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It's Important to Know!

BP202T — Pharmaceutical Organic Chemistry I

B.Pharm Semester 2 · Unit 3 — Alkyl Halides

Unit III: Alkyl Halides

SN1 and SN2 reactions

SN1 substitution has a slow ionisation step followed by nucleophile capture. It is favoured by substrates that form stable carbocations and by polar protic conditions. Because the carbocation is planar, stereochemical outcomes can include racemisation.

SN2 substitution occurs by backside attack in one concerted step. It gives inversion of configuration and is favoured by less hindered substrates, strong nucleophiles and suitable polar aprotic solvents. Steric hindrance slows SN2 reactions.

In an SN1 mechanism, the carbon-halogen bond ionises first. This produces a carbocation and a halide ion, and is usually the rate-determining step. A nucleophile then bonds to the planar carbocation. If the nucleophile is neutral, a final proton transfer may be needed to give a neutral product. The rate law is first order in the alkyl halide because nucleophile concentration is not involved in the slow ionisation step. A polar protic solvent can stabilise the ions. If the carbocation rearranges to a more stable one before capture, the product connectivity can change.

In an SN2 mechanism, the nucleophile approaches the carbon from the side opposite the leaving group. As the new bond forms, the carbon-halogen bond breaks in the same transition state. There is no isolable carbocation intermediate. The rate depends on both alkyl halide and nucleophile concentrations. Backside approach causes inversion at a stereogenic carbon. A polar aprotic solvent can keep an anionic nucleophile relatively reactive by solvating the counterion more strongly than the nucleophile.

For a practice prediction, compare two substrates with the same leaving group. A primary alkyl halide is relatively accessible to backside attack, so a strong nucleophile in a suitable polar aprotic solvent tends toward SN2. A tertiary alkyl halide is sterically crowded and can form a relatively stable carbocation, so ionisation and SN1 can be favoured in a polar protic solvent with a weak nucleophile. Secondary substrates can follow either route depending on the complete conditions. These are predictions of pathway preference, not guarantees of a single product.

Leaving groups and reaction factors

A leaving group is more effective when it can remain stable after departure. Halide leaving-group ability commonly follows iodide greater than bromide greater than chloride, while fluoride is usually poorer in ordinary substitution conditions. Nucleophile strength, solvent, substrate structure and temperature all matter. A strong base may also remove a beta hydrogen, giving elimination instead of substitution. Product analysis should therefore consider competing pathways.

Unit III: Frequently asked questions

Q: What is the stereochemical result of SN2 substitution?

A: Backside attack produces inversion of configuration at the reacting carbon.

Q: Why do tertiary substrates favour SN1 more than SN2?

A: Tertiary substrates can form relatively stable carbocations but are sterically crowded for backside attack.

Q: What is the main difference between SN1 and SN2 substitution?

A: SN1 substitution occurs in steps through a carbocation intermediate, while SN2 substitution occurs in one concerted step by backside attack.

Unit III: Key takeaways

- SN1 is stepwise and involves carbocation stability.
- SN2 is concerted and gives inversion.
- Steric hindrance strongly affects substitution pathways.
- Alkyl halide reactivity depends on substrate structure, nucleophile, solvent and mechanism.
- Compound-specific uses and tests require verified sources.

Unit III: Practical correlation

Practical correlation: qualitative analysis. A laboratory identification should compare the observed test, control result and expected reaction before a conclusion is recorded.