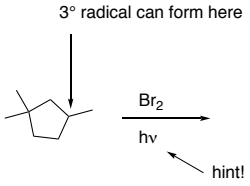
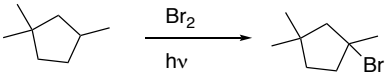
Reaction mechanism

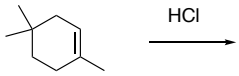
How to identify the most likely pathway for a reactant and it s reagents.

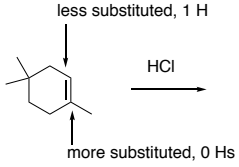
If the reagents or reaction conditions favor radicals, then it is likely to be a radical reaction. Look for hints like peroxide, AIBN, NBS, hν (UV light).

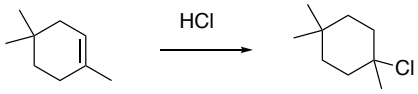




If the starting material is π-bonded and has no leaving group, then it is most likely an ADDITION reaction, but check for radicals, too. This is where Markovnikov's rule and carbocation mechanisms often occur. Note: addition can also happen when there is a leaving group present.







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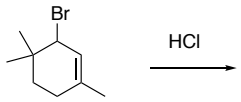

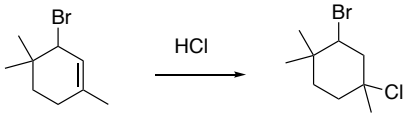

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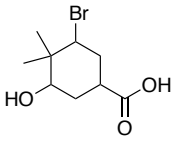
1. Identify the substrate (containing the leaving group), estimate its K_a value
2. If the nucleophile is a powerful enough base to react with the substrate in an acid/base reaction then that is the outcome because acid/base reactions are always very fast.

Estimate K_a



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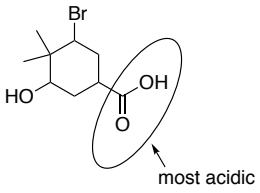
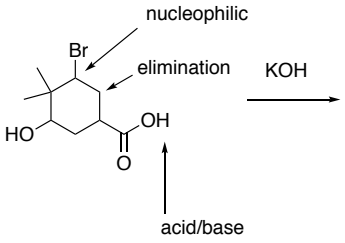
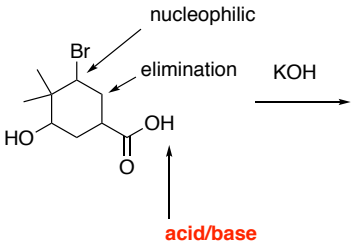
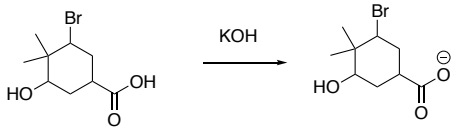


most acidic







OTHERWISE…

Determine the type of substrate based on the carbon with the leaving group. It is either methyl 1°, 2°, 3° or vinylic (leaving group attached to sp^2 carbon.

- If vinylic then no reaction will occur.
- If methyl – S_N2 substitution will happen.
- If 1° then S_N2 substitution is favored, except in the case of a nucleophile that is a very sterically hindered strong base like $(CH_3)_3CO^{(-)}$ in which case E2 elimination is favored.
- If 2°, then with a strong base (hydroxide or stronger) E2 elimination is favored, following Zaisev's rule; if the base is weaker than hydroxide, then S_N2 substitution is favored. Elimination is favored with higher temp and protic solvents. Lower temps and aprotic solvents favor substitution.
- If 3° then most likely pathway is elimination except in the case where the nucleophile is the solvent. This is called solvolysis which usually follows an S_N1 pathway, especially at lower temperatures. Higher temps and stronger bases favor E2 elimination.

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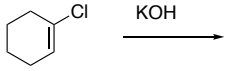

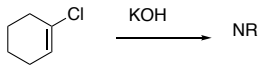

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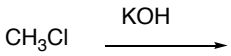

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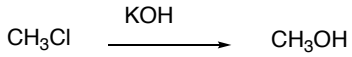

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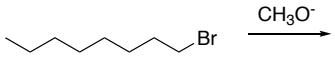

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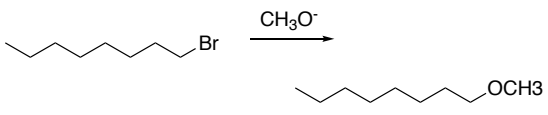

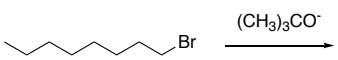

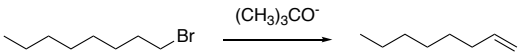

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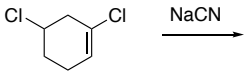
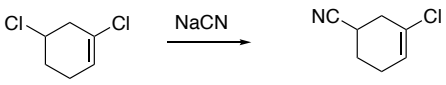
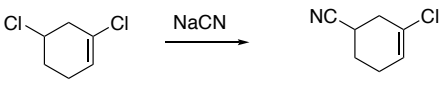


Note that $CN^{(-)}$ is a weaker base than $OH^{(-)}$



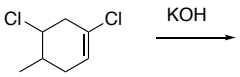
What temperature and solvent is best in this case?

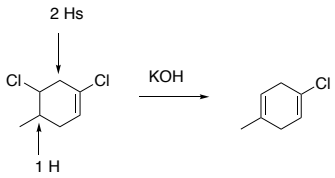


What temperature and solvent is best in this case?

- Room temperature or lower
- Aprotic polar solvents such as:
  - DMSO
  - Acetone
  - Diethyl ether
  - THF
  - DMF

Hydroxide is the starting point for elimination





What temperature and solvent is best in this case?

- Higher than rt (ex. 65 °C)
- Polar protic solvent, such as:
  - Alcohol
  - Water
  - Carboxylic acid
  - Amine

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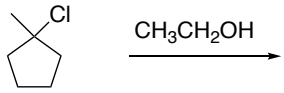
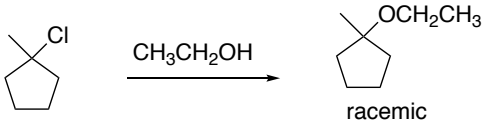
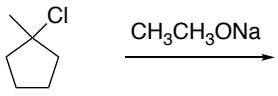
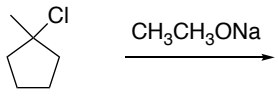


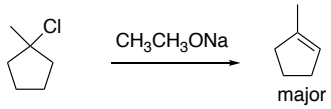
Why is it racemic?







What conditions are best? What is the minor product?



major