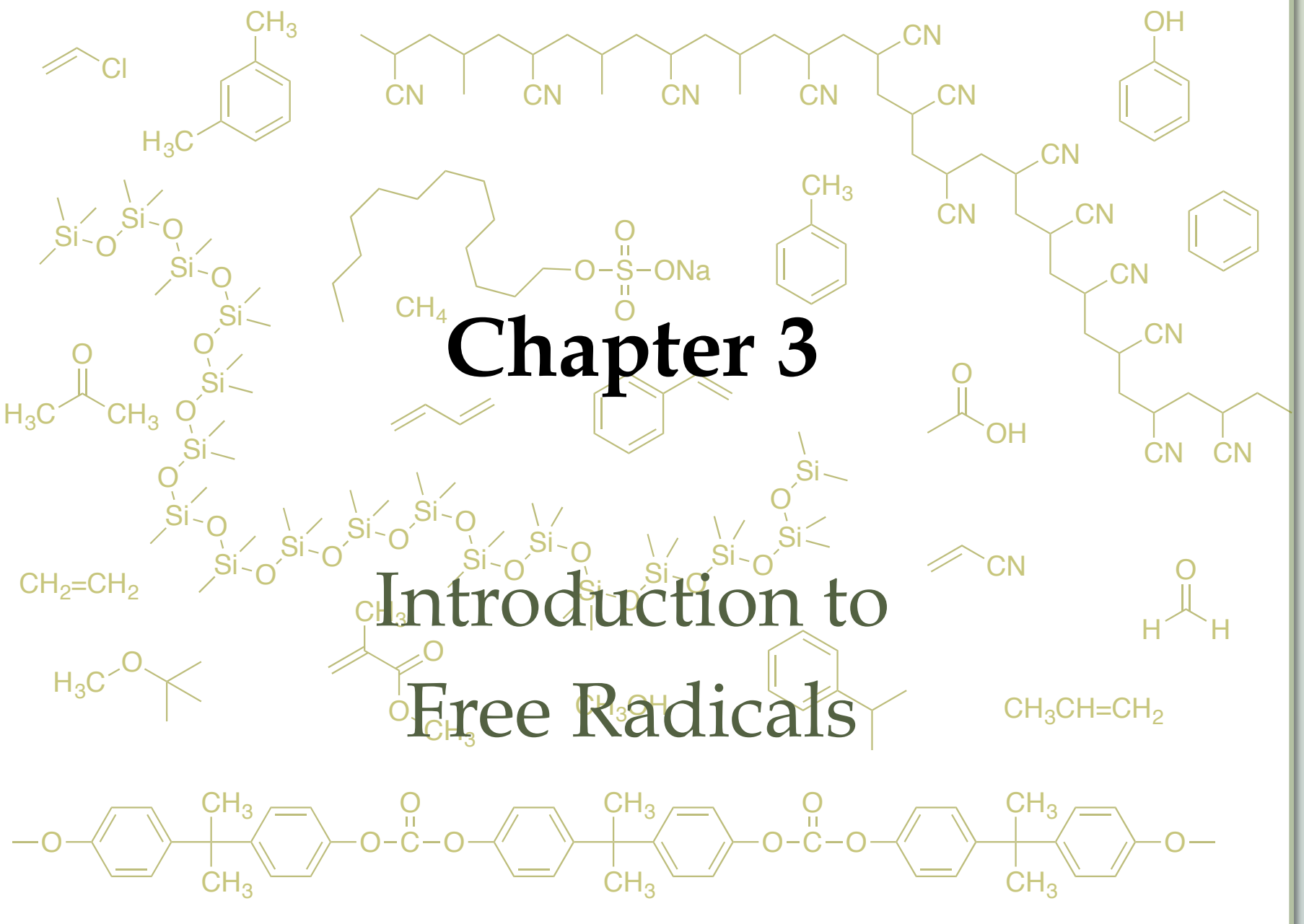


Chapter 3

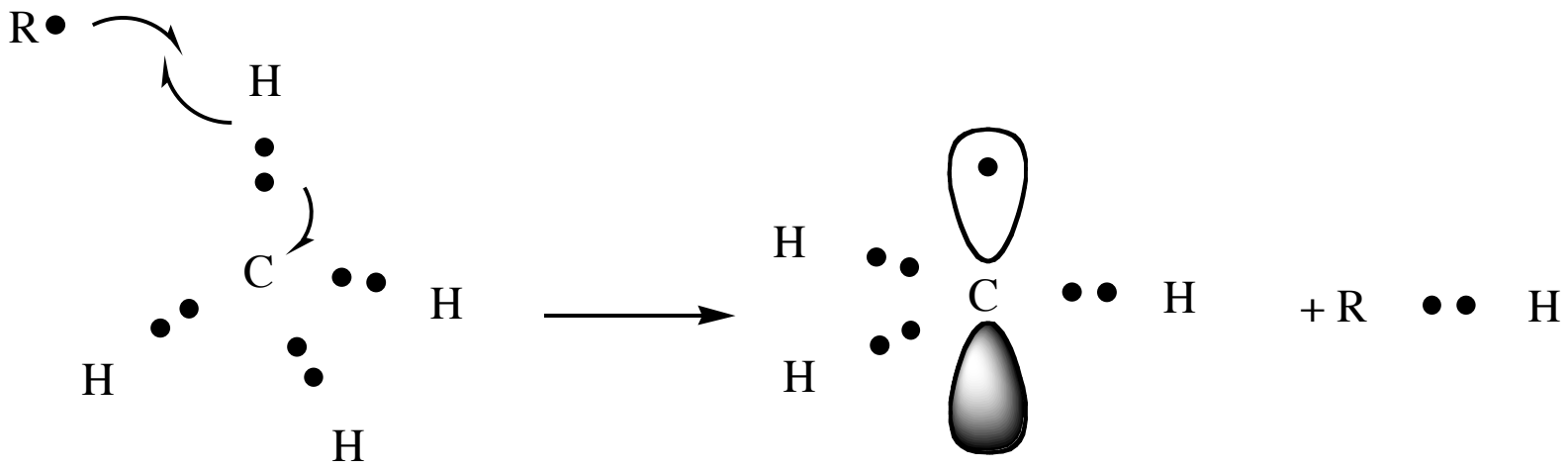
Introduction to Free Radicals

Introduction to free radicals

Free radicals play important roles in processes such as:

- Thermal cracking of petroleum products
- Hydrocarbon rearrangements
- Hydrocarbon halogenation
- Organic compound oxidation
- Vinyl polymerization

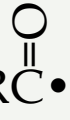
The methyl radical is planar



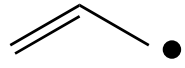
C is sp^3 **C is sp^2**

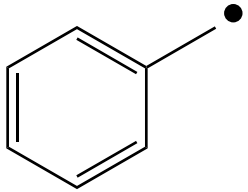
Hydrogen transfer or abstraction is a common free radical reaction. If R• above is a carbon centred radical (not methyl), is the reaction exothermic or endothermic?

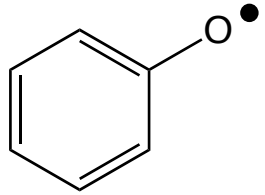
Free Radical Nomenclature

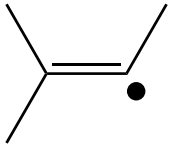
Alkyl radicals	R•	
Alkoxyl radicals	RO•	
Peroxyl radicals	ROO•	
Acyl radicals		
Acyloxyl radicals		

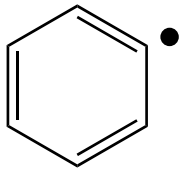
Some special radicals…

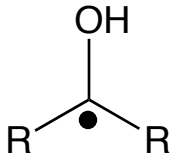






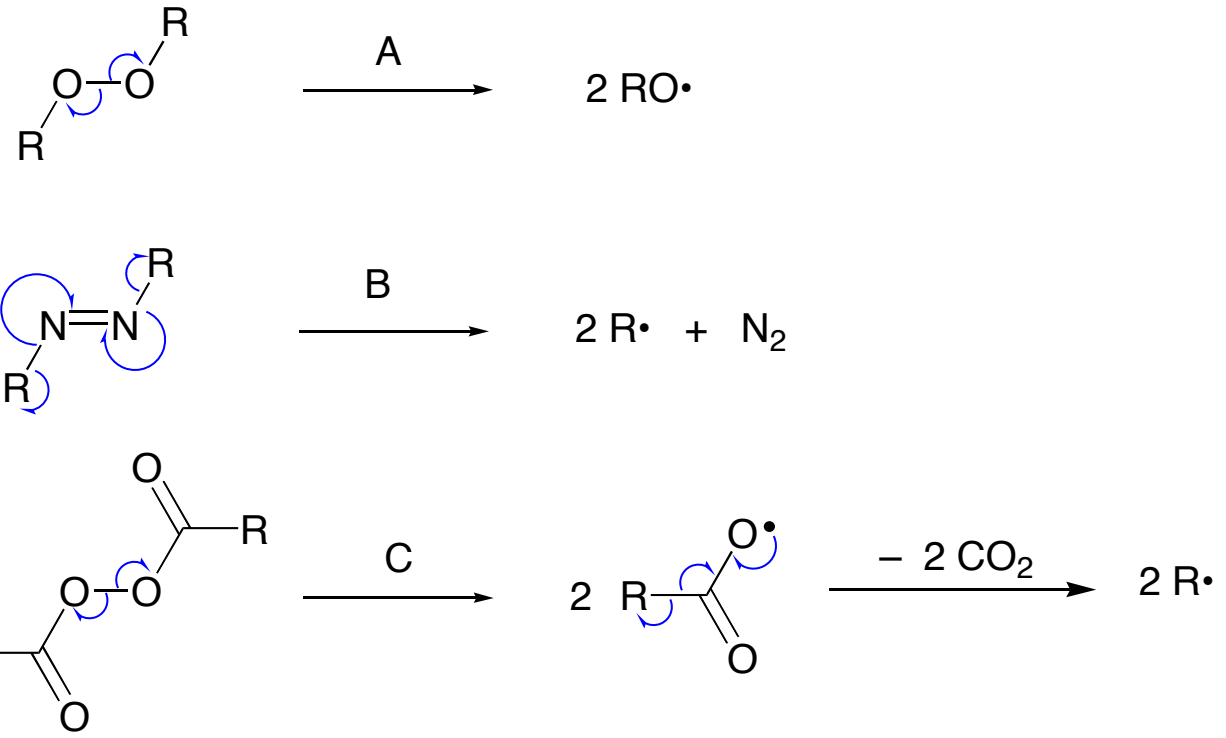




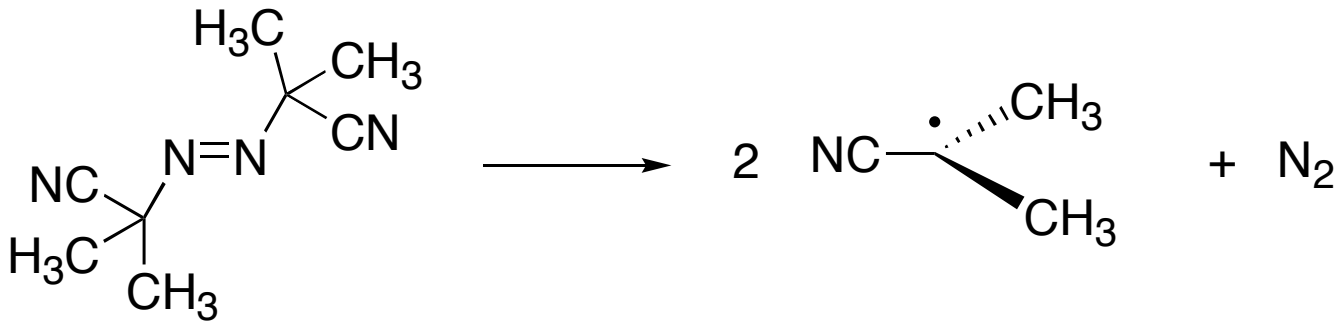


Making free radicals

- The majority of reactions that yield free radicals will produce them in pairs
- Radical production can be thermal or photochemical



A common azo compound: AIBN

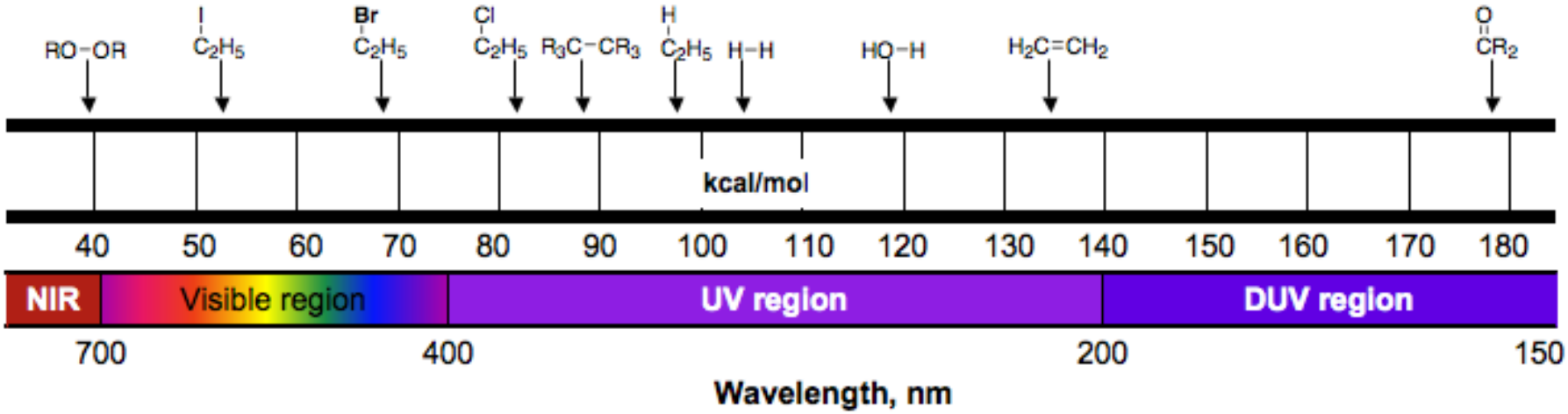


Activation energy = E_a = 31 kcal/mol

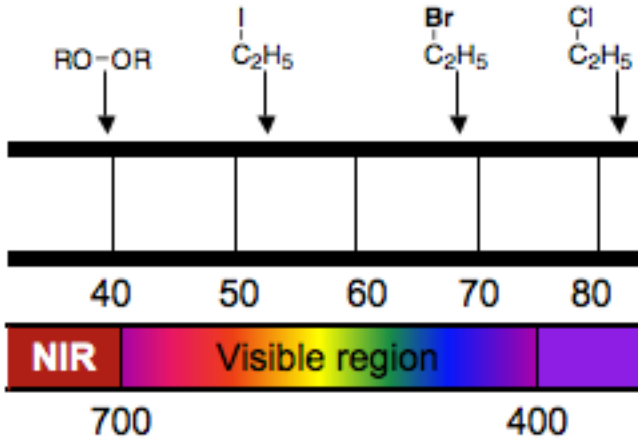
Occurs easily at easily accessible temperatures (<100°C)

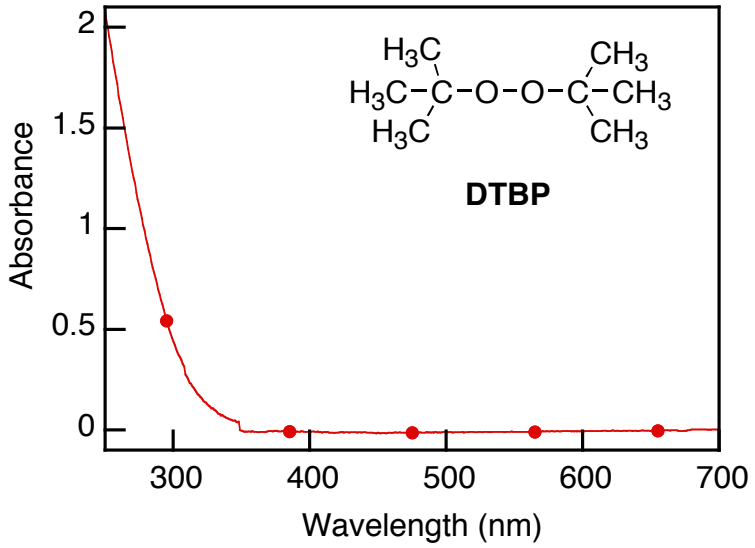
Wavelength and energy

- The necessary energy to break a bond can be delivered either thermally or photochemically



The 1st Law of Photochemistry





Only photons that are absorbed can induce a photochemical process

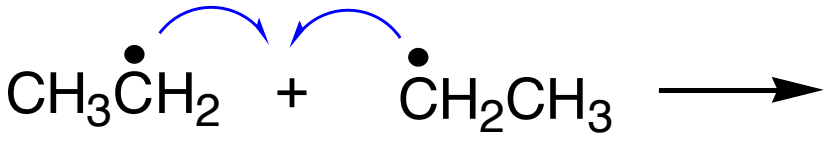
Geminate radical pairs

- A nascent radical pair is called a **"geminate"** radical pair for the brief period in which they remain close to each other.
- After initial separation, the **"free"** radicals can react with other free radicals or with other molecules present.

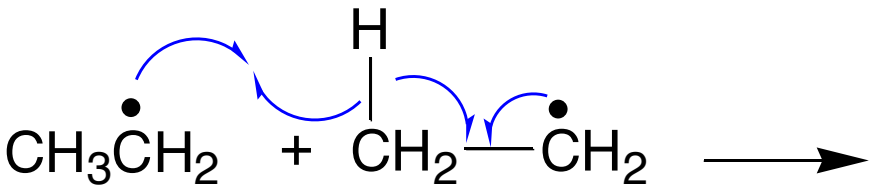
Why do they stay "close to each other" for some time, rather than separate immediately?

Radical-radical reactions

- two types: **combination** or **disproportionation**
- usually, these reactions are highly exothermic



$CH_3CH_2CH_2CH_3$ combination 85%



$C_2H_6 + C_2H_4$ disproportionation 15%

What are the criteria for disproportionation?

1. one radical must have at least **2 carbons**

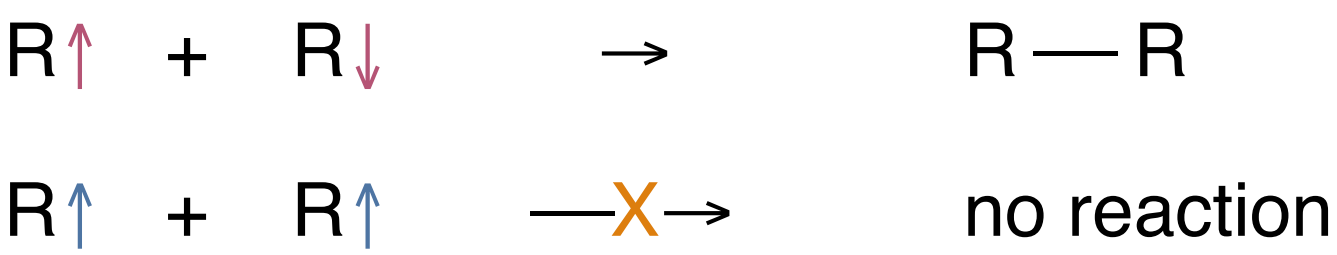
2. one radical must have at least **1 β-H**

Rate constants for radical-radical reactions

- In solution: $k_{max} = \frac{1}{4} \cdot k_{diff}$
  - this reflects spin statistical factors
- Typical rate constants: 1 – 5 x 10^9 $M^{-1}s^{-1}$ range

Radical	Solvent	Rate constant (M^{-1} s^{-1})
CH_3•	cyclohexane	4.5 x 10^9
c-C_6H_{11}•	cyclohexane	1.4 x 10^9
$PhCH_2$•	cyclohexane	1.0 x 10^9
$PhCH_2$•	benzene	0.9 x 10^9
CCl_3•	CCl_4	2.5 x 10^9

Why only one quarter…?



- Only 1 out of 4 encounters have the necessary spin configuration for reaction
- As a result when we say a reaction is diffusion controlled we mean that *all encounters with the correct spin configuration* lead to products

Activation energy for radical-radical reactions

- In the gas phase:

  $E_a \sim 0$

- In solution:

  $E_a \sim 2\text{-}3$ kcal/mol

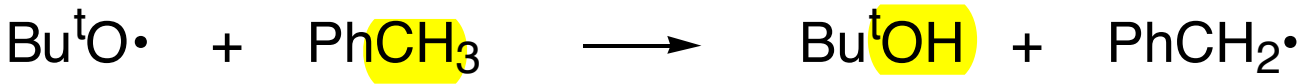
Types of radical-molecule reactions

1. Atom transfer or abstraction
2. Addition to π systems
3. Electron transfer
4. Homolytic substitution at polyatomic centres

1. Atom transfer or abstraction

This is a reaction that moves a hydrogen from one molecule to another. This transfers hydrogen atoms not protons. Typically in most cases the type of chemistry is controlled by thermodynamics deltaH. We are making a OH bond and breaking a C-H bond. The bond we are breaking is toluene and it is a relative weak bond because the product of the reaction has resonance

- usually, these are hydrogen abstractions
- favourable when a strong X-H bond is formed, or there is an increase in bond order

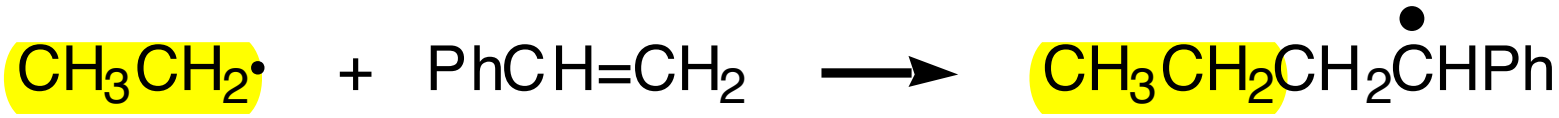


This is the most common type of hydrogen abstraction

stabilization. The bond we are breaking is 14kcal/mol less than the bond we are making.

2. Addition to π systems

- usually, to multiple bonds or aromatic rings
- constitutes the basis for *vinyl polymerization* (Ch. 10)
- important example: reaction with molecular oxygen

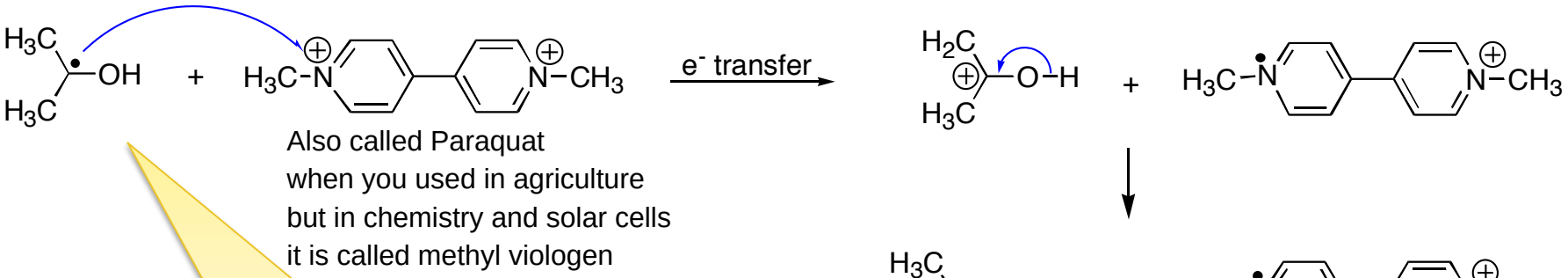


This is a reaction in which a carbon centered radical has to break to form a bigger radical molecule. The point of attack is the CH2 and this is the very first step in making polystyline. Why the CH2 and not the CH? The electron close to the benzene ring will cause a delocalized benzene ring.

3. Electron transfer

in this case you transfer an electron. The compound is popular because it is colorless.

Methyl viologen



Also called Paraquat
when you used in agriculture
but in chemistry and solar cells
it is called methyl viologen

Ketyl radicals are excellent hydrogen donors

Methyl viologen radical cation

4. S_H2 reactions

- less common
- possible with Lewis Acids

The H in SH2 reaction is homolytic substitution reaction pathway. Bimolecular helps homolytic substitution reaction. Not very common but it is one of the free radical reaction.

Some bond strengths – again, note the trends…

The more substitution, the weaker the bond. The more s character the bond has, the stronger the bond is.

Molecule	BDE, kcal/mol	
CH_3-H	105	methane
CH_3-CH_2-H	100	primary
$(CH_3)_2$CH-H	96	secondary
$(CH_3)_3$C-H	94	tertiary
CH_2=CH-H	106	vinyl
C_6H_5-H	111	phenyl
$C_6H_5CH_2$-H	88	benzyl
CH_2=$CHCH_2$-H	86	allyl
CH_3O-H	108	alcohol

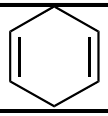
Rate constants for some radical-molecule reactions

When the radicals you make are very stable radical then the rate constants have a trend if not it will be higher than the rate constants of other reactions.

Reaction	Rate constant (M^{-1} s^{-1})
$^tBuO\cdot + PhCH_3 \longrightarrow {}^tBuOH + PhCH_2\cdot$	2.3×10^5
$^tBuO\cdot + PhCH_2CH_3 \longrightarrow {}^tBuOH + Ph\dot{C}HCH_3$	1.05×10^6
$^tBuO\cdot + CH_3CHOHCH_3 \longrightarrow {}^tBuOH + CH_3\dot{C}OHCH_3$	1.8×10^6
$^tBuO\cdot +$  $\longrightarrow {}^tBuOH +$ 	5.4×10^7
$^tBuO\cdot + {}^tBuOOH \longrightarrow {}^tBuOH + {}^tBuOO\cdot$	2.5×10^8
$CH_3\cdot + Bu_3SnH \longrightarrow CH_4 + Bu_3Sn\cdot$	1.1×10^7
$^tBu\cdot + Bu_3SnH \longrightarrow {}^tBuH + Bu_3Sn\cdot$	1.9×10^6
$C_6H_5\cdot + C_6H_5CH{=}CH_2 \longrightarrow C_6H_5CH_2\dot{C}HC_6H_5$	1.1×10^8
$C_6H_5\cdot + CH_3CHOHCH_3 \longrightarrow C_6H_6 + CH_3\dot{C}OHCH_3$	1.4×10^6
$C_6H_5\cdot + CCl_4 \longrightarrow C_6H_5Cl + CCl_3\cdot$	7.8×10^6
$C_6H_5CH_2\cdot + O_2 \longrightarrow C_6H_5CH_2OO\cdot$	3.4×10^9
$^tBu\cdot + O_2 \longrightarrow {}^tBuOO\cdot$	4.9×10^9

Perfect example
Higher rate constant.

Let's look at some selected examples…

Reaction	Rate constant (M^{-1} s^{-1})
$^{t}BuO\cdot$ + $PhCH_3$ ⟶ $^{t}BuOH$ + $PhCH_2\cdot$	2.3×10^5
$^{t}BuO\cdot$ + $PhCH_2CH_3$ ⟶ $^{t}BuOH$ + $Ph\dot{C}HCH_3$	1.05×10^6
$^{t}BuO\cdot$ + $CH_3CHOHCH_3$ ⟶ $^{t}BuOH$ + $CH_3\dot{C}OHCH_3$	1.8×10^6
$^{t}BuO\cdot$ +  ⟶ $^{t}BuOH$ + 	5.4×10^7

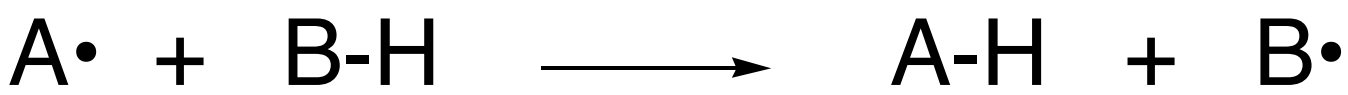
Reactions with oxygen

Reaction	Rate Constant ($M^{-1}s^{-1}$)
$C_6H_5CH_2\bullet + O_2 \longrightarrow C_6H_5CH_2OO\bullet$	3.4×10^9
$^tBu\bullet + O_2 \longrightarrow {}^tBuOO\bullet$	4.9×10^9

- these are *extremely* fast reactions, with rates approaching diffusion control

Do we need to know the number? No. If you are taking an antioxidant it doesn't matter if it reacts with the carbon centered radical but we have to make sure it traps the peroxyl radical because that is the one that will be going around.

How can we accelerate reaction rates? Example: Hydrogen Abstractions



- The formation of a strong bond
- The cleavage of a weak bond

} Favourable enthalpy change

- A large number of equivalent hydrogens
- Low steric hindrance
- In solution, a low viscosity
- High temperature

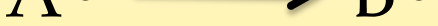
The more the equivalents the faster the reaction will be. High temperature helps twice because reactions have faster kinetics when the temperature is high and it also helps decrease the viscosity of the solvent assuming its a solvent.

Unimolecular radical reactions

- Two classes:

Fragmentations

Rearrangements

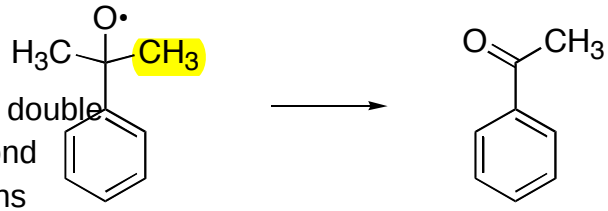


Radicals do unimolecular chemistry. They can fall apart and separate and also rearrange.

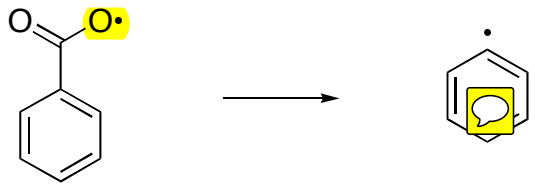
Fragmentation reactions

- radical → new radical + neutral molecule
- known as β-cleavage or β-scission
- break the weakest bond, when possible
- driving force: formation of a double bond and/or release of a small gaseous molecule

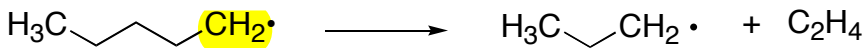
They all have something in common, in all examples we are making additions of a double. The formation of the extra bond is what is making the reactions stable. If one has a long molecule it will start loosing C2H4 gradually.



+ CH_3• (A)



+ CO_2 (B)



+ C_2H_4 (C)

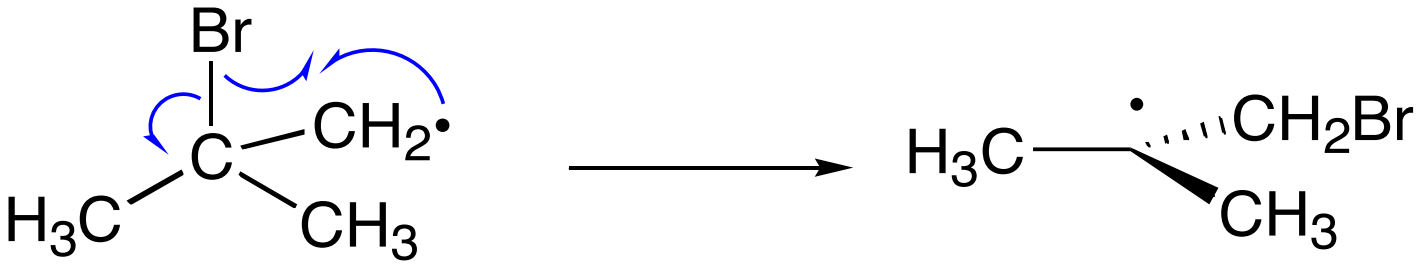
Rearrangements

- isomerizations, intramolecular atom transfers, etc.
- usually associated with a favourable enthalpy change

This means one radical on the left and on radical on the right, nothing else.

1,2-atom transfers

- not very common (compared to 1,2-H shifts in carbocations)

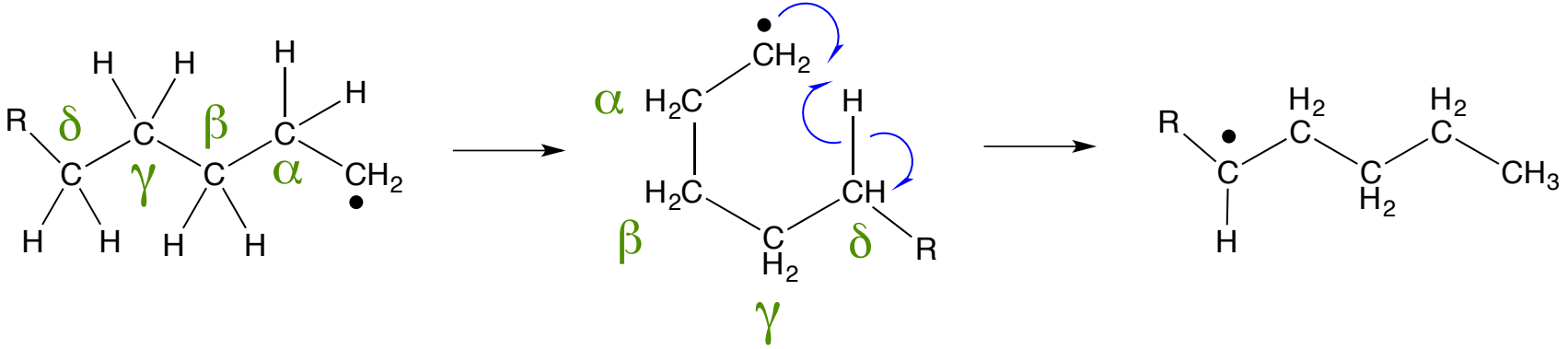


- what is the driving force?

Bromine is a big thing to move. The radical is most stable on a tertiary carbon. That is why the bromine has to move

1,5-atom transfers

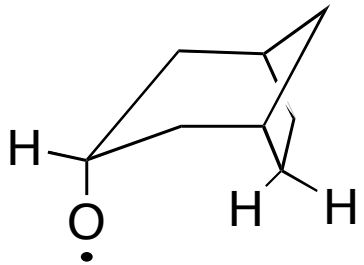
- more frequent: occur via a 6-membered transition state

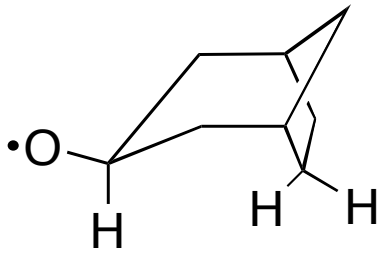


- sometimes known as the "back-biting" reaction

6-membered rings have no strain or stress. We went from a primary radical to a secondary radical which is more stable. If the product had an H attached to the carbon then it will be the same as the reagent.

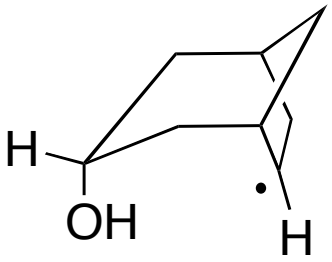
Stereochemical control:
Being in the right place at the right time





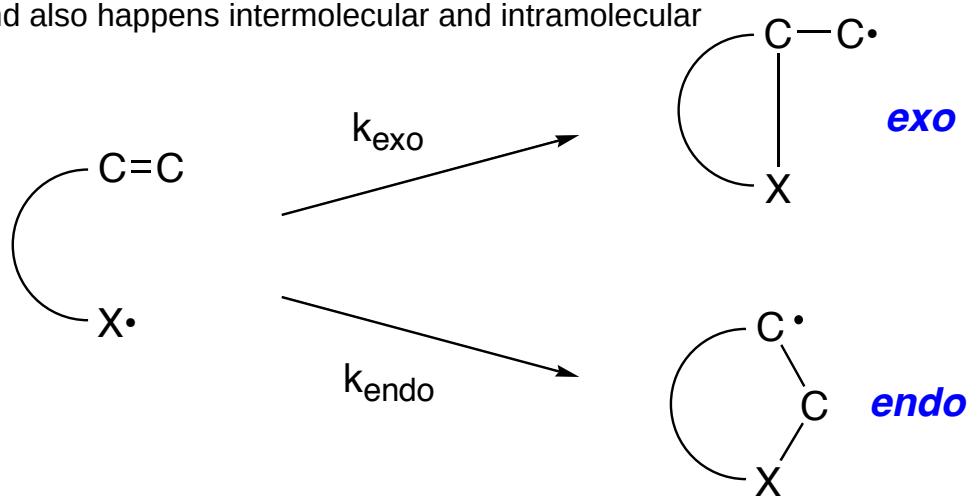
In this reaction, the oxygen is too far so transfer of atoms is far and not in close proximity to occur PROXIMITY is important.

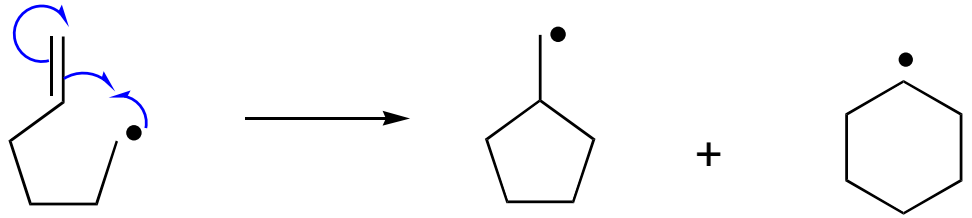
NO REACTION



Free radical rearrangements: Cyclizations *via* intramolecular π-addition

The addition to double bond also happens intermolecular and intramolecular





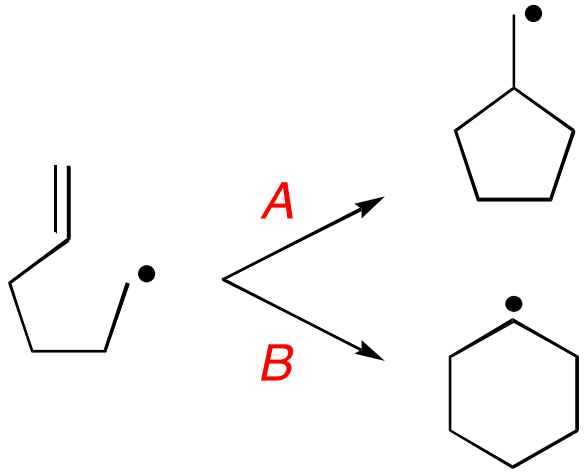
Hexenyl

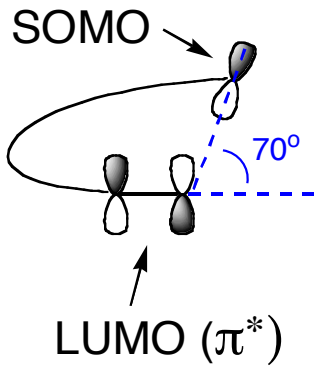
The product of this molecule does not follow the rules we have been talking about.

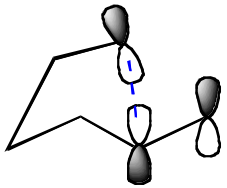
exo ***98%***

endo ***2%***

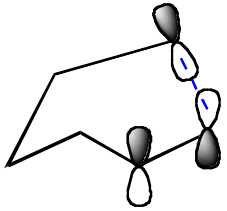
Why *exo* and not *endo*?







5-membered ring



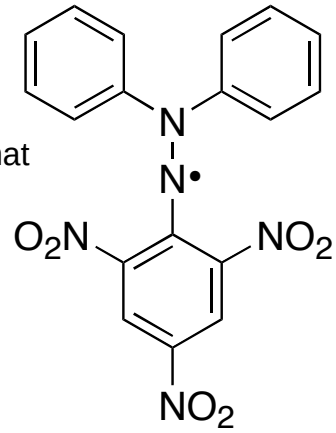
6-membered ring

Persistent radicals

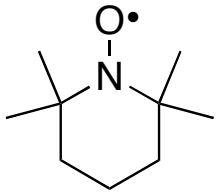
- "**stable**" radicals ⇒ thermodynamic term
- "**persistent**" radicals ⇒ kinetic term
- 2 criteria:
  - do NOT react with themselves
  - do NOT react (quickly) with oxygen

You can not buy many radicals because they have rich chemistry and can react with oxygen or with themselves. The persistent versus stable is just nomenclature

You can make free radicals that are stable enough to put in a bottle.



DPPH

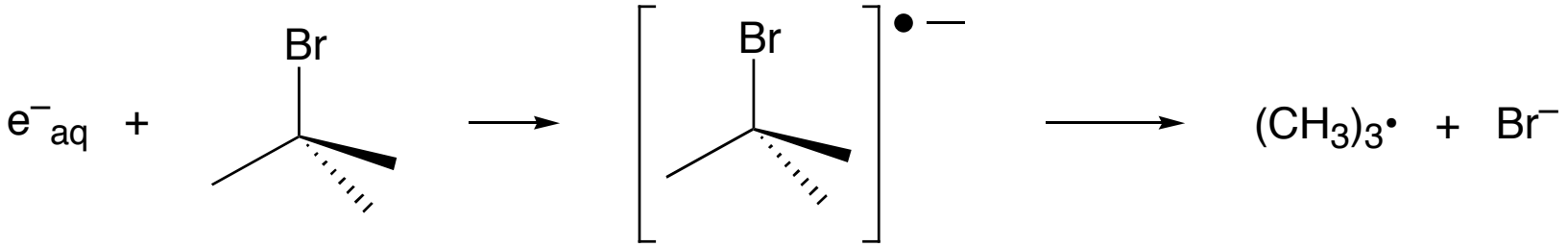


TEMPO

You can make electrons in many ways e.g. using electrodes.

The electron as a free radical (has an odd number of electrons)

- a "free" electron in solution
  - surrounded by solvent molecules: "solvated electrons"
  - if solvent = water: "hydrated electrons"
  - highly reactive ($k \sim k_{diff}$)



How would an electron react with *tert*-butyl acetate?

It is when things get together and stick together and they stick together for about 1 nanosecond. Molecules collide about a 100 times in the period of time when they encounter.

Diffusion-controlled reactions

- often, radical reactions are so fast they are referred to as "diffusion-controlled"

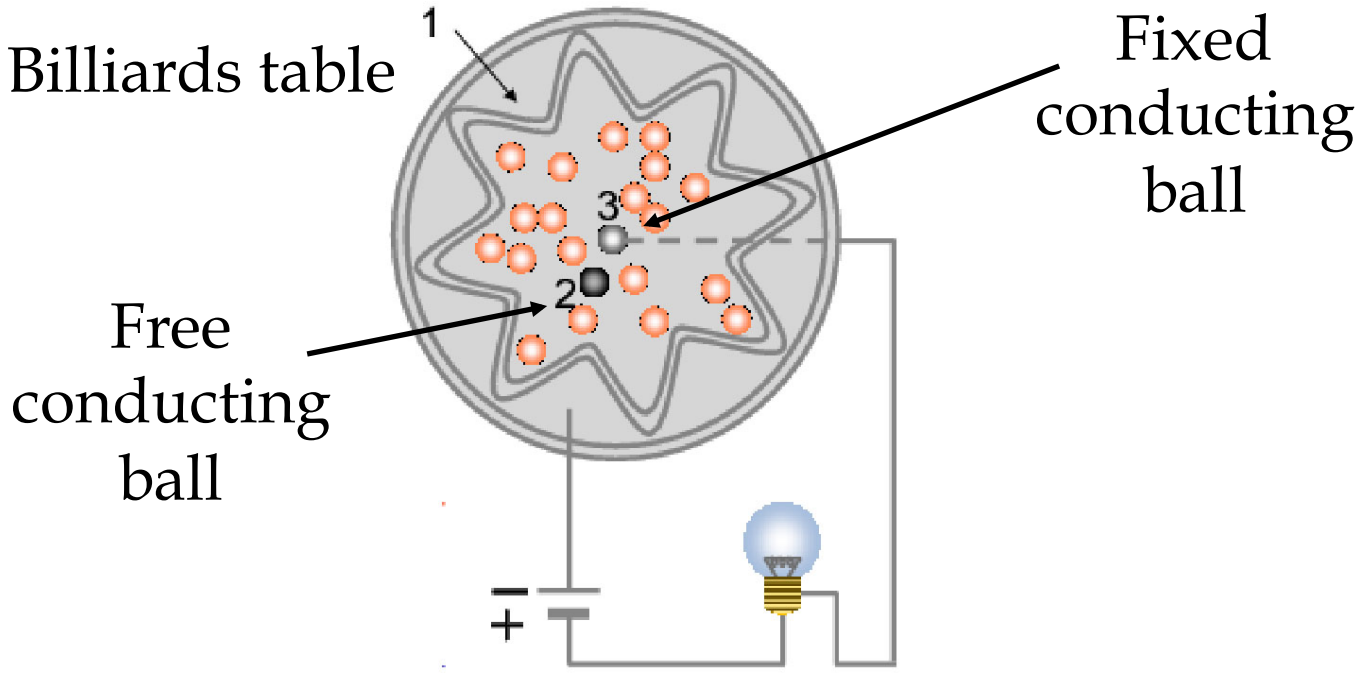
A diffusion controlled rate constant in solution at RT is typically:

$$k_{diff} \sim 10^{10}\ M^{-1}s^{-1}$$

But what does this really mean?

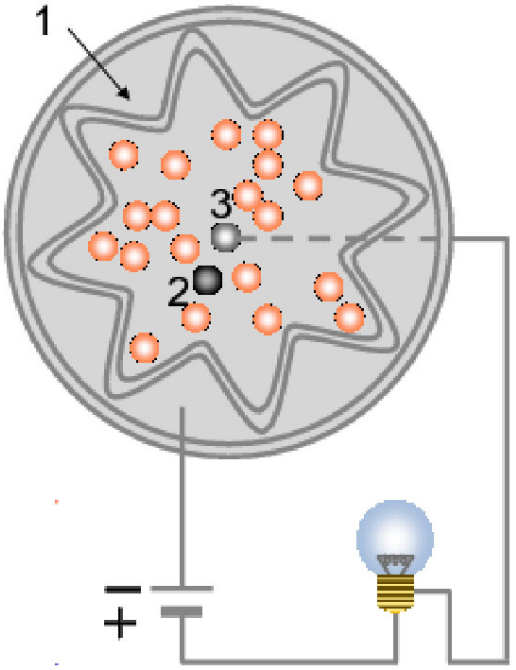
ENCOUNTERS AND THE CAGE EFFECT

A famous experiment by Rabinowitch and Wood (1936)



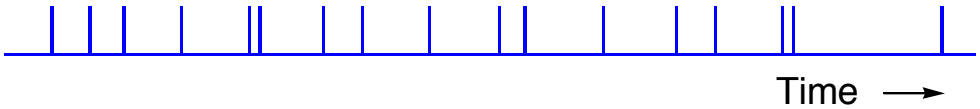
Source: "The Collison Mechanism and The Primary Photochemical Process in Solutions" E. Rabinowitch and W. C. Wood Trans. Faraday Soc., 32(1936) 1381-1387

A famous experiment by Rabinowitch and Wood (1936)

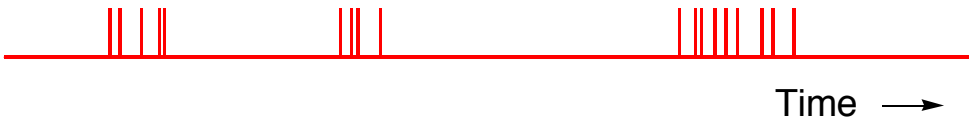


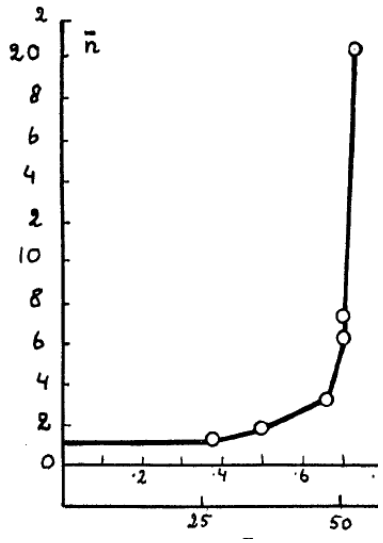
Source: "The Collison Mechanism and The Primary Photochemical Process in Solutions" E. Rabinowitch and W. C. Wood Trans. Faraday Soc., 32(1936) 1381-1387

(a) Low density - 25 wooden balls



(b) High density - 50 wooden balls

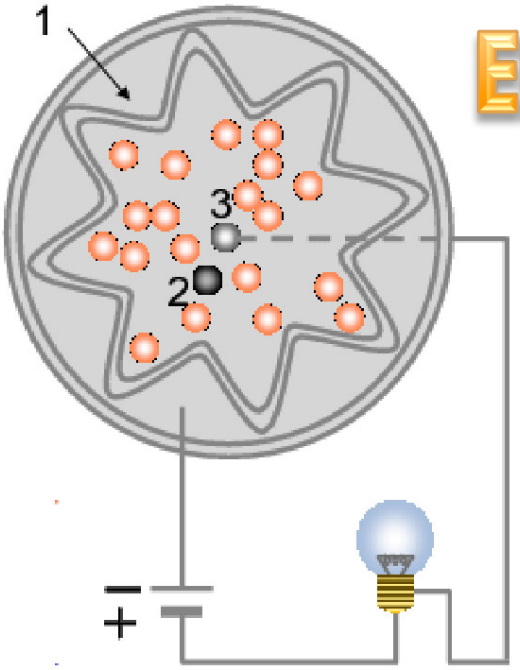




The way the collision occurred is different from how it occurred when the density was increased.

A famous experiment by Rabinowitch and Wood (1936)

They react every time they collide.



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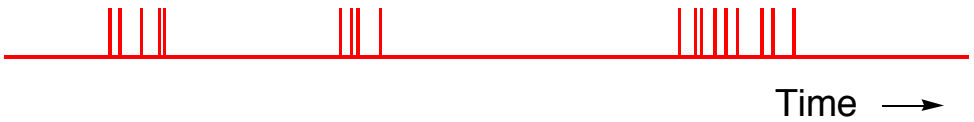
ENCOUNTERS AND THE CAGE EFFECT

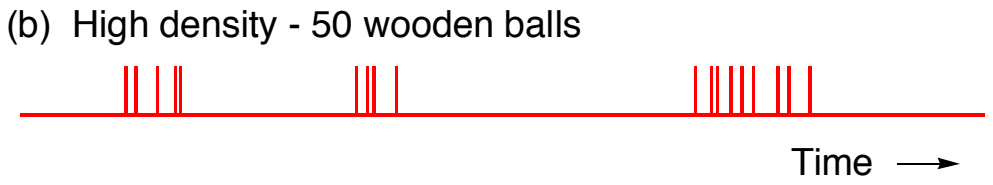
(b) High density - 50 wooden balls



Cage effect = surrounding solvent molecules prevent the separation of two species

Encounter = series of collisions between two species in solution

Encounters and diffusion control



- Let's assume that reaction probabilities are such that it takes 4 collisions for the reaction to occur
- In the above case, a reaction would therefore occur *at every encounter*
- The reaction can thus be described as "**encounter-controlled**"

DIFFUSION-CONTROLLED

Diffusion-controlled rate constants

- diffusion, or the time it takes for two species to meet in solution, determines the kinetics of the reaction A molecules have a diameter of 5 ounce strong in a perfect sphere and the same for solvent.

$$k_{diff} = \frac{8RT}{3000\eta}$$ The viscosity

η = viscosity, measured in *poise* ($g \bullet cm^{-1} \bullet s^{-1}$)
R = gas constant, 8.3145×10^7 $erg \bullet mol^{-1} \bullet K^{-1}$

Free radical chain reactions

- very common in free radical chemistry
- definition:
  - when there is more than one molecule of product formed for each free radical introduced in the system
  - when the difference is not due to trivial stoichiometric relationships

The essential steps

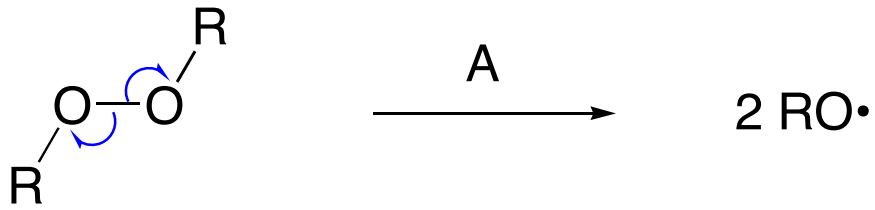
- Initiation
- Transfer
- Propagation
- Termination
- Branching

The lighter colors are steps that are done but not common and they do not cause a chain reaction. Propagation is the interesting one. Termination is the opposite of the initiation, it removes radicals. Making and removal of radical happens in pairs. Branching is a type of reaction where one radical produces more than one radical. Most radicals produce three radicals. Branching has the characteristics of combustion and increases the number of radicals in the system.

The essential steps

Initiation

- generates free radicals from a diamagnetic precursor
- radicals normally generated in pairs



The essential steps

Transfer (not always required)

- converts a radical formed in the initiation into one that participates in one of the propagation steps
- does not alter the number of radicals in the system
- in polymerizations, these reactions usually result in a decrease in the polymer MW

It is called an ID change when transfer occurs. It is also a trick to change the molecular weight of a polymer we are making and it goes in only one way. It will always reduce the molecular weight.

The essential steps

Propagation

- a sequence of two or more reactions that produce the actual products of the chain reaction
- the last step in the sequence regenerates a radical that normally participates in the first step
- sum of all propagation steps = the net reaction

If you have only one reaction for propagation, it is wrong. The reactions have to be two or more. The last step in the propagation reaction should be able to regenerate the first step.
Sum of all propagation steps never includes the free radical because when you add them up, the free radical has to cancel out. Otherwise its not a net reaction.

The essential steps

Termination

- removes radicals from the system giving diamagnetic products
- radicals are removed in pairs

Branching

- only some chain reactions involve branching, where a reaction (or series of reactions) leads to an increased number of radicals in the system

… see Chapter 5: explosions!

Initiation increase the number of total radicals in pairs. Branching is almost like an initiation from one radical to more radicals.

Do the initiation and termination also give products?

Yes, but:

- since the propagation occurs many times for each time the initiation or termination takes place, the products from these steps are **MINOR**
- the **MAJOR** products come from the net reaction (sum of propagation steps)

Chain length

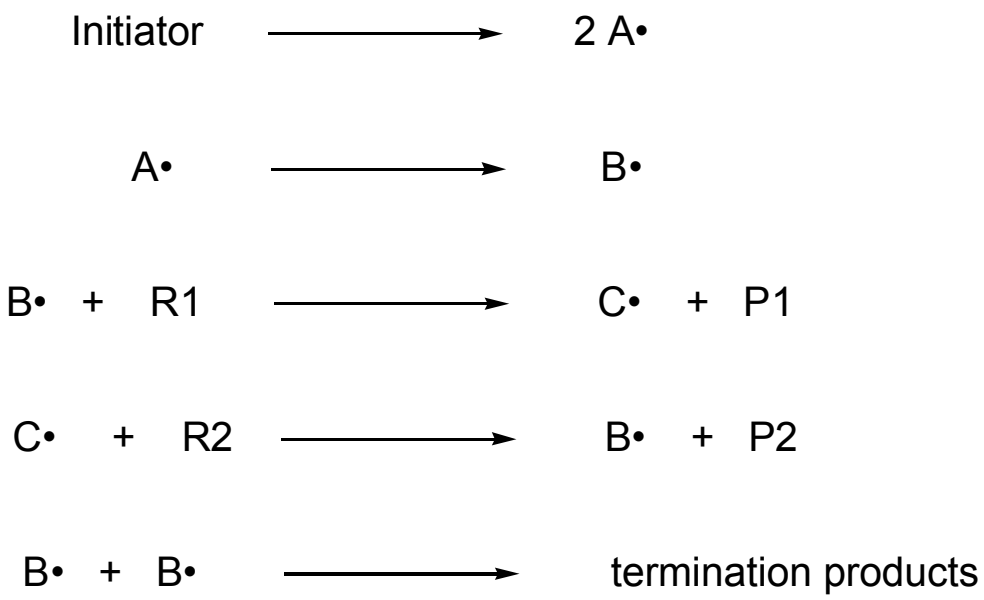
- indicates **how many times** the propagation steps occur for every time the initiation/termination steps take place

$$\text{Chain length} \propto \frac{\text{rate of propagation}}{\text{rate of initiation or termination}}$$

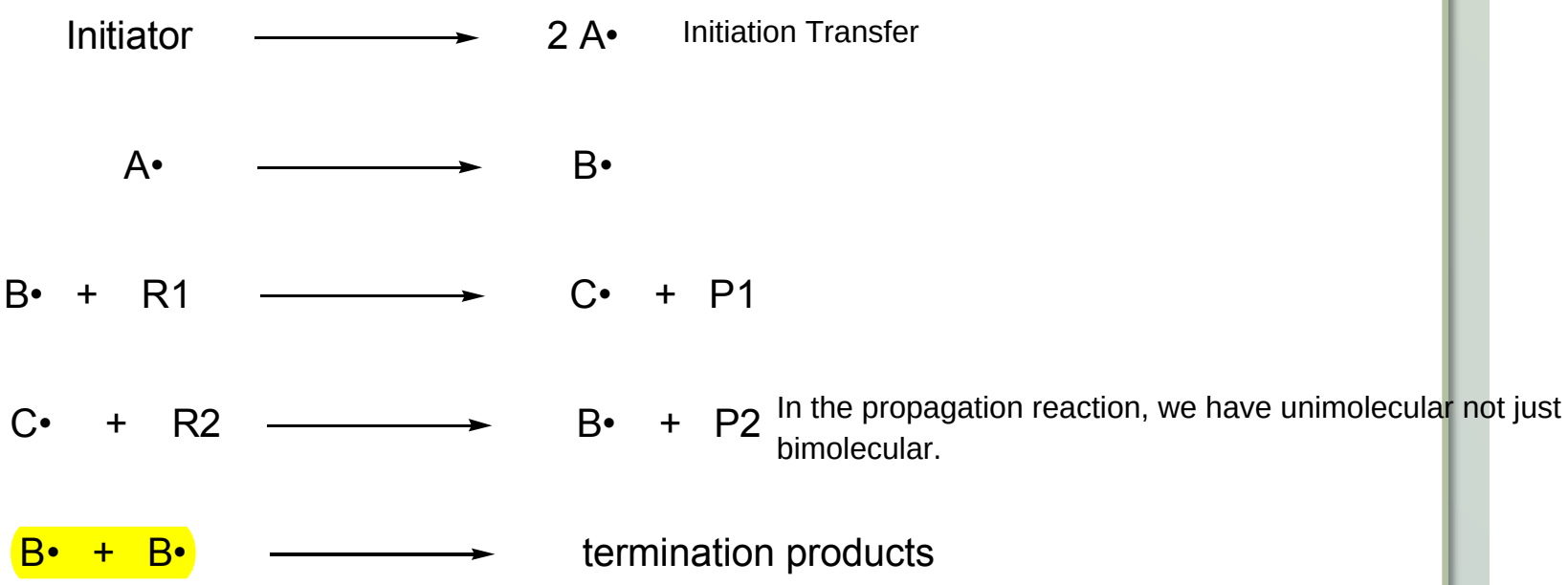
$$\text{Chain length} \propto \frac{\text{product of propagation}}{\text{product of initiation or termination}}$$

The initial rate of initiation and termination are always the same. If the termination is faster it wont be able to propagate for long because after it terminates it stops. If the initiation is faster than the termination reaction in an exothermic reaction then the reaction will be a run away reaction, will just make more radicals and be faster.

Determining the rate expression for a model chain reaction



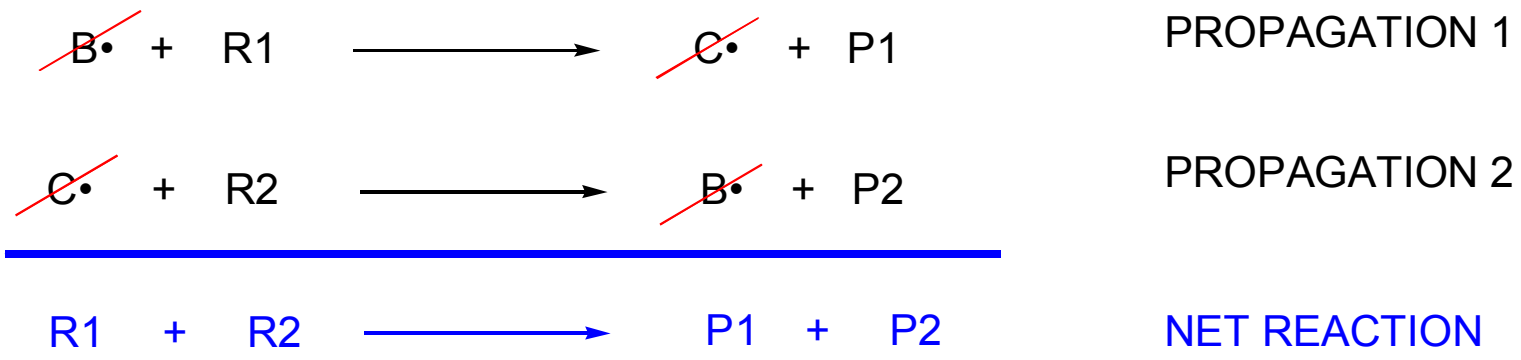
Step 1: Identify all the reaction steps



The two radicals are the same and they equal easy and two different radicals equal to a nightmare.

The Net Reaction

NET REACTION = SUM OF PROPAGATION STEPS



They occur the same number of time because one fits on the other. But they do have different rates though they occur at the same frequency.

- NOTE: If you end up with radicals in the net reaction, you picked the wrong propagation steps!

Step 2: Identify the rate determining step (the RDS)

- in the propagation cycle, one step will be slower than all the others – controls the kinetics of the entire chain!
- the RDS = the reaction bottleneck

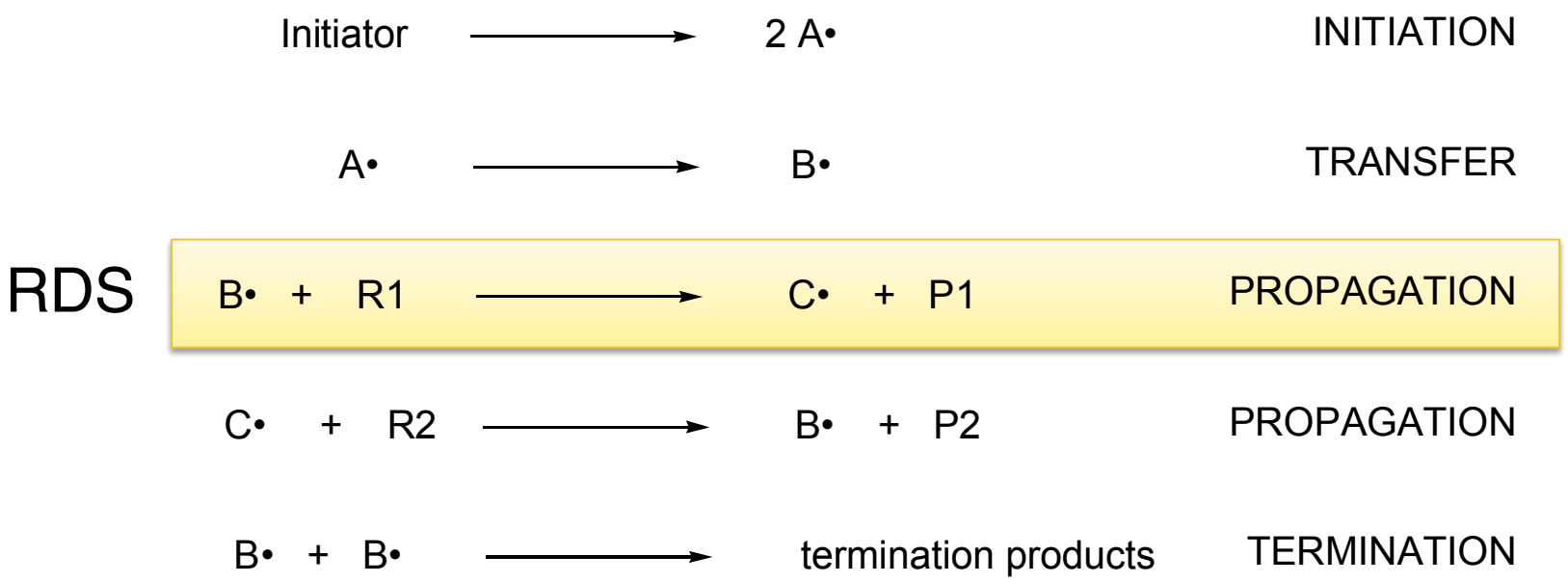
The one that sits around the longest because it has a hard time reacting is usually the one in the termination reaction.

ALL steps in the propagation occur with the same rate!

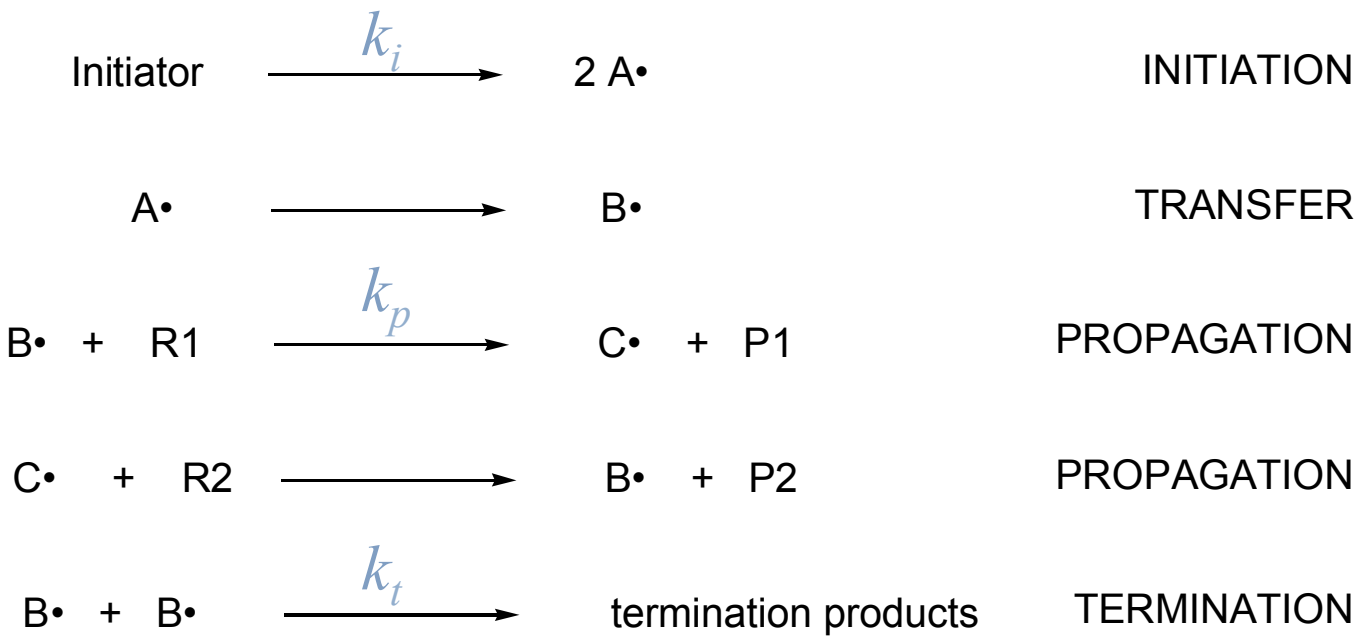
So, how do we identify the RDS?

Step 2: Identify the RDS

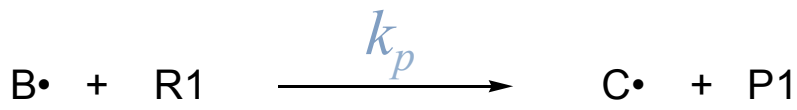
The radical that participates in the rate determining step usually participates also in the termination reaction



Step 3: Label the mechanism with the appropriate rate constants



Step 4: Write the rate equation for the RDS



PROPAGATION

This reactions are elementary steps. It happens the way we write it.

$$Rate = -\frac{d[\mathrm{R1}]}{dt} = +\frac{d[\mathrm{P1}]}{dt} = k_p[\mathrm{B\bullet}][\mathrm{R1}]$$

Usually unknown

Step 5: Use the steady-state approximation

- to solve the rate expression, use the SSA:
  - the rate of radical production is equal to the rate of radical consumption

rate of initiation = rate of termination

- if this wasn't valid, a chain reaction could not take place!
  - if $Rate_i < Rate_t$: the reaction will slow down/stop
  - if $Rate_i > Rate_t$: the reaction will accelerate out of control → explosion!

Step 5: Make the SSA

$$\text{Rate} = 2k_i[\text{Initiator}]$$

$$\text{Rate} = 2k_t[\text{B}\bullet]^2$$

Rate of initiation = Rate of termination

$$2k_i[\text{Initiator}] = 2k_t[\text{B}\bullet]^2$$

Step 6: Rearrange for the unknown radical concentration

$$2k_i[\text{Initiator}] = 2k_t[\text{B}\bullet]^2$$

$$[\text{B}\bullet] = \sqrt{\frac{2k_i[\text{Initiator}]}{2k_t}}$$

Step 7: Substitute back into the original rate expression

$$[\mathrm{B}\bullet] = \sqrt{\frac{2k_i[\mathrm{Initiator}]}{2k_t}}$$

$$Rate = -\frac{d[\mathrm{R1}]}{dt} = +\frac{d[\mathrm{P1}]}{dt} = k_p[\mathrm{B}\bullet][\mathrm{R1}]$$

$$Rate = k_p\left(\frac{2k_i}{2k_t}\right)^{1/2}[\mathrm{Initiator}]^{1/2}[\mathrm{R1}]$$

The overall recipe…

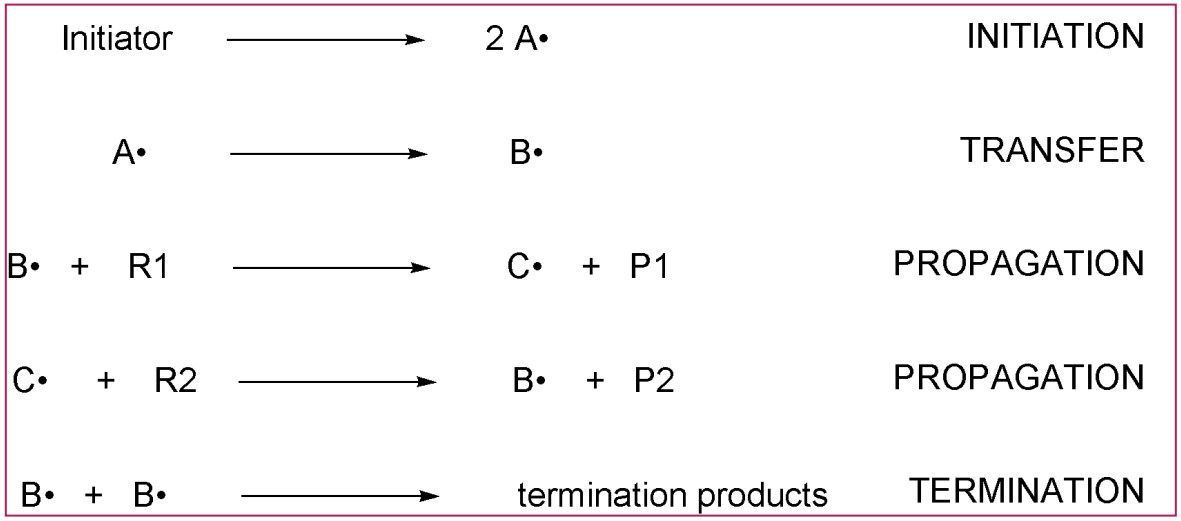
1. Label the inititation, transfer, propagation, and termination steps in the reaction. (Note: not all mechanisms have transfer steps.)
2. Determine the RDS of the mechanism: the radical that appears as a reactant in the RDS also participates in the termination step.
3. Label the mechanism with the appropriate rate constants.
4. Write the rate equation for the RDS. This will normally contain one or more radical concentration.
5. Write an equation that expresses mathematically that:

   rate of initiation = rate of termination
6. Rearrange (5) for the unknown radical concentration.
7. Substitute the radical concentration from (6) into equation (4). You should end up with an equation containing no radical concentrations.

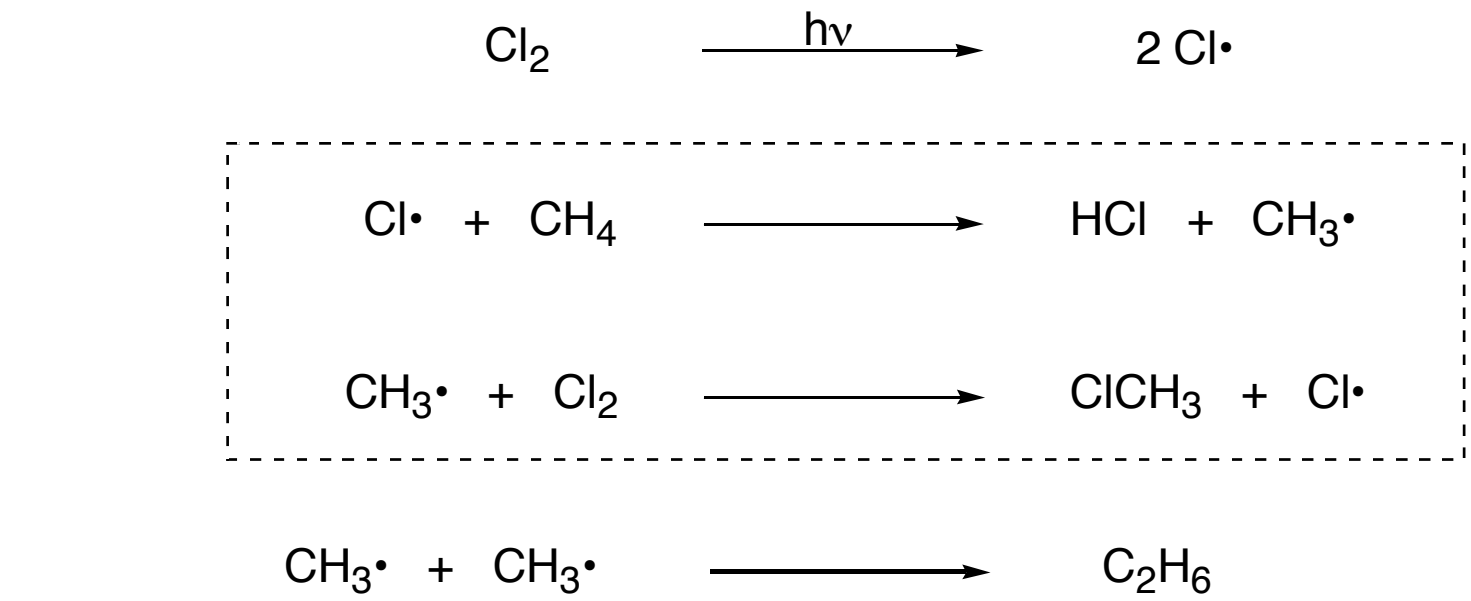
Some reactions do not have transfer steps. Branching and combustion goes together and we are going to have to find out which is the rate determining step and the radical that leaves its fingerprint is usually the one.

How will real chain reactions differ?

- Having more than two propagating steps
- Having some unimolecular reactions (R1 or R2 not involved)
- Having more than one/no transfer step
- Making two different radicals in the initiation
- Terminations involving different types of radicals (e.g., B• + C•)



Chlorination of hydrocarbons



The termination step is metabolical + metabolical to give ethane.

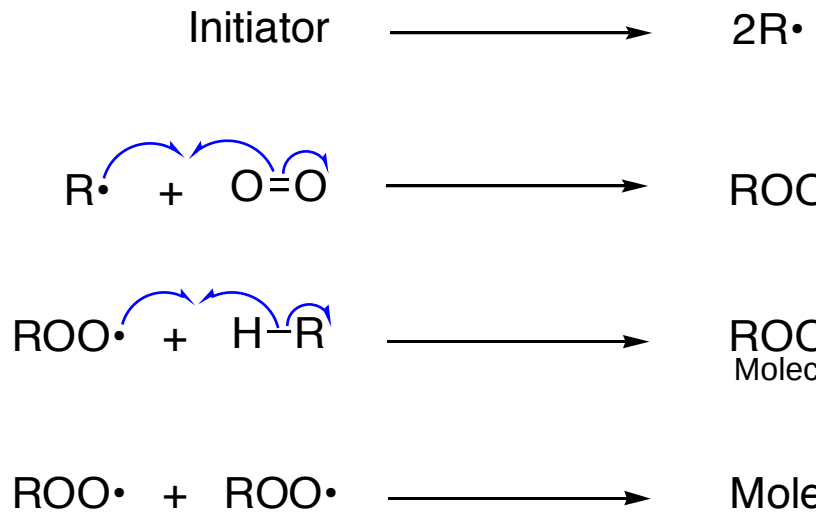
The overall reaction:

$$Cl_2 + CH_4 \xrightarrow{light} HCl + ClCH_3$$

There is no transfer mechanism. This is the easiest and simplest chlorination step. Chlorine is a sort of green gas, so it absorbs visible light. All the elements in the normal state have a heat of formation of zero. There are no endothermic reaction in our chain reactions. Always expect a negative answer otherwise if you get a positive answer it shows they don't happen.

The autooxidation chain reaction

- responsible for the degradation of many materials, the combustion of fuels, and even the ageing process



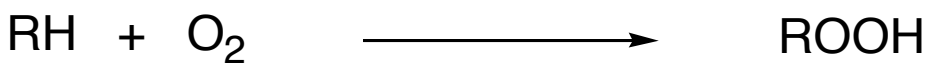
Initiator makes radical and we assume that the radical is carbon centered. Radicals normally react with oxygen very fast and form peroxide with two O's with R and H on both side.

Molecule that has a very weak bond.

More on autooxidation…

Peroxides are very unstable.

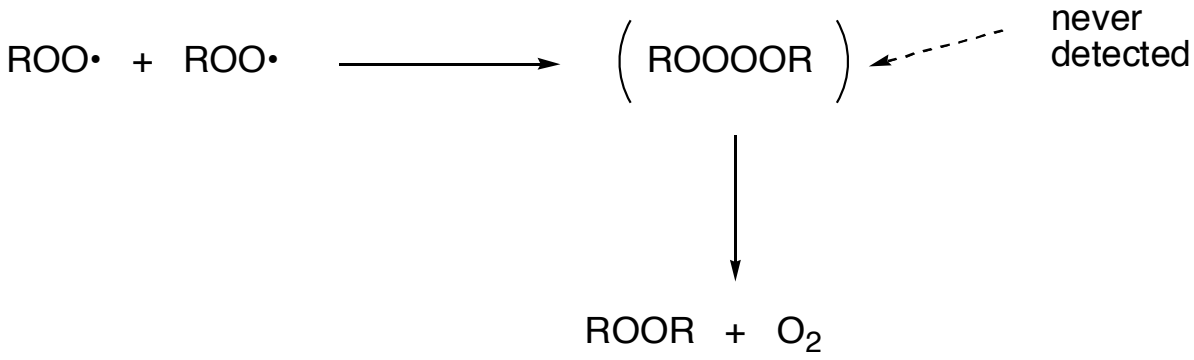
The overall reaction



The rate expression

$$\frac{d[ROOH]}{dt} = \left(\frac{k_i}{k_t}\right)^{1/2} k_p [initiator]^{1/2} [RH]$$

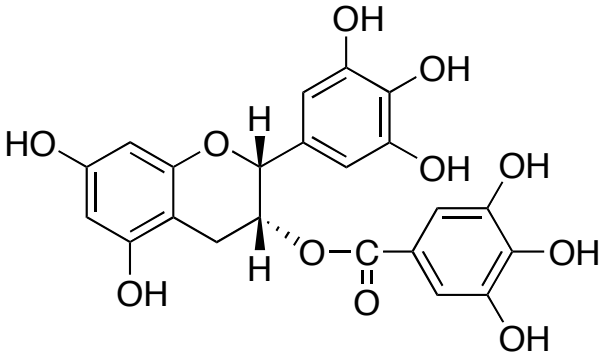
The termination reaction



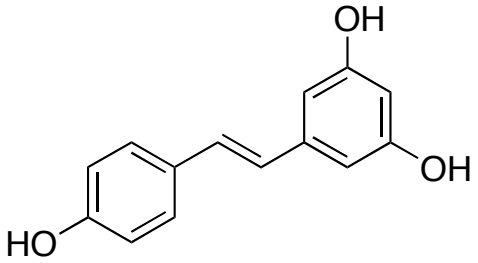
Antioxidants

- molecules which can "trap" radicals
  - they inhibit the autooxidation chain reaction
- two criteria:
  1. a good H donor (contain a weak X-H bond)
  2. produce a radical that does NOT react with oxygen

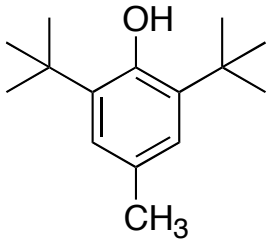
Common Antioxidants…



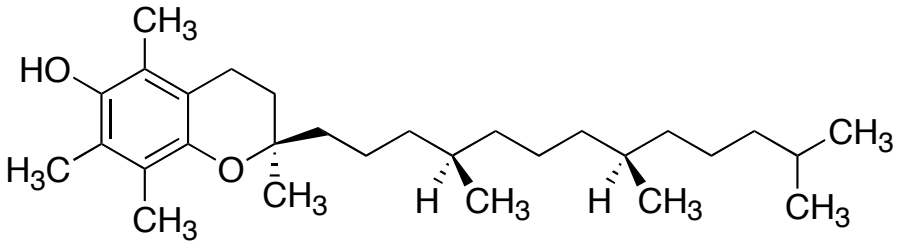
epigallocatechingallate (EGCG)



resveratrol

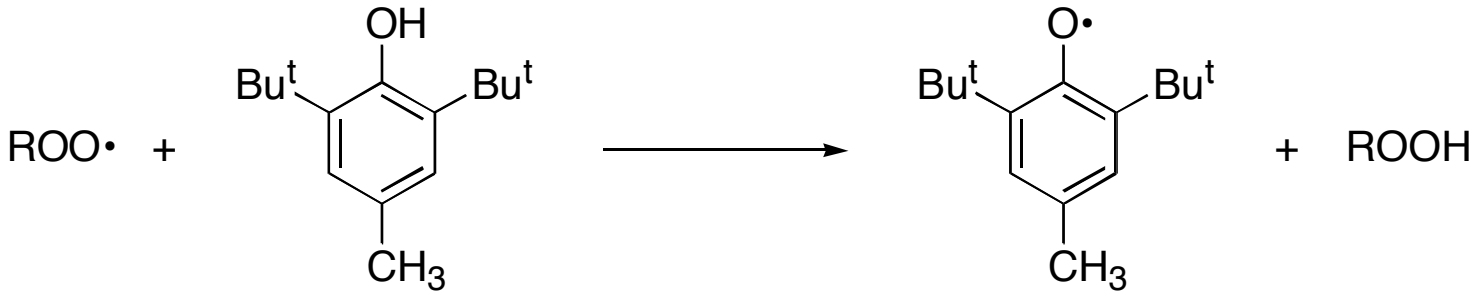


BHT



α-tocopherol (Vitamin E)

n: the stoichiometric factor



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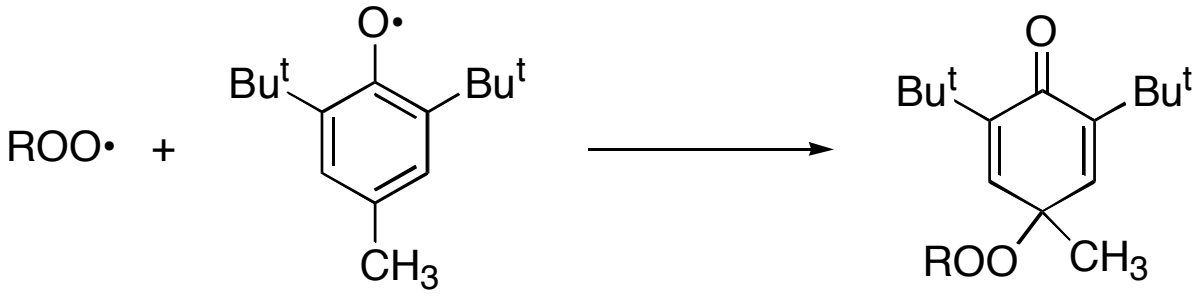
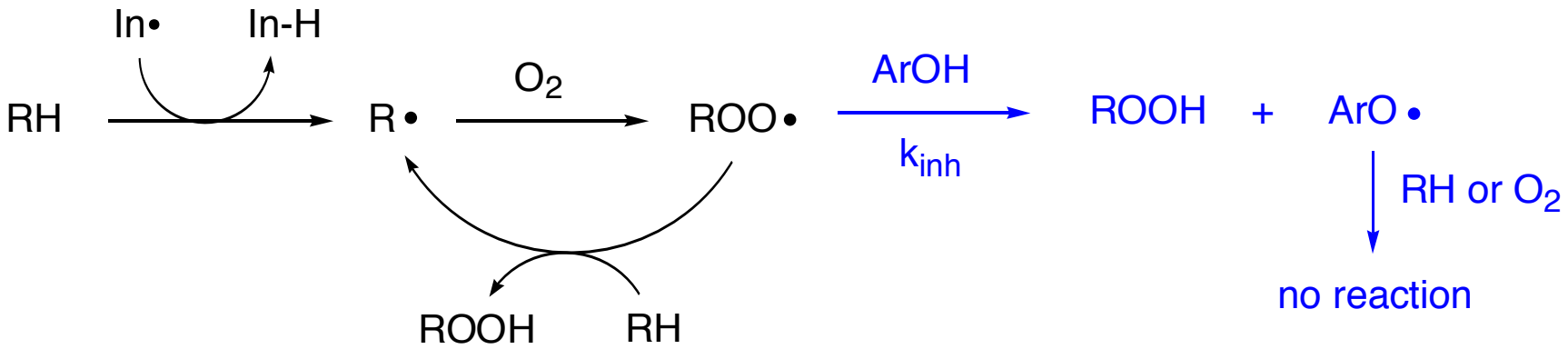


Inhibiting the autooxidation chain

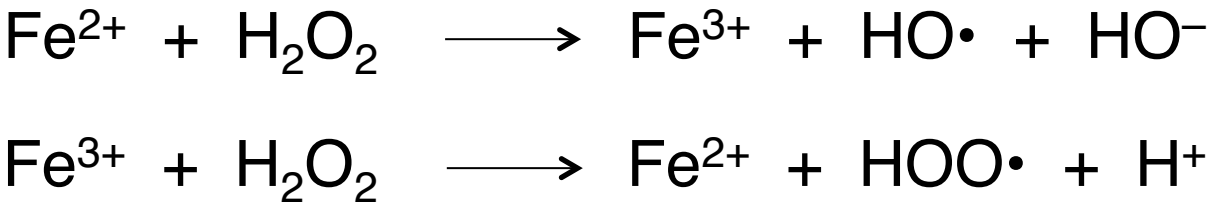
- a good H donor (contain a weak X-H bond)
- produce a radical that does NOT react with oxygen



Propagation simplified.
If you want to stop the consequences of oxidation you can do it in 3 different ways.
1. Stop the initiation. (Hardest way)
2. Eat the peroxy radical with something that is get rid of it.
3. Find some chemistry that gets rid of peroxide if it has already happened.

Fenton Chemistry (1894)

- two-step cycle:



- overall reaction: One way of decomposing peroxide is by using irons (Fe).

Up next…

Chapter 4: Organic Feedstocks