ^{13}C NMR δ 11.4, 15.4, 15.6, 33.1, 39.1, 39.4, 51.9, 57.2, 65.4, 66.8, 74.1, 132.3, 136.8, 172.3, 209.7; MS (EI) *m/z* (rel. intensity) 282 (M^+, 5), 254 (54), 180 (100), 165 (47), 137 (60); Anal Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.92; H, 7.74.

2,3-Diethoxy-1-methyl-4-phenylbicyclo[3.2.0]hept-2-en-7-one (16j). *oil* (Elution H-A 15:1); IR (neat) 1773, 1669 cm^{-1}; ^1H NMR δ 1.13 (3 H, t, *J*=7.0 Hz), 1.27 (3 H, t, *J*=7.0 Hz), 1.38 (3 H, s), 2.12 (1 H, dd, *J*=8.6, 5.8 Hz), 3.10 (1 H, dd, *J* =18.0, 5.8 Hz), 3.31 (1 H, dd, *J* =18.0, 8.6 Hz), 3.69 (1 H, s), 3.86 (2 H, q, *J* =7.0 Hz), 3.91 and 4.08 (each 1 H, dq, *J* =9.8, 7.0 Hz), 7.17-7.39 (5 H, m); ^{13}C NMR δ 15.5, 16.0, 37.2, 51.5, 53.5, 65.8, 66.8, 72.8, 127.3, 127.6 (2 C), 128.9, 129.1 (2 C), 135.0, 139.1, 143.8, 209.8; MS (EI) *m/z* (rel. intensity) 286 (M^+, 5), 258 (100), 229 (34), 213 (20), 201 (46); Anal Calcd for $C_{18}H_{22}O_3$: C, 75.50; H, 7.74. Found: C, 75.53; H, 7.71.

2,3-Diethoxy-1,4,4-trimethylbicyclo[3.2.0]hept-2-en-7-one (16k). *oil* (Elution H-A 15:1); IR (neat) 1773, 1669 cm^{-1}; ^1H NMR δ 1.05 (3 H, s), 1.14 (3 H, s), 1.20 (3 H, t,

J=7.0 Hz), 1.26 (3 H, t, *J*=7.0 Hz), 1.33 (3 H, s), 2.00 (1 H, d, *J*=8.4, 6.6 Hz), 2.85 (1 H, dd, *J* =17.8, 8.4 Hz), 3.21 (1 H, dd, *J* =17.6, 6.6 Hz), 3.51 and 3.90 (each 1 H, dq, *J* =9.6, 7.0 Hz), 4.04 and 4.27 (each 1 H, dq, *J* =9.8, 7.0 Hz); ^{13}C NMR δ 15.3, 15.6, 16.0, 19.5, 29.8, 40.6, 41.1, 46.1, 66.4, 66.9, 71.9, 131.0, 145.2, 210.7; MS (EI) *m/z* (rel. intensity) 238 (M^+, 12), 210 (100), 195 (70), 181 (57), 167 (44), 153 (68); Anal Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.57; H, 9.29.

5,6-Diethoxy-4-methyltricyclo[5.3.0.0^{1,4}]dec-5-en-3-one (16l). *oil* (Elution H-A 25:1); IR (neat) 1773, 1669 cm^{-1}; ^{1}H NMR δ 1.17 (3 H, s), 1.21 (3 H, t, *J*=7.0 Hz), 1.27 (3 H, t, *J*=7.0 Hz), 1.35-1.95 (6 H, m), 2.86 (1 H, dd, *J*=9.0, 4.0 Hz), 3.02 (1 H, d, *J* =18.4 Hz), 3.14 (1 H, d, *J* =18.4 Hz), 3.76 and 3.99 (each 1 H, dq, *J* =9.6, 7.0 Hz), 4.02 (2 H, q, *J* =7.0 Hz); ^{13}C NMR δ 11.8, 15.3, 15.6, 26.5, 31.0, 33.0, 42.6, 52.0, 54.6, 65.5, 66.6, 72.6, 131.2, 141.4, 211.6; MS (EI) *m/z* (rel. intensity) 250 (M^+, 7), 222 (100), 193 (40), 177 (24), 165 (94); Anal Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 72.02; H, 8.81.

Ring Expansion of Tricyclo[5.3.0.0^{1,4}]decenone 16l.

To a solution of **16l** (52 mg, 0.21 mmol) and *tert*-butyl diazoacetate (44 mg, 0.31 mmol) in dry dichloromethane (2 ml) was added BF_3•Et_2O (0.029 mL, 0.23 mmol) at 0 °C. After stirring for 30 min, the reaction mixture was quenched with 10% $NaHCO_3$ (5 mL) and extracted with dichloromethane (5 mL × 3). The extracts were dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 20:1) gave a triquinane derivative, *tert*-butyl 6,7-diethoxy-8-methyl-9-oxotricyclo[6.3.0.0^{1,5}]undec-6-ene-10-carboxylate **20** (41 mg, 54%) as a colorless oil; IR (neat) 1750, 1723, 1684 cm^{-1}; ^{1}H NMR δ 1.11 (3 H, s), 1.20 (3 H, t, *J*=7.0 Hz), 1.24 (3 H, t, *J*=7.0 Hz), 1.35-1.95 (6 H, m), 1.48 (9 H, S), 2.04 (1 H, d, *J*=12.8 Hz), 2.05 (1 H, d, *J* =9.0 Hz), 2.80 (1 H, dd, *J* =6.0, 4.8 Hz), 3.48 (1 H, dd, *J* =12.8, 9.0 Hz), 3.75 and 3.93 (each 1 H, dq, *J* =9.6, 7.0 Hz), 3.92 and 4.00 (each 1 H, dq, *J* =9.4, 7.0 Hz); ^{13}C NMR δ 14.2, 15.5, 15.6, 25.1, 28.1, 28.2 (3 C), 29.9, 36.5, 36.6, 50.7, 52.1, 53.8, 65.3, 67.4, 81.8, 134.1, 138.3, 169.5, 211.2; MS (EI)

m/z (rel. intensity) 64 (M^+, 3), 290 (10), 250 (17), 208 (100), 179 (36), 151 (17); Anal Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 69.26; H, 8.79.

Synthesis of Oxaspiro[3.5]nonenone 21 and Conversion to Oxatricyclo-[5.4.0.0^{2,5}]undecenone 22.

To a solution of **11a** (62 mg, 0.29 mmol) and **14g** (100 mg, 0.58 mmol) in dry dichloromethane (2 mL) was added BF_3•Et_2O (0.044 mL, 0.35 mmol) at 0 °C under a nitrogen atmosphere. After stirring for 0.5 h, the reaction mixture was quenched with 10% $NaHCO_3$ (5 mL) and extracted with dichloromethane (5 mL × 3). The extracts were dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue eluted with H-A 8:1 and then with H-A 4:1 gave the first diastereomer of **21** (12 mg, 19%) followed by the second diastereomer (47 mg, 73%). Thermolysis of **21** was carried out in the similar manner as described for **16** to give **22** in 94% yield.

Spectral data of the first eluted diastereomer. *oil*; IR (neat) 1755, 1624 cm^{-1}; ^1H NMR δ 1.43 (3 H, t, *J*=7.0 Hz), 1.70 (3 H, s), 1.59-2.08 (4 H, m), 2.55 (1 H, m), 3.89-4.17 (2 H, m), 4.39 (2 H, q, *J* =7.0 Hz), 5.02 (1 H, ddd, *J*=10.2, 1.8, 0.6 Hz), 5.11 (1 H, ddd, *J*=17.2, 1.8, 1.0 Hz), 5.64 (1 H, ddd, *J*=17.2, 10.2, 8.6 Hz); ^{13}C NMR δ 6.6, 15.2, 25.5, 27.5, 43.2, 67.5, 68.4, 94.3, 116.9, 122.9, 138.2, 179.8, 192.3; MS (EI) *m/z* (rel. intensity) 222 (M^+, 85), 194 (97), 165 (100), 149 (19), 137 (29); Anal Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.34; H, 8.06.

Spectral data of the second eluted diastereomer. *oil*; IR (neat) 1765, 1620 cm^{-1}; ^1H NMR δ 1.46 (3 H, t, *J*=7.0 Hz), 1.62-2.00 (4 H, m), 1.76 (3 H, s), 2.63 (1 H, m), 3.77-4.10 (2 H, m), 4.44 (2 H, q, *J* =7.0 Hz), 4.99-5.17 (2 H, m), 5.69 (1 H, m); ^{13}C NMR δ 7.1, 15.2, 24.6, 26.6, 41.0, 66.7, 68.9, 93.8, 116.7, 122.4, 137.5, 182.3, 190.8; MS (EI) *m/z* (rel. intensity) 222 (M^+, 52), 194 (96), 165 (100), 149 (19), 137 (33); Anal Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.24; H, 8.16.

Spectral data of 6-Ethoxy-5-methyl-8-oxatricyclo[5.4.0.$0^{2,5}$]undec-6-en-4-one (22). *oil* (Elution H-A 10:1); IR (neat) 1775, 1682 cm^{-1}; ^1H NMR δ 1.21 (3 H, t, *J*=7.0 Hz), 1.28 (3 H, s), 1.37-1.92 (4 H, m), 2.39 (1 H, ddd, *J*=8.6, 7.4, 6.6 Hz), 2.84 (1 H, m), 2.85 (1 H, dd, *J* =17.6, 8.6 Hz), 3.29 (1 H, dd, *J* =17.6, 6.6 Hz), 3.46 (1 H, m), 3.99 and 4.06 (each 1 H, dq, *J* =10.2, 7.0 Hz), 3.89-4.17 (1 H, m); ^{13}C NMR δ 14.6, 15.3, 23.7, 24.7, 33.2, 37.7, 45.0, 66.3, 68.9, 72.1, 133.1, 133.3, 209.3; MS (EI) *m/z* (rel. intensity) 222 (M^+, 17), 194 (100), 165 (91), 151 (30), 137 (39); Anal Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.34; H, 8.06.

Addition of Cyclobutenedione Monoacetal 11b to Allenylsilane 25.

To a solution of **11b** (231 mg, 0.83 mmol) and BF_3•Et_2O (0.21 mL, 1.67 mmol) in dry dichloromethane (2 mL) was added dropwise a solution of allenylsilane **25** (316 mg, 2.50 mmol) in dry dichloromethane (2 mL) at 0 °C under a nitrogen atmosphere. After stirring for 1 h, the same work-up as for **14a** and flash chromatography (Elution H-A 10:1) gave 4-(2-butynyl)-3,4-diethoxy-2-phenyl-2-cyclobutenone (**26**) (85 mg, 36 %) as a colorless oil; IR (neat) 2238, 1759, 1632, 1599 cm^{-1}; ^1H NMR δ 1.23 (3 H, t, *J*=7.0 Hz), 1.55 (3 H, t, *J*=7.0 Hz), 1.66 (3 H, t, *J*=2.6 Hz), 2.68 and 2.97 (each 1 H, dq, *J*=17.4, 2.6 Hz), 3.58 and 3.68 (each 1 H, dq, *J* =9.0, 7.0 Hz), 4.57 (2 H, q, *J* =7.0 Hz), 7.24-7.43 (3 H, m), 7.77-7.83 (2 H, m); ^{13}C NMR δ 3.5, 15.4, 15.5, 24.1, 31.0, 61.6, 69.5, 73.0, 80.4, 98.1, 126.0, 127.4 (2 C), 128.4, 128.8 (2 C), 181.3, 189.2; MS (EI) *m/z* (rel. intensity) 284 (M^+, 76), 255 (100), 227 (92) 145 (78); Anal Calcd for $C_{18}H_{20}O_3$: C, 76.03; H, 7.09. Found: C, 76.01; H, 7.11.

Addition of Cyclobutenedione Monoacetal 11a to Silyl Enol Ether 31.

To a solution of **11a** (162 mg, 0.70 mmol) and **31** (403 mg, 2.10 mmol) in dry dichloromethane (2 mL) was added BF_3•Et_2O (0.11 mL, 0.84 mmol) at 0 °C under a nitrogen atmosphere. After stirring for 5 h, the work-up as above and flash chromatography (Elution H-

A 4:1) gave 3,4-diethoxy-2-methyl-4-phenacylmethyl-2-cyclobutenone (**32**) (159 mg, 73 %) as a pale-yellow oil; IR (neat) 1763, 1680, 1622 cm^{-1}; ^1H NMR δ 1.19 (3 H, t, *J*=7.0 Hz), 1.43 (3 H, t, *J*=7.0 Hz), 1.69 (3 H, s), 3.33 and 3.63 (each 1 H, d, *J*=15.2 Hz), 3.50 and 3.57 (each 1 H, dq, *J* =8.8, 7.0 Hz), 4.40 and 4.48 (each 1 H, dq, *J* =9.8, 7.0 Hz), 7.40-7.61 (3 H, m), 7.94-8.00 (2 H, m); ^{13}C NMR δ 6.5, 15.1, 15.3, 40.9, 60.3, 68.8, 94.3, 124.2, 128.8 (2 C), 129.0 (2 C), 133.6, 137.4, 182.7, 192.0, 197.5; MS (EI) *m/z* (rel. intensity) 288 (M^+, 25), 260 (5), 244 (6), 183 (36), 155 (57), 127 (100); Anal Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 6.99. Found: C, 70.80; H, 7.00.

Addition of Cyclobutenedione Monoacetal 11a to Silyl Ketene Acetal 33.

To a solution of **11a** (147 mg, 0.69 mmol) and **33** (458 mg, 2.10 mmol) in dry dichloromethane (2 mL) was added trimethylsilyl triflate (2.3 M in dichloromethane; 0.15 mL, 0.35 mmol) at room temperature under a nitrogen atmosphere. After stirring for 3 h, the same work-up as above and flash chromatography (Elution H-A 4:1) gave benzyl (1,2-diethoxy-3-methyl-4-oxo-2-cyclobutenyl)acetate (**34**) (71 mg, 33 %) as a pale-yellow oil; IR (neat) 1765, 1738, 1624 cm^{-1}; ^1H NMR δ 1.18 (3 H, t, *J*=7.0 Hz), 1.39 (3 H, t, *J*=7.0 Hz), 1.61 (3 H, s), 2.83 and 2.98 (each 1 H, d, *J*=14.4 Hz), 3.47 and 3.54 (each 1 H, dq, *J* =9.0, 7.0 Hz), 4.32 and 4.39 (each 1 H, dq, *J* =9.8, 7.0 Hz), 5.06 and 5.13 (each 1 H, d, *J*=12.2 Hz), 7.33-7.36 (5 H, m); ^{13}C NMR δ 6.4, 15.0, 15.3, 38.1, 60.6, 66.7, 68.7, 93.8, 124.2, 128.6, 128.7 (2 C), 128.8 (2 C), 136.0, 169.4, 182.1, 191.4; MS (EI) *m/z* (rel. intensity) 318 (M^+, 100), 290 (24), 227 (6), 199 (24), 155 (53); Anal Calcd for $C_{18}H_{22}O_5$: C, 67.91; H, 6.97. Found: C, 67.92; H, 6.96.

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Chapter 3

Reaction of Alkoxycarbenium Ion Spiecies Generated from Squaric Acid Esters with Unsaturated Organosilanes

Section 3

Unprecedented 1,2-Silyl Migrative Ring-expansion Reaction of Cyclobutenedione Monoacetal with Alkynylsilane

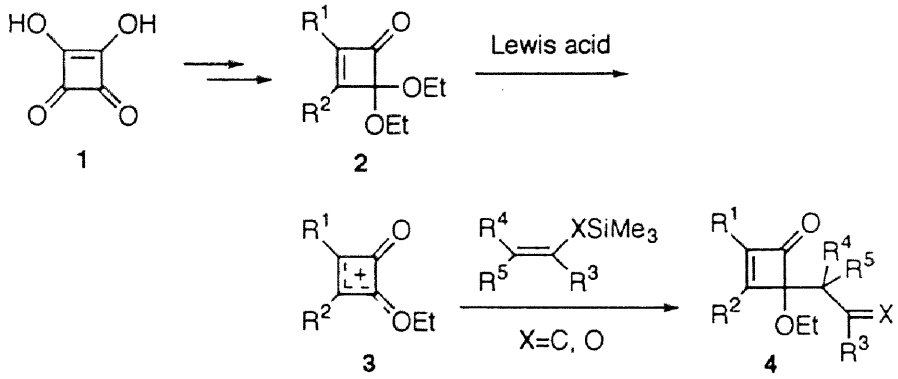
Abstract: An ethoxycarbenium ion intermediate, which was produced by the catalytic action of a Lewis acid on a cyclobutenedione monoacetal, reacted with phenyl(trimethylsilyl)acetylene at 0 °C to give a normal electrophilic substitution product. In sharp contrast, the same catalytic reaction with bis(trimethylsilyl)acetylene afforded a 2-methylene-4-cyclopentene-1,3-dione derivative instead of an alkynylation product. Butyl(trimethylsilyl)acetylene showed reactivity between them. This unprecedented rearrangement resulted from 1,2-silyl migration and subsequent ring-expansion of the formed vinyl cation intermediate. In the reactions of some alkyl-substituted silylacetylenes, both *E*- and *Z*-isomer of 2-(1-silylalkylidene)cyclopentene-diones were obtained, the ratio of which was found to be dependent on the reaction temperature and the amount of Lewis acid. The mechanism of the novel ring expansion induced by 1,2-silyl migration is discussed with the aid of semiempirical calculations.

2-Alkylidene-4-cyclopentene-1,3-dione, an attractive building block for synthesis of cyclopentanoids,[1] is accessible from ring-expansion routes starting from squaric acid. Liebeskind and co-workers have developed palladium- and mercury-catalyzed rearrangement of 4-alkynyl-4-hydroxycyclobutenones to a variety of 2-alkylidene-4-cyclopentene-1,3-dione derivatives.[2] The auther also found the similar type of reaction to furnish 2-iodomethylene-4-cyclopentene-1,3-diones, in which ionic rearrangement of a hypoiodite intermediate is believed to be involved.[3] These reactions are based on 1,2-acyl migration at the ring-expansion step. Moore *et al.* found that analogous ring-expansion products can be obtained by thermolysis of properly substituted 4-alkynylcyclobutenone.[4] On the other hand, Liebeskind demonstrated alternative [4+1] cycloaddition route using the reaction of covaltacyclopentenedione with terminal acetylenes.[5]

During the search for electrophilic addition reactions of cyclobutenedione monoacetal with alkynylsilanes, we found a novel type of ring expansion which was induced by 1,2-silyl migration. The 1,2-silyl migration is documented recently as a key step for ring construction based on allenyl-, allyl- and vinylsilanes.[6] In our case this migration was observed in the reaction of alkynylsilanes as the first example. This section deals with the silyl-migration aptitude of various alkynylsilanes, and the following ring-expansion process, which is best explained by Nazarov-type electronic cyclization on the basis of semiempirical calculations. The present method is intriguing as an alternative formal [4+1] route.

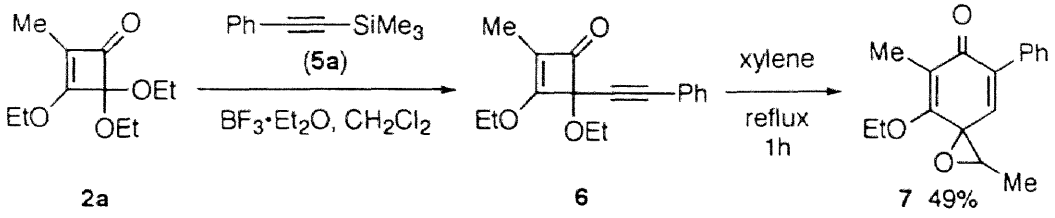
Results

In the previous section, the auther reported that catalytic action of a Lewis acid on monoacetal **2** prepared from commercially available squaric acid **1** could produced an ethoxycarbenium ion species **3**, which followingly reacted with allylsilane, silyl enol ether, and silyl ketene acetal regioselectively to afford adducts **4** (Scheme 1). This type of reaction using silylacetylenes was further studied. First examined was phenyl-substituted case (Scheme 2). Thus, phenyl(trimethylsilyl)acetylene **5a** (3 equiv.) was allowed to react with monoacetal **2a** in the



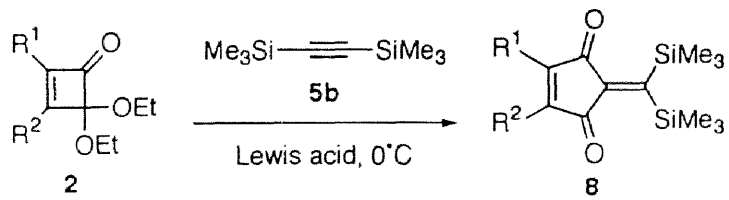
Scheme 1

presense of BF_3•Et_2O (1.2 equiv.) at 0 °C for 24h, and the expected 4-alkynyl-4-ethoxycyclobutenone **6** was obtained in 29 % yield after standard work-up and chromatographic separation. The yield was increased up to 81 % by use of 5 equivalents of the reagent, but the yield was rather low when the reaction was conducted at room temperature for 1h. The structural determination was based on the spectral inspections: MS peak at *m/z* 270 (M^+), IR absorption at 2224 cm^{-1} due to an alkynyl group and at 1769 and 1626 cm^{-1} due to an enone group, and ^1H NMR signals of two ethoxy groups and a phenyl group at δ 7.29-7.36 and 7.44-7.50 ppm. The obtained adduct **6** was transformed to an oxaspiro[2.5]heptadienone **7** according to the known process.[4] In sharp contrast, the reaction of **2a** with bis(trimethylsilyl)acetylene **5b** gave no alkynylation product such as **6** under the same conditions, but instead a less polar product was detected on TLC analysis. The IR spectrum showed no alkynyl absorption but a carbonyl absorption at 1682 cm^{-1}, which was no longer ascribable to a four-membered ketone. The ^1H NMR spectrum revealed the presence of two different trimethylsilyl groups together with only one ethoxy group. More importantly, the ^{13}C spectrum consisted of all sp^2-carbon signals (δ 134.8, 150.2, 167.0, 174.8, 188.3, and 191.0 ppm) except those of substituents. The molecular ion peak (M^+, *m/z* 310) in the mass spectrum and the elemental analysis supported the deacetalization. These data allowed to assign the structure as 2-[bis(trimethylsilyl)methylene]-4-ethoxy-5-methyl-4-cyclopentene-1,3-dione (**8a**) (Scheme 3). Table 1 shows optimization of the reaction conditions. While increasing amount of



Scheme 2

BF_3•Et_2O and silylacetylene improved the yield from 13 % to 50 % (entries a-d), a catalyst was critical; $TiCl_4$ (entry e), and more efficiently, $SnCl_4$ raised the yield up to 85 % (entry f). Under these catalytic conditions, phenyl-substituted **2b** (R^1=Ph, R^2=OEt) and alkynyl-substituted **2c** (R^1=PhC≡C, R^2=OEt) gave corresponding cyclopentenedione **8b** and **8c** (entries g and f) in moderate yields. The reaction of dimethyl-substituted monoacetal **2d** (R^1=R^2=Me) affirmed the above structural assignment (entry h); the ^{1}H NMR spectrum of the desired symmetrical product **8d** exhibited only a couple of singlet signals due to allylic methyl and trimethylsilyl groups, and the ^{13}C NMR spectrum only two sp^3-carbon and four sp^2-carbon signals. The reaction of 3-phenyl-substituted **2e** resulted in low yield even after prolonged reaction time probably because of a steric effect of a phenyl group at C_3 (entry i).



Scheme 3

The above results showed the different rearrangement aptitude between phenyl(trimethylsilyl)acetylene **5a** and bis(trimethylsilyl)acetylene **5b**. Obviously a substitutent on the acetylene influenced switching of the reaction course. Hence, we next investigated the reaction with various alkyl-substituted silylacetylenes. First, acetal **2a** was reacted with a butyl-substituted **5c** (3 equiv.) in the presence of BF_3•Et_2O (1.2 equiv.) at 0 °C for 24 h, and in this case, a ring-expansion product **9** with *E*/*Z* ratio of 81/19[7] and an alkynylation product **10** were obtained in 19 and 15 % yields, respectively (Scheme 4, Table 2). The stereoisomerism of the

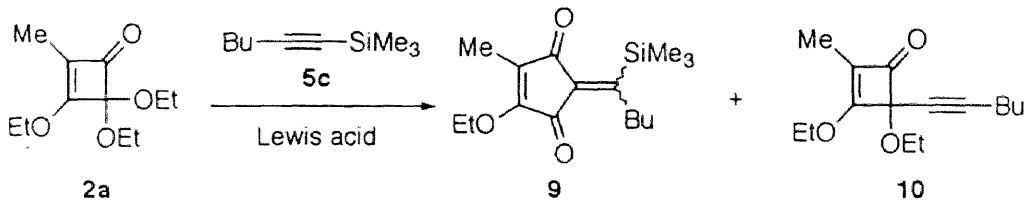
Table 1. Synthesis of Cyclopentenedione **8a-e** from acetals **2a-e**.

entry	2	R^1	R^2	Lewis acid (equiv.)	acetylene (equiv.)	time (h)	8 yield (%)
a	**2a**	Me	OEt	BF_3•OEt_2 (1.2)	3	24	**8a** (13)[a]
b	**2a**	Me	OEt	BF_3•OEt_2 (2)	3	24	**8a** (36)[a]
c	**2a**	Me	OEt	BF_3•OEt_2 (2)	6	24	**8a** (37)[a]
d	**2a**	Me	OEt	BF_3•OEt_2 (3)	6	24	**8a** (50)[a]
e	**2a**	Me	OEt	$TiCl_4$ (1.2)	3	1	**8a** (41)
f	**2a**	Me	OEt	$SnCl_4$ (1.2)	3	1	**8a** (85)
g	**2b**	Ph	OEt	$SnCl_4$ (1.2)	3	3	**8b** (63)
h	**2c**	PhC≡C	OEt	$SnCl_4$ (1.2)	3	1	**8c** (35)
i	**2d**	Me	Me	$SnCl_4$ (1.2)	3	1	**8d** (57)
j	**2e**	Me	Ph	$SnCl_4$ (1.2)	3	18	**8e** (19)[a]

[a]Deacetalized cyclobutene-1,2-diones were recovered in 66 % (entry a), 49 % (entry b), 32 % (entry c), 30 % (entry d), and 35 % (entry j) yields, respectively.

exo-olefin was influenced by reaction temperature and Lewis acid. From 0 °C to 10 °C, population of the *Z*-isomer was gradually increased (entries a-c), and the *E/Z* ratio was inversed and reached almost constant of ca. 3/7 at 0 °C-20 °C with 2 equivalents of BF_3•Et_2O (entries d-f). The best yield (49 %) of ring-expansion product **9** was attained by use of $SnCl_4$ (1.2 equiv.) (entry g). In this manner, reaction of **2a** with (hex-5-en-1-ynyl)trimethysilane **5d** afforded the corresponding product **11** with a comparable yield and *E/Z* ratio (Scheme 5). Similarly, the reaction of silylacetylenes such as methoxymethyl-substituted **5e** and benzyl-substituted **5f** gave cyclopentenediones **12** and **13**[8] in fair yields, but those of bromomethyl-substituted **5g** and unsubstituted **5h** resulted in low yield or worsely no product formed. In the

cases of **11-14**, alkynylation by-products were uncharacterized because they could not be isolated with an enough amount for analysis.

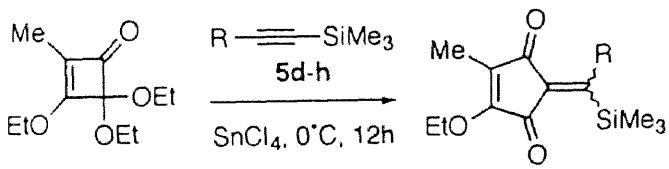


Scheme 4

Table 2. Reaction of Monoacetal **2a** and Alkynylsilane **5c**

entry	Lewis acid (equiv.)	temperature (°C)	time (h)	**9** yield (%) [*E*/*Z*][a]	**10** yield (%)
a	BF_3•OEt_2 (1.2)	0	24	19 [81/19]	15
b	BF_3•OEt_2 (1.2)	5	24	23 [56/44]	19
c	BF_3•OEt_2 (1.2)	10	24	24 [41/59]	18
d	BF_3•OEt_2 (2.0)	0	24	32 [28/72]	25
e	BF_3•OEt_2 (2.0)	10	24	31 [30/70]	21
f	BF_3•OEt_2 (2.0)	20	24	29 [29/71]	11
g	$SnCl_4$ (1.2)	0	1	49 [39/61]	13

[a]The *E*/*Z* ratio of **9** was determined by ^{1}H-NMR spectrum.



11: R=$(CH_2)_2CH{=}CH_2$, 45% (*E*/*Z*=43/67)
12: R=CH_2OMe, 34% (*E*/*Z*=21/79)
13: R=CH_2Ph, 32% (ND)
14: R=CH_2Br, 12% (*E*/*Z*=42/68)
15: R=H, 0%

Scheme 5

The stereochemistry of **9** was deduced by relative chemical shifts of trimethylsilyl and allylic methylene groups. As indicated in Figure 1, standard *E*- and *Z*-2-(1-trimethylsilyl-3-butenylidene)cyclopentenediones **17** (ratio: 79/21) were prepared from 4-hydroxy-4-trimethylsilylethynylcyclobutenone **16** by the Liebeskind's procedure,[2a] and compared with **9** obtained in entry a (Table 2); in the ^{1}H NMR spectra of these definite *E/Z* isomers, relative chemical shifts of the substituents at an allylic position due to major and minor isomers of **17** were well fitted with those of the corresponding isomers of **9**. Likewise the *E/Z* relationship of the other products **11-14** was determined and summarized in Scheme 5.

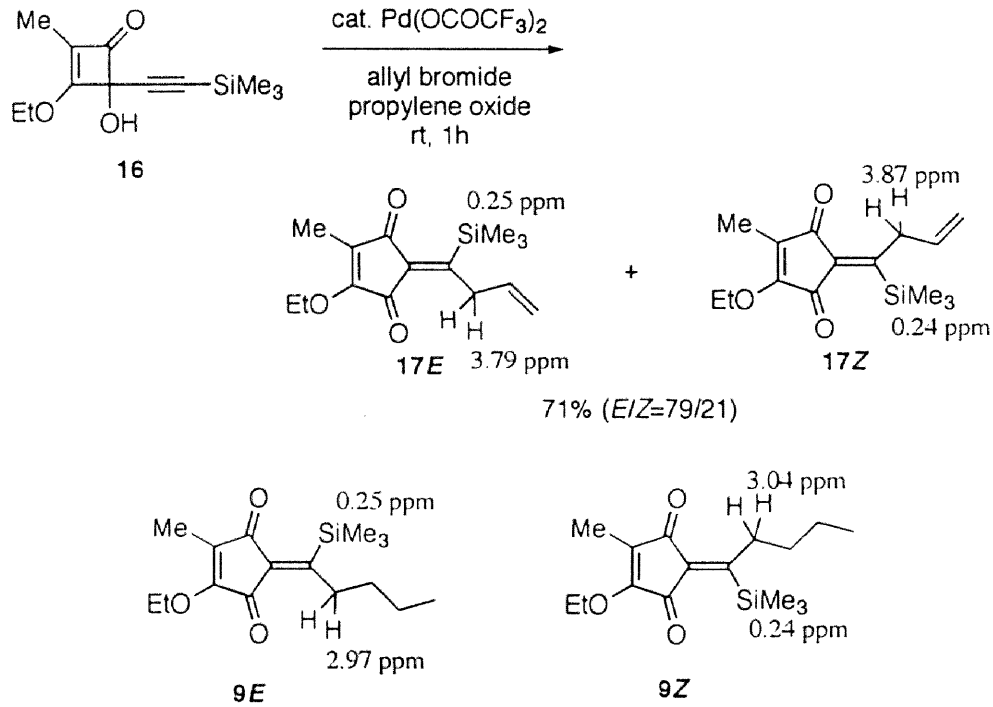
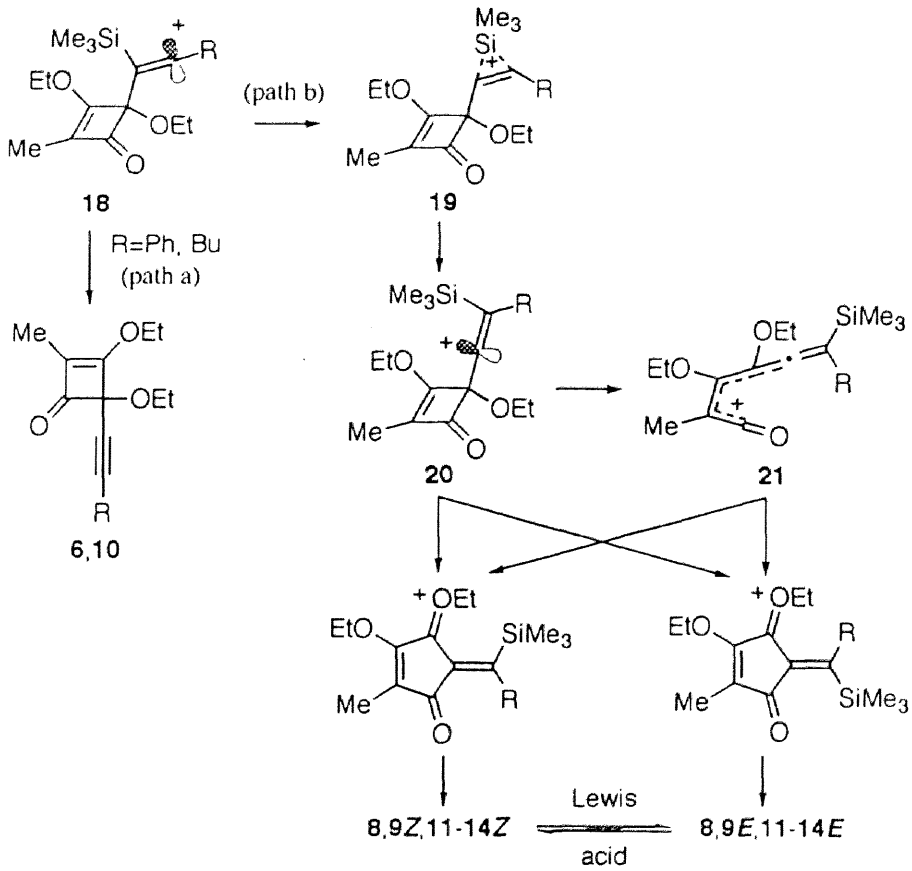


Figure 1

Discussion

Scheme 6 shows plausible mechanisms for the formation of alkynylation products **6,10** and ring-expansion products **8,9,11-14**. The reaction of ethoxycarbenium ion **3** and a silylacetylene **5** produces a vinyl cation intermediate **18**, which isomerizes to the other vinyl

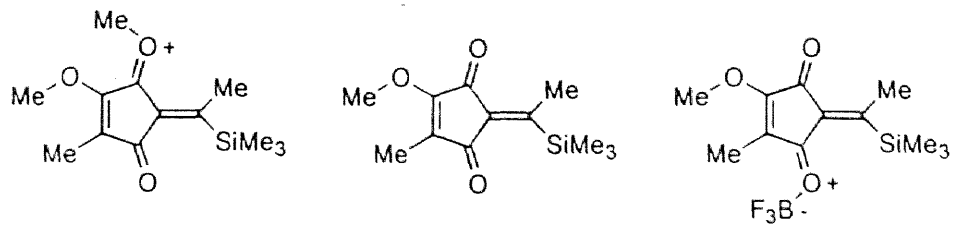
cation intermediate **20** *via* 1,2-silyl migration. At this stage, an acetylenic substituent R plays an important role to determine the course of reaction (path a *vs.* path b). In the case of phenyl(trimethylsilyl)acetylene (**5a**), the benzylic stabilization (*i.e.*, **18** R=Ph) allows straightforward desilylation (path a) to give 4-phenylethynylcyclobutenone **6**. In contrast, bis(trimethylsilyl)acetylene **5b** gave exclusively bis(trimethylsilyl)methylenecyclopentenedione **8** after 1,2-silyl migration (path b), because the rearranged cation **20** is more stabilized by β-effect of two silyl groups than the primarily formed cation **18**. Thus formed **20** is responsible for the following ring-expansion *via* two possible routes: simple 1,2-acyl shift followed by Nazarov-type after electrocyclization ring opening to pentadienoyl cation (see below). On the other hand, (1-hexynyl)trimethylsilane **5c** showed intermediate reactivity between **5a** and **5b** reactivity affording both the ring expansion product **9** and the alkynylation product **10**.



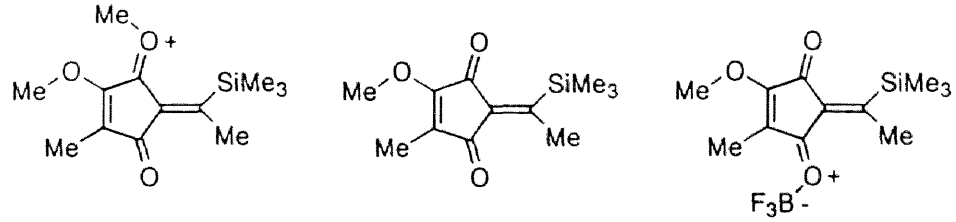
Scheme 6

The reaction of acetal **2a** with unsymmetrical acetylenes **5c-g** afforded a stereoisomeric mixture of 2-[(1-trimethylsilyl)alkylidene]-4-cyclopentene-1,3-diones. As described before, the *E/Z* ratio of the product **9** varied depending on the reaction conditions; the *E*-isomer of **9** was formed predominantly by employing 1.2 equivalents of BF_3•Et_2O at 0 °C, whereas the *Z*-isomer is favored at higher temperature, in excess amount of BF_3•Et_2O, and with a stronger Lewis acid such as $SnCl_4$. These observations suggest that the *E*-isomer was initially produced and converted into the thermodynamically favored *Z*-isomer by subsequent Lewis acid-catalyzed geometrical isomerization. Thus, a direct route to the *Z*-isomer *via* simultaneous stereospecific 1,2-acyl migration through a silyl-bridged cation **19** can be excluded. Then we considered predominancy of the *Z*-isomer over the *E*-isomer arising from the apparently participating vinyl cation intermediate **20**. To this end, stability of the model intermediates **22*E***, **22*Z*** and the corresponding products **23*E***, **23*Z*** were estimated by use of semiempirical calculations (Figure 2).[9] These were performed with the PM3 hamiltonian[10] involved in the MOPAC pakage. First, structure optimizations of metoxycarbenium ion intermediates **22** and cyclopentenediones **23** were carried out by the EF routine with the keyword PRECISE. As a result, it was revealed that the intermediate **22*E*** has a comparable energy to the *Z*-counterpart, but the product **23*E*** is 0.8 kcal/mol more stable than **23*Z***. This result may agree with the initial formation of **9*E***. Further calculation for BF_3 complex **24** supports the Lewis acid-catalyzed geometrical isomerization of **9**. In this case, the AM1 hamiltonian[11] was used since parameters for a boron atom are not available in PM3 calculations.[10] As shown in Figure 2, the coordination of BF_3 catalyst is estimated to be favored across b-methoxy enone moiety to produce thermodynamically more stable complex. In this situation, **24*Z*** was calculated to be more stable than **24*E*** by 0.3 kcal/mol. Hence, the initially produced **9*E*** is possibly converted into the more favorable *Z*-isomer with the aid of Lewis acid, as depicted in Scheme 7.

A possible ring-expansion pathway from the above intermediate **20** to **8,9,11-14** could be rationalized by considering ring opening to a strain-relieved and delocalized cation intermediate **21** and subsequent Nazarov type ring-closure. Semiempirical calculations support

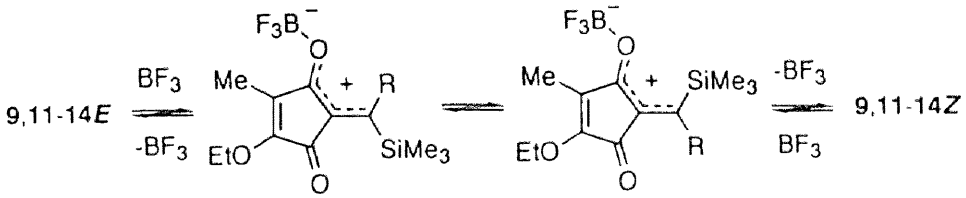


22*E* 50.3 kcal/mol　　23*E* -124.8 kcal/mol　　24*E* -387.5 kcal/mol



22*Z* 50.3 kcal/mol　　23*Z* -124.0 kcal/mol　　24*Z* -387.8 kcal/mol

Figure 2. Calculated Heat of Formations



Scheme 7

this option. For simplicity, we calculated the process of ring opening of the vinyl cation **25** and ring closure of the resulted cation **26**. Structures of intermediates **25**, **27**, transition states **26**, **28**, and a product cation **29** were fully optimized by the EF routine with the keyword PRECISE. The resulting transition structures were subjected to a vibrational analysis, and in each case, only one imaginary frequency was found. The obtained structures and corresponding heat of formations are summarized in Figure 3. These calculations revealed that the ring-opened **27** has a U-shaped structure and is 24.9 kcal/mol more stable than the parent vinyl cation **25**. The low energy barrier (2.6 kcal/mol) reflects the facile ring opening (**25** → **27**). Finally, Nazarov type cyclization of **27** proceeds with 15.7 kcal/mol energy barrier to afford a product cation **29**, which is 14.2 kcal/mol more stable than **27**. Thus, the process including these two steps seems to be a more reasonable route for the present ring-expansion

reaction. In this case, the stereochemistry of the primarily formed product is controlled by a torquoselectivity at the final Nazarov cyclization step. The energy profile is outlined in Figure 4.

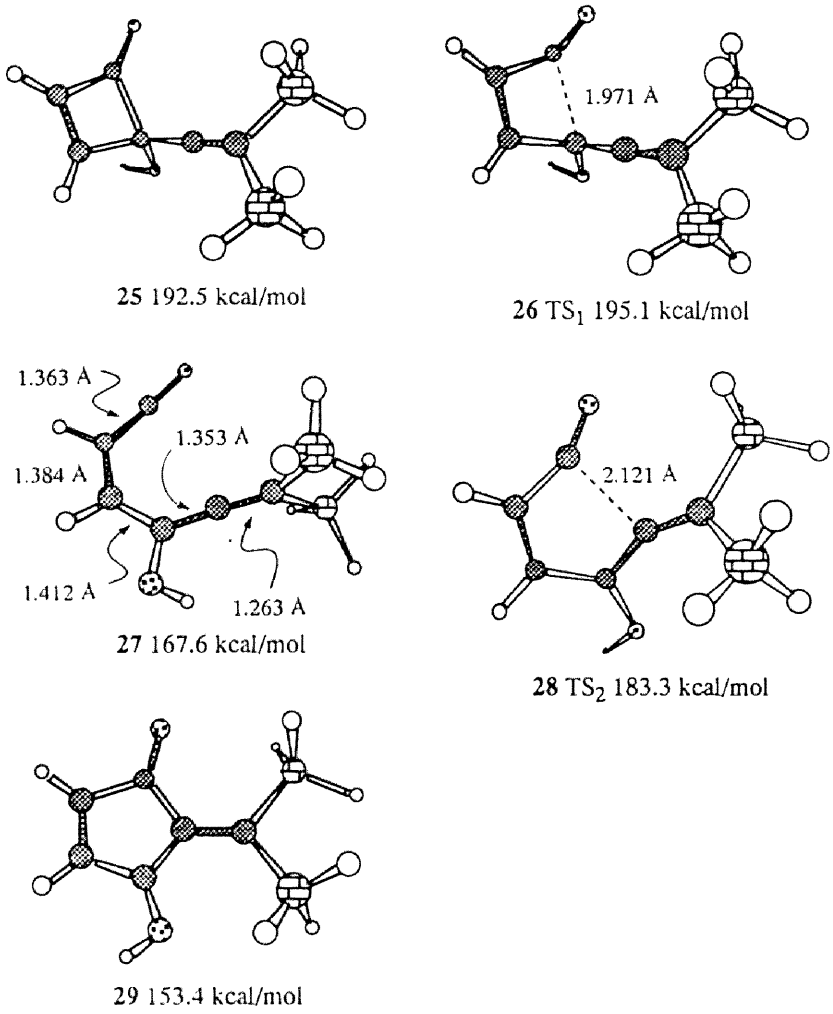


Figure 3. Optimized geometries and heat of formations of **19-23.**

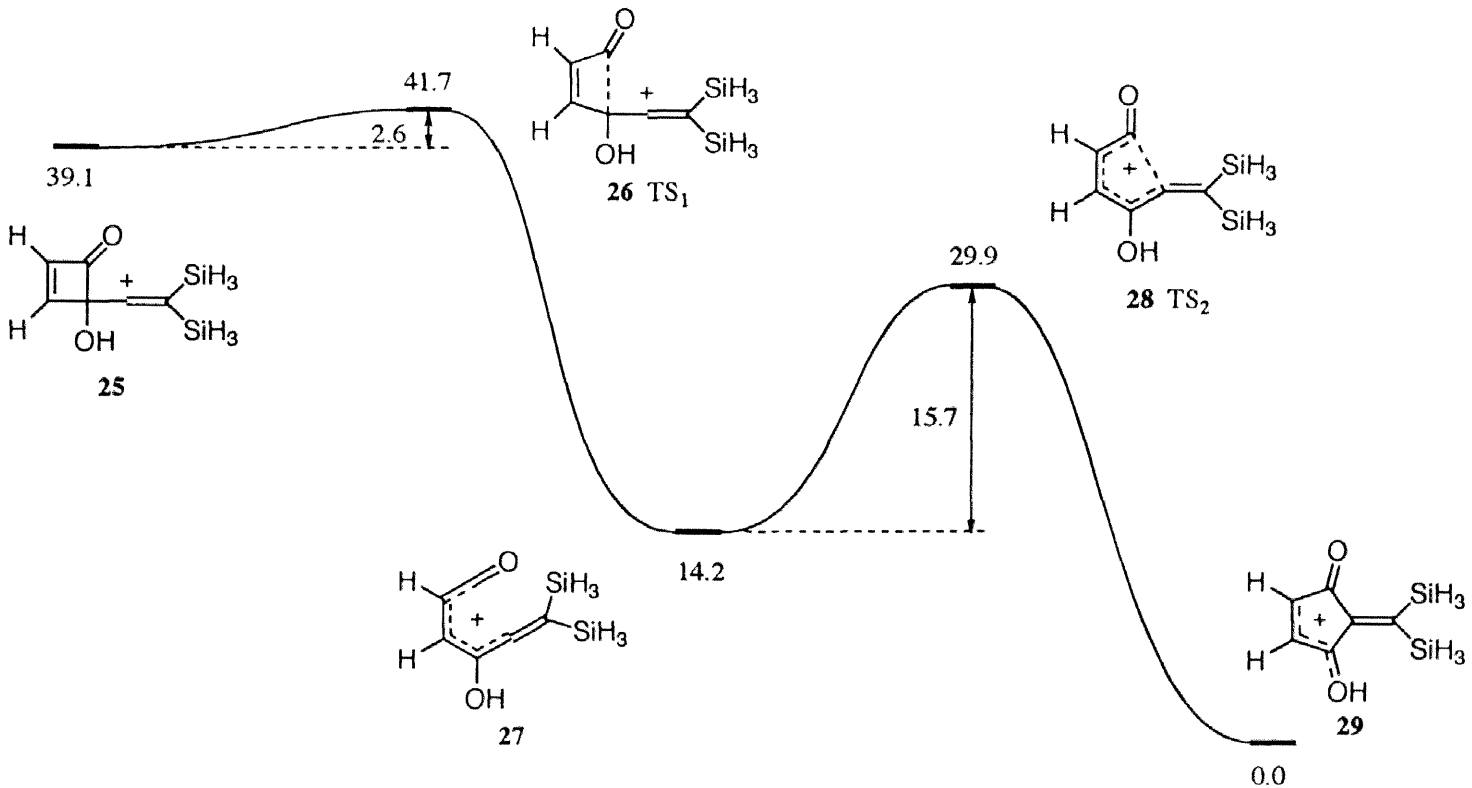


Figure 4. Schematic energy diagram for ring opening of **25** and Nazarov cyclization of resulted **27**. Indicated values show relative energies, ΔΔH in kcal/mol.

Conclusions

So far, cationic 1,2-silyl migration was mainly exploited in the cycloadition reactions using allenyl-, allyl-, and vinyltrialkylsilanes.[6] Particularly, this type of migration was often observed when bulky alkyl-substituents are placed on the silicon atom (probably to avoid the competitively occurring desilylation). In our hand, an unpresedented ring enlargement induced by 1,2-silyl migration emerged in the Lewis acid-catalyzed reaction of silylacetylenes with cyclobutenedione monoacetals. To our knowledge, the present 1,2-silyl migration is the first example on the alkynylsilane chemistry and for the ring-expansion reaction. This was significant in the reaction of bis(trimethylsilyl)acetylene since one of two silyl groups facilitated the migration of the other one, whereas phenyl-substituted silylacetylene gave a simple alkynylated product without the rearrangement and butyl-substituted silylacetylene gave both rearranged and alkynylated products. The similar reaction using some alkynylsilanes afforded *E*- and *Z*-isomers of (1-silylalkylidene)cyclopentenediones, in which the isomer ratio was dependent on the reaction temperature and the Lewis acid employed. Control experiments showed that the *E*-isomer was an initially formed product and converted to the *Z*-isomer by Lewis acid-catalyzed geometrical isomerization. From this result, it was suggested that the ring expansion proceeded with an acyl migration to an open vinyl cation rather than simultaneous silyl and acyl migrations through a silicon-bridged cation. Interestingly, a ring opening/Nazarov type ring-closure mechanism is considered as a possible ring-expansion route based on PM3 semiempirical calculations.

Experimental Section

General. IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ solution with $SiMe_4$ as an internal standard. Mass spectra were recorded on a JEOL JMS-AX 505 HA mass spectrometer. Flash chromatography was performed with a silica gel column (Fuji-Davison BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400S CHN elemental analyzer. Dichloromethane was dried over $CaCl_2$, distilled, and stored over 4Å molecular sieves. Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.

Synthesis of Cyclobutenedione Monoacetal 2d.

According to the reported procedure,[13] cyclobutenedione monoacetal **2d** was synthesized as follows; to a solution of monoacetal **2a** (2.13 g, 10.0 mmol) in dry THF (50 mL) was added methyllithium (30.0 mL, 31 mmol: 1.04 M solution in ether) at -78 °C under a nitrogen atmosphere, and the solution was stirred for 30 min. To this solution was added trifluoroacetic anhydride (2.1 mL, 15.0 mmol). The reaction mixture was stirred for 30 min, quenched with 10% $NaHCO_3$ (20 mL), and extracted with ether (20 mL × 3). The extracts were washed with brine (30 mL), dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 40:1) gave monoacetal **2d** (850 mg, 46%) as a colorless oil. Monoacetals **2a-c,e** were reported in the previous section.

4,4-Diethoxy-1,2-dimethyl-2-cyclobutenone (2d). IR (neat) 1765, 1644 cm^{-1}; ^1H NMR δ 1.23 (6 H, t, *J*=7.0 Hz), 1.75 (3 H, q, *J*=1.0 Hz), 2.17 (3 H, q, *J*=1.0 Hz), 3.74 (4 H, q, *J*=7.0 Hz); ^{13}C NMR δ 7.2, 11.5, 15.5 (2C), 61.1 (2C), 115.6, 152.7, 179.8, 195.7; MS (EI) *m/z* (rel. intensity) 184 (M^+, 2), 155 (25), 139 (13), 127 (100), 111 (18); Anal Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.50; H, 8.44.

Synthesis of 4-Alkynylcyclobutenone 6 and its Conversion to oxaspiro[2.5]octadienone 7.

To a solution of **2a** (129 mg, 0.57 mmol) and silylacetylene **5a** (316 mg, 2.50 mmol) in dry dichloromethane (2 mL) was added BF_3•Et_2O (0.091 mL, 0.72 mmol) at 0 °C under a nitrogen atmosphere. After stirring for 13 h, the reaction mixture was quenched with 10% $NaHCO_3$ (5 mL) and extracted with dichloromethane (5 mL × 3). The extracts were dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 8:1) gave 4-alkynylcyclobutenone **6a** (125 mg, 81 %) as a pale-yellow oil. Thermal rearrangement of **6** to **7** was carried out in the reported manner.[3]

3,4-Diethoxy-2-methyl-4-(phenylethynyl)-2-cyclobutenone (6). IR (neat) 2224, 1769, 1626 cm^{-1}; ^1H NMR δ 1.28 (3 H, t, *J*=7.0 Hz), 1.50 (3 H, t, *J*=7.0 Hz), 1.73 (3 H, s), 3.86 and 3.93 (each 1 H, dq, *J*=9.2, 7.0 Hz), 4.54 and 4.61 (each 1 H, dq, *J* =10.0, 7.0 Hz), 7.29-7.36 (3 H, m), 7.44-7.50 (2 H, m); ^{13}C NMR δ 6.6, 15.3, 15.6, 63.1, 69.4, 82.2, 88.3, 90.9, 122.3, 125.5, 128.7 (2 C), 129.3, 132.3 (2 C), 179.9, 186.8; MS (EI) *m/z* (rel. intensity) 270 (M^+, 12), 241 (37), 224 (73), 213 (100), 185 (59); Anal Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.57; H, 6.67.

4-Ethoxy-2,5-dimethyl-7-phenyl-1-oxaspiro[2,5]octa-4,7-dien-6-one (7). 49% (*ca.* 15:1 diastereomer mixture); *oil*; IR (neat) 1649, 1615 cm^{-1}; ^1H NMR (signals due to a minor isomer are indicated in bracket) δ 1.35 [1.37] (3 H, t, *J*=7.0 Hz) , 1.54 [1.72] (3 H, d, *J*=5.4 Hz), 1.97 [1.99] (3 H, s), 3.93 [3.92] (1 H, q, *J* =5.4 Hz), 3.98 and 4.08 [4.05 and 4.18] (each 1 H, dq, *J* =9.4, 7.0 Hz), 6.57 [6.37] (1 H, s), 7.34-7.45 (5 H, m); ^{13}C NMR δ 9.7, 14.5 [13.0], 15.8 [15.6], 58.1 [59.2], 61.6 [63.7], 70.3 [70.0], 127.7 [128.1], 128.5 [128.6] (2 C), 128.6 [128.3], 129.3 [129.1] (2 C), 136.1 [135.6], 138.6, 144.1 [143.8], 164.5, 186.8; MS (EI) *m/z* (rel. intensity) 270 (M^+, 36), 254 (100), 241 (53), 214 (29), 197 (89); Anal Calcd for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.49; H, 6.75.

Typical Procedure for Reaction of Cyclobutenedione Monoacetal 2 and Silylacetylene 5.

To a solution of monoacetal **2a** (146 mg, 0.68 mmol) and bis(trimethylsilyl)acetylene **5b** (348 mg, 2.04 mmol) in dry dichloromethane (2 mL) was added $SnCl_4$ (0.096 mL, 0.82 mmol) at 0 °C under a nitrogen atmosphere. After stirring for 1 h, the reaction mixture was quenched with 10% $NaHCO_3$ (5 mL) and extracted with dichloromethane (5 mL × 3). The extracts were dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 30:1) gave cyclopentenedione **8a** (179 mg, 85%) as a bright-yellow oil. Other cyclopentenediones **8b-e**,**9** and **11-14** were obtained according to the above procedure. Isolated yields are shown in Scheme 5 and Tables 1 and 2, in which the reactions of **2a-e** with **5b** and of **2a** with **5c** under various conditions are recorded.

2-[Bis(trimethylsilyl)methylene]-4-ethoxy-5-methyl-4-cyclopentene-1,3-dione (8a). IR (neat) 1682, 1620, 1248, 844 cm^{-1}; ^1H NMR δ 0.25 (9 H, s), 0.26 (9 H, s), 1.41 (3 H, t, *J*=7.0 Hz), 1.99 (3 H, s), 4.72 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 2.0 (3 C), 2.2 (3 C), 7.1, 15.9, 68.1, 134.8, 150.2, 167.0, 174.8, 188.3, 191.0; MS (EI) *m/z* (rel. intensity) 310 (M^+, 21), 295 (70), 281 (100), 267 (53), 251 (36); Anal Calcd for $C_{15}H_{26}O_3Si_2$: C, 58.02; H, 8.44. Found: C, 58.45; H, 8.00.

2-[Bis(trimethylsilyl)methylene]-4-ethoxy-5-phenyl-4-cyclopentene-1,3-dione (8b). mp. 82-85 °C; IR (KBr) 1672, 1585, 1246, 837 cm^{-1}; ^1H NMR δ 0.28 (9 H, s), 0.29 (9 H, s), 1.44 (3 H, t, *J*=7.0 Hz), 4.83 (2 H, q, *J*=7.0 Hz), 7.34-7.52 (3 H, m), 7.90-7.99 (2 H, m); ^{13}C NMR δ 2.0 (3 C), 2.3 (3 C), 16.0, 69.2, 128.6 (2 C), 129.3, 129.9, 130.2 (2 C), 132.4, 150.6, 165.6, 177.3, 188.5, 189.4; MS (EI) *m/z* (rel. intensity) 372 (M^+, 39), 357 (75), 343 (100), 329 (33), 313 (19); Anal Calcd for $C_{20}H_{28}O_3Si_2$: C, 64.47; H, 7.57. Found: C, 64.87; H, 7.17.

2-[Bis(trimethylsilyl)methylene]-4-ethoxy-5-phenylethynyl-4-cyclopentene-1,3-dione (8c). mp. 100-104 °C; IR (KBr) 2199, 1688, 1616, 1258, 849 cm^{-1}; ^1H NMR δ 0.27 (9 H, s), 0.30 (9 H, s), 1.56 (3 H, t, *J*=7.0 Hz), 4.93 (2 H, q, *J*=7.0 Hz), 7.34-7.42 (3

H, m), 7.52-7.58 (2 H, m); ^{13}C NMR δ 1.9 (3 C), 2.1 (3 C), 15.5, 69.0, 79.2, 107.1, 115.2, 122.5, 128.9 (2 C), 130.0, 132.1 (2 C), 148.2, 168.1, 182.6, 186.4, 187.6; MS (EI) *m/z* (rel. intensity) 396 (M^+, 26), 381 (100), 367 (38), 337 (5); Anal Calcd for $C_{22}H_{28}O_3Si_2$: C, 66.62; H, 7.12. Found: C, 66.63; H, 7.11.

2-[Bis(trimethylsilyl)methylene]-3,4-dimethyl-4-cyclopentene-1,3-dione (8d). IR (neat) 1686, 1640, 1246, 849 cm^{-1}; ^{1}H NMR δ 0.26 (18 H, s), 2.05 (6 H, s); ^{13}C NMR δ 2.0 (6 C), 9.2 (2 C), 149.0, 154.5 (2 C), 177.8, 193.4 (2 C); MS (EI) *m/z* (rel. intensity) 280 (M^+, 97), 265 (100), 250 (9), 237 (4); Anal Calcd for $C_{14}H_{24}O_2Si_2$: C, 59.94; H, 8.62. Found: C, 60.24; H, 8.24.

2-[Bis(trimethylsilyl)methylene]-3-methyl-4-phenyl-4-cyclopentene-1,3-dione (8e). mp. 67-70 °C; IR (neat) 1686, 1620, 1246, 845 cm^{-1}; ^{1}H NMR δ 0.30 (9 H, s), 0.31 (9 H, s), 2.24 (3 H, s), 7.45-7.57 (5 H, m); ^{13}C NMR δ 2.0 (3 C), 2.1 (3 C), 10.5, 128.9 (2 C), 129.9, 130.1 (2 C), 130.3, 149.1, 152.2, 153.6, 180.7, 192.0, 193.5; MS (EI) *m/z* (rel. intensity) 342 (M^+, 100), 327 (88), 312 (11), 299 (4); Anal Calcd for $C_{19}H_{26}O_2Si_2$: C, 66.61; H, 7.65. Found: C, 66.85; H, 7.41.

3-Ethoxy-4-methyl-2-[(1-trimethylsilyl)pentylidene]-4-cyclopentene-1,3-dione (9). IR (neat) 1680, 1628, 1246, 847 cm^{-1}; ^{1}H NMR signals due to *E*-isomer is indicated in brackets δ 0.24 [0.25] (9 H, s), 0.93 (3 H, t, *J*=7.4 Hz), 1.21-1.53 (4 H, m), 1.41 (3 H, t, *J*=7.0 Hz), 1.98 [1.97] (3 H, s), 3.04 [2.97] (2 H, t, *J*=7.4 Hz), 4.68 [4.69] (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ -0.5 [-0.2] (3 C), 7.0 (2 C), 13.9, 15.9, 23.3, 32.0 [31.6], 32.5 [32.3], 67.8, 133.6 [131.1], 134.4 [134.1], 164.9 [166.4], 170.7 [170.5], 189.9 [189.2], 192.4 [192.8]; MS (EI) *m/z* (rel. intensity) 294 (M^+, 100), 279 (72), 265 (31), 249 (77), 237 (30), 221 (99); Anal Calcd for $C_{16}H_{26}O_3Si$: C, 65.26; H, 8.90. Found: C, 65.20; H, 8.96.

3,4-Diethoxy-4-(1-hexynyl)-2-methyl-2-cyclobutenone (10). This was obtained with elution H-A 10:1 as a by-product after elution of **9**. IR (neat) 2232, 1771, 1634 cm^{-1}; ^{1}H NMR δ 0.91 (3 H, t, *J*=7.4 Hz), 1.23 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 1.32-1.55 (4 H, m), 1.68 (3 H, s), 2.29 (2 H, q, *J*=7.0 Hz), 3.74 and 3.82 (each 1 H, dq, *J*=9.2, 7.0

Hz), 4.48 and 4.55 (each 1 H, dq, *J*=9.8, 7.0 Hz); ^{13}C NMR δ 6.5, 13.6, 15.2, 15.5, 18.8, 22.0, 30.5, 62.6, 69.1, 73.2, 88.0, 92.4, 125.0, 180.5, 187.7; MS (EI) *m/z* (rel. intensity) 250 (M^+, 36), 221 (100), 205 (8), 193 (57), 165 (28); Anal Calcd for $C_{15}H_{20}O_3$: C, 71.97; H, 8.86. Found: C, 71.99; H, 8.84.

3-Ethoxy-4-methyl-2-[1-(trimethylsilyl)-4-pentenylidene]-4-cyclopentene-1,3-dione (11). IR (neat) 1680, 1624, 1246, 845 cm^{-1}; ^{1}H NMR signals due to *E*-isomer is indicated in brackets δ 0.24 [0.25] (9 H, s), 1.41 (3 H, t, *J*=7.0 Hz), 1.99 [1.98] (3 H, s), 2.10 (2 H, m), 3.13 [3.12] (2 H, q, *J*=7.6 Hz), 4.72 [4.68] (2 H, q, *J*=7.0 Hz), 4.93-5.10 (2 H, m), 5.76-5.97 (1 H, m); ^{13}C NMR δ -0.5 (3 C), 2.1 [2.2], 7.1, 15.9 [15.8], 34.4 [31.5], 68.1 [67.8], 115.4, 133.8 [135.0], 138.0 [134.7], 150.2, 167.0 [165.0], 169.2 [174.8], 189.8 [188.3], 192.3 [191.0]; MS (EI) *m/z* (rel. intensity) 292 (M^+, 100), 277 (45), 263 (23), 247 (26), 231 (24); Anal Calcd for $C_{16}H_{24}O_3Si$: C, 65.71; H, 8.27. Found: C, 65.61; H, 8.37.

3-Ethoxy-2-[2-methoxy-1-(trimethylsilyl)ethylidene]-4-methyl-2-cyclopentene-1,3-dione (12). IR (neat) 1680, 1626, 1246, 849 cm^{-1}; ^{1}H NMR signals due to *E*-isomer is indicated in brackets δ 0.22 [0.23] (9 H, s), 1.38 (3 H, t, *J*=7.0 Hz), 1.95 [1.96] (3 H, s), 3.27 [3.28] (3 H, s), 4.69 [4.68] (2 H, q, *J*=7.0 Hz), 4.82 [4.74] (2 H, s); ^{13}C NMR δ -0.5 [-0.2] (3 C), 7.1, 15.8 [15.9], 58.2, 68.1, 68.2 [67.8], 135.6 [133.6], 137.1 [136.8], 161.8 [161.6], 165.8 [167.0], 189.3 [188.9], 191.8; MS (EI) *m/z* (rel. intensity) 282 (M^+, 96), 267 (100), 238 (49), 223 (61), 207 (50); Anal Calcd for $C_{14}H_{22}O_4Si$: C, 59.54; H, 7.85. Found: C, 60.01; H, 7.38.

3-Ethoxy-4-methyl-2-[2-phenyl-1-(trimethylsilyl)ethylidene]-4-cyclopentene-1,3-dione (13). IR (neat) 1678, 1626, 1246, 849 cm^{-1}; ^{1}H NMR signals due to *E*-isomer is indicated in brackets δ 0.13 (9 H, s), 1.43 (3 H, t, *J*=7.0 Hz), 1.99 (3 H, s), 4.57 (2 H, s), 4.72 (2 H, q, *J*=7.0 Hz), 7.01-7.29 (5 H, m); ^{13}C NMR δ -0.3 (3 C), 7.1, 15.9, 36.7, 67.9, 126.3, 128.6 (2 C), 129.0 (2 C), 134.2, 136.4, 138.9, 165.2, 166.2, 189.6, 192.2; MS (EI)

m/z (rel. intensity) 328 (M^+, 100), 313 (24), 299 (7), 284 (64), 267 (14); Anal Calcd for $C_{19}H_{24}O_3Si$: C, 69.47; H, 7.36. Found: C, 69.67; H, 7.13.

2-[2-Bromo-1-(trimethylsilyl)ethylidene]-3-ethoxy-4-methyl-4-cyclopentene-1,3-dione (14). IR (neat) 1678, 1624, 1248, 849 cm^{-1}; ^1H NMR signals due to *E*-isomer is indicated in brackets δ 0.33 [0.34] (9 H, s), 1.41 [1.42] (3 H, t, *J*=7.0 Hz), 2.00 [1.99] (3 H, s), 4.72 [4.75] (2 H, q, *J*=7.0 Hz), 5.03 [4.93] (2 H, br s); ^{13}C NMR δ -0.7 [-0.4], 7.2 [7.1], 16.0 [15.9], 28.6 [28.0], 68.2 [68.3], 136.0 [135.8], 136.1 [136.0], 158.6 [158.9], 187.3 [166.2], 189.2 [188.4], 191.4 [191.7]; MS (EI) *m/z* (rel. intensity) 332 and 330 [ca. 1:1] (M^++2 and M^+, 14), 317 and 315 [ca. 1:1] (21), 289 and 287 [ca. 1:1] (17), 251 (100), 223 (15), 207 (34); Anal Calcd for $C_{13}H_{19}BrO_3Si$: C, 47.13; H, 5.78. Found: C, 47.00; H, 5.91.

Pd-Catalyzed Ring Expansion of 4-Hydroxy-4-(trimethylsilyl)ethynyl-cyclobutenone 16.

According to the reported procedure,[4] starting **16** was prepared as follows; to a solution of trimethylsilylacetylene (0.85 ml, 6.0 mmol) in dry THF (5 mL) was added ^{n}BuLi (3.71 mL, 6.0 mmol; 1.6 M in hexane) at 0 °C under a nitrogen atmosphere and the solution was stirred for 30 min. The resulted solution was then transferred to a solution of 3-ethoxy-4-methyl-3-cyclobutene-1,2-dione (701 mg, 5.0 mmol) in dry THF (20 mL) at -78 °C under a nitrogen atmosphere. The reaction mixture was stirred for 30 min, quenched with 10% $NaHCO_3$ (10 mL), and extracted with ether (10 mL × 3). The extracts were washed with brine (20 mL), dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 7:1) gave **16** (878 mg, 74%) as a yellow oil.

3-Ethoxy-4-hydroxy-2-methyl-4-(trimethylsilyl)ethynyl-2-cyclobutenone (16). IR (neat) 3337, 2166, 1763, 1624, 1252, 845 cm^{-1}; ^1H NMR δ 0.18 (9 H, s), 1.49 (3 H, t, *J*=7.0 Hz), 1.67 (3 H, s), 4.10 (1 H, br s), 4.59 (2 H, q, *J* =7.0 Hz); ^{13}C NMR δ -0.4 (3 C), 6.5, 15.2, 69.5, 83.4, 95.7, 99.3, 125.6, 180.7, 187.5; MS (EI) *m/z* (rel. intensity) 238 (M^+,

26), 223 (22), 209 (100), 195 (76), 181 (12); Anal Calcd for $C_{12}H_{18}O_3Si$: C, 60.47; H, 7.61. Found: C, 60.74; H, 7.34.

According to the reported procedure,[2a] ring expansion of cyclobutenones **16** was carried out as follows; a solution of **16** (238 mg, 1.0 mmol), allyl bromide (0.87 mL, 10 mmol), propylene oxide (1.75 mL, 25 mmol), and Pd(II) trifluoroacetate (17 mg, 0.05 mmol) in dry dichloromethane (8 mL) was stirred at ambient temperature under a nitrogen atmosphere for 1 h. The reaction mixture was quenched with saturated NH_4Cl (10 mL) and extracted with dichloromethane (5 mL × 3). The extracts were washed with brine (10 mL), dried (Na_2SO_4), and evaporated to dryness. Flash chromatography of the residue (Elution H-A 30:1) gave ring expansion product **17** (197 mg, 71%) as a yellow oil.

3-Ethoxy-4-methyl-2-[1-(trimethylsilyl)-3-butenylidene]-2-cyclopentene-1,3-dione (17). IR (neat) 1680, 1626, 1246, 847 cm^{-1}; ^1H NMR signals due to *E*-isomer is indicated in brackets δ 0.25 [0.24] (9 H, s), 1.41 [1.42] (3 H, t, *J*=7.0 Hz), 1.98 (3 H, s), 3.79 [3.87] (2 H, dt, *J*=6.0, 1.6 Hz), 4.70 (2 H, q, *J*=7.0 Hz), 4.90-5.06 (2 H, m), 5.70-5.90 (1 H, m); ^{13}C NMR δ -0.1 [-0.4] (3 C), 7.0 [7.1], 15.9 [15.8], 34.8 [35.3], 67.9 [67.8], 116.5, 132.0 [134.1], 135.5, 135.8 [135.2], 165.7 [165.2], 166.6 [166.0], 189.0 [189.6], 192.4 [192.2]; MS (EI) *m/z* (rel. intensity) 278 (M^+, 61), 263 (37), 249 (100), 233 (43); Anal Calcd for $C_{15}H_{22}O_3Si$: C, 64.71; H, 7.96. Found: C, 65.06; H, 7.61.

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1 a) H. Kikuchi, Y. Tsukitani, K. Iguchi and Y. Yamada, *Tetrahedron Lett.*, **23**, 25 (1982); b) K. Iguchi, S. Kaneta, K. Mori, Y. Yamada, A. Honda and Y. Mori, *Ibid.*, **26**, 5787 (1985); c) B. J. Baker, R. K. Okuda, P. T. K. Yu and P. J. Scheuer, *J. Am. Chem. Soc.*, **107**, 2976 (1985).

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3 See, Chapter 4, Section 2.

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7 No effort was made to separate these *E/Z* isomers.

8 *E*- or *Z*-Isomer was formed selectively. However, because of no data for relative chemical shifts, the stereochemistry could not be confirmed.

9 Semiempirical caiculations were carried out using MOPAC version 94.10 packaged in the CAChe Version 3.7.

10 J. J. P. Stewart, *J. Comp. Chem.*, **10**, 209 (1989).

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Chapter 4

Novel Ring-Transformation Methods for 4-Hydroxycyclobutenone Utilizing Reactive Intermediates

Chapter 4

Novel Ring-Transformation Methods for 4-Hydroxycyclobutenone Utilizing Reactive Intermediates

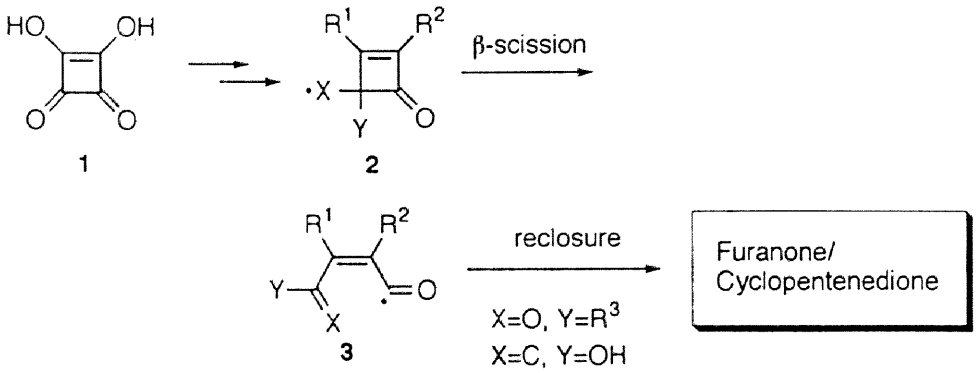
Section 1

Radical-Mediated Ring Enlargement of Cyclobutenones

Abstract: 4-Hydroxy-2-cyclobutenones, which are readily obtainable from diethyl squarate, reacted with lead tetraacetate to give 5-acetoxy-2(5*H*)-furanones and 5-alkylidene-2(5*H*)-furanones *via* oxy-radical-triggered ring-opening (β-scission) and subsequent 5-*endo* reclosure. This method was extended to saturated four-membered α-ketol, and applied to the synthesis of a natural product (*Z*-isomer of multicolanate). A carbon-centered radical-triggered reaction was also performed, in which photolysis of a mixed anhydride of thiohydroxamic acid and 4-oxo-2-cyclobutenylacetic acid afforded a 4-cyclopentene-1,3-dione rather than the furanone as a rearranged product. The similarity of these rearrangements is discussed using a PM3 calculation in terms of pentadienoyl radical to cyclopentenone radical cyclization and its oxa-version.

Cyclobutenes have received considerable attention as versatile synthetic intermediates because of their stereospecific ring-opening reactivity and its applicability to organic syntheses.[1] While these ring systems are obtainable primarily through cycloaddition, squaric acid **1** is a commercially available four-membered ring oxocarbon compound which has recently emerged as a C_4-synthon in the synthesis of highly substituted biologically active compounds based on the regioselective conversion to cyclobutenones and subsequent ring expansions.[2] Although various ring-transforming methods for the synthesis of naturally occurring products have been developed, previous studies principally focused on the electrocyclic ring-opening of cyclobutenones and successive ring-closure of the resulting vinyl ketene intermediates.[3] Nevertheless, some examples do not fall into this category; *e.g.*, the $Pd(OCOCF_3)_2$-catalyzed ring-enlargement of 4-alkynylcyclobutenone to alkylidenecyclopentenone[4] and the rhodium (I)-catalyzed ring-expansion of 4-cyclopropylcyclobutenones to cycloheptadienones[5] have been reported by Liebeskind and co-workers. With this perspective, the auther envisaged a novel ring transformation of 4-hydroxycyclobutenones *via* radical intermediates. In this method, ring-opening was effected by β-scission of a radical generated at the position adjacent to the cyclobutene ring, and the subsequent 5-*endo* reclosure of the resulting acyl radical intermediate gave rise to a cyclized product, 2(5*H*)-furanone, selectively.

This new ring transformation can be further extended to the case of a carbon-centered radical. Thus, as illustrated in Scheme 1, acyl radical intermediates **3**, which are generated by β-scission from the initial radicals **2** (X=O, C), contribute to subsequent intramolecular reclosure, in the 5-*endo* mode, to form five-membered ring systems. This section provides a detailed examination of both ring transformations from squaric acid including mechanistic considerations. Associated methodologies have recently been reviewed by Dowd and Zhang.[6]



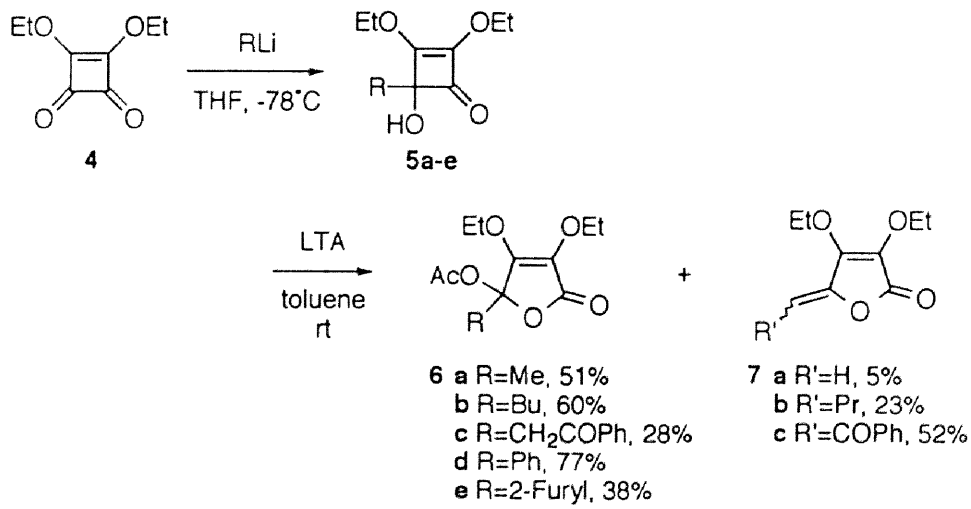
Scheme 1

Oxidative Rearrangement of 4-Hydroxycyclobutenones to 2(5*H*)-Furanones

The cycloalkoxy radical is a fascinating intermediate because it can be readily generated from a parent alcohol by various methods (*e.g.* nitrite ester photolysis, hypohalite thermolysis, one-electron oxidation, *etc.*).[7] Once formed, the oxy radical is so reactive that C-C bonds adjacent to the radical center are efficiently cleaved to produce a carbonyl and a new carbon radical (β-scission). These features have been exploited in organic synthesis. For example, the β-scission of a fused bond in bridgehead-hydroxylated bicyclic compounds results in the synthesis of medium and large rings.[8] Recyclization *via* the addition of a transient radical produced by β-scission to a radicophilic bond within the same molecule is also an important synthetic tactic.[9] Strained cyclobutoxy radicals inevitably undergo these types of reactions.[10] Accordingly, 4-hydroxycyclobutenones, which are derived from **1**, are believed to be susceptible to ring expansion *via* the oxy-radical.

The action of lead tetraacetate (LTA)[11] on alcohols is the preferred method for generating the oxy-radical in this system. The required alcohols **5a-e** were obtained from diethyl ester **4** and appropriate organolithium reagents.[12] Typically, the 4-methyl-substituted alcohol **5a** was treated with LTA (2 equiv.) in dry toluene at ambient temperature. The reaction was monitored by TLC, and was completed within 1 h. Standard work-up and separation by preparative TLC gave the rearranged products 5-acetoxy-2(5*H*)-furanone **6a** and 5-methylene-2(5*H*)-furanone **7a** in a ratio of 10/1 (total yield 56%) (Scheme 2). The structure of major product **6a** was

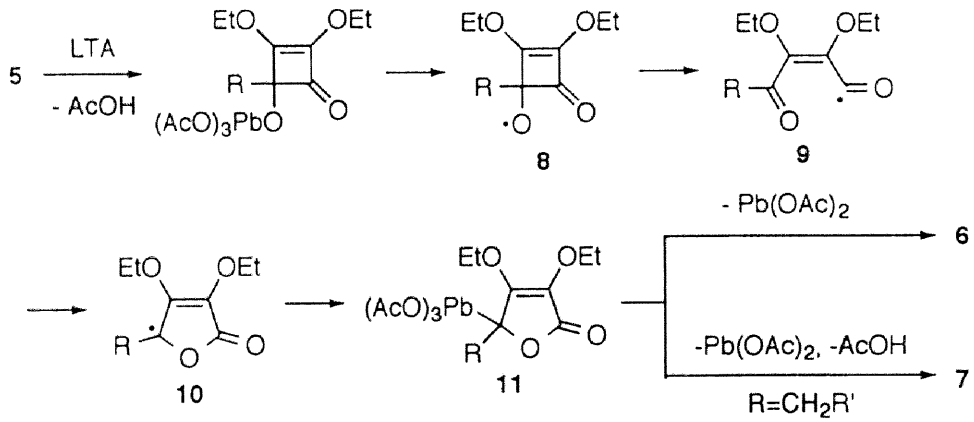
determined from spectral data. The IR spectrum indicated, instead of the hydroxy group of **5a**, two new carbonyl absorptions at 1782 and 1769 cm^{-1} corresponding to the acetoxy and furanone moieties. The ^{13}C NMR spectrum indicated the furanone structure due to the presence of one quaternary carbon (δ 99.1) and two pairs of olefinic and carbonyl carbons (δ 121.4, 156.4, 166.8 and 168.4). In the mass spectrum, the required M^+ (m/z 244, 85%) was observed together with the parent peak (*m/z* 202, M^+-H_2C=C=O). Minor product **7a** was characterized by carbonyl absorption at 1779 cm^{-1}, methylene signals in both the ^1H NMR (δ 4.95; s, 2 H) and ^{13}C NMR spectra (δ 92.1), and M^+ (*m/z* 184, 55%). In the same manner, rearranged products **6b** and **7b** were obtained in a ratio of 2.6/1 (total yield 83%) and **6c** and **7c** were obtained in a ratio of 1/2.4 (total yield 80%) from **5b** and **5c**, respectively. In these cases, (*Z*)-isomers were formed selectively, as deduced from ^1H NMR.[13] However, only 5-acetoxy-2(5*H*)-furanones **6d** and **6e** were produced from **5d** and **5e**, respectively, which have no α-hydrogens to eliminate (Scheme 2). With **5d**, in which a phenyl group is located at a position at which it might interact with the acyl radical,[14a] the reaction with a carbonyl group was unaffected (*vide infra*).



Scheme 2

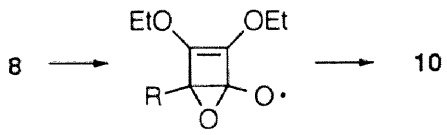
Scheme 3 illustrates a possible mechanism for the formation of furanones **6** and **7** from **5**. The initial alkoxy radical **8** generated from alcohol **5** and LTA undergoes β-scission to

produce acyl radical intermediate **9**. Recyclization (**9** → **10**) proceeds through addition of the radical to the carbonyl oxygen. The resulting lead (IV) intermediate **11** finally collapses *via* the reductive elimination of lead (II) acetate to give acetoxyfuranone **6** or alternatively *via* the concomitant elimination of acetic acid to give 5-ylidenefuranone **7**. A related *endo*-cyclization of the 4-oxo-2-butenyl radical has been reported in the photorearrangement of benzocyclobutenol to phthalide,[10d] and is supported by recent calculations.[15] Oxy radical **8** might be added to a carbonyl group intramolecularly to give a 5-oxabicyclo[2.1.0]pent-2-enyloxy radical intermediate which leads to the product by means of the process in Dowd's ring-expansion reaction.[16] However this route seems to energetically less favored (*vide infra*).



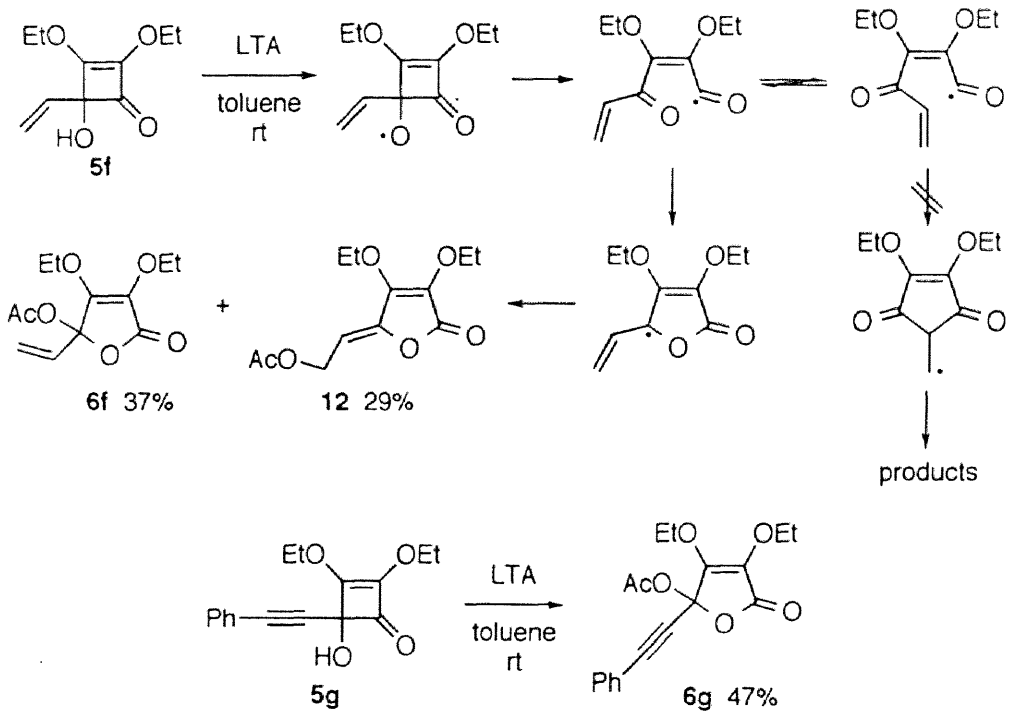
Scheme 3

Dowd's ring-expansion mechanism



In the mechanism described above, the ring-opened acyl radical intermediate recyclized with the carbonyl double bond, although it is possible in **5d** that the phenyl group participates in 6-*exo-trig* cyclization.[14a] To obtain further insight into this process, another typical cyclization, 5-*exo-trig*, was examined using 4-vinyl-substituted **5f**.[14b] As depicted in Scheme 4, however, 2(5*H*)-furanone **6f** and alkylidene-2(5*H*)-furanone **12**[13] were obtained in a ratio

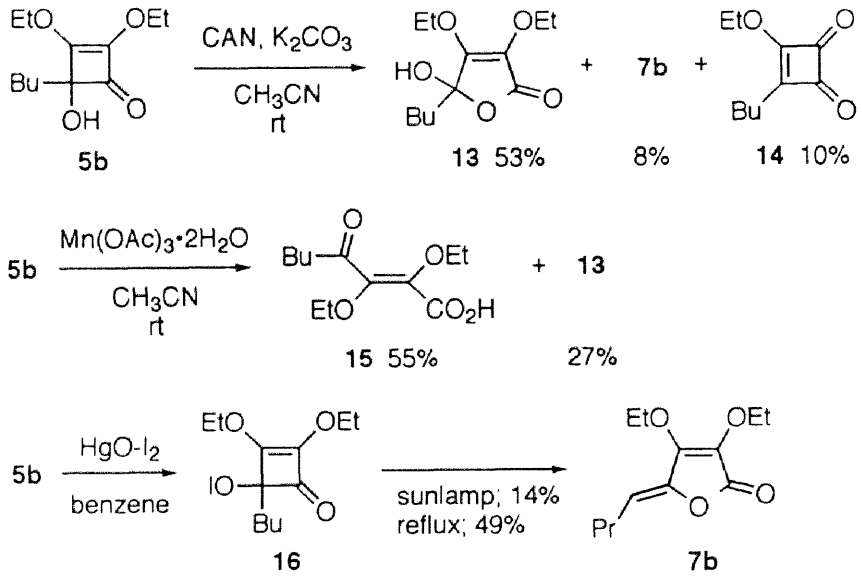
of 1.3/1 (total yield 66 %) rather than cyclopentenediones, which are 5-*exo-trig* cyclization products, under the same conditions. Similarly, 4-alkynyl-substituted **5g** gave 5-*endo* product **6g** at a yield of 47%. This selectivity implies that 5-*endo* cyclization involving a carbonyl terminus is a favorable process. This is supported by PM3 calculations (see Discussion). Alternatively, it can be explained by a cationic mechanism; *i.e.* oxidation of the acyl radical intermediate **9** with Pb(IV) or Pb(III) produces an acyl cation, which is responsible for the preferred interaction with a carbonyl group.[10g]



Scheme 4

Although LTA was effective in this rearrangement, other oxidants were also tested (Scheme 5). Oxidative rearrangement of **5b** with CAN [$(NH_4)_2Ce(NO_3)_6 \cdot H_2O$ (2 equiv.) / K_2CO_3 / CH_3CN, rt, 1 h] afforded 5-hydroxyfuranone **13** together with **7b** and 3-ethoxy-4-butyl-3-cyclobutene-1,2-dione (**14**). The structure of **13** was supported by acetylation to **6b**. In addition, Mn(III) oxidation of **5b** [$Mn(OAc)_3 \cdot 2H_2O$ (2 equiv.) / CH_3CN, rt, 1.5 h] afforded **13** together with **15**. However, anhydrous ferric chloride did not promote the

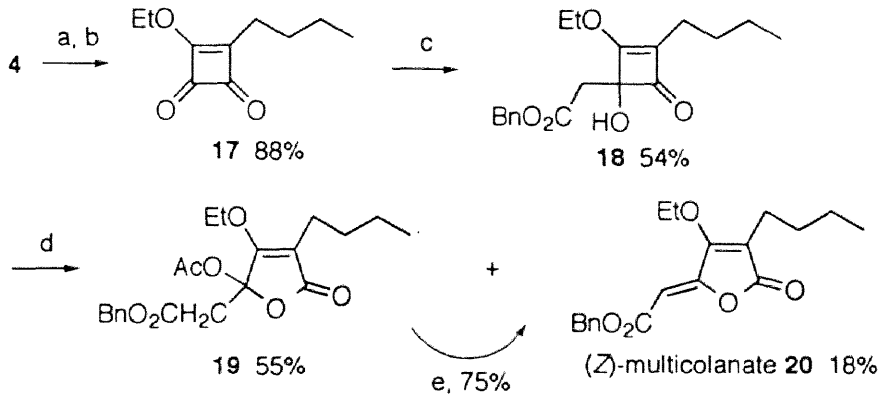
rearrangement of **5b**, and instead catalyzed the formation of **14** as a Lewis acid. Apart from this metallic oxidation, the reaction occurred through a distinct free radical pathway by photolysis and thermolysis of hypoiodite **16** generated from **5b** and HgO-I_2.[8a-c] A solution of **5b** in benzene was treated with HgO (3 equiv.) and I_2 (3 equiv.) followed by irradiation (sunlamp) for 1h to afford furanone **7b** at a yield of 14%, which was then refluxed in benzene for 1h to give a higher yield (49%). Thus, free radical mechanism undoubtedly participates in the formation of furanones (Scheme 3).



Scheme 5

A wide variety of 5-ylidenetetronic acid derivatives are found in nature,[17] and some show useful biological properties (*e.g.* agglomerin,[18a] tetronomycin,[18b] piperolide,[18c] pulvinic acid,[18d] and variabilin[18e]). The versatility of the furanone synthetic method described above was demonstrated in the stereoselective synthesis of (*Z*)-isomer **20** of multicolanate. Multicolanic acid[19] has a 4-acylmethylenetetronic acid skeleton, and its (*E*)-stereochemistry was previously established in the synthesis of a 1:3 mixture of methyl (*E*)- and (*Z*)-*O*-methylmulticolanate by the Wittig condensation of acid anhydride.[20] Our synthetic route is shown in Scheme 6. First, an alkyl side chain was introduced by reacting **4** with the corresponding Grignard reagent.[12b] The resulting **17** was functionalized with the lithium

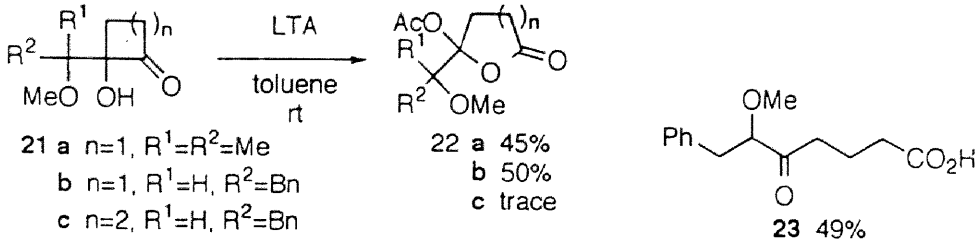
enolate of benzylacetate to 4-hydroxycyclobutenone **18** having an ester group at the 4-position. The oxidative rearrangement of **18** with LTA occurred smoothly to give **19** and **20** in a ratio of 1/3 (total yield 73%); acetoxy-tetronate **19** was converted to **20** in good yield with DBU in THF. The structure of **20** was confirmed by comparing the spectral data to that reported for the methyl ester.[20a]



[a]Key: (a) $CH_3(CH_2)_4MgBr$, THF, -78°C; (b) Cat. HCl, CH_2Cl_2, rt; (c) CH_2=COLi(OBn), THF, -78°C; (d) LTA, toluene, rt; (e) DBU, THF, rt.

Scheme 6[a]

Oxidative rearrangement with LTA was also attempted in a saturated ring system[21] (Scheme 7). Thus, α-hydroxycyclobutanones[22] **21a, b** were subjected to LTA oxidation to give the expected γ-acetoxy-γ-lactones **22a, b** in moderate yields. The success of this reaction implies that unsaturation is not required for ring closure. On the contrary, oxidation of the related α-hydroxycyclopentanone **21c** resulted in the formation of open-chain product **23** in a yield of 49 % together with a trace amounts of cyclized product **22c**; 6-*endo* cyclization of the acyl radical intermediate is disfavored.[23] Thus, the present oxidative rearrangement is realized in four-membered ring α-ketols.



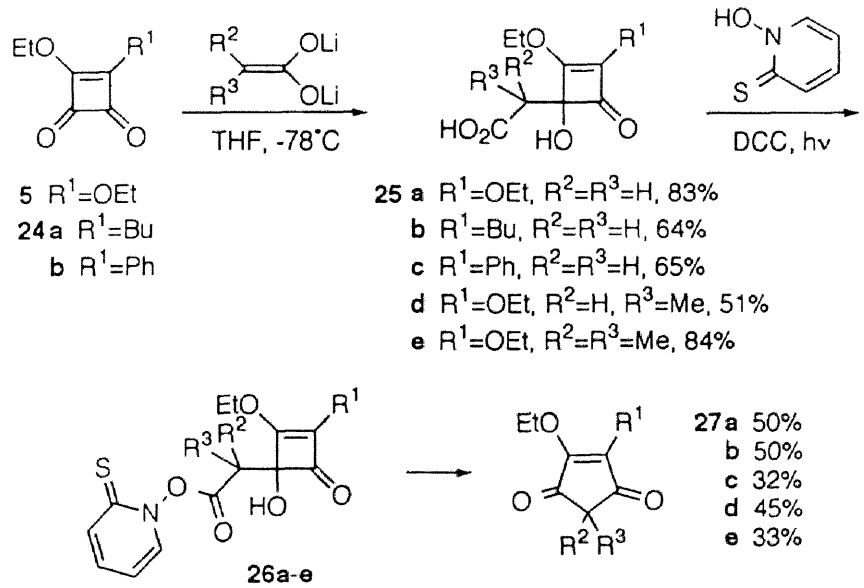
Scheme 7

Decarboxylative Rearrangement of (1-Hydroxy-4-oxo-2-cyclobutenyl)acetic Acid to 4-Cyclopentene-1,3-dione

Naturally occurring cyclopentenediones with interesting biological activities have been isolated (*i.e.* PGA derivatives,[24] pentenomycin,[25] terrein,[26] and similin A[27]). It may be useful to establish a general procedure for preparing highly substituted cyclopentenediones from substituted cyclobutenones.[28] In this respect, if the above oxidative rearrangement of 4-hydroxycyclobutenones can be realized faithfully with the carbon-centered radical as shown in Scheme 1, this class of compounds may be produced. Otherwise an enol-to-keto tautomerization may occur before rearrangement, leading to the furanones, exactly as with the oxy-radical. It would also be interesting to determine if there were any similarity, in the respective mechanisms, or synthetic dichotomy. Therefore, we decided to investigate the reactivity of 1-hydroxy-4-oxo-2-cyclobutenylmethyl radical (**2**, X=C, Y=OH in Scheme 1).

A mixed anhydride of thiohydroxamic acid and cyclobutenyl-substituted acetic acid (Barton's ester)[29] is the reagent of choice for generating the desired starting radical.[30] Acids **25a-e** were prepared from the addition of dilithioketeneacetals to cyclobutenediones **5** and **24** in 51-84% yields. Barton's esters **26a-e** were then obtained by condensing these acids with *N*-hydroxythiopyridone in the presence of *N*,*N*-dicyclohexylcarbodiimide (DCC), and used without further purification. Typically, **26a** was subjected to photolysis (500W tungsten lamp) in dichloromethane for 2 h. After removing the solvent, separation of the residue by flash chromatography gave the 5-*endo* cyclized product **27a** at a yield of 43%. When the reaction was carried out under high-dilution conditions, the yield was improved to 50 % (Scheme 8).

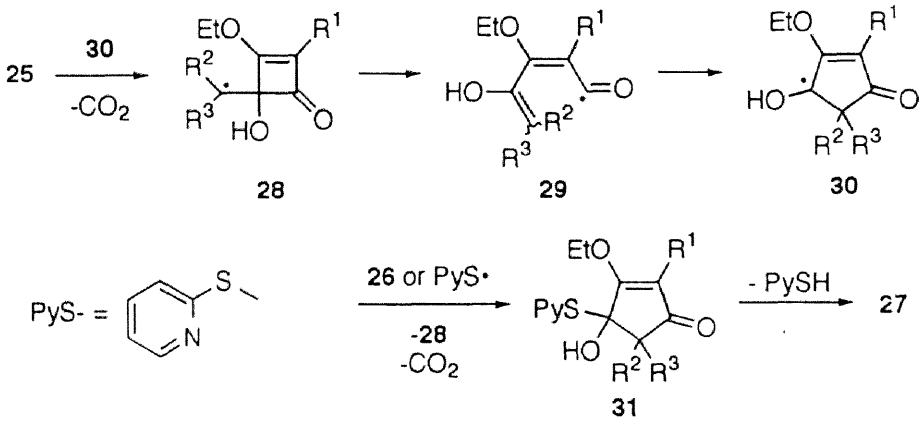
The cyclopentenedione structure of **27a** was confirmed as follows. The IR spectrum showed strong absorptions at 1694 and 1622 cm^{-1} due to an enedione moiety. In the ^1H NMR spectrum, a singlet signal due to a methylene moiety (δ 2.89) was observed together with signals at δ 1.39 (6 H, t, *J*=7.0 Hz) and 4.61 (4 H, q, *J*=7.0 Hz) due to two ethoxy groups. The ^{13}C NMR spectrum showed one sp^3 signal (δ 41.2) and two sp^2 signals (δ 151.9 and 192.3), which were assigned to the ring carbons. The required M^+ (*m/z* 184, 65 %) was demonstrated in the mass spectrum. Likewise, 3-butyl-substituted **25b** and 3-phenyl-substituted **25c** (in acetone) were transformed to the corresponding cyclopentenediones **27b** and **27c** at yields of 50 and 33 %, respectively. The reaction of α-substituted acids **25d, e** was also examined; photolysis of monosubstituted acid **25d** gave cyclopentenedione **27d** at a yield of 45 %, which is comparable to that of **27a**, while disubstituted **25e** gave **27e** at a lower yield (33 %) because of a steric effect at the 5-*endo* cyclization stage (**29** → **30** in Scheme 9).



Scheme 8

A proposed mechanism which accounts for the formation of **27** is outlined in Scheme 9. Photolysis of Barton's ester **26** produces a cyclobutenylmethyl radical **28**, which undergoes

β-scission to give an unsaturated acyl radical (pentadienoyl radical) **29**. Prior to enol-keto tautomerization, recyclization (**29** → **30**) proceeds through addition of the radical to an enol end, just as with **9** → **10** in the case of the oxy-radical-initiated reaction. Finally, a product-like radical **30** is trapped with a thiyl radical to give cyclopentenedione **27** after elimination. Again, involvement of a bicyclo[2.1.0]pent-2-enyloxy radical intermediate is less likely for the same reasons as cited above.[16, 31]



Scheme 9

Discussion

Both oxygen- and carbon-centered radicals generated at the position adjacent to a cyclobutenone ring induced the present rearrangement. Ring strain relief prompted ring-opening and the resulting terminal acyl radical underwent intramolecular 5-*endo* ring-closure as a carbonyl bond and an enol bond were formed. The resulting products were furanones from **5** and cyclopentenediones from **25**. If tautomerism were to predominate in **29**, the same furanone structure should result from the common intermediate. Furthermore, cyclization in **5f, g** occurred in the 5-*endo* mode rather than in the 5-*exo* mode. These facts indicate that the cyclization of pentadienoyl radical to cyclopentenone radical (**29** → **30**) and its oxa-version (**9** → **10**) occur with a relatively low energy barrier. To understand synthetically different but mechanistically similar results, we used UHF/PM3 calculations,[32] to study the energy of each

of the possible radical intermediates and the transition states. The default routines in MOPAC version 5.0 were used for full optimization of geometry and to compute the heats of formation using the keyword PRECISE. Geometry optimizations of transition structures were performed using the nonlinear least-squares (NLLSQ) minimization routine. The resulting transition structures were subjected to a FORCE analysis, and in each case only one negative value was found.

The calculation was first carried out for the 5-*endo vs.* 5-*exo* cyclization reactions; for simplicity, 2,3-diethoxy and phenyl substituents were omitted from **5g**. A schematic representation of the minimum-energy path for each cyclization is given in Figure 1. The resulting oxy-radical opens a cyclobutene ring with no saddle point to give an acyl radical with a carbonyl group inside, and with all of the atoms in the same plane. The formation of an ethynyl group inside results in a slightly higher energy. The 5-*endo* cyclized product (right hand) and 5-*exo* cyclized product (left hand) are then formed with an energy difference of 5.2 kcal. The former product is relatively more stable than the latter one. Thus, the 5-*endo* cyclization is an energetically favored process.

We next performed calculations for the rearrangement of the carbon-centered radical; again, the molecule was simplified by not considering substituents (Figure 2). In this case, the carbon radical generated opens a cyclobutenone ring with a very low-energy transition state (6.2 kcal). At this stage, the transition structure for forming a bicyclo[2.1.0]pentenoxy radical (*i.e.* Dowd's mechanism)[16] is estimated to have a much higher energy.[31] The acyl radicals formed have two extreme geometries with a hydroxyl group and a vinyl group inside. From these intermediates, the slightly stable radical which faces a vinyl group cyclizes, in the 5-endo mode, to a cyclopentenone radical with an energy barrier of only 14.4 kcal.

These calculations indicate that the resulting acyl radical is, in fact, a conjugated pentadienoyl radical with a flat U-shaped geometry, which can readily undergo rearrangement to a cyclopentenone radical. This is also true for the oxa-version (*i.e.* 5-oxapentadienoyl radical → furanone radical). Houk *et al.* discussed the analogous pattern of cationic and anionic

pentadienyl → cyclopentenyl rearrangement using *ab initio* quantum mechanics.[33] Facile pentadienyl radical to cyclopentenone radical cyclization seems to be associated with the Nazarov reaction, which includes pentadienone to cyclopentenone cyclization.

Conclusion

4-Hydroxycyclobutenones **5** prepared from diethyl squarate and organolithium reagents were transformed to 5-acetoxy-2(5*H*)-furanones and 5-ylidene-2(5*H*)-furanones by treatment with LTA. This novel oxidative rearrangement can be explained in terms of an oxy-radical triggered ring opening (β-scission) and subsequent ring closure with the addition of the resulting acyl radical to a carbonyl oxygen. Similarly, the oxidation of cyclobutenones with an alkenyl (alkynyl) substituent at the 4-position also gave 2(5*H*)-furanones. The versatility of this oxidative rearrangement was demonstrated in the stereoselective synthesis of the (*Z*)-isomer of multicolanate. This rearrangement was further extended to saturated four-membered α-ketols to give γ-lactones; however, in the case of a five-membered ring, 6-*endo* cyclization was disfavored. While cationic 5-*endo* cyclization could not be ruled out in the above metallic oxidation reactions (*e.g.* with LTA), the distinctive reaction with HgO/I_2 *via* a hypoiodite revealed that the radical intermediate was definitely involved in the ring-closure step.

In addition, an analogous ring enlargement triggered by a carbon-centered radical was realized by photolysis of Barton's esters **26** obtained from (1-hydroxy-4-oxo-2-cyclobutenyl)acetic acids **25** and *N*-hydroxythiopyridone. In this case, β-scission of the 4-oxo-2-cyclobutenylmethyl radical produced a pentadienoyl radical, which underwent the same 5-*endo* cyclization as above to give a cyclopentene-1,3-dione. As a result, a common rearrangement was observed in the reactions of both **5** and **26**; pentadienoyl radical to cyclopentenone radical cyclization (or its oxa-version) was a significant key process. In fact, this cyclization prevailed over keto-enol tautomerism as seen in **29** → **30** and 5-*exo-trig* ring closure as seen in **5f** → **6f**. PM3 calculations supported the energetic preference for this process.

In conclusion, new method involving cyclobutenone ring-opening suggests a new synthetic application for squaric acid. In addition, we believe that radical-mediated ring-opening of cyclobutene and subsequent 5-*endo* ring-closure may constitute a general ring-expansion methodology.

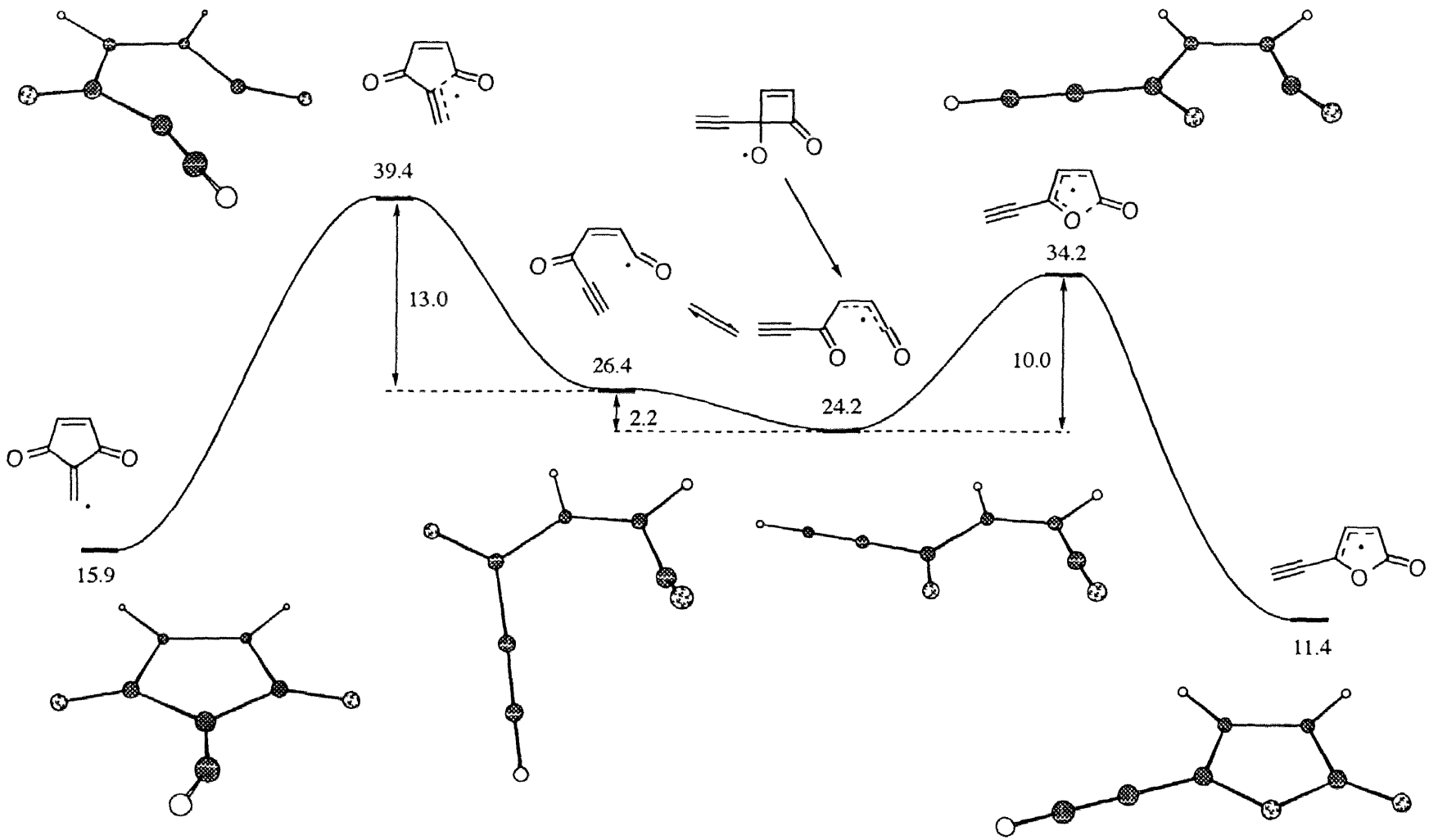


Figure 1. Schematic energy diagram for 5-*endo vs* 5-*exo* cyclizations from 1-ethynyl-4-oxo-2-cyclobutenyloxy radical. Indicated values show heat of formation, ΔH, in kcal/mol with optimized geometries (UHF/PM3).

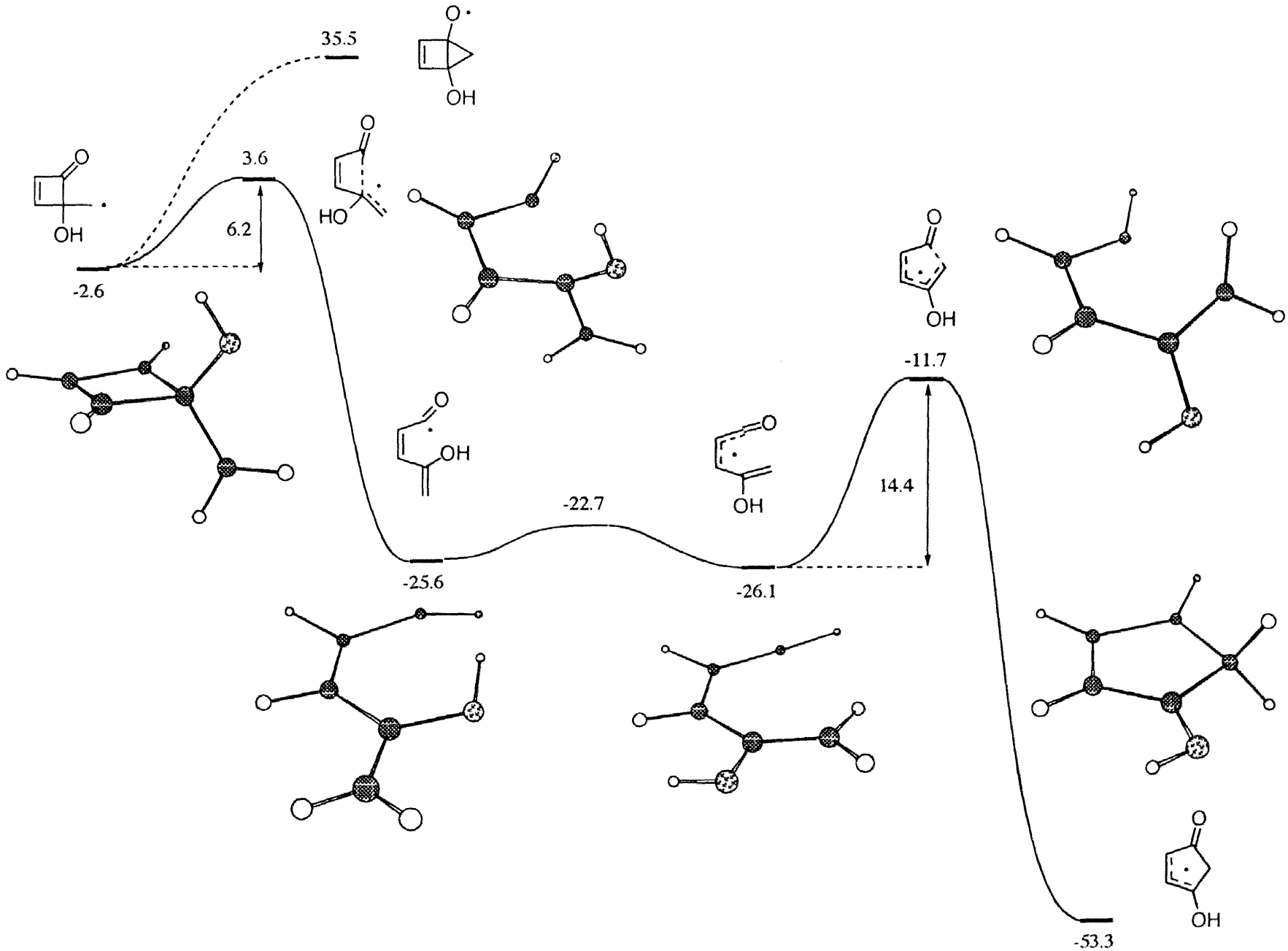


Figure 2. Schematic energy diagram for 5-*endo* cyclization from 1-hydroxy-4-oxo-2-cyclobutenylmethyl radical. Indicated values show heat of formation, ΔH, in kcal/mol with optimized geometries (UHF/PM3).

Experimental Section

General. IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ solution with $SiMe_4$ as an internal standard. Mass spectra were recorded on a JEOL JMS-AX 505 HA mass spectrometer. Flash chromatography was performed with a silica gel column (Fuji-Davison BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400S CHN elemental analyzer. THF was freshly distilled from Na and benzophenone. Toluene was dried over Na. Acetonitrile and diisopropylamine were dried over CaH_2, distilled, and stored over CaH_2. Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.

Synthesis of 4-Hydroxycyclobutenones 5. Alcohols **5a, d, e-g** were prepared from diester **4** and the corresponding organolithium reagents (vinyl magnesium bromide for **5f**) using procedures in previous reports[12] which have described **5b**.[12a]

2,3-Diethoxy-4-hydroxy-4-methyl-2-cyclobutenone (5a). 84 %; *oil* (Elution H-A 3:1); IR (neat) 3389, 1769, 1628 cm^{-1}; ^{1}H NMR δ 1.29 (3 H, t, *J*=7.0 Hz), 1.43 (3 H, t, *J*=7.0 Hz), 1.52 (3 H, s), 3.72 (1 H, br s), 4.28 (2 H, q, *J* =7.0 Hz), 4.44 and 4.51 (each 1 H, dq, *J*=7.0, 10.4 Hz); ^{13}C NMR δ 15.2, 15.5, 19.3, 66.8, 69.2, 83.4, 132.0, 169.3, 188.5; MS (EI) *m/z* (rel. intensity) 186 (M^+, 35), 169 (4), 129 (100), 113 (12); Anal Calcd for $C_9H_{14}O_4$: C, 58.05; H, 7.58. Found: C, 57.87; H, 7.76.

2,3-Diethoxy-4-hydroxy-4-phenyl-2-cyclobutenone (5d). 54 %; *oil* (Elution H-A 4:1); IR (neat) 3383, 1771, 1620 cm^{-1}; ^{1}H NMR δ 1.33 (3 H, t, *J*=7.0 Hz), 1.35 (3 H, t, *J*=7.0 Hz), 3.71 (1 H, br s), 4.34 (2 H, q, *J* =7.0 Hz), 4.31 and 4.44 (each 1 H, dq, *J*=7.0, 10.2 Hz), 7.30-7.55 (5 H, m); ^{13}C NMR δ 15.1, 15.6, 67.2, 69.6, 87.7, 126.2, 128.6, 128.9, 134.6, 137.8, 166.5, 184.7; MS (EI) *m/z* (rel. intensity) 248 (M^+, 100), 219 (41), 191 (82), 163 (24), 145 (48), 105 (88); Anal Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.74; H, 6.49.

2,3-Diethoxy-4-(2-furyl)-4-hydroxy-2-cyclobutenone (5e). 79 %; *oil* (Elution H-A 3:1); IR (neat) 3383, 1775, 1624 cm^{-1}; ^1H NMR δ 1.34 (3 H, t, *J*=7.0 Hz), 1.36 (3 H, t, *J*=7.0 Hz), 3.96 (1 H, br s), 4.35 (2 H, q, *J* =7.0 Hz), 4.35 and 4.47 (each 1 H, dq, *J*=7.0, 10.2 Hz), 6.38 (1 H, dd, *J*=1.8, 3.4 Hz), 6.46 (1 H, dd, *J*=1.0, 3.4 Hz), 7.40 (1 H, dd, *J*=1.0, 1.8 Hz); ^{13}C NMR δ 15.1, 15.5, 67.3, 69.6, 84.5, 108.6, 111.3, 135.2, 143.1, 150.6, 165.4, 182.9; MS (EI) *m/z* (rel. intensity) 238 (M^+, 100), 210 (14), 192 (15), 181 (22), 153 (38), 125 (16); Anal Calcd for $C_{12}H_{14}O_5$: C, 60.50; H, 5.92. Found: C, 60.31; H, 6.11.

4-Ethenyl-2,3-diethoxy-4-hydroxy-2-cyclobutenone (5f). 46 %; *oil* (Elution H-A 5:1); IR (neat) 3391, 1771, 1620 cm^{-1}; ^1H NMR δ 1.31 (3 H, t, *J*=7.0 Hz), 1.41 (3 H, t, *J*=7.0 Hz), 3.76 (1 H, br s), 4.30 (2 H, q, *J* =7.0 Hz), 4.39 and 4.47 (each 1 H, dq, *J*=7.0, 10.2 Hz), 5.36 (1 H, dd, *J*=1.0, 10.6 Hz), 5.54 (1 H, dd, *J*=17.4, 1.0 Hz), 5.98 (1 H, dd, *J*=17.4, 10.6 Hz); ^{13}C NMR δ 15.1, 15.5, 67.1, 69.5, 87.0, 109.9, 118.5, 135.0, 167.0, 185.4; MS (EI) *m/z* (rel. intensity) 198 (M^+, 55), 170 (31), 142 (71), 113 (100); Anal Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.55; H, 7.16.

2,3-Diethoxy-4-hydroxy-4-(phenylethynyl)-2-cyclobutenone (5g). 100 %; *oil* (Elution H-A 5:1); IR (neat) 3374, 2226, 1777, 1622 cm^{-1}; ^1H NMR δ 1.31 (3 H, t, *J*=7.0 Hz), 1.47 (3 H, t, *J*=7.0 Hz), 4.03 (1 H, br s), 4.32 (2 H, q, *J* =7.0 Hz), 4.59 (2 H, q, *J*=7.0 Hz), 7.25-7.50 (5 H, m); ^{13}C NMR δ 15.2, 15.5, 67.4, 69.8, 79.1, 83.6, 88.9, 122.1, 128.6, 129.2, 132.2, 135.0, 165.1, 181.5; MS (EI) *m/z* (rel. intensity) 272 (M^+, 15), 244 (28), 229 (53), 216 (46), 188 (32), 129 (100); Anal Calcd for $C_{16}H_{16}O_4$: C, 70.57; H, 5.92. Found: C, 70.58; H, 5.91.

Preparation of 2,3-Diethoxy-4-hydroxy-4-phenacyl-2-cyclobutenone (5c).

To a solution of LDA prepared from *n*-BuLi (0.51 ml of 1.6 M hexane solution, 0.82 mmol) and diisopropylamine (83 mg, 0.82 mmol) in dry THF (1 ml) at -78°C was added acetophenone (99 mg, 0.82 mmol) under a nitrogen atmosphere. The solution was stirred for 30 min and then transferred by syringe to a solution of diethyl squarate **4** (70 mg, 0.41 mmol)

in dry THF (1 ml) at -78°C. The solution was stirred for 30 min and then quenched with 5 % aq. NH_4Cl (5 ml) at -78°C. The product was extracted with dichloromethane (5 ml × 4), and the extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by flash chromatography (H-A 2:1) to afford alcohol **5c** (86 mg, 72 %). *oil* ; IR (neat) 3397, 2226, 1773, 1678, 1632 cm^{-1}; ^1H NMR δ 1.29 (3 H, t, *J*=7.0 Hz), 1.37 (3 H, t, *J*=7.0 Hz), 3.45 and 3.55 (each 1 H, d, *J*=17.2 Hz), 4.30 (2 H, q, *J*=7.0 Hz), 4.44 (2 H, q, *J*=7.0 Hz), 5.01 (1 H, br s), 7.43-8.00 (5 H, m); ^{13}C NMR δ 15.1, 15.5, 40.2, 67.0, 69.5, 84.2, 128.7, 129.0, 133.1, 134.2, 136.7, 166.9, 184.7, 200.0; MS (EI) *m/z* (rel. intensity) 290 (M^+, 2), 170 (31), 120 (32), 113 (17), 105 (100); Anal Calcd for $C_{16}H_{18}O_5$: C, 66.19; H, 6.25. Found: C, 66.10; H, 6.34.

Typical Procedure for Oxidation of Alcohol 5 with Lead Tetraacetate.

To a solution of $Pb(OAc)_4$ (444 mg, 0.70 mmol) in dry toluene (2 ml) at ambient temperature was added a solution of alcohol **5a** (65 mg, 0.35 mmol) in dry toluene (1 ml), and the solution was stirred for 1 h under a nitrogen atmosphere. The reaction mixture was poured into water (10 ml), and insoluble materials were filtered off. The products in the filtrate were then extracted with dichloromethane (5 ml × 4), and the extract was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by preparative TLC (H-A 3:1) to afford methylenefuranone **7a** (3 mg, 5 %) and acetoxyfuranone **6a** (44 mg, 51 %). The other alcohols **5b-e, g** were treated in the same manner to give products **6b-e, g** and **7b, c**. Furanones **6f** and **12** obtained from alcohol **5f** were separated by chromatography (H-A 15:1).

5-Acetoxy-3,4-diethoxy-5-methyl-2(5*H*)-furanone (6a). *oil*; IR (neat) 1782, 1769, 1694 cm^{-1}; ^1H NMR δ 1.32 (3 H, t, *J*=7.0 Hz), 1.38 (3 H, t, *J*=7.0 Hz), 1.68 (3 H, s), 2.06, (3 H, s), 4.17 (2 H, q, *J* =7.0 Hz), 4.48 and 4.55 (each 1 H, dq, *J*=7.0, 10.2 Hz); ^{13}C NMR δ 15.0, 15.2, 21.4, 23.5, 68.2, 68.3, 99.1, 121.4, 156.4, 166.8, 168.4; MS (EI) *m/z*

(rel. intensity) 244 (M^+, 85), 202 (100), 185 (33), 174 (39), 159 (21), 157 (52), 128 (68); Anal Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.02; H, 6.67.

3,4-Diethoxy-5-methylene-2(5*H*)-furanone (7a). *oil*; IR (neat) 1779, 1669, 1651 cm^{-1}; ^1H NMR δ 1.33 (3 H, t, *J*=7.0 Hz), 1.40 (3 H, t, *J*=7.0 Hz), 4.24 (2 H, q, *J* =7.0 Hz), 4.50 (2 H, q, *J*=7.0 Hz), 4.95 (2 H, s); ^{13}C NMR δ 15.3, 15.4, 67.9, 68.5, 92.1, 124.0, 148.2, 148.6, 165.4; MS (EI) *m/z* (rel. intensity) 184 (M^+, 55), 156 (27), 128 (100); Anal Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.66; H, 6.60.

5-Acetoxy-5-butyl-3,4-diethoxy-2(5*H*)-furanone (6b). 60 %; *oil*; IR (neat) 1782, 1692 cm^{-1}; ^1H NMR δ 0.90 (3 H, t, *J*=6.8 Hz), 1.32 (3 H, t, *J*=7.0 Hz), 1.37 (3 H, t, *J*=7.0 Hz), 1.35-1.43 (6 H, m), 2.06, (3 H, s), 4.18 (2 H, q, *J* =7.0 Hz), 4.48 and 4.53 (each 1 H, dq, *J*=7.0, 13.2 Hz); ^{13}C NMR δ 13.8, 15.2, 15.3, 21.6, 22.3, 24.0, 35.6, 68.2, 68.4, 101.0, 122.2, 155.4, 167.1, 168.5; MS (EI) *m/z* (rel. intensity) 286 (M^+, 83), 244 (100), 227 (27), 216 (50), 199 (20), 170 (39), 159 (40); Anal Calcd for $C_{14}H_{22}O_6$: C, 58.73; H, 7.74. Found: C, 58.73; H, 7.78.

5-Butylidene-3,4-diethoxy-2(5*H*)-furanone (7b). 23 %; *oil*; IR (neat) 1773, 1688, 1653 cm^{-1}; ^1H NMR δ 0.94 (3 H, t, *J*=7.2 Hz), 1.33 (3 H, t, *J*=7.0 Hz), 1.39 (3 H, t, *J*=7.0 Hz), 1.22-1.56 (2 H, m), 2.27 (2 H, q, *J*=7.2 Hz), 4.20 (2 H, q, *J* =7.0 Hz), 4.49 (2 H, q, *J*=7.0 Hz), 5.35 (1 H, t, *J*=8.0 Hz); ^{13}C NMR δ 13.8, 15.2, 15.3, 22.4, 27.2, 67.8, 68.6, 110.2, 123.0, 142.1, 149.0, 165.9; MS (EI) *m/z* (rel. intensity) 226 (M^+, 100), 198 (32), 169 (75), 156 (91), 141 (57), 128 (75), 113 (26); Anal Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.66; H, 8.06.

5-Acetoxy-3,4-diethoxy-5-phenacyl-2(5*H*)-furanone (6c). 28 %; *oil*; IR (neat) 1786, 1771, 1694 cm^{-1}; ^1H NMR δ 1.31 (3 H, t, *J*=7.0 Hz), 1.32 (3 H, t, *J*=7.0 Hz), 2.08 (3 H, s), 3.46 and 4.02 (each 1 H, d, *J*=15.2 Hz), 4.13 and 4.20 (each 1 H, dq, *J*=7.0, 10.0 Hz), 4.44 and 4.51 (each 1 H, dq, *J*=7.0, 10.0 Hz), 7.43-8.00 (5 H, m); ^{13}C NMR δ 15.1, 15.3, 21.7, 42.4, 68.3, 68.4, 99.0, 123.0, 128.8, 129.0, 134.0, 137.3, 154.4, 166.4,

168.3, 193.8; MS (EI) *m/z* (rel. intensity) 348 (M^+, 38), 261 (19), 233 (16), 105 (100); Anal Calcd for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79. Found: C, 62.12; H, 5.71.

3,4-Diethoxy-5-phenacylidene-2(5*H*)-furanone (7c). 52 %; *crystals* (mp. 89-91 °C); IR (KBr) 1786, 1657, 1618 cm^{-1}; ^1H NMR δ 1.35 (3 H, t, *J*=7.0 Hz), 1.44 (3 H, t, *J*=7.0 Hz), 4.34 (2 H, q, *J* =7.0 Hz), 4.56 (2 H, q, *J*=7.0 Hz), 6.48 (1 H, s), 7.42-7.99 (5 H, m); ^{13}C NMR δ 15.3, 15.4, 68.4, 68.6, 99.8, 125.3, 128.8, 128.9, 133.5, 138.4, 147.5, 150.8, 164.1, 188.4; MS (EI) *m/z* (rel. intensity) 288 (M^+, 26), 183 (24), 147 (18), 105 (100); Anal Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.59. Found: C, 66.61; H, 5.64.

5-Acetoxy-3,4-diethoxy-5-phenyl-2(5*H*)-furanone (6d). 77 %; *oil*; IR (neat) 1783, 1690 cm^{-1}; ^1H NMR δ 1.28 (3 H, t, *J*=7.0 Hz), 1.32 (3 H, t, *J*=7.0 Hz), 2.15 (3 H, s), 4.18 and 4.24 (each 1 H, dq, *J*=7.0, 9.8 Hz), 4.42 and 4.49 (each 1 H, dq, *J*=7.0, 10.2 Hz), 7.36-7.58 (5 H, m); ^{13}C NMR δ 15.0, 15.3, 21.6, 68.5 (2 C), 99.0, 121.6, 125.7, 128.8, 130.0, 135.6, 156.5, 167.1, 168.3; MS (EI) *m/z* (rel. intensity) 306 (M^+, 60), 264 (84), 247 (31), 191 (35), 105 (100); Anal Calcd for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.78; H, 5.88.

5-Acetoxy-3,4-diethoxy-5-(2-furyl)-2(5*H*)-furanone (6e). 38 %; *oil*; IR (neat) 1782, 1691 cm^{-1}; ^1H NMR δ 1.33 (3 H, t, *J*=7.0 Hz), 1.34 (3 H, t, *J*=7.0 Hz), 2.16 (3 H, s), 4.21 and 4.26 (each 1 H, dq, *J*=7.0, 9.8 Hz), 4.52 (2 H, q, *J*=7.0 Hz), 6.41 (1 H, dd, *J*=1.8, 3.4 Hz), 6.59 (1 H, dd, *J*=1.0, 3.4 Hz), 7.45 (1 H, dd, *J*=1.0, 1.8 Hz); ^{13}C NMR δ 15.1, 15.3, 21.5, 68.5, 68.6, 95.5, 109.9, 110.9, 122.4, 144.1, 147.3, 154.3, 166.5, 168.0; MS (EI) *m/z* (rel. intensity) 296 (M^+, 81), 254 (100), 237 (60), 209 (28), 181 (44); Anal Calcd for $C_{14}H_{16}O_7$: C, 56.76; H, 5.44. Found: C, 56.75; H, 5.45.

5-Acetoxy-5-ethenyl-3,4-diethoxy-2(5*H*)-furanone (6f). 37 %; *oil*; IR (neat) 1784, 1690 cm^{-1}; ^1H NMR δ 1.32 (3 H, t, *J*=7.0 Hz), 1.37 (3 H, t, *J*=7.0 Hz), 2.10 (3 H, s), 4.19 (2 H, q, *J*=7.0 Hz), 4.48 and 4.53 (each 1 H, dq, *J*=7.0, 10.2 Hz), 5.42 (1 H, dd, *J*=1.0, 10.6 Hz), 5.67 (1 H, dd, *J*=1.0, 17.4 Hz), 5.92 (1 H, dd, *J*=10.6, 17.4 Hz); ^{13}C NMR δ 15.1, 15.3, 21.6, 68.4 (2 C), 97.9, 120.0, 121.7, 132.1, 155.7, 166.8, 168.3; MS

(EI) *m/z* (rel. intensity) 256 (M^+, 65), 214 (100), 197 (35), 186 (50), 169 (27), 159 (14), 140 (47); Anal Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.35; H, 6.17.

5-(Acetoxyethylidene)-3,4-diethoxy-2(5*H*)-furanone (12). 29 %; *oil*; IR (neat) 1782, 1746, 1690, 1655 cm^{-1}; ^1H NMR δ 1.33 (3 H, t, *J*=7.0 Hz), 1.39 (3 H, t, *J*=7.0 Hz), 2.08 (3 H, s), 4.24 (2 H, q, *J*=7.0 Hz), 4.50 (2 H, q, *J*=7.0 Hz), 4.81 (2 H, d, *J*=7.2 Hz), 5.45 (1 H, t, *J*=7.2 Hz); ^{13}C NMR δ 15.2, 15.3, 20.8, 57.8, 68.0, 68.6, 102.0, 123.9, 144.7, 148.1, 164.6, 171.1; MS (EI) *m/z* (rel. intensity) 256 (M^+, 48), 214 (100), 185 (73), 157 (54), 141 (24); Anal Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.34; H, 6.19.

5-Acetoxy-3,4-diethoxy-5-(phenylethynyl)-2(5*H*)-furanone (6g). 51 %; *oil*; IR (neat) 2240, 1792, 1692 cm^{-1}; ^1H NMR δ 1.35 (3 H, t, *J*=7.0 Hz), 1.44 (3 H, t, *J*=7.0 Hz), 2.15 (3 H, s), 4.21 and 4.27 (each 1 H, dq, *J*=7.0, 9.6 Hz), 4.56 and 4.62 (each 1 H, dq, *J*=7.0, 10.2 Hz), 7.29-7.52 (5 H, m); ^{13}C NMR δ 15.1, 15.3, 21.4, 68.5, 68.8, 80.2, 87.7, 91.4, 120.8, 121.9, 128.7, 130.0, 132.5, 153.8, 165.8, 167.6; MS (EI) *m/z* (rel. intensity) 330 (M^+, 77), 287 (24), 273 (63), 215 (22), 175 (18), 129 (100); Anal Calcd for $C_{18}H_{18}O_6$: C, 65.45; H, 5.49. Found: C, 65.54; H, 5.40.

Oxidation of Alcohol 5b with Ceric Ammonium Nitrate.

To a mixture of alcohol **5b** (88 mg, 0.39 mmol) and powdered potassium carbonate (216 mg, 1.56 mmol) in dry acetonitrile (1 ml) at ambient temperature was added a solution of $(NH_4)_2Ce(NO_3)_6 \cdot H_2O$ (428 mg, 0.78 mmol) in dry acetonitrile (2 ml) dropwise over 40 min. The reaction mixture was stirred for 1 h under a nitrogen atmosphere, poured into water (10 ml), and extracted with dichloromethane (5 ml × 4). The extract was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by preparative TLC (H-A 3:1) to afford methylenefuranone **7b** (7 mg, 8 %), hydroxyfuranone **13** (50 mg, 53 %) and cyclobutenedione **14** (7 mg, 10 %).

5-Butyl-3,4-diethoxy-5-hydroxy-2(5*H*)-furanone (13). *oil*; IR (neat) 3378, 1767, 1752, 1682 cm^{-1}; ^1H NMR δ 0.87 (3 H, t, *J*=6.8 Hz), 1.15-1.45 (4 H, m), 1.31 (3 H, t,

J=7.2 Hz), 1.40 (3 H, t, *J*=7.2 Hz), 1.91 (2 H, m), 4.13 (2 H, q, *J* =7.2 Hz), 4.15 (1 H, br s), 4.50 (2 H, q, *J*=7.2 Hz); ^{13}C NMR δ 13.9, 15.2, 15.3, 22.4, 24.9, 35.7, 68.2, 68.8, 101.1, 121.1, 157.2, 168.6; MS *m/z* (rel. intensity) 244 (M^+, 84), 187 (76), 171 (31), 159 (56), 131 (100); Anal Calcd for $C_{12}H_{20}O_5$: C, 59.00 ; H, 8.25 . Found: C, 58.74 ; H, 8.51.

Oxidation of Alcohol 5b with Manganese (III) Acetate.

To a suspension of $Mn(OAc)_3 \cdot 2H_2O$ (113 mg, 0.42 mmol) in dry acetonitrile (2 ml) was added a solution of alcohol **5b** (49 mg, 0.21 mmol) in dry acetonitrile (1 ml) at ambient temperature. The reaction mixture was stirred for 1.5 h under a nitrogen atmosphere and poured into water (10 ml), and insoluble materials were filtered off. The products were then extracted with dichloromethane (5 ml × 4), and the extract was dried (Na_2SO_4) and evaporated to dryness. The residue was purified by preparative TLC (H-A 3:1) to afford carboxylic acid **15** (28 mg, 55 %) and hydroxyfuranone **13** (14 mg, 27 %).

(*E*)-2,3-Diethoxy-4-oxo-2-octenoic Acid (15). *oil*; IR (neat) 3341, 1763, 1686 cm^{-1}; ^1H NMR δ 0.89 (3 H, t, *J*=7.4 Hz), 1.15-1.45 (4 H, m), 1.32 (3 H, t, *J*=7 Hz), 1.42 (3 H, t, *J*=7 Hz), 1.85 (2 H, m), 4.16 (2 H, q, *J* =7 Hz), 4.54 (2 H, q, *J*=7 Hz), 9.82 (1 H, br s); ^{13}C NMR δ 13.8, 15.2, 22.5, 24.6, 31.8, 68.3, 68.7, 107.6, 122.6, 154.5, 168.9; MS *m/z* (rel. intensity) 244 (M^+, 5), 227 (100), 199 (35); Anal Calcd for $C_{12}H_{20}O_5$: C, 59.00 ; H, 8.25 . Found: C, 58.79 ; H, 8.46 .

Oxidation of Alcohol 5b with Mercury (II) Oxide and Iodine.

A solution of alcohol **5b** (76 mg, 0.33 mmol), HgO (214 mg, 0.99 mmol) and I_2 (251 mg, 0.99 mmol) in dry benzene (10 ml) was irradiated with a 500W-tungsten lamp at ambient temperature for 1 h. The reaction mixture was washed with 10 % $Na_2S_2O_3$ (5 ml), and the organic layer was dried (Na_2SO_4) and evaporated. The product was purified by preparative TLC (H-A 3:1) to afford methylenefuranone **7b** (15 mg, 14 %).

When a solution of **5b** (110 mg, 0.48 mmol), HgO (312 mg, 1.44 mmol) and I_2 (365 mg, 1.44 mmol) in dry benzene (10 ml) was refluxed for 1 h, the product was obtained at a yield of 49 % after the same work-up and separation.

Synthesis of Benzyl *O*-Ethyl-(*Z*)-multicolanate 20.

Preparation of 3-Ethoxy-4-pentyl-3-cyclobutene-1,2-dione (17). To a solution of diethyl squarate **4** (340 mg, 2.0 mmol) in dry THF (2 ml) at -78 °C was added a solution of pentylmagnesium bromide prepared from Mg (97 mg, 4.0 mmol) and 1-bromopentane (604 mg, 4.0 mmol) under a nitrogen atmosphere. The reaction mixture was stirred for 30 min, quenched with 5 % aq. NH_4Cl (10 ml), and extracted with dichloromethane (5 ml × 4). The extracts were dried (Na_2SO_4) and evaporated. The residue was treated with 2 drops of conc. HCl in dichloromethane (5 ml) for 1 h. The solution was then diluted with another 5 ml of dichloromethane and dried over K_2CO_3. After the solvent was evaporated, the residue was purified by chromatography (H-A 10:1) to afford cyclobutenedione **17** (308 mg, 80 %); *oil*; IR (neat) 1794, 1753, 1597 cm^{-1}; ^1H NMR δ 0.91 (3 H, m), 1.25-1.40 (4 H, m), 1.49 (3 H, t, *J*=7.2 Hz), 1.59-1.78 (2 H, m), 2.61 (2 H, t, *J*=7.2 Hz), 4.79 (2 H, q, *J* =7.2 Hz); ^{13}C NMR δ 13.9, 15.6, 22.2, 25.0, 25.5, 31.8, 70.7, 185.2, 194.8, 196.0, 199.0; MS *m/z* (rel. intensity) 196 (M^+, 9), 168 (20), 139 (100); Anal Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.28; H, 8.25.

Preparation of Benzyl 2-Ethoxy-1-hydroxy-4-oxo-3-pentyl-2-cyclobutenyl-acetate (18). To a solution of LDA prepared from *n*-BuLi (1.18 ml of 1.6 M hexane solution, 1.9 mmol) and diisopropylamine (192 mg, 1.9 mmol) in THF (2 ml) at -78°C was added benzyl acetate (285 mg, 1.9 mmol) by syringe. The solution was stirred for 30 min and then transferred by syringe to a solution of **17** (308 mg, 1.6 mmol) in dry THF (1 ml) at -78°C. The solution was stirred for 30 min and then quenched with 5 % aq. NH_4Cl (10 ml) at -78°C. The product was extracted with dichloromethane (5 ml × 4), and the extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by flash chromatography (H-A

4:1) to afford ester **18** (301 mg, 54 %). *oil* ; IR (neat) 3366, 1750, 1615 cm^{-1}; ^1H NMR δ 0.88 (3 H, t, *J*=6.8 Hz), 1.23-1.55 (6 H, m), 1.40 (3 H, t, *J*=7.2 Hz), 2.08 (2 H, t, *J*=7.4 Hz), 2.84 and 2.94 (each 1 H, d, *J*=20 Hz), 4.33 and 4.41 (each 1 H, dq, *J*=7.0, 9.6 Hz), 4.45 (1 H, br s), 5.14 and 5.21 (each 1 H, d, *J*=12.2 Hz), 7.37 (5 H, s); ^{13}C NMR δ 14.0, 15.0, 22.4, 22.7, 27.5, 31.8, 37.6, 67.3, 68.9, 88.1, 127.5, 128.8, 128.9, 129.0, 135.6, 171.4, 181.0, 190.7; MS (EI) *m/z* (rel. intensity) 300 (2), 253 (100), 213 (33), 209 (61): (CI), 347 (MH^+, 100); Anal Calcd for $C_{20}H_{26}O_5$: C, 69.34; H, 7.56. Found: C, 69.08; H, 7.82.

Oxidation of Alcohol 18 with Lead Tetraacetate.

As described for **5**, oxidation of **18** (301 mg, 0.87 mmol) with $Pb(OAc)_4$ (771 mg, 1.7 mmol), and chromatographic separation (H-A 8:1) afforded acetoxyfuranone **19** (195 mg, 55 %) and (*Z*)-multicolanate **20** (56 mg, 18 %).

Spectral Data for 19: *oil* ; IR (neat) 1773, 1744, 1676 cm^{-1}; ^1H NMR δ 0.89 (3 H, t, *J*=6.2 Hz), 1.23-1.56 (6 H, m), 1.33 (3 H, t, *J*=7.0 Hz), 2.01 (3 H, s), 2.28 (2 H, q, *J*=7.4 Hz), 3.04 and 3.22 (each 1 H, d, *J*=15.0 Hz), 4.27 and 4.35 (each 1 H, dq, *J*=7.0, 9.2 Hz), 5.06 and 5.14 (each 1 H, d, *J*=12.2 Hz), 7.35 (5 H, m); ^{13}C NMR δ 14.0, 15.1, 21.5, 22.4, 23.2, 29.4, 31.6, 40.4, 67.0, 67.9, 99.6, 104.6, 128.7 (2 C), 128.9, 135.6, 166.9, 167.0, 168.1, 171.2; MS (EI) *m/z* (rel. intensity) 404 (M^+, 15), 344 (7), 210 (16), 185 (55), 91 (100); Anal Calcd for $C_{22}H_{28}O_7$: C, 65.33; H, 6.98. Found: C, 65.27; H, 7.04.

Spectral Data for 20: *oil* ; IR (neat) 1790, 1725, 1638 cm^{-1}; ^1H NMR δ 0.89 (3 H, t, *J*=6.4 Hz), 1.2-1.6 (6 H, m), 1.42 (3 H, t, *J*=7 Hz), 2.45 (2 H, t, *J*=8 Hz), 4.40 (2 H, q, *J* =7 Hz), 5.24 (2 H, s), 7.3-7.5 (5 H, m); ^{13}C NMR δ 13.9, 15.2, 22.4, 23.6, 29.8, 31.6, 66.6, 68.0, 95.1, 107.4, 128.6 (2 C), 128.9, 136.1, 153.5, 161.2, 163.8, 169.6; MS *m/z* (rel. intensity) 344 (M^+, 2), 238 (100), 210 (26), 181 (32); Anal Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.62; H, 7.12.

Transformation of Acetoxytetronate 19 to 20. To a solution of **19** (96 mg, 0.24 mmol) in THF (1 ml) was added diazabicyclo[5.4.0]undec-7-ene (40 mg, 0.26 mmol), and the

solution was stirred for 10 min at ambient temperature. The reaction mixture was diluted with dichloromethane (10 ml), washed with water, and dried over Na_2SO_4. After evaporating the solvent, the residue was subjected to chromatography (H-A 8:1) to afford **20** (63 mg, 75 %).

General Procedure for Oxidation of Alcohols 21 with Lead Tetraacetate.

Alcohols **21a-c** were oxidized by the procedure described for **5**, and the products were separated by chromatography (eluent H-A 2:1).

4-Acetoxy-4-(1-methyl-1-methoxyethyl)-4-butanolide (22a). 45 %; *oil*; IR (neat) 1792, 1748 cm^{-1}; ^1H NMR δ 1.25 and 1.30 (each 3 H, s), 2.09 (3 H, s), 2.19-3.02 (4 H, m), 3.26 (3 H, s); ^{13}C NMR δ 18.0, 19.3, 21.8, 26.3, 29.4, 50.2, 77.8, 111.2, 169.7, 176.6; MS (EI) *m/z* (rel. intensity) 157 (7), 125 (20), 73 (100); (CI) 217 (MH^+, 13), 157 (100); Anal Calcd for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 55.51; H, 7.48.

4-Acetoxy-4-(2-phenyl-1-methoxyethyl)-4-butanolide (22b). 50 % (diastereomeric mixture *ca.* 3:1); *oil*; IR (neat) 1821, 1751 cm^{-1}; ^1H NMR δ 1.99 and 2.22 (1 H and 2 H, respectively, s), 1.5-3.1 (6 H, m), 3.23 and 3.34 (1 H and 2 H, respectively, s), 3.69 and 3.89 (1/3 H and 2/3 H, respectively, dd, *J*=5.0, 7.4 Hz), 7.12-7.34 (5 H, m); ^{13}C NMR δ 28.5 and 28.6, 32.8 and 32.7, 38.3 and 38.1, 58.7 and 60.6, 87.9 and 84.9, 109.7, 127.0 and 126.8, 128.7, 129.7 and 129.8, 1137.2 and 138.5, 169.1 and 168.9, 175.9; MS (EI) *m/z* (rel. intensity) 218 (23), 187 (17), 135 (100); (CI) 276 (MH^+, 4), 220 (100); Anal Calcd for $C_{15}H_{18}O_5$: C, 64.74; H, 6.52. Found: C, 64.55; H, 6.71.

6-Methoxy-5-oxo-7-phenylheptanoic acid (23). 49 %; *oil*; IR (neat) 3500-2500 (broad), 1713 cm^{-1}; ^1H NMR δ 1.84 (2 H, tt, *J*=7.0, 7.2 Hz), 2.33 (2 H, t, *J*=7.2 Hz), 2.43 and 2.56 (each 1 H, dt, *J*=7.0, 18.6 Hz), 2.88 (1 H, dd, *J*=7.4, 14.2 Hz), 2.98 (1 H, dd, *J*=5.2, 14.2 Hz), 3.32 (3 H, s), 3.84 (1 H, dd, *J*=5.2, 7.4 Hz), 7.17-7.34 (5 H, m), 10.03 (1 H, br s); ^{13}C NMR δ 17.9, 33.0, 37.4, 38.2, 58.6, 88.0, 127.0, 128.8, 129.7, 137.2, 179.7, 212.4; MS (EI) *m/z* (rel. intensity) (no molecular ion) 218 (11), 163 (1), 135 (100),

103 (27); (CI) 251 (MH^+, 100), 219 (29); Anal Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.00; H, 7.43.

Typical Procedure for Synthesis of Carboxylic Acids 25.

To a solution of LDA prepared from *n*-BuLi (3.71 ml of 1.6 M hexane solution, 6.0 mmol) and diisopropylamine (607 mg, 6.0 mmol) in THF (4 ml) at -78°C was added acetic acid (180 mg, 3.0 mmol) by syringe. The solution was stirred for 30 min and then transferred by syringe to a solution of diester 4 (170 mg, 1.0 mmol) in dry THF (2 ml) at -78°C. The solution was stirred for 2 h and then quenched with 1N HCl (10 ml) at -78°C. The product was extracted with dichloromethane (5 ml × 4), and the extracts were dried (Na_2SO_4) and evaporated to dryness. The residue was purified by flash chromatography (H-A 1:1) to afford carboxylic acid **25a** (190 mg, 83 %). The other acids **25b-e** were obtained in the same manner from the corresponding esters and alkanoic acids.

(2,3-Diethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)acetic Acid (25a). *oil* ; IR (neat) 3300, 1771, 1717, 1618 cm^{-1}; ^1H NMR δ 1.30 (3 H, t, *J*=7.0 Hz), 1.43 (3 H, t, *J*=7.0 Hz), 2.82 and 2.95 (each 1 H, d, *J*=16.0 Hz), 4.31 (2 H, q, *J*=7.0 Hz), 4.47 and 4.52 (each 1 H, dq, *J*=7.0, 10.2 Hz), 7.82 (2 H, br s); ^{13}C NMR δ 15.1, 15.5, 37.6, 67.2, 70.0, 83.0, 133.0, 167.0, 175.1, 185.7; MS (EI) *m/z* (rel. intensity) 230 (M^+, 75), 212 (12), 202 (67), 184 (64), 173 (25), 168 (42), 156 (89), 145 (68), 128 (62), 112 (100); Anal Calcd for $C_{10}H_{14}O_6$: C, 52.17; H, 6.13. Found: C, 52.40; H, 5.90.

(3-Butyl-2-ethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)acetic Acid (25b). This was obtained from **24a**[12a] and acetic acid in 64 % yield; *oil* (eluent H-A 1:1); IR (neat) 3300, 1748, 1717, 1605 cm^{-1}; ^1H NMR δ 0.90 (3 H, t, *J*=7.2 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 1.22-1.58 (4 H, m), 2.12 (2 H, t, *J*=8.4 Hz), 2.81 and 2.96 (each 1 H, d, *J*=15.6 Hz), 4.42 and 4.52 (each 1 H, dq, *J*=7.0, 9.6 Hz), 7.55 (2 H, br s); ^{13}C NMR δ 13.7, 15.0, 22.2, 22.6, 29.7, 38.2, 69.3, 87.6, 127.2, 174.3, 182.2, 193.2; MS (EI) *m/z* (rel. intensity) 242 (M^+,

19), 196 (48), 167 (22), 154 (48), 125 (100); Anal Calcd for $C_{12}H_{18}O_5$: C, 59.49; H, 7.49. Found: C, 59.15; H, 7.78.

(2-Ethoxy-1-hydroxy-4-oxo-3-phenyl-2-cyclobutenyl)acetic Acid (25c). This was obtained from **24b** and acetic acid in 65 % yield; *crystals* (mp. 159-162 °C) (eluent H-A 1:1); IR (KBr) 2970, 1740, 1709, 1620, 1593 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.45 (3 H, t, J=7.0 Hz), 2.84 (2 H, s), 4.56 and 4.64 (each 1 H, dq, J=7.0, 10.0 Hz), 6.85 (1 H, br s), 7.24-7.65 (5 H, m), 12.45 (1 H, br s); ^{13}C NMR (DMSO-d_6) δ 15.0, 39.4, 69.4, 90.3, 122.6, 126.5, 128.1, 129.1, 129.3, 170.9, 182.3, 188.8; MS (EI) *m/z* (rel. intensity) 262 (M^+, 16), 216 (100), 188 (9), 145 (21); Anal Calcd for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.15; H, 5.34.

2-(2,3-Diethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)propanoic Acid (25d). This was obtained from **4** and propanoic acid in 51 % yield (ca. 1:1 diastereomeric mixture); *oil* (eluent H-A 2:1); IR (neat) 3400, 1771, 1717, 1620 cm^{-1}; ^1H NMR δ 1.24 and 1.30 (each 3/2 H, d, J=7.2 Hz), 1.31 (3 H, t, J=7.0 Hz), 1.42 and 1.44 (each 3/2 H, t, J=7.0 Hz), 2.96 and 3.01 (each 1/2 H, q, J=7.2 Hz), 4.31 (2 H, q, J=7.0 Hz), 4.41-4.58 (2 H, m), 7.27 (2 H, br s); ^{13}C NMR δ 12.8 and 13.1, 15.5 (2 C) and 15.2 (2 C), 42.4 and 42.3, 67.2 (2 C), 70.1 and 70.0, 86.2 and 86.9, 133.6 and 133.9, 166.6 and 166.3, 178.2 and 177.6, 185.3 and 185.5; MS (EI) *m/z* (rel. intensity) 244 (M^+, 39), 198 (44), 170 (53), 142 (32), 113 (36), 85 (100); Anal Calcd for $C_{11}H_{16}O_6$: C, 54.09; H, 6.60. Found: C, 54.35; H, 6.30.

2-(2,3-Diethoxy-1-hydroxy-4-oxo-2-cyclobutenyl)-2-methylpropanoic Acid (25e). This was obtained from **4** and 2-methylpropanoic acid in 84 % yield; *oil* (eluent H-A 2:1); IR (neat) 3300, 1769, 1705, 1616 cm^{-1}; ^1H NMR δ 1.31 (3 H, d, J=7.0 Hz), 1.31 and 1.39 (each 3 H, s), 1.43 (3 H, t, J=7.0 Hz), 4.29 and 4.35 (each 1 H, dq, J=7.0, 10.2 Hz), 4.47 and 4.53 (each 1 H, dq, J=7.0, 10.2 Hz), 7.27 (2 H, br s); ^{13}C NMR δ 15.2, 15.6, 21.8, 22.1, 45.3, 67.2, 70.1, 89.1, 134.0, 166.3, 180.1, 185.8; MS (EI) *m/z* (rel. intensity) 258 (M^+, 34), 212 (61), 184 (63), 156 (51), 127, (42), 115 (100); Anal Calcd for $C_{12}H_{18}O_6$: C, 55.81; H, 7.02. Found: C, 56.02; H, 6.81.

Typical Procedure for Photorearrangement of Barton's Ester of Carboxylic Acid 25.

A solution of carboxylic acid **25a** (111 mg, 0.48 mmol) in dry dichloromethane (20 ml) was added dropwise to a solution of *N*-hydroxy-2-thiopyridone (74 mg, 0.58mmol) and *N*,*N*-dicyclohexylcarbodiimide (119 mg, 0.58 mmol) in dry dichloromethane (5 ml), while being irradiated with a 500W-tungsten lamp for 40 min (a Dimroth condenser was attached because the solution was heated to reflux). The solution was irradiated for an additional 3 h. Insoluble materials were filtered off and the filtrate was evaporated to dryness. Flash chromatography (H-A 10:1) of the residue afforded cyclopentenedione **27a** (44 mg, 50 %). The other carboxylic acids **25b-e** were treated similarly to give cyclopentenediones **27b-e**.

4,5-Diethoxy-4-cyclopentene-1,3-dione (27a). *oil* ; IR (neat) 1748 (sh), 1694, 1622 cm^{-1}; ^1H NMR δ 1.39 (6 H, t, *J*=7.0 Hz), 2.89 (2 H, s), 4.61 (4 H, q, *J*=7.0 Hz); ^{13}C NMR δ 15.7, 41.2, 68.2, 151.9, 192.3; MS (EI) *m/z* (rel. intensity) 184 (M^+, 65), 156 (21), 128 (34), 100 (100); Anal Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.49; H, 6.77.

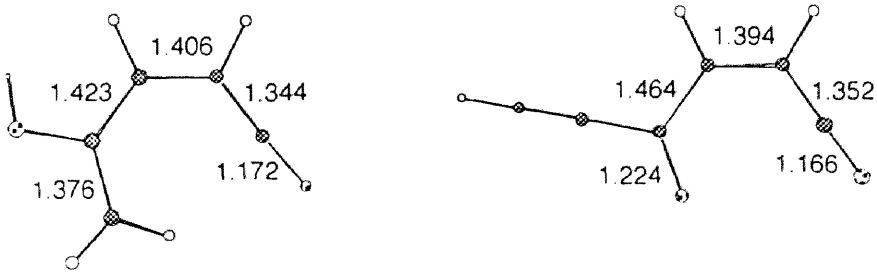
5-Butyl-4-ethoxy-4-cyclopentene-1,3-dione (27b). 50 %; *oil* (eluent H-A 10:1); IR (neat) 1742 (sh), 1696, 1616 cm^{-1}; ^1H NMR δ 0.92 (3 H, t, *J*=7.2 Hz), 1.38 (3 H, t, *J*=7.0 Hz), 1.24-1.56 (4 H, m), 2.39 (2 H, t, *J*=7.8 Hz), 2.89 (2 H, s), 4.69 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 13.8, 15.9, 21.7, 22.7, 29.7, 42.3, 68.0, 142.2, 166.5, 196.3, 196.9; MS (EI) *m/z* (rel. intensity) 196 (M^+, 5), 168 (100), 154 (66), 139 (43), 125 (73); Anal Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.27; H, 8.27.

4-Ethoxy-5-phenyl-4-cyclopentene-1,3-dione (27c). 32 %; *crystals* (mp. 41-43 °C) (eluent H-A 10:1); IR (KBr) 1736 (sh), 1688, 1586 cm^{-1}; ^1H NMR δ 1.41 (3 H, t, *J*=7.0 Hz), 3.06 (2 H, s), 4.76 (2 H, q, *J*=7.0 Hz), 7.38-7.91 (5 H, m); ^{13}C NMR δ 15.9, 42.7, 69.1, 128.4, 128.6, 129.9 (2 C + 1 C), 135.4, 164.8, 195.7, 196.1; MS (EI) *m/z* (rel. intensity) 216 (M^+, 71), 188 (54), 160 (100), 145 (59), 132 (77), 118 (79); Anal Calcd for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59. Found: C, 72.17; H, 5.63.

4,5-Diethoxy-2-methyl-4-cyclopentene-1,3-dione (27d). 45 %; *crystals* (mp. 57-58 °C) (eluent H-A 10:1); IR (KBr) 1682, 1620 cm^{-1}; ^1H NMR δ 1.24 (3 H, d, *J*=7.4 Hz), 1.39 (6 H, t, *J*=7.0 Hz), 2.75 (1 H, q, *J*=7.4 Hz), 4.58 and 4.64 (each 2 H, dq, *J*=7.0, 10.2 Hz); ^{13}C NMR δ 11.0, 15.7, 44.8, 68.1, 150.5, 196.3; MS (EI) *m/z* (rel. intensity) 198 (M^+, 100), 170 (21), 142 (37), 114 (94); Anal Calcd for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12. Found: C, 60.61; H, 7.10.

4,5-Diethoxy-2,2-methyl-4-cyclopentene-1,3-dione (27e). 33 %; *crystals* (mp. 54-55 °C) (eluent H-A 10:1); IR (KBr) 1680, 1624 cm^{-1}; ^1H NMR δ 1.18 (6 H, s), 1.39 (6 H, t, *J*=7.0 Hz), 4.61 (4 H, q, *J*=7.0 Hz); ^{13}C NMR δ 15.7, 20.2, 46.6, 68.0, 148.8, 199.6; MS (EI) *m/z* (rel. intensity) 212 (M^+, 100), 184 (27), 156 (81), 128 (31), 100 (18); Anal Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.20; H, 7.65.

Calculations. A semiempirical calculation (UHF/PM3) was carried out using MOPAC program Ver. 5.00 (QCPE No. 445): Stewart, J. P. *QCPE Bull.* **1989**, *9*, 10: Hirano, T. *JCPE Newsletter* **1989**, *1(2)*, 36; Revised as Ver. 5.01 by Toyoda, J. for Apple Macintosh®. The representative bond length (Å) of a pentadienoyl radical (left) and an oxa-analog (right) can be obtained as follows.



In the transition state to a cyclopentenone radical (or its oxa-analog), the partial C•••C=O single bond is 2.232 Å long (the O•••C=O single bond is 1.931 Å long).

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Chapter 4

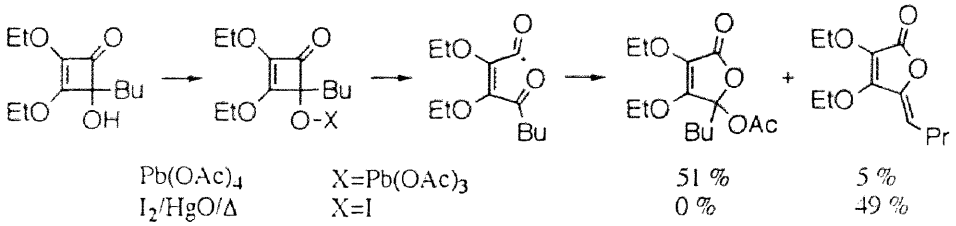
Novel Ring-Transforming Methods for 4-Hydroxycyclobutenone Utilizing Reactive Intermediates

Section 2

Ring Enlargement of 4-Alkynyl-4-hydroxycyclobutenone to 2-Iodomethylene-4-cyclopentene-1,3-dione *via* Ionic Rearrangement of Hypoiodite

Abstract: While hypoiodites generally produce oxy-radical intermediates upon photolysis or thermolysis, the reaction of 4-alkynyl-4-hydroxycyclobutenones with I_2/HgO, I_2/PhI(OAc)$_2$ and NIS all believed to form a hypoiodite afforded, even at room temperature, iodomethylenecyclopentene-1,3-diones as rearranged products *via* an ionic pathway.

Small ring compounds are known to undergo facile ring-opening induced by carbon- and hetero-radicals α to the ring, and this rearrangement aptitude is fruitfully applied in a variety of organic syntheses.[1] In the previous section, the author reported a radical-mediated rearrangement of 4-hydroxycyclobutenones to 2(5*H*)-furanones, in which ring-opening was triggered by an oxy-radical generated by action of lead tetraacetate (LTA) and the resultant acyl radical intermediate cyclized with a carbonyl group in a 5-*endo* mode to afford 2(5*H*)-furanones. In this oxidative rearrangement, the 5-*endo* cyclization might be elucidated by a cationic mechanism; *i.e.*, an acyl cation produced by further oxidation of the acyl-radical intermediate with Pb(IV) or Pb(III) is responsible for the observed interaction with a carbonyl group.[2] Then, in order to examine a distinct free radical pathway, the author performed the reaction *via* hypoiodite using I_2/HgO (hν or Δ).[3] As a result, it was recognized that the radical intermediate was actually operative in the cyclization step (Scheme 1).

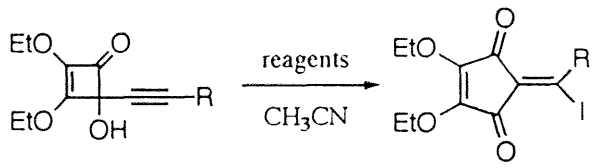


Scheme 1

Thereafter, our interest focused on the reaction of 4-alkynyl-4-hydroxycyclobutenones **1** which were obtained from diethyl squarate. In this case, 5-*endo* (with carbonyl) and 5-*exo* (with alkynyl) cyclizations are possibly to occur. Our own PM3 calculation for 1-ethynyl-4-oxocyclobutenoxy radical revealed that the former process was energetically favored by 5.2 kcal/mol (Chapter 4, Section 1). For the related reaction, the recent report also postulated that 2-formylbenzoyl radical cyclized in a 5-*endo* mode 10^3 times faster than 5-hexenoyl radical in a 5-*exo* mode.[4]

However, in contrast to the above expectation, the reaction of **1a** with I_2/HgO[5] was found to proceed without light or heating (Table 1, entry a), and the rearranged product was assigned as a cyclopentene-1,3-dione (5-*exo* cyclization) rather than a furanone (5-*endo*

cyclization). The structure of this ring expansion product was confirmed based on the following spectral features of **2a**. The IR spectrum showed disappearance of both hydroxyl and alkynyl groups. The formation of the methylenecyclopentene-1,3-dione ring was supported by an absorption at 1678 cm^{-1} due to an enone moiety in the IR spectrum, and four olefinic signals at δ 125.0, 129.0, 148.8 and 150.1 and two carbonyl signals at δ 183.9 and 184.3 in the ^{13}C NMR spectrum. Furthermore, a satisfactory molecular ion peak (*m/z* 378) was obtained together with a parent peak (*m/z* 251, M^+-I) in the mass spectrum.



1 **2**

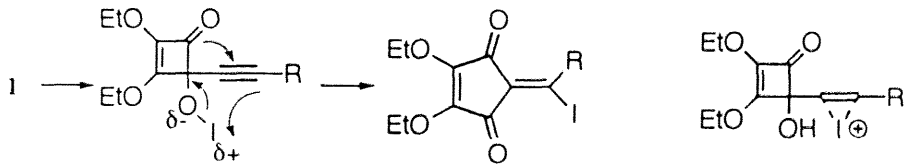
Table 1. Ring expansion of 4-alkynyl-4-hydroxycyclobutenone **1**.

entry	cyclobutenone	R	reagents (equiv.)	temp. (°C)	time (h)	product (yields, %)[a]
a	**1a**	Bu	I_2 (3.0)/HgO (3.0)	rt	1	**2a** (45)
b	**1a**	Bu	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	rt	1	**2a** (45)
c	**1a**	Bu	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	-15	1	**2a** (59)
d	**1a**	Bu	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	-30	3	**2a** (49)
e	**1b**	H	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	-15	1.5	**2b** (63)
f	**1c**	CH_2OMe	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	-15	2	**2c** (69)
g	**1d**	Ph	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	-15	3	**2d** (57)
h	**1e**	$SiMe_3$	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	-15	1.5	**2e** (68)
i	**1f**	I	I_2 (1.2)/$PhI(OAc)_2$ (1.3)	-15	1	**2f** (70)
j	**1a**	Bu	NIS (5.0)	rt	6	**2a** (44)

In addition, other reagents which are believed to form hypoiodite were also employed for the reaction of **1a-f**. In the reaction with iodine and iodobenzene diacetate (IBD), generation of an oxy-radical requires thermolytic or photolytic conditions.[6] However as shown in Table 1 (entry b), the reaction of **1a** with I_2/IBD was enough to be carried out in the dark at room temperature to afford **2a** in 45 % yield. The rearrangement took place even at -30 °C (entry d),

while the best yield (59 %) was achieved at -15 °C (entry c). Similarly, cyclobutenones **1b-f** (R=H, CH_2OMe, Ph, $SiMe_3$, I) were transformed to cyclopentene-1,3-diones **2b-f** in 57 ~ 70 % yields (entries e - f). The product **2i** has a symmetrical structure, and thus ^1H and ^{13}C NMR spectra indicated a very simple pattern: *e.g.* six ^{13}C NMR signals at δ 15.8, 18.8, 68.9, 133.5, 150.4, and 183.1. *N*-Iodosuccinimide (NIS)[7] was found to be also effective to give **2a** in 44 % yield (entry j).

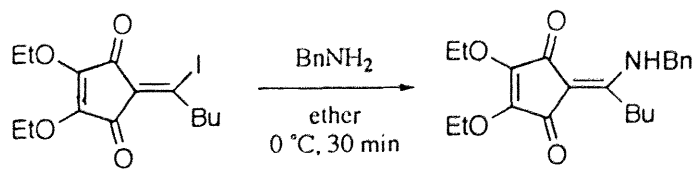
Thus, it is obvious that an oxy-radical intermediate (Scheme 1) is not involved in the above rearrangement. The results are best explained by an ionic mechanism as shown in Scheme 2; positive iodine atom transfer from a hypoiodite moiety in **3** to an alkyne terminus and concomitant 1,2-acyl migration may afford iodomethylenecyclopentene-1,3-dione **2**. As another possibility, the reaction might involve the bridged iodonium ion intermediate **4** which caused the 1,2-acyl migration.[8] However, the recent report indicated that such a reaction course was not realized in the reaction of 1-alkynyl-1-hydroxycycloalkane with I_2/IBD.[9] In any event, ring strain relief facilitated the 1,2-acyl migration, and hence ring expansion.



3 2 4

Scheme 2

In conclusion, switching of the rearrangement of 4-alkynyl-4-hydroxycyclobutenones from radical to ionic *via* hypoiodites provides a practical route to iodomethylenecyclopentene-1,3-diones from squaric acid.[10] These products may be useful for further conversion, for example, with a clue of iodine substitution. A simple case is demonstrated below.



2a 5 78 %

Scheme 3

Experimental Section

General. IR spectra were recorded on a JASCO FT/IR 5300 spectrophotometer. ^{1}H and ^{13}C NMR spectra were obtained with a Varian GEMINI-200 spectrometer at 200 and 50 MHz, respectively, for samples in $CDCl_3$ solution with $SiMe_4$ as an internal standard. Mass spectra were recorded on a JEOL JMS-AX 505 HA mass spectrometer. Flash chromatography was performed with a silica gel column (Fuji-Davison BW-300) eluted with mixed solvents [hexane (H), ethyl acetate (A)]. Microanalyses were performed with a Perkin-Elmer 2400S CHN elemental analyzer. Acetonitrile was dried over CaH_2, distilled, and stored over CaH_2. Squaric acid was supplied by Kyowa Hakko Kogyo Co. Ltd.

Synthesis of 4-Alkynyl-4-hydroxycyclobutenones 1.

Alcohols **1a, c-e** were prepared from diethyl squarate and the corresponding lithium acetylides using procedures in previous reports.[11] Alcohol **1d** was reported in the previous section.

2,3-Diethoxy-4-(1-hexynyl)-4-hydroxy-2-cyclobutenone (1a). 95%; *oil* (Elution H-A 4:1); IR (neat) 3387, 2236, 1779, 1634 cm^{-1}; ^{1}H NMR δ 0.90 (3 H, t, *J*=7.4 Hz), 1.31 (3 H, t, *J*=7.0 Hz), 1.45 (3 H, t, *J*=7.0 Hz), 1.25-1.59 (4 H, m), 2.26 (2 H, t, *J*=7.0 Hz), 3.36 (1 H, br s), 4.31 (2 H, q, *J*=7.0 Hz), 4.54 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 13.6, 15.2, 15.5, 18.6, 22.0, 30.4, 67.2, 69.5, 74.8, 78.8, 90.6, 134.8, 165.4, 182.0; MS (EI) *m/z* (rel. intensity) 252 (M^+, 2), 206 (17), 195 (4), 178 (13), 149 (100).

2,3-Diethoxy-4-hydroxy-4-(3-methoxy-1-propynyl)-2-cyclobutenone (1c). 85%; *oil* (Elution H-A 3:1); IR (neat) 3360, 2236, 1779, 1634 cm^{-1}; ^{1}H NMR δ 1.32 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 3.34 (3 H, s), 4.12 (2 H, s), 4.28 (1 H, br s), 4.30 (2 H, q, *J*=7.0 Hz), 4.55 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 15.1, 15.4, 57.8, 60.0, 67.3, 69.7, 78.5, 81.3, 84.7, 134.9, 164.9, 181.2; MS (EI) *m/z* (rel. intensity) 240 (M^+, 5), 208 (54), 193 (16), 180 (51), 165 (36), 152 (100).

2,3-Diethoxy-4-hydroxy-4-(trimethylsilylethynyl)-2-cyclobutenone (1e). 94%; *crystals* (Elution H-A 7:1); mp. 92-93 °C; IR (neat) 3256, 2168, 1775, 1626, 1252, 851 cm^{-1}; ^1H NMR δ 0.18 (9 H, s), 1.32 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 3.54 (1 H, br s), 4.31 (2 H, q, *J*=7.0 Hz), 4.55 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ -0.39, 15.2, 15.5, 67.3, 69.7, 79.0, 94.7, 99.3, 135.2, 164.8, 180.9; MS (EI) *m/z* (rel. intensity) 268 (M^+, 8), 253 (24), 239 (19), 225 (42), 211 (100), 197 (49).

Synthesis of Alcohols 1b, f.

Alcohol **1e** (807 mg, 3.0 mmol) was treated with tetrabutylammonium fluoride (87 mg, 0.30 mmol) in THF (5 mL) at 0 °C, and the solution was stirred for 2.5 h at ambient temperature. The reaction mixture was washed with water and dried (Na_2SO_4). After evaporation of the solvent the residue was purified by flash chromatography (H-A 3:1) to afford the alcohol **1b** (540 mg, 92 %) as an oil. This alcohol **1b** (234 mg, 1.2 mmol) was then treated with *N*-iodosuccinimide (321 mg, 1.4 mmol) and $AgNO_3$ (20 mg, 0.12 mmol) in acetone (5 mL) at ambient temperature for 1 h. The reaction mixture was washed with 10 % $Na_2S_2O_3$ (5 mL), and the organic layer was dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography (H-A 3:1) to afford the alcohol **1f** (305 mg, 80 %) as crystals.

2,3-Diethoxy-4-ethynyl-4-hydroxy-2-cyclobutenone (1b). IR (neat) 3289, 2114, 1779, 1630 cm^{-1}; ^1H NMR δ 1.32 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 2.81 (1 H, s), 3.86 (1 H, br s), 4.32 (2 H, q, *J*=7.0 Hz), 4.56 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 15.2, 15.5, 67.5, 69.9, 77.4, 78.5, 78.6, 135.3, 164.5, 180.7; MS (EI) *m/z* (rel. intensity) 196 (M^+, 23), 179 (6), 168 (15), 153 (16), 139 (100).

2,3-Diethoxy-4-hydroxy-4-iodoethynyl-2-cyclobutenone (1f). mp. 83-85 °C; IR (KBr) 3345, 2166, 1775, 1611 cm^{-1}; ^1H NMR δ 1.32 (3 H, t, *J*=7.0 Hz), 1.46 (3 H, t, *J*=7.0 Hz), 3.74 (1 H, br s), 4.31 (2 H, q, *J*=7.0 Hz), 4.54 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 8.4, 15.2, 15.5, 67.5, 70.0, 80.0, 89.0, 135.6, 164.7, 180.6; MS (EI) *m/z* (rel. intensity) (no molecular ion peak) 276 (44), 248 (30), 219 (100), 191 (43), 163 (28).

Oxidation of Alcohol 1a with Mercury (II) Oxide and Iodine.

A solution of alcohol **1a** (53 mg, 0.21 mmol), HgO (136 mg, 0.63 mmol) and I_2 (160 mg, 0.63 mmol) in dry acetonitrile (4 mL) was stirred at ambient temperature for 1 h. The reaction mixture was washed with 10 % $Na_2S_2O_3$ (5 mL), and the organic layer was dried (Na_2SO_4) and evaporated. The product was purified by preparative TLC (H-A 3:1) to afford cyclopentenedione **2a** (36 mg, 45 %) as a yellow oil.

4,5-Diethoxy-2-(1-iodohexylidene)-4-cyclopentene-1,3-dione (2a). IR (neat) 1678, 1628 cm^{-1}; ^1H NMR δ 0.94 (3 H, t, *J*=7.0 Hz), 1.40 (6 H, t, *J*=7.0 Hz), 1.25-1.67 (4 H, m), 3.55 (2 H, t, *J*=7.2 Hz), 4.60 (2 H, q, *J*=7.0 Hz), 4.67 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 13.9, 15.7, 15.8, 21.8, 32.2, 43.9, 68.5, 68.6, 125.0, 129.0, 148.8, 150.1, 183.9, 184.3; MS (EI) *m/z* (rel. intensity) 378 (M^+, 7), 251 (100), 223 (15), 195 (25), 167 (7).

Typical Procedure for Oxidation of Alcohol 1 with Iodobenzene Diacetate and Iodine.

A solution of alcohol **1a** (160 mg, 0.63 mmol), $PhI(OAc)_2$ (264 mg, 0.82 mmol) and I_2 (192 mg, 0.76 mmol) in dry acetonitrile (4 mL) was stirred at -15 °C for 1 h. The reaction mixture was washed with 10 % $Na_2S_2O_3$ (5 mL), and the organic layer was dried (Na_2SO_4) and evaporated. The same work-up as above afforded **2a** (140 mg, 59 %). Likewise cyclopentenediones **2b-f** were obtained and the yields are summarized in Table 1.

4,5-Diethoxy-2-(1-iodomethylene)-4-cyclopentene-1,3-dione (2b). *oil*; IR (neat) 1680, 1626, 1586 cm^{-1}; ^1H NMR δ 1.41 (3 H, t, *J*=7.0 Hz), 1.42 (3 H, t, *J*=7.0 Hz), 4.68 (2 H, q, *J*=7.0 Hz), 4.74 (2 H, q, *J*=7.0 Hz), 7.93 (1 H, s); ^{13}C NMR δ 15.8, 15.9, 68.7, 68.9, 89.2, 136.6, 149.6, 154.0, 182.9, 183.8; MS (EI) *m/z* (rel. intensity) 322 (M^+, 100), 307 (9), 294 (18), 279 (21), 266 (35).

4,5-Diethoxy-2-(1-iodo-2-methoxyethylidene)-4-cyclopentene-1,3-dione (2c). *oil*; IR (neat) 1678, 1630 cm^{-1}; ^1H NMR δ 1.40 (3 H, t, *J*=7.0 Hz), 1.41 (3 H, t, *J*=7.0 Hz), 3.37 (3 H, s), 4.63 (2 H, q, *J*=7.0 Hz), 4.71 (2 H, q, *J*=7.0 Hz), 4.89 (2 H, s); ^{13}C NMR δ

15.7, 15.8, 58.2, 68.7, 68.8, 73.7, 121.3, 131.5, 149.4, 151.3, 183.5, 183.6; MS (EI) *m/z* (rel. intensity) 366 (M^+, 15), 239 (100), 211 (7), 183 (31), 155 (79).

4,5-Diethoxy-2-(iodobenzylidene)-4-cyclopentene-1,3-dione (2d). *oil*; IR (neat) 1680, 1626 cm^{-1}; ^1H NMR δ 1.33 (3 H, t, *J*=7.0 Hz), 1.43 (3 H, t, *J*=7.0 Hz), 4.57 (2 H, q, *J*=7.0 Hz), 4.72 (2 H, q, *J*=7.0 Hz), 7.25-7.41 (5 H, m); ^{13}C NMR δ 15.7, 15.9, 68.6, 68.7, 112.8, 127.9 (3 C), 128.3, 130.0, 143.8, 148.9, 151.8, 181.8, 183.9; MS (EI) *m/z* (rel. intensity) 398 (M^+, 30), 271 (100), 243 (20), 215 (47), 187 (18).

4,5-Diethoxy-2-[iodo(trimethylsilyl)methylene]-4-cyclopentene-1,3-dione (2e). *oil*; IR (neat) 1680, 1622, 1248, 849 cm^{-1}; ^1H NMR δ 0.36 (9 H, s), 1.41 (6 H, t, *J*=7.0 Hz), 4.63 (2 H, q, *J*=7.0 Hz), 4.71 (2 H, q, *J*=7.0 Hz); ^{13}C NMR δ 1.6, 15.7, 15.9, 68.6, 68.8, 128.6, 141.3, 149.2, 152.2, 184.3 (2 C); MS (EI) *m/z* (rel. intensity) 394 (M^+, 18), 379 (100), 351 (72), 323 (51), 295 (6).

4,5-Diethoxy-2-(diiodomethylene)-4-cyclopentene-1,3-dione (2f). *crystals*; mp. 116-117 °C; IR (neat) 1671, 1620 cm^{-1}; ^1H NMR δ 1.41 (6 H, t, *J*=7.0 Hz), 4.67 (4 H, q, *J*=7.0 Hz); ^{13}C NMR δ 15.8, 18.8, 68.9, 133.5, 150.4, 183.1; MS (EI) *m/z* (rel. intensity) 448 (M^+, 100), 420 (13), 392 (12), 265 (71), 237 (28).

Oxidation of Alcohol 1a with *N*-Iodosuccinimide.

A solution of alcohol **1a** (90 mg, 0.36 mmol), *N*-iodosuccinimide (405 mg, 1.8 mmol) in dry acetonitrile (4 mL) was stirred at ambient temperature for 6 h. The same workup as above afforded **2a** (60 mg, 44 %).

Reaction of Iodomethylenecyclopentenedione 2a with Benzylamine.

A solution of cyclopentenedione 2a (52 mg, 0.14 mmol) and benzylamine (29 mg, 0.27 mmol) in ether (2 mL) was stirred at 0 °C for 30 min. The reaction mixture was washed with water and dried (Na_2SO_4). After evaporation of the solvent the residue was purified by flash chromatography (H-A 8:1) to afford the enamine **5** (38 mg, 78 %) as crystals.

2-[1-(Benzylamino)pentylidene]-4,5-diethoxy-4-cyclopentene-1,3-dione (5). mp. 100-102 °C; IR (KBr) 3246, 1642, 1591, 1497 cm^{-1}; ^1H NMR δ 0.92 (3 H, t, *J*=7.0 Hz), 1.35 (3 H, t, *J*=7.0 Hz), 1.36 (3 H, t, *J*=7.0 Hz), 1.19-1.59 (4 H, m), 2.85 (2 H, t, *J*=7.2 Hz), 4.38 (2 H, q, *J*=7.0 Hz), 4.41 (2 H, q, *J*=7.0 Hz), 4.50 (2 H, d, *J*=6.4 Hz), 7.23-7.42 (5 H, m), 9.71 ; ^{13}C NMR δ 13.8, 15.6 (2 C), 22.9, 26.7, 30.5, 46.1, 67.9, 68.0, 94.8, 127.2 (2 C), 128.2, 129.3 (2 C), 137.4, 141.8, 143.1, 165.7, 188.2, 193.2; MS (EI) *m/z* (rel. intensity) 357 (M^+, 100), 328 (37), 300 (15), 266 (6).

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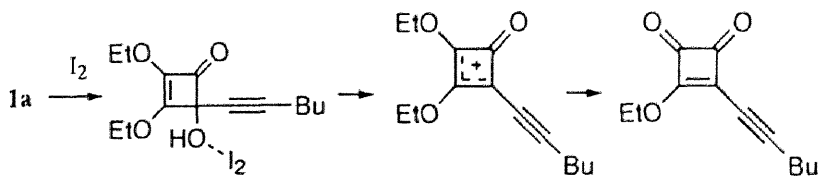
8 This type of rearrangement has been reported by Liebeskind (see refs. 10a-c). The simple treatment of **1a** with I_2, which may lead to the intermediate **4**, resulted in the formation of the other rearranged product as shown below.



9 a) P. Bovonsombat and E. McNelis, *Tetrahedron*, **49**, 1525 (1993); in the following paper, they described that a phenyl substituent at the acetylenic end altered the reaction mechanism [Idem., *Tetrahedron Lett.*, **34**, 8205 (1993)]. This is not the case for the present reaction (Table 1, entry g).

10 Related synthetic methods using squaric acid derivatives were reported; a) L. S. Liebeskind, D. Mitchell and B. S. Foster, *J. Am. Chem. Soc.*, **109**, 7908 (1987); b) D. Mitchell and L. S. Liebeskind, *Ibid.*, **112**, 291 (1990); c) L. S. Liebeskind and A. Bombrun, *J. Org. Chem.*, **59**, 1149 (1994); d) L. S. Liebeskind and R. Chidambaram, *J. Am. Chem. Soc.*, **109**, 5025 (1987); e) M. Zora and J. W. Herndon, *J. Org. Chem.*, **59**, 699 (1994).

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List of Publications

Chapter 2-1

1,2- vs. 1,4- Addition of 3,4-Dichlorocyclobut-3-ene-1,2-dione with Unsaturated Organosilanes

M. Ohno, Y. Yamamoto, and S. Eguchi, *J. Chem. Soc. Perkin Trans., 1* **1991**, 2272-2273.

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Chapter 2-2

Synthesis of γ-Acylmethylenetetronates from Squaric Acid

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Acylmethylenetetronate by Thermal Rearrangement: New Synthetic Aspect of Squaric Acid as a C_4-Synthon

Y. Yamamoto, M. Ohno, and S. Eguchi, *Tetrahedron*, **50**, 7783-7798 (1994).

Chapter 3-1

Cyanohydrins from Squaric Acid Ester with Trimethylsilyl Cyanide and Their Ring Opening Reactions

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Triethyloxonium Tetrafluoroborate Mediated Addition Reaction of Unsaturated Organosilanes to Squaric Acid Esters

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Chapter 3-2

BF_3-Catalyzed Reaction of Cyclobutene-1,2-dione Monoacetal and Its Vinylog with Allylsilanes. Regioselective Synthesis of 4-Allyl-4-ethoxycyclobutenones from Squaric Acid and Their Conversion to Bi- and Tricycloalkanones

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Regioselective Derivatization of Squaric Acid via Lewis Acid-Catalyzed Reaction of Cyclobutenedione Monoacetal and Its Vinylog with AllylSilanes, Silyl Enol Ether, and Silyl Ketene Acetal, and Subsequent Ring Transformations of the Adducts

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Chapter 4-1

Oxidative Rearrangement of 4-Hydroxy-2-cyclobutenone. A. New Route to Highly Substituted Furanones from Squaric Acid

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Chapter 4-2

Unexpected Ionic Rearrangement of Hypoiodite. Ring-Expansion of 4-Alkynyl-4-hydroxycyclobutenone to Iodomethylenecyclopentene-1,3-dione

Y. Yamamoto, M. Ohno, and S. Eguchi, *Tetrahedron Lett.*, **36**, 5539-5542 (1995).

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