

ACCOUNTS of CHEMICAL RESEARCH®

JANUARY 2001

Registered in U.S. Patent and Trademark Office; Copyright 2001 by the American Chemical Society

Photoinduced Ortho [2 + 2] Cycloaddition of Double Bonds to Triplet Benzenes

PETER J. WAGNER*

Chemistry Department, Michigan State University, East
Lansing, Michigan 48824

Received June 20, 2000

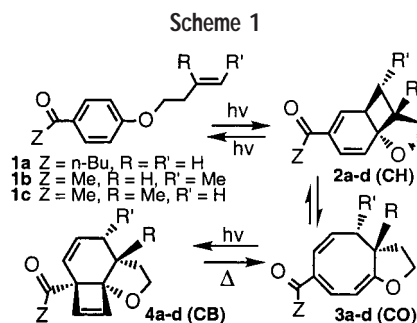
ABSTRACT

The triplet states of certain phenyl ketones and benzoic acid derivatives undergo regioselective and stereoselective intramolecular ortho cycloaddition to remote double bonds, triggering an array of photochemical and thermal pericyclic rearrangements among various novel polycyclic products.

Introduction

Aromatic resonance protects benzene rings from thermal rearrangements, but photoinduced reactions can destroy that aromaticity. The excited singlet states of aromatic compounds undergo all sorts of rearrangements and additions, of which the meta cycloaddition of alkenes has attracted the most synthetic and mechanistic interest.¹ In 1987, we discovered that the excited triplet states of several *p*-(3-alken-1-oxy)alkanophenones such as **1** undergo rapid intramolecular reaction with their remote double bonds,² forming ortho [2 + 2] cycloadducts that undergo the interesting series of electrocyclic rearrangements shown in Scheme 1.³ The precedent for such ortho [2 + 2] cycloadditions was slim for benzenes in general¹ and non-existent for acylbenzenes, although a few benzonitriles had been found to react in such a way.⁴ We have since surveyed the scope of this novel reaction, which provides a new synthetic route to some bi- and tricyclic structures as well as unique information about both the chemistry

of benzene triplets and substituent effects on electrocyclic equilibria. This Account summarizes what has been learned so far.

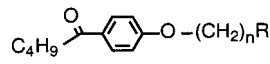


Discovery

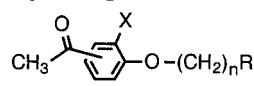
Our initial goal was simply to compare a vinyl group to a tertiary amino group in their ability to quench a π, π^* benzene triplet intramolecularly. To our surprise, the vinyl was a better quencher than the more easily oxidized amine. Noting that an irradiated solution of **1a** had become yellow, we subjected it to gas chromatography and isolated the yellow cyclooctatriene **3a**. We assumed that the tricycloxaundecadiene **2a** was formed by a [2 + 2] cycloaddition and then opened thermally to **3a** in the hot GC injector. However, NMR analysis of irradiated **1a** yielded **4a** as the only detectable product at all percent conversions, there being no sign of any **2a** or **3a**. Where did **4a** come from? Direct irradiation of isolated **3a** established it as the precursor of **4a**. Since **3a** absorbs light much more strongly than does **1a**, its concentration never gets high enough to be observable by NMR. Monitoring the reaction of 0.01 M **1a** by UV revealed that an intense peak with λ_{max} at 350 nm had grown after only 15 s of irradiation and demonstrated that **3a** is formed very rapidly at ambient temperatures. So how, exactly, is **3a** formed? Fortunately, **1b** provided the answer, the NMR spectrum of a partially irradiated solution showing the presence of both **2b** and **4b**. The steric interactions caused by the methyl group poking inside the boat cyclooctatriene structure of **3b** raise its energy sufficiently to

Peter Wagner was born in Chicago on Christmas, 1938. He received a B.S. degree from Loyola University, Chicago, and a Ph.D. with Cheves Walling at Columbia University. After a postdoctoral year with George Hammond at Caltech, he joined the Chemistry Department at Michigan State University, where he is currently University Distinguished Professor. His research interests involve various mechanistic and exploratory aspects of molecular photochemistry.

* E-mail: wagnerp@pilot.msu.edu.

Table 1. Reaction Rate Constants of Triplet *p*-Alkenoxyvalerophenones


<i>n</i>	R	<i>k_r^a</i>
1	H	0
1	CH=CH ₂	0.3
1	CH=CHMe	0.7
2	CH=CH ₂	89
2	C(Me)=CH ₂	120
2	CH=CHMe	277
2	CH=CMe ₂	2220
3	CH=CH ₂	2.3
3	CH=CMe ₂	6.6
4	CH=CH ₂	≤0.1
9	CH=CH ₂	≤0.1

^a Units of 10⁶ s⁻¹ at 24 °C.**Table 2. Kinetics for Triplet Decay of *o*-, *m*-, and *p*-Alkenoxyacetophenones in Toluene**


R	X	log <i>A</i>	<i>E_a^a</i>	<i>k_r^b</i>
Para				
-CH=CH ₂	CN	10.6	3.1	22
-CH=CH ₂	Cl	10.8	4.0	9.0
-CH=CH ₂	H	10.5	3.9	4.5
-CH=CH ₂	CH ₃	10.5	4.3	2.0
-CH=CH ₂	OCH ₃	10.7	5.0	1.2
Meta				
-CH=CH ₂	H			≤0.2
-CH=CMe ₂	H			≤0.3
Ortho				
-CH=CH ₂	H	10.2	3.5	3.7

^a In kcal/mol. ^b Units of 10⁷ s⁻¹ at 24 °C.

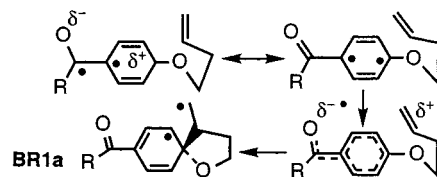
change the equilibrium between **2** and **3**. Both **2a** and **2b** open to **3** very rapidly, but only **3b** reverts to **2** fast enough to compete with photocyclization to **4**.

The three polycyclic products depicted in Scheme 1 will be identified in general as **CH**, **CO**, and **CB**. The overall process can be broken down into two separate topics: the initial photoinduced [2 + 2] cycloaddition to form **CH**, and the ensuing thermal and photochemical electrocyclic rearrangements originating with **CH**. We had much more to learn about how sensitive the various interconversions in Scheme 1 are to structure. Only when we found isolable **CH**s did their photoreversion to phenyl ketone become evident.

Nature and Mechanism of Triplet Reactivity

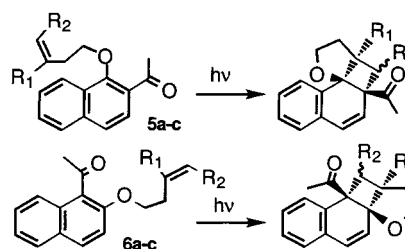
Tables 1 and 2 list rate constants for the intramolecular reaction of various acylbenzene triplets with their alkenoxy groups. The variation of these rate constants with structure strongly suggests that triplet **1** behaves like a biradical, one radical site adding to the remote double bond the way a 5-hexenyl radical would cyclize, generating the 1,4-biradical **BR1a** that couples to form structure **2**.

The fact that a double bond reacts with the acylbenzene triplet faster than does a tertiary amino group clearly indicates that the quenching is not a simple charge-transfer (CT) process. That the cycloaddition occurs only for alkanophenones, not for benzophenones, identifies the



reactive triplet as π, π^* and not n, π^* . The same state dependence was found for intramolecular CT quenching by amino groups; such regioelectronic control of reactivity is due to excitation being localized differently in the two types of triplets.⁵ In the case of this cyclization, the difference between the two types of triplets represents their different spin densities at the para position, the π, π^* triplet having full radical character at the para carbon, the n, π^* triplet having only partial radical character. The fact that both ortho- and para-substituted ketones react, but not meta-substituted ketones, is consistent with the amount of unpaired electron density at those three positions in the π, π^* triplet, the meta position having very little.⁶ That the reaction is rapid only when three atoms separate the double bond from the benzene ring is exactly analogous to the cyclization of 5-hexenyl radical to cyclopentylmethyl being faster than cyclization of 6-heptenyl radical to cyclohexylmethyl.⁷ Likewise, the effect of alkyl substituents on the double bond is the same as in hexenyl radical cyclization.⁷ There does appear to be some charge-transfer nature to the process, since electron-withdrawing substituents ortho to the alkenoxy group enhance reactivity, while electron-donating substituents depress reactivity.⁸

The final indication that the triplet reacts as a biradical is provided by the behavior of some butenoxycetophenones, which undergo [2 + 2] cycloaddition cleanly.⁹ The products do not open to cyclooctatrienes, since that would destroy the aromaticity of both rings. Apart from the rarity of cycloadditions to triplet naphthalenes,¹⁰ the large kinetic differences between isomers **5** and **6** are very informative. Isomer **5** reacts faster than **6** because the unpaired



electron density in triplet naphthalenes resides mainly at α rather than β positions.¹¹ Alkyl groups on the double bond again affect rate constants just as they do in hexenyl radical cyclizations. The smaller quantum yields for **6** vs **5** reflect slower and less efficient biradical cyclization. Table 3 summarizes the photokinetics for **5a-c** and **6a-c**.

Biradical Behavior

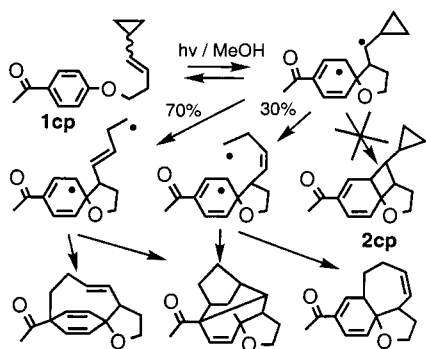
The first nonkinetic indication that a biradical is involved was the observation that *cis* → *trans* isomerization of the double bond occurs in **1c** with a quantum yield of 27%.²

Table 3. Photokinetics for (3-Buten-1-oxy)acetophenones^a

ketone	R ¹	R ²	Φ_{cyc}	k_r^a
5a	H	H	0.23	7.8
6a	H	H	0.01	2.0
5b	CH ₃	H	0.17	5.7
6b	CH ₃	H	0.04	0.7
5c	H	C ₂ H ₅	0.31	11.5
6c	H	C ₂ H ₅	0	

^a Units of 10⁵ s⁻¹ at 24 °C.

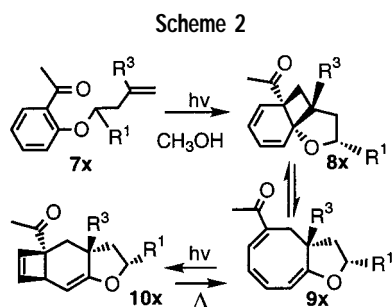
This cannot be due to triplet energy transfer, which would be 9–10 kcal/mol endothermic and thus too slow to compete. It appears that about half of the 1,4-biradicals revert to ground-state alkenoxyacetophenone in competition with their cyclization. Confirmation that a biradical intermediate is involved was provided by the fact that **1cp** does not form any of the products expected from **2cp**, but



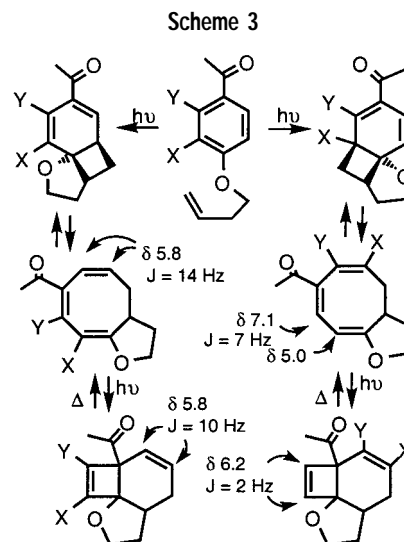
rather a mixture of products resulting from opening of the cyclopropyl ring,¹² which is known to have a rate constant of $7 \times 10^7 \text{ s}^{-1}$ for cyclopropylethyl radicals. This experiment suggests that closure of the 1,4-biradical is relatively slow, $\leq 10^6 \text{ s}^{-1}$, probably due to its allylic and enolate conjugation.

Regioselectivity

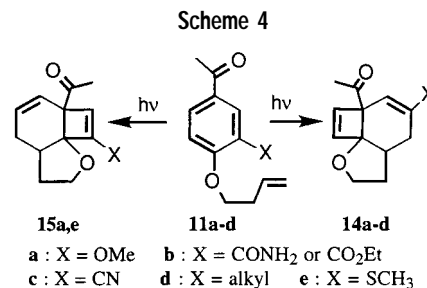
Compounds in which the alkenoxy tether is ortho to the acyl group undergo addition solely at the bond between the two substituents (Scheme 2). This high selectivity reflects a positive combination of steric and electronic effects, as will be discussed below. A ring substituent on



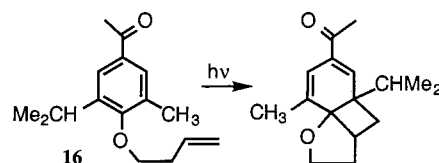
the *p*-alkenoxy ketones allows the possibility of two modes of cycloaddition, one directed toward and one directed away from the substituent. Scheme 3 shows the various possibilities and how NMR spectra can easily distinguish between them. As shown in Scheme 4, substituents ortho



to the alkenoxy tether direct the addition 100% toward themselves, with the exception of methoxy and thiomethoxy, which direct addition 80% and 100% to the other side of the benzene ring, respectively.¹³ Such high regioselectivity clearly is exciting from a synthetic viewpoint; it is equally exciting from a mechanistic viewpoint, there being several possible contributors to the overall effect.

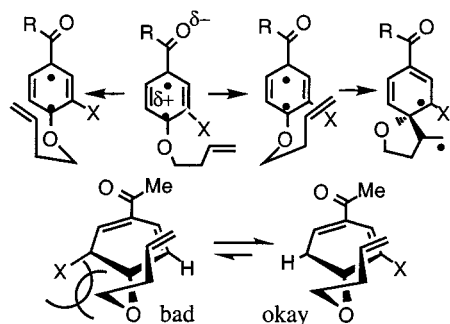


The selectivity appears to have both electronic and steric components. That alkyl groups produce the same selectivity as do strong electron-withdrawing groups clearly is a steric effect, as indicated by the preference for addition toward isopropyl rather than methyl in **16**. Scheme 5



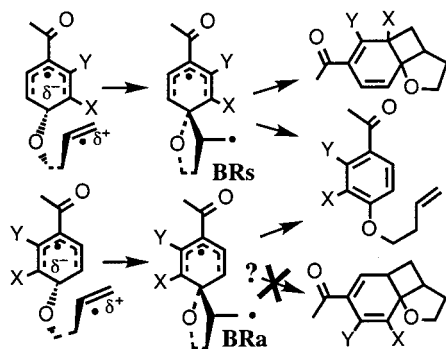
portrays this steric effect in terms of the chairlike transition state expected for a hexenyl radical cyclization, the methylene group next to oxygen preferring to avoid interaction with X. Since the double bond approaches the benzene ring from the top, it does not interact much with X. An electronic effect is indicated by both the opposite regioselectivities and the opposite effects on rate constants produced by strong electron-donating and -withdrawing groups. The strong electron-donating ability of the methoxy and thiomethoxy substituents seems to counteract the steric effect, which is lessened by their methyl groups twisting away from the tether. Scheme 6 portrays two

Scheme 5



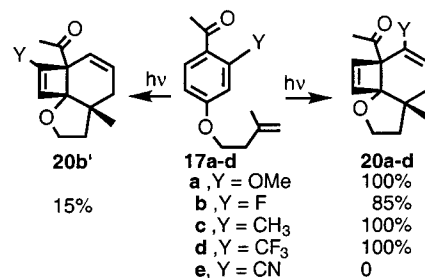
stages of the reaction that are possibly subject to electronic effects. Since the kinetics suggest that an exciplex precedes biradical formation, the preferred orientation of the exciplex probably determines selectivity. The relatively weak alkene donor should approach the side of the benzene ring with the lower electron density, not one with a strong donor attached. However, we cannot overlook the possibility that both biradicals are formed and that one of them entirely reverts to the ground state of reactant. There are many precedents for biradical partitioning determining product ratios,¹⁴ including the [2 + 2] cycloaddition of alkenes to cycloalkenes.¹⁵ In this case, it is difficult to understand how X could *entirely* prevent **BRa** from coupling. An electron-withdrawing X may lower the unpaired electron density at the other end of the pentadienyl radical moiety, but not enough to prevent cyclization, and one would think that the steric effect of X that makes **BRa** less likely to form would also make **BRs** less likely than **BRa** to cyclize. Substituents ortho to the

Scheme 6

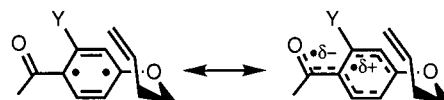


acetyl group also promote high regioselectivity, cycloaddition taking place next to both electron donors and acceptors,¹⁶ as shown in Scheme 7. The efficiency of photocyclization is greatly diminished by strong electron-withdrawing groups. The cyano derivative **17e** does not react at all, and the trifluoromethyl derivative **17d** reacts very sluggishly and furnishes the cyclooctatriene precursor to **20d** as the only stable product. Such lower reactivity contrasts to that measured for cyano ortho to the tether and indicates different electronic effects on the reaction. The fluoro derivative **17b** was the only one to undergo addition in both directions. What causes this remarkable selectivity? Substituents meta to the tether cannot cause any direct steric hindrance to exciplex formation, biradical

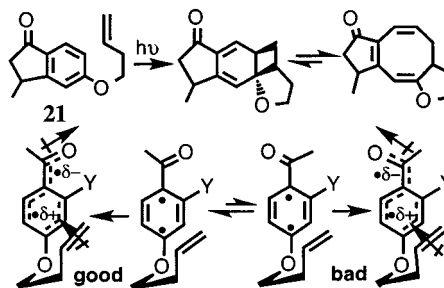
Scheme 7



formation, or final cyclization. Since the substituents are at nodes in the pentadienyl radical portion of the 1,4-biradical, they cannot affect unpaired electron density and thus biradical partitioning. Therefore, we surmised that the electronegative substituents (all but methyl) increase positive charge on that side of the benzene ring in the triplet, thus attracting the nucleophilic double bond. Semiempirical calculations indeed indicate strong positive charge in the triplet states of **17a,b,d** on the carbon bearing the substituents, in accord with the picture below.

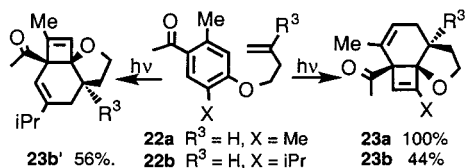


This charge-induced orientation picture does not explain how the weakly electron-donating methyl group induces regioselectivity. The fact that fluorine, the smallest substituent studied, is the only one that produces both possible cyclization modes suggests that the direction of the C=O bond somehow induces the regioselectivity. The fact that indanone **21**, its carbonyl pointed away from the 2-alkyl group, undergoes clean photocyclization with the *inverse* selectivity supports this notion. The major con-



former of all compounds **17** has the carbonyl oxygen syn to the 2-substituent; the larger the substituent, the lower the population of the conformer with the acetyl methyl pointed toward the substituent. All of these facts suggest a strong inductive effect due to dipole orientation. Given the initial CT component of the reaction, the dipole associated with charge transfer from double bond to benzene ring likely prefers to align itself perpendicular, not parallel, to the C=O dipole.

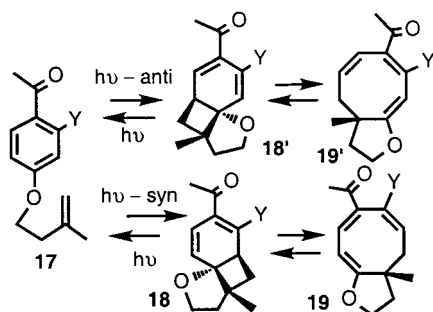
The 2-methyl-5-alkyl compounds **22** were studied to see which is more influential: substitution ortho to the tether or ortho to the acyl group. Their behavior indicates that the inductive effect of substituents ortho to the acyl



group is stronger than the steric effect of those ortho to the tether. It is especially noteworthy that when R³ is methyl, reaction is totally suppressed, presumably because the severe steric interactions caused by the 2-methyl's orientational dominance force the tether to pucker toward the 5-alkyl group.

As was mentioned above and will be described below, substituents greatly affect the electrocyclic equilibrium between **CH** and **CO**. Scheme 8 depicts these competitions for **17–19**. Relative rates and equilibrium constants for interconversion between **18** and **19** could also affect regioselectivity, since **18** undergoes very efficient photo-reversion to **17**, thus preventing the conversion of **19** to photostable **20**. However, the behavior of **17b** indicates that the **18** ⇌ **19** equilibrium is not a major contributor to the 6:1 **20b/20b'** selectivity. The **18b/19b** equilibrium ratio is 5:6, while the **18b'/19b'** ratio is 1:10. This difference in the equilibrium constants favors formation of the anti adduct and thus would have *depressed* rather than enhanced the syn/anti selectivity in biradical formation.

Scheme 8



Stereoselectivity

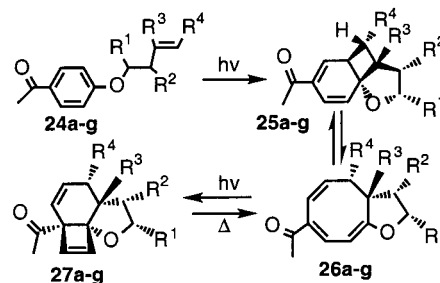
As Scheme 9 and Table 4 indicate, this photoreaction proceeds with significant diastereoselectivity with regard to substituents on the butenoxy carbons.¹⁷ Nonbonded steric interactions at three different stages of the process determine different selectivities. The relative configura-

Table 4. Diastereomer Excess (R³ Trans to R¹, R², or R⁴) in Cycloaddition Products

reactant ^a	de (%)		
	2	3	4
24a , R ⁴ = Me	≥90	≥90	≥90
24b , R ¹ = Me		56	41
24c , R ¹ = iPr		61	67
24d , R ¹ = R ³ = Me		80	80
24e , R ¹ = iPr, R ³ = Me		≥95	≥95
24f , R ² = R ³ = Me	92		
24g , R ¹ , R ³ , R ⁴ = Me ^b	80		80
24g , R ¹ , R ³ , R ⁴ = Me ^c	>95		>95
24x , R ¹ = iPr, R ³ = Me		80	80

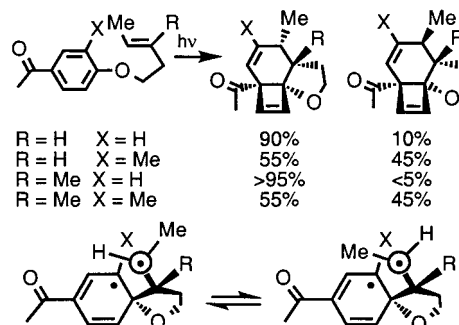
^a R^x = H unless noted. ^b (R³/R¹). ^c (R³/R⁴).

Scheme 9

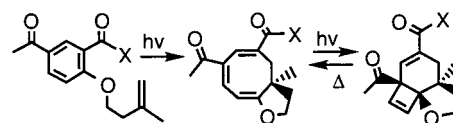


tions of R¹, R², and R³ are controlled by the normal preference for equatorial positioning in the chairlike transition state for biradical formation. However, the large preference for R³ and R⁴ being trans occurs during closure of the 1,4-biradical to a bicyclo[4.2.0]octadiene. How can a biradical cyclize with complete stereoselectivity? We have addressed this question regarding other photocyclizations;¹⁸ the answer is that rings can restrict biradicals to certain preferred geometries. Despite free bond rotation in the biradical, an R⁴ methyl must prefer to be twisted out away from the benzene ring, so that coupling places it trans to R³ (methyl or H). Scheme 10 shows evidence for this intuitively simple idea in that a methyl group ortho to the tether (which forces addition toward itself) destroys the trans selectivity, presumably because now R⁴ has steric interactions with something below it in either possible biradical geometry. Since this reaction produces a per-

Scheme 10



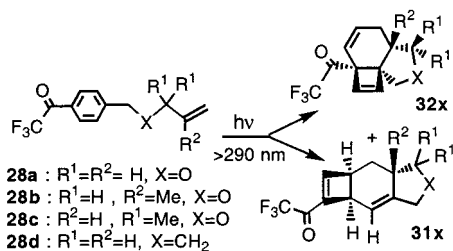
manent stereocenter in **CO**, we attached several chiral auxiliaries X as esters and amines. They promoted diastereomeric excess as high as 90%.¹⁹ The example below shows the major enantiomers formed with X = (+)-camphorsultam.



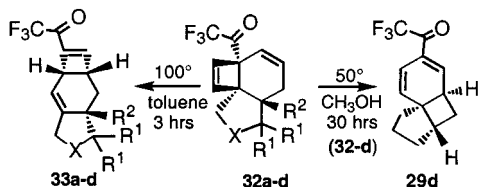
Carbon Anchors

We studied several trifluoroacetophenones **28** with a methylene group anchoring the tether to see how a change from oxygen might affect the reaction. Trifluoroacetophenones were chosen in order to maintain as strong a donor–acceptor interaction as possible. Scheme 11 shows the results.²⁰ Changing the anchoring atom from oxygen

Scheme 11



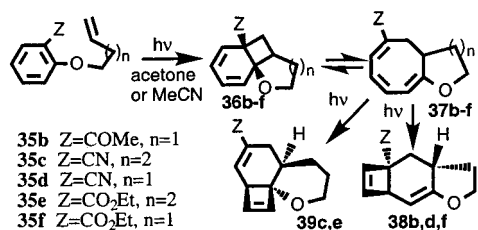
to carbon does not change the initial photoinduced [2 + 2] cycloaddition. Both linear (**31**) and angular (**32**) **CB** isomers are formed from **CO**, and the stereochemistry of their formation is the same as that found in oxygen-anchored systems. However, rates of the subsequent electrocyclic rearrangements are changed substantially, so that the competitive photochemistry of **CH** and **CO** lowers overall quantum efficiencies for formation of products. Likewise, the **32** → **CO** ring opening is so slow that at high temperatures Cope rearrangement **32** → **33** dominates. Interestingly, **33** is an epimer of **31**, and both are quite temperature stable.



Benzoic Acid Derivatives

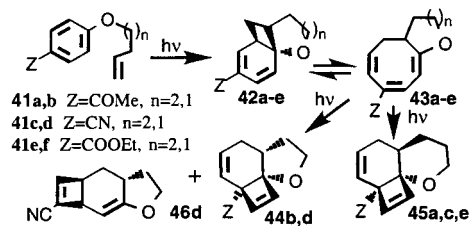
This cycloaddition is not restricted to just phenyl ketones. *o*- and *p*-butenoxy- and pentenoxy-substituted benzonitriles and benzoate esters undergo the same photoreaction upon both direct irradiation²¹ and triplet sensitization.²² Schemes 12 and 13 show that the three functional groups display identical excited-state behavior and also how the electrocyclic regioselectivity diverges depending on tether length. That this reaction can be sensitized widens the

Scheme 12



scope of the reaction considerably and indicates that direct irradiation of the nitriles and benzoate esters produces mainly triplet-state reaction of the aromatic, as Gilbert and co-workers also found.²¹ A useful benefit of acetone sensitization is revealed by the behavior of **35c** and **35e**, which cyclize only to **39c** and **39e** when irradiated in acetone. Upon irradiation at 254 nm in acetonitrile, some di- π -methane rearrangement products of **39c** and **39e** were also obtained. It is curious that **41f**, with a three-atom tether, is unreactive. All of the reactants with four-

Scheme 13

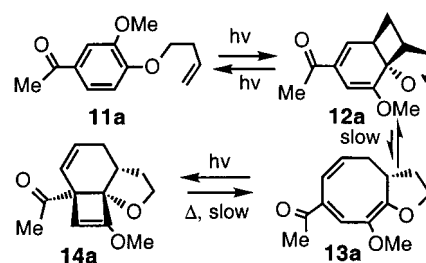


atom tethers undergo the same ortho photocycloaddition as do compounds with three-atom tethers. Triplet *p*-alkenoxyacetophenones with four-atom tethers react only 1% as fast as those with three-atom tethers.² Nonetheless, the initial [2 + 2] cycloaddition proceeds efficiently for both, unlike the situation usually encountered for intramolecular singlet-state meta cycloadditions.¹ However, the ensuing electrocyclic reactions depend on the size of the new ether ring, as is discussed below.

CH ⇌ CO Equilibrium

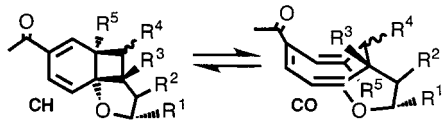
This equilibrium is sensitive to structural variations involving substituents on both the tether and the benzene ring. Table 5 lists how the former affect the equilibrium, which can range between the extremes of only the **CH** or the **CO** being detectable by NMR. As mentioned above, R³ is forced inside the boat cyclooctatriene structure; when it is an alkyl group it causes steric interactions that raise **CO**s energy relative to that of **CH**. The reason that an alkyl group at R⁴ also increases the population of **CH** is not so clear.

What start as ring substituents on the phenyl ketones end up having large effects on the electrocyclic interconversions of the photoproducts. That **12a** formed from **11a** is a stable, isolable product, with its barely populated **CO** isomer detectable only by UV, is the most striking example. Efficient photoreversion of the stable **12a** to **11a**



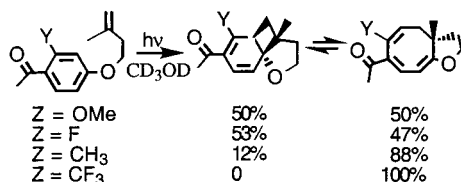
is responsible for the very low observed quantum efficiency for conversion of **11a** to **14a**. The thermal stability of **12a** indicates that the normal acceleration of **CH** → **CO** ring-opening by charge transfer from oxygen to the acyl group is greatly diminished by the electron-donating methoxy group on the acceptor cyclohexadiene π system.

Substituents originally ortho to the acyl group show the same behavior, the equilibrium **CO** population increasing with the electron-withdrawing power of Z. Scheme 14, listing the relative amounts of **CH** and **CO** formed thermally from **CB**, shows how this electronic effect can alter the steric effect of R³, which a CF₃ group overwhelms.

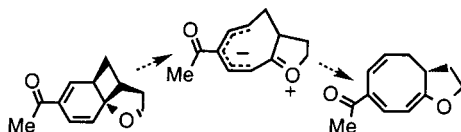
Table 5. CH \rightleftharpoons CO Equilibria


R ¹	R ²	R ³	R ⁴	R ⁵	CH (%)	CO (%)
H	H	H	H	H	<5	>95
Me	H	H	H	H	<5	>95
iPr	H	H	H	H	<5	>95
Me	H	Me	H	H	25	75
H	Me	Me	H	H	>90	<10
H	H	Me	Me	H	>95	<5
H	H	H	Me	H	~10	~90
H	H	H	iPr	H	>90	<10
H	H	Me	Me	Me	>95	<5
H	H	H	Me	Me	<5	>95

Scheme 14



That the normal rapid **CH** to **CO** opening requires the oxygen atom of the tether is proven by the relative stability of the **CH** structures **29** formed with a methylene group anchoring the tether.



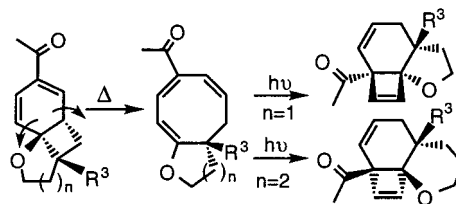
CO \rightleftharpoons CB Interconversion

All of the compounds studied form **COs**, which undergo disrotatory photocyclization to **CBs** with a cis 4/6 ring fusion. These **CBs** undergo thermal reversion to the same **COs** from which they were formed, but obviously not by a concerted *conrotatory* electrocyclic mechanism, which would not regenerate the all-cis **CO**. Structural variations affect both the regio- and stereoselectivity of the **CO** \rightarrow **CB** conversion and both the rate and chemoselectivity of **CB** reactions.

CO \rightarrow CB

Four **CB** isomers are possible based on which diene unit cyclizes and on how it puckers relative to the attached ring. With three-atom tethers the five-ring fused to the excited cyclooctatriene forces the developing four-ring to pucker away from it, cyclization thus producing a cis 5/6 ring fusion, such that R³ is cis and the five-ring trans to the cyclobutene ring. With four-atom tethers (Schemes 12 and 13), the more flexible six-ring allows a diene unit of the excited **CO** to pucker to form a **CB** with a trans 6/6 ring fusion and R³ trans to the cyclobutene ring.

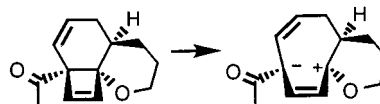
Geometric differences between the 8/5-fused and 8/6-fused **COs** appear to control regioselectivity, with formation of mainly angular **CBs** from the latter. Most of the



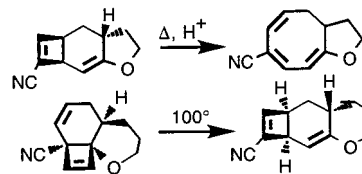
oxygen-tethered ketones that we have studied produce only a **CB** with the acyl group at the bridgehead (Schemes 1, 3, 6, and 8–10). The strong oxygen-to-carbonyl donor–acceptor conjugation present in one diene unit of **CO** probably localizes excitation mostly on that diene unit. The **COs** formed from methylene-tethered compounds and benzoic acid derivatives form both linear and angular **CB** photoproducts (Schemes 11–13). In the former case, a CH₂ group provides no π conjugation, making the two diene units of the triene electronically similar. Cyano and carboxy groups apparently are not sufficiently electron-withdrawing to localize excitation in just one diene unit, regioselectivity depending mainly on the size of the fused ring.

CB \rightarrow CO

This thermal reversion is an acid-catalyzed reaction that involves heterolysis of the weak 4/6 bridgehead bond, for which there is ample precedent.²³ Closure of the intermediate to an all-cis **CO** is likely sterically controlled. Its rate varies with the degree of donor/acceptor conjugation in the **CB**.



Ring substituents, tether anchor, Z (Scheme 13), and the number of bonds between ether oxygen and Z all affect that conjugation and thus the rates for both **CH** and **CB** converting to **CO**. As already described, Cope rearrangements can compete with ring-opening, as in the products of **11c**, **28**, and **41c**.



Concluding Remarks

Discovering a previously overlooked new reaction should be rewarding enough, but finding one that provides high regio- and stereoselectivity is a real blessing. A very helpful referee suggested that I would not lose my reputation as a physical organic chemist by revealing actual chemical yields of products; I am happy to note that in most cases yields from 0.01 M reactant have been nearly quantitative except when the products themselves are photolabile. I hope our work is followed by critical analysis of which

other ortho [2 + 2] cycloadditions to substituted benzenes involve excited triplets rather than singlets and that this chemistry proves to be synthetically useful.

This work was accomplished by an excellent group of students who are listed in the various references. We all are grateful for support from both NSF and NIH. I also thank Tito Scaiano at Ottawa University for providing access to his flash kinetics apparatus.

References

- (1) Mattay, J. Selectivity and Charge Transfer in Photoreactions of Arenes with Olefins 2. Modes of Cycloaddition. *Tetrahedron* **1985**, *41*, 2405. Wender, P.; Siggel, L.; Nuss, J. Arene-Alkene Cycloaddition Reactions. In *Organic Photochemistry*; Padwa, A., Ed.; Dekker: New York, 1989; Vol. 10, p 357. Cornelisse, J. The Meta Photocycloaddition of Alkenes to Arenes. *Chem. Rev.* **1993**, *93*, 615.
- (2) Wagner, P. J.; Nahm, K. Regiospecific Intramolecular Reaction of an Alkene Group with the Benzene Ring of a Triplet Ketone. *J. Am. Chem. Soc.* **1987**, *109*, 4404.
- (3) Wagner, P. J.; Nahm, K. Interconversion of Bicyclooctadienes and Cyclooctatrienes Formed by Intramolecular Photocycloaddition of Phenyl Ketones Containing Remote Double Bonds. *J. Am. Chem. Soc.* **1987**, *109*, 6528.
- (4) Atkinson, J. G.; Ayer, D. E.; Buchi, G.; Robb, E. W. Photochemical Reactions XII. Addition Reactions of Olefins and Acetylenes with Benzonitrile. *J. Am. Chem. Soc.* **1963**, *85*, 2257. Al-Jalal, N.; Drew, M. G. B.; Gilbert, A. Competitive arene substitution and ortho-cycloaddition in the photochemical reactions of methoxybenzene-acrylonitrile systems. *J. Chem. Soc., Chem. Commun.* **1985**, 85.
- (5) Wagner, P. J.; Siebert, E. J. Regioelectronic Control of Intramolecular Charge-Transfer Quenching in Excited Triplet *p*-Acylbenzoate Esters. *J. Am. Chem. Soc.* **1981**, *103*, 7335.
- (6) Wagner, P. J.; May, M. J. Triplet EPR of fluorobenzonitriles. *Chem. Phys. Lett.* **1976**, *39*, 350.
- (7) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; deMayo, P., Ed.; Academic Press: New York, 1980; Vol. 1, pp 185–201.
- (8) Wagner, P. J.; Sakamoto, M. Electronic Effects on the Addition of Double Bonds to Triplet Benzenes: What is the Rate-Determining Step in Biradical Formation? *J. Am. Chem. Soc.* **1989**, *111*, 8723.
- (9) Wagner, P. J.; Sakamoto, M. Intramolecular Triplet State Cyclization of But-3-enoylacetophenones. *J. Am. Chem. Soc.* **1989**, *111*, 9254.
- (10) Dopp, D.; Krüger, C.; Memarian, H. R.; Tsay, Y.-H. 1,4-Photocycloaddition of α -Morpholinoacrylonitrile to 1-Acyl-naphthalenes. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1048.
- (11) Hirota, N.; Hutchison, C. A.; Palmer, P. Hyperfine Interactions and Electron Spin Distribution in Triplet State Naphthalene. *J. Chem. Phys.* **1964**, *40*, 3717. Mispelter, J.; Grivet, J.-Ph.; Lhoste, J.-M. ESR of Phosphorescent Fluorine-Substituted Aromatics: 1-Fluoronaphthalene and 2-Fluoronaphthalene. *Mol. Phys.* **1971**, *21*, 999; 1015.
- (12) Cheng, K.-L.; Wagner, P. J. Biradical Rearrangements during Intramolecular Cycloaddition of Double Bonds to Triplet Benzenes. *J. Am. Chem. Soc.* **1994**, *116*, 7945.
- (13) Wagner, P. J.; Sakamoto, M.; Madkour, A. E. Regioselectivity in Intramolecular Cycloaddition of Double Bonds to Triplet Benzenes. *J. Am. Chem. Soc.* **1992**, *114*, 7298.
- (14) Sauers, R. R.; Huang, S.-Y. Analysis of Norrish Type II Reactions by Molecular Mechanics Methodology: Cyclodecanone. *Tetrahedron Lett.* **1990**, *31*, 5709.
- (15) Hastings, D. J.; Weedon, A. C. Origin of the Regioselectivity in Photochemical Cycloaddition Reactions of Cyclic Enones with Alkenes: Chemical Trapping Evidence for the Structure, Mechanism of Formation, and Fates of the 1,4-Biradical Intermediates. *J. Am. Chem. Soc.* **1991**, *113*, 8525.
- (16) Smart, R. A.; Wagner, P. J. Regioselectivity in Intramolecular Cycloaddition of Double Bonds to Triplet Acylbenzenes. II. Effects of Substituents Meta to the Tether. *Tetrahedron Lett.* **1995**, *36*, 5131.
- (17) Wagner, P. J.; Cheng, K.-L. Stereoselectivity in the intramolecular cycloaddition of double bonds to triplet benzenes. *Tetrahedron Lett.* **1993**, *34*, 907.
- (18) Wagner, P. J.; Meador, M. A.; Zhou, B.; Park, B.-S. Photocyclization of α -(*o*-Tolyl)acetophenones: Triplet and 1,5-Biradical Reactivity. *J. Am. Chem. Soc.* **1991**, *113*, 9630.
- (19) Wagner, P. J.; McMahon, K. Chiral Auxiliaries Promote both Diastereoselective Cycloaddition and Kinetic Resolution of Products in the Ortho Photocycloaddition of Double Bonds to Benzene Rings. *J. Am. Chem. Soc.* **1994**, *116*, 10827.
- (20) Wagner, P. J.; Alehashem, H. Intramolecular ortho [2 + 2] photocycloaddition of 5-(*p*-acylphenyl)-1-penten-1-ones. *Tetrahedron Lett.* **1993**, *34*, 911.
- (21) Gilbert, A.; Al-Qaradawi, S. Y.; Cosstick, K. B. Intramolecular Photocycloaddition of Substituted 4-Phenoxy-1-butenes. *J. Chem. Soc., Perkin Trans. 1* **1992**, 1145.
- (22) Wagner, P. J.; Smart, R. P. Acetone Sensitized Intramolecular ortho Photocyclization of Substituted 4-Phenoxybut-1-enes and 5-Phenoxy-pent-1-enes. *Tetrahedron Lett.* **1995**, *36*, 5135.
- (23) Schell, F. M.; Cook, P. M. Intramolecular Photochemistry of a Vinyllogous Amide and Some Transformations of the Photoproducts. *J. Org. Chem.* **1984**, *49*, 4067. Winkler, J. D.; Hey, J. P. Inside–Outside Stereoisomerism: The Synthesis of *trans*-Bicyclo[5.3.1]undecan-11-one. *J. Am. Chem. Soc.* **1986**, *108*, 6425.

AR000113N