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It's Important to Know!

BP202T — Pharmaceutical Organic Chemistry I

B.Pharm Semester 2 · Unit 4 — Alcohols and Carbonyl Compounds

Unit IV: Alcohols and Carbonyl Compounds

Alcohols

Alcohols contain a hydroxyl group attached to a saturated carbon. Their properties depend on hydrogen bonding, carbon skeleton and substitution. Oxidation of primary alcohols can lead to aldehydes and then carboxylic acids, while secondary alcohols can form ketones. Tertiary alcohols resist simple oxidation because the carbon bearing the hydroxyl group lacks a hydrogen.

Qualitative tests may distinguish classes of alcohols using oxidation or substitution behaviour.

Alcohols are classified as primary, secondary or tertiary by the number of carbon groups attached to the carbon bearing the hydroxyl group. Hydrogen bonding raises boiling points compared with similar-sized compounds that cannot donate hydrogen bonds. Small alcohols mix well with water; water solubility generally falls as the nonpolar carbon chain becomes longer.

Oxidation provides a useful reactivity comparison. A primary alcohol loses hydrogen during oxidation to form an aldehyde. Further oxidation, often with an aqueous oxidising reagent, can produce a carboxylic acid. A secondary alcohol is oxidised to a ketone. A tertiary alcohol does not undergo this simple oxidation because the hydroxyl-bearing carbon has no hydrogen to remove without breaking a carbon-carbon bond. Actual reagent, solvent and work-up determine whether an aldehyde can be isolated or proceeds to acid.

Alcohols can undergo substitution to form alkyl halides under suitable conditions. In a typical acid-assisted route, the hydroxyl group is protonated so water can leave more readily. The subsequent pathway depends on substitution at carbon: a stable carbocation may support an SN1 route, while a less hindered substrate and a strong nucleophile can support SN2 displacement. Strongly acidic conditions can also cause dehydration to an alkene, so temperature and reagent choice are important.

Dehydration removes water from an alcohol. Under acid and heat, protonation converts hydroxyl into a better leaving group. Loss of water and removal of a neighbouring hydrogen then form an alkene. Depending on substrate, this can follow an E1 or E2 pathway. Rearrangements are possible when a carbocation intermediate forms. Product orientation often favours the more substituted alkene, subject to structure and conditions.

Pharmaceutical and laboratory examples

The syllabus names several halogenated compounds and alcohols for structure, properties and uses. Learn their official names, functional groups, hazards and approved uses from a verified monograph. Do not infer a use from a name.

Structure and reactivity

Aldehydes and ketones contain a polar carbonyl group. The carbonyl carbon is electrophilic and can undergo nucleophilic addition. Aldehydes are generally more reactive than ketones because they have less steric hindrance and fewer electron-releasing alkyl groups.

Nucleophilic addition can be described in a short sequence. A nucleophile donates an electron pair to the carbonyl carbon. The carbon-oxygen pi bond shifts toward oxygen, giving an alkoxide intermediate. Protonation of the alkoxide gives an addition product. In acid-catalysed reactions, protonation of oxygen can first increase electrophilicity, after which a weak nucleophile attacks and a proton transfer completes the process. The exact sequence depends on reagent and medium.

For a simple comparison, an aldehyde usually reacts faster than a ketone toward the same nucleophile. The aldehyde has one hydrogen and one carbon substituent at the carbonyl carbon, while a ketone has two carbon substituents. This usually means less steric crowding and less electron donation in the aldehyde. Conjugation or unusual substituents can alter the trend.

Reduction converts aldehydes to primary alcohols and ketones to secondary alcohols when an appropriate hydride donor is used, followed by protonation. Oxidation readily converts aldehydes to carboxylic acids because aldehydes have a hydrogen on the carbonyl carbon. Ketones resist ordinary mild oxidation; strong oxidative cleavage can occur under more forcing conditions. Reagent identity and work-up must be specified for a laboratory procedure.

Condensation reactions

Aldol condensation involves enolate or enol formation followed by carbon-carbon bond formation and dehydration under suitable conditions. Crossed aldol reactions use two different carbonyl compounds and can produce mixtures unless one reaction partner is controlled.

Cannizzaro reaction occurs with aldehydes that lack an alpha hydrogen under strongly basic conditions. One molecule is oxidised and another is reduced. Benzoin condensation joins aromatic aldehyde units through a cyanide or thiazolium-type catalytic pathway. Perkin condensation forms an unsaturated aromatic acid derivative from an aromatic aldehyde and an acid anhydride in the presence of base.

In an aldol reaction, a base removes an alpha hydrogen from a carbonyl compound that has one, forming an enolate. The enolate carbon attacks the carbonyl carbon of another molecule. Protonation gives a beta-hydroxy carbonyl compound, the aldol addition product. Heating or other suitable conditions can remove water to produce a conjugated carbonyl compound. In a crossed aldol reaction, two different carbonyl compounds may each form enolates and can give a mixture. Selectivity improves when one partner cannot form an enolate or when conditions control which enolate is generated.

The Cannizzaro reaction is a disproportionation of a non-enolisable aldehyde in concentrated base. Hydroxide adds to one aldehyde molecule. A hydride equivalent is then transferred to a second aldehyde molecule through a coupled step. The donor molecule becomes a carboxylate,

while the acceptor becomes an alcohol after work-up. The reaction requires aldehydes without an alpha hydrogen because those with alpha hydrogens can undergo aldol chemistry instead.

Benzoin condensation is a carbon-carbon bond-forming reaction between aromatic aldehydes. A catalyst temporarily changes the reactivity of one aldehyde so it can act as a nucleophilic partner toward another aldehyde. Proton transfers and catalyst regeneration yield an alpha-hydroxy ketone. Perkin condensation combines an aromatic aldehyde with an acid anhydride in the presence of base; after condensation and work-up, an unsaturated aromatic acid derivative is obtained. Reagent scope and specific named-reaction conditions depend on substrate and are best learned from the prescribed reaction examples.

Qualitative tests

Carbonyl compounds may be investigated using tests for aldehydes, ketones or reducing behaviour.

Unit IV: Frequently asked questions

Q: How do primary and secondary alcohol oxidation products differ?

A: Primary alcohols can be oxidised to aldehydes and further to carboxylic acids, while secondary alcohols form ketones.

Q: Why are carbonyl compounds susceptible to nucleophilic addition?

A: The carbonyl bond is polar, leaving the carbonyl carbon electron-poor and open to nucleophile attack.

Q: What happens in the Cannizzaro reaction?

A: Two aldehyde molecules without alpha hydrogen undergo simultaneous oxidation and reduction under basic conditions.

Q: What is aldol condensation?

A: It is carbon-carbon bond formation involving an enolate or enol followed by dehydration to an unsaturated carbonyl compound.

Unit IV: Key takeaways

- Primary alcohols can oxidise through aldehydes to carboxylic acids, while secondary alcohols form ketones.
- The carbonyl carbon is electrophilic.
- Aldehydes usually undergo nucleophilic addition more readily than ketones.
- Aldol reactions form carbon-carbon bonds.
- Cannizzaro reactions involve oxidation and reduction of aldehydes.
- Qualitative test details must be learned with their limitations.

Unit IV: Practical correlation

Practical correlation: impurity testing. Carbonyl tests can support identity or detect a reactive group, but a single colour or precipitate is not a complete quality decision.