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It's Important to Know!

BP202T — Pharmaceutical Organic Chemistry I

B.Pharm Semester 2 · Unit 2 — Alkanes, Alkenes and Conjugated Dienes

Unit II: Alkanes, Alkenes and Conjugated Dienes

Alkanes

Alkanes contain carbon-carbon single bonds and have tetrahedral carbon atoms described as sp^3 hybridised. Their main reactions are substitution and combustion. Free-radical halogenation proceeds through initiation, propagation and termination. Selectivity and product distribution depend on radical stability and reaction conditions.

In chlorination under light or heat, initiation breaks a chlorine-chlorine bond homolytically and produces chlorine radicals. During propagation, a chlorine radical abstracts hydrogen from an alkane, producing hydrogen chloride and an alkyl radical. The alkyl radical then abstracts chlorine from another chlorine molecule, yielding an alkyl chloride and regenerating a chlorine radical. In termination, two radicals combine and remove radical species from the chain. This is a chain reaction because propagation regenerates the radical carrier.

For an alkane with more than one distinct type of hydrogen, substitution can yield multiple constitutional products. Product proportions depend on the number of each hydrogen type and how readily each hydrogen is abstracted. A more stable radical pathway can be favoured, but a product prediction should account for both statistical abundance and relative reactivity. Extensive halogenation can continue unless reagent ratio and reaction time are controlled.

Alkenes and addition

Alkenes contain a carbon-carbon double bond with sp^2 hybridised carbon atoms. The π bond is electron-rich and can undergo electrophilic addition. Markovnikov orientation places hydrogen so that the more stable carbocation intermediate is formed when the mechanism proceeds through a carbocation.

Free-radical addition can give anti-Markovnikov orientation in appropriate peroxide-mediated addition of hydrogen bromide. This rule is not general for every reagent. Ozonolysis cleaves the double bond and produces carbonyl fragments after work-up.

For acid-catalysed hydration of a simple unsymmetrical alkene, the mechanism can be followed in three stages. First, the π bond accepts a proton, giving the more stable carbocation pathway where alternatives exist. Second, water attacks the carbocation to form a protonated alcohol.

Third, another water molecule removes a proton, yielding the neutral alcohol and regenerating acid. Rearrangements may occur if a more stable carbocation can form. The product prediction therefore depends on substrate structure and conditions.

Ozonolysis is useful for inferring the position of an alkene bond. Ozone reacts with the double bond, and work-up converts the resulting intermediates into carbonyl compounds. Reductive work-up generally preserves aldehydes and ketones, while oxidative work-up can further oxidise aldehyde products. To work a product example, split the carbon-carbon double bond conceptually, replace each alkene carbon's unsatisfied valence with a carbonyl oxygen, and determine whether each fragment is an aldehyde or ketone from its attached groups. No structure drawing is needed for this reasoning.

E1 and E2 elimination

E1 elimination occurs in two steps through a carbocation. Its rate depends mainly on substrate ionisation. E2 elimination occurs in one concerted step and its rate depends on substrate and base. Carbocation rearrangement can occur in E1 pathways. Saytzeff orientation generally favours the more substituted alkene when steric and electronic factors do not override it.

In E1, the leaving group departs first to form a carbocation. A base then removes a hydrogen from a neighbouring carbon, and the electrons from that carbon-hydrogen bond form the double bond. Because carbocation formation is the slow step, a more stable carbocation usually makes ionisation easier. Polar protic solvents can stabilise ions. Rearrangement by hydride or alkyl shift is possible before elimination if it produces a more stable cation.

In E2, a base removes a beta hydrogen as the leaving group departs from the adjacent carbon. Formation of the double bond and leaving-group departure occur in one concerted event. The beta hydrogen and leaving group generally need an anti-periplanar arrangement for effective orbital overlap. A strong base and suitable substrate favour this pathway. Since no carbocation intermediate forms, a simple E2 reaction does not undergo carbocation rearrangement.

To compare substitution and elimination, inspect the substrate first, then the reagent, solvent and temperature. A strong, hindered base often favours elimination; a good nucleophile that is not strongly basic can favour substitution in suitable substrates. Heating often increases the contribution of elimination. These are qualitative trends, not substitutes for evaluating the actual substrate and conditions.

Conjugated dienes

Conjugated dienes have alternating double and single bonds. Delocalisation stabilises the system. Electrophilic addition can give products from kinetic and thermodynamic control. The Diels-Alder reaction is a concerted cycloaddition between a conjugated diene and a dienophile. Allylic rearrangement involves movement of a double bond through a resonance-stabilised allylic intermediate.

When an electrophile adds to a conjugated diene, the first step forms an allylic carbocation. Resonance distributes positive charge across the terminal positions, so a nucleophile can attack at more than one site. Lower temperature and shorter reaction time can favour the product formed faster, called the kinetic product. Higher temperature and reversible conditions can favour the more stable product, called the thermodynamic product. Which product dominates depends on the actual reaction conditions.

The Diels-Alder reaction joins a conjugated diene and an alkene or alkyne dienophile in a concerted step. The diene must adopt a suitable conformation, and electron-withdrawing substituents on a dienophile commonly increase its reactivity. The reaction creates a six-membered ring framework and can form stereogenic relationships. When analysing an example, identify the four diene atoms and the two dienophile atoms, then track which new bonds form and whether substituent relationships are retained. This is a verbal atom-mapping exercise, not a structure drawing.

Unit II: Frequently asked questions

Q: What is the difference between E1 and E2 elimination?

A: E1 is stepwise through a carbocation, while E2 is concerted and occurs in one step.

Q: What is Markovnikov orientation?

A: In a typical electrophilic addition to an unsymmetrical alkene, the product orientation follows formation of the more stable intermediate.

Q: Why are conjugated dienes more stable?

A: Their pi electrons are delocalised across the conjugated system, lowering the overall energy.

Unit II: Key takeaways

- Alkanes are saturated and commonly undergo radical substitution.
- Alkenes are unsaturated and commonly undergo electrophilic addition.
- E1 is stepwise, while E2 is concerted.
- Ozonolysis cleaves carbon-carbon double bonds into carbonyl fragments.
- Conjugation stabilises dienes and supports Diels-Alder chemistry.

Unit II: Practical correlation

Practical correlation: reaction safety. Organic reactions should be planned from substrate, reagent, solvent, temperature, mechanism and expected hazards.