



Photochemistry of Carbonyl Compounds

Molecular Photochemistry

CHEM 4801

Primary Photochemical Processes of Carbonyl (n, π^*) States

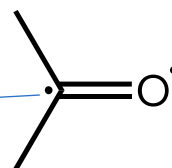
Photochemistry of the Carbonyl Group

Primary Reactions of (n,π^*) States

Carbonyl (n,π^*) states are essentially diradicaloid in nature regardless of spin. The reactivity of (n,π^*) under a given set of conditions depends on whether the n or π^* orbital is involved.

$^1(n,\pi^*)$ or $^3(n,\pi^*)$

π^* initiated (reactions with electrophiles)



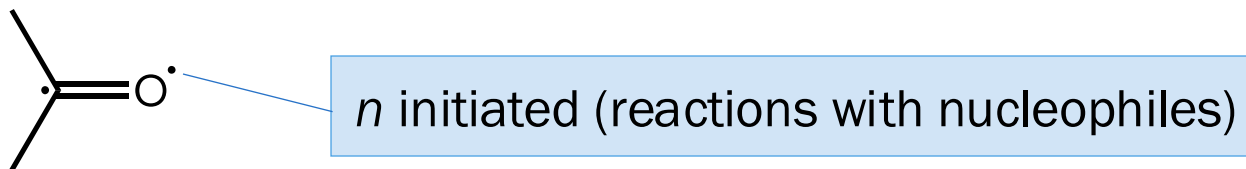
n initiated (reactions with nucleophiles)

- Radical reactions
 - Atom abstractions
 - Radical additions
 - β -Cleavage
- Electron donation

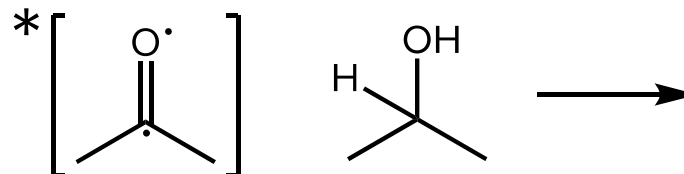
- Radical reactions
 - Atom abstractions
 - Radical additions
 - α -Cleavage
- Electron acceptance

n -Initiated Primary Reactions

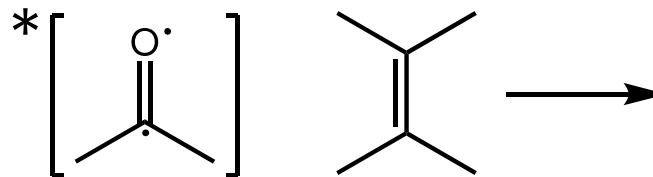
The n orbital of an (n,π^*) state is electrophilic and can thus accept an electron, abstract an atom in a nucleophilic bond (e.g. C-H), engage in electrophilic addition, or facilitate α -cleavage.



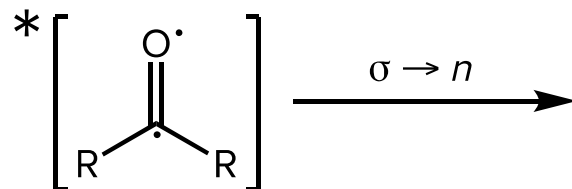
Atom abstraction from “nucleophilic” bonds



Radical additions to unsaturated groups



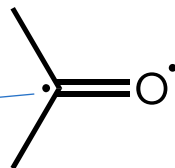
α -Cleavage ($\sigma \rightarrow n$)



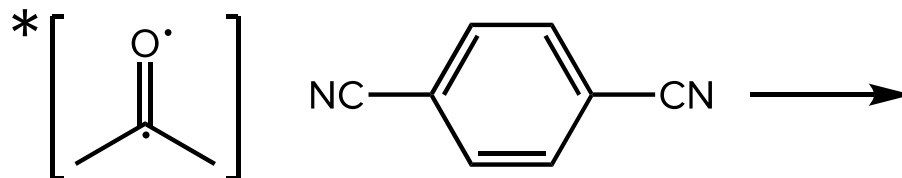
π^* -Initiated Primary Reactions

The π^* orbital of an (n,π^*) state is nucleophilic and can thus donate an electron, engage in nucleophilic addition, or facilitate β -cleavage.

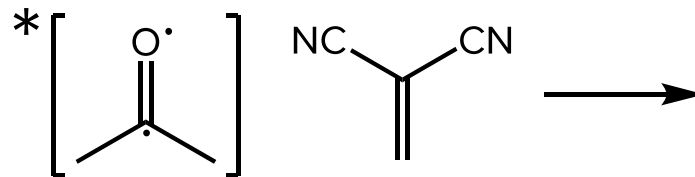
π^* initiated (reactions with electrophiles)



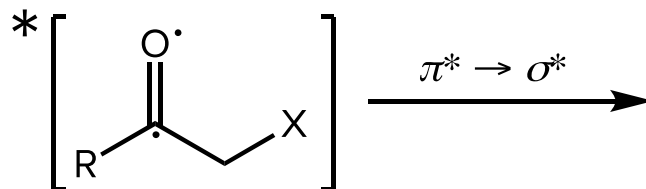
Donation of an electron



Radical additions to unsaturated groups



β -Cleavage ($\pi^* \rightarrow \sigma^*$)

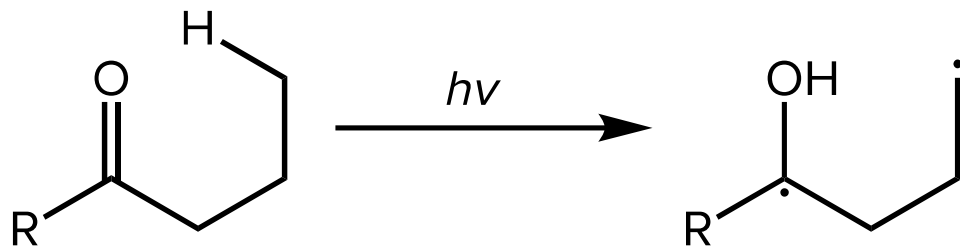


Secondary Thermal Processes of Radicals Derived from Carbonyls

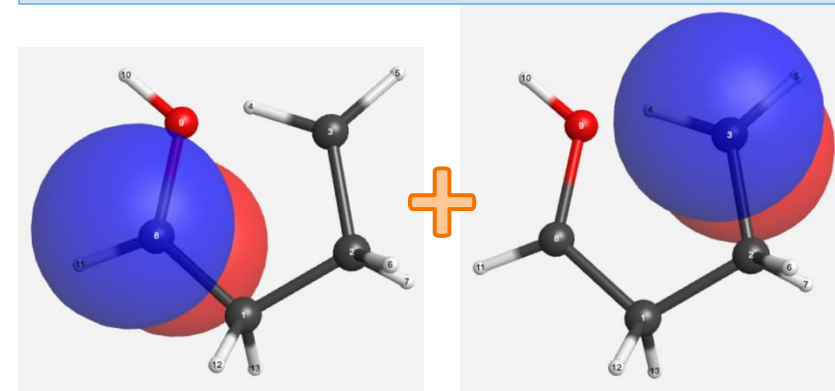
Photochemistry of the Carbonyl Group

Secondary Processes: Fates of Diradicals

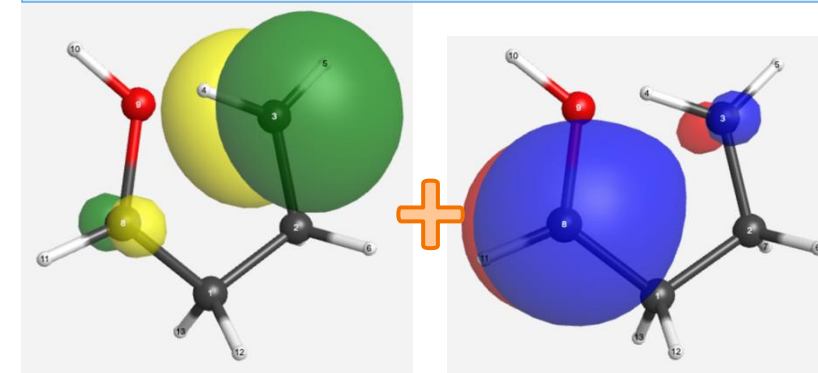
Many reactions of (n,π^*) states of carbonyls lead to biradical (BR) or radical pair (RP) intermediates. These ground-state species may undergo radical coupling, fragmentation, or addition processes.



Triplet diradical (D_3)



Singlet diradical/zwitterion (D_1/Z)



Exemplary State Diagrams for Ketones

Photochemistry of the Carbonyl Group

Dialkyl Ketones: Acetone

Alkyl ketones generally have small ΔE_{ST} for (n,π^*) . S_1 and T_1 are pure (n,π^*) , which results in a relatively *slow* rate for ISC in accordance with El-Sayed's rules.

(π,π^*) S_2 —————

(π,π^*) T_2 —————

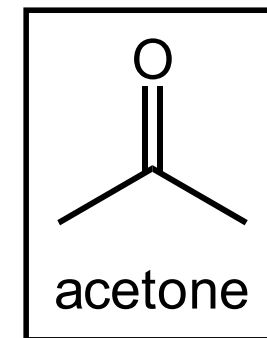
(n,π^*) S_1 —————

T_1^\ddagger —————

$$k(S_1 \rightarrow T_1) = 10^7 - 10^8 \text{ s}^{-1}$$

(n,π^*) T_1 —————

S_0 —————



Diaryl Ketones: Benzophenone

Diaryl ketones have much lower energy (π, π^*) states, such that $E(S_1) \approx E(T_2)$. Intersystem crossing from $^1(n, \pi^*)$ to $^3(n, \pi^*)$ is often very rapid—faster than many reactions.

$(\pi, \pi^*) S_2$ —————

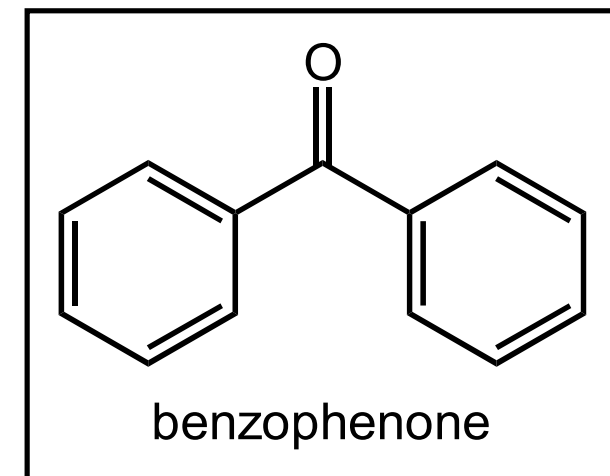
$(n, \pi^*) S_1$ —————

$(\pi, \pi^*) T_2$ —————

$(n, \pi^*) T_1$ —————

$$k(S_1 \rightarrow T_1) = 10^{10} - 10^{11} \text{ s}^{-1}$$

S_0 —————




Configurations of T_1 and T_2 can depend on solvent and substituents.

Strongly Delocalized Ketones


For strongly delocalized ketones, S_1 and T_1 are (π, π^*) . Intersystem crossing from $^1(\pi, \pi^*)$ to $^3(n, \pi^*)$ may be very rapid and compete with primary processes.

(n, π^*) S_2 

(π, π^*) S_1 

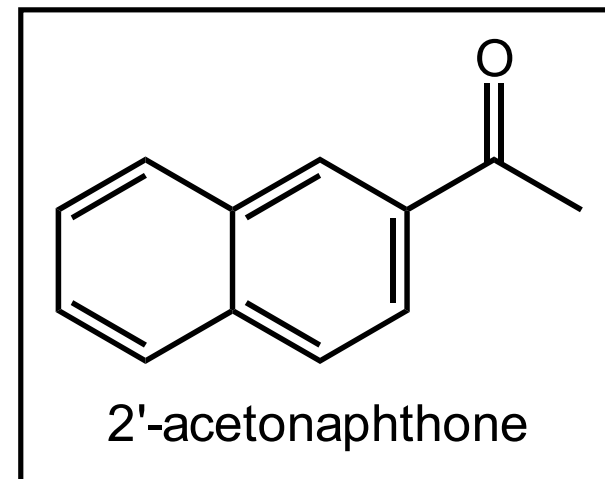
(n, π^*) T_2 

$$k(S_1 \rightarrow T_1) = 10^{10} - 10^{11} \text{ s}^{-1}$$

(π, π^*) T_1 

Lifetimes can be very long for $^3(\pi, \pi^*)$.

S_0 

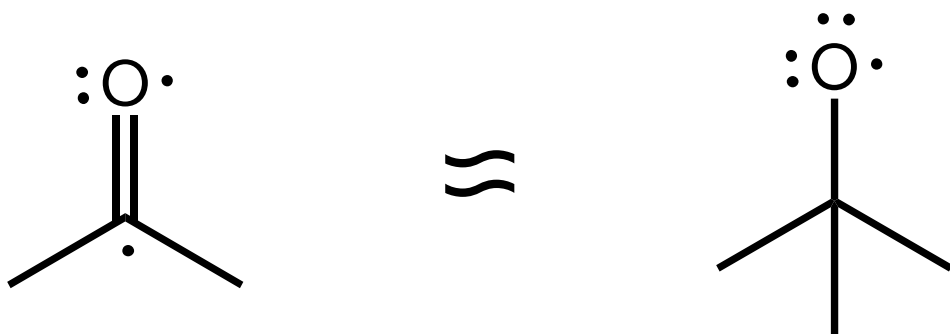


Alkoxy Radical as (n,π^*) Analogue

Alkoxy radicals contain a half-filled n_o orbital analogous to the one found in (n,π^*) states of carbonyl compounds. They have been used as benchmarks for reactivity of (n,π^*) states.

(n,π^*)

Alkoxy radical



Hydrogen atom abstraction

Addition to $C=C$

α -Cleavage

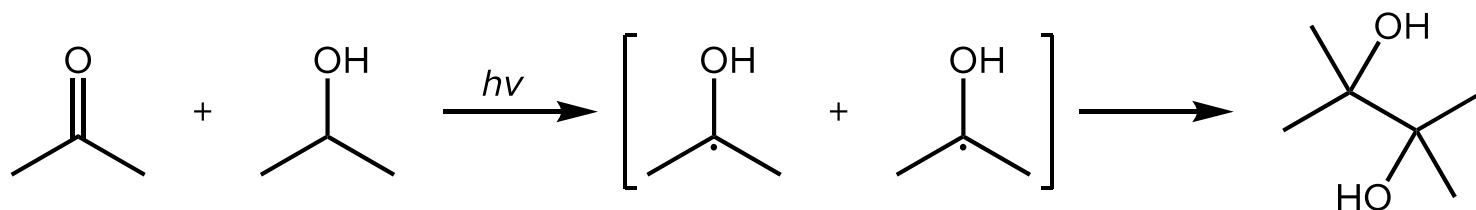
Intermolecular Hydrogen Atom Abstraction by Ketones

Photochemistry of the Carbonyl Group

Hydrogen Abstractions of Alcohols

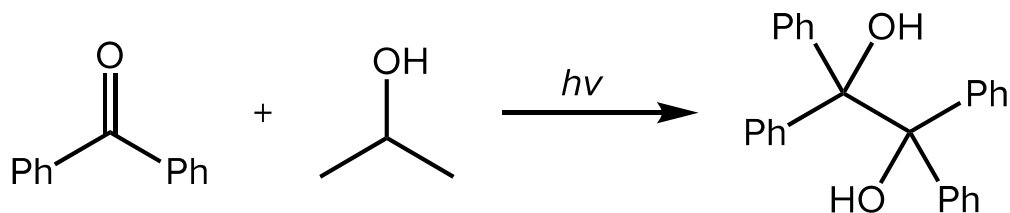
$S_1(n,\pi^*)$ or $T_1(n,\pi^*)$ can abstract hydrogen from ROH to form α -hydroxy radicals. The key orbital interaction is $\sigma_{CH} \rightarrow n$ and radical formation is followed by ISC and radical coupling.

Irradiation of acetone in isopropanol



Reaction mechanism: benzophenone + IPA

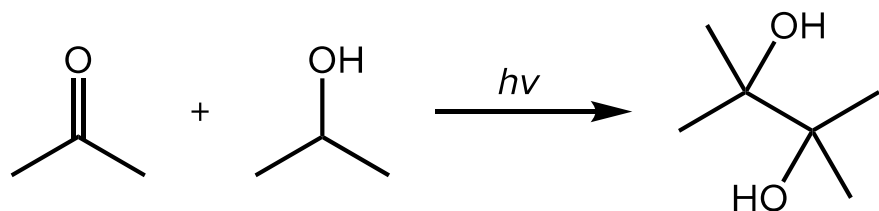
Irradiation of benzophenone in isopropanol: an interesting result



Hydrogen Abstractions of Alcohols

$S_1(n,\pi^*)$ or $T_1(n,\pi^*)$ can abstract hydrogen from ROH to form α -hydroxy radicals. The key orbital interaction is $\sigma_{\text{CH}} \rightarrow n$ and radical formation is followed by ISC and radical coupling.

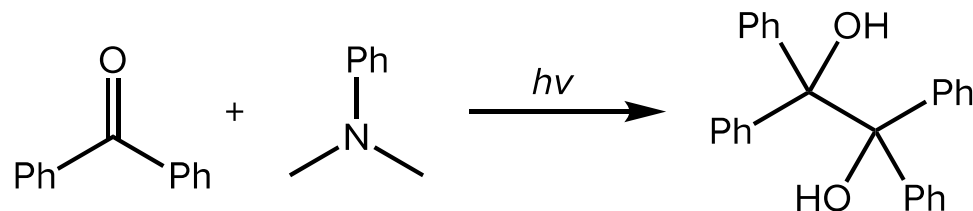
Reaction mechanism: [1. ISC ($S_n \rightarrow T_1$)]; 2. $\sigma_{\text{CH}} \rightarrow n$; [3. ISC ($T \rightarrow S$)]; 4. $n \leftrightarrow n$



Ketones and Amines: Abstraction via et

Amines react with photo-excited ketones to form either pinacols or 2-aminoalcohols. Unlike the reactions with alcohols, electron transfer (et) is typically involved in these reactions.

Reaction mechanism: [1. ISC ($S_n \rightarrow T_1$);] 2. et ($n_N \rightarrow n_O$); 3. pt; [4. ISC;] 5. $n \leftrightarrow n$



Evidence for Electron Transfer

Rate constants of quenching by alcohols and amines support significantly different mechanisms for the two classes of hydrogen donors.

Ketone	E_T	T_1	k_q (M ⁻¹ s ⁻¹)	
			Me ₂ CHOH	NEt ₃
Me ₂ CO	78	n, π^*	1×10^6	4×10^8
4-CF ₃ C ₆ H ₄ COPh	74	n, π^*	2×10^6	—
PhCOMe	72	n, π^*	1×10^6	7×10^7
4-MeC ₆ H ₄ COPh	70	π, π^*	1×10^5	—
Ph ₂ CO	69	n, π^*	1×10^6	2×10^9
4-PhC ₆ H ₄ COPh	61	π, π^*	1×10^4	—
MeCOCOMe	56	n, π^*	5×10^3	5×10^7
2-Acetylnaphthalene	56	π, π^*	—	5×10^5

For amines, rate of quenching is negatively correlated with the ionization potential of the amine.

Even $T_1(\pi, \pi^*)$ has a high rate of reaction with amines despite generally slow reaction with ROH.

Structure-Reactivity Relationships

(n,π^*) states are considerably more reactive than (π,π^*) states as evidenced by the data below. Solvent-based switching of the configuration of T_1 can dramatically affect k .

Ketone	E_T	T_1	k_q ($M^{-1} s^{-1}$)	
			Me ₂ CHOH	NEt ₃
Me ₂ CO	78	n,π^*	1×10^6	4×10^8
4-CF ₃ C ₆ H ₄ COPh	74	n,π^*	2×10^6	—
PhCOMe	72	n,π^*	1×10^6	7×10^7
4-MeC ₆ H ₄ COPh	70	π,π^*	1×10^5	—
Ph ₂ CO	69	n,π^*	1×10^6	2×10^9
4-PhC ₆ H ₄ COPh	61	π,π^*	1×10^4	—
MeCOCOMe	56	n,π^*	5×10^3	5×10^7
2-Acetylnaphthalene	56	π,π^*	—	5×10^5

Rate of PhCOMe + Me₂CHOH

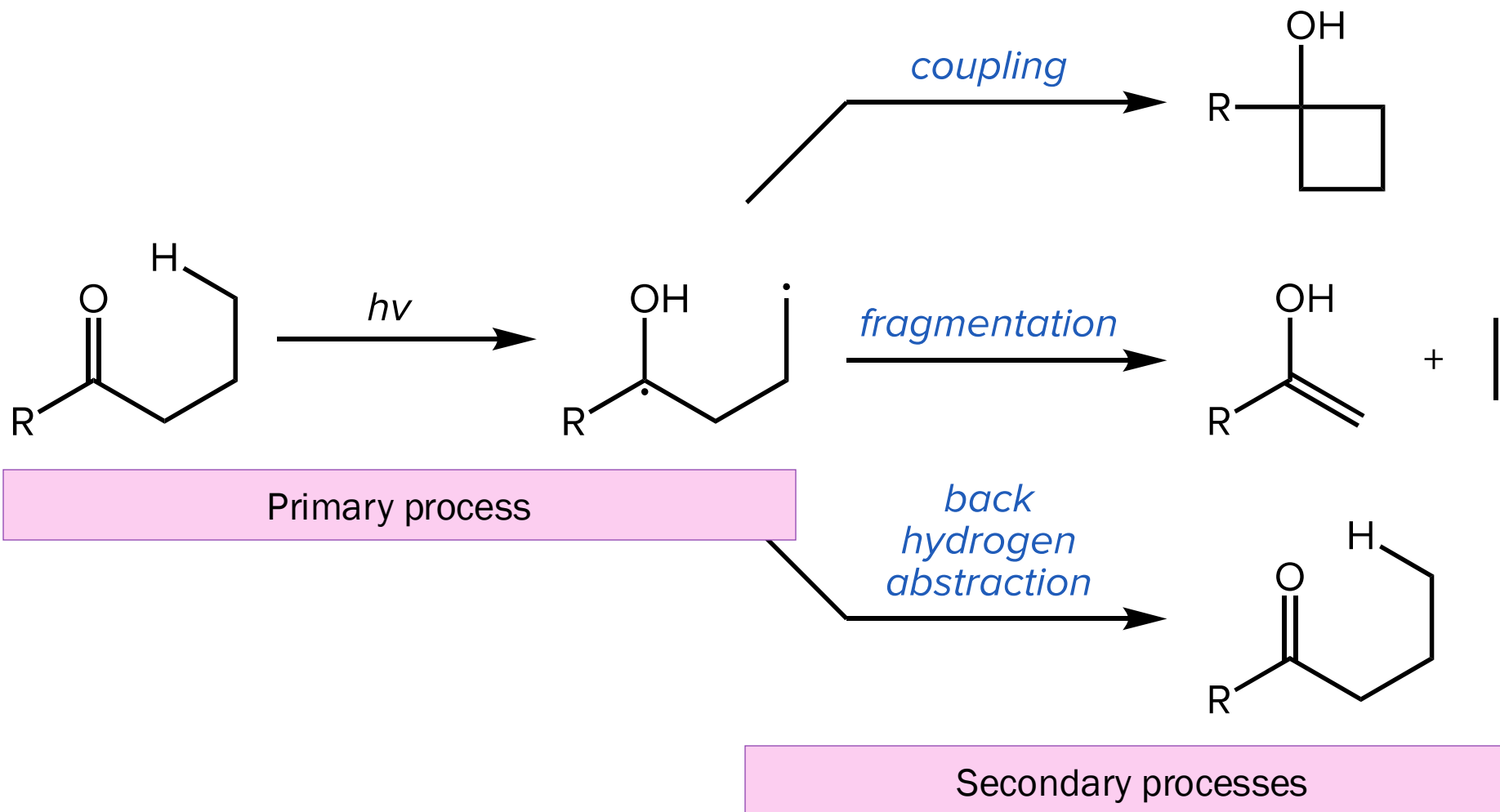
Solvent	k_q ($M^{-1} s^{-1}$)
Benzene	2×10^6
Acetonitrile	10^3

Intramolecular Hydrogen Atom Abstraction and Norrish Type II

Photochemistry of the Carbonyl Group

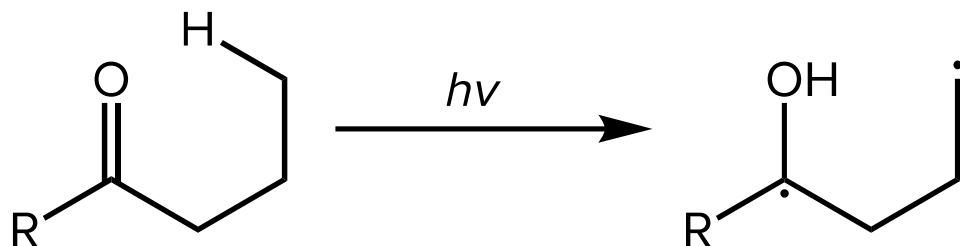
Intramolecular γ -Hydrogen Abstraction

Intramolecular hydrogen abstraction is called **Norrish type II reaction** or **γ -hydrogen abstraction (γ -HA)**. A 1,4-biradical is produced that may undergo fragmentation or coupling.



Intramolecular γ -Hydrogen Abstraction

Intramolecular hydrogen abstraction is called *Norrish type II reaction* or *γ -hydrogen abstraction (γ -HA)*. A 1,4-biradical is produced that may undergo fragmentation or coupling.



$\sigma_{\text{CH}} \rightarrow n$ or $\sigma_{\text{CH}} \rightarrow \pi$ remains the key orbital interaction in the abstraction step.

This particular abstraction has a favorable six-membered cyclic transition state.

Structure-Reactivity Relationships

As in intermolecular hydrogen abstraction, (n, π^*) is more reactive than (π, π^*). Relative reactivity of hydrogens is tertiary > secondary > primary.

Ketone	T_1	Φ_{IHA}	k_q (ns ⁻¹)
PhCOCH ₂ CH ₂ <u>CH</u> ₃	n, π^*	1.0 (0.36)	0.8
PhCOCH ₂ CH ₂ <u>CH</u> ₂ CH ₃	n, π^*	1.0 (0.33)	10
PhCOCH ₂ CH ₂ <u>CH</u> (CH ₃) ₂	n, π^*	1.0 (0.25)	50
4-ClPhCOCH ₂ CH ₂ <u>CH</u> ₂ CH ₃	n, π^*	0.8	3
4-MeOPhCOCH ₂ CH ₂ <u>CH</u> ₂ CH ₃	π, π^*	0.3	0.6
4-MeOPhCOCH ₂ CH ₂ <u>CH</u> (CH ₃) ₂	π, π^*	—	0.3
4-CF ₃ PhCOCH ₂ CH ₂ <u>CH</u> ₂ CH ₃	n, π^*	1.0	30
MeCOCH ₂ CH ₂ <u>CH</u> ₃	n, π^*	0.8 (0.4)	1
MeCOCH ₂ CH ₂ <u>CH</u> ₂ CH ₃	n, π^*	0.1 (0.3)	10
MeCOCH ₂ CH ₂ <u>CH</u> (CH ₃) ₂	n, π^*	0.1 (0.9)	40

Singlet Reactivity of Dialkyl Ketones

Dialkyl ketones undergo slow intersystem crossing, so S_1 is also reactive in γ -hydrogen abstraction. S_1 is generally much more reactive than T_1 (why?)

Ketone	Configuration	Φ_{IHA}	k_q (ns ⁻¹)
MeCOCH ₂ CH ₂ <u>CH</u> ₃	$T_1(n,\pi^*)$	0.8 (0.4)	1
	$S_1(n,\pi^*)$	0.06 (0.06)	20
MeCOCH ₂ CH ₂ <u>CH</u> ₂ CH ₃	$T_1(n,\pi^*)$	0.1 (0.3)	10
	$S_1(n,\pi^*)$	0.1 (0.1)	100
MeCOCH ₂ CH ₂ <u>CH</u> (CH ₃) ₂	$T_1(n,\pi^*)$	0.1 (0.9)	40
	$S_1(n,\pi^*)$	0.3 (0.3)	200

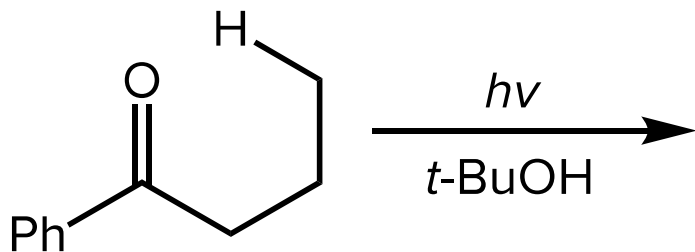
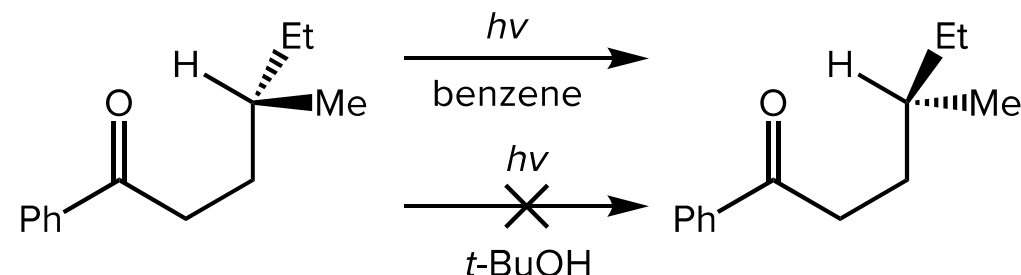
Recall our state energy diagram for acetone.

Solvent Effects

Quantum yields of γ -HA products are often higher in alcoholic solvents. The new hydroxyl group hydrogen bonds to solvent, arresting back hydrogen abstraction and increasing Φ .

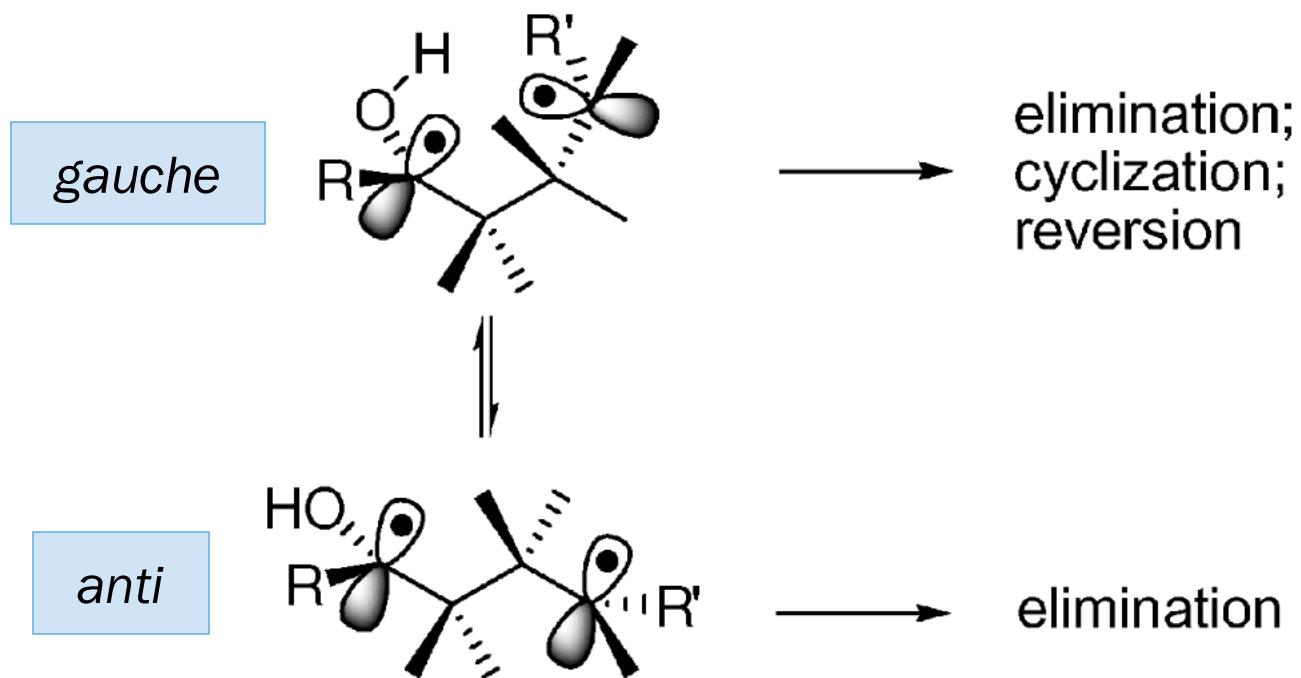
Ketone	T_1	Φ_{IHA} ROH	Φ_{IHA} benzene
$\text{PhCOCH}_2\text{CH}_2\text{CH}_3$	n, π^*	1.0	0.36
$\text{PhCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	n, π^*	1.0	0.33
$\text{PhCOCH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$	n, π^*	1.0	0.25
$\text{MeCOCH}_2\text{CH}_2\text{CH}_3$	n, π^*	0.8	0.4
$\text{MeCOCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	n, π^*	0.1	0.3
$\text{MeCOCH}_2\text{CH}_2\text{CH}(\text{CH}_3)_2$	n, π^*	0.1	0.9

Hydrogen bonding also prevents racemization of γ -stereogenic ketones.



Fate of the Biradical Intermediate

The distribution of final (closed-shell) products from T_1 depends on (1) the populations of possible conformers of the biradical and (2) their intrinsic rates of intersystem crossing, which depend on the distances between the radical centers.

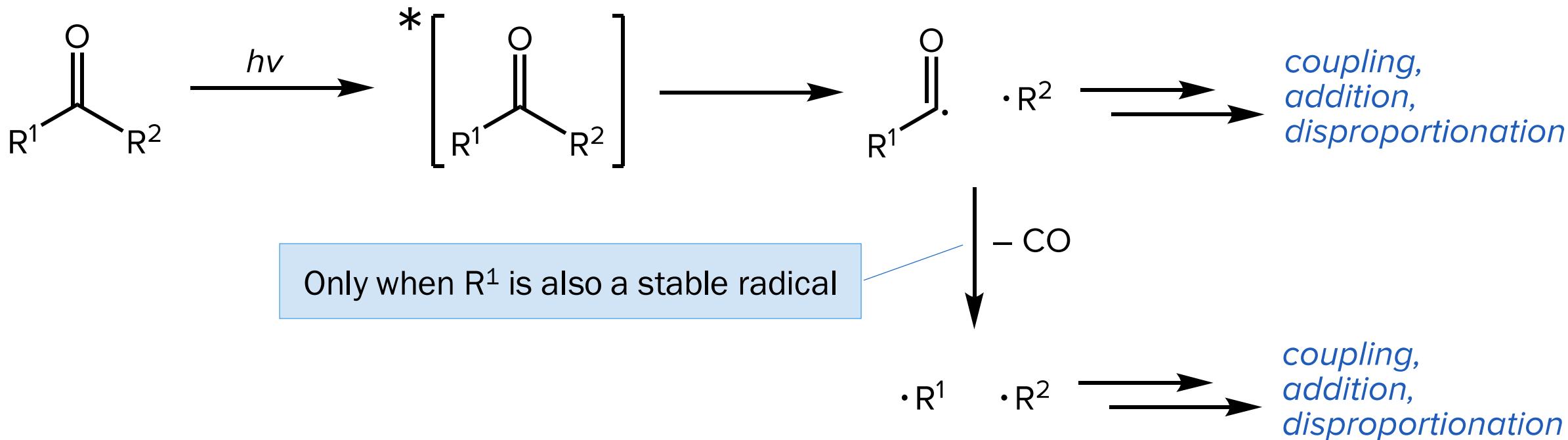


α -Cleavage of Carbonyl Compounds and Norrish Type I

Photochemistry of the Carbonyl Group

α -Cleavage of Excited Carbonyls

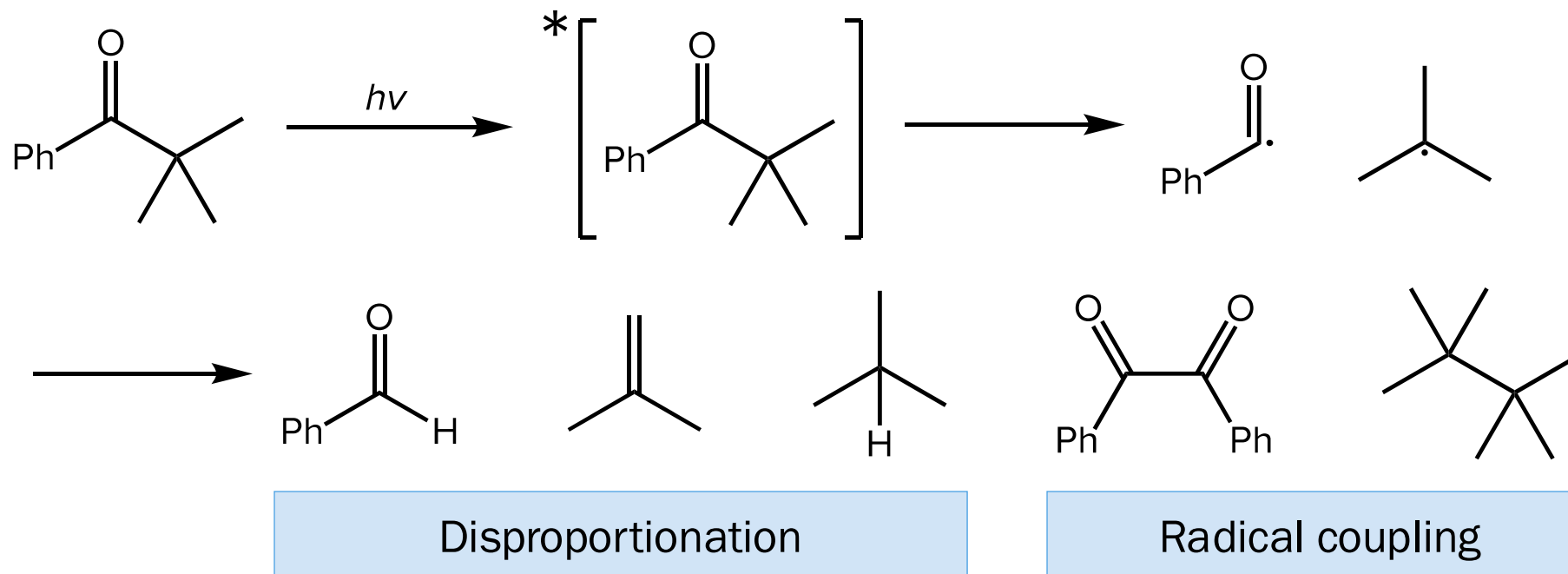
Excited carbonyls may undergo **α -cleavage** or **Norrish type I reaction**. A bond between the carbonyl carbon and an α -carbon breaks. A variety of secondary processes of the resulting RP are possible.



Formation of a relatively stable radical is required (at least secondary) and Φ and rate parallel the stability of the (non-acyl) radical formed and the bond dissociation energy of the broken bond.

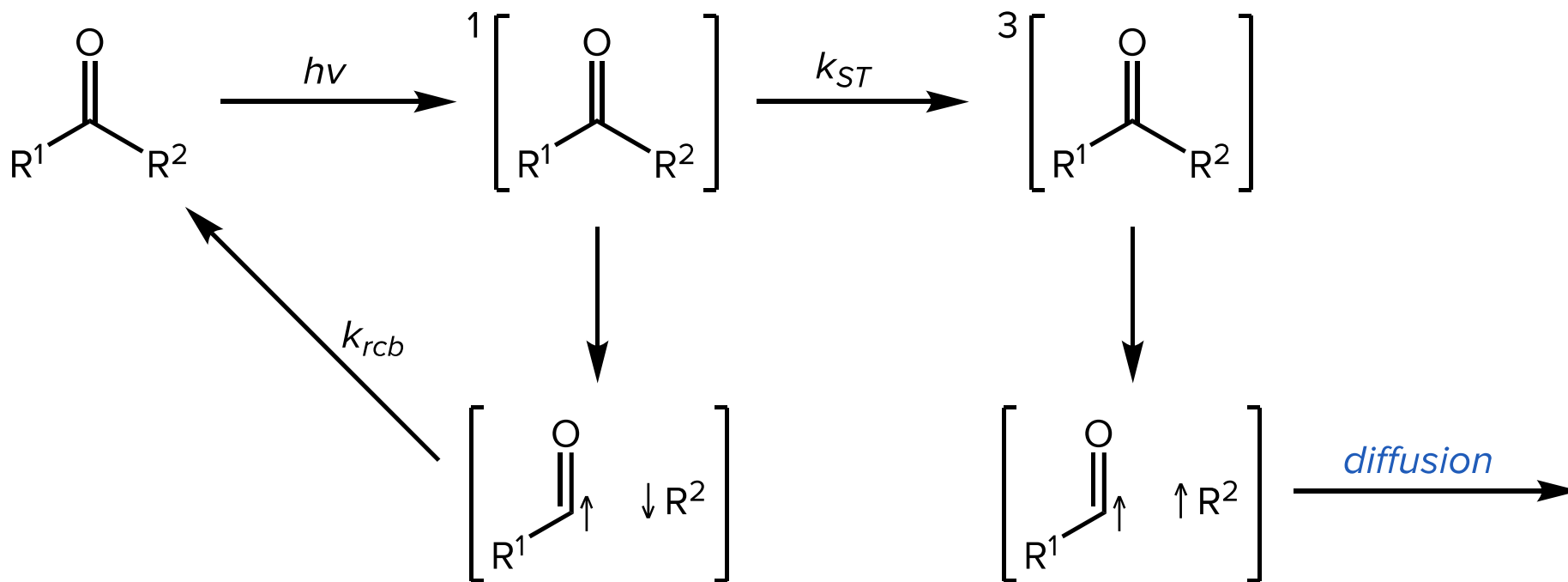
α -Cleavage of Excited Carbonyls

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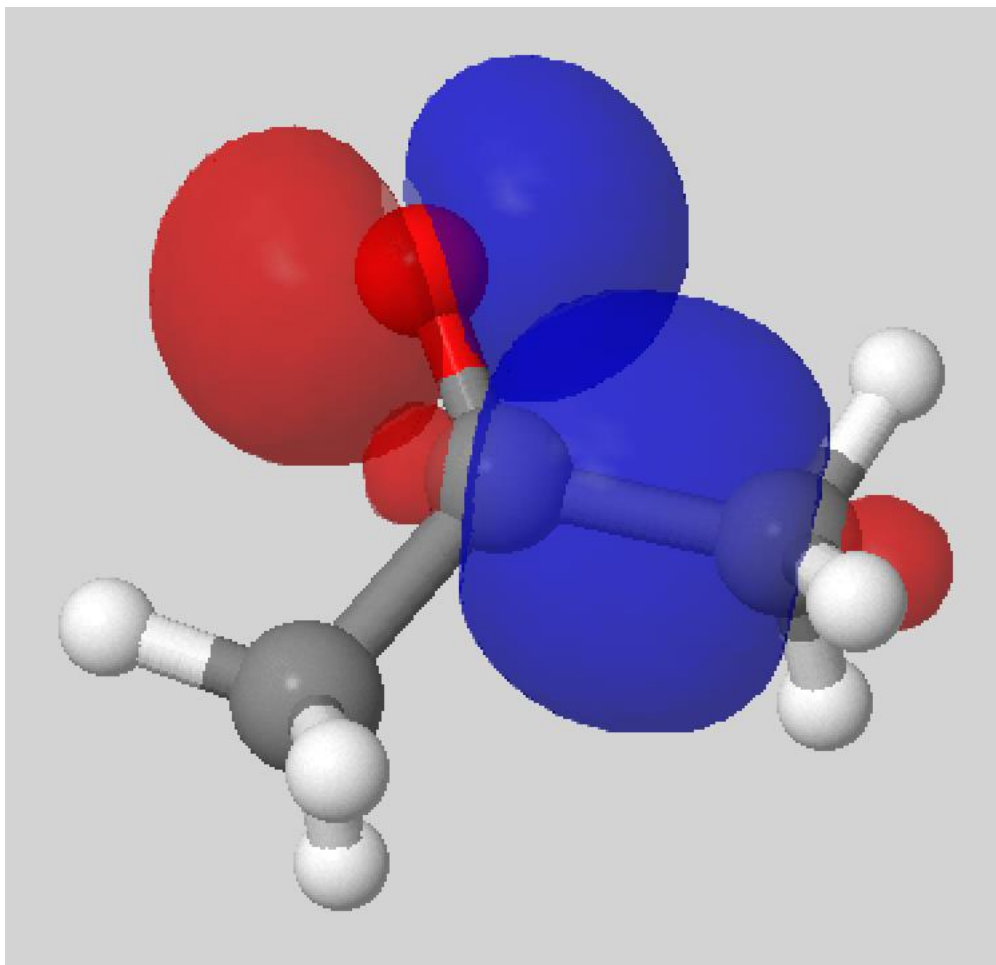
Fate of the Radical Pair

S states yield singlet radical pairs, which can rapidly recombine to form starting material. T states cannot immediately recombine and the radicals typically escape the solvent cage and react randomly.



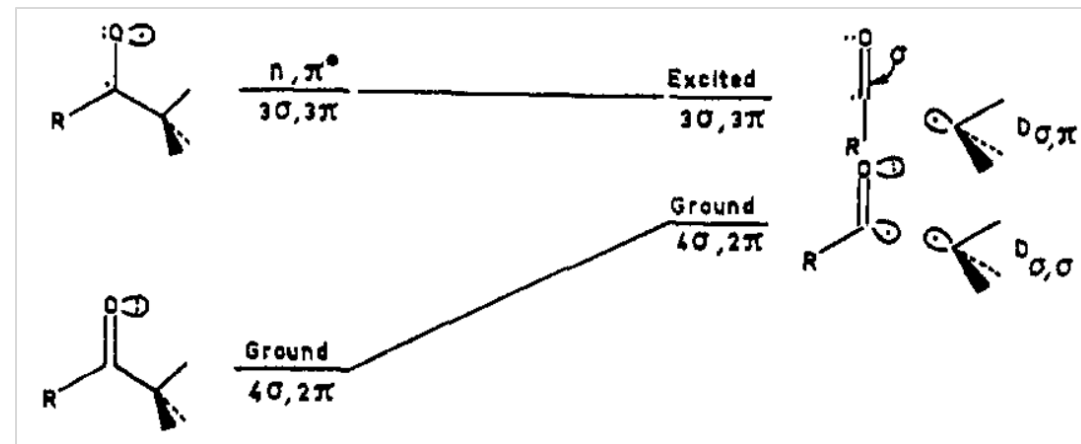
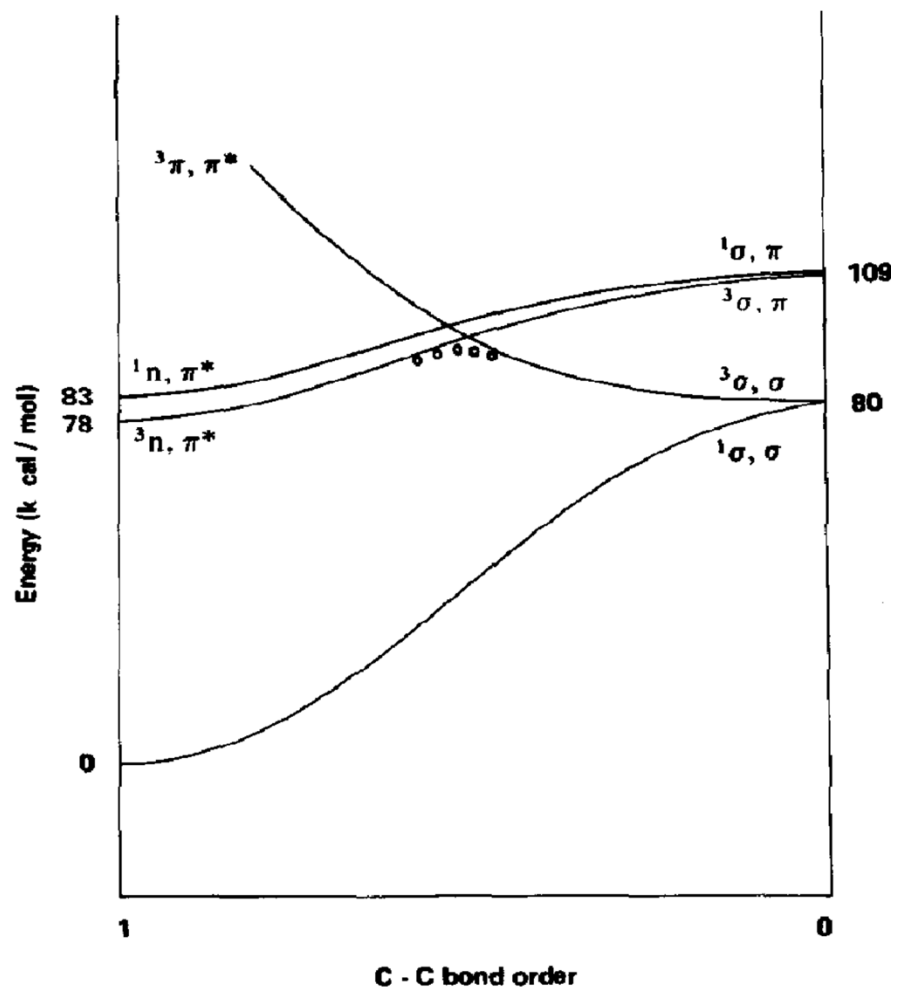
Orbital Analysis of the Primary Process

(n, π^*) states are much more reactive than (π, π^*) states because the half-filled n orbital overlaps well with the σ_{CC} orbital of the breaking bond. The key orbital interaction is $\sigma_{CC} \rightarrow n$.



State Correlation Diagram

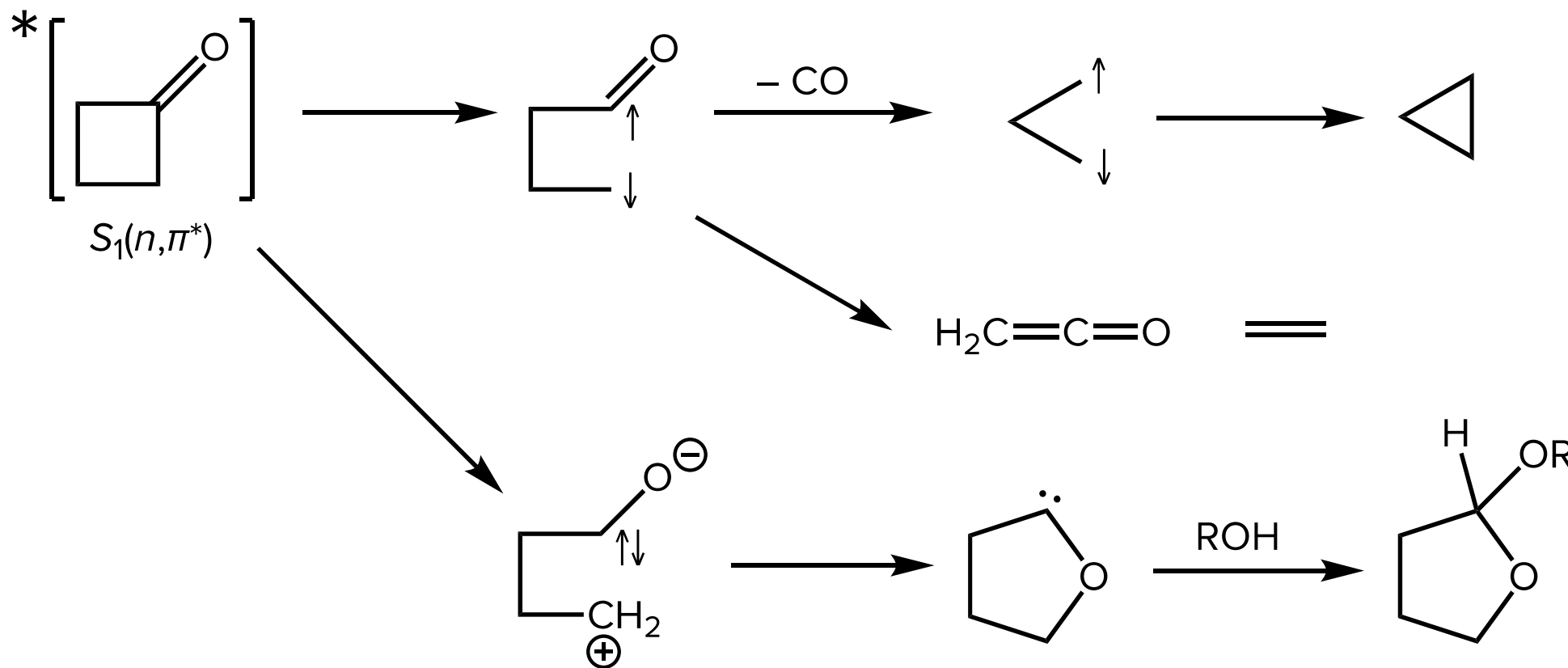
A state correlation diagram for α -cleavage shows that reactions of both S and T are expected to exhibit an activation barrier starting from the excited state, either (n,π^*) or (π,π^*) .



The (n,π^*) state correlates with the *linear* acyl radical and the ground and (π,π^*) states correlate with the *bent* acyl radical. A surface crossing and avoided crossing save the day.

α -Cleavage of Cyclobutanones

Cyclobutanones readily open via α -cleavage after photo-excitation. Decarbonylation or elimination may take place; conversion to a zwitterionic intermediate followed by ring closure may also occur.



Reactions of the 1,4-BR are extremely rapid, as all three processes are stereospecific with respect to C4.

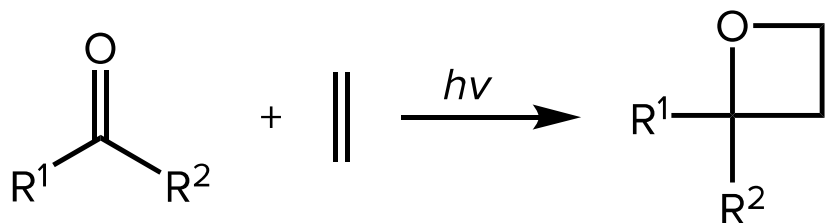
Cycloadditions of Excited States of Carbonyls to Alkenes

Photochemistry of the Carbonyl Group

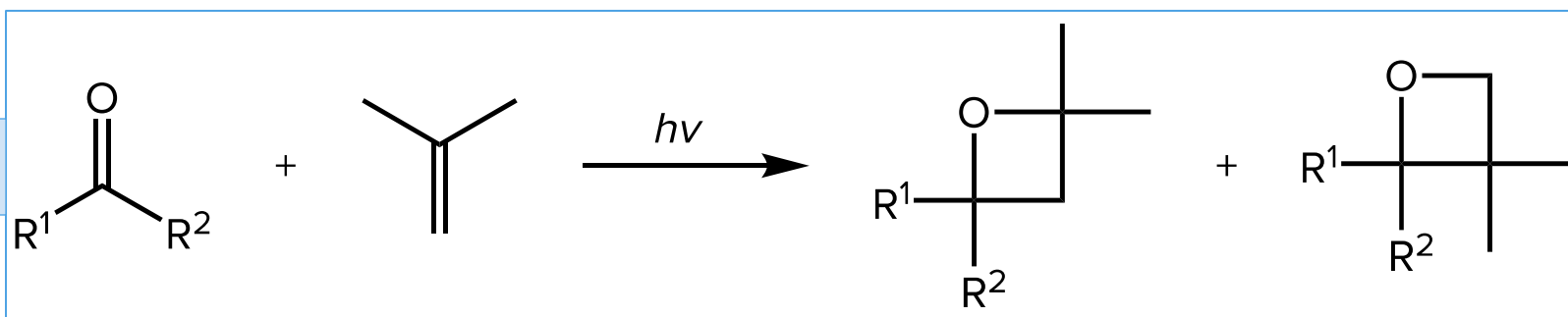
Electron-rich Alkenes + Excited Carbonyls



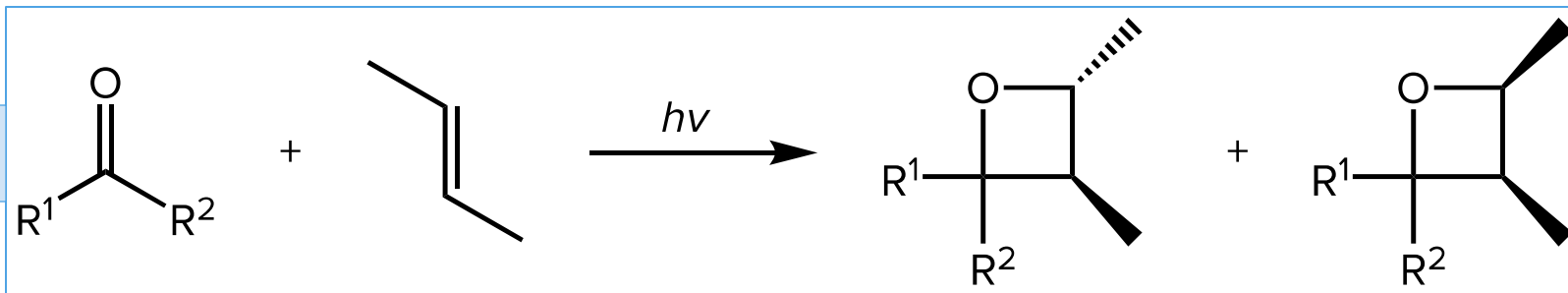
Excited ketones and aldehydes (n,π^*) react with alkyl- and EDG-substituted alkenes in a [2 + 2] cycloaddition process called the *Paterno-Büchi reaction*.



Regioselectivity?



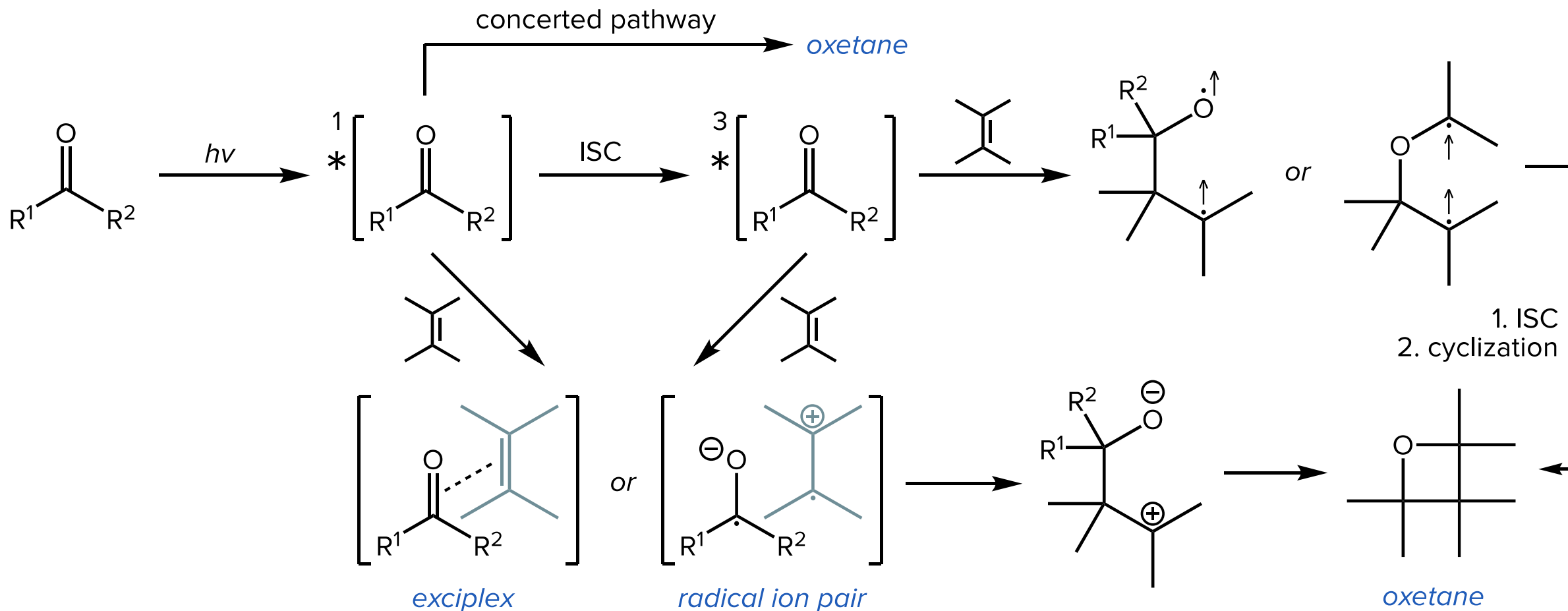
Stereoselectivity?



Electron-rich Alkenes + Excited Carbonyls



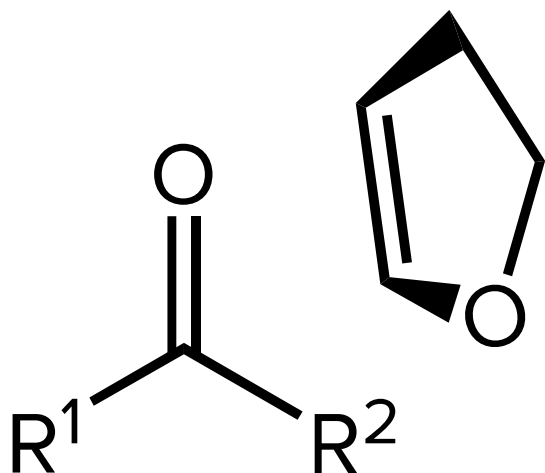
Both singlet and triplet states can react, although the selectivity of the reaction and its underlying mechanism depend on the multiplicity of the (n,π^*) state.



Key Orbital Interactions

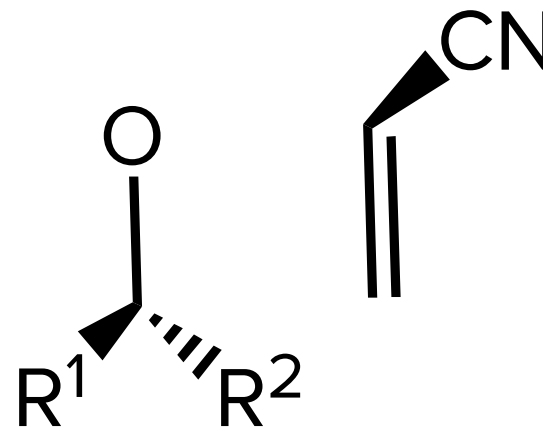
The key orbital interactions for electron-rich and electron-poor olefins are different not only in the orbitals involved, but in their symmetry and stereochemistry. Distinct biradicals are formed.

Electron-rich olefins. $\pi \rightarrow n$



Perpendicular
approach

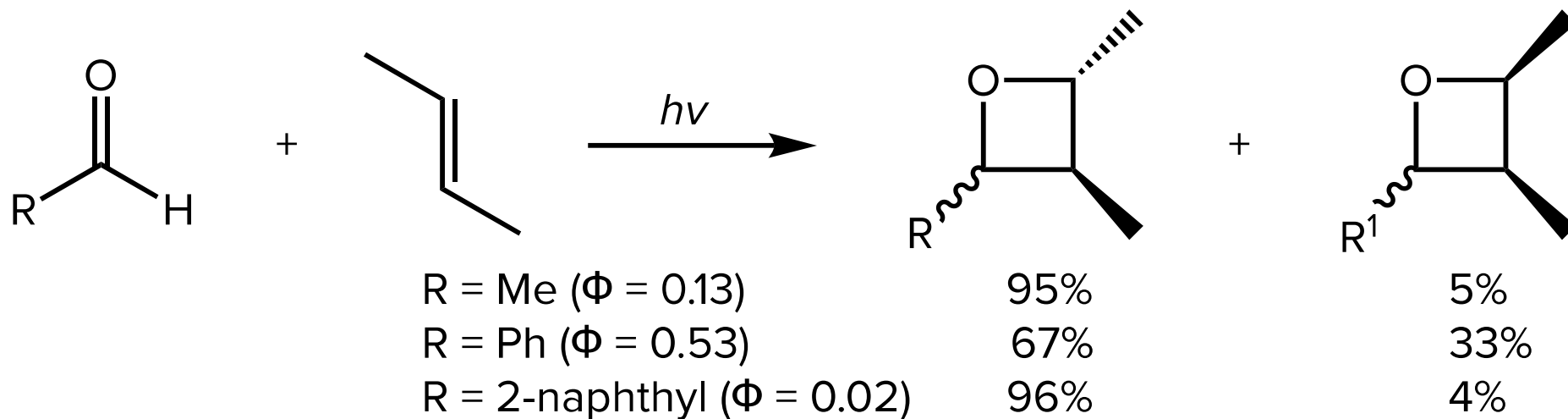
Electron-poor olefins. $\pi^*_{CO} \rightarrow \pi^*_{CC}$



Parallel
approach

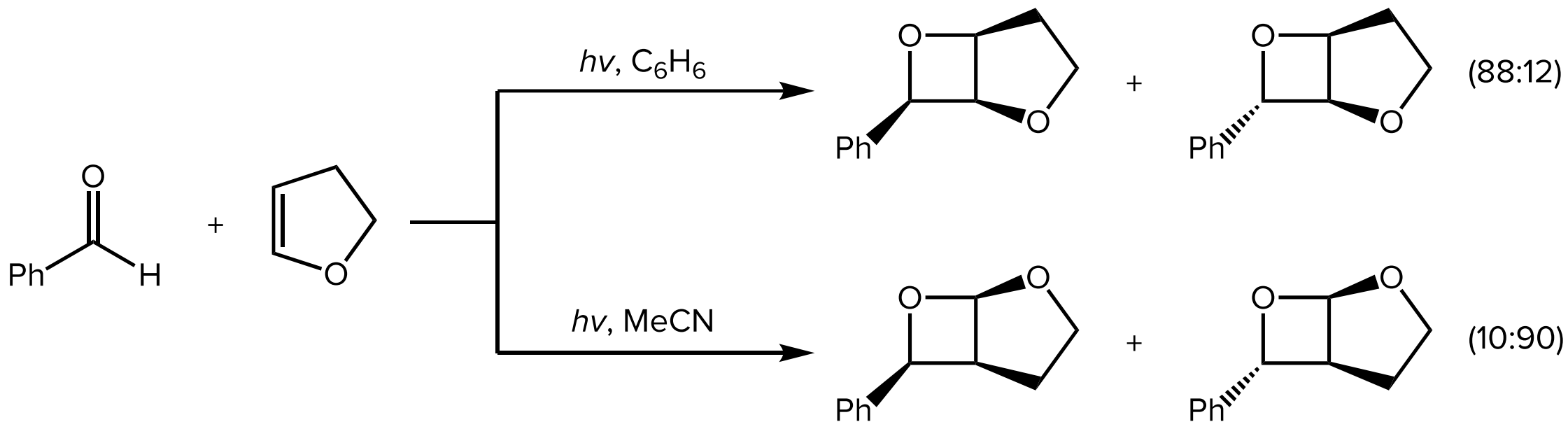
Multiplicity-dependent Reactivity

The stereoselectivity of addition of excited acetaldehyde to (*E*)-2-butene is significantly greater than the selectivity of the corresponding reaction of benzaldehyde. Why?



Solvent-dependent Reactivity

Changing the polarity of the solvent can have a profound effect on the mechanism and alter both stereo- and regioselectivity.



Via triplet biradical intermediate

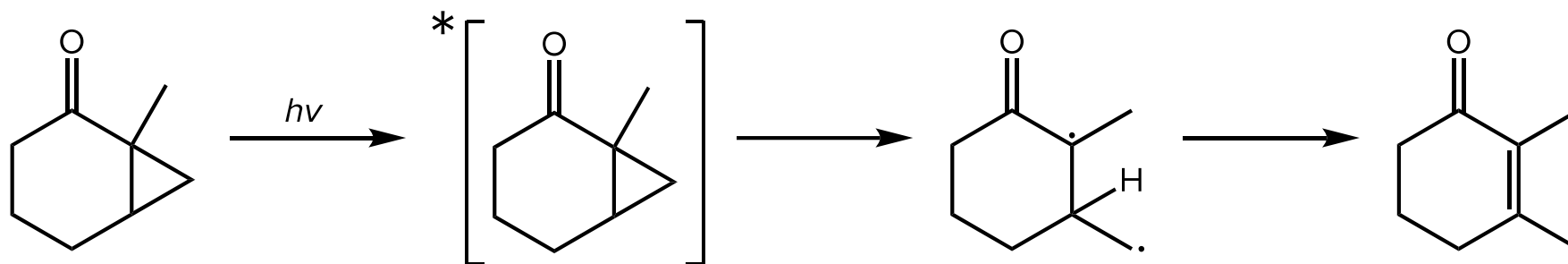
Via electron transfer

β -Cleavage of Excited Carbonyl Compounds

Photochemistry of the Carbonyl Group

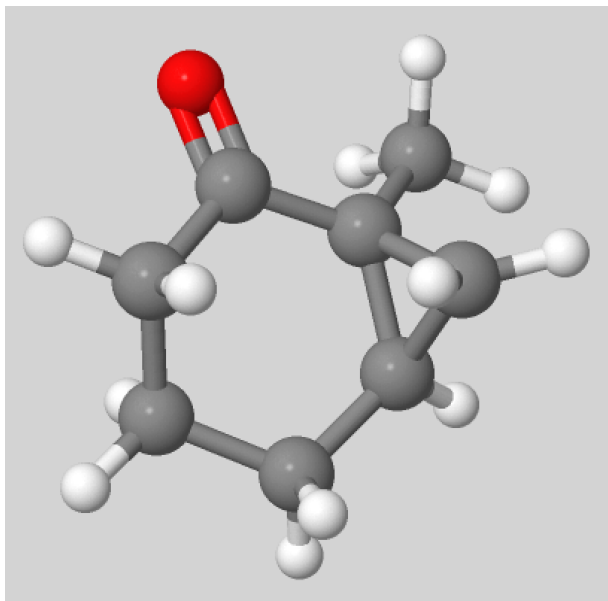
β -Cleavage of Excited Carbonyls

A $\pi^* \rightarrow \sigma^*$ interaction facilitates cleavage of *weak* bonds β to the carbonyl group in (n, π^*) or (π, π^*) states. In the latter case, a $\sigma \rightarrow \pi$ interaction may also be relevant.



Ring strain

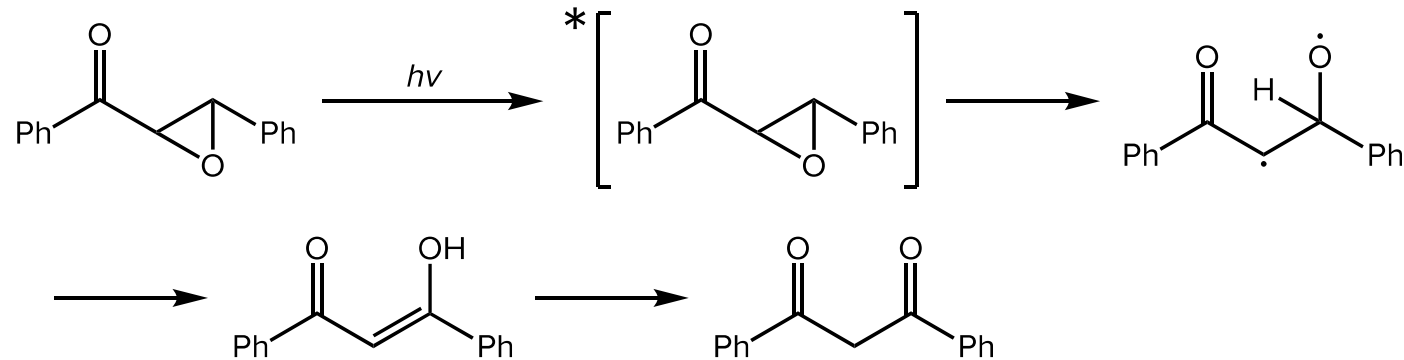
Low bond energy



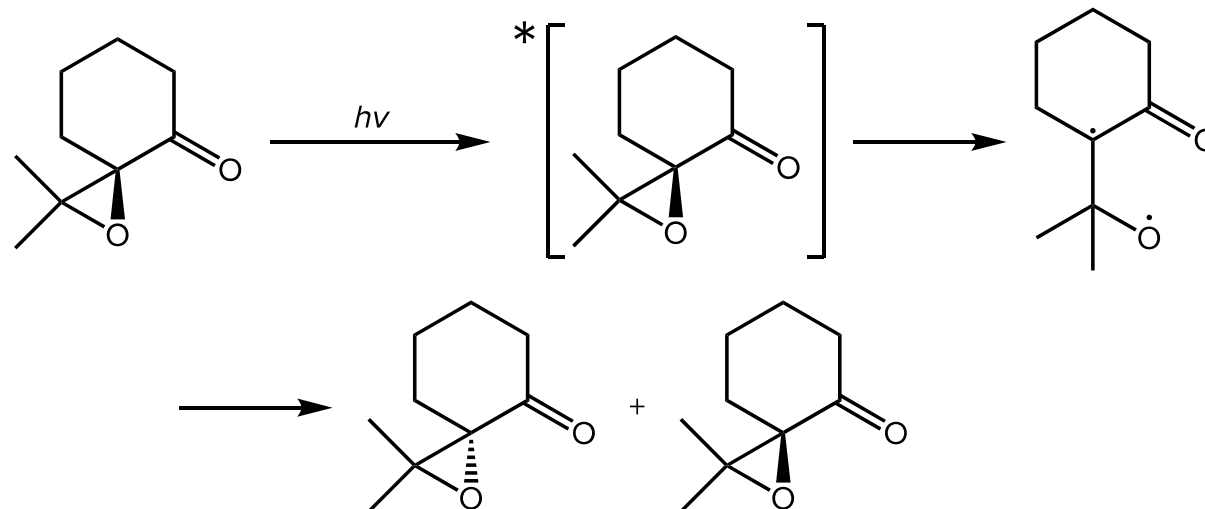
α,β -Epoxy Ketones or Aldehydes

β -Cleavage of α,β -epoxy ketones or aldehydes may lead to rearrangement or stereoisomerization of the starting material.

Rearrangement to β -diketones

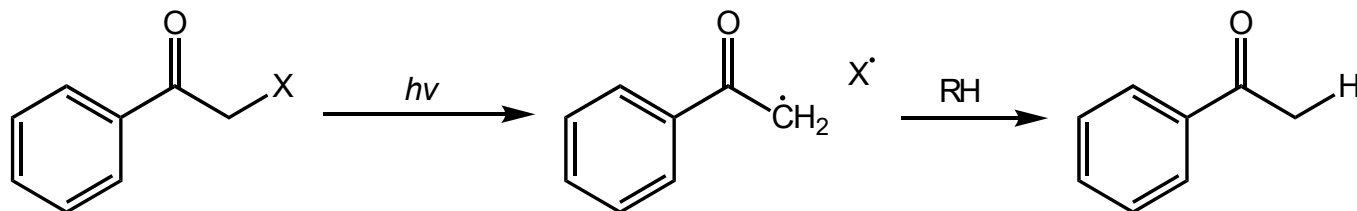


Epimerization at the α -carbon



Fragmentations Initiated by β -Cleavage

Reasonably good leaving groups can be lost from the β -position following excitation of the carbonyl group. Benzoin's are an interesting case study in this regard.



Ionic cyclization of benzoin's to benzofurans

