Reactions of Alkanes: Radical Chain Halogenation

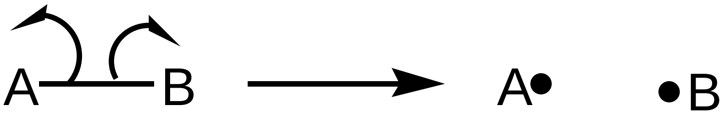
Radicals and Homolysis

Radicals are molecules with unpaired electrons. Radicals can be charged or neutral (e.g. O_2^+ radical and O radical). Radicals can have just one or several unpaired electrons (e.g. O_2 has two unpaired electrons). Here, we will be mostly concerned with the simplest systems: Radicals that are neutral and that have one unpaired electron. These radicals are called **doublets**. Radicals with one unpaired electron can have their unpaired electron either "spin up" or "spin down" (example methyl radical). Because there are these two possibilities for the spin, we call these radicals **doublets**. Closed shell systems have just one possibility for their spin; those systems are **singlets**. Radicals with two unpaired electrons can have their spins up-up, down-down, up-down, and down-up. The latter two "mix" so that there is one spin state with the electron parallel and one where they are antiparallel. The antiparallel case is called an open-shell singlet. The other three spin arrangements have the spins parallel aligned; this is a **triplet** spin state.

Simple rule: Count unpaired electrons and add 1 to get the **multiplicity**.

Lewis Notations. The unpaired electron is shown as a dot (examples for the halogen radicals and so on). The generic radical is denoted R• or X• depending on the EN of the radical carrying atom. Halogen radicals are shown as Cl• even though there also are three lone pairs (goes without saying by now).

Formation by Homolysis. Homolysis describes the breaking of a bond to form **radicals**, that is, a molecule with an odd number of electrons. The homolysis of a bond to form free radicals requires the **bond dissociation energy**. We will be mostly interested in C-H and C-X bonds. Homolysis is indicated with two curved arrows in that each arrow points to the atom on which the electron will end up after the homolytic bond cleavage.



	H	**F**	**Cl**	**Br**	**I**
H-	104	135	103	87	71
Me-	105	110	85	71	57
Et-	98	107	80	68	53
***i*-propyl**	95	106	81	68	53
***t*-butyl**	93	110	81	67	52

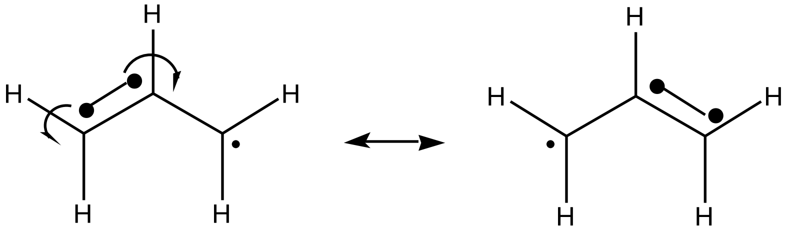
Factors Affecting Radical Stability

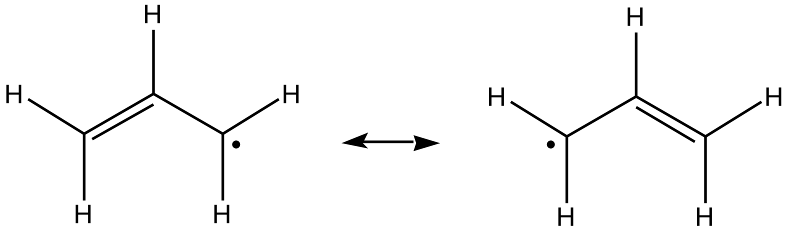
Radicals are **electron deficient** species. Everything that helps to reduce the deficiency stabilizes the radical. Radical site C-atoms are sp^2 hybridized: This puts the remaining electrons as close to the core as possible! (There are some exceptions). In addition: One needs to add electron donors.

(1) Allyl Radical - Stability due to Conjugation

Write the two degenerate resonance forms of allyl radical.

$H_2C{=}CH{-}CH_2\bullet$ $\qquad\qquad$ $\bullet H_2C{-}CH{=}CH_2$

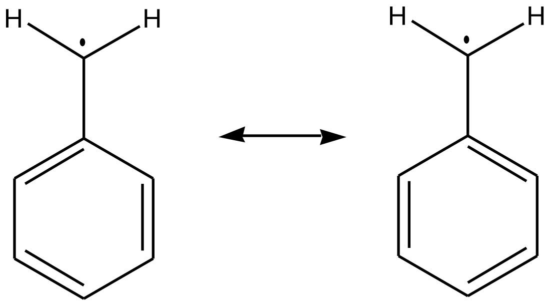




To generate a new resonance from of a radical: Disconnect the π-bond as indicated by the curved arrows above. Then combine two unpaired electrons to form the new resonance form.

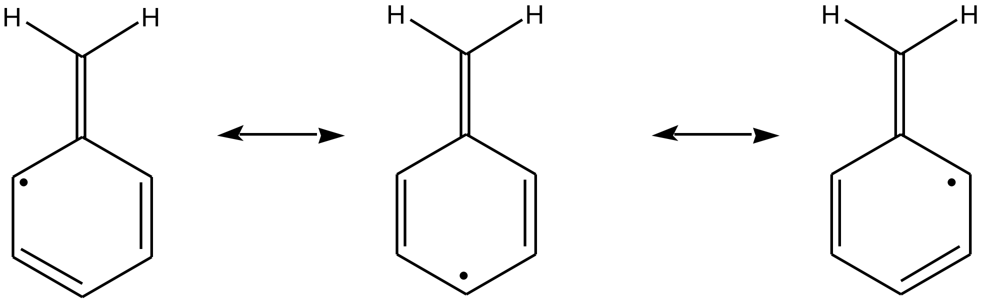
(2) Benzyl Radical - Stability due to Conjugation

(a) Two resonance forms with **exocyclic** radical site



Resonance forms of radicals in which the radical site does not change are generated in the usual fashion by **shifting pairs of electrons** around.

(b) Three resonance forms with **endocyclic** radical position

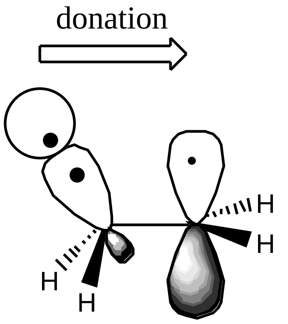


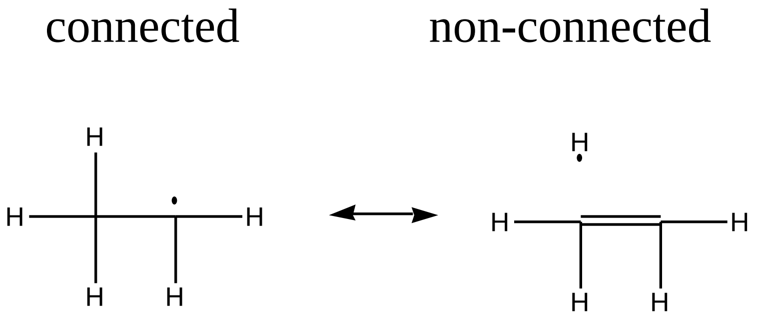
Resonance forms that contain the radical site at different sites are generated in the same fashion as discussed for the allyl radical. Disconnect the π-bond that is next to the radical site. The recombine unpaired electrons to get the new resonance form.

(3) Alkyl Substitution of Radicals - Hyperconjugation

methyl	primary	secondary	tertiary
$H_3C\bullet$	$H_3C\text{-}H_2C\bullet$	$Me_2HC\bullet$	$Me_3C\bullet$

“Hyperconjugation” refers to the notion that electron pairs **from σ-bonds** are being delocalized to reduce the electron deficiency of the radical site. In ethyl radical, the methyl group is aligned such that the C-H bond is parallel to the p-AO of the radical. This arrangement allows for some overlap and some donation.

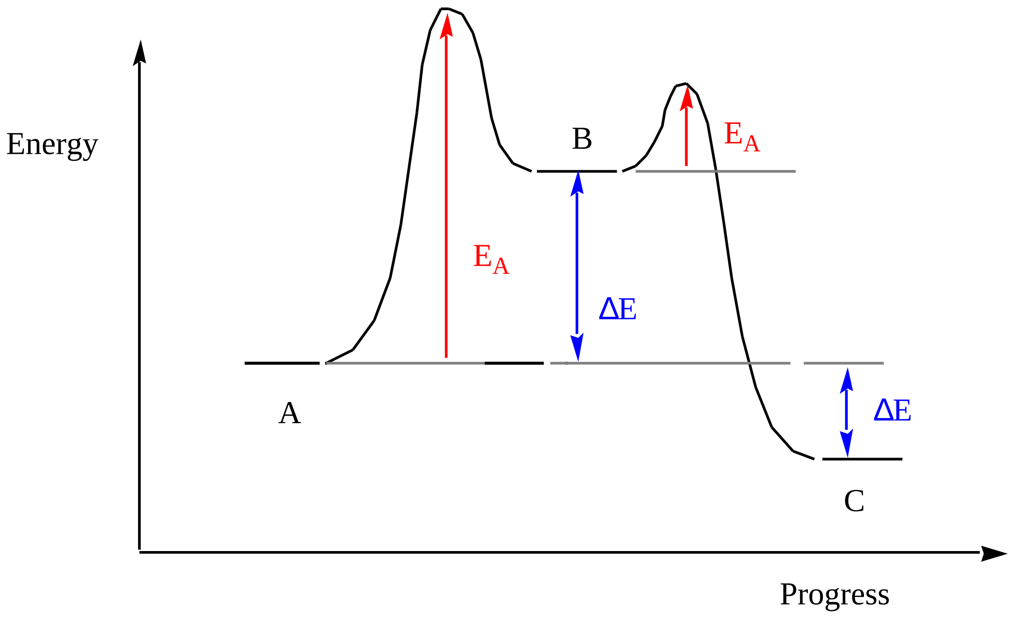




Formally, the hyperconjugation resonance forms are generated very much like the other resonance forms for conjugated radicals. Again we break a bond to the atom that is a next neighbor to the radical site. Then we recombine the electrons forming a new π-bond and leaving the H-atom “unconnected”.

Reaction Energy or Potential Energy Surface Diagram

The vertical axis is **energy**. The horizontal axis is **reaction progress**. This is often called the **reaction coordinate**. In most reactions, several internal coordinates vary and some combination of all of these have to be used to describe the progress.

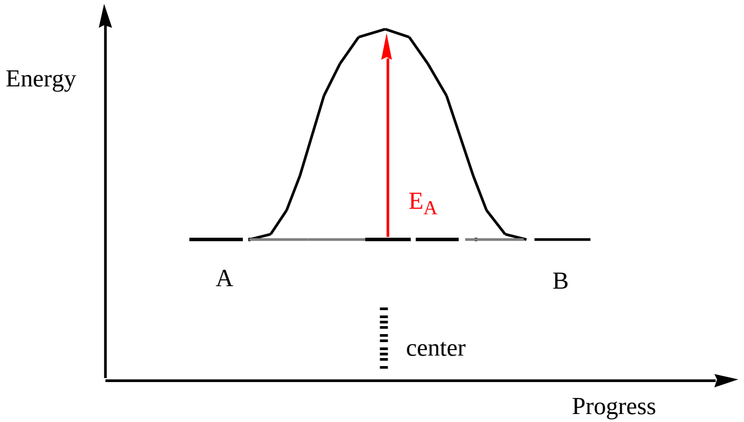


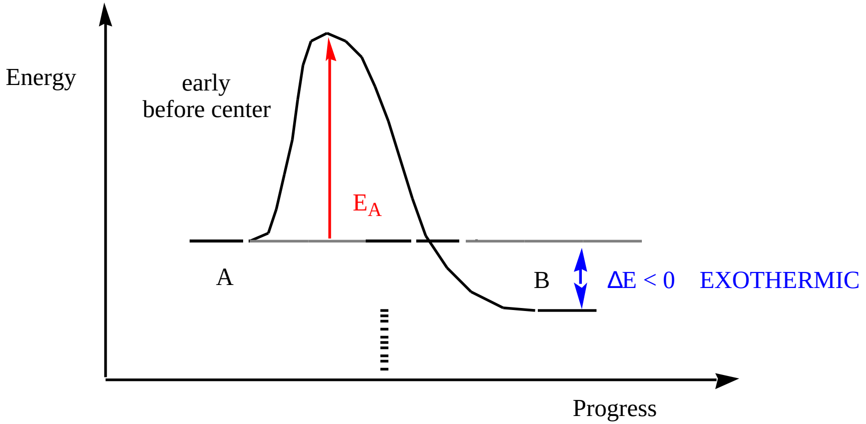
The **extrema** are critical. Minimum (pl. minima) correspond to **stable structures** and **intermediates**. Maximum (pl. maxima) correspond to **transition state** structures.

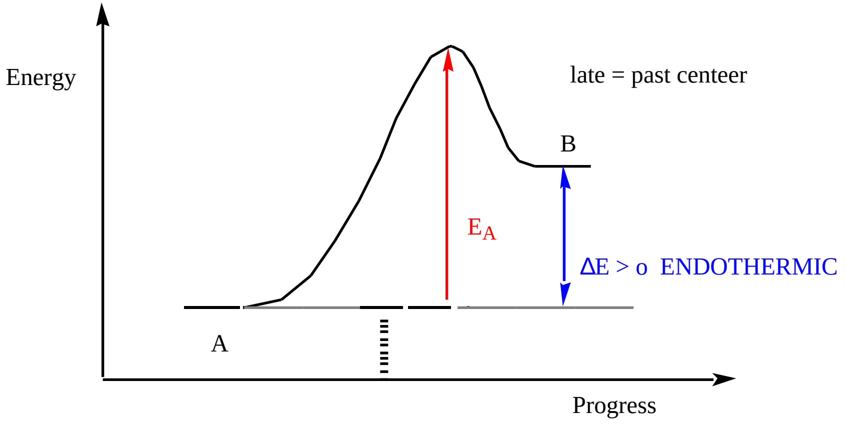
The difference between minima and maxima are **activation barriers** E_A. They control kinetics.
The differences between minima are **reaction energies** **ΔE**. They control thermodynamics.

Hammond’s Postulate

The location of the transition states in PES diagrams can be approximated by the **Hammond Postulate**. The postulate states that the transition state is closer to the high-energy minimum. Early TS in exothermic reactions. Late TS in endothermic reactions.







Kinetics

The rate of a reaction is determined by the rate of the slowest step. The rate can often be expressed by an equation that depends on the concentrations of the starting materials.

$$A + B \dashrightarrow C + D$$

$$\text{Rate} = k\,[A]^a\,[B]^b$$

The orders of the reaction with respect to A and B are a and b, respectively. The **reaction order** is (a+b).

Units of "rate" are concentration change per time: mol / (l sec). Units of the "rate constant" k depends on the reaction order.

The rate constants are related to the activation energies by way of the **Arrhenius Equation**:

$$k = A \exp(-\Delta E/RT)$$

A is the pre-exponential factor. This number has to do with the number of productive *versus* unproductive collisions. Having enough energy is not enough, if the reagent hits the substrate at the wrong place. A typical A can be as small as 10^{-6}.

Thermodynamics

Thermodynamics control the equilibrium of the reaction. The equilibrium constant K depends on the change in the **free energy** of the system.

$$K = \exp(-\Delta G/RT) \quad \text{or} \quad -\Delta G = -2.303\ RT \log(K)$$

The change in free energy during the reaction depends on the change in **enthalpy** and the change in **entropy** during the reaction.

$$\Delta G = \Delta H - T\Delta S$$

ΔG = change in free energy = G(products) - G(reagents)
ΔH = change in enthalpy = H(products) - H(reagents)
ΔS = change in entropy = S(products) - S(reagents)

Common Approximation in Organic Solution Chemistry:

$$\Delta G \approx \Delta H$$

ΔH is accessible via the tabulated values for the bond dissociation energies.

Chlorination of Methane

Overall Reaction: Methane reacts with chlorine under the influence of UV light to form HCl and chloromethane.

$$CH_4 \;+\; Cl_2 \;\text{---->}\; HCl \;+\; H_3CCl$$

The reaction is exothermic.

C-H bond in methane: 105	C-Cl bond formed: 85
Cl-Cl bond: 58	H-Cl bond formed: 103
NEED: 163 kcal/mol	OUT: 188 kcal/mol

So, why does the reaction not proceed right away? To answer this question, we need study the **mechanism** of the reaction.

Mechanism of reaction: A step-by-step description of all of the changes in bonding and energy that occur along the **reaction path** or **reaction coordinate**.

The chlorination of alkanes involves a radical **chain reaction mechanism**. Chain reactions are characterized by regenerating one of the molecules involved in the chain. All in all, there are three types of steps:

(1) **initiation** reaction to start the chain reaction,

(2) **propagation** reactions (2 or more reactions) to keep the reaction going, and

(3) **termination** step (or several).

Initiation Reaction - Make Reactive Radicals

Homolysis of chlorine with heat (300 ˚C) or UV light.

Cl_2 ----> 2 Cl• requires 58 kcal/mol

Propagation Steps I & II - Productive Radical Reactions

Step 1: Cl• abstracts H from methane to give H_3C• and HCl

Cl• + H-CH_3 ----> Cl-H + H_3C•

Step 2: H_3C• reacts with Cl_2 and forms product and a new Cl•

H_3C• + Cl_2 ----> Cl-CH_3 + Cl•

Steps 1 & 2 combined: The chlorine atom acts as a catalyst!

Cl• + CH_4 + Cl_2 ----> H_3CCl + HCl + Cl•

The propagation reaction yields the product, the chlorinated alkane and also a new chlorine radical. Each initially formed Cl radical will end up producing lots and lots of product. The number of cycles per initial radical is called the **turnover** or **chain length**. The **quantum yield** of the photoreaction is very high. For every photon that was absorbed, there will be many molecules of product formed.

Kinetics of Step 1: Endothermic by 2 kcal/mol!
BDE(C-H) = 105 is higher than BDE(H-Cl) = 103.

Kinetics of Step 2: Exothermic by 27 kcal/mol!
BDE(Cl-Cl) = 58 is lower than BDE(C-Cl) = 85 kcal/mol.

Chain Termination - Destroy Reactive Radicals

Any reaction that sabotages any of the propagation steps.

In the propagation steps the radical reacts with a closed shell system and because of that a new radical is produced always. This works well so long as there are many more closed shell systems then radicals. If that is no longer true, then radicals will bump into radicals. **When radicals collide then they will combine to form closed shell systems**. There are two types of radicals involved; so we have three different possibilities for their pair collisions. Each possibility happens.

Step 1: $Cl\bullet + H\text{-}CH_3 \text{ ---->} \ Cl\text{-}H + H_3C\bullet$
Step 2: $H_3C\bullet + Cl_2 \text{ ---->} \ Cl\text{-}CH_3 + Cl\bullet$

Two chlorine atoms recombine: $2\ Cl\bullet \text{ ---->} \ Cl\text{-}Cl$
Two methyl radicals combine: $2\ H_3C\bullet \text{ ---->} \ H_3C\text{-}CH_3$
Chlorine atom and methyl radical combine. This forms product but **not** in the productive way: $Cl\bullet + H_3C\bullet \text{ ---->} \ Cl\text{-}CH_3$

Larger alkyl radicals also terminate via **disproportionation**. This involves an H-atom transfer:

$$2\ H_3C\text{-}CH_2\bullet \text{ ---->} \ H_3C\text{-}CH_3 + H_2C{=}CH_2$$

Formation of Mixtures

This is a big problem with all of these radical reactions. That's why they are used mainly in industrial processes (with subsequent separation) but not so often in the laboratory.

Note that in the propagation the chlorine reacts with an alkane. Initially just the alkane is present and there is no problem. As the reaction goes on for some time, we will have the alkane and also some already chlorinated alkane present. The chlorine radical is so reactive that it can abstract a H from either one. So, the initial product can become the substrate - the result is poly-chlorination. And so on. The reaction of methane thus yields H_3CCl, H_2CCl_2, $HCCl_3$, and CCl_4.

Homework: Write down all the reaction steps that are involved in the chlorination of chloromethane. (All that is required is to write the propagation steps with chlorinated alkanes.) Also write down all the termination steps that are possible with the polychlorinated species. (Think first about the maximum number of termination reactions. Then write.)

To prevent the formation of mixtures, we play with the concentrations to affect the statistics. For example: High [alkane] ---> high yield of monohalogenation.

Other Halogenations of Methane

Fluorine, chlorine, and bromine all can halogenate alkanes. Why not iodine? Why does fluorine do it so explosively?

Does the reason lie with the initiation reaction?

F_2	37 kcal/mol	Cl_2	58 hardest to break!
Br_2	46	I_2	36 easy to break! same as F_2.

The reason lies with the propagation steps?

Halogen radicals will <u>not always</u> abstract hydrogens from alkanes. The first step is exothermic only for F but not for the others. The abstraction of a H-atom from methane is getting harder and harder in the order F > Cl > Br > I since the H-X bond strength weakens.

Alkyl radicals <u>always</u> will cleave the X_2 molecule. All of the second steps are exothermic. The exothermicity is reduced as the EN of X decreases. The second step always is exothermic but is not exothermic enough for the case of iodine.

	Step 1	**Step 2**	**Overall**	
F	-30	-73	-103	Explosive!!
Cl	+2	-27	-25	**OK**
Br	+18	-25	-7	mild!
I	+34	-21	+13	NO GO!

How do chlorination and bromination get started? A few of the X radicals will always have enough energy ... (Boltzmann)

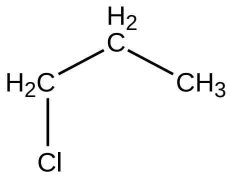
Chlorination of Higher Alkanes: Relative Reactivity and Selectivity.

Ethane reacts instead of Methane

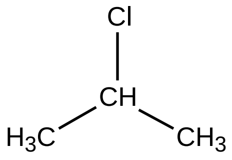
Propagation Step 2 is now exothermic by 5 kcal/mol. Only 98 kcal/mol required to break the CH bond in ethane; 7 less than in methane.

Propane - Now there is a choice of Regiochemistry!

Regiochemistry a matter of statistics!
6 H-atoms in methyls and 2 H-atoms in methylene.
Statistics: methyl:methylene = 3:1
Regiochemistry a matter of Radical Stability?
Will the methyl group react? Less stable radical. BDE = 98.
Will the methylene react? More stable radical. BDE = 94.5.
Winner! Actual outcome: methyl:methylene = 43:57.



1-chloropropane



2-chloropropane

The definition of selectivity:

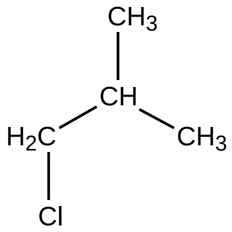
```
yield from methylene / # methylene Hs     57/2
-------------------------------------  =  ----   =  4
  yield from methyl  /  # methyl Hs       43/6
```

(Wade says 4.5, close)

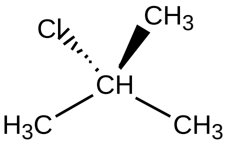
Butane

There are two isomers of butane. The straight chain butane is pretty much like the case discusssed for propane except that there are now two methylene groups. The more interesting case is the branched butane.

Two products from branched butane:
Isobutylchloride from reaction at methyl.
Butylchloride from reaction at tertiary site.



iso-butylchloride



tert.-butylchloride

Statistics: Isobutyl vs butyl = 9 : 1
Actual: Isobutyl vs butyl = 64 : 36 (@ 25 ˚C)
Selectivity = 5.1 (Wade gives the number 5.5, close)

Higher T reduces the selectivity and the ratio becomes more what statistics will tell you.
Actual: Isobutyl vs butyl = 80 : 20 (@ 600 ˚C)

2-Methylbutane

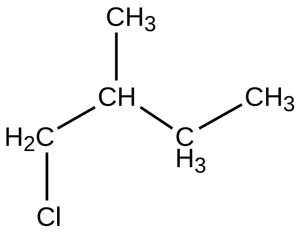
Four products:

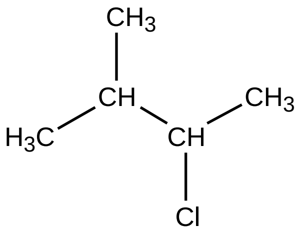
Chlorinate at one of the two methyl groups	6H	27%
Chlorinate at the unique methyl group	3H	14%
Chlorinate at methylene	2H	36%
Chlorinate at the tertiary site	1H	23%

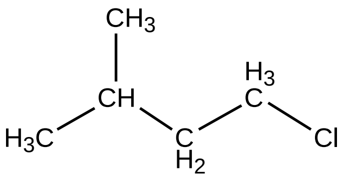
Prim : Sec : Tert = (27+14)/9 : 36/2 : 23/1 =about= 1 : 4 : 5

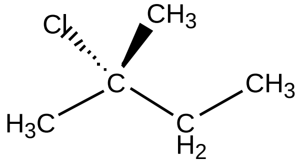
Wade's numbers are Prim : Sec : Tert =about= 1 : 4.5 : 5.5

The four products are shown and you can name them for your exercise.





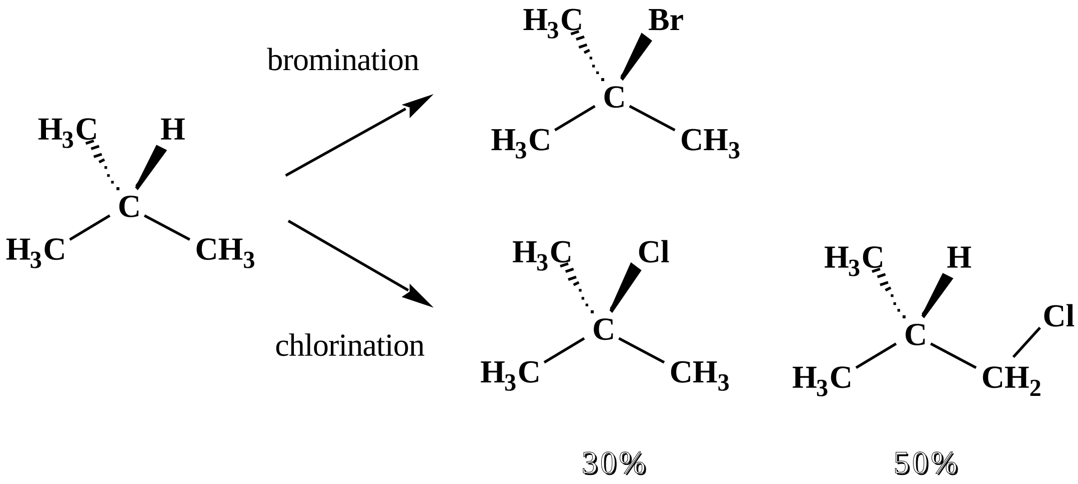




High Selectivity in Radical Halogenation with Bromine

Tertiary Butane

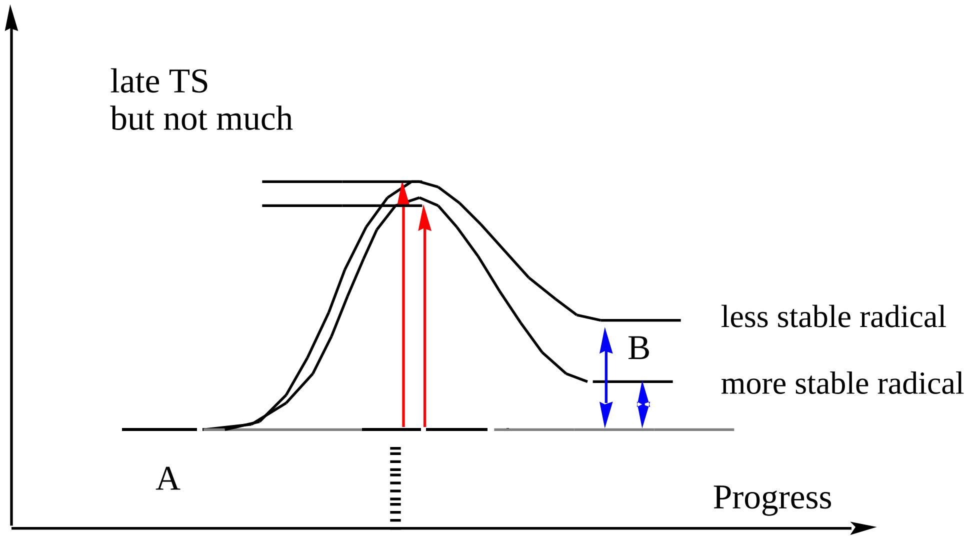
Bromination of *tert.*-butane is highly selective producing *tert.*-butyl bromide > 99% and *iso*-buty bromide < 1%.

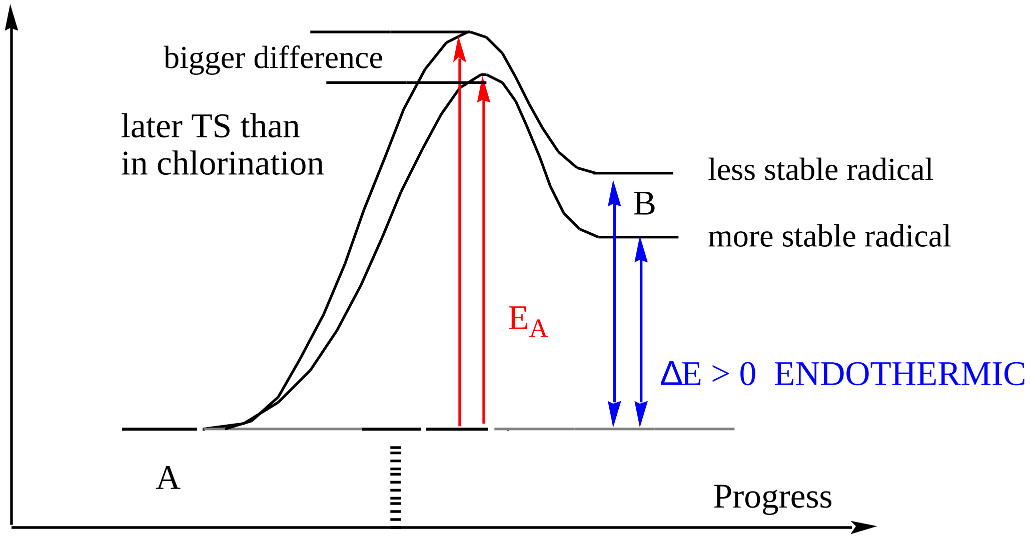


The **rate-limiting step** is the H-abstraction from the alkane. This step is **more endothermic for bromination** then for chlorination. The potential energy surfaces for the first steps of the chlorination and bromination reactions can explain the selectivity.

Hammond Postulate: Endothermic reactions have late transition states.

Consequence of HP: If the transition state is late, then the transition states of two competing pathways already reflect the stability differences of the alternative radicals formed. See PES schemes on next page.





The transition states leading to both possible radicals are later than in the case of the chlorination. The radical character of the forming radicals is more fully expressed in these late transition states. The difference in the two transition states equals a larger fraction of the energy difference of the isomeric radicals formed in this step. This is what causes the selectivity, the difference in the relative energies of the two transition state structures that lead to the isomeric products.

Fluorination, Chlorination and Bromination of Methane Transition State Structured for H-Abstraction

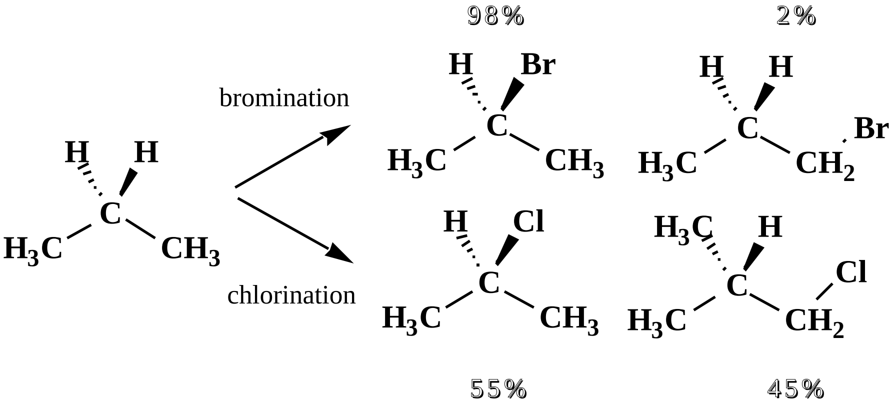
The transitions state structures for the H-abstraction from methane by fluorine, chlorine and bromine have been determined with quantum-mechanical methods and the structures are shown in the visualization center.

	F	Cl	Br
C-H in TS	1.153	1.438	1.600
C-H in CH_4	1.085	1.085	1.085
H-X in TS	1.350	1.431	1.527
H-X in HF	0.934	1.280	1.436

The later the transition state, the more radical character there is in the hydrocarbon fragment. The more radical character, the more differentiation is possible between primary, secondary and tertiary carbons.

Chlorination and Bromination of Propane

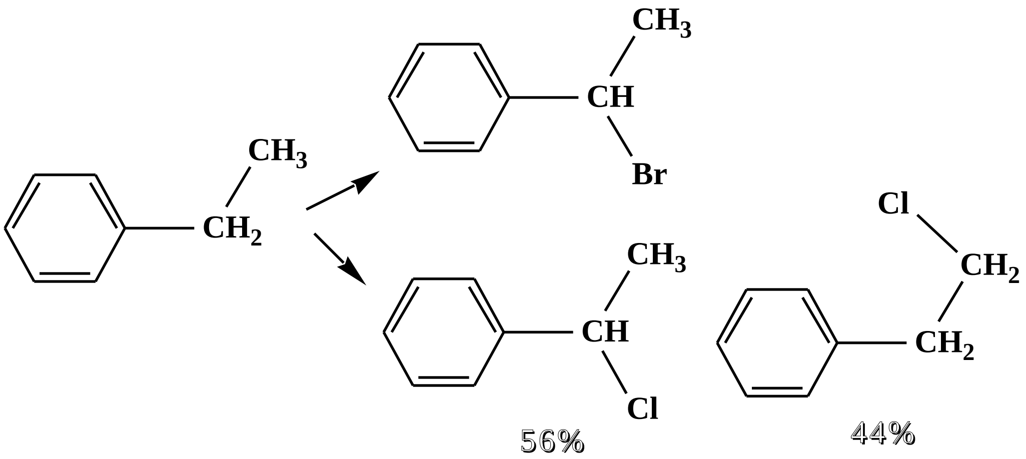
There are two types of Hs and they come in different numbers. Two are at a secondary carbon, six are at primary carbons. Two products are formed in the chlorination (note that the product formed from the more stable radical dominates although there are fewer Hs of that type to be extracted). Bromination is rather selective. As before: The H-abstraction by bromine radical is more endothermic and the TS is late, that is, it more fully reflects the factors that stabilize the radical formed.



Reactivity ratio for Chlorination: Prim. vs. Sec. = 1 : 4.5.
Reactivity ration for Bromination: Prim. vs. Sec. = 1 : 97.

Toluene and Ethylbenzene

There will not be any halogenation of the aromatic ring!
Just the side chain will be halogenated and the rules are just the same as for the alkanes themselves. Toluene gives benzylhalides. Ethylbenzene gives selective bromination of the benzylic carbon. Chlorination of ethylbenzene also gives chlorination of the methyl group as a side product.



Synthetic Uses of Radical Halogenations of Alkanes

Example 1: Methane

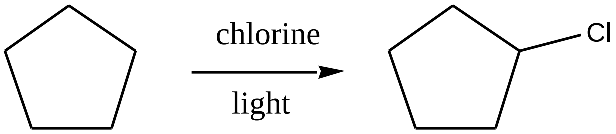
Used to be most important. To make chlorinated solvents.

Tetrachloromethane, TETRA
Chloroform, $HCCl_3$
Methylenechloride, H_2CCl_2

The more chlorine is used the higher is the probability for polyhalogenation.

Example 2: Cyclopentane (using light, in 93% yield)

Only one product possible. No selectivity problems.



Example 3: Brominations in the research laboratory.

Advantages: Bromine is a liquid, more selective reagent.

Solvent: Chlorinated methanes (at least 2 Cl).

Examples of Radical Reactions

Pyrolysis of Alkanes

Thermal decomposition of alkanes at high temperatures without oxygen. For example: Butane. If you heat it high enough, then eventually a CC bond will break (initiation). Now you have two alkyl radicals. Two things can happen. Recombine the radicals; that is the boring option (a termination step). Use the radical to abstract an H from another butane. This leads to a smaller alkane and a butane radical. What can the butane radical do? Three things: Recombine with some radical. Break a CC bond and produce an olefine and a radical. Abstract a H from some other butane. In the end, you end up with small alkanes and small alkenes.

Homework: Write the equations down. Do the same with propane and pentane until you catch on.

Oxygen in Autoxidations

The “rancid butter problem”. Butter contains fats of various sorts. When exposed to light or heat and air butter goes bad. Why? Oxygen is a biradical and it can do all the types of reactions discussed. “Luckily” oxygen diradical is quite stable, so these reactions occur slowly.

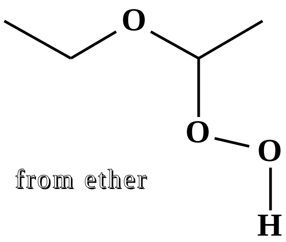
Initiation: Not necessary because O_2 is a biradical as it is! O_2 takes an H and produces an **alkyl radical**.

Propagation: The alkyl radical adds an oxygen biradical to produce an hydroperoxide monoradical. The generated radical abstracts an H from the next fatty acid to produce a hydroperoxide and an **alkyl radical**. The propagation is carried on by the **alkyl radical.**

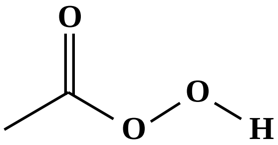
Termination: Any combination of radicals present.

The overall reaction is the insertion of O_2 into CH bonds to form hydroperoxides. These products are quite reactive themselves and go on to do many things such as producing acids (the bad smell is butanoic acid).

Other autooxidations include (i) the autooxidation of ethers (very dangerous!) and (ii) the autooxidation of aldehydes to acids (peroxyacetic acid reacts with aldehyde to give to molecules of the acid.



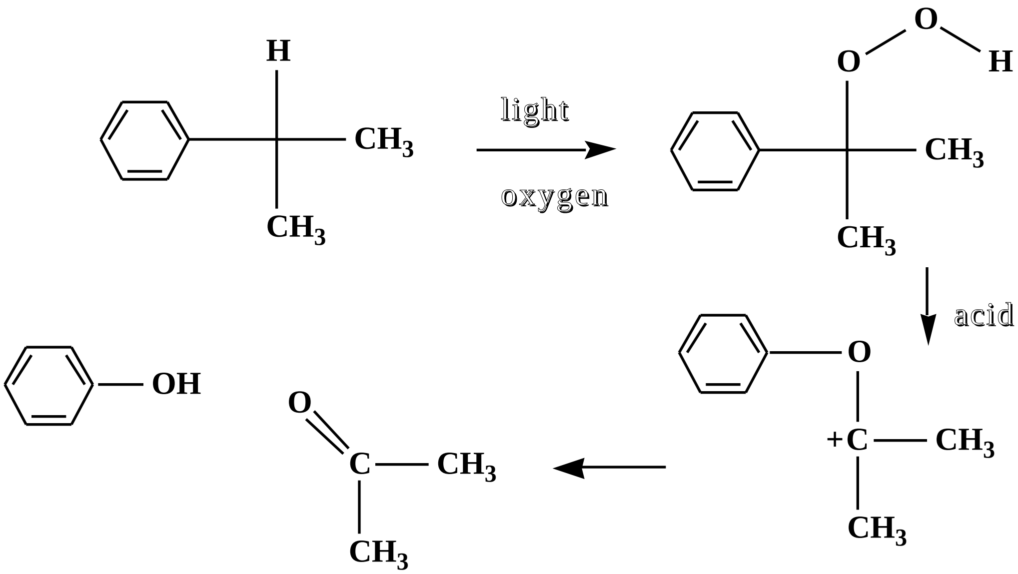
from ether



from aldehyde

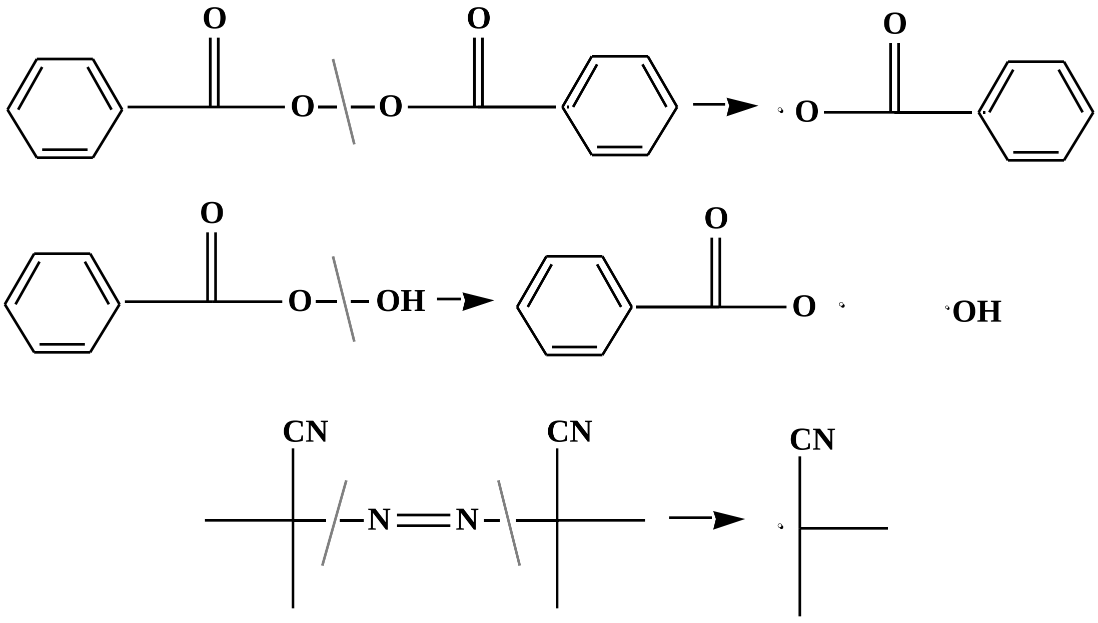
Cumene Process

Very important process to produce phenol and acetaldehyde in large quantities. The first step is the formation of a hydroperoxide by radical oxidation in air (requires heat). Addition of acid protonates the terminal OH. Water gets eliminated and the phenyl group moves to the remaining O. The rearranged cation adds water, and loses a proton, and kicks out a phenoxide.



Initiators and Inhibitors

A free radical initiator is anything that can produce radicals that can start a radical chain reaction. For the halogenations, **light** is the initiator. Light cleaves X_2 to produce two X• radicals. Chemicals with very small bond dissociation energies are often used. These just need to be heated to from radicals. Some of the more often used ones are
(i) Benzoyl peroxide
(ii) Peroxybenzoic acid
(iii) Azobisisobutyronitrile (AIBN).



Common Initiators of Free Radical Reactions

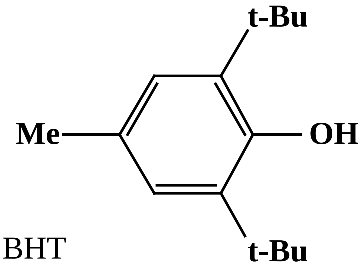
An inhibitor is anything that converts a reactive radical into a stable nonreactive radical. Most usually such compounds are phenols. The products are radicals that are very much stabilized by resonance. These compounds “trap” radicals. If they trap radicals that would otherwise lead to autooxidation, then they will prevent the oxidation. Thus, we call such inhibitors “antioxidants”. Antioxidants are important as food preservatives. Let’s look at how phenol acts as an inhibitor and then let’s look at some specific phenols that are used as food preservatives.

The Phenol Trap

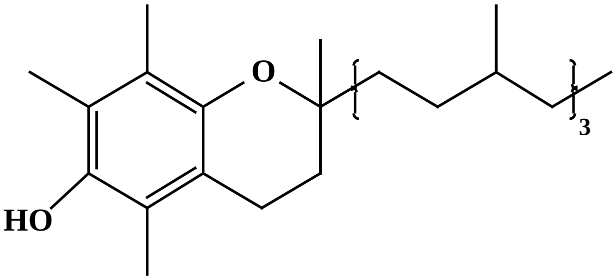
The phenol H is easily abstracted by a reactive radical. The reactive radical becomes unreactive in the process and the phenoxy radical is formed. The phenoxy radical is very stable. Many resonance forms.

BHT and Vitamin E

Synthetic and natural phenol based preservatives.



BHT
Butylated hydroxytoluene



α

Arylamines

Aromatic amines function just like aromatic alcohols. The reactive radical picks up the amino-H and leaves an unreactive resonance-stabilized radical. The N-phenyl-2-naphthylamine is used in rubber products. There are two aromatic rings to use for resonance. Write down the resonance forms (for fun).