Predicting the pathway of a reaction

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 <u>is</u> a leaving group present.

If the starting material has a leaving group (for example, a halogen atom) then look for ACID/BASE, Nucleophilic SUBSTITUTION or ELIMINATION as the likely pathway.

First, since all nucelophiles are bases, check to see if the reaction an ACID/BASE reaction.

1. identify the substrate (containing a 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 since acid/bases reactions are always fast.

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 <u>no reaction</u> 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 Zaitsev's rule; if the base is weaker than hydroxide, then S_N2 SUBSTITUTION is favored. Elimination is favored with higher temp and protic solvents.

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.