

Week 3

More Types of Reactions

3.1 Radical Chemistry

1/25:

- Reviews mass spectroscopy.
- Radical chemistry allows us to do some reactions that we cannot do in a two-electron manifold.
 - If we want to attach a nucleophile to the C2 position of propane, heat alone will not make the hydrogen on that position leave (hydrides are terrible leaving groups).
- Presents how easy (in terms of ΔH) it is to homolytically cleave various C–H bonds in alkanes.
- Radical stability is the same as carbocation stability.
 - In terms of decreasing stability,
$$\text{benzylic} \approx \text{allylic} > \text{tertiary} > \text{secondary} > \text{primary} > \text{methyl}$$
 - Note that a benzylic or allylic *primary* radical is still more stable than a tertiary radical with no resonance stabilization.
- Three steps (initiation, propagation, and termination).
 - Initiation is either started by light ($h\nu$) or heat (Δ).
- You can lose CO_2 in a radical mechanism.

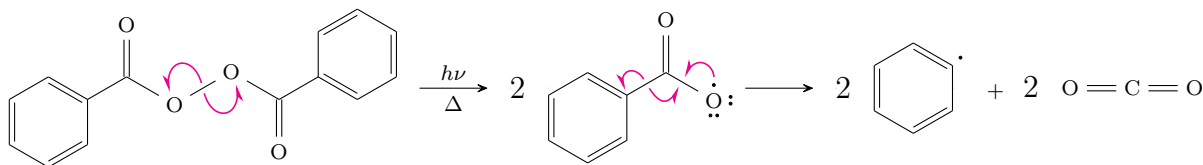


Figure 3.1: Losing CO_2 in a radical mechanism.

- The second step is strongly favored by entropy (ΔS).
- Chlorination of alkanes.
 - If multiple types of C–H bonds are present, they will all be functionalized but in differing amounts.
 - The mechanism is sensitive both to the number of available hydrogens of each type, how sterically accessible hydrogens are, and (most importantly) radical stability.
 - You can also get polychlorinated products.

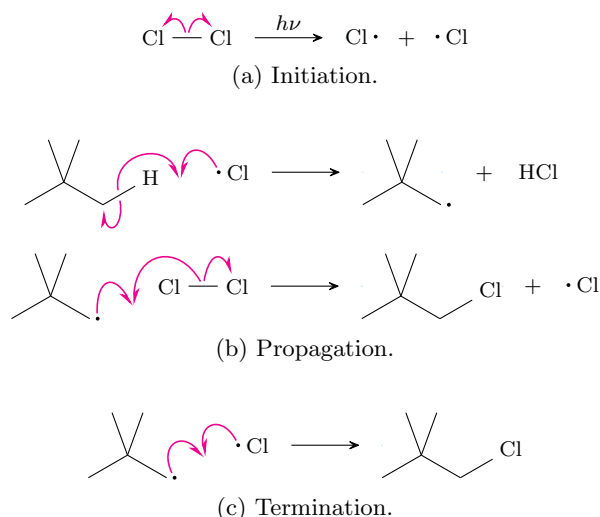


Figure 3.2: Chlorination of alkanes.

- Take-home message: If we use this, we only do so when all hydrogens are symmetric and we use excess starting material.
- Bromination of alkanes is basically the same.
 - One difference is that bromination is incredibly sensitive to radical stability, so whatever is the most stable radical will be the brominated one.
- Multistep synthesis example.
 - Propane to propane-1,2-diol.
 - Use radical bromination to put a bromine on C2, then β -elimination, then dihydroxylation.
- Allylic/benzylic halogenation.
- General form.

$$\text{---} \xrightarrow[h\nu]{\text{Br}_2} \text{---Br}$$
 - A possible side reaction is bromination of the alkene, but this requires a high temperature and low concentration.
 - The mechanism is entirely analogous to that of chlorination.
- HBr addition to alkenes.
 - The hydrohalogenation mechanism produces the Markovnikov product.
 - Morris Kharasch at UChicago in 1933 proposed that a radical mechanism produced the anti-Markovnikov product.
 - In particular, when run in the presence of air, it proceeds quickly even at low temperatures and with the help of an organic peroxide.
- Mechanism.
 - In hydrohalogenation, the hydrogen adds into the double bond to form the most stable carbocation.
 - In this mechanism, the bromine adds into the double bond to form the most stable radical.

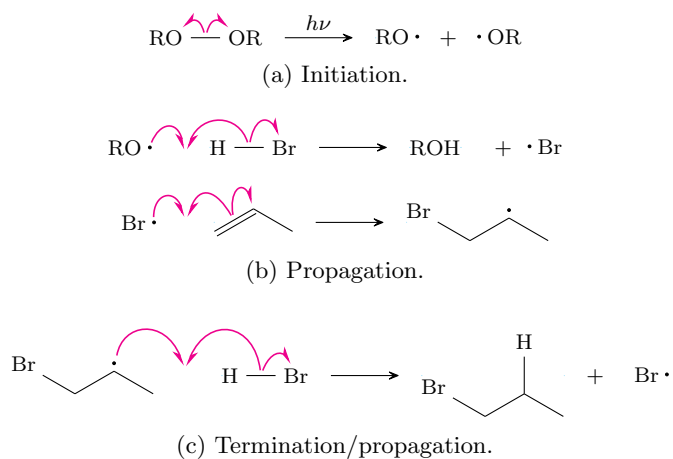


Figure 3.3: Radical hydrohalogenation.

3.2 Office Hours (Snyder)

1/26:

- We use excess substrate in radical chlorination reactions to avoid polychlorination — kinetically, we make it more likely for a chloride radical to collide with the reactant than the product.
- Problem set 1, Question 6.
 - Six is greater than exam strength.
 - 4 peaks in the aromatic region of ^{13}C means gives you a benzene ring.
 - From the ^{13}C NMR, we have 4 peaks in the aromatic region, so it is not a disubstituted asymmetric aryl ring. It's at least symmetric.
 - Once we get reasonably close, draw all possible structures and then analyze.
 - For isomer A, the two easiest lost groups are CH_3 and Cl , which both form benzylic carbocations. We also have that lower down primary methyl peak in the ^{13}C NMR.