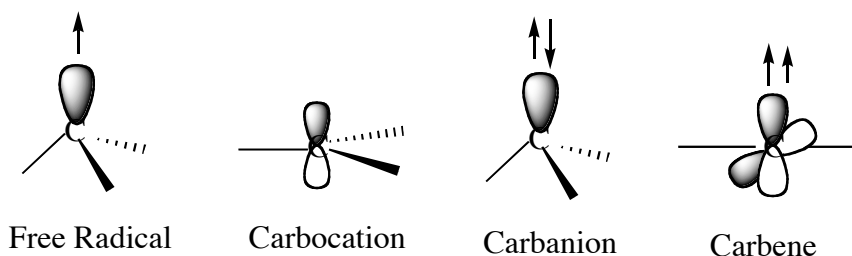


## FREE RADICALS

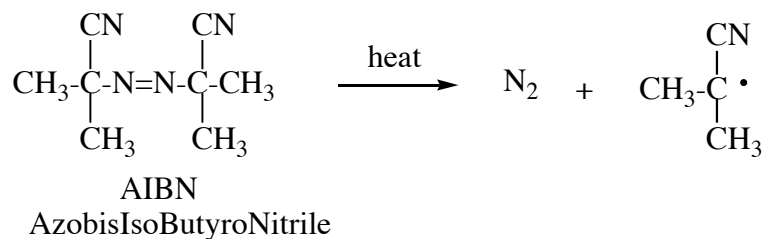
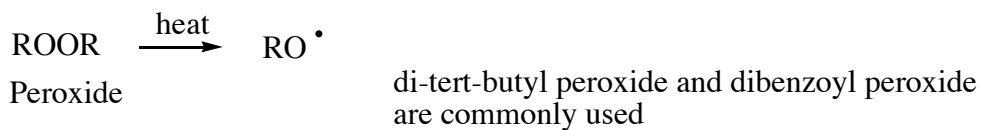


Radical Reaction Characteristic---three step process

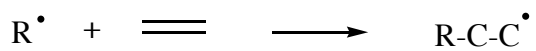
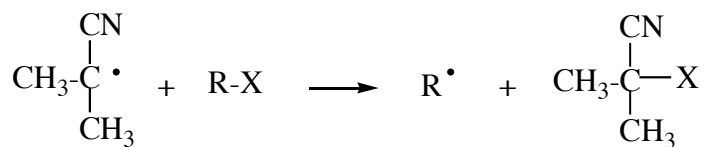
- 1) Initiation Step---required to get a free radical
- 2) Propagation Steps--- The reaction of the radical and production of new radicals.
- 3) Termination steps---Required to remove radicals from the reaction

### Initiation Step

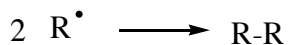
Chemical species known as initiators are required, or photons.



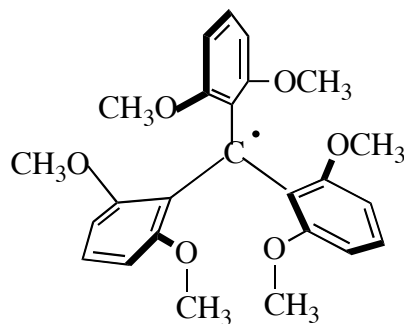
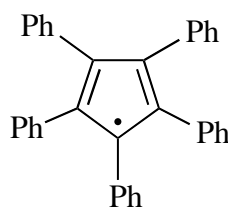
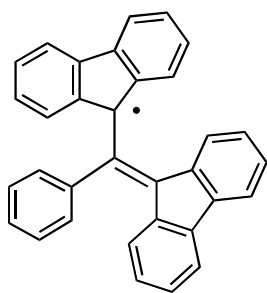
Propagation---The first formed radical now produces new radicals and reactions



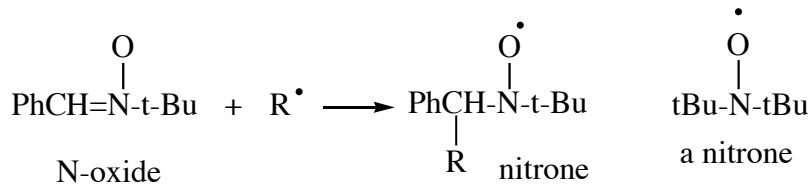
Termination---any reaction that removes the radical



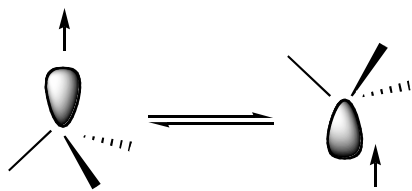
Stable Free Radicals



shape prevents dimerization

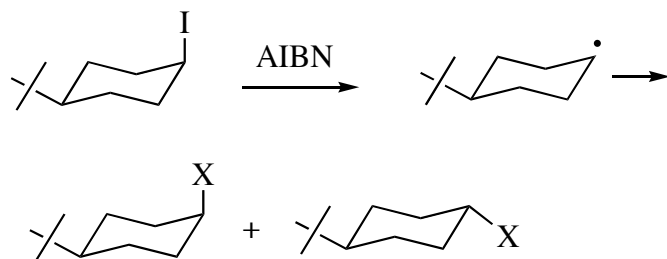
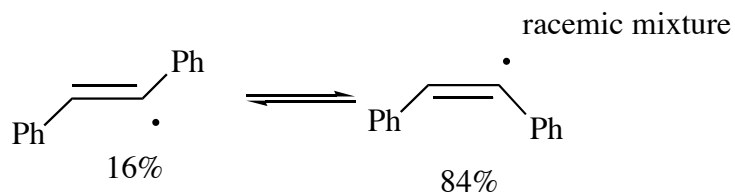
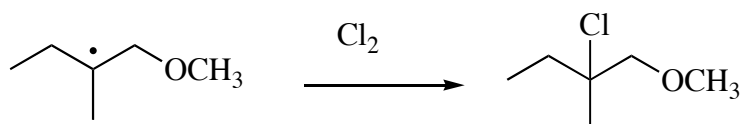


The reaction above produces a stable nitrone radical from a reactive Radical. The ESR signal of the nitrone can be used to analyze the radical. Tables of nitrone ESR spectra with different R groups are in the literature

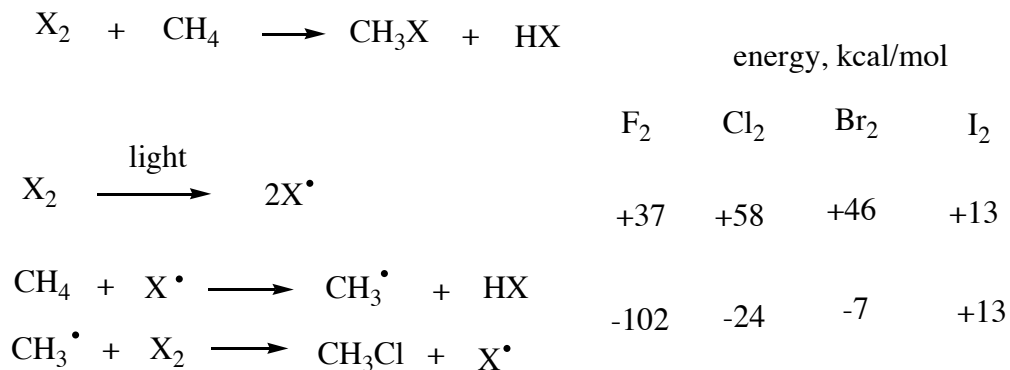


Free Radical

Nearly  $sp^3$  hybrid with inversion of stereochemistry



## Halogenation



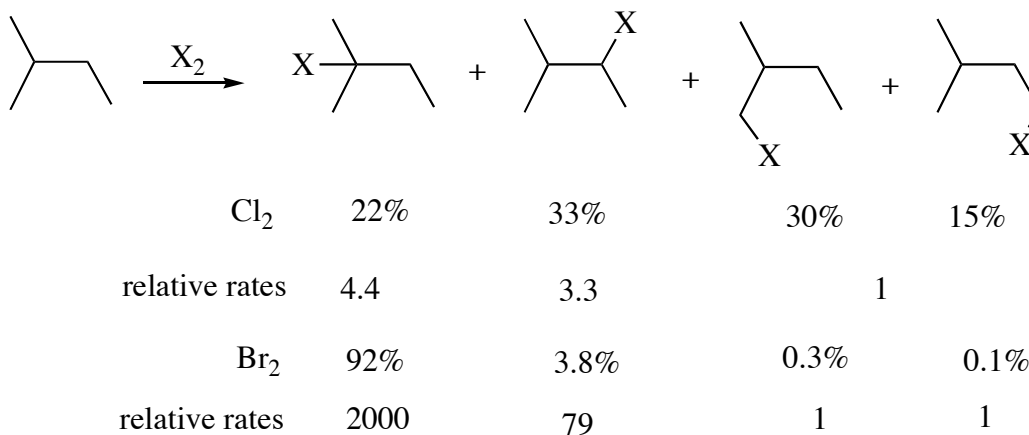
Fluorination--Propagation energy is so large that the reaction is uncontrollable and explosions result

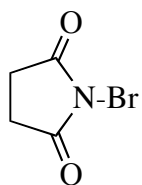
Chlorination--can control the production of Cl radicals by the light source to give a useful process

Bromination--The termination step is of low energy and the reactions are very selective for tertiary CH bonds

Iodination--Reaction too difficult to go to completion

Bromination is much more selective than chlorination

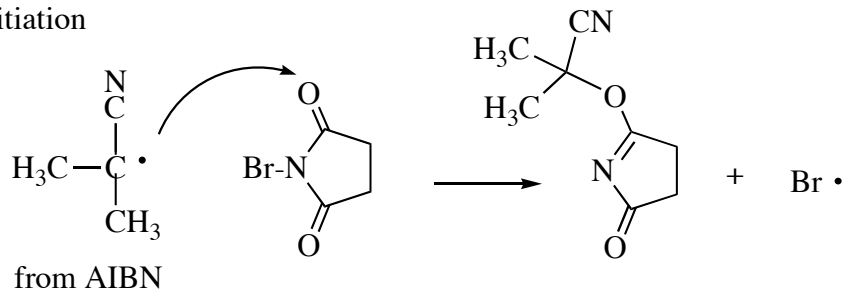




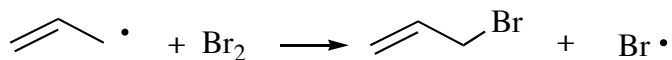
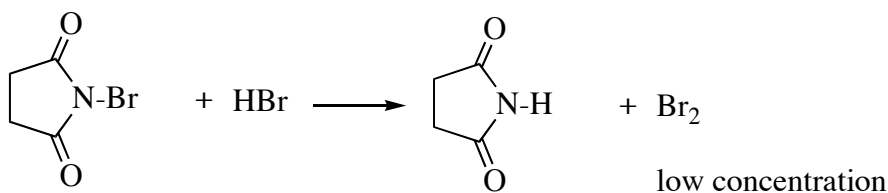
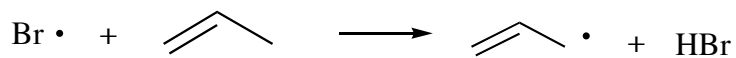
NBS, N-BromoSuccinimide

Mild bromination of allylic and benzylic radicals

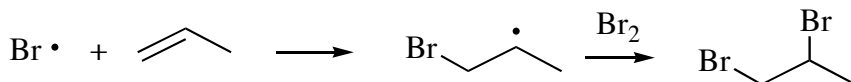
Initiation



Propagation

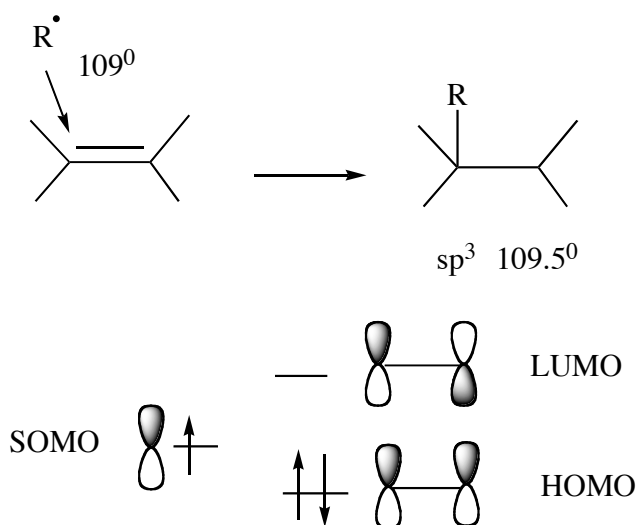


Br<sub>2</sub> concentration too low for alkene addition



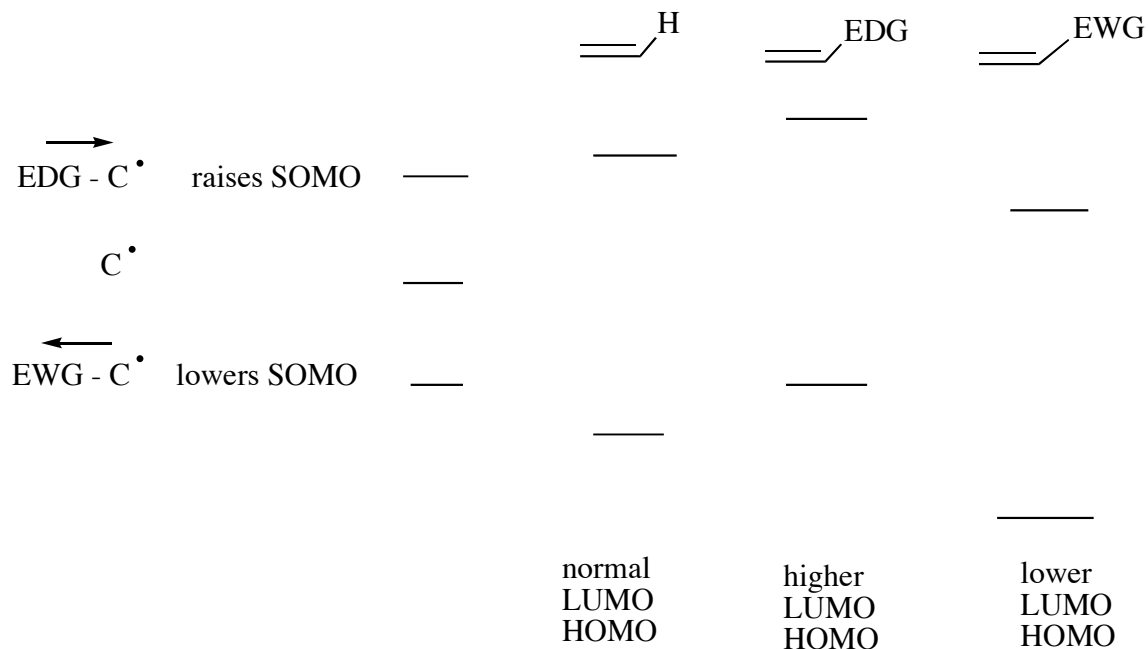
$$\frac{d [\text{radical substitution}]/dt}{d [\text{addition}]/dt} = k / \text{Br}_2$$

## Radical addition to alkene theory



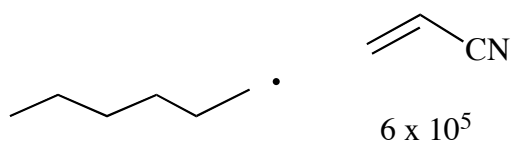
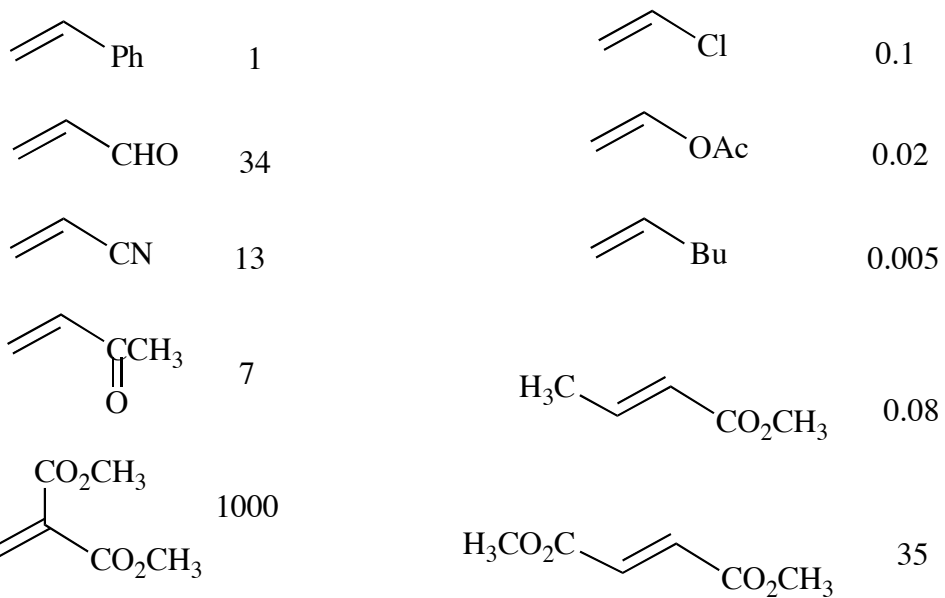
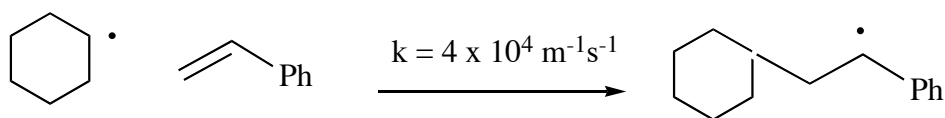
The SOMO orbital of a free radical reacts with the LUMO or HOMO of more similar energy with the SOMO. Electron donating groups raise the SOMO level and make the radical nucleophilic (SOMO-LUMO). Electron withdrawing groups lower the SOMO and make it electrophilic (SOMO-HOMO).

On the alkene, EWG lower LUMO and HOMO; EDG raise HOMO and LUMO



## SOMO - LUMO

Nucleophilic radicals contain EDG and add to the LUMO of alkenes.

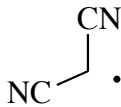
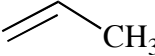
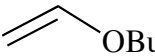
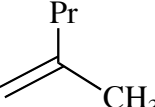
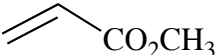
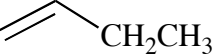
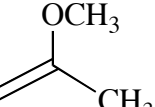
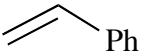


SOMO 3 > 2 > 1



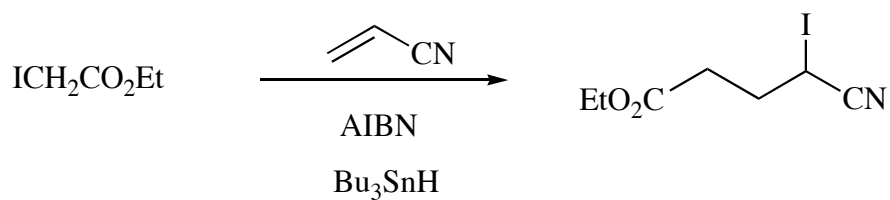
## SOMO-HOMO

Electrophilic Radicals contain EWG and add to the HOMO of alkenes

		low HOMO	
	low SOMO		10 <sup>-3</sup>
			1
			30
			16
		high HOMO	
	$\cdot \text{CH}_2\text{CO}_2\text{Et}$		20
	neutral reacts with LUMO and HOMO levels		1
			2
	$(\text{CF}_3)_3\text{C} \cdot$	$\text{Et}_3\text{Si-H}$	$10^8 \text{ m}^{-1}\text{s}^{-1}$
	most electrophilic radical known		$10^8 \text{ m}^{-1}\text{s}^{-1}$
	$(\text{CH}_3)_3\text{C-O} \cdot$	$\text{Et}_3\text{Si-H}$	$10^6 \text{ m}^{-1}\text{s}^{-1}$

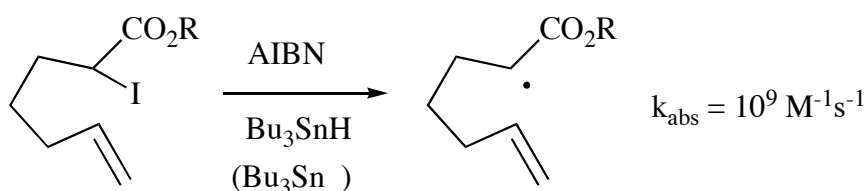


## Atom Transfer Reaction

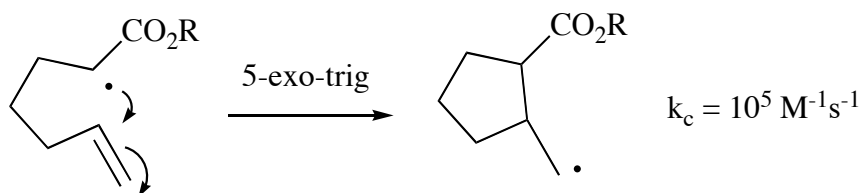


The iodine atom is transferred from the starting iodo compound to the new radical to form the product.

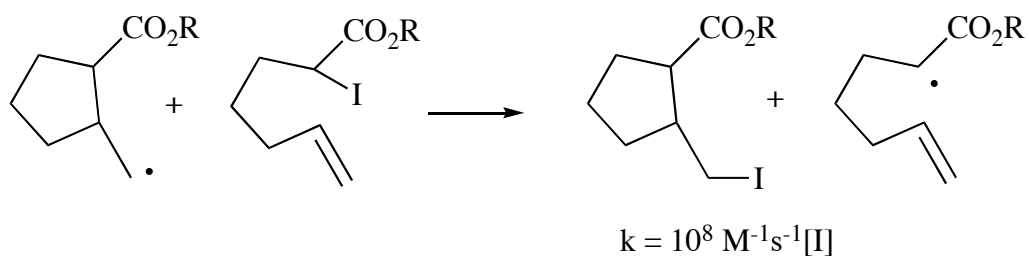
### 1) Radical Formation



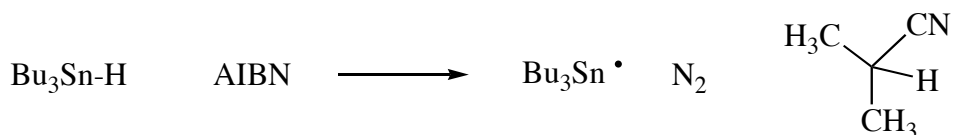
### 2) Cyclization



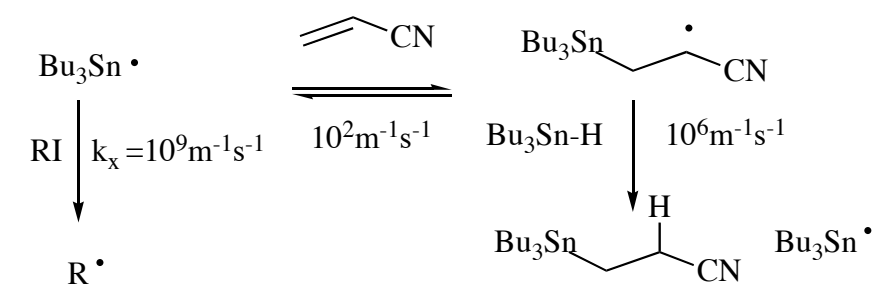
### 3) Atom transfer and propagation



Initiation

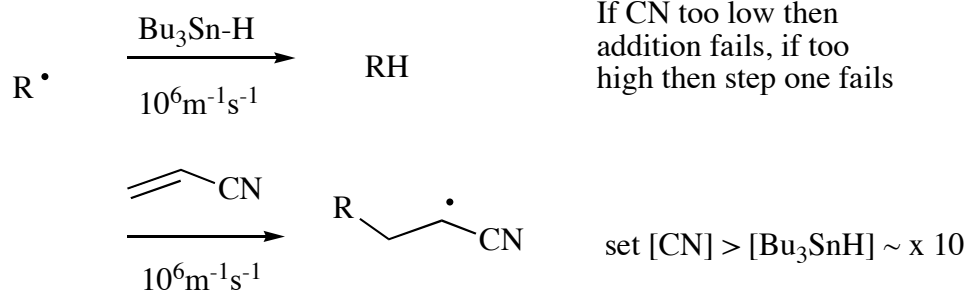


STEP 1

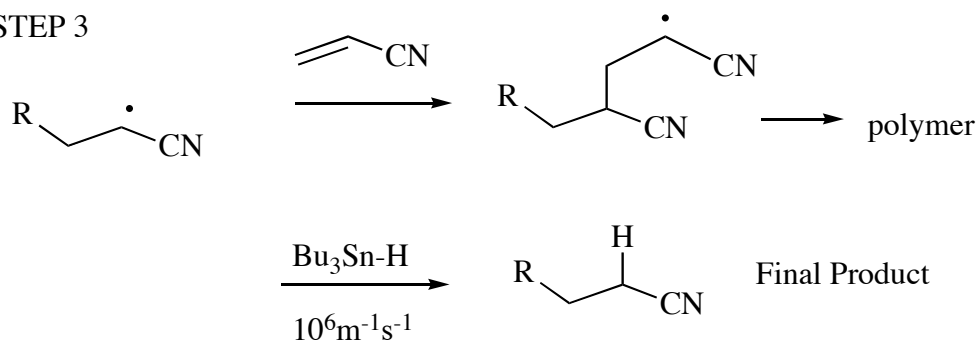


If  $K_x[\text{RI}] < 10^2$   
This step stops

STEP 2

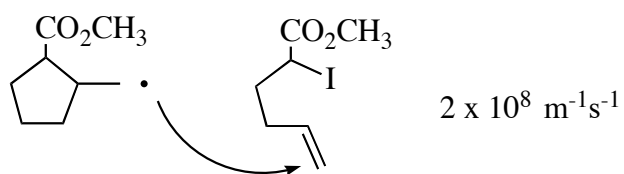
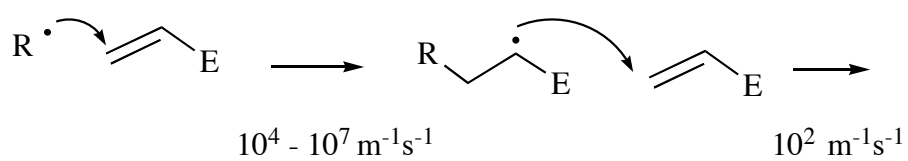
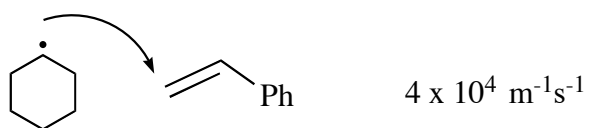
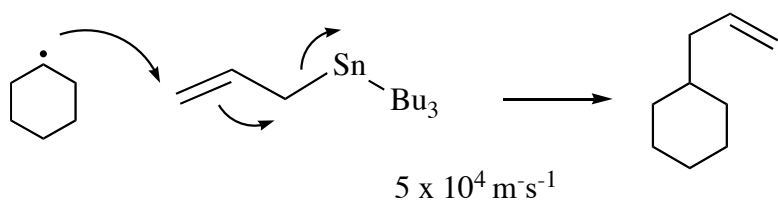


STEP 3

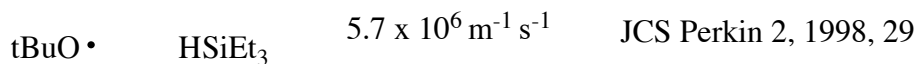
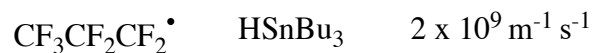


$$[\text{Bu}_3\text{Sn-H}] 10^6\text{m}^{-1}\text{s}^{-1} > [\text{CN}] 10^2\text{m}^{-1}\text{s}^{-1} \quad 1 \times 10^6 > 10 \times 10^2$$

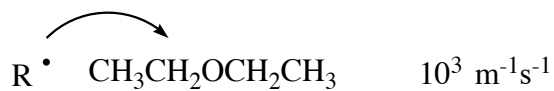
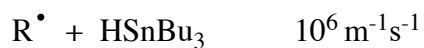
## Addition to alkenes



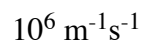
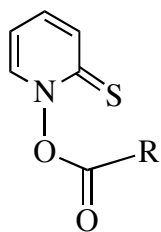
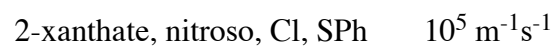
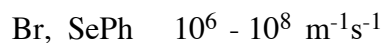
Abstraction of H



Dolbier, JOC, (1998) 63, 5687

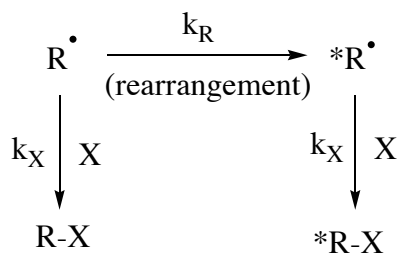


Abstraction of X



## Clock Reactions

When a radical intermediate rearranges to another radical intermediate, and both intermediates compete for a reagent, then the values for the rate constants of the reactions involved can be determined. This "clock" allows for the timing of the steps.



$$d \text{*R}^\bullet / dt = 0 = k_R [\text{R}^\bullet] - k_X [\text{X}] [\text{*R}^\bullet]$$

$$\frac{\text{*R}^\bullet}{\text{R}^\bullet} = \frac{k_R}{k_X [\text{X}]}$$

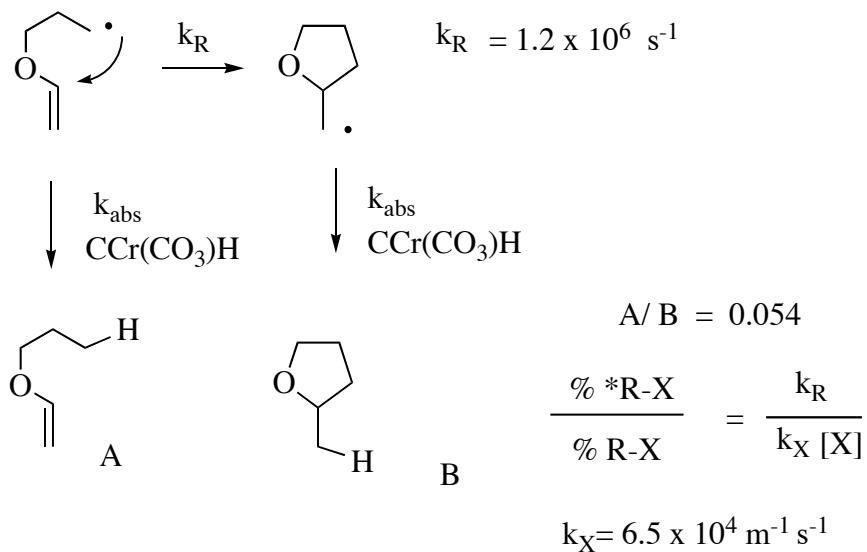
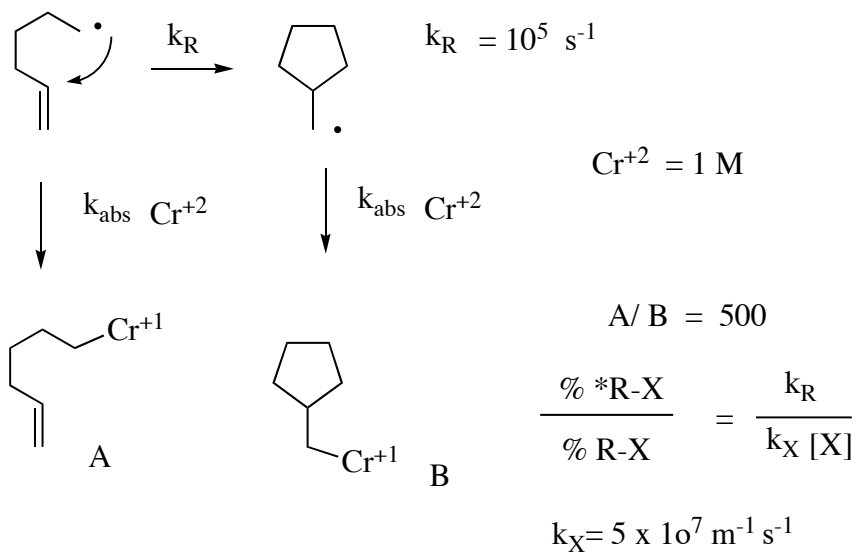
$$\frac{d [\text{*RX}] / dt}{d [\text{RX}] / dt} = \frac{k_X [\text{X}] [\text{*R}^\bullet]}{k_X [\text{X}] [\text{R}^\bullet]} = \frac{\text{*R}^\bullet}{\text{R}^\bullet}$$

$$\frac{\% \text{*R-X}}{\% \text{R-X}} = \frac{k_R}{k_X [\text{X}]}$$

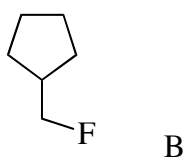
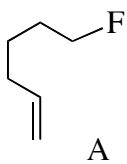
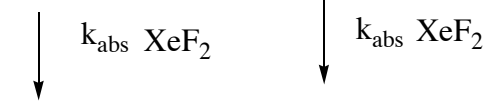
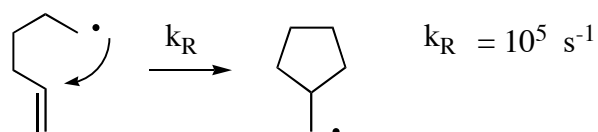
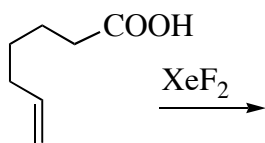
The percentages of the products can thus be used to obtain a rearrangement constant or an abstraction constant. One of the constants must be known and many are known and tabulated.

## Clock reactions in the 5-exo-trig cyclization

5-hexenyl radicals cyclize to give five membered rings exclusively. This is important for the synthesis of 5-membered rings and for obtaining information about the rates of radical reactions



### Xenon Difluoride Reaction



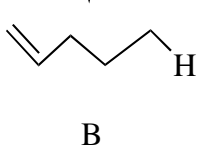
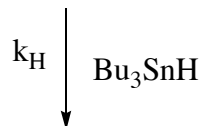
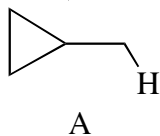
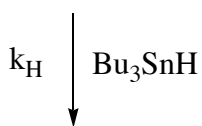
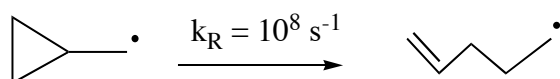
$$\text{XeF}_2 = 0.27 \text{ M}$$

$$A/B = 0.2$$

$$\frac{\% \text{ *R-X}}{\% \text{ R-X}} = \frac{k_R}{k_X [\text{X}]}$$

$$k_X = 1.2 \times 10^6 \text{ m}^{-1} \text{ s}^{-1}$$

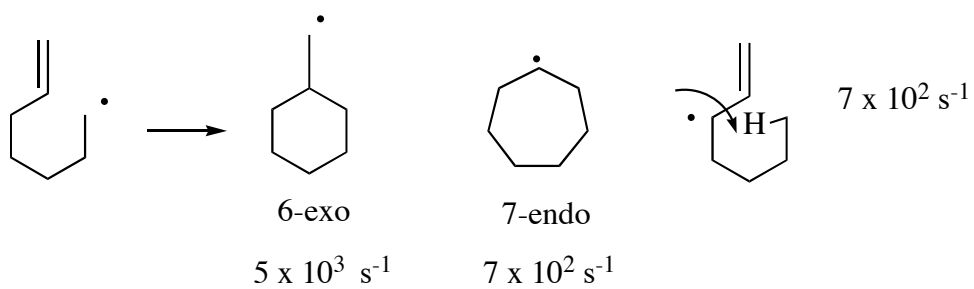
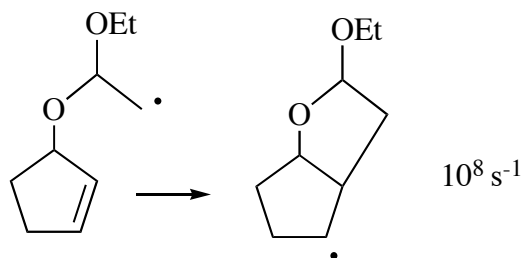
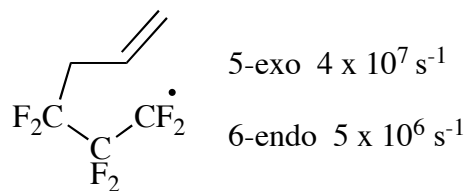
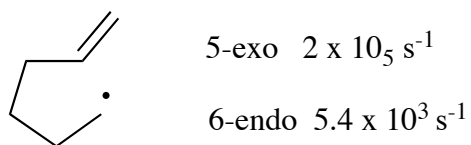
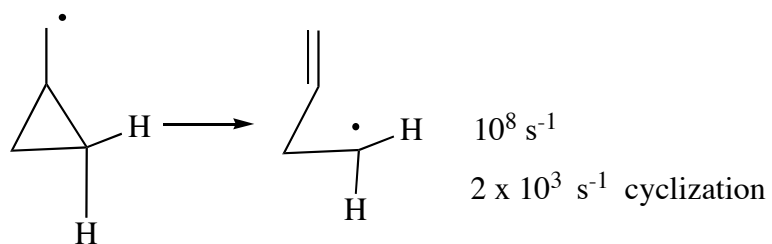
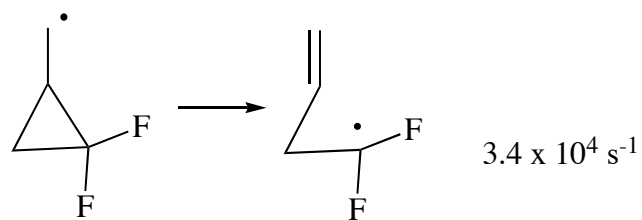
### Cyclocarbonyl radical (rapid ring opening)



$$A/B = 0.011$$

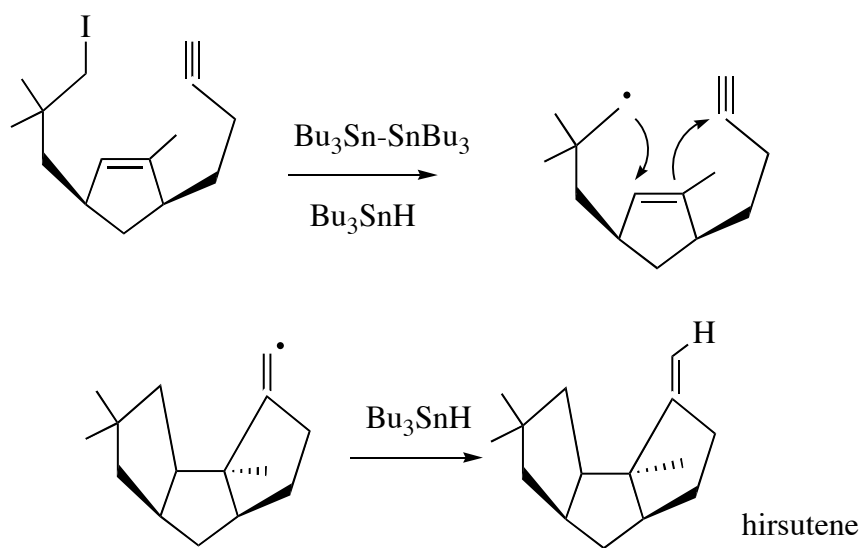
$$k_H = 1.4 \times 10^6 \text{ m}^{-1} \text{ s}^{-1}$$

Cyclization k values

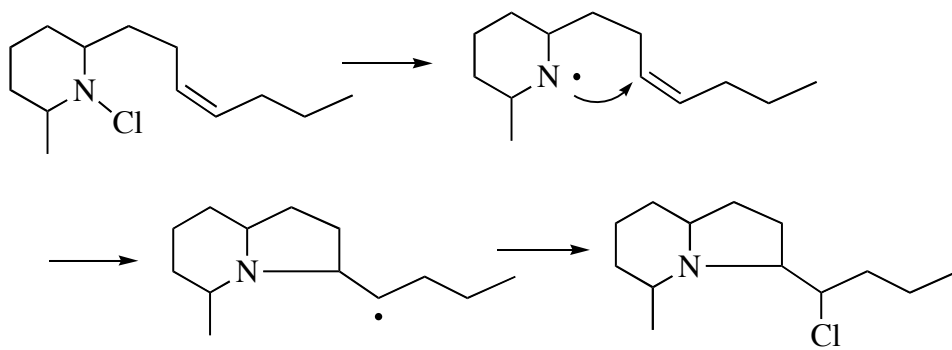




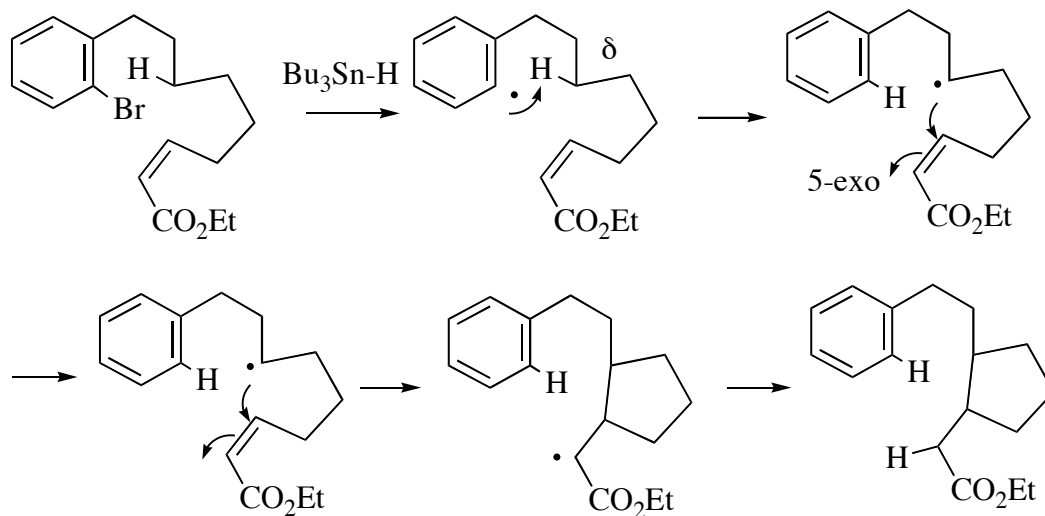
## Tandem Reactions



## 5-exo-trig



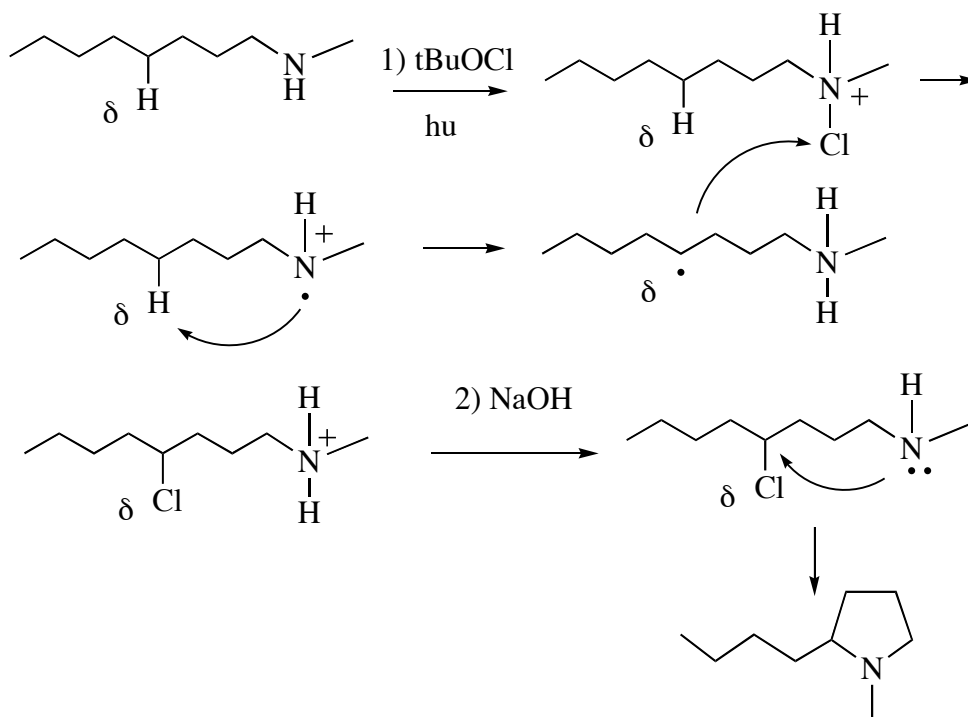
Abstract the delta ( $\delta$ ) hydrogen



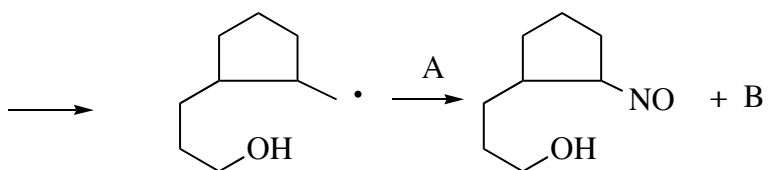
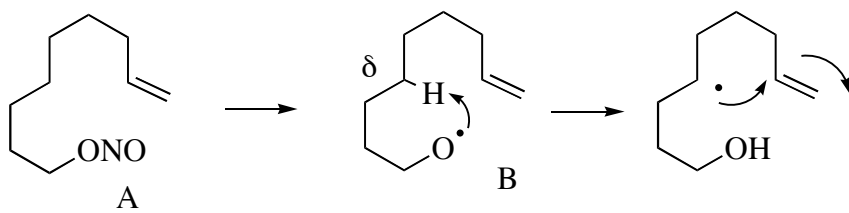
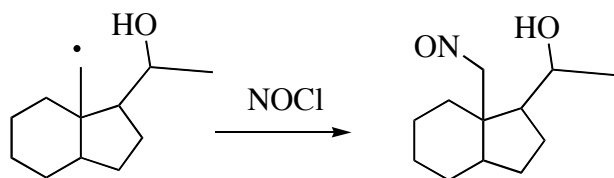
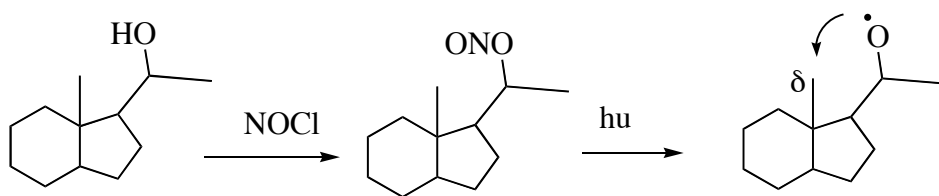
Tet Lett (1990) 31. 6911 and 5181

JACS (1998), 110, 5900

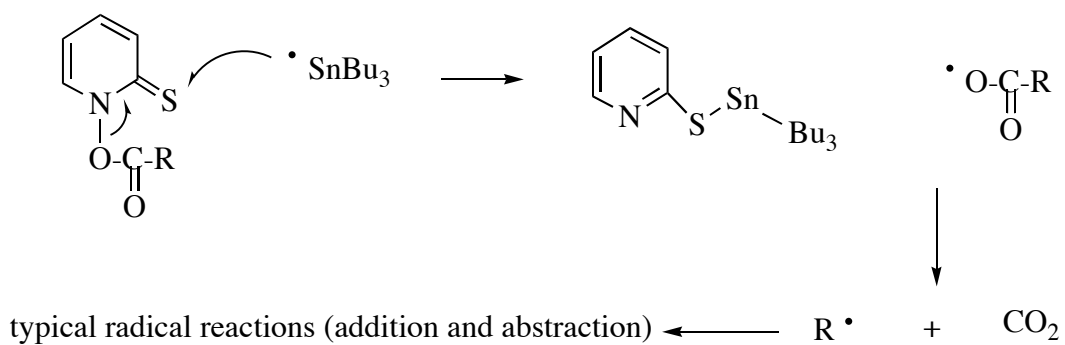
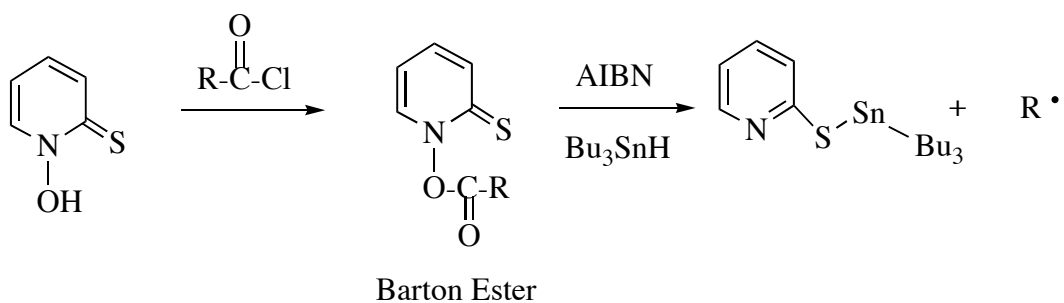
Hofmann-Loeffler Reaction



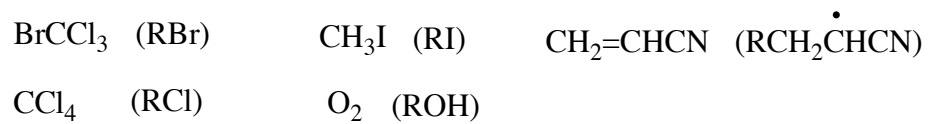
Barton



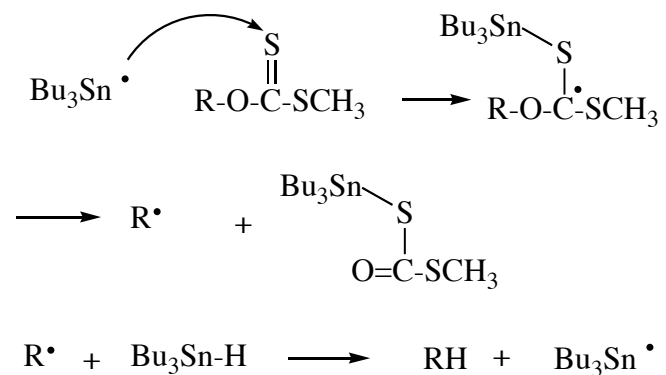
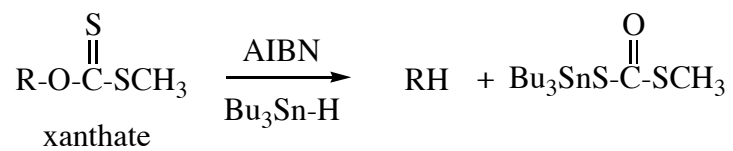
### Barton Ester Method



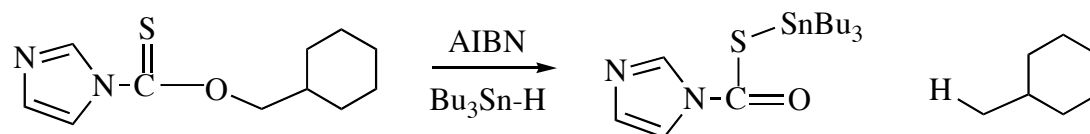
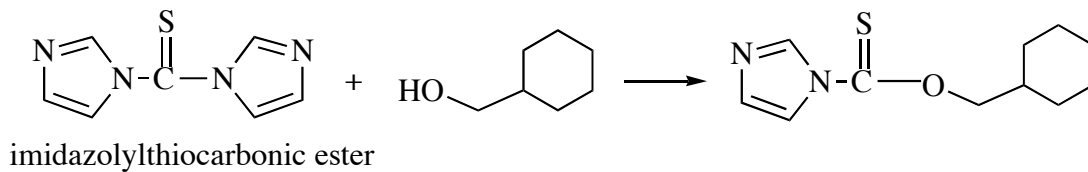
Some common reactions of R•



Barton-McOmbie reduction of OH

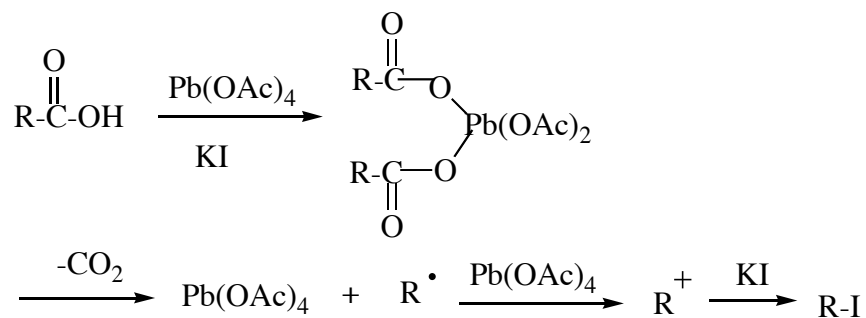


Similar Process

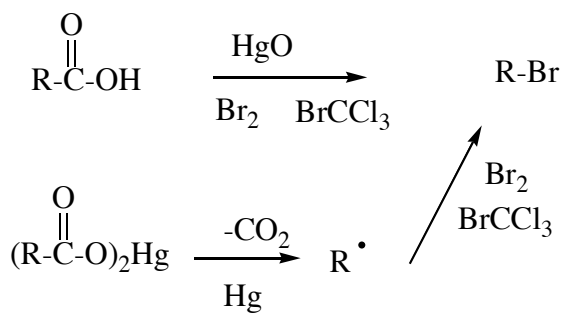


## Halo-decarboxylations

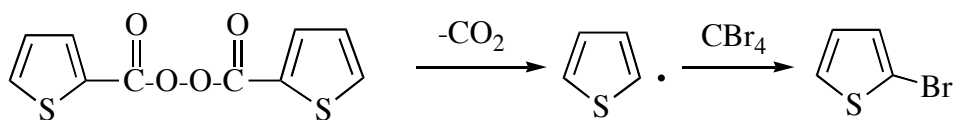
### Kochi



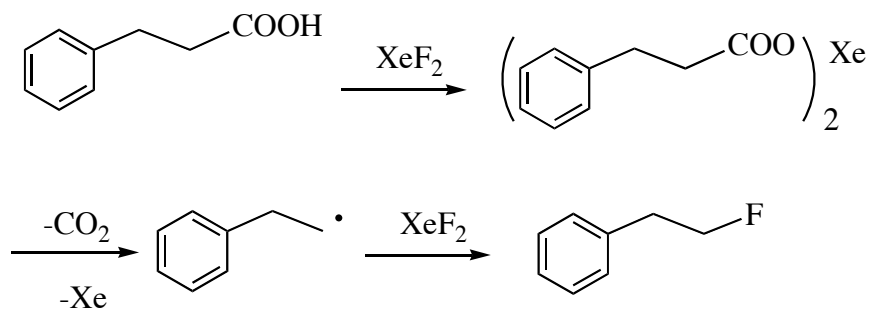
### Hunsdiecker-Borodine



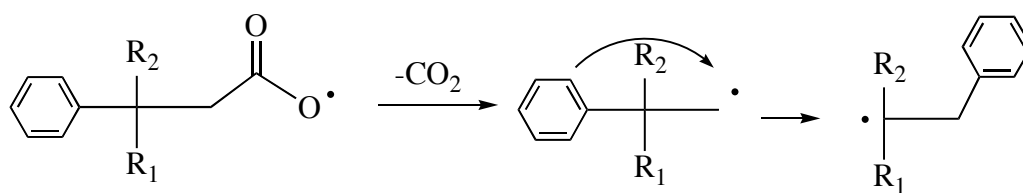
### Peroxide



### SIUE

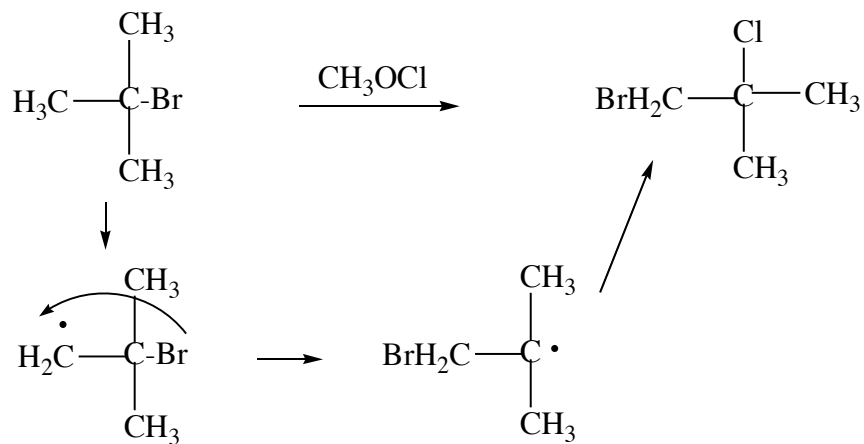
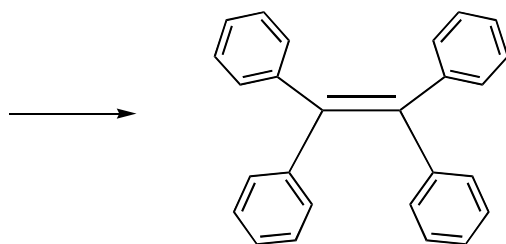
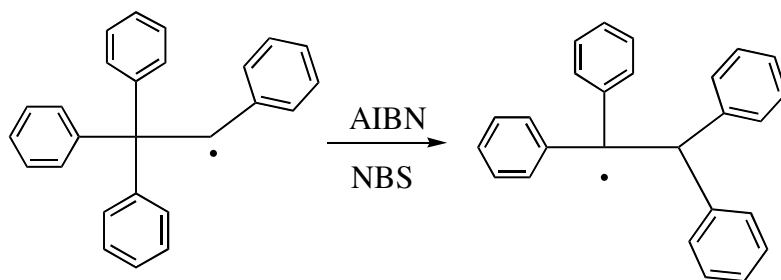


## Rearrangements

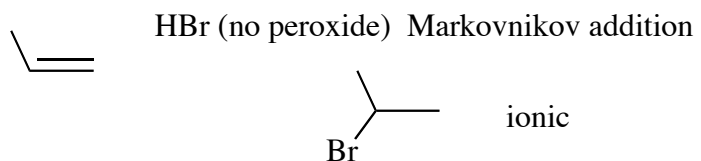


R <sub>1</sub>	R <sub>2</sub>	% rearrangement
CH <sub>3</sub>	H	39
Ph	H	63
Ph	Ph	100

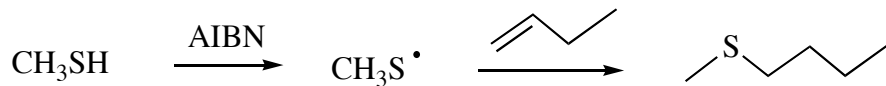
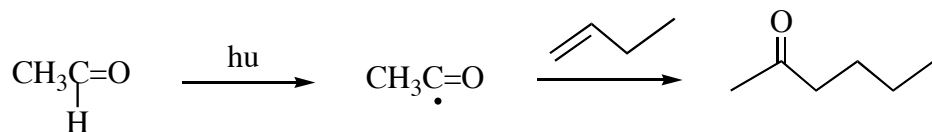
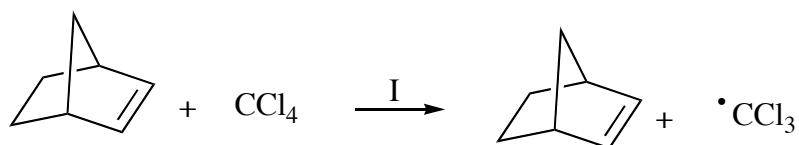
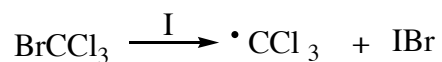
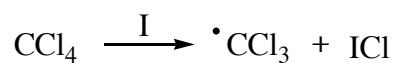
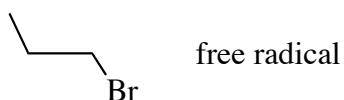
rearrangement increases as the stability of the tert radical increases.



## Additions to Alkenes

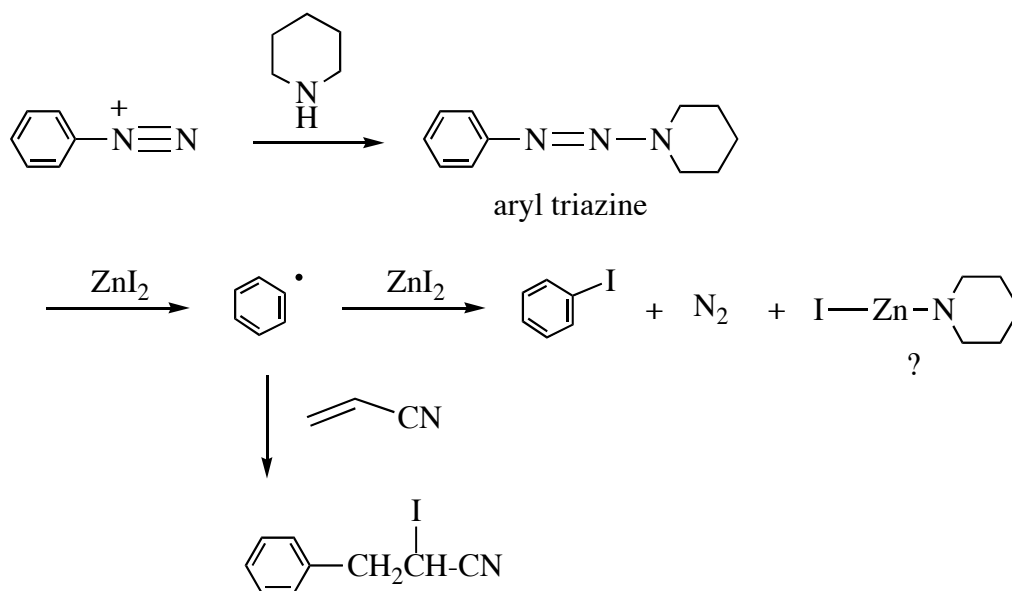
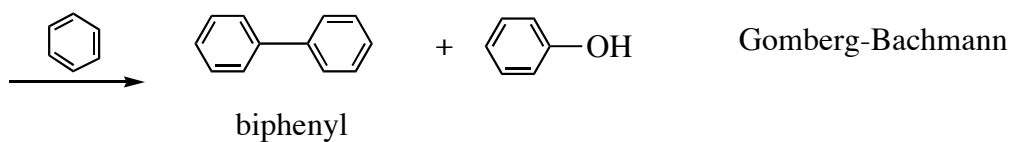
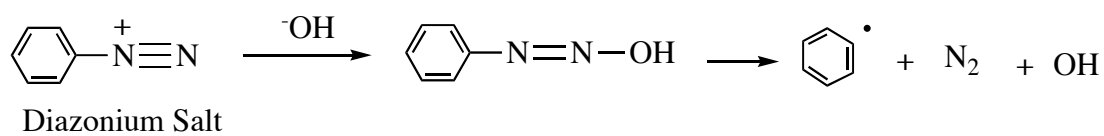
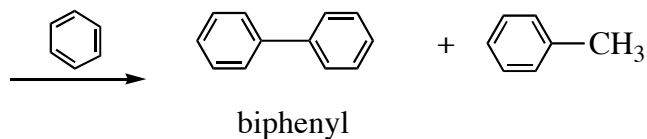
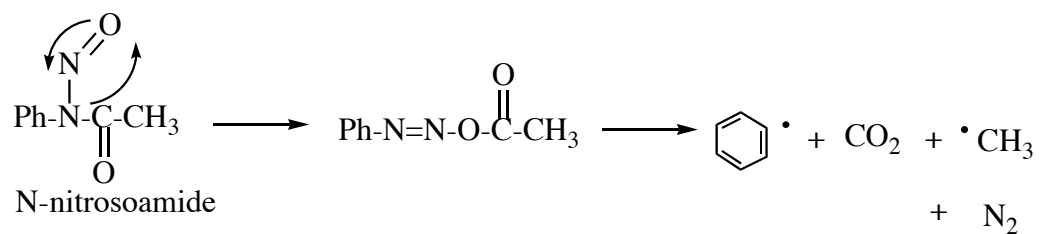


HBr (peroxide) Anti Markovnikov addition

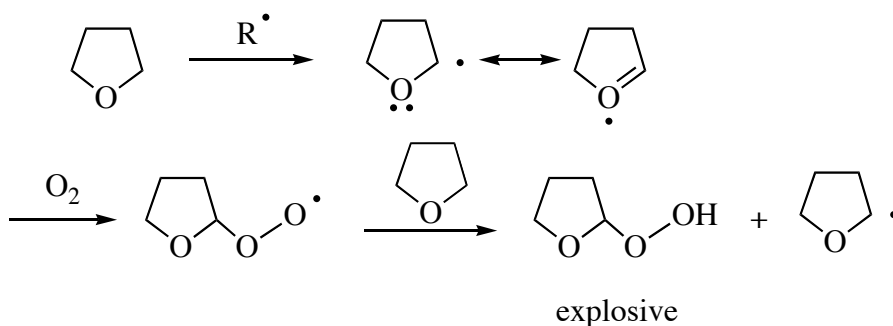
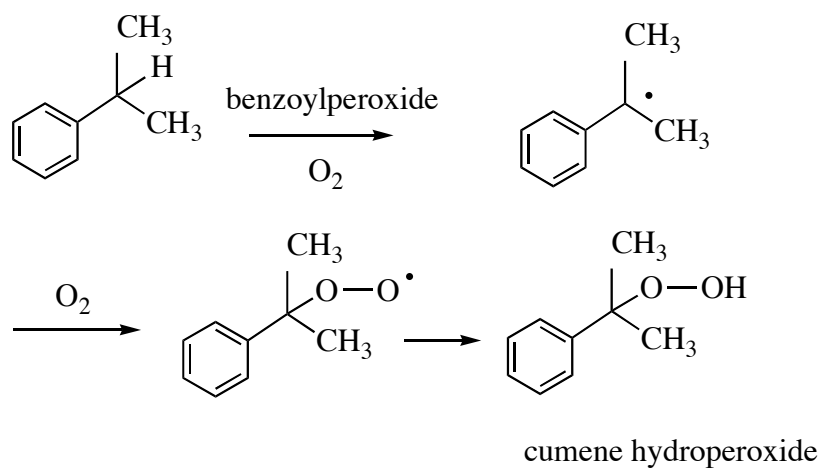




## Aryl Radicals



Autooxidation--oxidation by oxygen



Ethers (THF, diethyl ether, diisopropyl ether) form peroxides on standing when oxygen is present. The initiator is uncertain. The peroxides are unstable and can detonate on agitation. Thus ether that has been standing in a previously opened container for a long period can explode when handled.