Chem. Rev. 1993, 93, 3-22

New Insights into an Old Mechanism: [2 + 2] Photocycloaddition of Enones to Alkenes

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Received August 27, 1992 (Revised Manuscript Received November 4, 1992)

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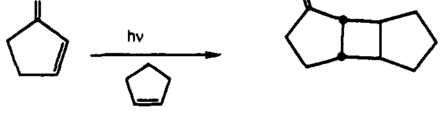
I. Introduction

Following his original discovery of the photocyclodimerization of 2-cyclopentenone in 1962,[1] Eaton reported the photocycloaddition of this enone to cyclopentene, shown in eq 1.[2] In 1964, Corey and his co-workers reported analogous [2 + 2] photocycloadditions of 2-cyclohexenone to a variety of alkenes,[3] and established many of the characteristic features of this reaction, as will be discussed below. The potential of this type of reaction as a key step in the synthesis of natural products was first shown by Corey in his landmark synthesis of caryophyllene.[4] The photochemical step in this synthesis is shown in eq 2.



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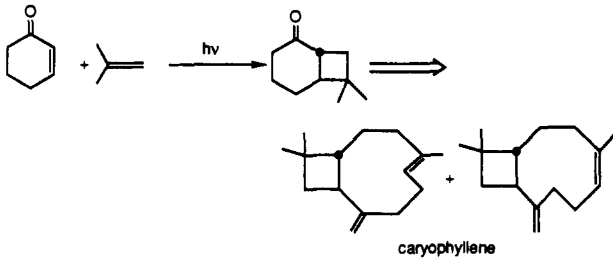

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Following these pioneering studies, inter- as well as intramolecular [2 + 2] photocycloadditions have become part of the standard repertoire of synthetic organic chemists, and this process is now probably the most widely used photochemical reaction in synthetic organic chemistry.[5] This review will focus on new insights into the mechanism of this classic photochemical process which have been provided by recent research in several different laboratories. The picture which emerges, which still needs definition in some respects, is significantly different from that presented in recent reviews which focus primarily on the synthetic applications of this reaction.[5]

II. Basic Characteristics of Photocycloaddition Reactions of Enones

In this section, the basic structural and mechanistic features of enone [2 + 2] photocycloaddition reactions will be briefly summarized, with key literature citations. Since numerous reviews of this subject have been published, the intention here is not to cover the literature encyclopedically, but rather to highlight those observations of greatest mechanistic significance.

A. Triplet Excited States of Enones as Reactive Intermediates

Photodimerization of simples enones in solution to give mixtures of cis-anti head-to-head (HH) and head-to-tail (HT) [2 + 2] photodimers occurs via the lowest enone triplet, in the cases of cyclopentenone (CP), cyclohexenone (CH), and isophorone (3,5,5-trimethyl-2-cyclohexenone). This was established using triplet sensitization and quenching techniques in pioneering studies done by Hammond,[6] Leermakers,[7] Chapman,[8] de Mayo,[9] and Wagner.[10,11] In 1969, Wagner presented data indicating that the moderately low quantum yields (on the order of 0.3) observed for CP photodimerization

0009-2665/93/0793-0003$12.00/0

David I. Schuster is a native New Yorker. He graduated from Far Rockaway High School in 1952, and from Columbia College in 1956, magna cum laude. He went west to pursue doctoral studies at Caltech with John D. Roberts, and received a Ph.D. in chemistry and physics in 1961. He was urged by George Hammond to pursue postdoctoral research with Howard Zimmerman at the University of Wisconsin—Madison, and their study of the photochemistry of cyclohexadienones is considered a milestone in mechanistic organic photochemistry. He joined the faculty of New York University in 1961, where he has remained to this day, becoming Professor in 1970. He has remained acitve in the area of organic photochemistry, in which he has published extensively. During 1968–1969, he was a Visiting Scientist at the Royal Institution in London in association with George Porter (now Lord Porter) doing research using flash photolysis. He has been one of the pioneers in the use of fast reaction techniques to solve mechanistic problems in organic photochemistry, from microsecond and nanosecond flash photolysis to time-resolved photoacoustic calorimetry. Following a sabbatical leave at Yale in 1975–1976, he has also been active in research in neurochemistry, aimed at chemical characterization of neuroreceptor binding sites in the central nervous system, and understanding the mechanism of action of antipsychotic drugs and related substances. This work currently extends from synthesis of novel medicinal agents to isolating, characterizing, and cloning neuroreceptor proteins. A serious and dedicated pianist, he has appeared in recent years in solo recitals as well as in chamber music concerts with fellow chemist–musicians. He is a member of the board and writes the program notes for The Fairfield Orchestra, Connecticut's leading orchestra, and frequently attends musical and theatrical performances in New York and elsewhere with his wife Carlotta. He is an authority on restaurants in the New York area and elswhere, has written two restaurant guides, and maintains a large collection of fine wines. He likes to challenge students to tennis and racquetball matches, which he occasionally wins.

George Lem was born in Mozambique, Africa, on September 19, 1966. He has lived in Europe and South American before settling in the United States, where he obtained his B.A. and M.S. degrees in chemistry from New York University. He is currently working toward a Ph.D. in D. I. Schuster's laboratory studying the photocycloaddition of enones in zeolite matrices.

Nikolas Kaprinidis was born in Salonica, Greece, on September 5, 1962. He received his B.S. in chemistry from the University of Ioannina, Ioannina, Greece. In 1989 he received his M.S. in chemistry from New York University. He is currently fulfilling the requirements for his Ph.D. under the supervision of D. I. Schuster at New York University studying mechanistic aspects of the [2 + 2] photocycloaddition reactions of enones with alkenes. His current interests are focused on the determination of the dynamics of triplet 1,4-biradical species using photoacoustic calorimetry.

were not attributable to either a low efficiency of intersystem crossing nor to rapid CP triplet decay competitive with triplet attack on ground state CP.[10] He suggested the inefficiency was principally associated with reversion of initially formed dimeric adducts, possibly 1,4-biradicals, to two ground-state CP molecules. For example, at 1.0 M CP in acetonitrile, this reversion occurred to the extent of 64%. It was also recognized that the fraction of dimeric adducts (triplet biradicals) which undergo reversion is probably different for HH as opposed to HT dimerization. Wagner noted that there was no direct relationship between quantum efficiencies of dimer formation and triplet state reactivities, a phenomenon that he suggested was probably common in nonconcerted reactions involving triplet excited states[10] (see section II.F. for further discussion on this point). De Mayo came to similar conclusions at the same time regarding addition of CP triplets to alkenes (cyclohexene, cyclopentene, *trans*-3-hexene), where kinetic data suggested that reversion of one or more intermediates to starting materials competed with product formation. The authors left open the question as to whether the critical intermediate in this case was a π-complex or a 1,4-biradical, or possibly both.[12]

In a classic mechanistic investigation of CP and CH photodimerization in acetonitrile, Wagner and Bucheck derived rate constants for unimolecular enone triplet decay (k_d) and for bimolecular interaction of enone triplets with enone ground states (k_a).[11] These rate constants were obtained from quantum yield measurements and Stern–Volmer slopes for quenching of the dimerization by dienes (1,3-pentadiene and 1,3-cyclohexadiene), assuming diffusion-controlled quenching occurred with a rate constant k_q of 1.0×10^{10} M^{-1} s^{-1}. The values of the derived rate constants were 0.4×10^8 and 3.0×10^8 s^{-1}, for k_d, and 6.6×10^8 and 1.1×10^8 M^{-1} s^{-1} for k_a, for CP and CH, respectively. Thus the triplet state lifetimes for CP and CH under these conditions were found to be quite small, 25 and 3.3 ns, respectively, while the second-order rate constants associated with bimolecular triplet–ground-state interactions (self-quenching) were quite large. In later studies by Schuster,[13,14] these rate constants were directly

Table I. Rate Constants for Quenching of Enone Triplets by Alkenes[a] and Quantum Yield for Adduct Formation[b]

		$k_q \times 10^{-7}$ M^{-1} s^{-1}		$\Phi_{add}{}^c(\Phi_{tc})^d$	
ketone	alkene	MeCN	C_6H_{12}	MeCN	C_6H_{12}
cyclopentenone	(Cl)(CN)C=CH_2	200	520	0.04 (0.28)	0.05 (0.67)
	(CN)CH=CH_2	63	180	0.08 (0.95)	0.03 (0.96)
	trans-(CN)CH=CH(CN)	160	460	0.00 (0.22)	(0.77)
	cyclohexene	33	42	0.64 (0.94)	0.42 (0.96)
	$Cl_2C{=}C(Cl)_2$	65		0.00 (0.91)	0.00
	cyclopentene	15	40	0.56 (0.85)	0.26 (0.87)
	$Me_2C{=}C(Me)_2$		99	0.71	0.29 (0.97)
	$Cl_2C{=}CH_2$	78		0.18 (0.91)	0.15
	$(MeO)_2C{=}CH_2$	3			
3-methylcyclohexenone	(Cl)(CN)C=CH_2	46	35	0.10 (0.95)	0.07 (0.91)
	(CN)CH=CH_2	15	11	0.14 (0.84)	0.08 (0.29)
	trans-(CN)CH=CH(CN)	50	67	0.28 (0.95)	(0.95)
	cis-(CN)CH=CH(CN)	70		0.36 (0.96)	
	cyclohexene	5.2	0.5	0.16 (0.66)	0.07 (0.12)
	$Cl_2C{=}C(Cl)_2$	1.2	2.0	0.00 (0.31)	0.00 (0.41)
	cyclopentene	<0.1	0.5	0.21	0.10 (0.14)
	$Me_2C{=}C(Me)_2$	<0.1		0.08	0.03
	$(MeO)_2C{=}CH_2$	0.7			
	$Cl_2C{=}CH_2$			0.07	0.04
testosterone acetate	(CN)CH=CH_2	24			
	cyclopentene	5.9		0.38^e $(1.00)^e$	
bicyclo[4.3.0]non-1(6)-en-2-one	(CN)CH=CH_2	130		1.60^f	
	cyclohexene	27		4.16^f	
	cyclopentene	3.8		$1.00,^f$ 0.048^e (0.91)	
	$(MeO)_2C{=}CH_2$	26		0.62^f	
	trans-(CN)CH=CH(CN)	4.5			
	cis-(CN)CH=CH(CN)	4.5			

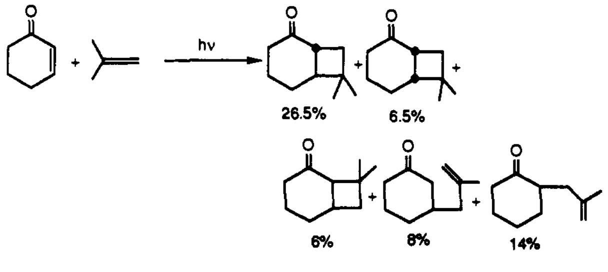
[a] Determined from lifetimes of enone triplet decay at 280 nm on flash excitation at 355 nm as a function of alkene concentration. [b] Adducts determined by GC/MS. Conversion <10%. [c] Quantum yield for photoaddition at 313 nm at 0.50 M alkene. [d] Quantum yields for enone capture at alkene concentrations used in determining Φ_{add}. [e] Quantum yield at 313 nm in neat cyclopentene. [f] Relative quantum yield at 0.75 M alkene.

measured by laser flash photolysis. It was shown that Wagner's estimated rate constants were too high by about 1–2 orders of magnitude, due to the fact that dienes typically quench enone triplets at substantially less than the diffusion-controlled limiting rate. Speculation on the origin of this effect is given elsewhere.[13]

On the basis of extensive triplet sensitization and quenching studies, de Mayo concluded that enone photocycloadditions to alkenes also proceed exclusively via enone triplet excited states.[12,15] On the basis of earlier spectroscopic studies of steroid enones[16] and calculations of energies of relaxed n,π* and π,π* states,[17] de Mayo concluded that the lowest energy enone triplet state and the one responsible for photoaddition reactions was probably the π,π* state.[15] This conclusion has been amply confirmed by recent studies by Schuster and co-workers using transient absorption spectroscopy[13] and time-resolved photoacoustic calorimetry.[18] Estimates by de Mayo[12,15] of the rate constants k_d and k_a for enone triplet decay and for additions of enone triplets to alkenes, respectively, were made, as in Wagner's photodimerization study,[11] from quenching kinetics using piperylene and acenaphthene as triplet quenchers, assuming as above that enone triplet quenching occurred at the diffusion-controlled rate. Schuster and co-workers measured triplet lifetimes in solution of a number of cyclic enones using flash photolysis[13] and demonstrated that alkenes directly quench these triplets.[19] The rate constants for a large number of enone–alkene combinations were measured and are shown in Table I.[19,20] Trends in these values will be discussed later in section II.F., but it should be noted here that in overlapping systems these rate constants are about an order of magnitude smaller than de Mayo's estimated rate constants,[12,15] again because of the overly high value assumed for the rate constant of triplet energy transfer. In any event, there appears to be general agreement that these enone-alkene photocycloadditions proceed via enone π,π* triplet states, although in some cases (specifically rigid enones) the lowest n,π* and π,π* triplets may be close in energy.[5a,13,21]

B. Stereochemistry of Ring Fusions of Cycloadducts

Corey established early on that formation of cycloadducts on photoaddition of 2-cyclohexenone to simple alkenes is often accompanied by formation of products resulting from disproportionation, as shown in eq 3 in the case of 2-methylpropene.[3] Such disproportionation suggested the intermediacy of 1,4-biradicals in these reactions. This reaction also illustrates the formation of trans-fused as well as cis-fused cycloadducts, one of the key features of this process. As expected, the relatively strained trans-fused cycloadduct can be isomerized to the more stable cis-fused



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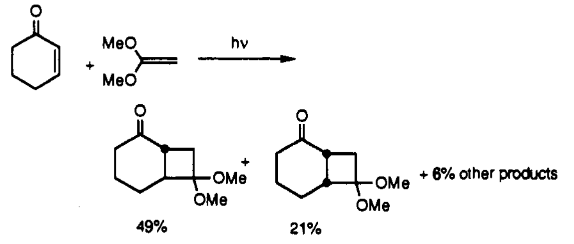
adduct on treatment with base.[3] It is therefore striking that trans-fused adducts are formed in greater yield in this case, as well as in photoadditions of cyclohexenone to 1,1-dimethoxyethylene (eq 4) and cyclopentene (eq 5).



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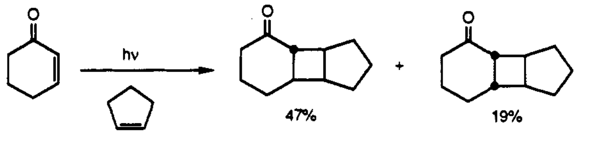

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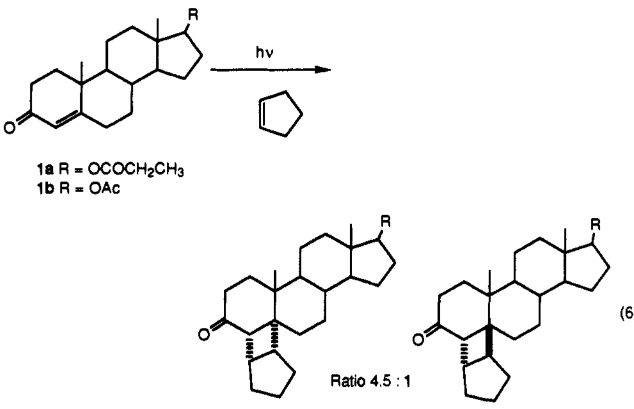
This is not an observation that is confined to simple monocyclic enones. Rubin reported that testosterone propionate **1a** gives both cis- and trans-fused photoadducts (**2a** and **3a**) with cyclopentene, in a ratio of 4.5:1 (eq 6) while the vinylogous dienone **4** gives exclusively a trans-fused adduct (eq 7).[22] Adduct structures were assigned from ORD curves, ^{1}H NMR spectra, and base epimerization studies. Rubin also reported that the product ratio was dependent upon the alkene concentration as well as temperature. The reaction of the corresponding acetate **1b** with cyclopentene has been investigated recently by Schuster and co-workers,[23] who obtained X-ray crystal structures for **2b** and **3b**, thereby confirming Rubin's assignments. They found that the principal product at short reaction times was **3b** (trans), but shifted in favor of **2b** (cis) over time. This is the result of secondary phototransformations of the adducts which preferentially consume **3b**.[24] Thus, even with steroid enones, formation of cycloadducts with trans ring junctions is preferred. This selectivity must have a kinetic rather than thermodynamic basis, since the cis-fused structure with a boat cyclohexanone ring and a relatively flat cyclobutane ring is thermodynamically more stable than the corresponding trans-fused structure which has diequatorial linkage of a twisted cyclobutane ring to a relatively undistorted half-chair cyclohexanone ring.[23] The difference in energies of these two types of linkages was estimated by molecular mechanics to be 3.0 kcal/mol in addition of 2-cyclohexenone to 2,3-dimethyl-2-butene, but increased to be 7.4 kcal/mol for cyclohexenone–cyclopentene adducts corresponding to **2** and **3**.[23] We will return later to this question of preferred formation of trans-fused adducts from alkenes and photoexcited cyclohexenone. It is noteworthy in this connection that Demuth has found that cis-fused adducts are formed exclusively on [2 + 2] photocycloaddition of octalones of structure **5** to 2-(trimethylsiloxy)-1,3-butadiene (see eq 8).[25] A referee has pointed out that this atypical stereochemistry may denote a different reaction mechanism, perhaps involving triplet energy transfer from **5** to the diene, followed by attack of diene triplets on ground-state **5**.



1a R = OCOCH$_2$CH$_3$
1b R = OAc

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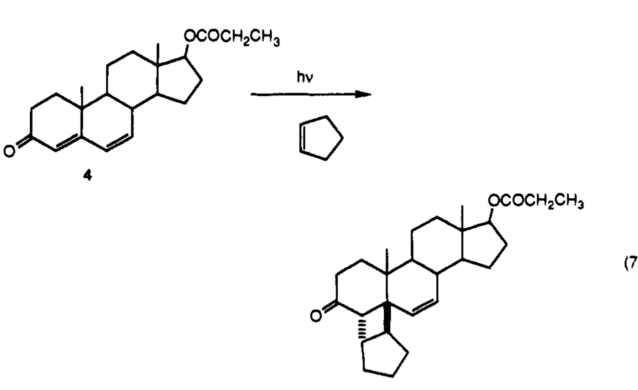
2a R = OCOCH$_2$CH$_3$
2b R = OAc

3a R = OCOCH$_2$CH$_3$
3b R = OAc



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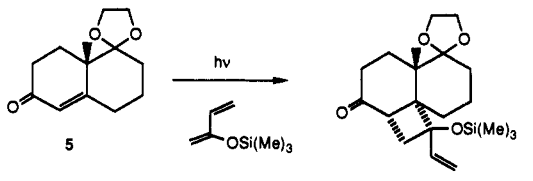

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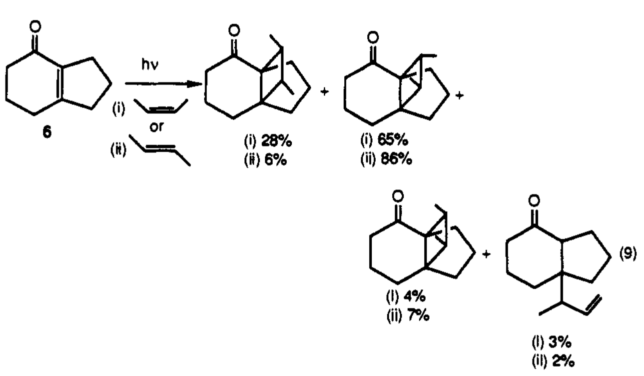
C. Stereochemical Integrity of the Alkene Component in Photocycloadditions

1. Intermolecular Photocycloadditions

Corey reported that an identical mixture of cycloadducts was obtained from photoaddition of cyclohexenone to either (*Z*)- or (*E*)-2-butene, indicating that the stereochemistry of the alkene component is lost in the course of formation of cycloadducts.[3] Recovery of the alkene component at various reaction times indicated <1% isomerization of the starting material had occurred. This finding unequivocally demonstrated that stereomutation occurred at some intermediate reaction stage, and that the two new σ bonds in the cycloadduct are formed sequentially. The most reasonable mechanistic interpretation involves rotationally equilibrated triplet 1,4-biradicals as precyclization intermediates. The lack of isomerization of the starting materials indicated that, at least in this system, reversion of these 1,4-biradicals to starting material by fragmentation is not competitive with cyclization.

Cargill and coworkers found that bicyclo[4.3.0]non-1(6)-en-2-one (BNEN, **6**) gives the same four products on photoaddition to either (*Z*)- or (*E*)-2-butene, as shown in eq 9.[26] Although the product ratios derived from each of the isomeric alkenes are not identical in this case, it is clear that the stereochemical integrity of the alkene component is lost during the reaction. The

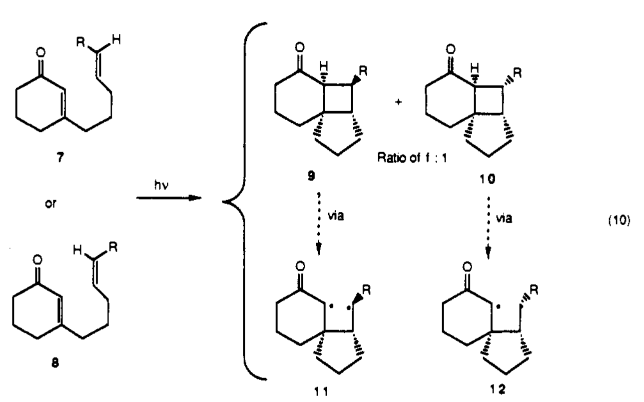


results were again rationalized in terms of a mechanism involving sequential formation of the new σ bonds and rotameric equilibration of the various possible 1,4-biradical intermediates. A similar study involving photoaddition of cyclopentenone to (*Z*)- and (*E*)-1,2-dichloroethene was reported by Dilling and co-workers.[27] In these cases, the possibility of reversion of the biradicals to starting materials which would result in *Z*–*E* isomerization of the alkene was not explicitly considered or investigated. McCullough found that at 2% conversion in the photoaddition of 3-phenylcyclohexenone to (*Z*)-2-butene, recovered alkene contained 9% of the *E* alkene,[28] supporting the proposal that biradical reversion to the ground state starting materials is a major source of inefficiency in these reactions, as anticipated by Wagner and de Mayo (see above).[10,12]

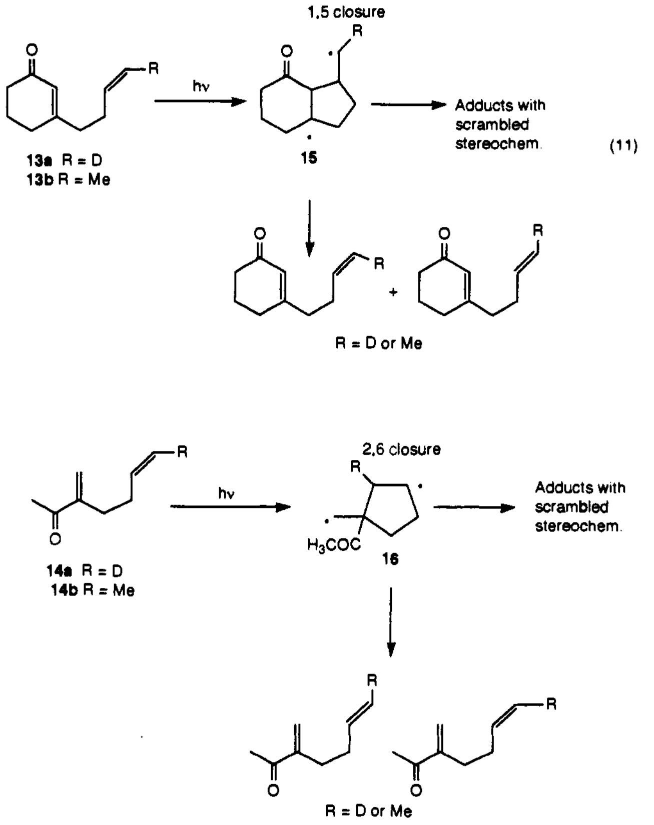
Biradical reversion appears to be a much more important process in enone additions to electron-deficient alkenes. Thus, Schuster and co-workers found that in the reaction of 3-methylcyclohexenone with (*Z*)- and (*E*)-1,2-dicyanoethene (maleo- and fumaronitrile) isomerization of the alkenes accompanies formation of cycloadducts.[29] On the basis of quantum yields for all processes and rate constants for quenching of the enone triplet by these alkenes, it was concluded that alkene isomerization occurred by reversion of 1,4-biradical intermediates (i.e., a Schenck-type mechanism) rather than by triplet-energy transfer from the enone to the alkenes. The latter process was a distinct possibility because of the relatively low triplet energies of these particular alkenes.[30] The full significance of biradical reversion in affecting the course of enone photocycloadditions has only emerged recently, and will be discussed later in section III.D.

2. Intramolecular Photocycloadditions

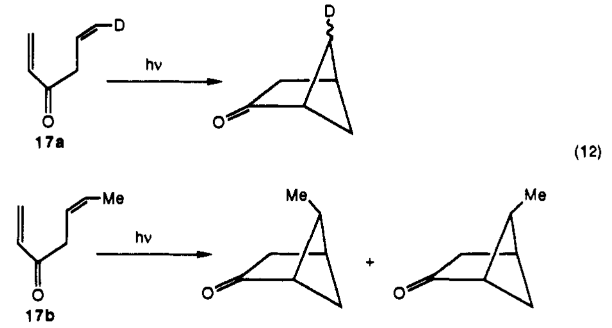
Stereochemical scrambling in intramolecular photocycloadditions of enones with tethered alkene moieties has been investigated by Becker[31] and Agosta.[32] Becker found that the isomeric β-linked 1-acyl-1,6-heptadienes **7** and **8** (R = CH_3) give a 1:1 mixture of stereoisomeric cycloadducts **9** and **10** but that the dienes do not equilibrate during the irradiation.[31] Similar results were later obtained with **7** (R = isopropyl) and with a *cis*-dideuterio dienone, demonstrating that steric effects did not influence the course of the reaction. The results indicate that initial bonding in these systems occurs between C_2 (the β-carbon of the enone) and C_6 of the heptadiene moiety in accord with the famous "rule of five"[33] to give triplet 1,4-biradicals whose lifetimes are sufficiently long to allow complete rotational equilibration prior to ring closure. Thus, as shown in eq 10, the reaction proceeds via a completely equilibrated mixture of 1,4-biradicals **11** and **12**, which do not revert to starting materials.



In contrast, Agosta found that the 1-acyl- and 2-acylhexadienes **13** and **14** undergo scrambling of the label (D or CH_3) on the C=C bond competitive with formation of photoproducts.[32] (The latter system was studied under conditions of triplet sensitization because of competing reactions via the enone singlet on direct photoexcitation). For **13**, reaction most likely occurs via 1,4-biradicals of type **15** formed by initial 1,5-bonding to the α-carbon of the enone (eq 11), in which inversion and rotation at the radical center occur prior to fragmentation or cyclization. The proposed mechanism for **14** involves preferential cyclization to biradical **16** in which the label becomes scrambled as a result of conformational interconversion. These modes of cyclization are consistent with extensive studies of analogous compounds. Based upon the measured quantum yields, the ratio of rates of biradical reversion (k_r) to product formation (k_p) are 0.75 for **15a**, 1.81 for **15b**,



2.53 for **16a**, and 9.30 for **16b**. There is no measurable scrambling of the label in the 3-acylhexadienes **17a** and **17b**, although the label is completely scrambled in the products, shown in eq 12. This indicates formation of a nonreverting biradical (not otherwise specified) whose lifetime is sufficiently long to permit scrambling of the label. Thus, the competition between the various pathways for biradical formation and decay depends critically on the substitution pattern in these systems.



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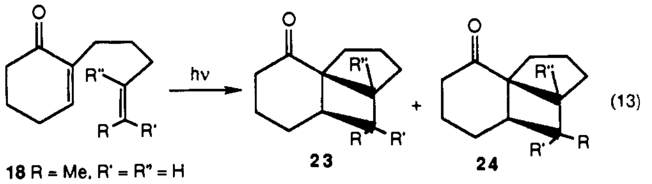
Returning to 2-acyl-1,6-heptadienes, Becker[31] investigated the photoreactions of the α-linked enones **18**–**22**. Here again, no *Z*–*E* isomerization of the starting materials was observed. While mixtures of stereoisomeric cycloadducts were formed in each case, no simple pattern of reactivity emerges. Thus, both **18** and **19** preferentially afford diastereomer **23**, but the ratio of **23** to **24** is quite different in each case (eq 13), indicating the reaction is more complicated than that of the analogous β-linked dienones. Thus, the products cannot be derived exclusively via rotationally equilibrated 1,4-biradicals of structure **25**, which would be generated by 1,5-ring closure to the α-carbon of the enone, a process which has ample precedent. A similar anomaly is found with the propyl-substituted dienones **20** and **21**, where again products of structure **23** are formed in preference to **24**, but to different extents. Even with the dideuterio dienone **22**, diastereoselectivity is observed on ring closure. Clearly, these results require the participation of several competing reaction pathways which have yet to be fully elucidated.



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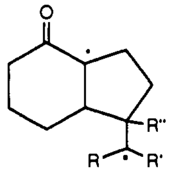
18 R = Me, R' = R'' = H
19 R' = Me, R = R'' = H
20 R = *i*-Pr, R = R'' = H
21 R' = *i*-Pr, R = R'' = H
22 R = R'' = D, R' = H

Ratio of 23 : 24 = 35 : 1 for 18
Ratio of 23 : 24 = 5.8 : 1 for 19
Ratio of 23 : 24 = 3.8 : 1 for 20
Ratio of 23 : 24 = 1.4 : 1 for 21
Ratio of 23 : 24 = 2 : 1 for 22



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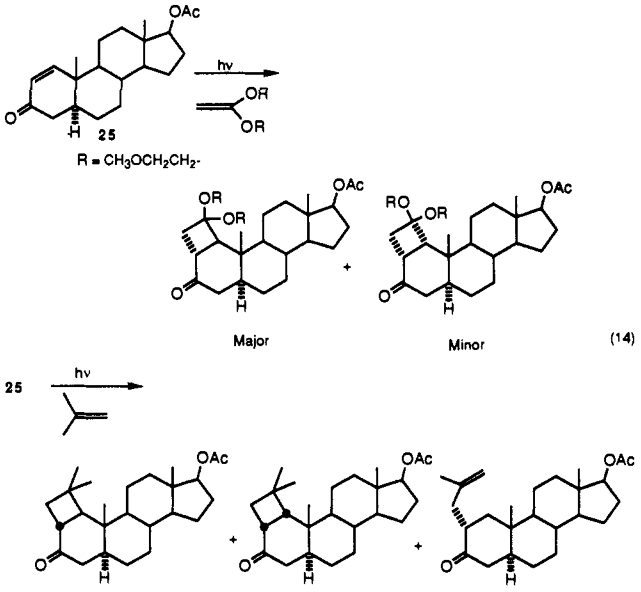
D. Regiochemistry of Enone–Alkene [2 + 2] Photocycloadditions

One of the most significant findings in Corey's pioneering study was that photocycloadditions of enones to unsymmetrical alkenes were invariably regioselective.[3] Thus, in the addition of cyclohexenone to 2-methylpropene (eq 3) and 1,1-dimethoxyethene (eq 4), a clear preference for formation of head-to-tail (HT) vs head-to-head (HH) adducts is observed. This selectivity was also found by Corey for photoaddition of cyclohexenone to allene, vinyl acetate, methyl vinyl ether, and benzyl vinyl ether and by Cantrell[34] for addition of 3-methylcyclohexenone (3-MCH) to 1,1-dimethoxyethene (DME). HT adducts with both cis and trans ring fusions are also formed exclusively upon photoaddition of the steroid enone **25** to a 1,1-dialkoxyethene and 2-methylpropene, as shown in eq 14.[35] Corey suggested that, in contrast, HH adducts are preferentially formed between cyclohexenone and acrylonitrile (eq 15a), although the adduct structures (including stereochemistry) in this reaction were not firmly established.[3] Consistent with Corey's finding, Cantrell[34] reported that photoaddition of 3-MCH to acrylonitrile gave mainly two HH adducts (see eq 15b), whose structures were assigned on the basis of ^{1}H NMR spectra; the structure of a third adduct was not firmly established. More recently, Rao and co-workers established that the major photoadduct from 4,4-dimethylcyclohexenone and acrylonitrile had a HT structure (eq 16a),[36] while Weedon and co-workers established that the ratio of HH:HT adducts formed from 2-cyclopentenone and acrylonitrile was 3:4.8 (see eq 16b).[37] Thus, Corey's proposal[3] that the regiospecificity in [2 + 2] photocycloadditions is generally reversed in enone additions to electron-deficient vis a vis electron-rich alkenes is incorrect.



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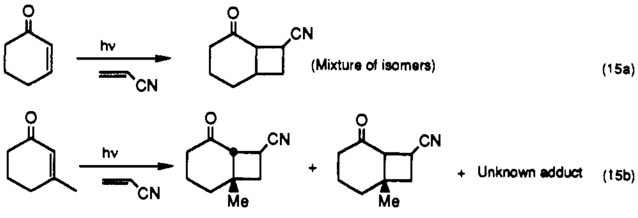

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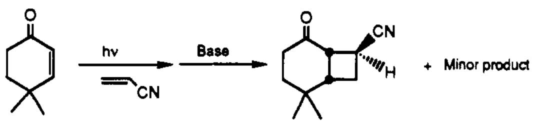
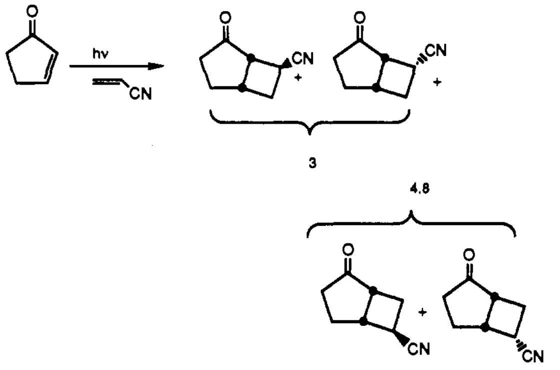
(15b)

Strong evidence that regiospecificity in [2 + 2] photocycloadditions does not follow a simple rule comes

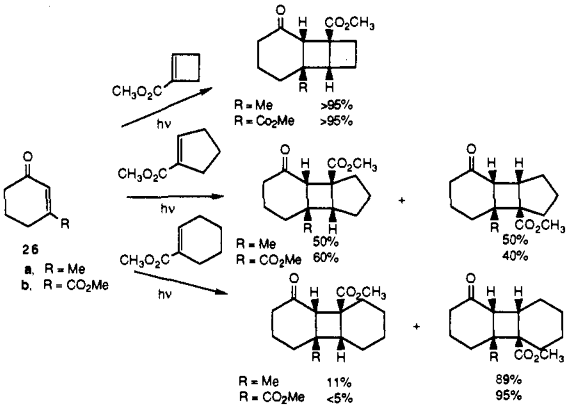


(16a)



(16b)

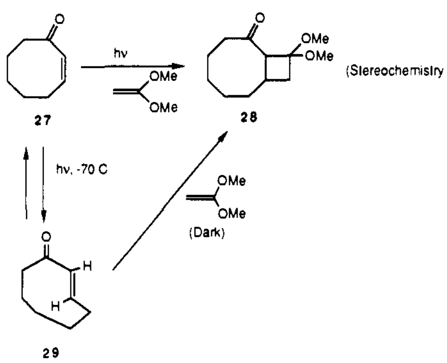
from a study by Lange on addition of enones **26a** and **26b** to a series of methyl 1-cycloalkene-1-carboxylates (eq 17).[38] Similar observations were made in an earlier



(17)

but less complete study of some of these systems by Tada and Nieda.[39] While additions to the cyclobutenyl ester gave exclusively HH adducts, in line with Corey's generalization, increasing amounts of HT adducts were obtained as the ring size of the alkene was increased, resulting eventually in a reversal of regioselectivity. Thus, the HH:HT adduct ratio with the cyclopentenyl ester was 1:1 for **26a** and 60:40 for **26b**, but became 1:9 for reaction of the cyclohexenyl ester with **26a** and <5:>95 for addition to **26b**. The regiochemistry associated with enone–alkene photocycloadditions is clearly more complex than originally envisioned by Corey.[3] Mechanistic rationalization of these findings will be deferred until the later discussion.

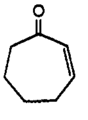
E. [2 + 2] Photocycloaddition Reactions of Medium-Ring Enones



(18)

Corey briefly investigated the effect of ring size of the enone component in [2 + 2] photocycloadditions.[3] While 2-cycloheptenone did not undergo photocycloaddition to DME, a HH adduct **28** was observed with 2-cyclooctenone **27** (eq 18). A special pathway appears to operate in this case, since the same cycloadduct could be obtained if DME was added in the dark to a solution of **27** which had been preirradiated at dry ice temperatures in the absence of DME, followed by warming of the mixture to room temperature. Since irradiation causes isomerization of **27** to its ground-state trans isomer **29**,[40] it is very likely that the photoadduct with DME arises from thermal [2 + 2] cycloaddition of DME to **28**.[3] It is also interesting to note the reversal of regioselectivity from HT to HH that occurs under these conditions in contrast to photochemical addition of cyclohexenone and cyclopentenone to DME.

The ability of 2-cycloheptenone (**30**) to undergo photocycloadditions to alkenes has been more thoroughly investigated by Schuster and co-workers.[41] While the lack of reactivity of **30** with electron-rich alkenes such as DME and 2,3-dimethyl-2-butene was verified, photoadditions to electron-deficient alkenes were observed. In the absence of added alkenes, **30** is known to undergo photodimerization, which probably involves initial generation of ground-state *trans*-cycloheptenone **31**.[42] Irradiation of **30** in the presence of electron-deficient alkenes such as acrylonitrile, α-chloroacrylonitrile (CAN), maleic anhydride, and chloroalkenes leads to 1:1 adducts (detected by GC/MS analysis) at the expense of the photodimerization of **30**. Aside from the GC/MS analyses, these new adducts have been incompletely characterized, except for one adduct with CAN which has been shown by X-ray crystallography to be the trans-fused HT adduct **32**. Attempts to determine using flash photolysis whether cycloheptenone–alkene adducts arise by capture by alkenes of the reactive trans isomer **31** gave inconclusive results.[41] It is evident, in any event, that [2 + 2] photocycloaddition reactions do indeed occur with medium-ring enones, but these reactions may be mechanistically quite different from the analogous reactions of cyclohexenones and cyclopentenones.



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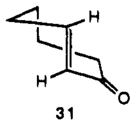

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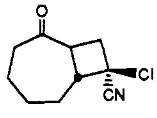

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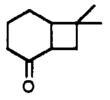
F. Reactivity of Alkenes toward Photoexcited Enones

Corey and co-workers determined "relative reactivities" for additions of alkenes to photoexcited 2-cyclohexenone.[3] The ratio of the total products derived from each alkene, as determined quantitatively by gas chromatography, was taken to be a measure of relative rates of addition. The "relative rate factors" shown in Table II were derived from irradiation of 2-cyclohexenone in the presence of 9–10 equiv of each of two alkenes, and are normalized to take account of formation

Table II. Competition between Cyclopentene and Various Olefins for Excited 2-Cyclohexenone

olefin	observed ratio of products from olefin and cyclopentene	relative rate factor
1,1-dimethoxyethene	2.33	4.66
methoxyethene	0.785	1.57
cyclopentene		1.00[a]
isobutylene	0.266	0.40,[b] 0.13[c]
allene	0.234	0.234[a]

[a] Factors of two were applied to observed ratios in the case of cyclopentene and allene in which there are two modes of addition which lead to the same product. [b] Refers to formation of



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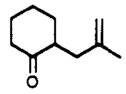
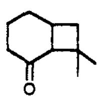


[c] Refers to formation of



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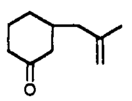


of identical adducts from symmetrical alkenes by two modes of attack. Corey notes that acrylonitrile was much less "reactive" than any of the other alkenes listed, and that DME and cyclopentene had similar "relative reactivities" toward cyclopentenone as with cyclohexenone. On the basis of these data, Corey concluded that photoexcited cyclohexenone was a moderately electrophilic species toward alkenes.

These data were critical elements in the formulation of mechanistic hypotheses by Corey[3] and others, and for a long time were generally accepted by most reviewers[5b-d] and subsequent workers as proper measures of alkene reactivity in photocycloadditions. However, it has been long recognized that product ratios in photochemical processes are measures of relative quantum efficiencies for disappearance of starting materials and/or formation of products, and cannot be equated with relative rates of reaction.[5a,10,12,43] The lack of a relationship between overall quantum efficiencies and rate constants of reaction was dramatically demonstrated many years ago by Wagner in the case of Norrish type II reactions of aromatic ketones, where quantum efficiencies were determined entirely by the competition between reversion of 1,4-biradical intermediates to starting material and progress on pathways leading to products.[44] There was absolutely no correlation between these quantum efficiencies and the rate constants for formation of the biradicals from the ketone triplet states. A similar situation exists with enone photocycloaddition to alkenes, where 1,4-biradicals also play a crucial role, as suggested earlier and amply confirmed by recent observations to be discussed below in section III.D. Thus, one should not expect relative yields of enone–alkene photoadducts to directly reflect the rates of the initial interaction of alkenes with enone triplet excited states, as clearly pointed out by de Mayo in 1971[15] and later by Cargill,[45] Weedon,[5a] and Schuster.[19,43] As already seen, analogous considerations hold for enone photodimerization, which is essentially an example of addition of an enone triplet to a deactivated C=C bond, as specifically noted by de Mayo.[15]

Rate constants for interaction (quenching) of triplet excited states of cyclic enones with alkenes can be directly measured using transient absorption spectroscopy.[13,19] Such data were first reported by Schuster et al. a few years ago.[19,20] The rate constants shown in Table I were obtained from measurements of triplet-state lifetimes τ_T as a function of alkene concentration using nanosecond transient absorption spectroscopy (laser flash photolysis).[13] The decay of enone triplet absorption at 280 nm could be conveniently followed following excitation of the enones [cyclopentenone (CP), 3-methylcyclohexenone (3-MCH), testosterone acetate (TA), bicyclo[4.3.0]non-1(6)-en-2-one (BNEN, **6**)] in acetonitrile and cyclohexane at 355 nm using the third harmonic of a Nd:YAG laser. In all cases, decays were cleanly first order. The rate constants k_q are obtained from the relationship $(\tau_T)^{-1} = (\tau_o)^{-1} + k_q[\text{alkene}]$, where τ_o is the limiting triplet lifetime of the enone at the concentration utilized in the absence of alkene. Also given in Table I are the quantum efficiencies for formation of enone–alkene adducts. Quantum efficiencies for capture of enone triplets by alkenes, ϕ_{tc}, are given by $k_q\tau_T[\text{alkene}]$ using the experimentally determined values of k_q and τ_T.

It is obvious from inspection of Table I that there is absolutely no correlation between the rate constants k_q for interaction of the enone triplets with the alkenes and the overall quantum efficiency for formation of products derived from this interaction. In general, higher quantum yields are seen with electron-rich alkenes while higher rate constants are found for electron-deficient alkenes. Moreover, the values of ϕ_{tc} at the alkene concentrations at which the product quantum yields were measured (0.5 M in most cases) are always higher than the efficiency of product formation, often much higher. This is perhaps the clearest evidence for efficient formation of intermediates which revert to starting materials in competition with progress to adducts. There is no correlation of the rate constants k_q in Table I with ionization potentials of the alkene, as would be expected if quenching involved formation of a donor–acceptor complex with the enone acting as the electron acceptor. In fact, the data suggest that the enone π,π^* triplet is not particularly electrophilic. There is also no significant difference in k_q measured in polar and nonpolar solvents, indicating a lack of charge development in the transition state for addition.

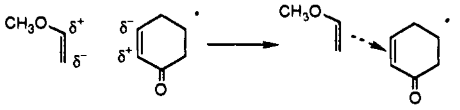
The presence of strong electron-withdrawing groups on the C=C bond of alkenes results in lowering of the energy of both the planar and perpendicular alkene triplet, sometimes below that of the enone triplet.[30] For such systems, triplet-energy transfer from the enone to the alkene becomes a distinct possibility, whereas this is energetically unfavorable for simple alkenes which possess very high energy triplets. In principle, two distinctly different quenching mechanisms could be operating in the systems included in Table I, a Schenck-like addition mechanism involving 1,4-biradical formation and triplet-energy transfer. As discussed earlier, it was shown that quenching of 3-methylcyclohexenone by 1,2-dicyanoethenes involves a Schenck mechanism,[29] while interaction of high-energy triplets of the rigid enone BNEN with the same alkenes clearly involves transfer of triplet excitation.[21,29] The difference can be attributed to inhibition of triplet-energy transfer from 3-MCH and similar conformationally flexible enones by the Dexter exchange mechanism due to poor

π-overlap between the twisted chromophore of the twisted triplets and the alkenes.[46] No such inhibition would be involved with the conformationally constrained enone BNEN.

III. Mechanistic Proposals

A. The Corey–de Mayo Exciplex Mechanism

On the basis of the regiochemistry and the "relative rate factors" observed in his studies of alkene additions to photoexcited cyclohexenone (see above), Corey proposed in 1964 that the first step of the [2 + 2] photocycloaddition of enones to alkenes involved interaction of a polarized enone excited state, which most likely was a triplet state, with the ground-state alkene to given an "oriented π-complex" **33**.[3] The complex for the key case of addition of cyclohexenone to methoxyethene was depicted as shown. The reactive excited state of the enone was assumed to be an n,π^* state, which was predicted by extended Hückel calculations to have the charge polarization as shown, with electron density higher at C_β than at C_α.[47] In the donor–acceptor π-complex, the alkene ground state was proposed to act as the electron donor and the enone excited state as the electron acceptor, the two moieties being held together by coulombic attraction. The modest range of alkene "reactivities" argued against formation of a highly polar donor–acceptor complex. Corey noted[3] that it was likely that the π-complex model could not be extended to enone photodimerization nor to reactions of enones with alkenes possessing strong electron-withdrawing substituents such as CN or COOR. Steric factors remained to be assessed with respect to the proposed model.



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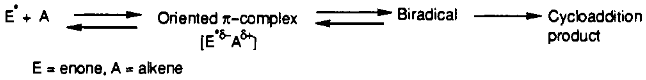
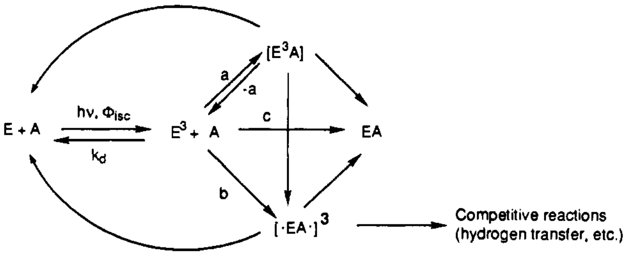
Corey rejected the alternative hypothesis that the regiospecificity in enone photocycloadditions is governed by preferences in formation of alternative adduct 1,4-biradicals, since this did not explain (in his opinion) the observed selectivity in photoaddition of cyclohexenone to DME, and does not account for the olefin reactivity shown in his "relative rate factors". However, biradicals were invoked to rationalize the formation of disproportionation products in some cases (see eq 3) and also the loss of alkene stereochemistry on photoaddition of cyclohexenone to the 2-butenes. The original Corey mechanism for enone–alkene photocycloadditions is shown in Scheme I.[3]

Corey did not explicitly consider the possibility that the proposed intermediates might decay to regenerate ground-state reactants competitive with formation of products. This deficiency of the Corey mechanism was explicitly pointed out by de Mayo in his studies of photocycloaddition reactions (photoannelations) of cyclopentenone (CP) and cyclohexenone (CH).[9,12,48] Quantum yields for formation of adducts from CP and a variety of alkenes were in no case greater than 0.50, even in neat alkene. This was interpreted to mean that some intermediate(s) on the reaction pathway could partition between reversion to ground-state starting materials and progress to products. De Mayo originally concluded that this intermediate was Corey's π-complex, now termed an exciplex, rather than a biradical derived from the exciplex, since little if any alkene isomerization occurred (Φ < 0.033) on irradiation of CP in the presence of 3-hexene.[48] The general mechanism shown in Scheme II was proposed. The possibility that adducts might arise at least in part directly from the exciplex, bypassing the biradical, was included in this scheme, since such a process could not be excluded on the basis of the available data. In his 1971 review,[15] de Mayo clearly indicates that the tetramethylene 1,4-biradical is the key intermediate, whether formed directly from the enone triplet or via the exciplex. The fact that lowering the temperature led to an increase in the quantum yield for photoaddition of cyclopentenone to both cyclopentene and cyclohexene could most easily be explained in terms of changes in the partitioning of the 1,4-biradical intermediate, since fission of such intermediates is generally favored at higher temperatures.[49] Later work by Loutfy and de Mayo demonstrated, however, that the ratio of rates of cyclization to fission can either increase or decrease with temperature, depending on the system.[50]

Scheme I



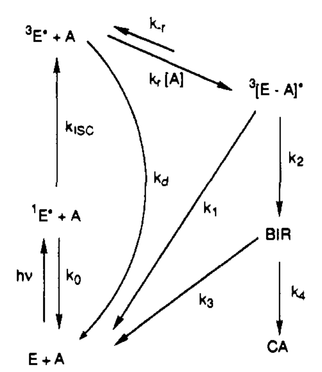
Scheme II



E = enone, A = alkene, [E^{3}A] = triplet exciplex, [· EA·]^3 = triplet biradical, EA = adduct

On the basis of the dependence of quantum yields on temperature and alkene concentration, as well as results of quenching by 2,5-dimethyl-2,4-hexadiene, Loutfy and de Mayo[50] arrived at the following general conclusions regarding photoaddition of enones to alkenes: (a) a triplet exciplex is first formed, irreversibly, from the enone triplet and the alkene ground state; (b) the exciplex collapses to one or more 1,4-biradicals; (c) the biradicals either cyclize or revert to ground-state starting materials; (d) biradical reversion represents the main source of inefficiency (energy wastage) in the cycloaddition reaction; (e) the addition reaction is temperature dependent because of the differences in activation energy of biradical closure and fragmentation. Problems in accounting for formation of both cis- and trans-fused cycloadducts remained, complicated by Chapman's report[8] that stereoisomeric adducts might not originate from a common triplet intermediate. This turned out to be an artifact, arising from the use of di-*tert*-butyl nitroxyl as the triplet quencher,[8] since later studies using naphthalene as the quencher showed clearly that cis- and trans-fused adducts in a model system (see below) arise from a common enone triplet state.[51] Loutfy and de Mayo[50] also noted that insuf-

Scheme III



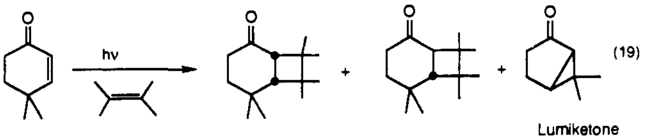
E = enone, A = alkene, BIR = 1,4-biradical, CA = cycloadducts

ficient evidence was available to indicate whether the first bond in the adduct is formed α or β to the enone carbonyl group. However, despite their acceptance of the exciplex hypothesis, Loutfy and de Mayo's data in no way *requires* formation of an exciplex precursor to biradicals in enone [2 + 2] photocycloadditions. In contrast, Caldwell concluded that some kind of complex was an obligatory intermediate prior to formation of triplet 1,4-biradicals in the analogous process of oxetane formation from benzophenone and alkenes, on the basis of comparison of secondary kinetic isotope effects for initial quenching of the ketone triplet, for formation of oxetanes, and for cis–trans isomerization of the alkenes.[52] The identity and structure of this complex (exciplex) could not be described with certainty, but Caldwell argues that most likely it is a π-complex involving interaction of the n-orbital of benzophenone with the π molecular orbital of the alkene (the reactive triplet in this case is the n,π^* triplet state of benzophenone). No such kinetic test for exciplex intermediates prior to formation of triplet 1,4-biradicals in enone photocycloadditions has been reported.

The final version of the Corey–de Mayo mechanism is shown in Scheme III.[50]

B. Identification of the Reactive Enone Intermediate

De Mayo's studies provided strong evidence that the reactive excited state of the enone component in [2 + 2] photocycloadditions to alkenes is a triplet state, and that most likely it has a π,π^* configuration.[12,15,50] This conclusion was strongly supported by studies of Schuster and co-workers on 4,4-dimethylcyclohexenone (**34**), which gives the products shown in eq 19 upon irradiation in the presence of tetramethylethylene.[43,51,53] The results of these studies can be summarized as follows: (a) alkenes quench the well-known lumiketone photorearrangement of this enone; (b) cis- and trans-fused cycloadducts are formed at the expense of photorearrangement products as the alkene concentration is increased; (c) Stern–Volmer slopes for quenching of the formation of lumiketone and cycloadducts by naphthalene and 1-methylnaphthalene are identical; (d) cis- and trans-fused cycloadducts arise from the same enone triplet, in contrast to an earlier report.[8] Since it has previously been concluded that the rearrangement of cyclohexenones to lumiketones proceeds via the enone $^3\pi,\pi^*$ state and not the ^{3}n,π^* state,[43,51,54,55] the former must necessarily be the reactive excited state in the [2 + 2] photocycloadditions shown in eq 19. Confirmation of this conclusion comes from irradiation of this enone in neat alkene, which affords the oxetane **35** in addition to [2 + 2] cycloadducts and lumiketone, as reported previously.[56] Tucker[53] found that the Stern–Volmer slope for quenching of formation of **35** by naphthalene is different from that for quenching of the formation of all the other products in eq 19. It is generally accepted[57] that oxetanes are produced from n,π^* triplet excited states of ketones. This unequivocally demonstrates that all products, except for **35**, arise from the triplet π,π^* state of **34**, including the [2 + 2] cycloadducts.



(19)

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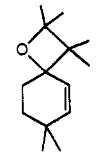

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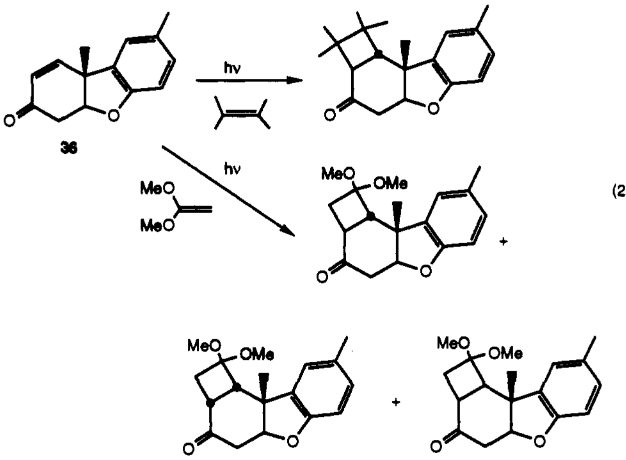
There is now good evidence from transient absorption spectroscopy[13] and photoacoustic calorimetry[18] to show that relaxed π,π^* triplets of simple cyclohexenones are highly twisted, as expected by analogy with medium-ring enones,[40,42] simple alkenes,[57,58] and cyclohexenes such as 1-phenylcyclohexene[59] and 1-acetylcyclohexene.[60] While interaction of twisted cyclohexenone triplets with alkenes would help to rationalize the formation of trans-fused cycloadducts, the fact remains that steroid enone triplets which are not twisted to a significant extent[13,16] also preferentially form trans-fused adducts with alkenes.[22,23]

Prior to direct determination of rate constants for alkene interception of enone triplets using flash photolysis,[19] the ability of alkenes to quench the photoisomerization of 4,4-dimethyl-2-cyclohexenone was studied.[43,51,61] Stern–Volmer quenching slopes $k_q\tau_T$ were obtained for each alkene. Since the lifetime of the triplet state of this enone is known from flash photolysis studies to be 25 ns,[62] the alkene quenching data can be used to obtain the rate constants for interaction of the alkenes with this particular enone triplet. There is absolutely no correlation between these quenching rate constants for 16 alkenes and 3 alkynes and the 17 ionization potentials.[61] Again, there is absolutely no correlation between these quenching rate constants and the ionization potentials of the alkenes. The most reactive compound in the series investigated was *cis*-1,2-dichloroethene, which was 4 times more reactive than the next most reactive material, cyclopentene. The least reactive quenchers were maleic anhydride, 4-octyne, and 3,3-dimethyl-1-butyne. Those alkenes with the lowest and highest ionization potentials, respectively, were 2,3-dimethyl-2-octene and maleic anhydride. No obvious pattern of reactivity has been derived from these data. The adducts were not structurally characterized in most of these systems.

A mechanistic anomaly relating to the photochemistry of 34 still has not been resolved. The Stern–Volmer slopes for quenching of the rearrangement of 34 by alkenes do not agree with the values of $k_q\tau_T$ obtained from direct measurements of the effect of these alkenes on the rate of enone triplet decay.[63] A possible rationalization of this discrepancy is that the route to cycloadducts in this case does not involve interaction of alkenes directly with the short-lived enone triplet, but rather with a secondary species derived from the triplet, such as a ground-state *trans*-cyclohexenone.[63] The intermediacy of such a species would also help to explain the preferential formation of trans-fused cycloadducts with alkenes. Photoisomerization of 1-acetylcyclohexene to a ground-state trans isomer is well-established,[60,64,65] but the corresponding photochemical isomerization of *cis*-cyclohexenones to more highly strained ground-state *trans*-cyclohexenones must still be regarded as speculative.[43,65,67] Probably the best evidence for formation of a *trans*-cyclohexenone exists for Pummerer's ketone (36), where the stereospecificity associated with formation of methanol adducts is the same as in methanol addition to medium-ring enones, where adducts have been postulated to arise by syn-addition to ground-state trans enones.[68] [4 + 2] adducts with a trans ring junction are formed on irradiation of 36 in the presence of furan, and are thought to arise by trapping of the ground-state trans isomer of 36 by furan.[69] Photoaddition of 36 to tetramethylethylene gives *exclusively* a trans-fused cycloadduct, while addition to DME gives a mixture of cis- and trans-fused adducts, consistent with (but not requiring) the intermediacy of a *trans*-cyclohexenone (see eq 20).[69]

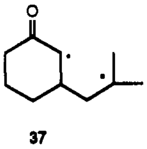


(20)

Because of the very short triplet-state lifetime of 36, it has not yet been possible to determined if these alkenes are intercepting the excited triplet or the ground-state trans isomer of 36. Rudolph and Weedon[70] have argued that *trans*-cyclohexenones are immediate precursors of carbocations in acid-catalyzed photodeconjugation and methanol photoaddition reactions of isophorone (3,5,5-trimethyl-2-cyclohexenone) and related cyclohexenones. Their kinetic data suggest that is not the enone triplet which is protonated, but rather a longer-lived (>1 μs) intermediate, which they propose to be the ground-state twisted *trans*-cyclohexenone. However, recent flash studies by Schuster and co-workers on 3-methylcyclohexenone, which undergoes the same acid-catalyzed photoreactions as isophorone, indicate that it is indeed the enone triplet which is protonated under the reaction conditions.[71] The results of photoacoustic studies of simple cyclohexenones also argue against the formation in appreciable yield of long-lived (>1 μs) ground-state intermediates, since formation and radiationless decay of the very short-lived enone triplets account for >98% of the excitation energy, i.e., the "heat discrepancy" which would be associated with formation of a long-lived ground-state trans isomer (as is observed for 1-acetylcyclohexene) is <2%.[18] Thus, the role of *trans*-cyclohexenones in the photochemistry of conformationally flexible cyclohexenones remains controversial.

C. Bauslaugh's Biradical Proposal

Twenty-three years ago, Bauslaugh[72] proposed that the regiochemistry in [2 + 2] photocycloadditions of enones could be explained without invoking exciplexes, by considering the partitioning of 1,4-biradicals between cyclization and fragmentation pathways. Thus, for the addition of cyclohexenone to 2-methylpropene, one needs to consider the four biradicals 37–40. On the basis of radical stabilization, he proposed that the rate of formation of 37 should be fastest and 40 the slowest. In fact, it was considered unlikely that 40 played any role in the reaction, as has been confirmed recently (see below). Because of its relative stability, 37 would be the most likely member of the set to undergo reversion to starting materials; 37 is also the probable source of HH adducts. Thus, cyclization was predicted to occur preferentially from 38 and 39, leading predominantly to HT adducts, as observed. The fact that the analogous addition of cyclopentenone to propene gives about a 1:1 ratio of HH and HT adducts (see eq 21)[65] was attributed to reduced importance of biradical reversion to cyclopentenone vis a vis cyclohexenone because of ring strain. While this explanation has a decided ad hoc flavor, the regioselectivity in eq 21 raises additional doubts about the validity of the exciplex hypothesis. As for the addition of cyclohexenone to DME (eq 4), Bauslaugh[2] suggests that formation of HH adducts would require juxtapositioning of polar groups in 41 prior to ring closure, which should be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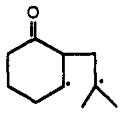
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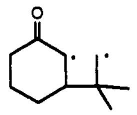
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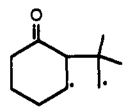
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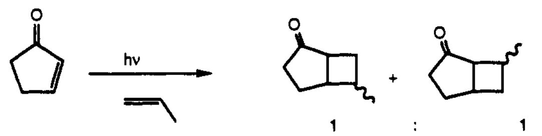

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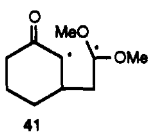

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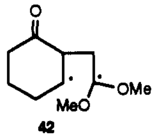
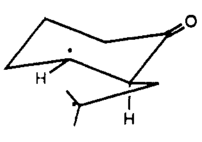


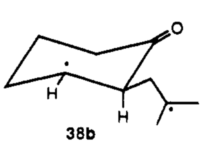
42

be energetically unfavorable compared with cyclization of the biradical **42**. (More recent studies by Weedon (see below) suggest that **41** and **42** are indeed formed in a 1:1 ratio, but undergo reversion to starting materials to different extents.)

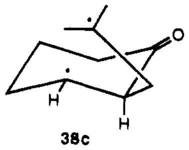
Bauslaugh also was able to account for formation of trans-fused products from cyclohexenones by considering the possible conformations of the intermediate 1,4-biradicals. Thus, in the addition of cyclohexenone to 2-methylpropene, there are three staggered conformations for biradical **38**, the most likely source of HT adducts, as shown below. Conformation **38a** would lead to the trans-fused adduct by equatorial ring closure at C_3, while **38c** would give the cis-fused adduct by axial attack at C_3; the extended conformation **38b** is unable to give either adduct and would presumably undergo fragmentation. Bauslaugh suggests that **38a** is conformationally more stable than **38c**, and would therefore be favored on equilibration of these three conformations. Moreover, the steric problems associated with ring closure of **38c** to give a cyclobutane are more severe than with **38a**. A similar conformational analysis of biradical **37** leads to the conclusion that **37a** is better suited to undergo ring closure to HH adducts than **37b**, while **37c** is most likely to undergo fragmentation. However, Bauslaugh sees no compelling preference for formation of a trans as opposed to cis-fused HH adduct from **37a**; indeed only a cis-fused HH adduct was isolated by Corey.[3]



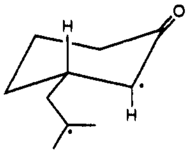
38a



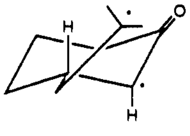
38b



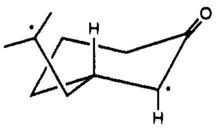
38c



37a



37b

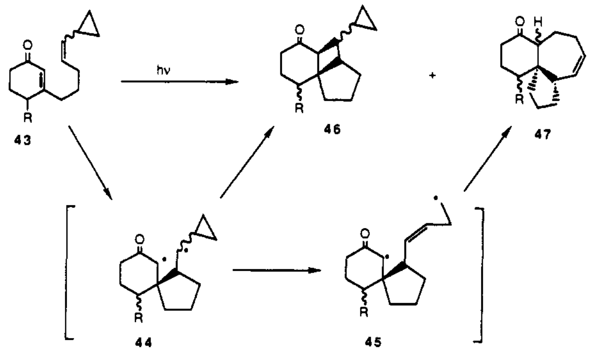


37c

Facial selectivity in the [2 + 2] photocycloaddition of steroid enones to allene was rationalized by Wiesner[73] using a similar type of conformational analysis, coupled with the suggestion that the β-carbon of enones becomes pyramidal in the reactive excited state. The latter point is now generally recognized probably as being correct.[13,18,43] Wiesner's argument was that the precise configuration at C_β of the excited enone will be that which is preferred thermodynamically on the basis of ring strain and nonbonded interactions. However, this model is inherently deficient since it does not explicitly take biradical reversion into account.

D. Detection and Trapping of Biradical Intermediates in Photocycloadditions

As has been seen, the intermediacy of triplet 1,4-biradicals in enone [2 + 2] photocycloaddition reactions is well established, and there is strong experimental support to the hypothesis that biradical reversion to starting materials is competitive with product formation. Recently, significant progress has been made in detecting and trapping biradical intermediates in enone [2 + 2] photocycloadditions, and in clarifying the mechanism of formation of these biradicals from photoexcited enones and alkenes. One approach has been to estimate triplet 1,4-biradical lifetimes by generation of biradicals which are capable of undergoing competitive rearrangement to alternative products at a known rate. Since the rate constant of ring opening of cyclopropylcarbinyl to 3-butenyl radicals is known from several independent investigations,[74] this process can be used as a "radical clock" for estimation of biradical lifetimes. Thus, Becker and co-workers generated diradicals **44** from the dienones **43** with a cyclopropyl substituent on the C═C bond in the side chain.[75] They isolated rearrangement products of type **47** as well as normal [2 + 2] cycloadducts **46** in a ratio of 45:55, showing that the ring-opening of biradical **44** to give **45** occurred at roughly the same rate as ring closure (see eq 22). On this basis, they estimated the lifetime of biradical **44** to be on the order of 50 ns. In a related study, Rudolph and Weedon[76] found that photoaddition of cyclopentenone to vinylcyclopropane gave HH and HT cycloadducts **48** and **49** as well as products **50** and **51** derived from ring opening of the intermediate biradicals; the expected cyclization products **52** and **53** were not observed (see eq 23). Again,



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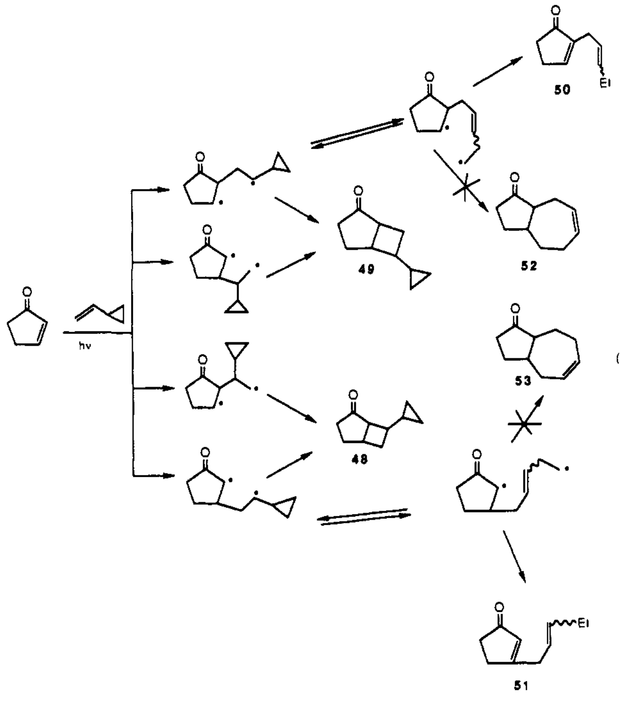
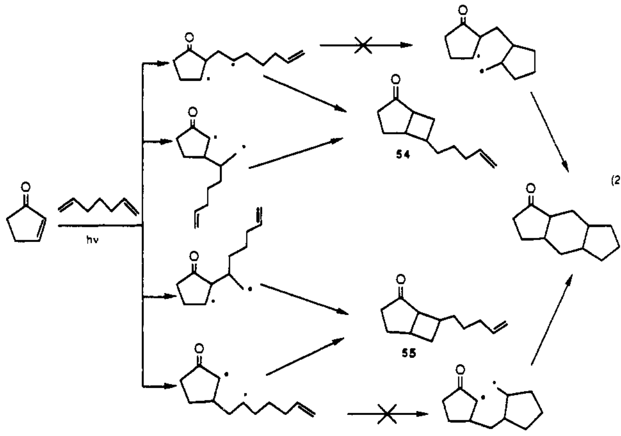


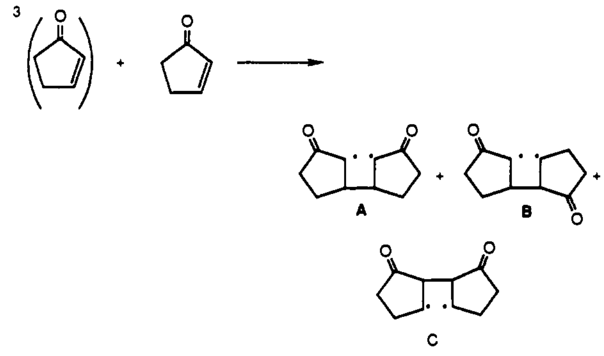
(23)

the lifetimes of the initially formed triplet 1,4-biradicals were estimated to be ca. 50 ns. It is worth noting that initial bond formation between the enone and alkene in this system occurs at both C_α and C_β. In a related study, these authors[76] found that the photoaddition of cyclopentenone to 1,6-heptadiene gave only the expected [2 + 2] cycloadducts 54 and 55 (see eq 24); no products were isolated arising from competitive rearrangement of the initial 1,4-biradicals within the side chain to give 1,6-biradicals. Since the rate of rearrangement of 1-hexenyl to cyclopentylmethyl radicals is $<10^5\ s^{-1}$,[77] the lifetimes of the initially formed triplet 1,4-biradicals in eq 24 must be substantially less than 10 μs. A similar observation was made[75] in analogous intramolecular photoadditions using cyclohexenones with a tethered diene moiety.



(24)

Direct detection of triplet 1,4-biradicals in enone cycloadditions has been achieved recently by Schuster, Caldwell, and co-workers.[14] Laser flash excitation of cyclopentenone (CP) in acetonitrile gives complex transient decay profiles at 280 nm which can be resolved into two first-order decays, one which is dependent on the concentration of the enone and a second which is not. The former is concluded to be the CP triplet, which has been a controversial subject of study.[6,11,12,64c,65] It is known from studies of CP photodimerization that quenching of CP triplets by ground-state CP (self-quenching), the primary process leading to CP cyclodimers, is unusually fast.[6,11] Indeed, plots of reciprocal CP lifetimes [measured by transient absorption spectroscopy (TAS)] vs CP concentration give a self-quenching rate constant of $5 \times 10^8\ M^{-1}\ s^{-1}$, higher than for any other enone.[13,14] The limiting CP triplet lifetime in acetonitrile is 380 ± 75 ns, much higher than Wagner's estimate of only 3 ns[11] and the value of 30 ns reported by Bonneau[64c] in his pioneering study of enone triplet states. Bonneau's value is consistent with the value of 37 ns for the concentration-independent lifetime of the second transient observed using TAS by Schuster and Caldwell,[14] a value proposed to be the (weighted) average lifetime of the mixture of HH and HT adduct triplet 1,4-biradicals formed by CP self-quenching, depicted in eq 25. (Note that each of these biradicals is a mixture of two diastereomers, since two stereogenic centers are generated on formation of the first C-C bond, so that six possible 1,4-biradicals are in fact formed in this reaction.) Thus, at even moderate CP concentrations (>0.05 M), essentially the only detectable transient species are the dimeric triplet biradicals. Measurements using time-resolved photoacoustic calorimetry (PAC) at moderate CP concentrations allow detection of a transient which again is concluded to be the mixture of dimeric biradicals.[14] The biradical lifetime was in perfect agreement with that from the TAS study, and its energy (relative to a pair of CP ground state molecules) was found to be 47.4 ± 1.7 kcal/mol. Using the Benson group additivity technique,[78] the energies of the HH and HT biradicals (A and B) were estimated to be 44 and 51 kcal/mol, respectively, consistent with the experimental average energy. These are the first such data available for triplet 1,4-biradicals derived from cyclic enones.

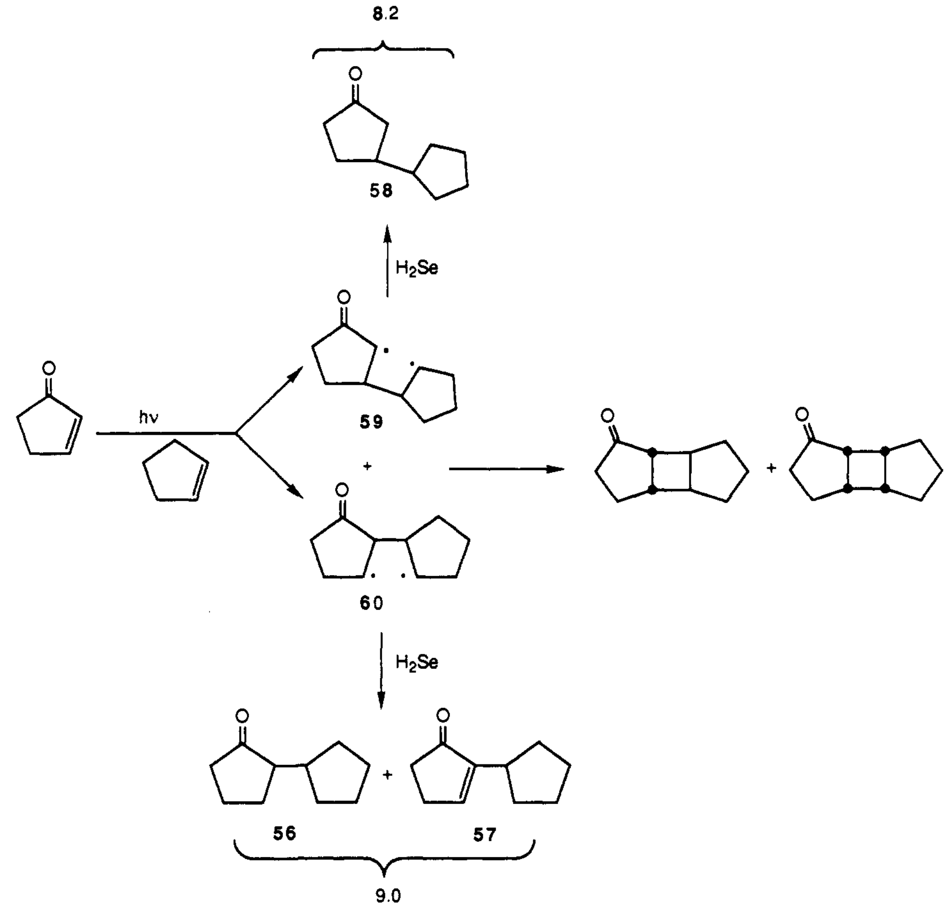


(25)

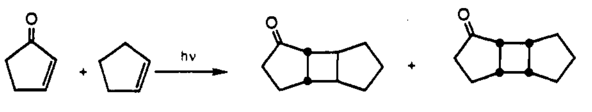
More recently, the PAC technique has been used to measure lifetimes and energies of triplet 1,4-biradicals derived from some model enones and alkenes, as the first step in a broad study of such species.[79] The biradical lifetimes vary from 15 to 900 ns. The shortest lifetimes are for biradicals derived from 3-methylcyclohexenone and cyanoalkenes, while the longest is for the same enone and 2,3-dimethyl-2-butene. A typical value is 59 ± 5 ns for the biradical(s) derived from testosterone acetate and cyclopentene. The triplet biradical lifetimes estimated by Becker[75] and Weedon[76] (see above) lie in this quite broad range. As already mentioned, these values are the weighted average lifetimes for the group of biradicals formed in the given interaction, some of which may not yield products to a significant extent. The average energies of these biradicals also vary over a considerable range, from 36 to 60 kcal/mol, relative to the ground states of the reactants. These values are in good agreement with estimates based on Benson's additivity rules.[78] Further discussion of these data will be presented in due course. It is clear, however, that these triplet biradicals have lifetimes which allow complete conformational equilibration, as has been implied by many of the observations discussed previously.

Many of the problems and anomalies associated with enone photocycloadditions would be resolved if one knew (a) the quantum efficiency for formation of the several possible triplet 1,4-biradicals obtainable from a given enone and alkene pair, (b) the lifetime and energy of each biradical, and (c) the extent to which each biradical undergoes reversion to starting material and conversion to cycloadducts. As was suggested by Schuster in his recent review of enone photochemistry,[43] a and c could be achieved if a method were found to trap enone-derived biradicals analogous to those used by Wagner and Scaiano to trap triplet 1,4-biradicals in

Scheme IV



the Norrish type II reaction.[80] Such a method has recently been discovered by Weedon using H_2Se as the trapping reagent.[37,81] This reagent was shown to be effective in trapping Norrish II biradicals[82] while the enone–alkene biradicals were not efficiently intercepted by more standard trapping agents such as thiols and stannanes.[81] The viability of H_2Se as an effective biradical trap was first demonstrated in the photoaddition of cyclopentenone to cyclopentene in benzene.[2] Hastings and Weedon[81] showed that this reaction gives a mixture of cis-syn-cis and cis-anti-cis adducts (eq 26).

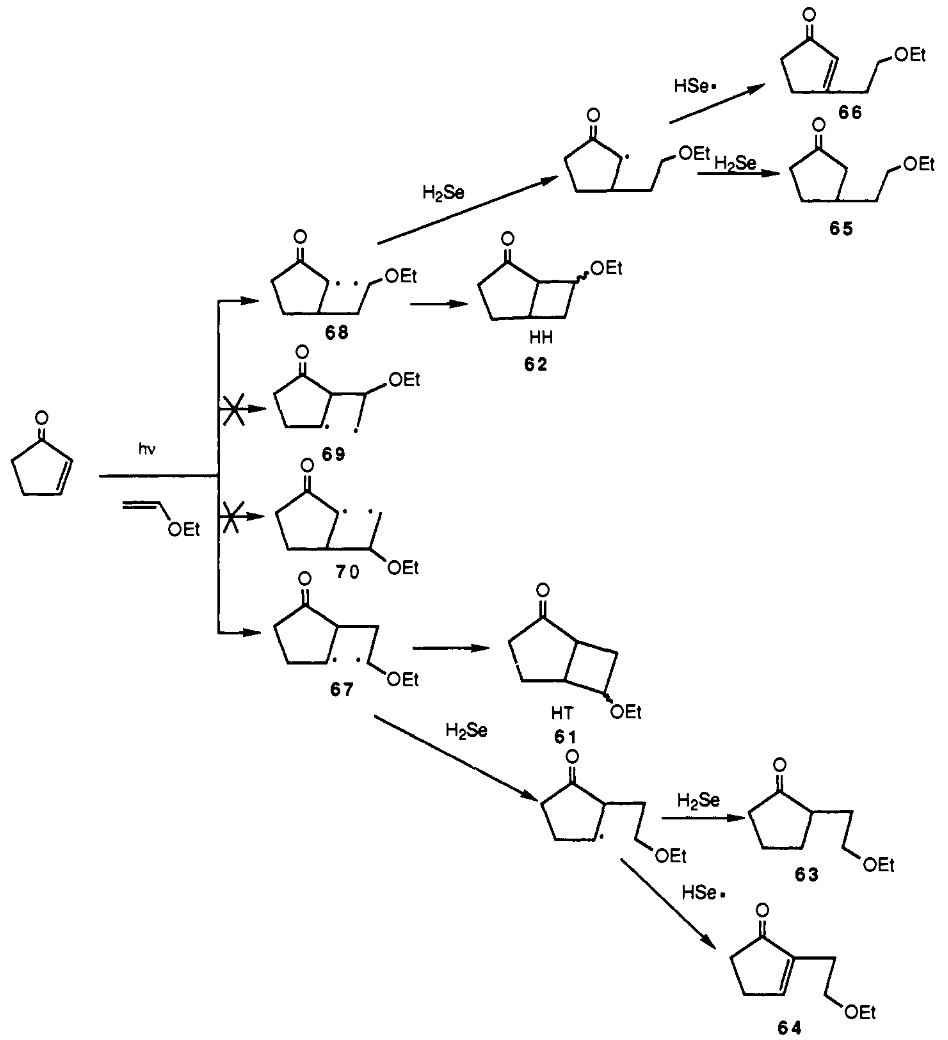


(26)

When the reaction was carried out under identical conditions (0.06 M enone, 1.2 M alkene) in the presence of 0.3 M H_2Se, no cycloadducts were formed. In addition to some products from dark reactions of cyclopentene and H_2Se, three additional products (**56**–**58**) derived from photochemical processes were formed, shown in Scheme IV. These are obviously derived from the putative 1,4-biradical intermediates **59** and **60** by radical reduction and disproportionation reactions. The fact that the ratio of HH to HT products [(**56** + **57**):**58**] is 9.0:8.2 suggests that the biradicals **59** and **60** are formed in similar amounts. This in turn indicates that in the absence of constraints there is essentially no difference in reactivity between the α and β carbons of the enone triplet as far as initial bonding to the alkene is concerned, resolving a long-standing controversy in this field.[3,5,12,15,23,31,37,50]

An even more revealing study involved the photoaddition of cyclopentenone to ethyl vinyl ether (EVE).[37,81] As reported previously,[83] photoaddition of CP to EVE gives a mixture of HT and HH cycloadducts **61** and **62** in a ratio of 3.1:1.0. When the reaction is carried out in the presence of H_2Se, adduct formation is totally suppressed. Instead, compounds **63**–**66** are formed (see Scheme V). Compounds **63** and **65** most reasonably arise by reduction of intermediate biradicals **67** and **68** by H-transfer from H_2Se, while **64** and **66** are proposed to arise by disproportionation of the partially trapped biradicals by HSe radicals, as shown in Scheme V. The ratio of the products arising from biradical trapping is 5.7:1.0:3.2:3.5. No products derived by trapping of biradicals **69** and **70** were detected, indicating that these biradicals which contain a primary radical center are either not produced on addition of CP triplets to EVE or revert to starting materials faster than they are trapped. If the former explanation is correct, which seems more likely given that no cycloadducts are formed in the presence of H_2Se, the results demonstrate that the excited enone become attached exclusively to the less substituted alkene carbon to give the more stable intermediate HT and HH biradicals **67** and **68**. Moreover, the ratio of products of trapping of **67** and **68** is essentially 1:1, which indicates that these biradicals are formed in a 1:1 ratio, and therefore that the rates of their formation from the triplet excited enone and EVE are essentially the same. Thus, the rates of alkene attack at the α and β positions of the enone are not significantly different, implying that there is no kinetic advantage associated

Scheme V



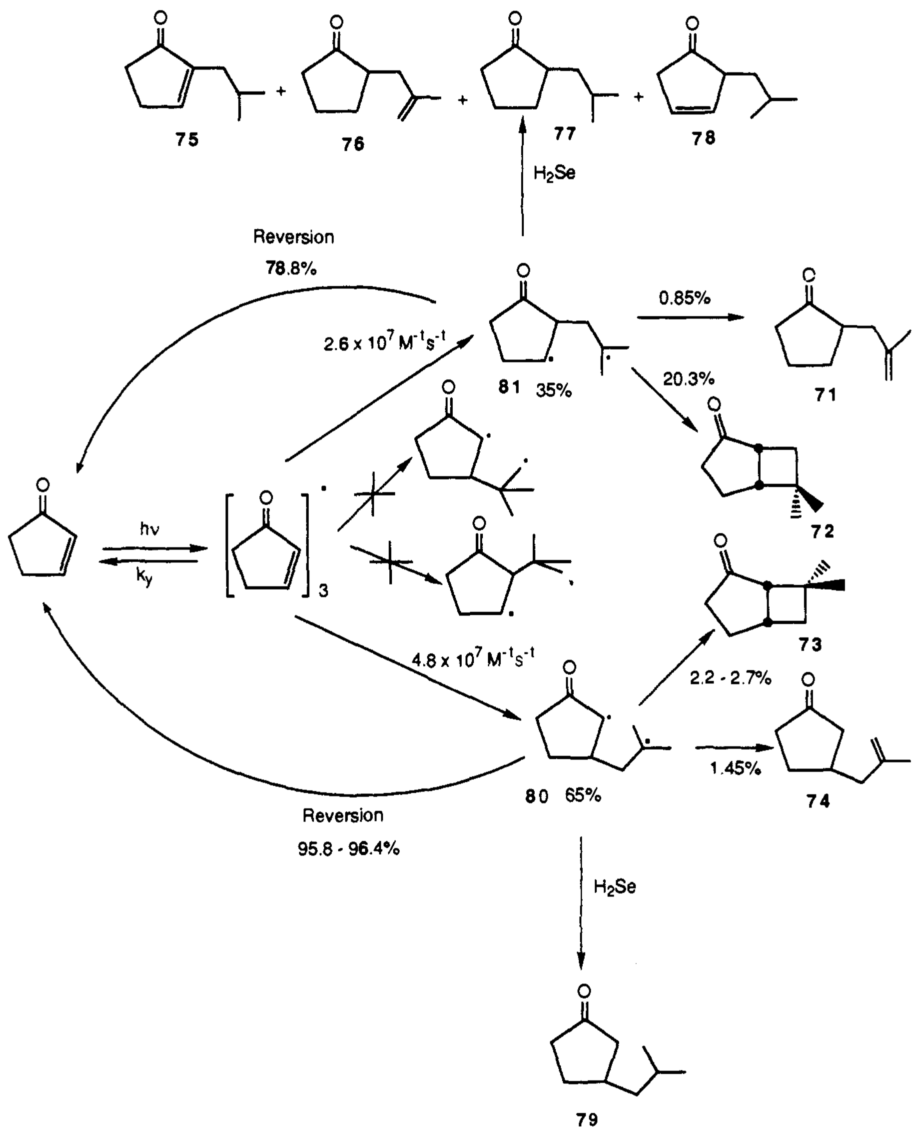
with generation of a radical center α to the carbonyl group.

The most important conclusion to be derived from this study is that the HT:HH regioselectivity observed in formation of cycloadducts from CP and EVE does *not* result from selectivity in formation of HT and HH biradical intermediates **67** and **68**, but has its origin in the differing extent to which these biradicals revert to starting material in competition with closure to products. If the rate of the former process is designated k_2 and the latter k_1, then the fraction ρ of biradicals giving adducts is given by $k_1/(k_1 + k_2)$. The data reported do not allow determination of individual ρ values for formation of HH and HT adducts, for which quantum yield measurements are necessary, but they do allow calculation of the ratio ρ_{HT}/ρ_{HH}, which is 2.64. Thus, the critical question which needs to be addressed in future studies is fundamental to understanding biradical reactivity; i.e., why does the HT biradical **67** have so much greater a preference to undergo cyclization vs fragmentation vis a vis the HH biradical **68**? This probably relates to differing populations of extended vs closed conformations for each of these biradicals, but there are as of yet no experimental or theoretical studies which provide information on this question. As will be seen below, this HT/HH preference is not unique to the CP/EVE system.

Scheme VI summarizes the data of Andrew and Weedon[37] for addition of cyclopentenone to 2-methylpropene. The products obtained in the absence of H_2Se are **71–74**, while in the presence of H_2Se the products obtained are **75–79**. From the ratios of photoproducts, the HT/HH selectivity is 72.4/27.7 = 2.61. The yields of products originating from trapping of biradicals **80** (HH) and **81** (HT) by H_2Se, four of which are derived from **81** and only one (**79**) from **80**, are 35% and 65%, respectively (HT/HH = 1.86). As above, biradicals in which the enone becomes attached to the more substituted carbon of the alkene appear not to be formed in detectable amounts, since little or no products derived from trapping such species were observed. Once again there is a greater tendency of the HT biradical **81** to give adducts (from both cyclization and disproportionation) than the HH biradical **80**. Knowledge of the quantum yields for adduct formation and the enone triplet lifetime of 22 ns (calculated from data in ref 14) allows estimates of the second-order rate constants for formation of each of the biradicals **80** and **81** and the fraction of each which revert to starting materials or go on to products. These parameters are all given in Scheme VI.

Similar analyses have been made by Weedon and co-workers[37] for reactions of cyclopentenone with (*Z*)- and (*E*)-2-butene, 2-methylcyclopentenone with 2-methylpropene, and 3-methylcyclopentenone with 2-methylpropene. In the latter two systems, essentially all the chemistry is associated with formation of the more substituted biradicals on the alkene moiety

Scheme VI



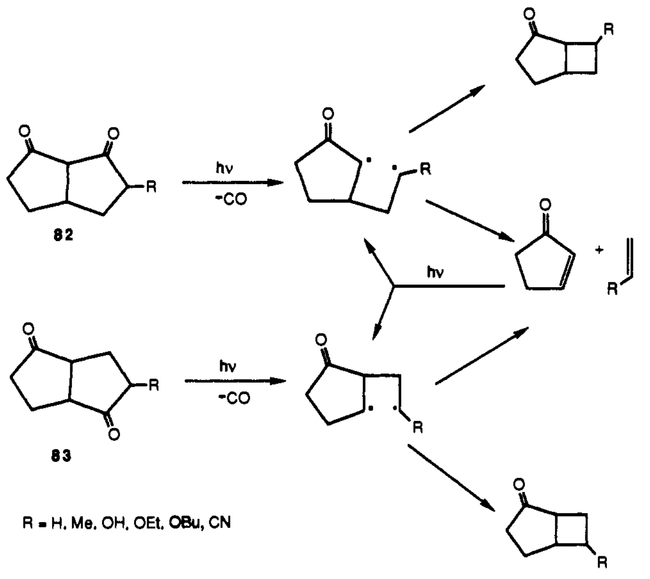
resulting from bonding to both the α and β carbons of the enone. No general trend with respect to the parameter ρ (see above) is observed, however. In some systems, ρ is larger for HT biradicals and in others it is larger for HH biradicals. Steric as well as electronic effects evidently play a role in determining the fragmentation/cyclization rate ratio.

Griesbeck et al.[84] have recently determined the location (i.e., exo or endo) of the OEt moiety in adducts 61 and 62 using NMR techniques. They found that the endo:exo ratio for the HT adduct 61 is 57:43 and for the HH adduct 62 is 62:38. Thus, there is moderate endo diastereoselectivity in formation of both adducts, which they rationalize in terms of the optimum geometry of the intermediate biradicals 67 and 68 which minimizes nonbonding interactions with the hydrogen on the radical center of the five-membered ring. Similar diastereoselectivity was found for adducts of CP with isopropyl and phenyl vinyl ethers and with 2,3-dihydrofuran.

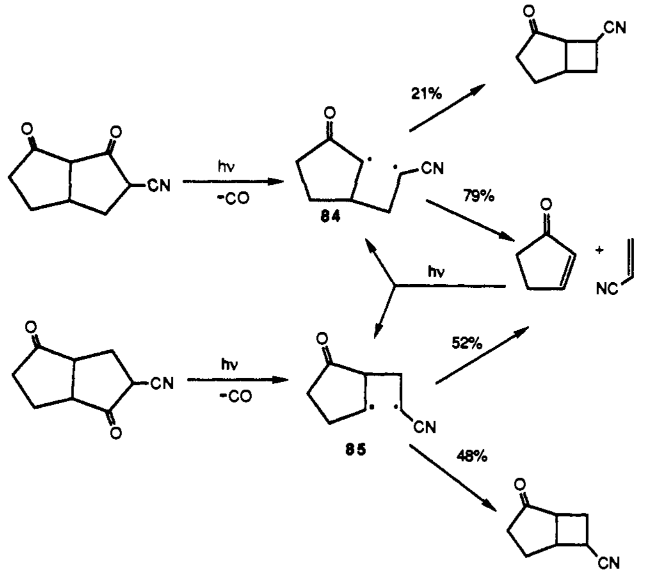
E. Generation of Adduct 1,4-Biradicals by an Independent Route

One final case that has interesting features is the photoaddition of cyclopentenone to acrylonitrile.[37,85] As shown in equation 16b, a mixture of four cycloadducts is formed, two HH (40%) and two HT (60%). Once again, Corey's suggestion[3] that the regioselectivity in photoaddition of enones to electron-deficient alkenes favors formation of HH adducts is not observed. In the CP–acrylonitrile system, alone among those studied to date, H_2Se proved to be ineffective in trapping intermediate biradicals. Possible explanation for this finding will be discussed below. In order to determine ρ values for this system, an alternative approach was employed, involving generation of the putative intermediate biradicals by a different route. The route chosen for independent generation of HH and HT biradicals involves photodecarbonylation of diketones of structure 82 and 83, respectively, and determination of the ratio of cyclization products to fragmentation products (alkene + cyclopentenone), as shown in Scheme VII. In the event, this route to 1,4-diradicals failed for R = H, methyl, hydroxy, ethoxy, and *tert*-butoxy, and only disproportionation products (ketenes and unsaturated aldehydes) derived from the intermediate acyl–alkyl 1,5-biradicals were obtained.[83] However, this approach proved to be successful for R = CN upon irradiation of 82 and 83 at 254 nm in benzene, and gave the results shown in Scheme VIII. Thus, the HH

Scheme VII



Scheme VIII



diradical 84 mainly undergoes fragmentation ($\rho = 0.21$), while the HT diradical 85 fragments and cyclizes to about the same extent ($\rho = 0.52$). From the cycloadduct ratios in the [2 + 2] cycloaddition reaction, the data allow estimation of the relative yields of these biradicals in the cycloaddition as 61% HH and 39% HT, i.e., the ratio of the rates of formation of the biradicals $k_{HH}/k_{HT} = 1.54$. Thus, in this case, the HH biradical is formed faster but preferentially undergoes fragmentation to regenerate starting materials rather than cyclization.

An important mechanistic consideration is whether the spin multiplicity of the biradicals produced by photodecarbonylation of the diketones shown in Scheme VII is identical with that of the biradicals derived from attack of enone triplets on alkenes. It is well-known that the Norrish type I fragmentation reaction of aliphatic ketones occurs from both singlet and triplet excited states, and that loss of CO from the resulting acyl–alkyl biradicals is usually a very fast process.[88] Thus, both singlet and triplet 1,4-biradicals might well be produced by the route shown in Scheme VII. The cyclization/fragmentation ratio is expected to be very different from these two species, since the singlet biradical lifetime should be much too short to allow complete equilibration between the various biradical conformations, some of which would favor cyclization and others which would favor fragmentation. The stereochemistry associated with ring closure may also be quite different for singlet and triplet 1,4-biradicals. Rudolph and Weedon[37,85] argue that the decarbonylation of 82 and 83 which occurs upon excitation at 254 nm in benzene occurs by photosensitization, leading to triplet states of the diketones and hence to triplet 1,4-biradicals, since the same products in roughly similar proportions were seen upon direct excitation of the diketones in benzene at 313 nm. (However, only a single run was performed at 313 nm for 82 and 83 using very low ketone concentrations, which did not allow for accurate measurement of product ratios by gas chromatography.) Thus, we feel that some degree of caution must yet be exercised with respect to the conclusion[37,85] that the photodecarbonylation reaction occurs exclusively via triplet 1,4-biradicals, and that these findings are therefore relevant to the [2 + 2] photocycloaddition of CP and acrylonitrile. In our opinion, additional data are required to justify the conclusions drawn from these experiments.

Weedon suggests that the failure to intercept biradicals 84 and 85 from the addition of cyclopentenone (CP) to acrylonitrile (AN) with H_2Se suggests that this particular reaction does not proceed via the lowest enone triplet excited state.[37] On xanthone-sensitized irradiation of CP in the presence of AN, CP dimers rather than CP–AN cycloadducts were obtained. Furthermore, under direct irradiation conditions, the quantum yield of enone dimer formation increases with increasing CP concentration, while the quantum yield for CP–AN adduct formation is constant. Weedon concludes that the two reactions occur via different CP excited states, and that the CP singlet excited state may be the species interacting with AN.[37] Schuster and co-workers[87] have found that CP photodimerization is quenched by AN, which itself does not distinguish between reaction of AN with CP singlet and triplet excited states. However, 1-methylnaphthalene quenches formation of both CP dimers and CP–AN adducts, although the Stern–Volmer quenching slopes are not precisely identical. This suggests that the CP–AN photocycloaddition may occur via a CP triplet which is different from that leading to CP dimers. Clearly more work is needed to resolve this problem. Thus, photodimerization of cyclohexenone may also arise from a triplet state different from that responsible for other photochemical reactions including [2 + 2] photocycloaddition.[43]

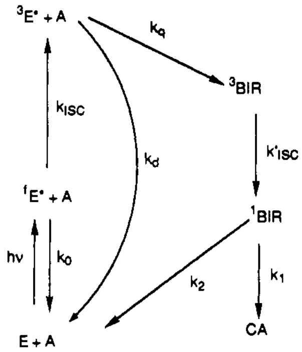
There is obvious concern that acrylonitrile and other electron-deficient alkenes could be quenching enone triplets by triplet-energy transfer. Acrylonitrile (AN) is known to undergo triplet-sensitized photodimerization via a low-energy (ca. 60 kcal/mol) triplet excited state.[88] It was found, however, that AN dimers, which are readily detectable on benzophenone-sensitized excitation of AN, are formed in at most trace quantities upon irradiation of cyclopentenone, 3-methylcyclohexenone, cyclohexenone, and BNEN in neat AN under conditions that lead in the first three cases to good yields of enone–AN adducts.[19] The same result was found using α-chloroacrylonitrile in place of AN. To ascertain whether these adducts might possibly be formed by a route involving triplet energy transfer to AN followed by attack of AN triplets on ground state enone, AN triplets were generated by benzophenone sensitization in neat AN in the presence of 0.2 M cyclopentenone under conditions where benzophenone absorbed 97% of the incident light. Under these conditions, only AN photodimers[88] and none of the CP-AN photoadducts (see eq 16) could be detected.[19] Thus, a sensitization-addition mechanism for the [2 + 2] photocycloaddition can be excluded, at least in this case.

As previously mentioned, the triplet biradicals derived from 3-methylcyclohexenone and fumaronitrile or acrylonitrile are unusually short-lived, on the order of 20 ns.[79] These lifetimes are much shorter than anticipated for biradicals stabilized by a cyano group at one of the radical centers, and are indeed shorter than the lifetimes of any other 1,4-biradicals studied thus far. Assuming that a similar situation holds for the biradicals formed from CP and acrylonitrile, this may explain why Weedon's H_2Se trapping experiment failed uniquely in this particular case. The loss of stereochemistry on photoaddition of 3-MCH to fumaro- and maleonitrile implies that adduct triplet biradicals with sufficient lifetimes to undergo conformational equilibration are indeed formed in this reaction. Biradical trapping has not been reported as yet for this or indeed for any photocycloaddition reaction involving cyclohexenones.

F. The Bauslaugh–Schuster–Weedon Biradical Mechanism for Enone–Alkene Photocycloadditions

While the Corey–de Mayo exciplex mechanism[3,15,50] for photocycloaddition of enones to alkenes has certainly provided a stimulus for workers in this field, and has undoubtedly had heuristic value in accounting for experimental observations in a vast number of reactions,[5] it is now very clear that there is no experimental support to justify the proposal that the initial interaction of enone excited states and alkenes involves formation of an enone–alkene exciplex. Several of the most critical experimental findings on which the exciplex hypothesis was based have turned out to be seriously flawed. The most prominent of these are (1) the enone excited state actually responsible for the reaction (π,π^*) has a different polarization than the state (n,π^*) originally thought to be involved;[3] (2) the reactivity scale of alkenes in these photochemical addition reactions as measured directly using nanosecond laser flash techniques[13,19,20] is quite different from the reactivity scale derived originally from competition studies,[3] which did not take into account biradical reversion to starting materials; (3) the regioselectivity for addition of enones to electron-deficient alkenes is not as a general rule reversed from that for additions to electron-rich alkenes; and (4) the frequently observed regioselectivity in additions of enone triplets to unsymmetrical alkenes arises in all cases studied thus far from the competition between reversion of intermediate adduct 1,4-biradicals to ground-state starting materials and formation of products by cyclization and disproportionation reactions. Thus, there is no evidence to support the original hypothesis[3] that there is a preferred orientation of the enone triplet and the alkene in a polarized donor–acceptor complex. Furthermore, as demonstrated by the data in Table I, there is essentially no effect on the rate constant for interaction of a large number of enone triplets with alkenes upon changing from a polar (acetonitrile) to a nonpolar (cyclohexane) solvent, indicating no significant development of charge in the transition state for this process. Since no evidence *requiring* exciplex precursors to biradicals has been reported for these photocycloadditions, and since exciplexes are not necessary to explain the course of these reactions, we see no reason why exciplexes should continue to be invoked in mechanistic discussions of enone [2 + 2] photocycloaddition reactions. The mechanism shown in Scheme IX, essentially that postulated by Bauslaugh in 1970, is sufficient to explain the course of these reactions. In this mechanism, the only intermediates invoked are enone triplet excited states, adduct triplet 1,4-biradicals, and the corresponding singlet 1,4-biradicals. Firm evidence to support the involvement of all of these species has been presented. Examples may yet be uncovered, particularly involving analogous heterocyclic systems, in which evidence will be obtained *requiring* initial formation of exciplexes. Until such time, we recommend that the mechanism of Scheme IX be used as the framework for discussion of [2 + 2] photocycloadditions of enones to alkenes.

Scheme IX



E = enone, A = alkene, BIR = 1,4-biradical, CA = cycloadducts

One of the possible benefits of this revised mechanism is that more attention may now be paid to photoadditions of enones to electron-deficient alkenes. While these are sometimes accompanied by unwanted side reactions, as in enone additions to acrylonitrile which invariably lead to formation of acrylonitrile polymers,[13,34] these reactions oftentimes proceed quite cleanly, as in the examples described by Lange.[38] Just as [2 + 2] photoaddition of enones to electron-rich alkenes have been extensively and profitably used by synthetic chemists,[5] there is no reason why analogous reactions using electron-poor alkenes should not also find synthetic utility, now that the mechanistic bias against them has been removed.

IV. Future Directions

The focus of attention in future mechanistic work on [2 + 2] photocycloadditions must necessarily be centered on the triplet 1,4-biradical intermediates derived from enone triplets and alkenes. The physical and chemical properties of such species need to be determined in a systematic fashion for a wide range of systems, with emphasis on biradical lifetimes and energies. Such an effort is ongoing in our laboratory at this time.[79] The factors (electronic and steric) which control the rates of fragmentation and cyclization of these biradicals need to be elucidated. Theoretical calculations will surely be of some assistance in this connection, as will increased understanding of the dynamic properties of flexible triplet biradicals.[89] For example, it is not at all obvious why addition of cyclohexenone to (*Z*)- and (*E*)-2-butene is not accompanied by at least partial isomerization of the recovered alkene, as reported by Corey,[3] or why there is no loss of stereochemistry in the alkene moiety of recovered starting material in the intramolecular photocycloadditions reported by Becker which give mixtures of stereoisomeric products.[31] Assuming these observations are correct, the triplet biradicals involved in these particular reactions do not appear to revert to ground-state starting materials to a significant extent. It should be noted that cycloaddition quantum efficiencies were not reported in these cases. An obvious goal is to attempt to correlate the extent of isomerization in the reactant alkene with independently determined biradical partitioning factors.

The possibility of altering the course of enone [2 + 2] photocycloadditions by modification of reaction conditions needs to be investigated. One approach would be to carry out such reactions in nonhomogeneous media. Thus, photodimerization of coumarin in cyclodextrins[90] and of cyclopentenone and cyclohexenone in dry zeolites[91] and Norrish type II reactions in zeolites[92] give product distributions which are quite different from those in fluid solution. Stereochemical and regiochemical control of [2 + 2] photocycloadditions in solution has not been possible for reasons which are now totally clear, but these goals may ultimately be achievable if these reactions can be successfully carried out in other kinds of environments. Developments along these lines would further increase the synthetic value of a reaction which is already the most frequently used organic photochemical process.

A completely satisfactory theory is still not at hand to explain the stereochemistry associated with formation of adducts from cyclohexenones. It is clear that both cis- and trans-fused cycloadducts arise from the same enone triplet, and that twisting of the enone triplet is not a prerequisite for the formation of trans-fused adducts. While the involvement of ground-state *trans*-cyclohexenones in cycloadditions cannot be excluded,[51,63,65,70] the general involvement of such species is at best highly speculative, as discussed earlier. Thus, in one recent case involving photoaddition of 4,4-dimethylcyclohexenone to acrylonitrile,[36] where such a species was invoked to rationalize the "abnormal" regioselectivity observed, it is now clear that the course of this reaction was entirely normal.

One final point concerns the rates of reaction of enone triplets with alkenes. The second-order rate constants for these reactions (Table I) are orders of magnitude larger than for reaction of carbon-centered radicals with alkenes[93] or for processes such as addition of diene triplets to diene ground states.[94] The rate constants in Table I are similar in magnitude to the rate constants found for quenching of aromatic ketone triplets by alkenes leading to oxetanes, but in that case evidence has been presented which supports a mechanism involving initial formation of a complex.[52] Rapid formation of some kind of bimolecular complex from enone triplets and alkenes is one way of rationalizing the large rate constants for this interaction, as explicitly noted by Wagner[11] and de Mayo.[15,50] Thus, one might argue that the magnitude of the rate constants observed is inconsistent with direct formation of triplet biradicals from enone triplets and alkenes. However, one might also argue that reaction of monoradicals with alkenes is not an appropriate model for the corresponding reaction of enone triplets, since the latter is predicted to be more exothermic by at least 10–20 kcal/mol, based on the relative energies of the triplet 1,4-biradicals and the enone triplets.[13,18,79] The exothermicity of the addition reaction can also be used to rationalize the fact that enone triplets react nonselectively with alkenes at the α and β carbons, according to Weedon's recent findings;[37,81] i.e., enone triplets are very indiscriminate reagents, at least toward alkenes. These fundamental questions will undoubtedly receive further attention in the future.

Acknowledgments. Research at NYU on enone photochemistry has been supported by grants from the National Science Foundation and the Petroleum Research Fund, for which we are deeply grateful. We are also grateful to Professor Alan Weedon at the University of Western Ontario (UWO) for sending us preprints of recent manuscripts prior to publication as well as unpublished experimental results relating to enone photocycloadditions. We also thank Andreas Rudolph for permission to quote results from his recently submitted Ph.D. dissertation at UWO.

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