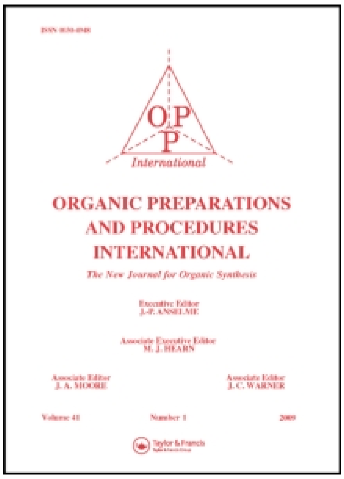

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Hashem, Ahmed I. , Senning, Alexander and Hamad, Abdel-Sattar S.(1998) 'PHOTOCHEMICAL TRANSFORMATIONS OF 2(5*H*)-FURANONES. A REVIEW', Organic Preparations and Procedures International, 30: 4, 401 — 425

To link to this Article: DOI: 10.1080/00304949809355303

URL: http://dx.doi.org/10.1080/00304949809355303

ORGANIC PREPARATIONS AND PROCEDURES INT., 30 (4), 401-425 (1998)

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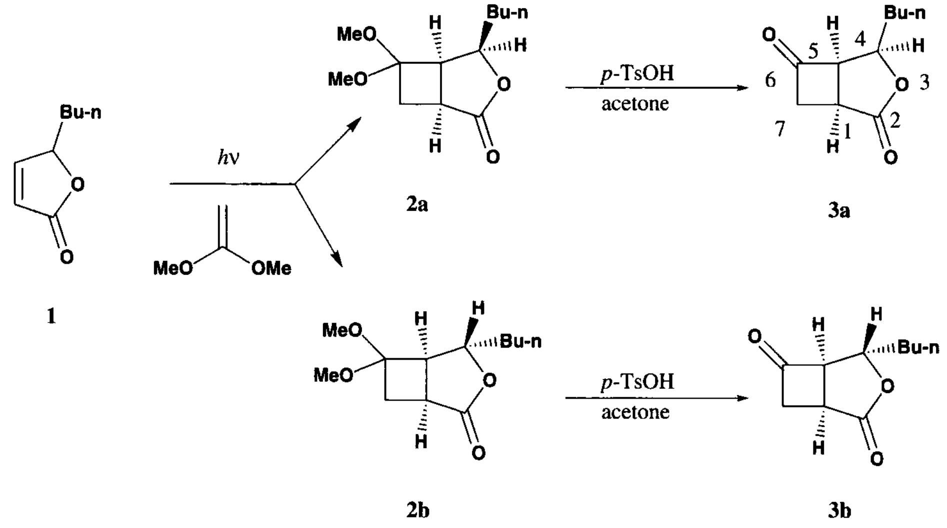
INTRODUCTION

2(5*H*)-Furanones are often the core skeletons of naturally occurring heterocycles.[1] Moreover, they occur as intermediates in the synthesis of many products of biological interest. The anti-inflammatory agent vulpinic acid,[2] the antibiotic aspertetronins,[3] and vitamin C[4] exemplify simple 2(5*H*)-furanone derivatives, although this subunit can also be found in highly complex structures such as the tetrocarcin family of antitumor agents and kijanimicin.[5] The photochemical behavior of these unsaturated lactones has been the subject of extensive studies during the past few decades. In 1990, a review dealing with the photochemistry of these compounds was published,[6] and therefore the present survey will emphasize recent developments of the last seven years (until end of 1996). The majority of reactions encountered during this period are [2+2] photocycloadditions. Such reactions constitute a versatile methodology for the construction of the skeletons of many natural products.

I. ADDITIONS REACTIONS

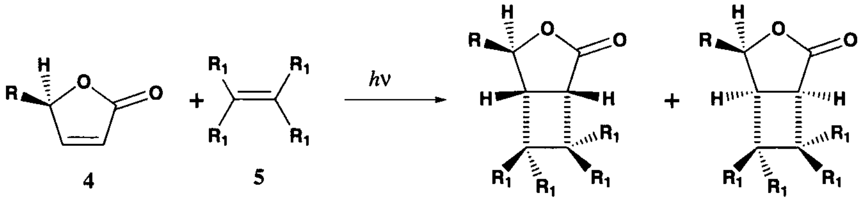
1. Addition of Alkenes

Substituted cyclobutane rings are present in some natural products spatane diterpenes,[7] bourbonene,[8] caryophyllene sesquiterpenes,[9] and the monoterpene (+)grandisol.[10] The [2+2] photocycloaddition of 2(5*H*)-furanones to alkenes has been successfully utilized for the generation of such rings in the total synthesis of some of these substances,[11] Kosugi *et al.*[12] reported that irradiation of the furanone **1** in the presence of excess 1,1-dimethoxyethylene in benzene gave a mixture of stereoisomeric adducts which were separated by column chromatography into *endo*-**2** and *exo*-**2**, respectively. The orientation of the dimethyl acetal group and the configuration of the butyl group were rigorously established on the basis of the ^{1}H-NMR coupling pattern in the hydrolysis products *endo*-**3** and *exo*-**3**, obtained by treatment of **2a** and **2b** with *p*-toluenesulfonic acid in acetone (*Scheme 1*).



Scheme 1

If a certain control for this cycloaddition could exist and the starting 2(5*H*)-furanone were homochiral, such reactions could lead to good diastereomeric excesses and ultimately to enantiomerically pure natural products.[13] Steric and stereoelectronic effects can force the olefin to approach the furanone from its less hindered side, thus creating a diastereofacial differentiation. To clarify this point, the stereoselective course of the photochemical cycloadditions of furanones **4** to tetramethylethylene ($R_1 = R_1 = CH_3$) and ethylene ($R_1 = R_1 = H$) was investigated.[13] Two cycloadducts, *endo*-**6** and *exo*-**6**, were obtained (*Scheme 2*) whose relative configurations were determined by inspection of their NMR coupling constants. The major cycloadduct had the smallest *J* values and was assigned the *exo* structure.



a) $R_1 = CH_3$ (TME) b) $R_1 = H$ (ethylene) **exo-6** **endo-6**

Scheme 2

The ratios of the *exo* and *endo* isomers led to the conclusion that there is some interaction between R of the furanone and the olefin.[13] Steric interactions can account for facial diastereoselectivities, the β-side of the furanone being encumbered by R. In addition, stereoelectronic effects, i. e., the n-π interaction between the non-bonding electrons of the ester oxygen of R and the π-orbitals of the furanone, could induce a preferential α-attack (*Fig. 1*).

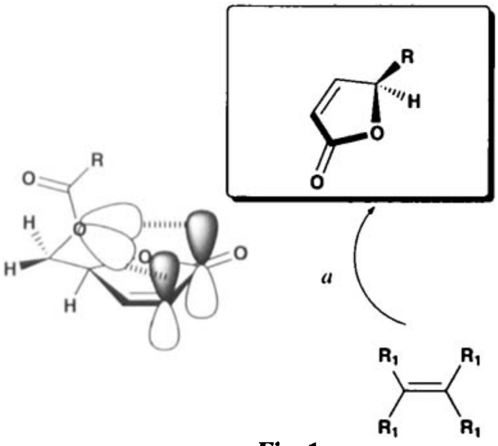
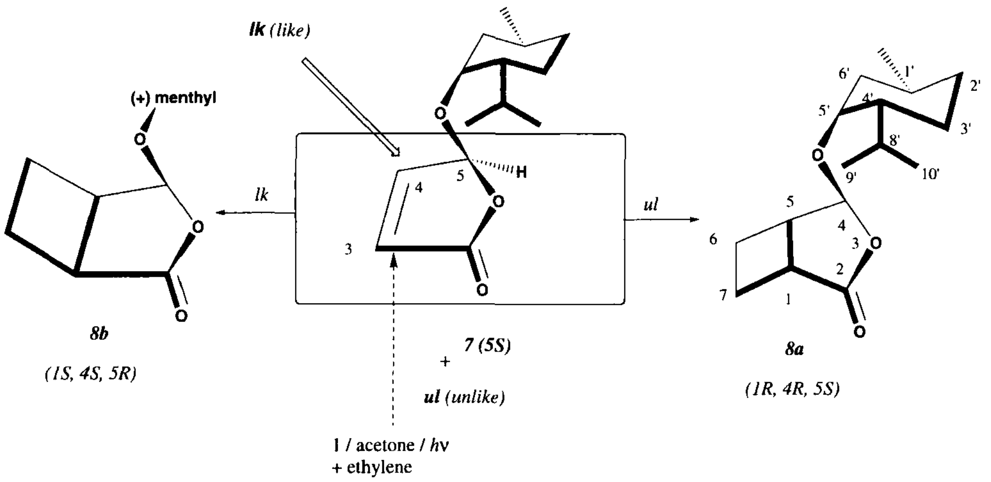


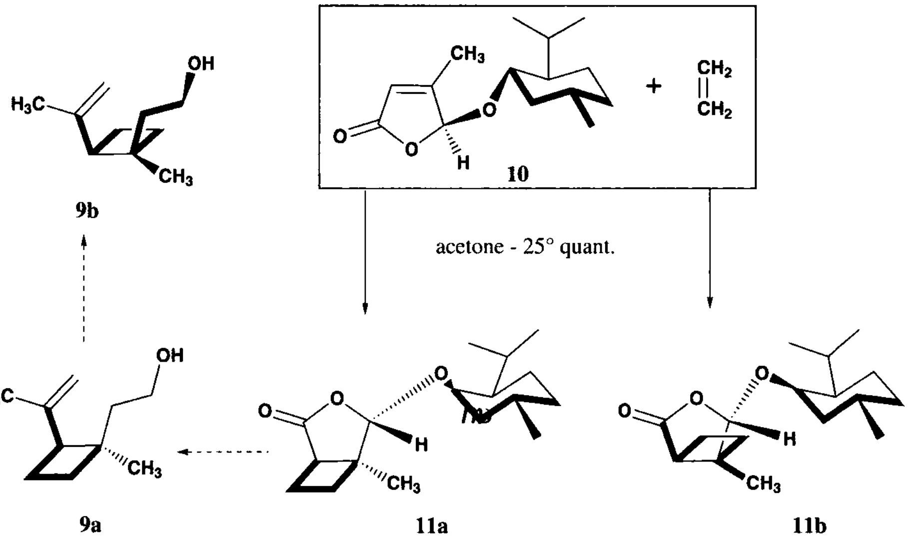
Fig. 1

Hofmann *et al.* studied the diastereoselective course of the acetone-sensitized photocycloaddition of ethylene to the chiral furanone (5*S*)-**7**. A diastereomeric mixture of *endo*-**8** and *exo*-**8** was obtained in high yield (*Scheme 3*). The relative configurations of these isomers were determined by the NMR coupling of the acetal proton at position 4 with the proton at position 5. It was concluded that *ul*-attack (unlike-attack) is preferred and that the diastereoselectivity can be improved by lowering the reaction temperature.[14]



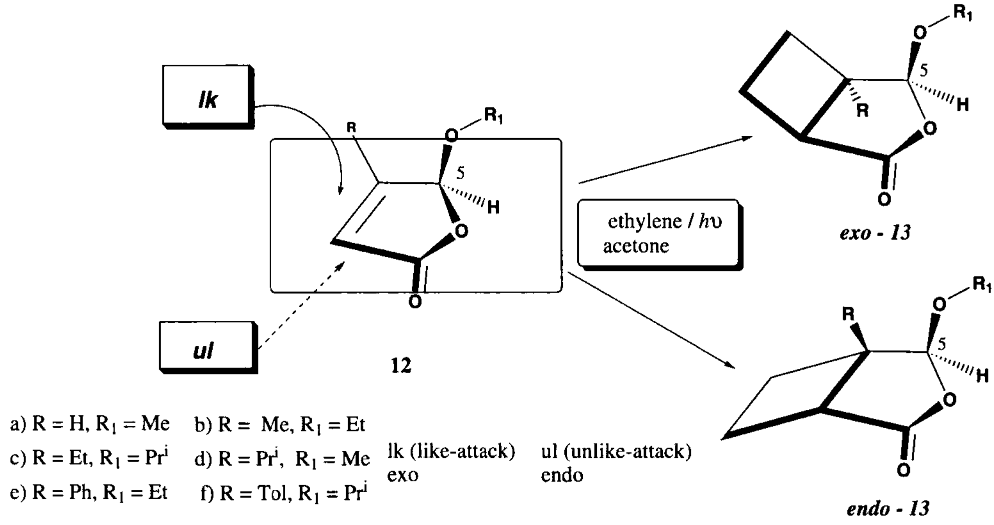
Scheme 3

The total synthesis of (+)grandisol **9a,** which is found in the aggregation pheromone of the boll weevil (*Anthonomus grandis*), the most important insect pest in cotton production in the southern USA,[15] has been described by Hoffmann and Scharf.[16] The first step of this synthesis involved an acetone-sensitized photocycloaddition of ethylene to (5*S*)-5-[(+)-menthyloxy]-4-methyl-2(5*H*)-furanone **10**. Two diastereomeric cyclobutanes, **11a** and **11b**, were obtained (*Scheme 4*) and easily separated by column chromatography.



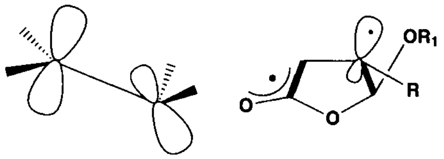
Scheme 4

(+) Grandisol was formed from the isomer **11a** while **11b** could be converted to (-) grandisol **9b**. The mechanism of the stereoselective [2+2] photocycloaddition of ethylene to 5-alkoxy-2(5*H*)-furanones **12** has been intensively investigated.[17] The furanones (*Scheme 5*) were irradiated in the presence of ethylene in acetone as solvent and sensitizer.



Scheme 5

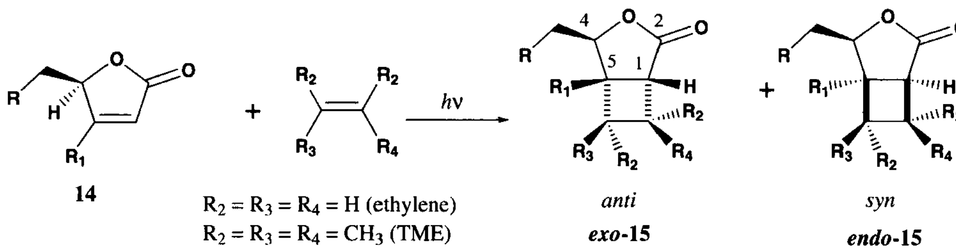
The ratios of the diastereomeric cyclobutanes *exo*-**13** and *endo*-**13** were determined by ^{13}C NMR. The differences in the activation parameters $\Delta\Delta H^{\ddagger}$ and $\Delta\Delta S^{\ddagger}$ for the overall reaction were also calculated. The diastereoselectivity of the photocyclobutane formation was found to depend predominantly on the achiral substituent R. The influence of R_1 was of minor importance. Remarkable differences in the enthalpy and entropy for the formation of the excess diastereomer were observed in the reaction with ethylene of the furanones carrying an isopropyl substituent compared to those carrying an aryl substituent and those without β-substitution. In the former case, the *lk*-attack (like-attack) was favored by enthalpy control and entropically disfavored; thus, on balance the *ul*-attack (unlike-attack) is favored. The same authors concluded that the diastereoselection is dominated by only one mechanistic step which is the approach of ethylene to the vibrationally relaxed $^3\pi\pi^*$ excited furanone (*Fig. 2*).



Possible Transition State of the [2+2]Cycloaddition of Ethylene to a Triplet Excited 5-Alkoxy-2(5*H*)-Furanone

Fig. 2

Recently, Alibés *et al.*[18] studied in detail the photocycloaddition of furanones**14** to ethylene, extending the scope to other olefins, mainly tetramethylethylene (TME) and vinylene carbonate (*Scheme 6*).



14

$R_2 = R_3 = R_4 = H$ (ethylene)
$R_2 = R_3 = R_4 = CH_3$ (TME)
$R_3 = R_4 = OCOO$, $R_2 = H$
Vinylene carbonate

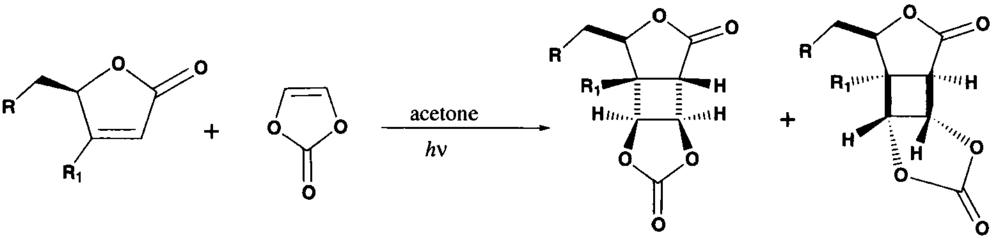
exo-**15**

endo-**15**

a) R = H, R_1 = H; b) R = OH, R_1 = H;
c) R = CF_3COO, R_1 = H; d) R = CH_3COO, R_1 = H;
e) R = $(CH_3)_3CCOO$, R_1 = H_3 ; f) R = $PhCH_2O$, R_1 = H;
g) R = $(CH_3)_3CCOO$, R_1 = CH_3 ; h) R = CH_3COO, R_1 = CH_3

Scheme 6

The cycloadducts were separated by column chromatography and their relative configurations determined by NMR. When the alkene is vinylene carbonate four new stereogenic centers are created.[18] However, only the *anti-anti* and the *syn-anti* isomers could be detected and isolated.

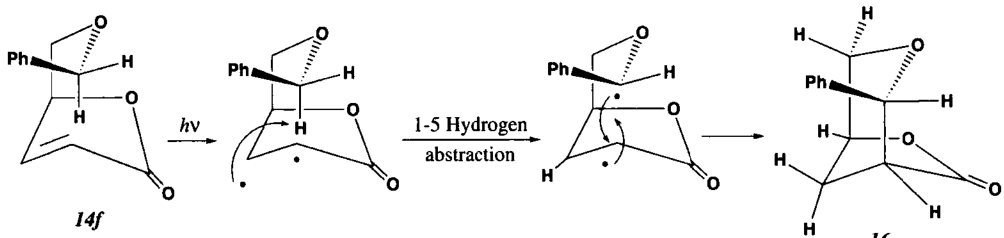


anti-anti

syn-anti

Scheme 7

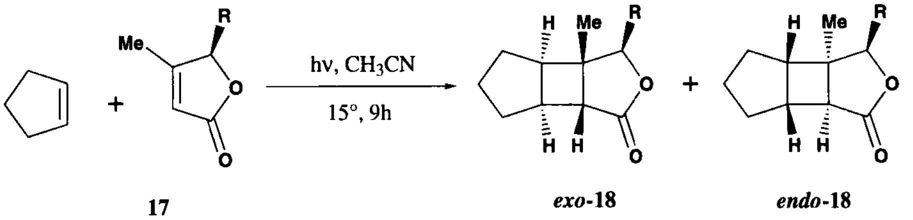
The authors investigated the effect on the *anti/syn* ratios of R, R_1, R_2, R_3 and R_4, the temperature, the solvent and the filter. Their results revealed a strong influence of the solvent. An electron-rich olefin such as TME gave a good yield in ether under direct irradiation, but not in acetone and with a pyrex filter. On the other hand, electron-poor olefins reacted efficiently in acetone with a pyrex filter, but not in ether with a quartz filter. This behavior of electron-poor olefins was explained in terms of the triplet, *i. e.* the $^3\pi\pi^*$ excited 2(5*H*)-furanone which can be generated by sensitization in acetone[19] and by the avoidance of photodecomposition of the cycloadducts or their precursors by filtering with pyrex (acetone is still excited at $\lambda > 290$ nm). The acetone provides for the formation of the reactive triplet of the enone, and the pyrex filter prevents photodegradation. With respect to the effect of the R group, it was found that increasing the bulk of R^1 increases the *anti/syn* ratio regardless of the olefin. In the case of furanone **14f**, no cycloadducts could be isolated, but instead the bicyclic lactone **16** was obtained as the only product. All ^1H and ^{13}C NMR peaks were rigorously assigned and a configurational analysis of the newly formed stereogenic centers of **16** carried out. The photochemical formation of **16** is thought to involve the following steps (*Scheme 8*).[18]



Scheme 8

2. Additions of Cycloalkenes and Cycloalkenones

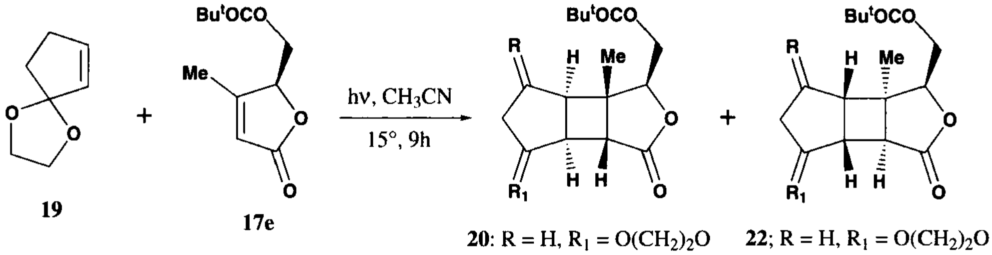
Irradiation of furanones **17** and cyclopentene in acetonitrile with a low pressure mercury lamp at 15° leads to the formation of two new cycloadducts: *endo*-**18** and *exo*-**18** (*Scheme 9*). These products were isolated by column chromatography and their relative amounts and stereochemistry determined by NMR.



a) R = $CH_2OC(Ph)_3$; b) R = CH_2OH; c) R = $CH_2OCH_2OCH_3$; d) R = $CH_2OCOCH(CH_3)_2$
e) R = $CH_2OCO(CH_3)_3$; f) R = $CH_2OSi(CH_3)_2C(CH_3)_3$; g) R = $C(CH_3)_2OH$

Scheme 9

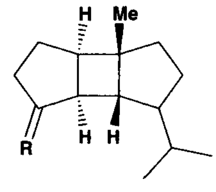
It was expected that the *exo* and the *endo* isomer would be the major and the minor product, respectively, consistent with the least hindered approach. The efficiency of the diastereofacial differentiation correlates with the bulk of the substituents; **17b** and **17c** showed almost no selectivity while **17e** gave the highest ratio. A [2+2] photocycloaddition of **19** to **17e** under the same conditions afforded the four cycloadducts **20-23** *(Scheme 10)*, with **20** being the major product.[11]



20: $R = H, R_1 = O(CH_2)_2O$ **22**; $R = H, R_1 = O(CH_2)_2O$

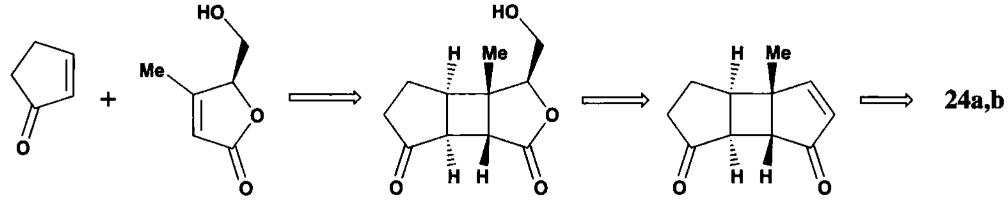
21: $R = O(CH_2)_2O, R_1 = H$ **23**; $R = O(CH_2)_2O, R_1 = H$

Scheme 10



24 a) $R = CH_2$ b) $R = O$

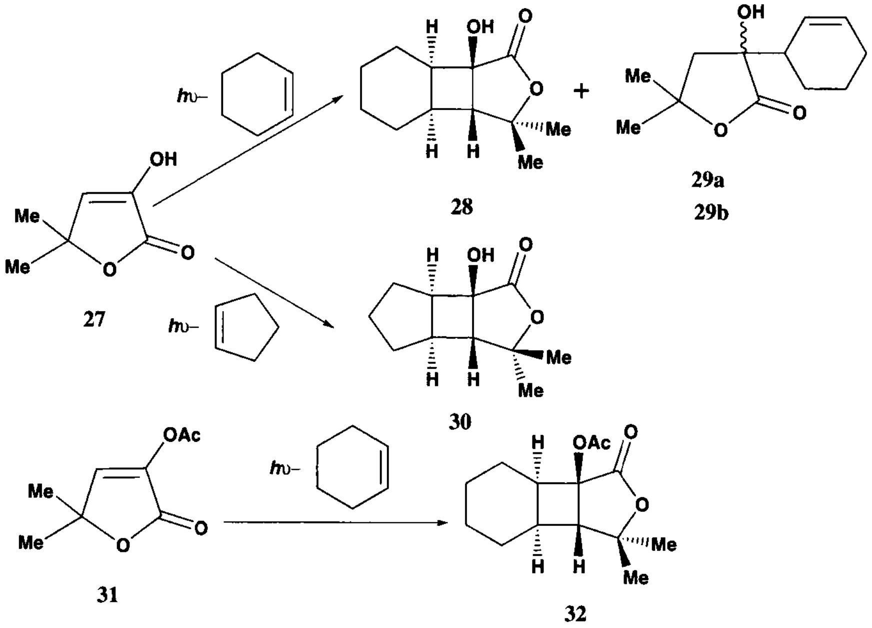
The major product **20** was used as starting material for a total synthesis of (-)β-bourbonene (**24a**), a representative of the bourbonene sesquiterpenes. The first step of this total synthesis[20] of (-)β-bourbonene **24a** and (-) norbourbonene **24b** involves a [2+2] photocycloaddition of 2-cyclopentenone to the furanone **17b** (*Scheme 11*). The least hindered approach of the cyclopentenone to the furanone creates the chiral centers of the products **25** and **26**, resulting in the subsequent formation of optically pure **24a** and **24b**.



17b **25** **26**

Scheme 11

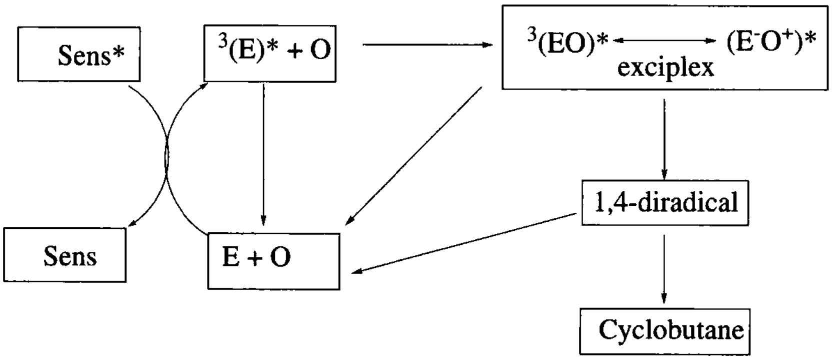
Hatsui *et al.*[21] have reported photocycloadditions of 3-hydroxy-5,5-dimethyl-2(5*H*)-furanone **27** with cyclohexene and cyclopentene, respectively (*Scheme 12*). With cyclohexene the products **28** and **29** were obtained after chromatographic separation. The 1:1 adduct **28** is the major product while ^{13}C NMR of the minor product disclosed the presence of the isomers **29a** and **29b** in a 2:1 ratio. Similarly, the reaction of the furanone **27** with cyclopentene was examined[21] and gave a single product **30** which was identified, as the [2+2] cycloadduct based on spectroscopic data. Irradiation of 3-acetoxy-5,5-dimethyl-2(5*H*)-furanone **31** and cyclohexene afforded the photocycloadduct **32** (*Scheme 12*)



Scheme 12

3. Mechanisms of the [2+2] Photocycloadditions

Despite a number of elaborate and elegant studies, many details of these reactions remain to be elucidated.[22] The lack of mechanistic uniformity notwithstanding, several arguments lead to a working hypothesis (*Scheme 13*)[12,17,23] which may serve as the basis for rational predictions of the regio- and stereochemical outcome of many photocycloadditions.[22]



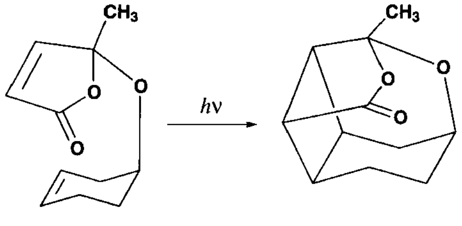
Mechanism of ThePhotosensitized [2+2] Cycloaddition; Sens: Sensitizer, E: Enone, O: Olefi

Scheme 13

In many cases, the exciplex is not directly detectable. Therefore many authors have assumed the direct formation of the diradical from the excited enone.[24-27] The 1,4-diradical intermediates can then recombine to form cyclobutanes. Such diradicals have been trapped by intermolecular hydrogen abstraction from H^2Se as hydrogen donor.[27] In this mechanistic cycle, the exciplex as well as the 1,4-diradical may revert to starting material. In their study of the photosensitized [2+2] cycloaddition of ethylene to 5-alkoxy-2(5*H*)-furanones, Hoffmann *et al.*[17] stated that the formation of the 1,4-diradical intermediate is predominate in the selection step. These authors postulated a possible transition state (Fig. 2, p. 407) involving approach of the ethylene molecule to the vibrationally relaxed $^3\pi\pi^*$ excited furanone.

4. Intramolecular Photocycloadditions

Regio- and stereochemical control can be excellent in many examples of intermolecular photochemical [2+2] cycloadditions, but the frequency of cases where the selectivity is low or unpredictable, has inhibited the widespread use of this otherwise highly efficient reaction.[24h] This problem can virtually be overcome by incorporation of the two sites of unsaturation in the same molecule. Although many early examples of [2+2] photocycloadditions were in fact intramolecular, this reaction variant saw only limited use in the synthesis of complex molecules until the 1970's where its potential for the smooth and efficient construction of a wide array of complex polycyclic carbon skeletons was fully recognized. During his attempts at the synthesis of reserpine, Pearlman found that photolysis of the furanone **33** leads to the formation of the cycloadduct **34** in 45% yield (*Scheme 14*).[23c]

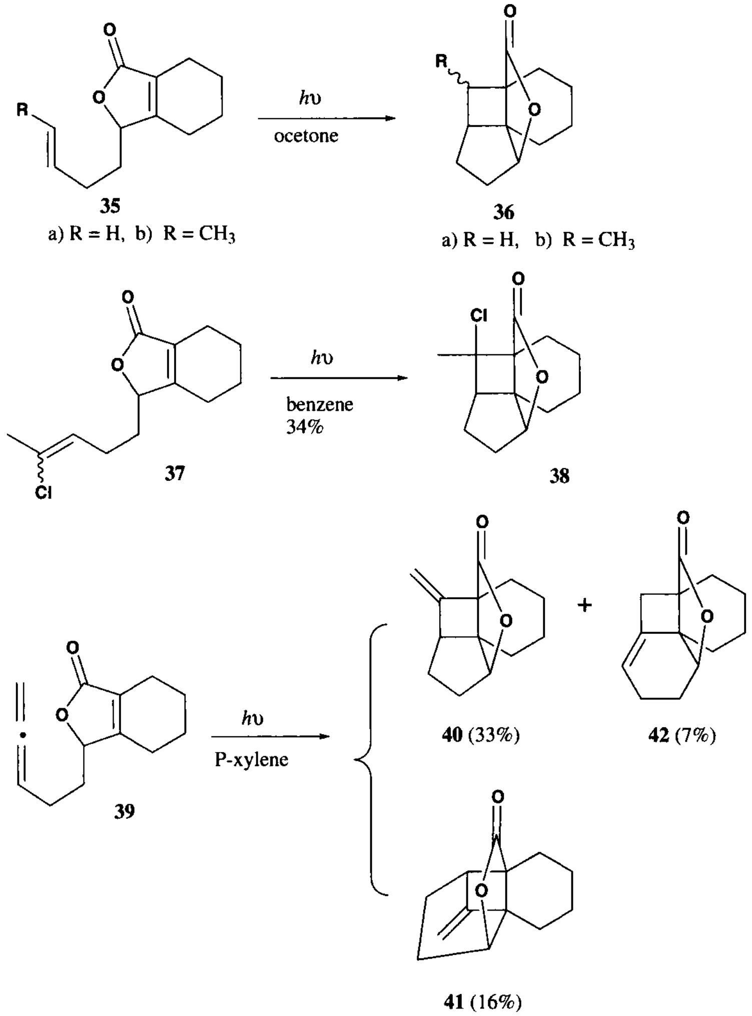


Scheme 14

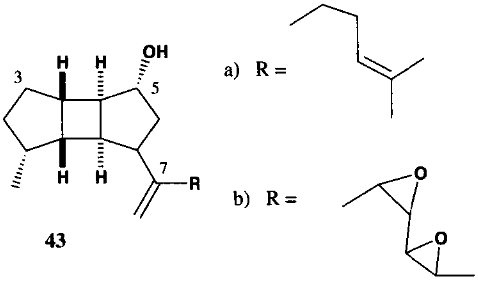
Intramolecular photochemical [2+2] cycloadditions of fused furanones bearing alkenyl side-chains at position 5 have been described by Coates and coworkers (*Scheme 15*).[28] Irradiation of furanones **35** in acetone in quartz vessels affords the tricyclic lactones **36**. The photocycloaddition of (chloropentenyl)furanones **37** in benzene proceeds by a factor of 50 more slowly than that of the methyl derivative **35b** to give the adduct **38**. In contrast to the apparently high regioselectivity in the photocycloadditions of the butenyl and pentenyl substituted furanones **35** and **37**, irradiation of the (3,4-pentadienyl)furanone **39** in *p*-xylene affords the cycloadducts **40** and **41** as major products with a small amount of a third product **42** formed by cycloaddition to the terminal double bond of the allene system.

The *cis,anti,cis*-tricyclo[5.3.0.0^{2,6}]decane ring system found in spatane diterpenes (such as stoechospermol **43a** and spatol **43b**) was constructed by means of an intramolecular asymmetric [2+2] photocycloaddition.[29]

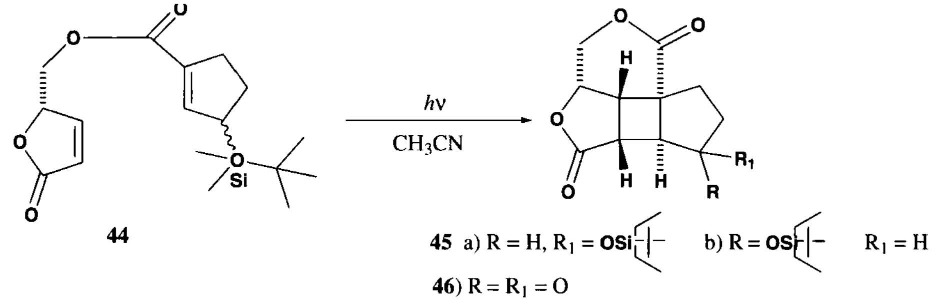
Upon UV irradiation in acetonitrile, furanone ester **44** is transformed to a 1:1 mixture of **45a** and **45b** (*Scheme 16*). After subsequent desilylation and oxidation, both diatereomers give the same keto lactone **46**.



Scheme 15



This was considered as an indication that the regio- and stereoselectivity of this intramolecular cycloaddition is fully controlled by the chiral center of the furanone moiety and is independent of that of the cyclopentene portion. In more recent work,[30] the same authors employed a highly regioand stereoselective intramolecular [2+2] photocycloaddition as the key step of the construction of an optically pure tricyclo[5.3.0.0^{2,6}]decane ring system from an optically pure furanone. They were thus able to synthesize optically pure (+) stoechospermol. Molecular models of the transition states and of the intramolcular cycloadducts of furanone **47** (*Scheme 17*) indicated that the ester linkage between the furanone and cyclopentene parts can be expected to control the regio- and stereochemistry of this reaction. This control allows the cyclopentene moiety to approach from the sterically more hindered face of the furanone to afford **46**.

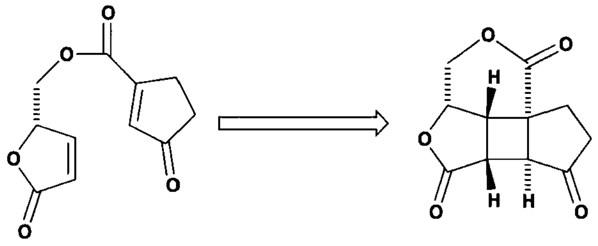


44

45 a) R = H, R_1 = OSi b) R = OS R_1 = H

46) R = R_1 = O

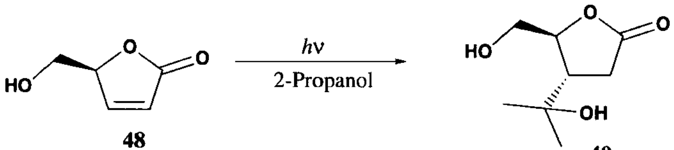
Scheme 16



47 **Scheme 17** **46**

5. Addition of Alcohols and Amines

Reaction of (*S*)-5-hydroxymethyl-2(5*H*)-furanone **48** with 2-propanol under irradiation with a low pressure mercury lamp yields the photoadduct **49** (*Scheme 18*).[31]

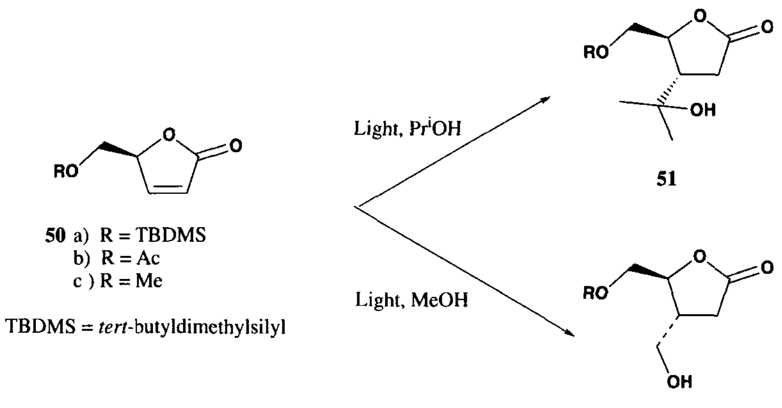


48 **49**

Scheme 18

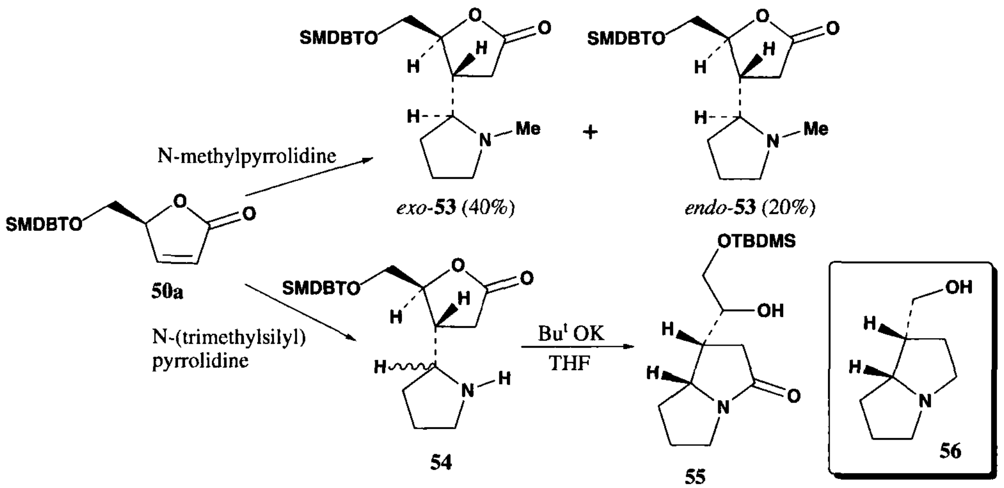
The regiospecific and (apparently) stereospecific addition of various alcohols to furanones **50** under irradiation in the presence of benzophenone was studied by Mann and Wilson (*Scheme 19*).[32]

The photoadducts **51** and **52** were used as intermediates in the synthesis of *cis*-chrysanthemic acids and novel nucleosides. In an attempt to widen the scope of this procedure, de Alvarenga and Mann studied the photoinduced addition of *N*-substituted pyrrolidines to 2(5*H*)-furanones.[33] It



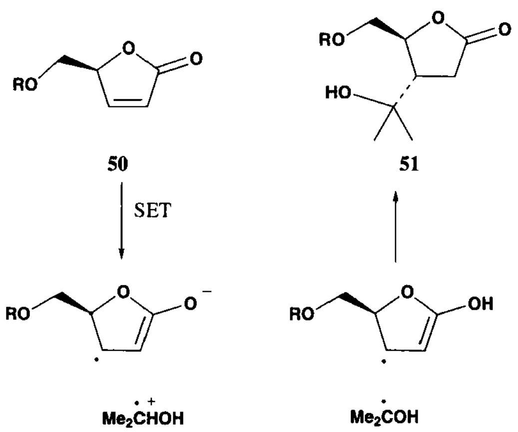
Scheme 19

was found that co-irradiation of furanone **50a** and *N*-methylpyrrolidine in acetonitrile in the presence of benzophenone leads to the formation of two photoadducts, *i. e. exo*-**53**, and *endo*-**53**, in 40 and 20% yield respectively (*Scheme 20*). This photoreaction was repeated with *N*-(trimethylsilyl)pyrrolidine instead of *N*-methylpyrrolidine. The photoadduct thus obtained was treated with potassium *tert*-butoxide in THF to give 1-azabicyclo[3.3.0]-2-octanone **55**. The latter possesses the ring skeleton and stereochemistry of the pyrrolizidine alkaloid lindelofidine **56**.[33]



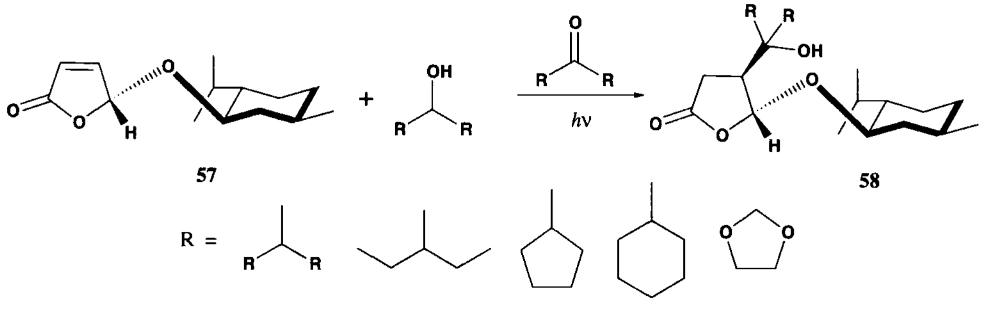
Scheme 20

According to Weymouth-Wilson and Mann, it is possible to effect photoaddition of 2-propanol to furanones **50** by use of a low pressure mercury lamp without addition of benzophenone as sensitizer. These additions are completely regiospecific and apparently, face-selective as well as efficient (94% yield).[33] These authors also concluded that this reaction might be initiated by a single electron-transfer (SET) process, and subsequently proceeds *via* a radical-chain reaction (*Scheme 21*).[34,35]



Scheme 21

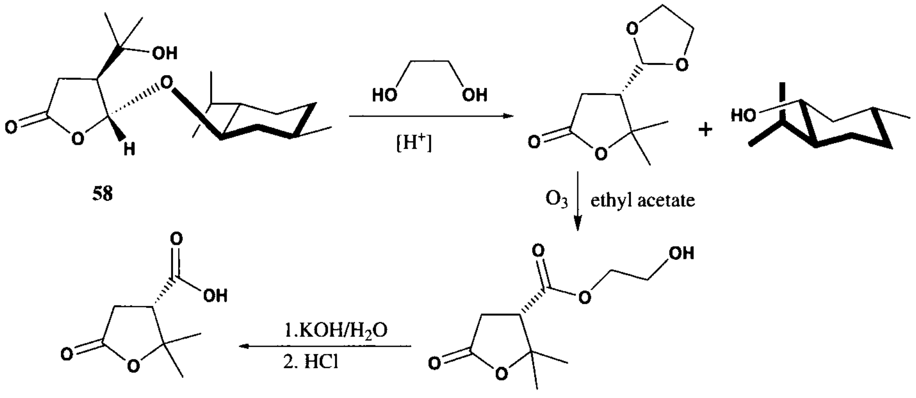
It was impossible to add methanol to these furanones under the same conditions since the initially formed ketyl radical •CH_2OH is certainly less stable than the tertiary radical •CMe_2OH.[34] In the opinion of the authors, the mechanism of this photoinduced reaction appears analogous to that proposed by Fraser-Reid *et al.*[36] for similar systems. This mechanism involves excitation of benzophenone to the triplet, *i. e.* the $^3n\pi^*$ excited state and subsequent abstraction of a hydrogen atom from methanol and Michael addition of the so formed radical to the furanone. The addition of hydroxyalkyl radicals, generated photochemically from alcohols by hydrogen abstraction by $^3n\pi^*$ excited carbonyl compounds, to (5*R*)-(-)-5-menthyloxy-2(5*H*)-furanones **57** has been described by Hoffmann (*Scheme 22*).[37] The diastereoselectivity as well as the product ratio resulting from the competing



Scheme 22

reactions of two different ketyl radicals (generated from the alcohol and the ketone, respectively) were measured by ^{13}C NMR.[37] It could be shown in all cases that the diastereoselectivity is > 95%.

In order to determine the site of the attack, adduct **58** was converted to (-) terebic acid (*Scheme 23*) whose optical rotation and absolute configuration are known. This transformation revealed that the furanone **57** is attacked by the radicals from the *unlike* side.

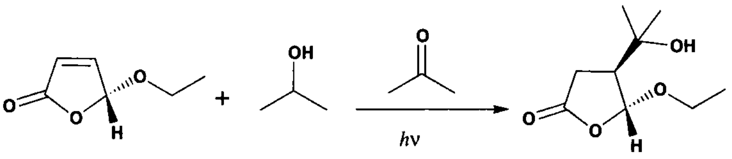


58

(-) terebic acid
yield 32%

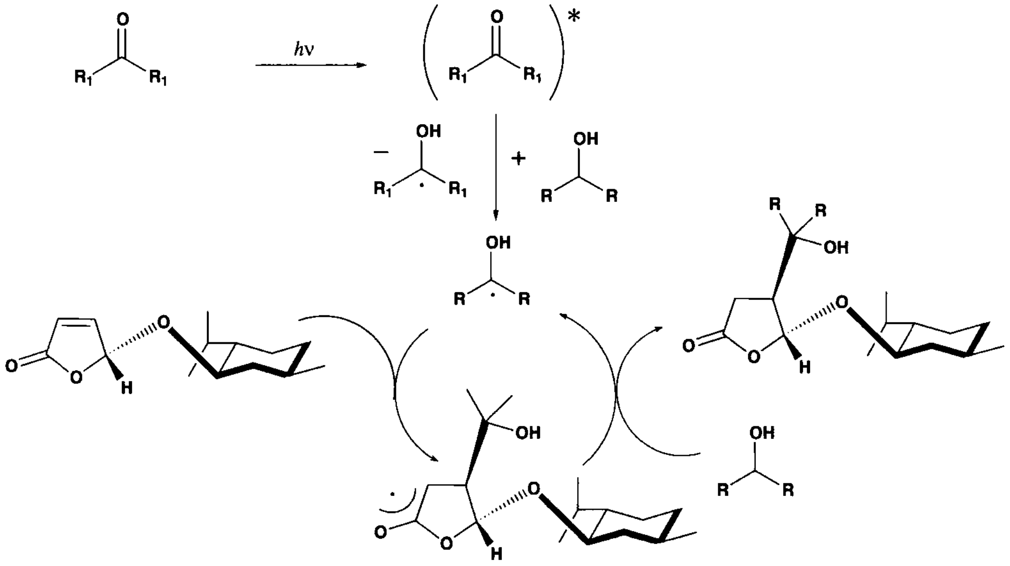
Scheme 23

The reaction of 2-ethoxy-2(5*H*)-furanone **59** with 2-propanol (*Scheme 24*) has been studied kinetically.[37]



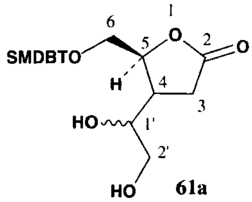
59 **Scheme 24** **60**

In the absence of acetone, no reaction takes place in the dark. These results as well as the fact that this reaction is still very efficient even when acetone is present in low concentration led the author to conclude that a radical chain mechanism is operative (*Scheme 25*)[37,38] as was pointed out earlier by Pitts *et al.*[39]



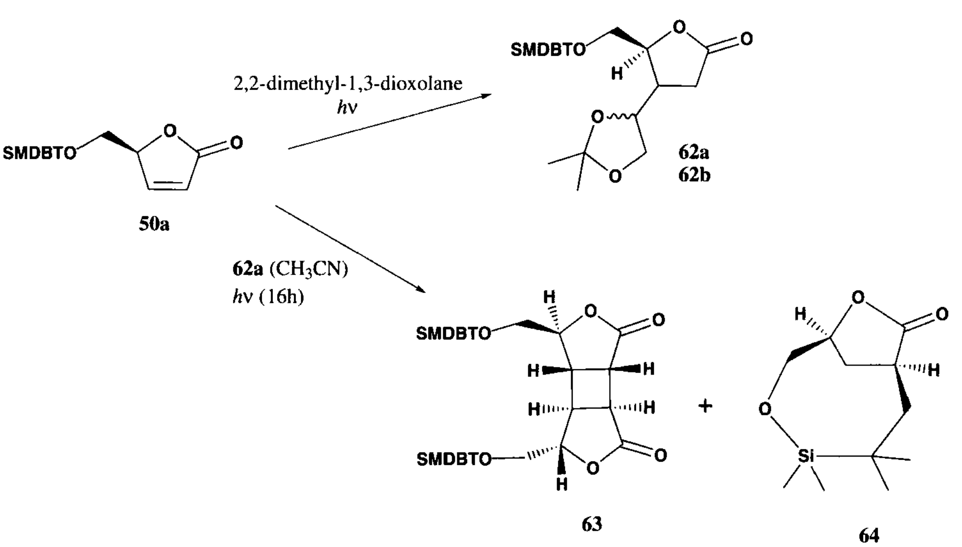
Scheme 25

Ethylene glycol reacts with furanone **50a** under irradiation (254 nm) to give a mixture of the diastereomers **61a** and **61b**, *i. e.* [(4*R*,5*S*)-5-*tert*-butyldimethylsilyoxymethyl)-4-(*R*,*S*)-(1,2-dihydroxyethyl)tetrahydro]-2(5*H*)-furanone. This mixture could be separated after conversion to the corresponding acetonides.[32]



61a
61b

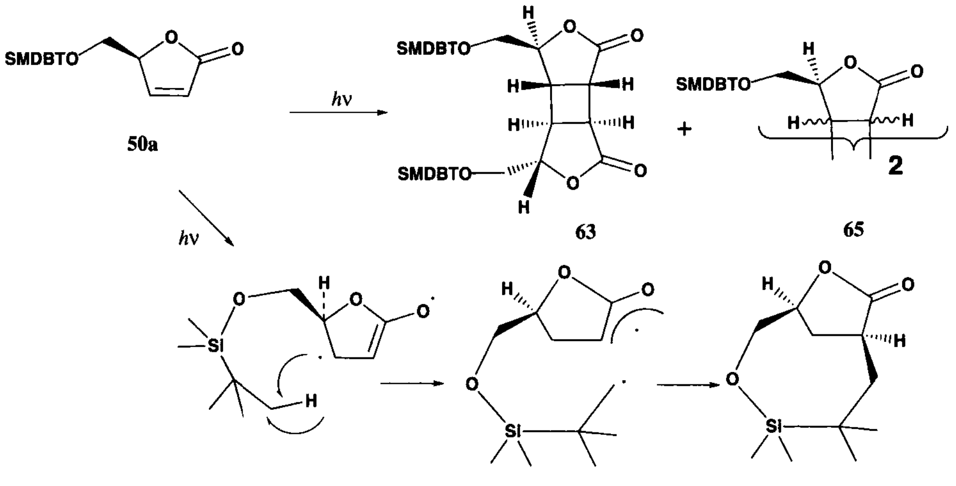
Brown *et al.*[40] have reported that irradiation of furanone **50a** in the presence of 2,2-dimethyl-1,3-dioxolane yields the two photoadducts **62a** and **62b**, *i. e.* {[(4*R*,5*S*)-5-*tert*-butyldimethylsilyloxymethyl-4-[*O*-isopropylidene-(*R*,*S*)-1,2-dioxyethyl]tetrahydro-2(5*H*)-furanone} (*Scheme 26*). The two anomers could be separated in low yield (13 and 17%, respectively) by flash chromatography. In an attempt to improve this synthesis, the authors irradiated furanone **50a** (CH^3CN, 254 nm) in the presence of excess (*S*)-isomer **62a**, whereby two new products were obtained (Scheme 26). These two products were shown by NMR to be the furanone dimer **63** and the intramolecular photoadduct **64**. The structure of **63** was confirmed by X-ray crystallography.



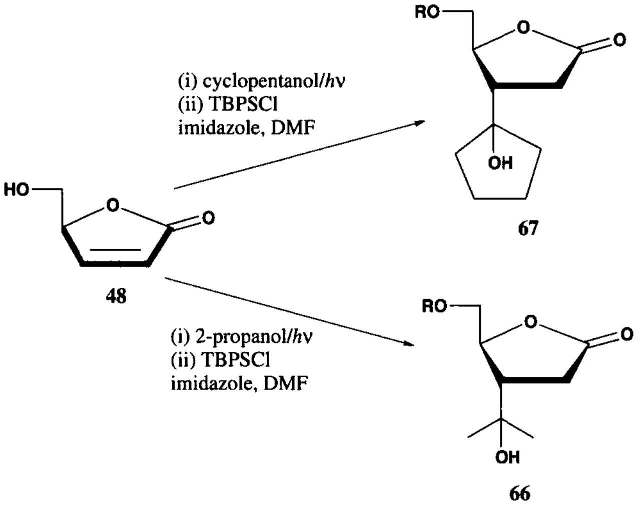
Scheme 26

A minor dimeric product **65** was also detected. The proposed mechanism for the formation of these products (*Scheme 27*) involves initial generation of a 1,3-biradical.[40]

The photoaddition of 2-propanol and of cyclopentanol to (*S*)-hydroxymethyl-2(5*H*)-furanone **48** has recently been described.[41] These additions were carried out by irradiation with a medium pressure mercury lamp in the presence of benzophenone, followed by selective protection of the primary hydroxyl group by reaction with *tert*-butyldiphenylsilyl chloride (TBDPSCl) and imidazole in DMF. The photoadducts **66** and **67** (*Scheme 28*) were then used as key synthons for several biologically important 3'-C branched 2',3'-dideoxynucleosides.[41]

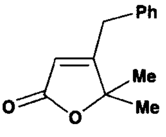


Scheme 27

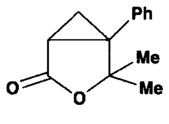


Scheme 28

II. REARRANGEMENTS AND ISOMERIZATIONS



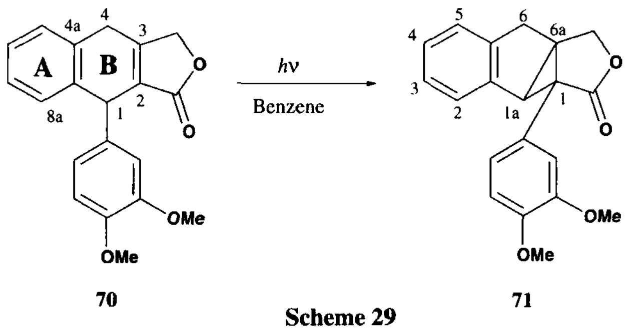
68



69

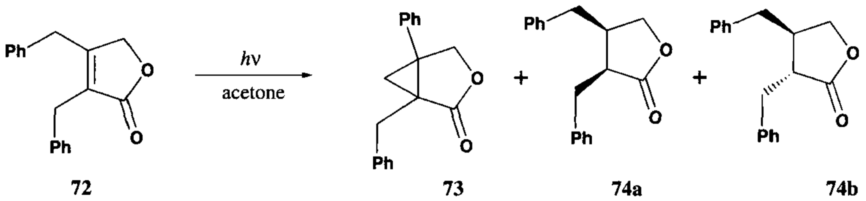
The di-π-methane rearrangement[42] is a particularly general photochemical reaction with a fascinating mechanistic complexity and esthetic appeal. The requirement for this reaction is a reactant with two π-moieties attached to a single sp^3-hybridized carbon atom. Thus, acetone photosensitized irradiation of 4-benzyl-5,5-dimethyl-2(5*H*)-furanone **68** leads to the formation of 4,4-dimethyl-5-phenyl-3-oxabicyclo[3.1.0]-2-hexanone **69** *via* a di-π-methane rearrangement.[43]

Momose *et al.* have reported the di-π-methane rearrangement of β-apolignan (**70**), a naturally occurring naphthalide lignan with a γ -lactone moiety. Thus, irradiation of **70** in benzene with pyrex filtered light led to the photoproduct **71** (*Scheme 29*). The formation of **71** was explained in terms of $C^1 \rightarrow C^2$ dimethoxyphenyl migration and C^1–C^3 bond formation.[44]



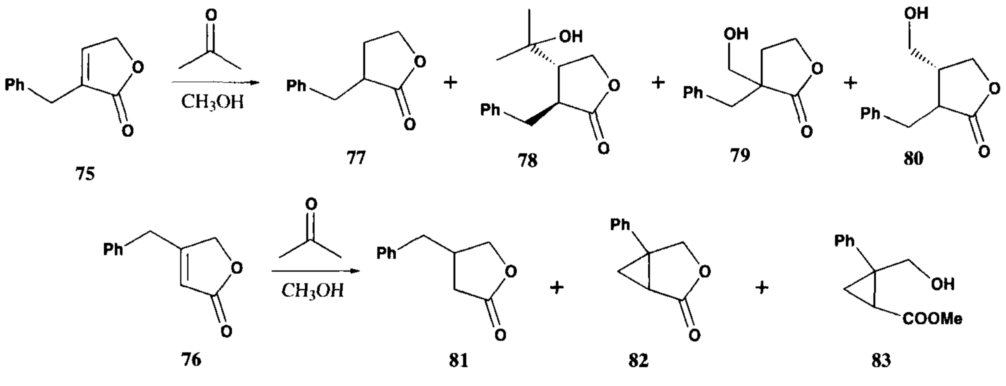
Scheme 29

Irradiation of 3,4-dibenzyl-2(5*H*)-furanone **72** in acetone leads to a mixture of the rearranged photoproduct **73** and the two dihydrofuranones **74a** and **74b** (*Scheme 30*).[45]



Scheme 30

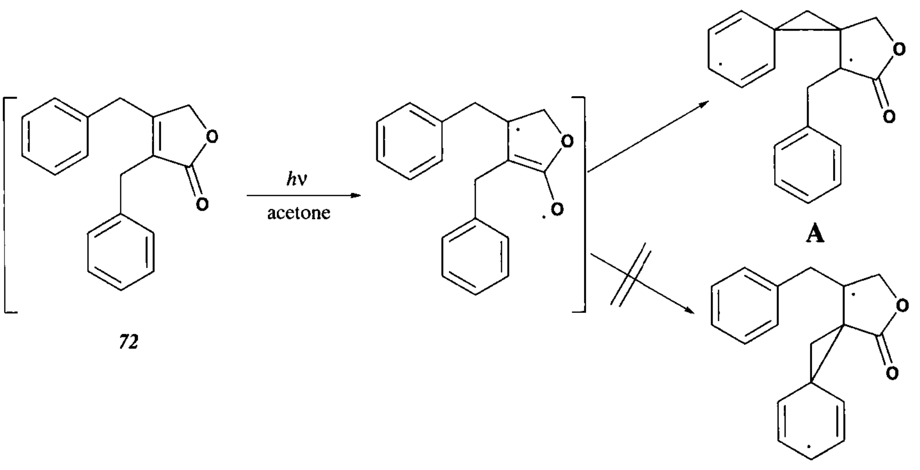
The formation of the 3-benzyl derivative **73** indicates that it is the 4-benzyl group which migrates. In order to confirm this specific migratory aptitude of the 4-benzyl group of **72**, the authors also examined the di-π-methane rearrangements of 3- and 4-benzyl-2(5*H*)-furanone **75** and **76** (*Scheme 31*). Irradiation of **75** in acetone led to the dihydrofuranone **77** as well as 3-benzyl-4-(2-hydroxy-2-propyl)dihydro-2(3*H*)-furanone **78**. Irradiation in methanol gave three products: The



Scheme 31

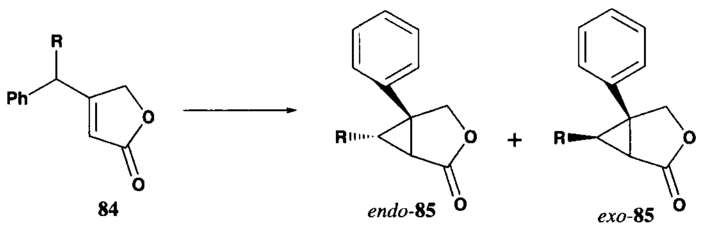
dihydrofuranone **77**, 3-benzyl-3-(hydroxymethyl)dihydro-2(3*H*)-furanone (**79**) and 3-benzyl-4-(hydroxymethyl)dihydro-2(3*H*)-furanone (**80**). On the other hand, irradiation of **76** in acetone gave the dihydrofuranone **81** and the cyclopropanolactone **82**. When methanol was used as solvent an additional product, *i. e.* methyl 2-(hydroxymethyl)-2-phenyl-1-cyclopropanecarboxylate (**83**), was formed.[45]

These results led the authors to conclude that in the photolysis of aryl butenolidyl di-π-methane systems lacking a rigid stereochemistry, the migratory aptitudes are reversed compared to the β-apolignan system.[44] As far as the rearrangement of β-apolignan **70** is concerned, it appears obvious that a pendant phenyl group locked in a *quasi-axial* conformation is essential for the rearrangement and fulfills the specific stereoelectronic requirements.[46] The superior migratory aptitude of the 4-benzyl group of the dibenzylfuranone **72** has been explained by invoking two possible intermediates (*Scheme 32*).[47] One of them, **A**, with its unpaired electron to the carbonyl group, is considered to be more stable than **B**.



Scheme 32

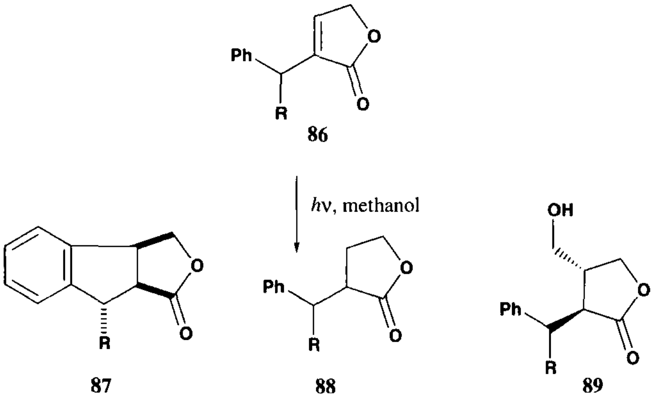
Muraoka *et al.*[48] have studied the effect of central methane substitution on the di-π-methane rearrangement of 4-substitutedbenzyl-2(5*H*)-furanones **84**. Direct irradiation of **84** in methanol gave two photorearranged isomers, the 6-substituted *endo*- and *exo*-5-phenyl-3-oxabicyclo[3.1.0]-2-hexanones *endo*-**85** and *exo*-**85** (*Scheme 33*).



a) R = CH_3 ; b) R = C-hexyl ; c) R = Ph

Scheme 33

Acetone-sensitized irradiation of **84** resulted in the formation of the same products. A comparison of the yields obtained with the different substituents revealed that the efficiency of the rearrangement can be ascribed both to the effects of the substituents on the central methane carbon atom on facile migration via radical fission and to the inherent inability of the furanone's ring double bond to suffer photoinitiated (*E*,*Z*)-isomerization, an otherwise competing reaction path. The photoreactivity of α-substituted 3-benzyl-2(5*H*)-furanones **86** has also been investigated for cases with alkyl substituents on the central methane carbon atom.[49] Thus, irradiation of **86a-86e** in methanol affords the corresponding photocyclized 3,3a,8,8a-tetrahydro-1*H*-indeno[1,2-*c*]-1-furanones **87**, together with the photoreduced products **88** and the methanol adducts **89** (*Scheme 34*).



a) R = CH_3 ; b) R = C-hexyl ; c) R = Et; d) R = Pr^n ; e) R = Pr^i ; f) R = Ph

Scheme 34

The predominant photochemical arylation was attributed to the facile formation of a radical at the β-position of the enone system (cf. *Scheme 32*). It was found that the efficiency of the cyclization of **86** increases with increasing bulk of the substituent at the central carbon atom. Inspection of a Newman projection of **86e** suggested that the phenyl and the butenolidyl π-planes are highly restricted in their rotation by the isopropyl methyl groups and thus forced close to each other (*Fig. 3*).

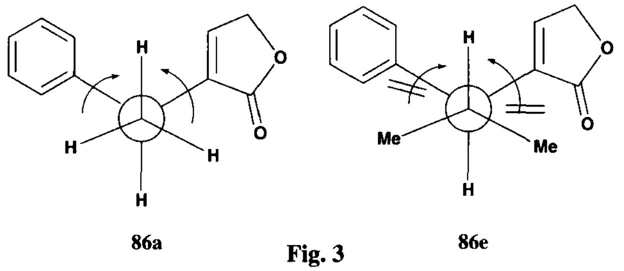
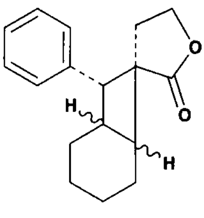
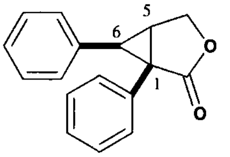


Fig. 3

In more recent work, the behavior of the 3-substitutedbenzyl-2-(5*H*)-furanones **86** upon irradiation was reinvestigated.[50] It was found that irradiation of 3-benzyl-2(5*H*)-furanone **75** in methanol gave, in addition to the products **77**, **79**, and **80** obtained in the earlier study,[45] a small amount of the photocyclization product **87** (R = H). Upon reexamination of the irradiation of **86b**, the cyclobutane **90** was found as a minor product. It could also be shown that upon irradiation in methanol, **86f** yielded the di-π-methane rearrangement products *exo*- and *endo*-1,6-diphenyl-3-oxabicyclo[3.1.0]-2-hexanone *exo*-**91** and *endo*-**91** as well as the photocyclized product **87f**.

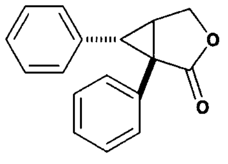


90



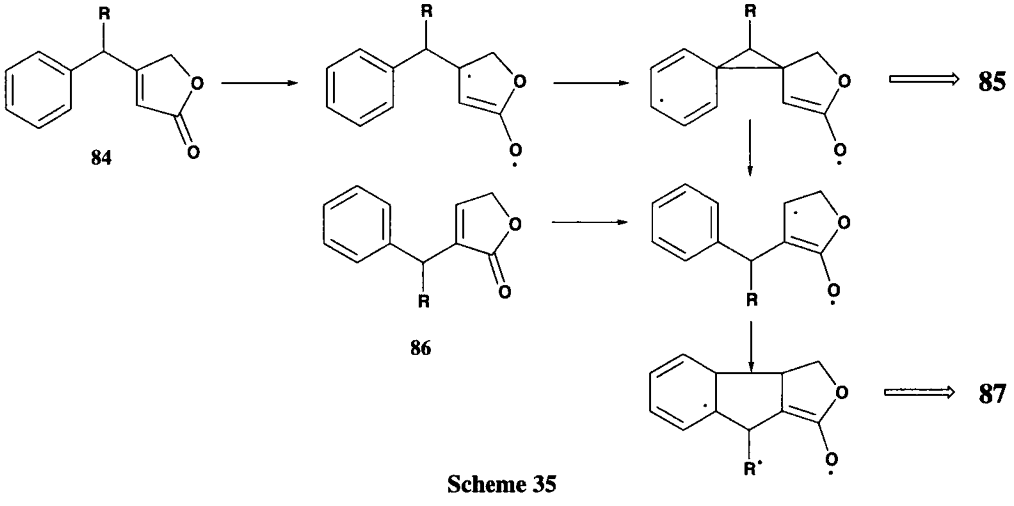
exo-**91**

\+



endo-**91**

Recently, Muraoka *et al.* studied the photochemical behavior of α-substituted 4-benzyl-2(5*H*)-furanones **84** in order to understand the difference in their chemoselectivity and that of their 3-benzyl counterparts **86**. Direct irradiation of **84** in methanol afforded the corresponding di-π-methane rearranged products, the 6-substituted *endo*- and *exo*-5-phenyl-3-oxabicyclo[3.1.0]-2-hexanones *endo*-**85** and *exo*-**85**, in 77-93% yield.[51] This difference vis-à-vis **86**, where typically photocyclization takes place, was explained in terms of the stability of intermediate biradicals. The formation of a radical at the β-position in preference to the position α to the carbonyl group could be responsible for the observed reaction traits (*Scheme 35*).



Scheme 35

III. CONCLUSIONS

2(5*H*)-Furanones undergo inter- and intramolecular [2+2] photocycloadditions with the formation of four-membered carbo- and heterocycles, respectively. The intramolecular version is thought to be more predictable with regard to regiochemical and stereochemical control. Photochemical additions of alcohols and amines are efficient, regiospecific and face-selective. 2(5*H*)-Furanones containing a methane moiety undergo the di-π-methane rearrangement.

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(Received November 24, 1997; in final form May 7, 1998)