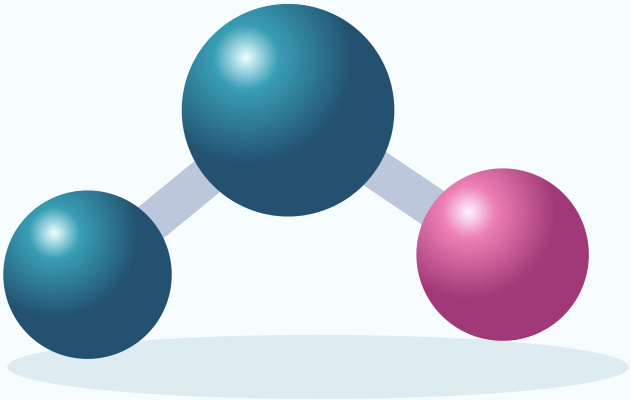
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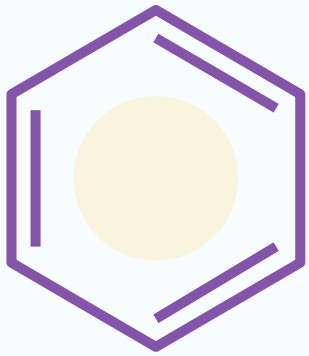
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01	IUPAC Nomenclature	3
02	Purification Techniques	21
03	Isomerism	24
04	General Organic Chemistry	50
05	Organic Analysis	74
06	Hydrocarbons	80
07	Haloalkanes & Haloarenes	102
08	Alcohols, Phenols & Ethers	129
09	Carbonyls & Carboxylic Acids	145
10	Amines	165
11	Biomolecules	173

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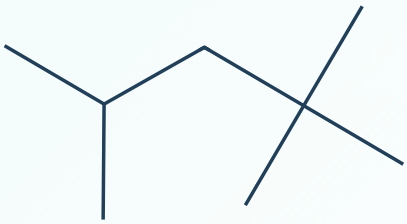
IUPAC Nomenclature

Choose the chain · number · name

01

01 Degree of carbon and hydrogen

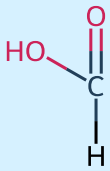
- Degree of a carbon = number of carbon atoms directly attached to that carbon. A primary (1°), secondary (2°), tertiary (3°) or quaternary (4°) carbon has 1, 2, 3 or 4 carbon neighbours respectively.



$CH_3–CH(CH_3)–CH_2–C(CH_3)_2–CH_3$

Carbon count: five 1° carbons, one 2° carbon, one 3° carbon and one 4° carbon.

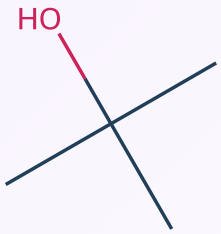
- A hydrogen has the degree of the carbon to which it is attached. In the same molecule: 1° H = 15; 2° H = 2; 3° H = 1. A 4° hydrogen is impossible because a quaternary carbon already has four C–C bonds.

- Classroom term: "superprimary" carbon has no carbon neighbour. Examples: 

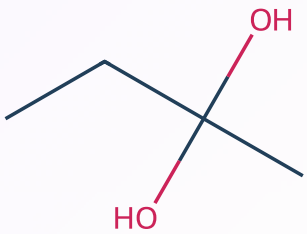
, CH_4, CH_3OH and CH_3Cl. Its formal carbon degree is zero.

02 Degree of alcohol and amine

- Degree of an alcohol = degree of the carbon bearing –OH. Count that carbon's carbon neighbours, not the number of –OH groups.



Tertiary (3°) alcohol



Geminal diol: each OH is on a secondary carbon

The –OH-bearing carbon decides the class.

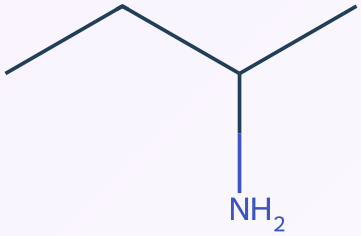
IUPAC Nomenclature

Degree of alcohol and amine · Degree of unsaturation: two ways to count

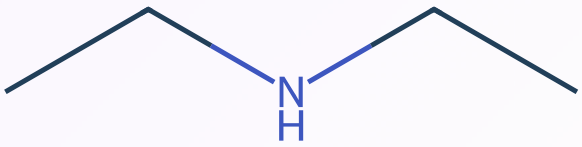
02 Degree of alcohol and amine

continued

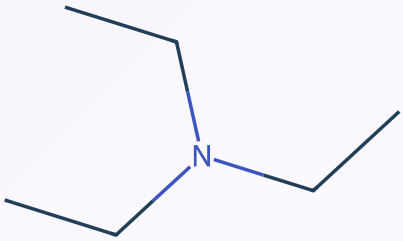
- Degree of an amine = number of carbon groups directly attached to nitrogen. One group: 1° amine; two: 2°; three: 3°. Four groups on N^+ form a quaternary ammonium salt.



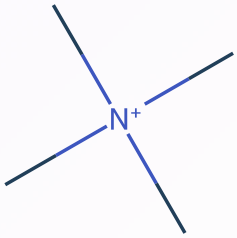
1° amine: butan-2-amine



2° amine: diethylamine



3° amine: triethylamine



Quaternary ammonium cation; counter-ion omitted

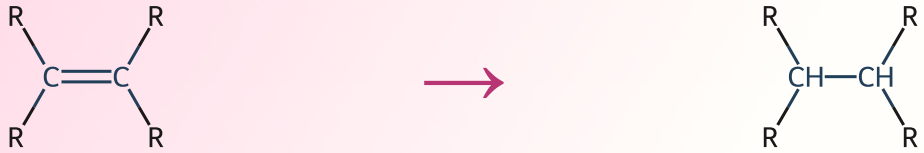
An amine's degree is counted at nitrogen.

03 Degree of unsaturation: two ways to count

- For multiple bonds, count the H_2 molecules needed for complete hydrogenation: one C=C uses one H_2; one C≡C uses two H_2. Each π bond contributes one degree of unsaturation (DU). Each ring contributes one DU: opening one ring adds two hydrogens.

1 H_2

Hydrogenation



One double bond = one π bond = one DU.

2 H_2

Complete hydrogenation



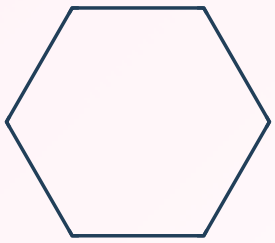
One triple bond = two π bonds = two DU.

IUPAC Nomenclature

Degree of unsaturation: two ways to count · σ bonds, π bonds, lone pairs and hybridization

03 Degree of unsaturation: two ways to count

continued



Cyclohexane: one ring, DU = 1



Open-chain saturated comparison: hexane

Ring opening adds the equivalent of one H_2.

$$\mathrm{DU} = C + 1 - \frac{H + X - N}{2}$$

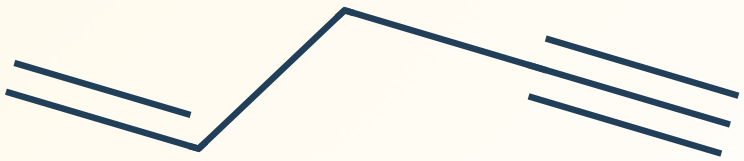
C, H and N are atom counts; X is the total halogen count. Oxygen and divalent sulfur do not change this expression for ordinary closed-shell formulas.

04 σ bonds, π bonds, lone pairs and hybridization

Bond	σ bonds	π bonds
A–B	1	0
A=B	1	1
A≡B	1	2

$$\text{Lone pairs on an atom} = \frac{\text{valence electrons} - \text{electrons contributed to bonding}}{2}$$

Use the appropriate electron count for formal charge; 'sharing electrons' means that atom's contributed bonding electrons.



$HC{\equiv}C{-}CH_2{-}CH{=}CH_2$

Following $HC{\equiv}C{-}CH_2{-}CH{=}CH_2$: sp, sp, sp^3, sp^2, sp^2.

- *π bonds are not counted as separate hybrid orbitals. In $HC{\equiv}C{-}CH_2{-}CH{=}CH_2$, the five carbons have 2σ, 2σ, 4σ, 3σ and 3σ respectively.*

IUPAC Nomenclature

σ bonds, π bonds, lone pairs and hybridization · Homologous series and the name-building order

04 σ bonds, π bonds, lone pairs and hybridization

continued

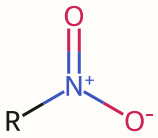
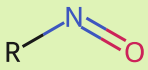
$$\mathrm{EN}(sp) > \mathrm{EN}(sp^2) > \mathrm{EN}(sp^3)$$

More s character means greater electronegativity. Comparison: F > O > C(sp) > N > C(sp²) > C(sp³).

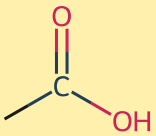
05 Homologous series and the name-building order

- A homologous series has the same functional group and general formula. Successive members differ by one $-CH_2-$ unit, so molecular formula and molecular mass change. Example: $CH_4 \rightarrow C_2H_6 \rightarrow C_3H_8$, adding CH_2 each time.

- Name-building order: secondary prefix + primary prefix + word root + primary suffix + secondary suffix. The primary prefix is 'cyclo' for a ring. The secondary prefix names branches/substituents.

Prefix group	Examples / name
Alkyl branches	$-CH_3$ methyl; $-C_2H_5$ ethyl; general $-R$ alkyl
–OR	Alkoxy
–X	Halo
	Nitro
	Nitroso
$-C_6H_5$ / –Ph	Phenyl

06 Word root and suffixes

- The word root gives the number of carbons in the parent chain: 1 meth-, 2 eth-, ..., 11 undec-. Primary suffix: C–C → -ane; C=C → -ene; C≡C → -yne. Secondary suffix identifies the principal functional group, such as  or $-SO_3H$.

07 Four basic naming rules

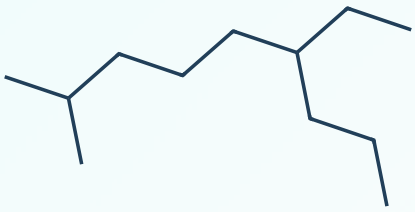
- 1. Identify the appropriate longest parent carbon chain.
- 2. Number it so substituents receive the lowest set of locants, after higher-priority naming features have been considered.
- 3. List different alkyl substituents alphabetically.
- 4. Repeated identical substituents use di-, tri-, tetra-, etc. The multiplicative prefixes di-, tri- and tetra- are ignored when ordinary substituents are alphabetized.

IUPAC Nomenclature

Four basic naming rules · Complex alkyl branches

07 Four basic naming rules

continued



6-Ethyl-2-methylnonane

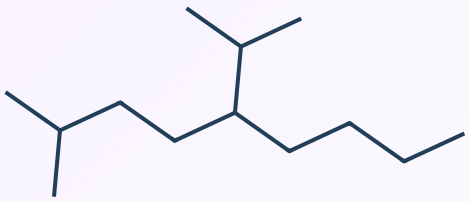


2,4-Dimethylpentane

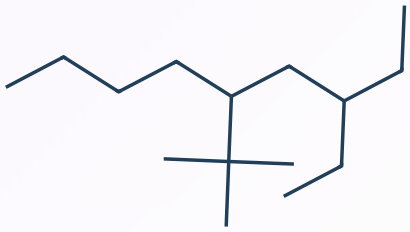
Number first; then write substituent names in alphabetical order.

08 Complex alkyl branches

- *Number a complex substituent from its point of attachment to the parent. Enclose its name in parentheses. The complete complex-substituent name is used for alphabetizing; internal di-/tri- can therefore count. Different branches still follow alphabetical order.*

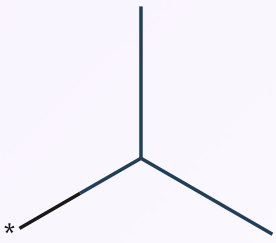


5-Isopropyl-2-methylnonane; 2-methyl-5-(1-methylethyl)nonane

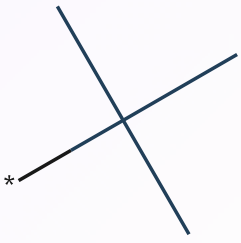


5-(1,1-Dimethylethyl)-3-ethylnonane; 5-tert-butyl-3-ethylnonane

Isopropyl = 1-methylethyl; tert-butyl = 1,1-dimethylethyl.



Isopropyl / propan-2-yl



tert-Butyl / 1,1-dimethylethyl

The star marks the bond to the parent skeleton.

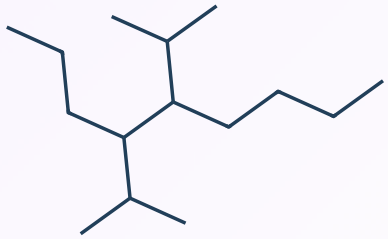
- *When the same complex substituent appears more than once, use bis-, tris-, tetrakis-, pentakis-, etc. Example: 4,5-bis(1-methylethyl)nonane, also written 4,5-diisopropylnonane in common substituent nomenclature.*

IUPAC Nomenclature

Complex alkyl branches · Unsaturated branches: alkenyl and alkylidene

08 Complex alkyl branches

continued

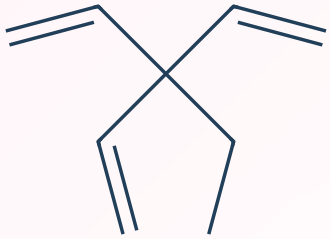


4,5-Bis(1-methylethyl)nonane

The two identical complex branches have separate attachment locants.

09 Unsaturated branches: alkenyl and alkylidene

Substituent (left bond attaches to parent)	Name(s)
$-CH=CH_2$	Ethenyl / vinyl; also: eth-1-enyl
$-CH=CH-CH_3$	Prop-1-en-1-yl; also: prop-1-enyl / propenyl
$-CH_2-CH=CH_2$	Prop-2-en-1-yl / allyl
$=CH_2$	Methylidene (often called methylene)
$=CH-R$	Alkylidene
$=CH-CH_3$	Ethylidene



3-Ethenyl-3-ethylpenta-1,4-diene; 3-ethyl-3-vinylpenta-1,4-diene

The parent contains two double bonds; the third $=CH_2$-containing branch is ethenyl (vinyl).

10 Alkynyl branches and multiple-bond numbering

Substituent	Name(s)
$-C\equiv CH$	Ethynyl; also: eth-1-ynyl
$-C\equiv C-CH_3$	Prop-1-yn-1-yl; also: prop-1-ynyl
$-CH_2-C\equiv CH$	Prop-2-yn-1-yl / propargyl

IUPAC Nomenclature

Alkynyl branches and multiple-bond numbering · Combining suffixes and naming a substituted side chain

10 Alkynyl branches and multiple-bond numbering

continued

- When double and triple bonds coexist, choose the lowest set of multiple-bond locants. If numbering is still tied, give the double bond the lower locant. With two or more double/triple bonds, retain the connecting 'a' in names such as buta-1,3-diene.

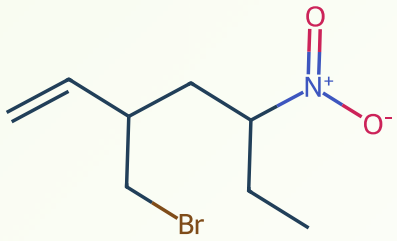


Buta-1,3-diene: $CH_2=CH-CH=CH_2$

Two C=C bonds begin at carbons 1 and 3.

11 Combining suffixes and naming a substituted side chain

- When suffixes meet, drop the terminal 'e' where required before a vowel-containing suffix. Example: $CH_2=CH-C\equiv CH$ is but-1-en-3-yne (not but-1-ene-3-yne).



3-(Bromomethyl)-5-nitrohept-1-ene

If a carbon lies between the parent chain and Br, the branch is bromomethyl, not bromo.

- Name order: secondary prefix + primary prefix + word root + primary suffix + secondary suffix. Selection guide: principal functional group (PFG) → multiple bonds → longest carbon chain → maximum substituents → lowest locants → alphabetical tie-break. Numbering priority: secondary suffix > primary suffix > secondary prefix.

12 Functional groups: suffix, prefix and ring suffix

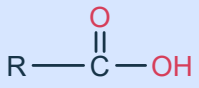
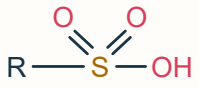
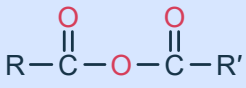
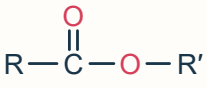
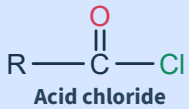
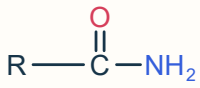
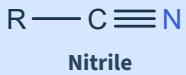
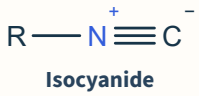
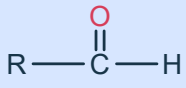
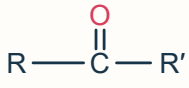
- Use the table as a functional-group naming guide. A lower-priority group becomes a prefix. Use the special suffix when the functional-group carbon lies outside the chosen parent skeleton, especially with rings. Isocyanide is included for recognition; do not treat it as an ordinary suffix-bearing priority row.

IUPAC Nomenclature

Functional groups: suffix, prefix and ring suffix

12 Functional groups: suffix, prefix and ring suffix

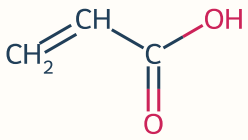
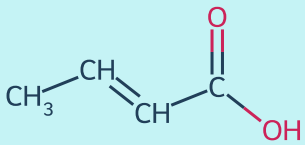
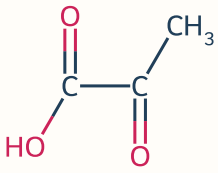
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Functional group	Usual suffix	Prefix when subordinate	Special suffix / ring form
 Carboxylic acid	-oic acid	carboxy-	-carboxylic acid
 Sulfonic acid	-sulfonic acid	sulfo-	-sulfonic acid
 Acid anhydride	-oic anhydride	—	—
 Ester	-oate	alkoxycarbonyl-	-carboxylate
 Acid chloride	-oyl chloride	chlorocarbonyl-	-carbonyl chloride
 Amide	-amide	carbamoyl-	-carboxamide
 Nitrile	-nitrile	cyano-	-carbonitrile
 Isocyanide	isonitrile (classroom term)	isocyano-	—
 Aldehyde	-al	oxo- (C included); formyl- (C outside parent)	-carbaldehyde
 Ketone	-one	oxo- (also called keto-)	-one
 Alcohol	-ol	hydroxy-	-ol
 Thiol	-thiol	sulfanyl- (also: mercapto-)	-thiol
 Amine	-amine	amino-	-amine

IUPAC Nomenclature

Common acid-name roots remembered · Principal group and alphabetical prefixes

13 Common acid-name roots remembered

Carbon skeleton / acid family	Common root
C_1	form-
C_2	acet-
C_3	propion-
C_4	butyr- (normal / iso)
C_5	valer- (normal / iso / neo)
 **Acrylic acid**	acryl-
 **Crotonic acid**	croton-
 **Pyruvic acid**	pyruv-

14 Principal group and alphabetical prefixes

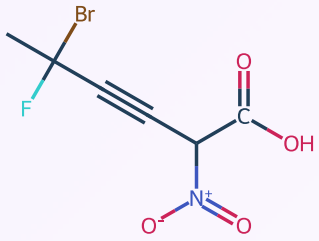
- When several functional groups are present, choose the principal group using priority, but write the remaining prefixes in alphabetical order.

IUPAC Nomenclature

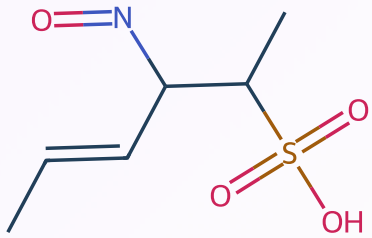
Principal group and alphabetical prefixes · When a functional group becomes a prefix

14 Principal group and alphabetical prefixes

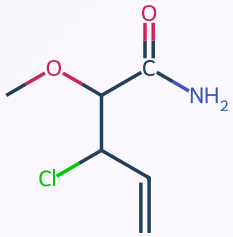
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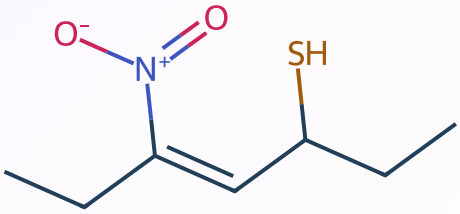
5-Bromo-5-fluoro-2-nitrohex-3-ynoic acid



3-Nitrosohex-4-ene-2-sulfonic acid

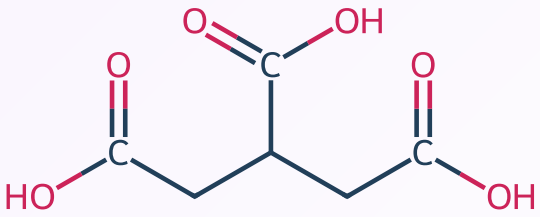


3-Chloro-2-methoxypent-4-enamide



5-Nitrohept-4-en-3-thiol

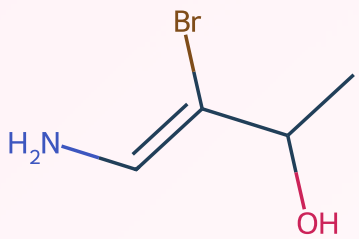
Four worked examples: acid, sulfonic acid, amide and thiol as the principal group.



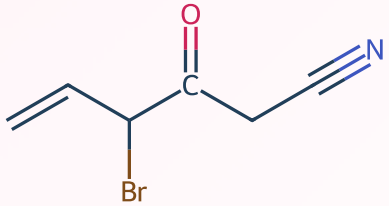
Propane-1,2,3-tricarboxylic acid

With three –COOH groups, name the carbon skeleton and use the tricarboxylic-acid suffix.

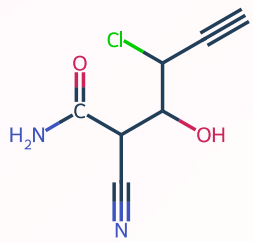
15 When a functional group becomes a prefix



4-Amino-3-bromobut-3-en-2-ol



4-Bromo-3-oxohex-5-enenitrile



4-Chloro-2-cyano-3-hydroxyhex-5-ynamide

Retain every subordinate group as an alphabetized prefix.

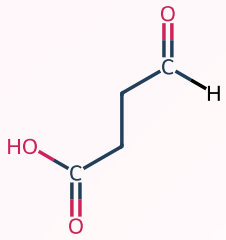
IUPAC Nomenclature

When a functional group becomes a prefix · Cyclic ethers: epoxy and oxirane names

15 When a functional group becomes a prefix

continued

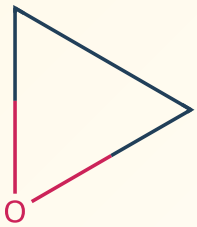
- A subordinate aldehyde is named oxo- when its carbon is included in the parent chain; use formyl- when  is treated as a side group outside that chain. HOOC–CH_2–CH_2–CHO is 4-oxobutanoic acid. The alternative parent description is 3-formylpropanoic acid. "Aldo" is a classroom shorthand; use oxo- in the systematic name.



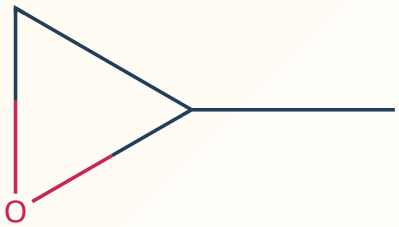
4-Oxobutanoic acid: terminal –CHO carbon included

Oxo versus formyl is decided by whether the aldehyde carbon belongs to the parent.

16 Cyclic ethers: epoxy and oxirane names



1,2-Epoxyethane = oxirane



1,2-Epoxypropane = 2-methyloxirane

Oxirane numbering begins at oxygen (position 1).

17 Anhydrides, esters and N-substituted compounds

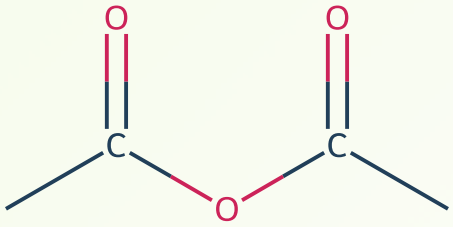
- A symmetrical anhydride is named from one acid: alkanoic anhydride. A mixed anhydride names both acids alphabetically, followed by 'anhydride'.

IUPAC Nomenclature

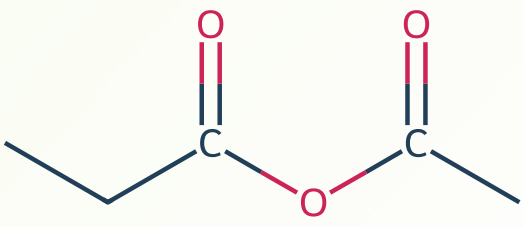
Anhydrides, esters and N-substituted compounds

17 Anhydrides, esters and N-substituted compounds

continued



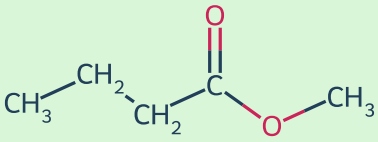
Ethanoic anhydride



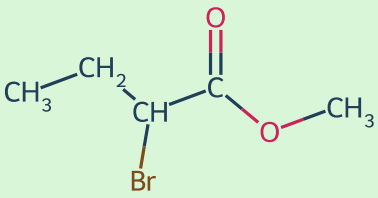
Ethanoic propanoic anhydride

Symmetrical and unsymmetrical acid anhydrides.

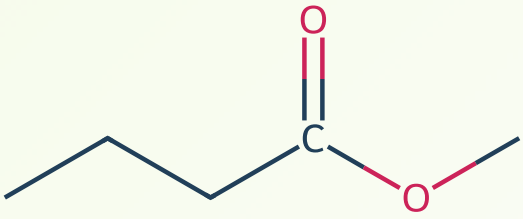
- *Ester naming: write the O-bound alkyl group first, then the acid-derived alkanoate.*



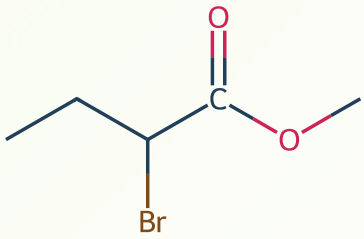
is methyl butanoate. Adding Br at carbon 2 gives



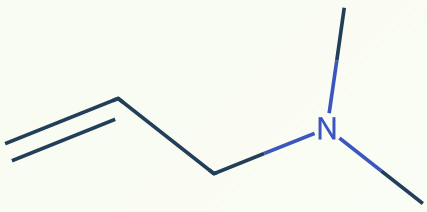
, methyl 2-bromobutanoate.



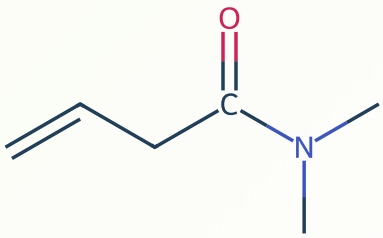
Drawn structure: methyl butanoate



Named brominated example: methyl 2-bromobutanoate



N,N-Dimethylprop-2-en-1-amine



N,N-Dimethylbut-3-enamide

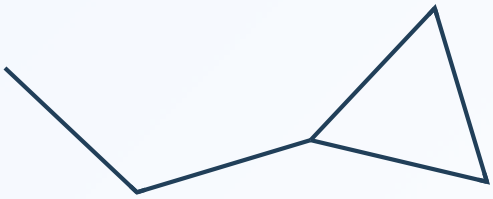
Use N-locants for groups attached directly to nitrogen.

IUPAC Nomenclature

Choosing a ring or chain parent · Ring functional groups and numbering

18 Choosing a ring or chain parent

- *Cyclo-compound naming uses prefix + cyclo + root + unsaturation suffix + principal-group suffix (or special suffix). Decision order: principal functional group → multiple bond → longer chain/ring. With equal carbon counts and no higher-priority feature, choose the ring. A carbon-containing principal group directly attached to a ring is often named with a special suffix.*



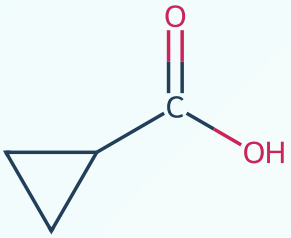
Ethylcyclopropane: ring has 3 carbons, chain 2



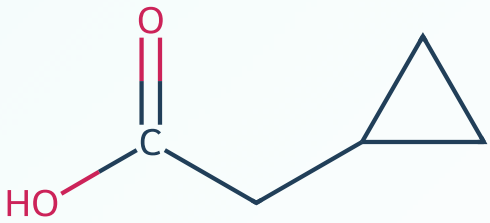
Propylcyclopropane: ring and chain each have 3 carbons

When the carbon counts tie in these examples, the ring is the parent.

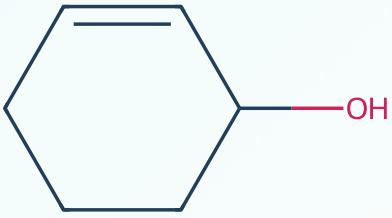
19 Ring functional groups and numbering



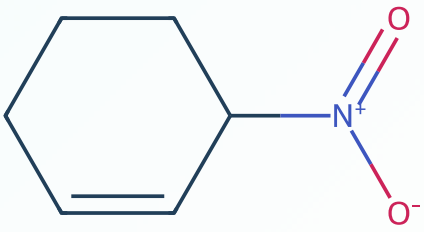
Cyclopropanecarboxylic acid



2-Cyclopropylethanoic acid



Cyclohex-2-en-1-ol



3-Nitrocyclohex-1-ene

Numbering priority: principal suffix > multiple-bond suffix > prefix.

20 Retained names of benzene derivatives

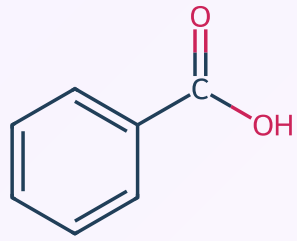
- *Many monosubstituted benzene derivatives retain familiar names. Some systematic alternatives are shown alongside them.*

IUPAC Nomenclature

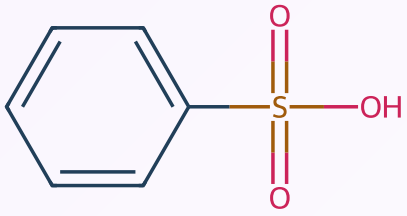
Retained names of benzene derivatives

20 Retained names of benzene derivatives

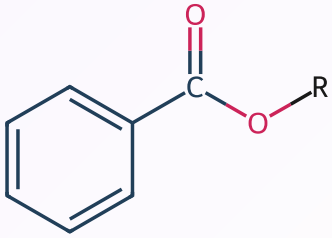
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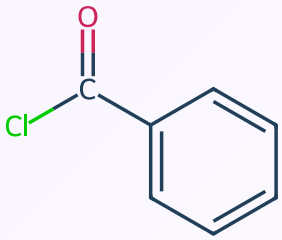
Benzoic acid / benzenecarboxylic acid



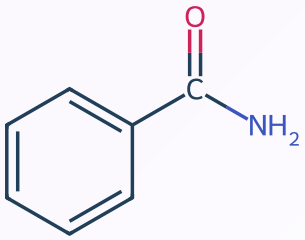
Benzenesulfonic acid



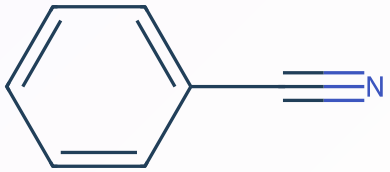
R benzoate / R benzenecarboxylate



Benzoyl chloride / benzenecarbonyl chloride

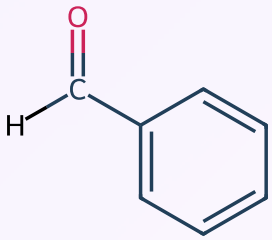


Benzamide / benzenecarboxamide

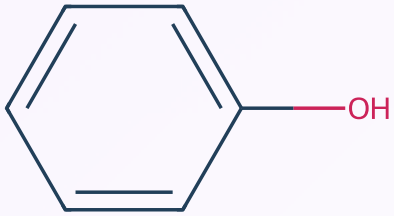


Benzonitrile / benzenecarbonitrile

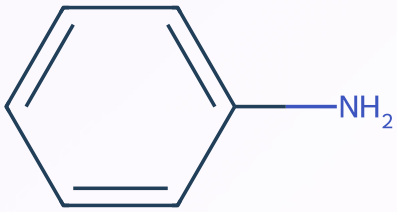
Carbon-containing functional groups attached to benzene.



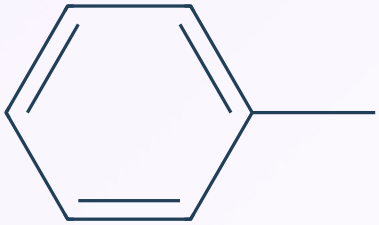
Benzaldehyde



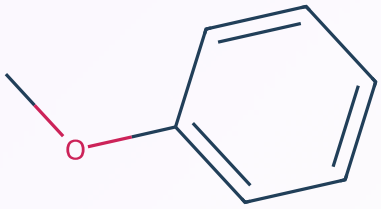
Phenol



Aniline



Toluene



Anisole

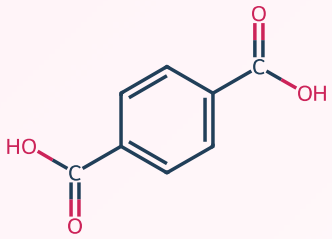
The remaining five retained aromatic names.

IUPAC Nomenclature

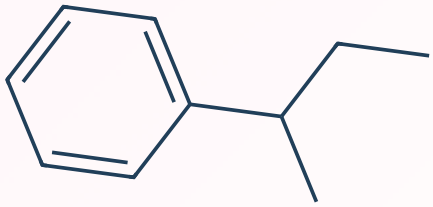
Several groups: ring or side chain?

21 Several groups: ring or side chain?

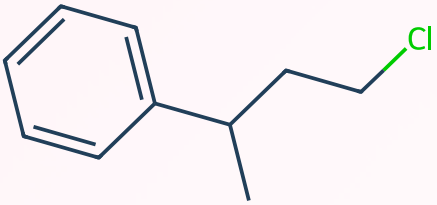
- *For more than one group, number according to the naming rules. The part containing the principal functional group normally governs parent selection. Benzene can be named as a phenyl substituent in the longer open-chain examples below; toluene and ethylbenzene are familiar aromatic names.*



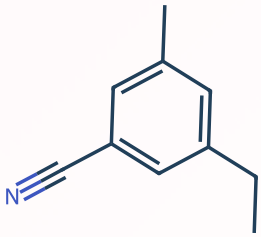
Benzene-1,4-dicarboxylic acid



2-Phenylbutane



1-Chloro-3-phenylbutane



3-Ethyl-5-methylbenzonitrile

Worked numbering and parent-selection examples.

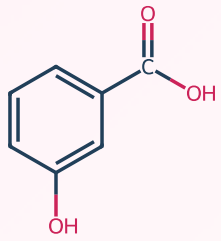
- *When more than one principal-group candidate is present, use functional-group priority, then number the ring and alphabetize the prefixes. If the same kind of group occurs on the open-chain part and on the ring, the illustrated worked examples choose the open-chain parent.*

IUPAC Nomenclature

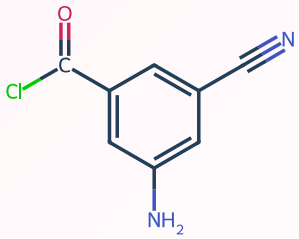
Several groups: ring or side chain? · Ortho, meta and para

21 Several groups: ring or side chain?

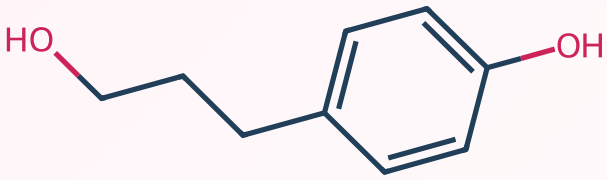
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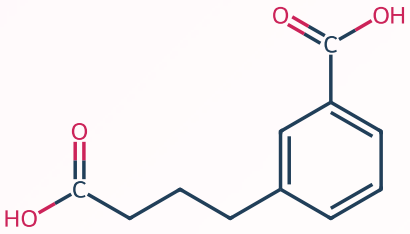
3-Hydroxybenzoic acid



3-Amino-5-cyanobenzoyl chloride



3-(4-Hydroxyphenyl)propan-1-ol



4-(3-Carboxyphenyl)butanoic acid

Examples with two or more functional groups.

22 Ortho, meta and para

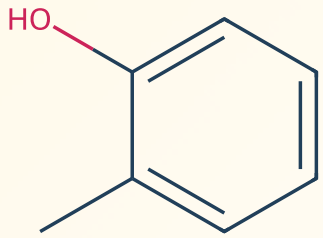
- *Relative to a group at benzene position 1: positions 2 and 6 are ortho (o-); 3 and 5 are meta (m-); 4 is para (p-).*

IUPAC Nomenclature

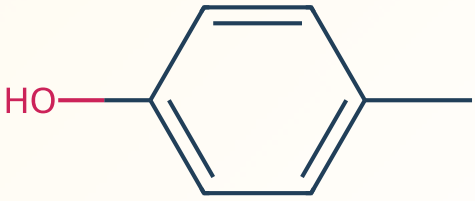
Ortho, meta and para · Common hydrocarbon-derived substituents

22 Ortho, meta and para

continued



o-Cresol / 2-methylphenol



p-Cresol / 4-methylphenol

The illustrated two cresol examples.

23 Common hydrocarbon-derived substituents

Group (free bond marks attachment)	Name
CH_3-	Methyl (from CH_4)
$CH_3CH_2CH_2-$	n-Propyl / propan-1-yl
$(CH_3)_2CH-$	Isopropyl / propan-2-yl (also: sec-propyl)
$CH_3CH_2CH(CH_3)-$	sec-Butyl / butan-2-yl
$(CH_3)_2CHCH_2-$	Isobutyl / 2-methylpropyl
$(CH_3)_3C-$	tert-Butyl / 1,1-dimethylethyl
$CH_3CH_2CH_2CH(CH_3)-$	Pentan-2-yl; may be chiral when attached to an appropriate group (also: active sec-pentyl)
$(CH_3CH_2)_2CH-$	Pentan-3-yl (also: sec-pentyl)
$(CH_3)_3CCH_2-$	Neopentyl / 2,2-dimethylpropyl

Purification Techniques

Separate · purify · identify

02

01 Five common purification methods

- Purification means removing impurities. Useful methods include sublimation, crystallization, distillation, differential extraction and chromatography. Sublimation and crystallization are mainly used for solids; the other techniques are selected according to the mixture and its physical properties.

02 Sublimation: solid directly to vapour

- Some solids change directly into vapour on heating without passing through the liquid state. Separate a sublimable compound from non-sublimable impurities by collecting the condensed solid. Examples in the also: iodine, camphor, naphthalene and ammonium chloride.

03 Crystallization: use a solubility difference

- Crystallization relies on different solubilities of the desired compound and impurities in a suitable solvent. Dissolve the impure solid in a solvent in which it is sparingly soluble at room temperature but appreciably soluble at higher temperature. Cooling then gives crystals.

- If a compound is very soluble in one solvent but only slightly soluble in another, use a suitable mixture of the two solvents. Examples: purification of sugar and potash alum.

04 Distillation: four useful choices

- Distillation separates a volatile liquid from non-volatile impurities, or separates liquids with sufficiently different boiling points.

Method	Choose it when...	Example
Simple distillation	The liquids have well-separated boiling points; rule of thumb: difference >20 °C.	Chloroform (334 K) and aniline (457 K)
Fractional distillation	The boiling points are close; rule of thumb: difference <20 °C.	Different crude-oil fractions in the petroleum industry
Reduced-pressure distillation	A liquid has a very high boiling point or decomposes at/below its atmospheric-pressure boiling point.	Glycerol from spent lye in the soap industry
Steam distillation	The substance is steam-volatile and immiscible or nearly immiscible with water.	Aniline from aniline–water mixture

- The 20 °C separation is a classroom guide, not a universal sharp boundary; the suitable method also depends on composition and vapour–liquid behaviour.

05 Differential extraction

- This method uses the different solubilities of an organic compound in different solvents. Shake its aqueous solution with an organic solvent in which it is more soluble. The organic solvent and water must be immiscible so they form two distinct layers. Separate the layers with a separating funnel.

Purification Techniques

Recover the extracted compound · Chromatography: purpose and phases

06 Recover the extracted compound

- After separating the organic layer in the separating funnel, remove the organic solvent by distillation or evaporation to recover the organic compound.

07 Chromatography: purpose and phases

- Chromatography is used to purify compounds, separate mixtures and test purity. It has a stationary phase and a mobile phase. In adsorption chromatography the stationary phase is a solid; the mobile phase is a liquid or gas. In partition chromatography the stationary phase is a liquid held on a support.

Main type	Basis
Adsorption chromatography	Different substances are adsorbed to different extents on a solid surface.
Partition chromatography	Different substances distribute differently between two phases.

08 Adsorption chromatography

- Common adsorbents are silica gel and alumina. The two methods are column chromatography and thin-layer chromatography (TLC).

- Column chromatography: pack a glass tube with adsorbent (stationary phase) and pass the mixture/mobile phase through it. More strongly adsorbed components are retained near the top for longer; less strongly adsorbed components travel farther down. Here retention means adsorption onto the solid, not dissolution in it.

- TLC: coat a glass plate with a thin adsorbent layer. Components move up with the solvent to different distances because their adsorption strengths differ; this produces separation.

$$R_f = \frac{x}{y} = \frac{\text{distance travelled by component from baseline}}{\text{distance travelled by solvent front from baseline}}$$

The retardation factor compares a component's travel with the solvent front under the same conditions. Measure both distances from the same baseline.

09 Partition chromatography: paper chromatography

- In the paper example, the stationary phase is water trapped in cellulose chromatography paper; the mobile phase is a liquid solvent or solvent mixture. Suspend the spotted paper so the solvent can rise through it.

- The solvent rises by capillary action and passes over the sample spot. Components are retained differently because they partition differently between the trapped water and the moving solvent. Repeated differential partitioning separates the mixture. The developed paper strip is called a chromatogram.

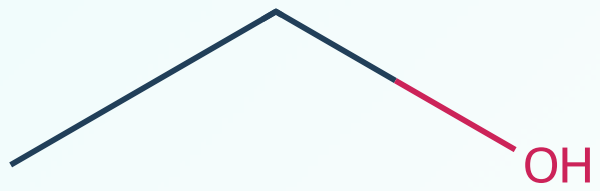
Isomerism

Connectivity · configuration · conformation

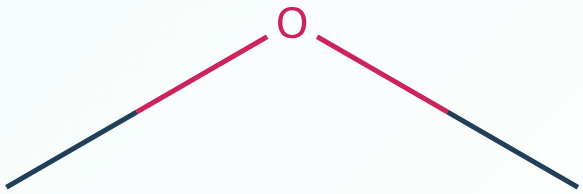
03

01 What are isomers?

- Isomers are different compounds having the same molecular formula. Example: C_2H_6O can be ethanol (CH_3CH_2OH) or dimethyl ether (CH_3OCH_3).



Ethanol



Dimethyl ether

C_2H_6O: same formula, different connectivity.

- Isomers have the same molecular formula, molar mass, empirical formula, degree of unsaturation and ideal-gas vapour density. They differ in at least one physical or chemical property.

Structural isomers	Stereoisomers
Different atom connectivity	Same connectivity; different arrangement in space
Different constitutional IUPAC names	Same constitutional name; stereodescriptors distinguish them

02 Chain isomerism

- Chain isomers have different carbon skeletons or parent-chain arrangements.



Butane: 4-carbon parent



2-Methylpropane: 3-carbon parent

Both are C_4H_{10}.

Isomerism

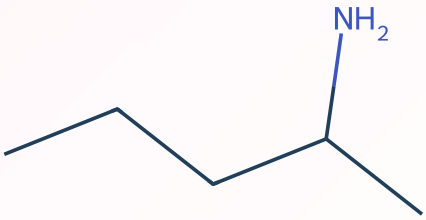
Position isomerism

03 Position isomerism

- Position isomers have the same parent skeleton but differ in the position of a substituent, multiple bond or functional group. Example: the $-NH_2$ group moves from carbon 1 to carbon 2 of pentane.



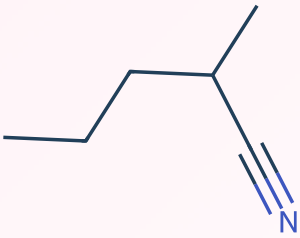
Pentan-1-amine



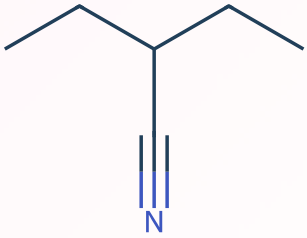
Pentan-2-amine

Same five-carbon skeleton; different amine position.

- Classroom shortcut for comparing only chain versus position isomerism: write XY, where X is the number of carbons in the chosen parent and Y is the number of carbon branches. Equal XY suggests position isomerism; different XY suggests chain isomerism. This is a classroom shortcut, not a universal definition.



2-Methylpentanenitrile: comparison code 51



2-Ethylbutanenitrile: comparison code 41

For nitriles, the –C≡N carbon participates in the parent count.

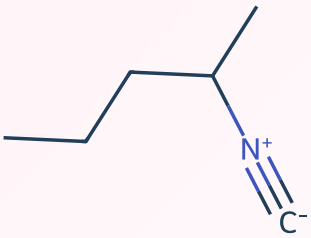
- Compare $CH_3CH(NC)CH_2CH_2CH_3$ and $CH_3CH_2CH(NC)CH_2CH_3$: both have comparison code 50 and are position isomers. In isocyanides the attached atom is N, so the terminal isocyano carbon is not added to the alkane parent. Classification priority: chain > position.

Isomerism

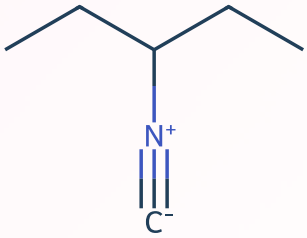
Position isomerism · Metamerism: groups on two sides of a bridge

03 Position isomerism

continued



2-Isocyanopentane: comparison code 50

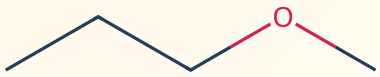


3-Isocyanopentane: comparison code 50

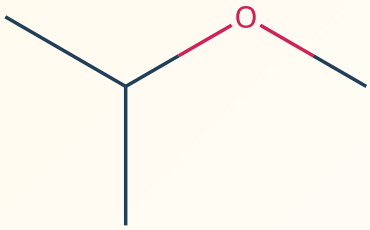
The pentane skeleton stays the same; the isocyano group changes position.

04 Metamerism: groups on two sides of a bridge

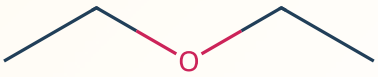
- *Metamers have the same molecular formula and the same bridging functional group but a different distribution of carbon groups on its two sides.*



Methyl n-propyl ether: 3C + 1C

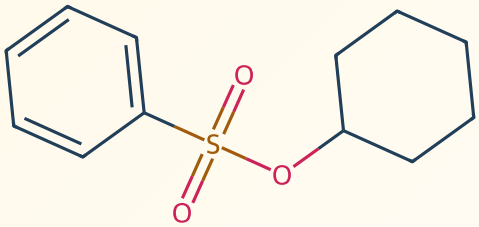


Methyl isopropyl ether: branched 3C + 1C

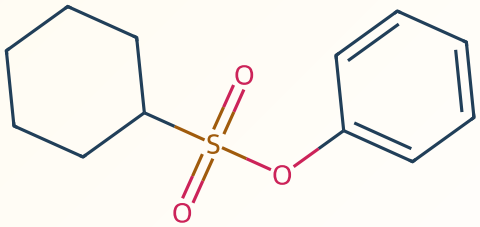


Diethyl ether: 2C + 2C

$C_4H_{10}O$ ethers: compare the groups on either side of oxygen.



Cyclohexyl benzenesulfonate



Phenyl cyclohexanesulfonate

Swap phenyl and cyclohexyl across the $–SO_2–O–$ linkage.

Isomerism

Metamerism: groups on two sides of a bridge · Functional isomerism: important pairs

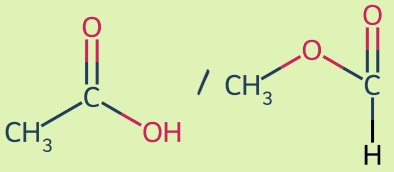
04 Metamerism: groups on two sides of a bridge

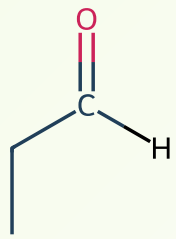
continued

- Use the classification order metamerism > chain > position when more than one classroom description seems possible.

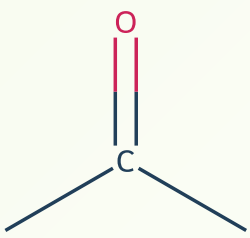
05 Functional isomerism: important pairs

- Functional isomers share a molecular formula but have different functional-group arrangements.

Pair	Examples
Aldehyde / ketone	Propanal / propanone
Alcohol / ether	Propan-1-ol / methoxyethane
Carboxylic acid / ester	
1°, 2°, 3° amines	Propan-1-amine / N-methylethanamine / trimethylamine
1°, 2°, 3° amides	Propanamide / N-methylethanamide / N,N-dimethylmethanamide
Cyanide / isocyanide	
Diene / alkyne	Buta-1,3-diene / but-2-yne
Phenol / alcohol	Phenol and a suitable alcohol can form a same-formula functional-isomer pair.



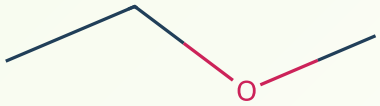
Propanal



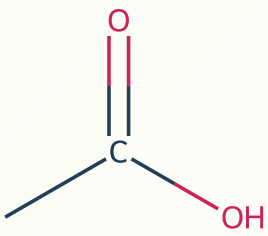
Propanone



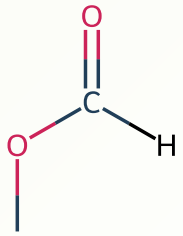
Propan-1-ol



Methoxyethane



Ethanoic acid



Methyl methanoate

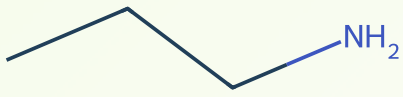
Worked aldehyde/ketone, alcohol/ether and acid/ester examples.

Isomerism

Functional isomerism: important pairs · Ring–chain isomerism

05 Functional isomerism: important pairs

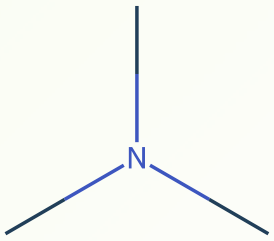
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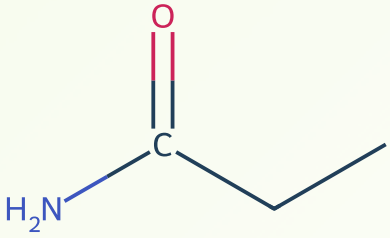
1° amine



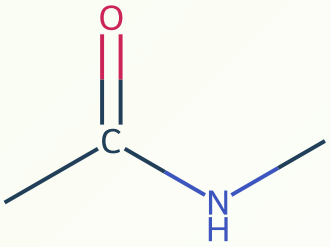
2° amine



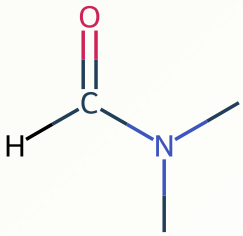
3° amine



1° amide

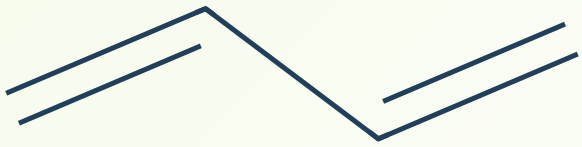


2° amide



3° amide

Amines and amides: compare primary, secondary and tertiary substitution.



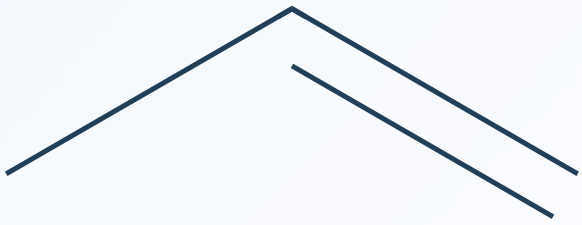
Buta-1,3-diene



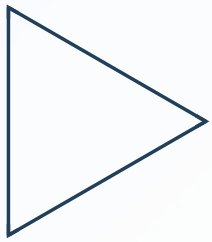
But-2-yne

Diene and alkyne: both C_4H_6.

06 Ring–chain isomerism



Propene: open chain



Cyclopropane: ring

Both have formula C_3H_6.

Isomerism

Ring–chain isomerism · Tautomerism: movement of H and a π bond

06 Ring–chain isomerism

continued

- Ring–chain isomerism compares an open-chain structure with a cyclic structure. This is also often grouped with functional isomerism.

07 Tautomerism: movement of H and a π bond

- Tautomers interconvert through proton transfer together with a change in bond position. For ordinary keto–enol tautomerism, the carbonyl compound needs an α-hydrogen on an initially sp^3 α-carbon. Examples include 1,3-, 1,5- and 1,2-shift systems.

- In a 1,3-system, transfer H from site 3 to site 1 and move the π bond from 1–2 to 2–3. The usual catalysed process need not be a single direct intramolecular proton jump.

Reversible tautomeric equilibrium



Keto ⇌ enol.

Reversible tautomeric equilibrium



Nitro ⇌ aci-nitro.

Reversible tautomeric equilibrium



Nitroso ⇌ oxime.

Reversible tautomeric equilibrium



Imine ⇌ enamine.

Isomerism

Tautomerism: movement of H and a π bond · 1,5- and 1,2-systems

07 Tautomerism: movement of H and a π bond

continued

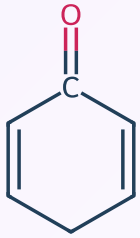
Reversible tautomeric equilibrium



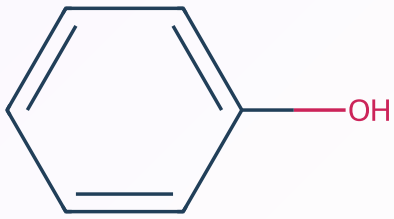
Amide ⇌ imidic acid (also: imidol).

08 1,5- and 1,2-systems

- *For a conjugated system where the simple 1,3-shift is not available, consider the longer conjugated 1,5-shift shown.*



Cyclohexa-2,5-dien-1-one



Phenol

1,5 keto–enol example: formation of an aromatic phenol.

Reversible tautomeric equilibrium



The illustrated 1,2-system: HCN ⇌ HNC; HNC is represented with appropriate formal charges in a full Lewis structure.

- *Tautomers may also be classed as functional isomers. In the depicted acetone/enol pair, each has 9 σ bonds, 1 π bond and 2 lone pairs. Use this bond-count comparison as a quick check.*

09 Classification guide

- *When several school-level labels appear possible, use the guide R > T > F > M > C > P: ring–chain > tautomerism > functional > metamerism > chain > position. Mnemonic: "Raat ko F.M. chalao pyaar se."*

Isomerism

How many constitutional alkane isomers? · Worked count: C_4H_8

10 How many constitutional alkane isomers?

Carbon count	Number of structural isomers
C_1	1
C_2	1
C_3	1
C_4	2
C_5	3
C_6	5
C_7	9
C_8	18
C_9	35
C_{10}	75

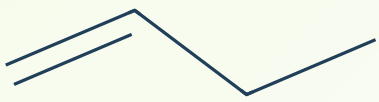
$$\mathrm{DU} = C + 1 - \frac{H + X - N}{2}$$

DU = 0: no rings or π bonds. DU = 1: one ring or one π bond. DU = 2: two rings, two π bonds, or one ring plus one π bond.

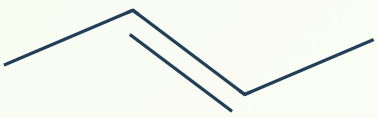
11 Worked count: C_4H_8

$$\mathrm{DU} = 4 + 1 - \frac{8}{2} = 1$$

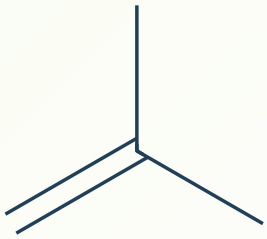
Either one C=C or one ring.



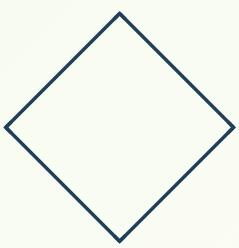
But-1-ene



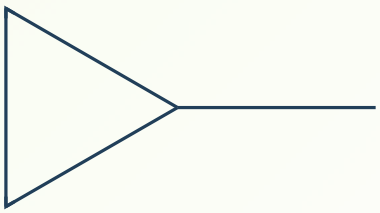
But-2-ene



2-Methylpropene



Cyclobutane



Methylcyclopropane

Five structural isomers; cis/trans forms of but-2-ene are not counted separately in this structural count.

Isomerism

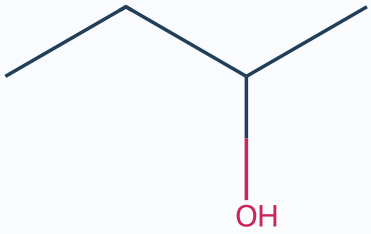
Worked count: $C_4H_{10}O$ · Benzenoid positional patterns

12 Worked count: $C_4H_{10}O$

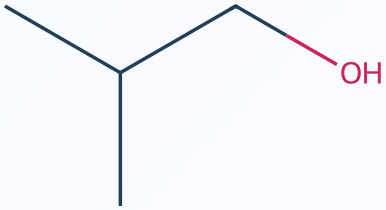
- DU = 0. With one oxygen, consider alcohols and ethers. There are four alcohols and three ethers.



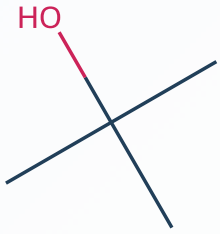
Butan-1-ol



Butan-2-ol



2-Methylpropan-1-ol



2-Methylpropan-2-ol

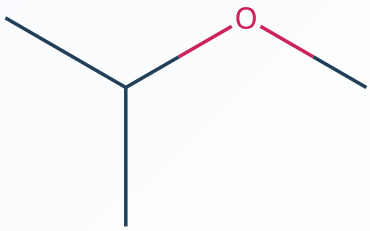
Four alcohol structures.



Ethoxyethane



1-Methoxypropane



2-Methoxypropane

Three ether structures; total = seven structural isomers.

13 Benzenoid positional patterns

- Common benzenoid counting patterns: C_6H_5X; $C_6H_4X_2$; C_6H_4XY; $C_6H_3XY_2$; $C_6H_2XY_3$; C_6HXY_4; and C_6H_3XYZ. X, Y and Z stand for substituent types. The worked result is $C_6H_3BrCl_2$ → six distinct benzenoid arrangements.

14 Stereoisomerism and restricted rotation

- Stereoisomers have the same connectivity but a different arrangement in space. The two classes considered here are geometrical and optical isomerism; stereodescriptors distinguish names that otherwise share the same constitution.

Isomerism

Stereoisomerism and restricted rotation · Cis/trans and E/Z

14 Stereoisomerism and restricted rotation

continued

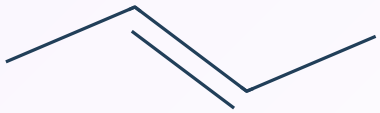
- Geometrical isomerism arises from restricted rotation, for example around C=C, suitable C=N or N=N groups, and within rings. A simple C=O group alone cannot have E/Z isomers because oxygen does not carry two distinguishable substituents.

- Geometrical isomers are diastereomers: they are not mirror images. Their substituent distances differ, and differences in physical properties often allow separation. For the illustrated A/H disubstituted alkene, the distance between A groups is shorter in cis (ℓ_1) than trans (ℓ_2): $\ell_2 > \ell_1$.

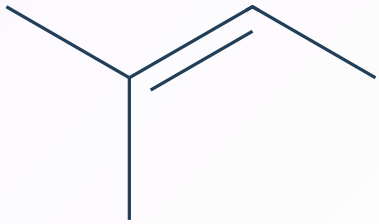
- Condition for a C=C pair: each double-bond carbon must carry two different groups. $CH_3CH=CHCH_3$ qualifies; $(CH_3)_2C=CHCH_3$ does not. Isotopes count as different groups.



cis-But-2-ene



trans-But-2-ene



2-Methylbut-2-ene: no E/Z pair

Identical groups on one alkene carbon prevent geometrical isomerism.

15 Cis/trans and E/Z

- Cis: matching groups are on the same side. Trans: matching groups are on opposite sides. E/Z works more generally: compare the higher-priority group at each end. Same side = Z; opposite sides = E.

- Cahn–Ingold–Prelog (CIP) priority: 1. Higher atomic number of the directly attached atom gives higher priority. 2. If tied, compare the next attached atoms in descending order at the first point of difference. 3. For isotopes of the same element, higher mass number has higher priority. 4. Treat multiple bonds using duplicate-atom comparisons; do not use bond order before checking atom identities.

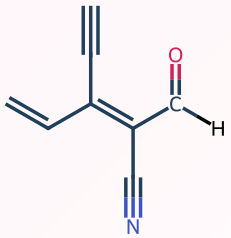
Source comparison	Priority result
Same attached atom types	Triple-bond duplicate set > double > single in the listed simple comparisons
Carbon groups	−C≡C > −C=C > −C−C
Nitrogen-containing groups	−C≡N > −C=N > −C−N
Carbonyl versus alcohol carbon	−C=O > −C−O when the remaining comparison is tied
C=O versus C≡C	Carbonyl side higher because O > C
C≡N versus C−O	C−O side higher because O > N
C=C versus C−O	C−O side higher because O > C
C=N versus C≡C	C=N side higher because N > C

Isomerism

Cis/trans and E/Z · C=N: syn/anti oximes

15 Cis/trans and E/Z

continued

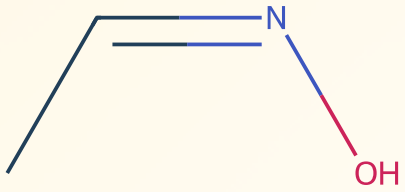


E/Z example: CHO and C≡CH on the same side

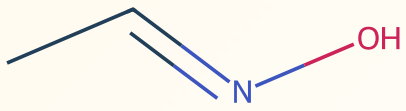
CHO outranks CN (O > N); ethynyl outranks vinyl. The depicted arrangement is Z.

16 C=N: syn/anti oximes

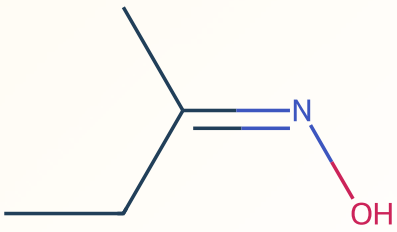
- *Aldoxime: when the aldehydic H and –OH lie on the same side of C=N, it is called syn; opposite sides are anti. For ketoximes, specify the reference alkyl group when using syn/anti.*



Anti-acetaldoxime: H and OH opposite



Syn-acetaldoxime: H and OH same side

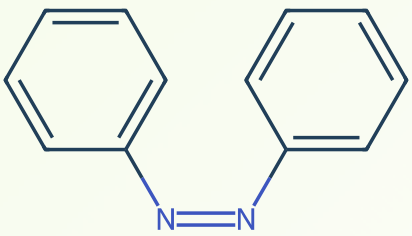


Methyl ethyl ketoxime geometry

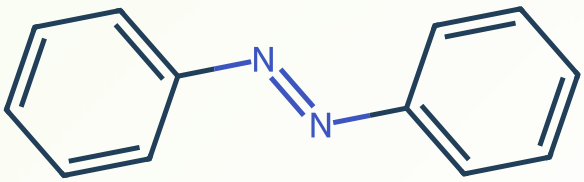
For the ketoxime shown, OH is syn to ethyl and anti to methyl.

- *The ketoxime can be described as syn to ethyl or anti to methyl; always identify the reference group.*

17 N=N and cycloalkanes



Syn / cis azobenzene



Anti / trans azobenzene

For N=N, compare whether the phenyl groups lie on the same or opposite side.

Isomerism

N=N and cycloalkanes · Reading ring stereochemistry

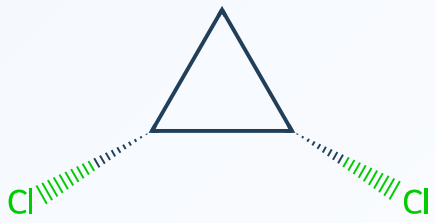
17 N=N and cycloalkanes

continued

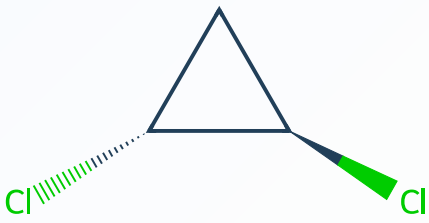
- In a cycloalkane, substituents may point above or below the ring plane. In cyclopropane, one H at each carbon is above the ring plane and the other is below. On the same face = cis; on opposite faces = trans.

18 Reading ring stereochemistry

- In 1,2-dichlorocyclopropane, both Cl groups on the same face give cis; one Cl above and one below give trans. Solid wedge = toward the reader / above the drawing plane; hashed wedge = away / below; plain line = in the drawing plane.



cis-1,2-Dichlorocyclopropane



trans-1,2-Dichlorocyclopropane

Use the two Cl bond directions to distinguish cis and trans.

- For ring geometrical isomerism, the relevant substituents are on different sp^3 ring atoms; they can be the same or different groups.

Cyclopropane substitution pattern	Number of geometrical arrangements
One a substituent	No cis/trans pair
a,a or a,b on the same ring carbon	No cis/trans pair
a,a or a,b on two different ring carbons	2
a,a,a on three ring carbons	2
a,a,b on three ring carbons	3
a,b,c on three ring carbons	4

- These are counts of relative cis/trans arrangements, not separate counts of every enantiomer.

19 Special restricted systems

- Cumulenes: with an odd number of consecutive C=C bonds, the terminal substituents lie in the same plane and geometrical isomerism is possible if $a \neq b$ and $x \neq y$. Skeleton: (a)(b)C=C=C=C(x)(y).

- Spiranes: the illustrated chain of three consecutive spiro rings has terminal Cl/H pairs; an odd number of such rings can give geometrical isomerism if each terminal pair differs.

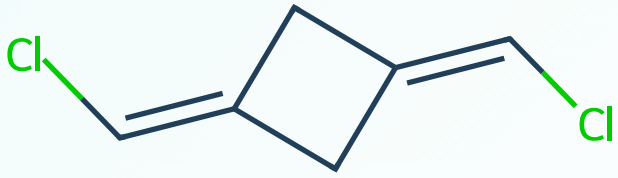
Isomerism

Special restricted systems · Exocyclic alkenes: compare the two ring paths

19 Special restricted systems

continued

- *Combined spirane + cumulene system: consider a four-membered ring with two opposite exocyclic C=C bonds, each terminal carbon carrying Cl and H. One ring + two double bonds is odd, and the drawing is marked "GI yes".*

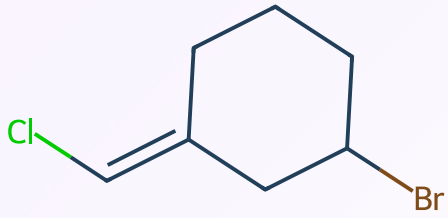


Opposite exocyclic chloromethylene groups on a four-membered ring

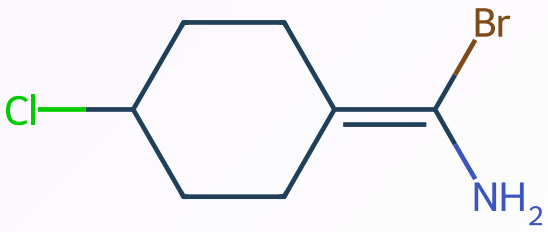
Combined ring-plus-double-bond example; Cl/H differ at both ends.

- *These odd/even shortcuts apply to the specific idealized terminal-substitution systems drawn, with the required substituent differences.*

20 Exocyclic alkenes: compare the two ring paths



Different ring paths: GI possible



Equivalent ring paths: no exocyclic E/Z pair

In the first ring Br makes the two paths different; the symmetric opposite-ring Cl in the second leaves them equivalent.

- *The exocyclic carbon must also have two different groups. Here they are Cl/H in the first example and Br/NH_2 in the second.*

21 Cycloalkenes and fused rings

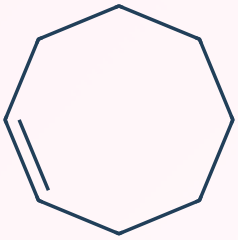
- *For ordinary cycloalkenes, isolable trans forms become possible from an eight-membered ring upward. A simple-ring stability guide: cis > trans for rings of 8–10 carbons; trans > cis from 11 onward. Treat this as the illustrated simple-ring comparison, not a general rule for every substituted ring.*

Isomerism

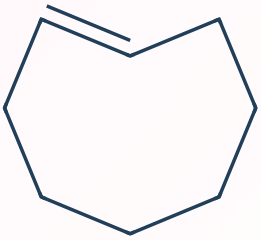
Cycloalkenes and fused rings · Nitrogen heterocycles

21 Cycloalkenes and fused rings

continued

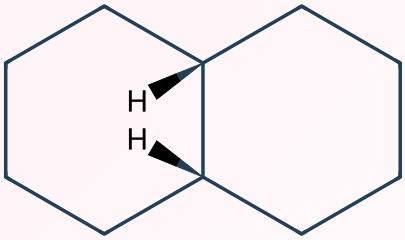


cis-Cyclooctene (Z)

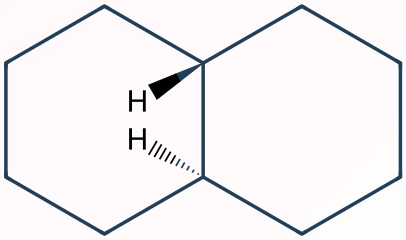


trans-Cyclooctene (E)

The illustrated cis/trans cyclooctene sketches.



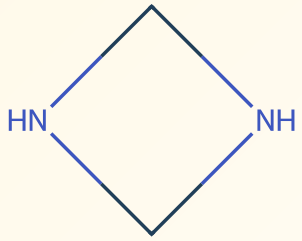
One decalin ring-junction configuration



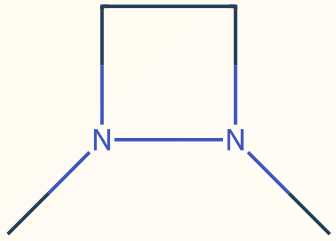
The other decalin ring-junction configuration

For decalin, same-face bridgehead H atoms are cis; opposite-face bridgehead H atoms are trans.

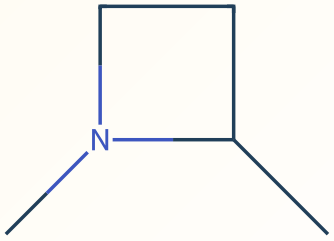
22 Nitrogen heterocycles



Four-membered ring with opposite NH groups



Adjacent N-methyl groups in a four-membered ring



N-methyl / C-methyl four-membered heterocycle

Relative cis/trans arrangements can be drawn; check nitrogen-inversion stability.

Isomerism

Nitrogen heterocycles · Counting independent geometrical elements

22 Nitrogen heterocycles

continued

- Nitrogen pyramidal inversion can rapidly interconvert some such arrangements. A drawn relative arrangement does not by itself establish isolable stereoisomers; the inversion barrier and ring constraints must be considered.

23 Counting independent geometrical elements

$$\text{Maximum geometrical isomers} = 2^n$$

For an unsymmetrical system without further equivalences; n = number of independent E/Z elements.

- Example: $CH_3–CH=CH–CH=CH–CH_2Br$ has different end groups, n = 2 and $2^2 = 4$ geometrical isomers.

24 A symmetrical polyene counting formula

$$G = 2^{n-1} + 2^{p-1},$$

$$p = \begin{cases} n/2 & n \text{ even} \\ (n+1)/2 & n \text{ odd} \end{cases}$$

This formula assumes equivalent ends and the simple linear-polyene symmetry illustrated, not every symmetrical molecule.

- Example: $CH_3–CH=CH–CH=CH–CH=CH–CH_3$. Here n = 3; p = 2; G = $2^2 + 2^1 = 6$.

25 Cis/trans property comparisons

Property	Source trend for comparable simple examples
Dipole moment	cis > trans
Boiling point	cis > trans; stronger intermolecular polarity can raise boiling point
Crystal lattice cohesion	cis < trans in the illustrated packing comparison
Melting point	cis < trans when the more symmetric trans form packs better
Thermodynamic stability	cis < trans for the usual acyclic disubstituted-alkene examples
Solubility	Source: cis > trans; actual order depends on solvent and crystal packing

- These are useful example trends, not universal laws. Melting point, solubility and stability must be assessed for the actual compounds. Here lattice energy means the energy needed to break up one mole of crystal.

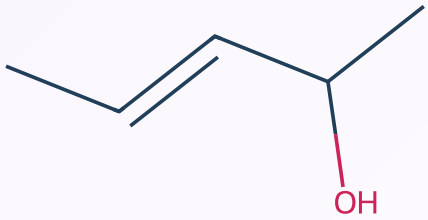
Isomerism

Chiral centres versus independent stereogenic elements · Optical activity terminology

26 Chiral centres versus independent stereogenic elements

- A tetrahedral chiral centre has four different attached groups. A chiral carbon is an sp^3 carbon attached to four different groups. Every such chiral centre is stereogenic, but a stereogenic element need not be a tetrahedral chiral carbon.

- The participating-atom counts the two atoms at each geometrically stereogenic C=C as two "stereocentres": participating-atom count = chiral centres + 2 per GI double bond. For counting stereoisomers, however, one independently variable E/Z double bond is one element.



CH_3–CH(OH)–CH=CH–CH_3

Participating-atom count: 1 tetrahedral centre + 2 alkene atoms = 3 marked sites; there are 2 independent binary stereogenic elements.

- Two further counting sketches mark two sites in a substituted cyclohexane fragment plus one E/Z double bond (marked-site total 2 + 2 = 4), and a CH_3–CH^*–CH^*–CH=CH–CH=CH–CH_3 chain (marked-site total 2 + 4 = 6). The extra groups at the starred CH sites are not fully written, so their chirality cannot be independently checked from these incomplete sketches.

27 Optical activity terminology

- An achiral compound is optically inactive. An enantiomerically enriched chiral sample may be optically active. Clockwise rotation is dextrorotatory, d or (+); anticlockwise is laevorotatory, l or (–). Chirality alone does not make a racemic sample rotate light.

28 Plane and centre of symmetry

- A plane of symmetry (POS) divides a molecular arrangement into mirror-related halves. A molecule may have more than one such plane. Examples: meso-2,3-dichlorobutane in a Fischer projection, and cis-1,2-dimethylcyclopropane.

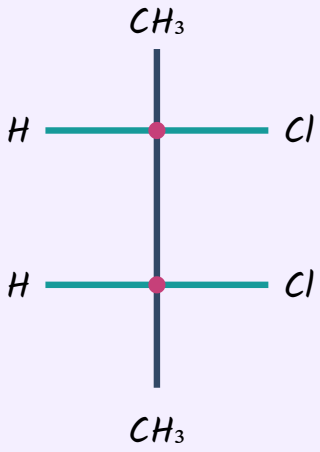
Isomerism

Plane and centre of symmetry · Fischer projection convention

28 Plane and centre of symmetry

continued

Mirror plane through middle



The two Cl groups on the same side of this Fischer projection give an internally compensated meso arrangement.

- A centre of symmetry (COS) is a point through which every atom/group has an identical counterpart at the opposite equal displacement. There is at most one inversion centre. Suitable substitution on an even-membered ring can give inversion symmetry.

Ring arrangement	COS result
Opposite Br substituents on a cyclobutane, one solid wedge and one dashed wedge	Yes in the idealized source drawing
Same opposite Br substituents, both solid wedges	No
cis-Dimethylcyclopropane sketch	No inversion centre
Opposite methyl groups on cyclobutane with opposite up/down orientations	Yes in the idealized source drawing

- Presence of a POS or COS guarantees achirality. The table labels POS/COS = yes/yes, yes/no and no/yes as optically inactive, and no/no as active. The last shortcut is incomplete: absence of both is not sufficient; all improper rotation symmetry must be absent, and a sample must not be racemic.

29 Fischer projection convention

- In a Fischer projection, horizontal bonds point toward the viewer and vertical bonds point away. The intersection is the tetrahedral centre.

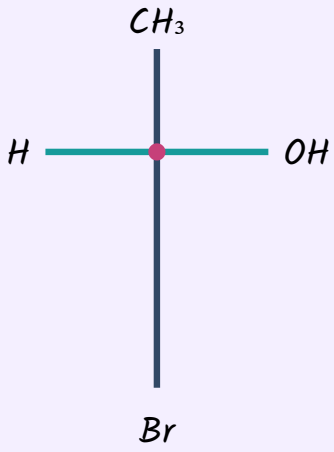
Isomerism

Fischer projection convention · Assign R/S using CIP priorities

29 Fischer projection convention

continued

Four different groups; no POS



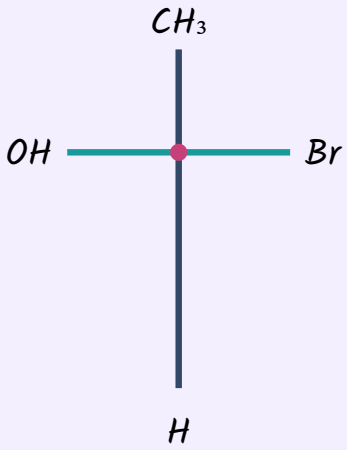
Fischer example: CH_3 above, Br below, H left and OH right.

30 Assign R/S using CIP priorities

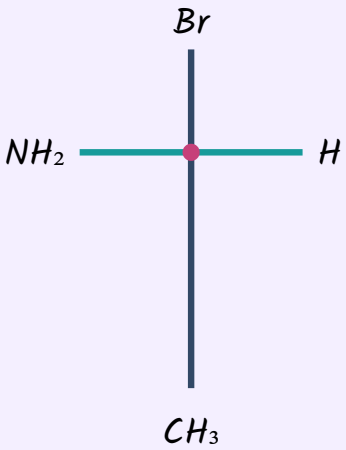
- Assign priorities 1 > 2 > 3 > 4. With group 4 pointing away, clockwise 1→2→3 is R and anticlockwise is S. These descriptors do not predict (+)/(−) rotation.

- Fischer projection: group 4 on a vertical bond points away, so use the observed sense. Group 4 on a horizontal bond points toward you, so reverse the observed result.

R: 4 is vertical



R: 4 is horizontal; reverse



Worked Fischer examples: Br highest, H lowest; the middle-priority group is O or N before carbon.

Isomerism

Assign R/S using CIP priorities · Relating stereoisomers

30 Assign R/S using CIP priorities

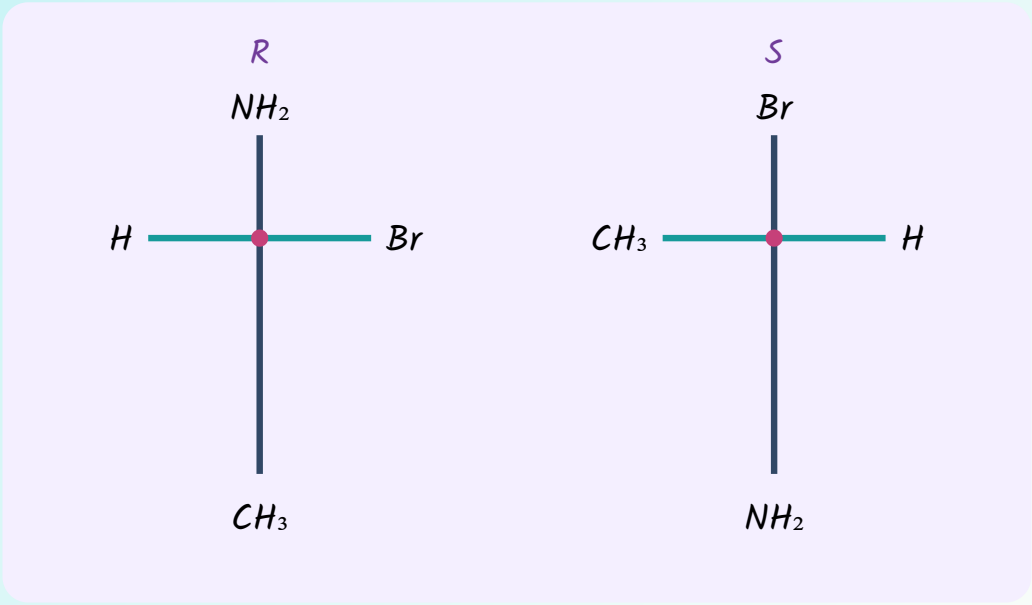
continued

- Wedge–dash drawing: if 4 is dashed, read normally; if 4 is a solid wedge, reverse. If 4 lies in the drawing plane, interchange it with an away-pointing group, assign the temporary structure, then reverse because a single interchange inverts the configuration.

- Halogen example: I > Br > Cl > F. F is initially in-plane, Cl is dashed and Br is on a solid wedge. Swap F and Cl to put priority 4 away; the temporary drawing reads S, so the starting structure is R.

31 Relating stereoisomers

- With one chiral centre and the same connectivity: R/R or S/S are identical; R/S are enantiomers. Enantiomers are non-superimposable mirror images.



Opposite configurations: an enantiomeric pair.

- With two or more chiral centres: all configurations unchanged → identical; all inverted → mirror-image candidates (check for a meso identity); some but not all inverted → diastereomers. Diastereomers are stereoisomers that are not mirror images.

Two-centre comparison (no meso equivalence assumed)	Relationship
RR versus SS	Enantiomers
RS versus SR	Enantiomers
RR versus RS or SR	Diastereomers
SS versus RS or SR	Diastereomers
RR versus RR; RS versus RS	Identical

Isomerism

Relating stereoisomers · Meso compounds

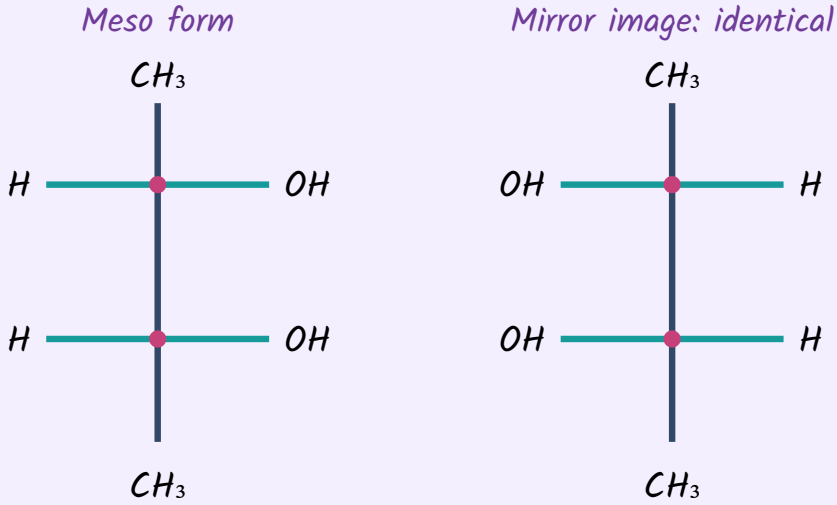
31 Relating stereoisomers

continued

- POS is a useful quick check in these open-chain examples; check both POS and COS in the ring examples. The general symmetry and sample-composition cautions on the preceding page still apply.

32 Meso compounds

- A meso compound is achiral despite containing stereogenic centres; this describes its optical inactivity as internal compensation. Common examples have at least two chiral carbons and a symmetry plane or inversion symmetry. Its mirror image is identical after appropriate reorientation.



The two Fischer drawings represent the same meso-2,3-butanediol.

- A cis-1,2-disubstituted cyclopropane with identical substituents is meso: two stereogenic carbons, a mirror plane and internal compensation.

33 Racemic mixture and resolution

- A racemic mixture contains equal amounts of two enantiomers. Each pure enantiomer is optically active under the measurement conditions, but equal and opposite rotations cancel in the mixture: external compensation.

$$(+40^\circ) + (-40^\circ) \longrightarrow \theta_{\text{net}} = 0$$

Illustration: equal amounts of enantiomers A and B, measured under matching conditions.

Isomerism

Racemic mixture and resolution · Observed and specific rotation

33 Racemic mixture and resolution

continued

- Resolution means separating a racemic mixture into its enantiomers: inactive (A+B) → active A + active B.

34 Observed and specific rotation

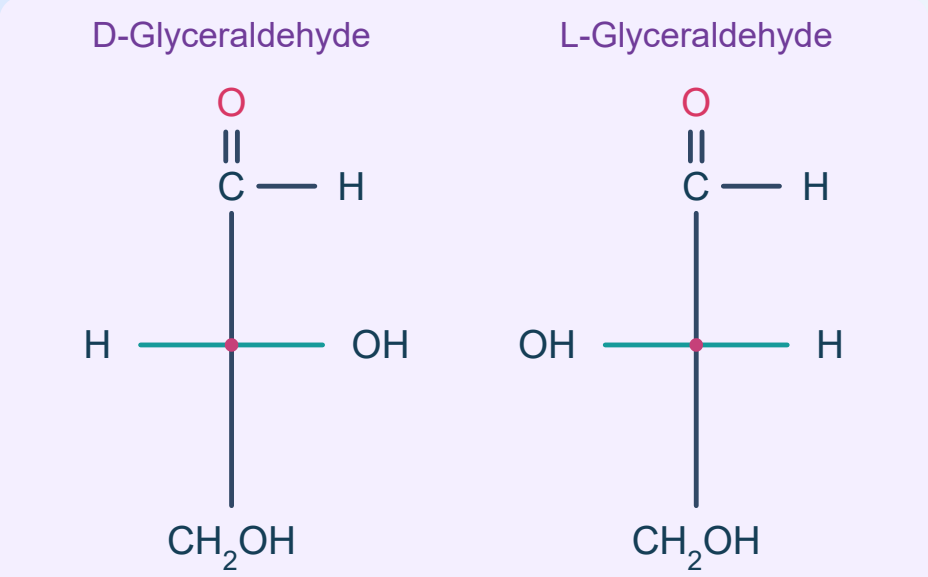
$$[\alpha]_{\lambda}^{T} = \frac{\theta}{c\,l}$$

θ = observed rotation; c = concentration in g mL⁻¹; l = path length in dm. State temperature T and wavelength λ for a specific rotation.

35 D/L is not d/l

- In the standard Fischer convention for the appropriate sugar or amino-acid reference, a diagnostic OH (or NH_2) on the right gives D and on the left gives L. This cannot be assigned from an arbitrary Fischer orientation without the required reference convention. D/L describes relative configuration; d/l or (+)/(−) describes measured optical rotation.

36 D/L and erythro/threo examples



The reference D/L Fischer pair.

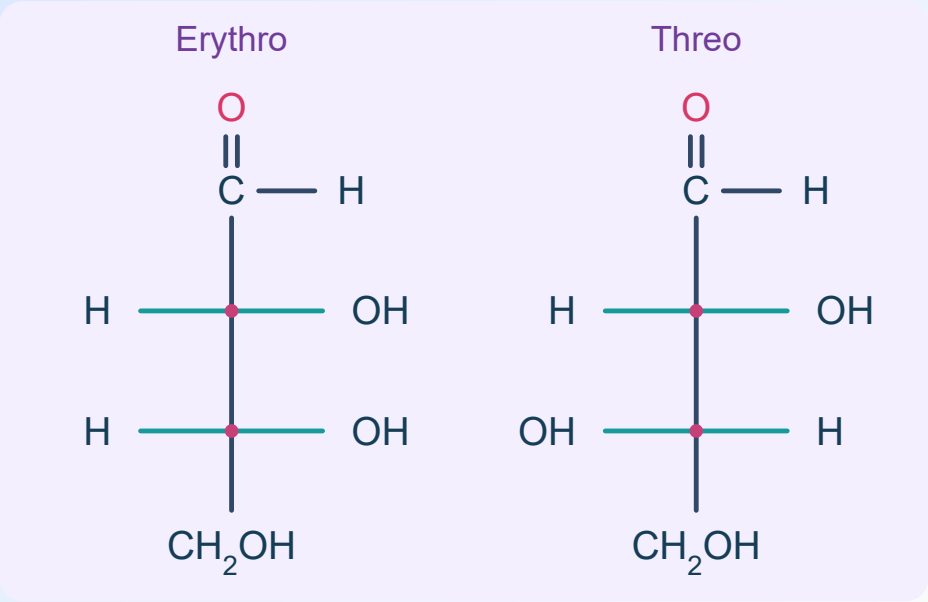
- Erythro/threo is used for suitable molecules with two adjacent stereogenic centres in the specified Fischer convention. Similar groups on the same side → erythro; on opposite sides → threo.

Isomerism

D/L and erythro/threo examples · Counting optical stereoisomers

36 D/L and erythro/threo examples

continued



Worked two-centre Fischer examples.

37 Counting optical stereoisomers

$$\text{Unsymmetrical: total} = 2^n,$$
$$\text{OA} = 2^n,$$
$$\text{meso} = 0,$$
$$\text{pairs} = \frac{\text{OA}}{2}$$

Assumes n independent tetrahedral stereogenic centres and no symmetry reduction. "OA" means individual chiral stereoisomers; each enantiomeric pair can form one racemate.

$$n \text{ even: total} = 2^{n-1} + 2^{n/2-1}$$

For the illustrated idealized symmetrical-chain class: chiral forms = 2^(n−1), meso forms = 2^(n/2−1), enantiomeric pairs = chiral forms/2.

$$n \text{ odd: total} = 2^{n-1},$$
$$\text{meso} = 2^{(n-1)/2}$$

Symmetric-chain shortcut: chiral forms = total − meso; enantiomeric pairs = chiral forms/2. These special formulas are not universal for every symmetric molecular skeleton; use explicit symmetry analysis when their assumptions fail.

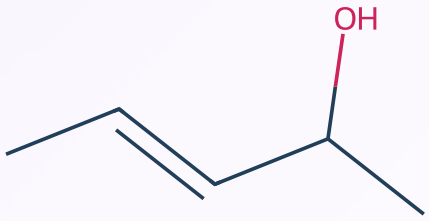
Isomerism

Combine optical and geometrical elements · Optical activity without a tetrahedral chiral carbon

38 Combine optical and geometrical elements

$$\text{Maximum total stereoisomers} = 2^n$$

Here n = independent chiral centres + independent E/Z elements, before symmetry reductions.



CH_3–CH=CH–CH(OH)–CH_3

One E/Z element and one tetrahedral centre give n = 2, hence four stereoisomers. Three atoms participate, but there are only two independent elements.

39 Optical activity without a tetrahedral chiral carbon

- *Cumulenes with an even number of consecutive double bonds can have axial chirality when terminal substituents differ: A ≠ B and X ≠ Y. Allene skeleton: (A)(B)C=C=C(X)(Y), with the two terminal substituent planes perpendicular.*

- *Consider two consecutive spiro rings with terminal A/B and X/Y pairs. Appropriate even-ring spiro systems can be chiral when each terminal pair differs.*

- *Restricted biphenyl rotation can give atropisomers. Bulky ortho groups hinder rotation, and each ring must have distinguishable substituent environments around the axis. A sufficiently high rotational barrier is also required.*

Steric comparison	Examples
Listed as bulky	NO_2, COOH, Cl, Br, I, SO_3H, alkyl R
Listed as relatively small	H, D, T, F, OH, NH_2, CN

- *The bulky/small list is a classroom guide. Axial chirality and configurational stability depend on the full substitution pattern and rotational barrier, not this list alone.*

40 Conformational isomerism

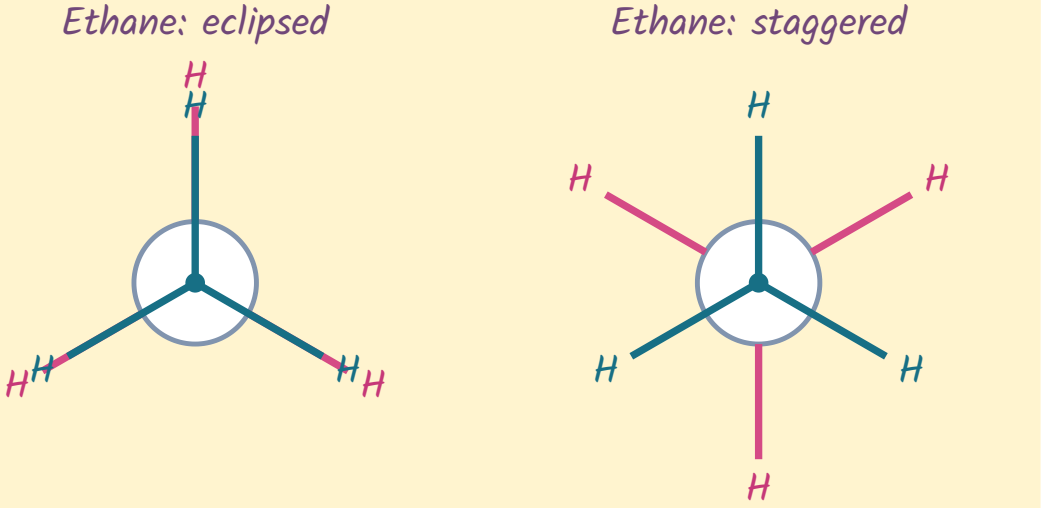
- *Conformers interconvert by rotation about σ bonds without breaking connectivity. Rotation gives a continuous range of conformations. Methane has no C–C bond and therefore no distinct C–C rotational conformers.*

Isomerism

Conformational isomerism

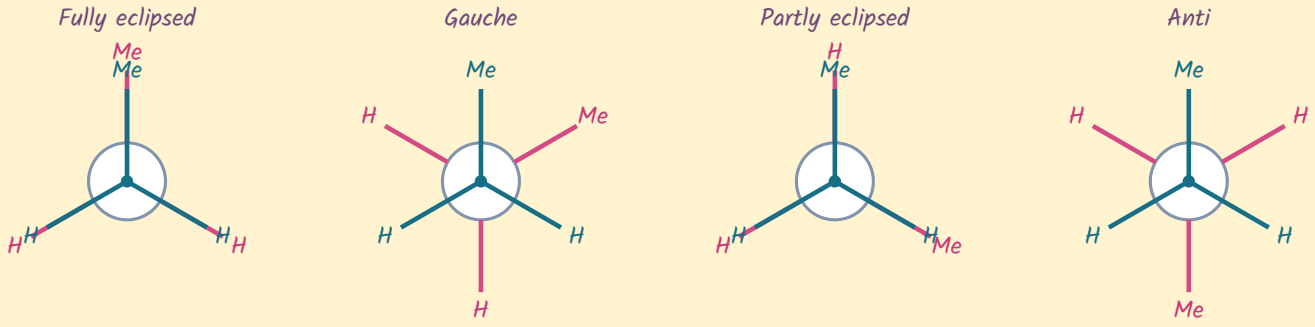
40 Conformational isomerism

continued



A 60° rotation changes eclipsed ethane into staggered ethane. Front bonds are teal; rear bonds are pink.

- Ethane stability: staggered > intermediate skew > eclipsed. Energy order is the reverse: staggered < skew < eclipsed. Lower energy means greater stability.



Butane viewed along the central C–C bond: successive 60° rotations.

- Butane stability: anti > gauche > partly eclipsed > fully eclipsed. Energy: anti < gauche < partly eclipsed < fully eclipsed.

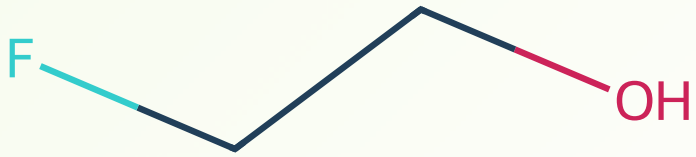
Alkane	Strain emphasized by source
Ethane	Torsional strain
Propane	Torsional strain
Butane	Torsional strain plus van der Waals / steric repulsion

Isomerism

Gauche effect and intramolecular hydrogen bonding · Cyclohexane conformations

41 Gauche effect and intramolecular hydrogen bonding

- A gauche arrangement can be more stable when it permits a favourable intramolecular interaction, such as the illustrated hydrogen-bonded F–CH_2–CH_2–OH sketch. The H on OH approaches F, producing a ring-like interaction geometry. Recall F–H, O–H and N–H in hydrogen-bonding comparisons.



2-Fluoroethanol: a gauche conformer can bring O–H near F

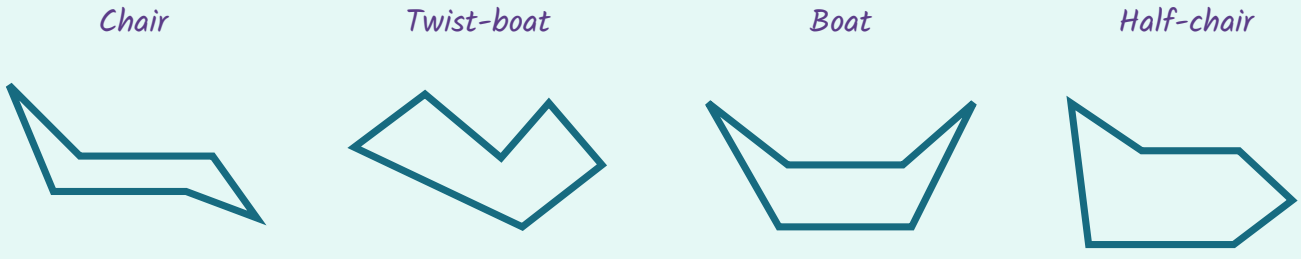
Example of conformational stabilization by an internal contact.

- For the favourable hydrogen-bonding example, the preference can be gauche > anti > partly eclipsed > fully eclipsed. This is conditional; gauche effects are not universally caused by hydrogen bonding.

42 Cyclohexane conformations

- Four conformations: chair (C), twist-boat (TB), boat (B) and half-chair (HC). The two handed twist-boat forms are conformational enantiomers.

Comparison	Order
Stability	Chair > twist-boat > boat > half-chair
Energy	Chair < twist-boat < boat < half-chair



Schematic 3D projections · bond lengths are not to scale

Redrawn cyclohexane conformational outlines.

General Organic Chemistry

Electronic effects · stability · reactivity

04

01 Start with electron density

- Organic reactivity depends strongly on where electron density lies. For a comparable localized charge, a smaller region has greater charge density. Across C, N, O and F, size decreases: C > N > O > F; a similar negative charge is increasingly concentrated.

- For the same atom, increasing negative charge increases electron density, while increasing positive charge decreases it: $A^{3-} > A^{2-} > A^{-} > A > A^{+} > A^{2+}$. Treat these as qualitative comparisons, not exact mathematical proportionalities.

02 Inductive effect: transmission through σ bonds

- The inductive effect acts through σ bonds and produces partial charges. It is distance-dependent and falls rapidly as the substituent moves away; in simple comparisons it is often small beyond the first few carbon atoms. +I groups donate inductively; −I groups withdraw.

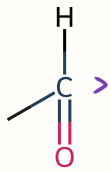
+I donor order listed in this guide

$-CH_2^- > -NH^- > -O^- > -COO^-$ > tertiary alkyl > secondary alkyl > primary alkyl > methyl

Isotope comparison: −T > −D > −H; H is the reference (zero)

−I withdrawing order listed in this guide

$-NF_3^+ > -NR_3^+ > -SR_2^+ > -NH_3^+ > -NO_2 > -SO_3H > -CN$

Then  > −COR > −F > −Cl > −Br > −I > −OR > −OH > −C≡CH

Then $-NH_2$ / $-NR_2$ > phenyl > alkenyl > H

- Inductive-effect rankings depend on the comparison and environment. Keep the listed order as the notes' classroom sequence; do not treat every neighbouring pair as a universal quantitative scale.

- Memory line for the long −I sequence: "Na Farhan, na Hrithik, Shah Rukh; na Himesh, na Om Puri; Salman, cyano; Ali ki car mein father collector beta inspector; aur alcohol ki mummy alkyne; nahi hai benzene hai." The chemistry order above is the primary reference.

03 Acid strength: stabilize the conjugate base

- For comparable solutions, a stronger acid has larger K_a and lower pK_a; at the same concentration it usually gives greater $[H^+]$ and lower pH. pH and pK_a are logarithmic quantities, so these are trends rather than inverse-proportionality equations.

General Organic Chemistry

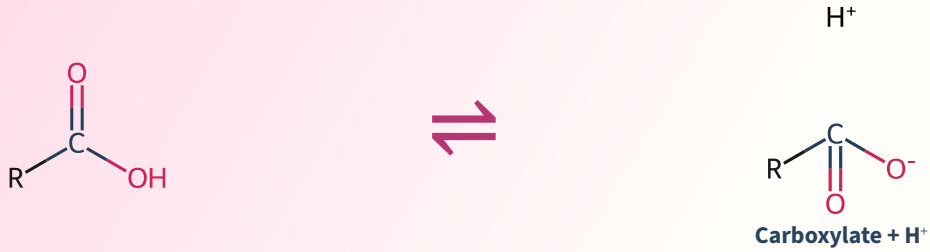
Acid strength: stabilize the conjugate base · Amine basicity: induction and solvation

03 Acid strength: stabilize the conjugate base

continued

Acid dissociation

Reversible



Carboxylate + H^+

A −I substituent stabilizes the carboxylate; +I tends to destabilize it.

- *For aliphatic carboxylic acids (open-chain or cyclic, without aromatic resonance effects): stronger −I generally increases acidity; stronger +I generally decreases it. Apply the same conjugate-base idea to alcohols: ROH ⇌ RO^- + H^+.*

- *Comparison mnemonic: D > N > P, "Do Not Play": Distance first, then Number of withdrawing groups, then their withdrawing Power. It is a guide for the comparable examples used in these notes.*

04 Amine basicity: induction and solvation

- *Greater available electron density on N usually increases basicity. +I helps; −I opposes it. RNH_2, R_2NH and R_3N are primary, secondary and tertiary amines.*

Condition	Order / observation
Simple gas-phase alkylamines	3° > 2° > 1° in the listed inductive comparison
Aqueous methylamines	2° > 1° > 3°
Aqueous ethylamines	2° > 3° > 1°
Solvation tendency alone	1° > 2° > 3°
Inductive donation alone	3° > 2° > 1°

- *For propyl, butyl and larger alkyl groups, do not use an unconditional 3° > 2° > 1° aqueous rule: solvation and steric effects must be compared for the actual compounds.*

05 Charged intermediates

- *Carbocations: electron donation by +I groups generally stabilizes the electron-deficient carbon; −I tends to destabilize it. Carbanions: −I stabilizes negative charge; +I tends to destabilize it. Always also check resonance, hybridization and solvation.*

06 Free radicals and hyperconjugation

- *In the usual simple alkyl-radical comparison, electron-donating alkyl groups help stabilize the radical. Hyperconjugation (Baker–Nathan effect; "no-bond resonance" notation) describes donation from a σ bond into an adjacent suitable orbital.*

General Organic Chemistry

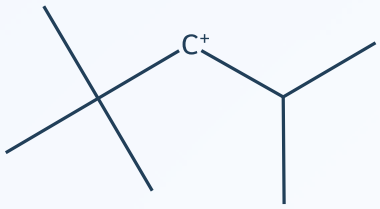
Free radicals and hyperconjugation · Reverse hyperconjugation and stability comparisons

06 Free radicals and hyperconjugation

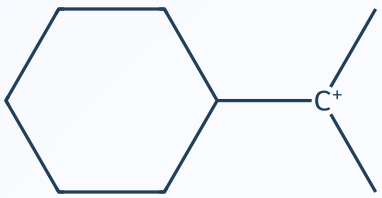
continued

- For the C–H version emphasized here, an adjacent α-carbon is sp^3 and bears α-H. The number of C–H no-bond contributors = number of α-hydrogens. Including the normal structure, total contributors in this counting convention = α-H + 1.

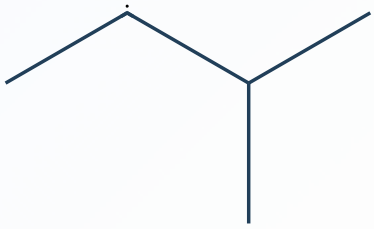
Accepting centre	Orbital interaction
Carbocation	σ bond → vacant p orbital
Free radical	σ bond → half-filled p orbital
Alkene	σ bond → π^* orbital



Left adjacent quaternary C: no α-H; right CH: one α-H



Two methyls (3+3) and one ring CH (1): seven α-H



Radical: three α-H on CH_3 plus one on CH = four

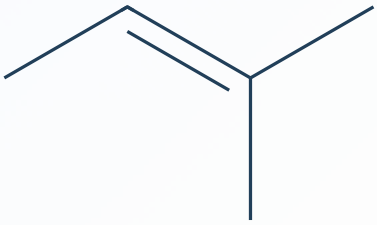
Count hydrogens on carbons immediately adjacent to the electron-deficient or radical centre.



An adjacent CH_2 supplies α-H: hyperconjugation possible



Adjacent quaternary carbon: no α C–H contributor



Three adjacent methyl groups: nine α-H

All three alkene comparisons.

07 Reverse hyperconjugation and stability comparisons

- Reverse (negative) hyperconjugation is represented here for $X_3C–CH=CH_2$, where X is a halogen: donation from the π system into a neighbouring C–X antibonding interaction is shown using charge-separated no-bond forms.

$$X_3C-CH=CH_2 \leftrightarrow X^- + X_2C=CH-CH_2^+$$

There are corresponding forms for each of the three C–X bonds; the notation is a resonance representation, not a claim of free ions in the stable molecule.

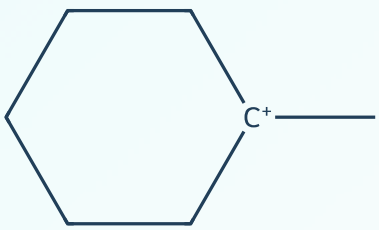
General Organic Chemistry

Reverse hyperconjugation and stability comparisons · Resonance: contributors and the real molecule

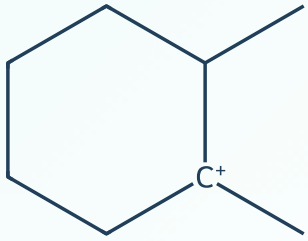
07 Reverse hyperconjugation and stability comparisons

continued

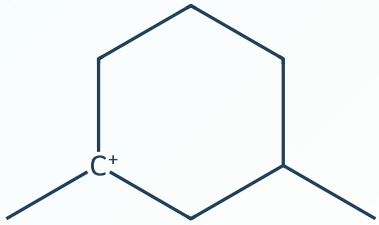
- Within comparable structures, more effective hyperconjugative donors generally increase the stability of carbocations, radicals and alkenes. Comparison guide H > I: hyperconjugation before induction when the two effects compete in the illustrated cases.



A: seven α-H



B: six α-H



C: seven α-H plus a remote methyl

Illustrated order: C > A > B. Hyperconjugation first separates B; induction distinguishes C and A.

08 Resonance: contributors and the real molecule

- Resonance contributors are alternative Lewis descriptions, not separately existing rapidly interconverting molecules. The resonance hybrid is the actual delocalized structure. Move electrons, not atoms: σ connectivity and nuclear positions stay fixed.

$$O=O^{+}-O^{-} \leftrightarrow {}^{-}O-O^{+}=O$$

Ozone has two equivalent contributors. In the hybrid the two O–O bonds have equal length; the two terminal oxygens share the negative charge (−½ each in this simple representation).

- Conjugation needs appropriately aligned orbitals and a continuous path for overlap. Planarity of the relevant conjugated fragment helps; the whole molecule need not be planar. A saturated sp^3 interruption or orthogonal orbitals can stop ordinary π delocalization.

09 Which resonance contributors matter more?

Comparison	Preferred contribution
Neutral versus unnecessarily charge-separated forms	Neutral generally contributes more when octet satisfaction is otherwise comparable
Complete octets / more covalent bonds	Usually favoured over incomplete-octet alternatives
Negative-charge location	More electronegative atoms across a period, or larger polarizable atoms down a group, usually stabilize it
Opposite charges	Less unnecessary separation is generally favoured
Other factors	Compare octets, aromaticity and charge placement before applying shortcuts

General Organic Chemistry

Which resonance contributors matter more? · Keep repelling electron-rich sites apart

09 Which resonance contributors matter more?

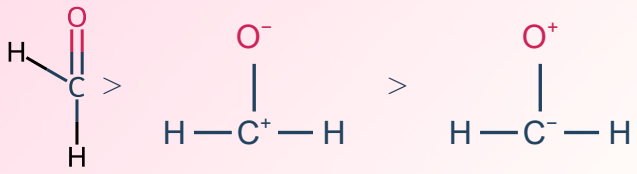
continued

$$CH_2 = CH - Cl \; > \; {}^{-}CH_2 - CH = Cl^{+}$$

The neutral vinyl chloride contributor is favoured over the charge-separated one.

$$^{+}CH_2 - F \; < \; CH_2 = F^{+}$$

The octet-complete contributor is important despite putting positive formal charge on F; octet completion must be considered before electronegativity alone.



Illustrated formaldehyde ordering: neutral > negative charge on O > negative charge on C.

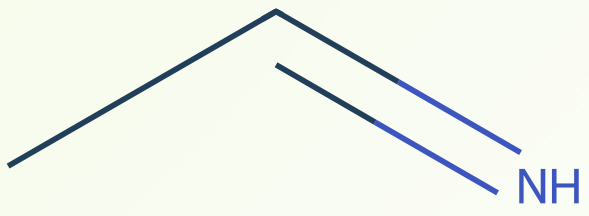
- *Negative-charge stabilization across a period: C^- < N^- < O^- < F^-. For halide ions down the group: F^- < Cl^- < Br^- < I^- in the illustrated size/polarizability comparison.*

- *Phenol's charge-separated contributors have O^+ and negative charge at an ortho or para ring carbon. The closer ortho charge pair is favoured over the more widely separated para pair in this isolated comparison; the total hybrid includes all allowed contributors.*

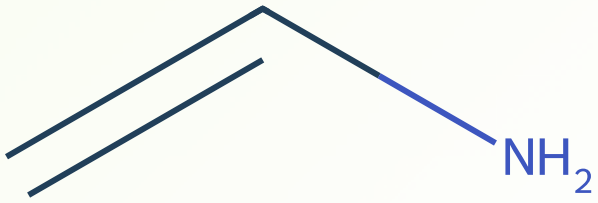
10 Keep repelling electron-rich sites apart

- *Adjacent like charges are unfavourable. Compare a negative charge close to a lone pair with one farther away: $^{-}CH_2$–CH=CH–NH_2 is favoured over CH_2=CH–CH^{-}–NH_2 in this isolated electron-repulsion comparison. Nearby negative charge/lone-pair density repels more strongly.*

11 Localized and delocalized lone pairs



CH_3–CH=NH: N lone pair localized outside the C=N π system



CH_2=CH–NH_2: N lone pair can conjugate with C=C

A lone pair participates in resonance only when a suitable adjacent orbital pathway is available.

General Organic Chemistry

Localized and delocalized lone pairs · Bredt's rule and bridgehead geometry

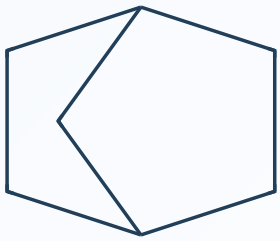
11 Localized and delocalized lone pairs

continued

- A localized lone pair does not participate in the indicated resonance path. A delocalized lone pair overlaps with the neighbouring π system and is shared through resonance.

12 Bredt's rule and bridgehead geometry

- A small bridged bicyclic framework cannot easily give a bridgehead the approximately planar geometry required for an ordinary bridgehead alkene. Bridgehead C=C and planar-carbocation geometries can therefore be strongly disfavoured; an adjacent O lone pair remains localized if the required alignment is prevented.



Norbornane-type bridged skeleton; the two junction atoms are bridgeheads

Identify the bridgeheads before testing whether the required orbital alignment is possible.

- Bredt's rule is a restriction for sufficiently small/strained bridged systems, not a universal ban on every sp^2 bridgehead: larger frameworks and special electronic structures need separate treatment.

13 Extended versus cross conjugation



Extended conjugated path ending at OMe



Two vinyl groups coupled through oxygen

Continuous conjugation versus branching conjugated paths.

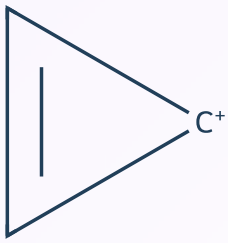
- Extended conjugation spreads electron density along a continuous path; cross conjugation offers branches that do not all share one uninterrupted conjugated sequence. The drawn cyclohexadienyl-cation comparison favours the more extended resonance path over the cross-conjugated arrangement; apply this only after verifying the actual connectivity.

General Organic Chemistry

Equivalent resonance contributors · Fries-type benzenoid comparison

14 Equivalent resonance contributors

- *Equivalent contributors have the same energy and contribute equally by symmetry. The cyclopropenyl cation has three equivalent contributors, with the positive charge and double bond drawn at different positions. Its actual aromatic hybrid is more stable than any one localized contributor and distributes charge equally (+⅓ on each carbon).*

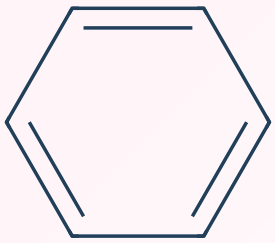


Cyclopropenyl cation: three equivalent resonance forms

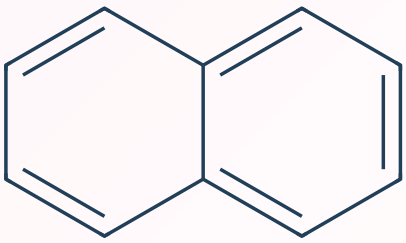
Hybrid > contributor I = contributor II = contributor III.

15 Fries-type benzenoid comparison

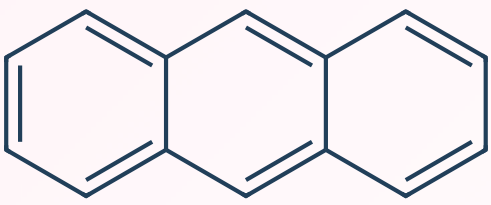
- *For alternative benzenoid resonance descriptions of the same framework, contributors with more complete aromatic sextets generally make a larger contribution. Separated aromatic sextets are favoured over representations that force a sextet to be shared.*



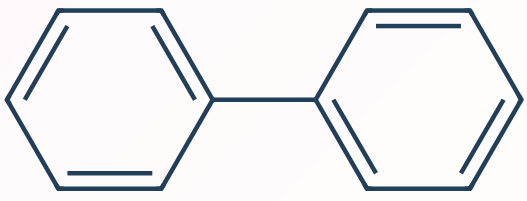
Benzene



Naphthalene



Anthracene



Biphenyl

One, two and three benzenoid rings; separated versus fused rings.

General Organic Chemistry

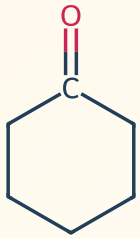
Fries-type benzenoid comparison · Bond length and bond strength

15 Fries-type benzenoid comparison

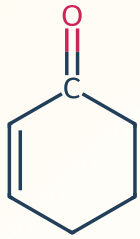
continued

- Do not compare the total "stability" of molecules with different formulas solely by counting rings. The useful rule concerns resonance contribution and aromatic stabilization in a properly matched comparison.

16 Bond length and bond strength



Cyclohexanone: localized C=O, length x



Conjugated cyclohexenone: C=O length y

Conjugation reduces localized C=O bond order in this comparison, so y > x.

Property	Qualitative order for comparable atom pairs
Bond strength / bond energy	Triple > double > partial double > single
Bond length	Triple < double < partial double < single

17 Resonance / mesomeric effect

- The mesomeric effect is a permanent redistribution of electron density through a conjugated π system. It can be transmitted along a conjugated pathway rather than dying away like a simple inductive effect. Charge-separated Lewis contributors are bookkeeping forms; they do not mean atoms bear their full formal charge in the hybrid.

- Mesomeric substituent effects are an application of resonance. Resonance is the broader idea; not every resonance comparison is described as a substituent mesomeric effect.

- +M / +R: a group donates a p-orbital lone pair into an attached alkene or benzene ring. In arrow notation, a lone pair becomes a bonding pair and another π pair moves to a lone-pair position.

$$\mathrm{CH_2=CH-G \leftrightarrow {}^{-}CH_2-CH=G^{+}}$$

Generic +M representation for a suitable lone-pair donor G directly attached to the π system.

18 +M and –M: recognize the attachment atom

- +M donors usually have a lone pair on the atom directly attached to the alkene or aromatic ring. Alkyl groups can donate through hyperconjugation (+H); this is often discussed alongside resonance donation, but is distinct from ordinary lone-pair mesomerism.

General Organic Chemistry

+M and −M: recognize the attachment atom · Comparing +M power

18 +M and −M: recognize the attachment atom

continued

$$CH_3 - CH = CH_2 \leftrightarrow H^+ + CH_2 = CH - CH_2^-$$

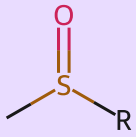
Formal no-bond representation of alkyl donation. It is not an equilibrium producing free H^+.

- *−M / −R groups withdraw through the conjugated π system. A common sign is a π bond from the first attached atom to an electronegative atom, as in a carbonyl group.*



The carbonyl withdraws by resonance.

- *$-CX_3$ groups can withdraw by negative hyperconjugation. The corresponding X^- + $X_2C{=}CH{-}CH_2^+$ contributor was shown earlier.*

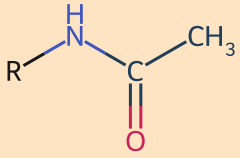
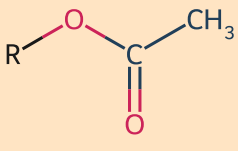
- *Groups such as −N=O and*  *can have both donating and withdrawing resonance possibilities because the attachment atom has both a lone pair and a multiple-bond pathway. The direction depends on the full conjugated system; $CH_2{=}CH{-}N{=}O$ illustrates the two competing pathways.*

19 Comparing +M power

- *Effective donation depends on electron availability and orbital overlap. Comparable orbital sizes improve overlap. In a simple C/N/O comparison, NH_2 > OH for lone-pair donation; compare charge/electron density before size.*

$$-NH^- > -O^- > -NH_2 > -OH$$

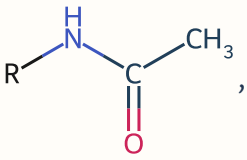
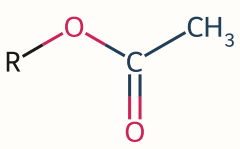
Classroom +M donor sequence for comparable attachment and geometry.

- *A lone pair already shared with a carbonyl is less available for donation into another π system: $-NH_2$ >*  *and −OH >*  *. Direct lone-pair donation can exceed alkyl hyperconjugation: −OH > $-CH_3$ in the stated +M/+H comparison.*

General Organic Chemistry

Competing electronic effects · Ortho effect and steric inhibition of resonance

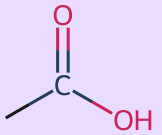
20 Competing electronic effects

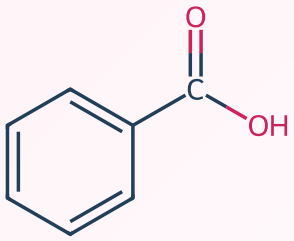
Guide	Examples / limitation
M > H > I	Useful priority in comparable conjugated examples, not a universal energy scale
+M often outweighs −I	$-NH_2$, $-OH$, $-OR$,  ,  at appropriate aromatic positions
−I important for $-CX_3$	Compare its induction with negative hyperconjugation
Halogens	−I withdrawers but +M donors; net ring deactivation with ortho/para direction
Meta position	Direct resonance forms do not put the substituent-induced charge at meta; inductive and other effects remain

- Halogen −I order in this guide: F > Cl > Br > I. The listed +M overlap trend is also F > Cl > Br > I in the simple orbital-size picture. Net withdrawal cannot safely be ranked by subtracting these qualitative lists; it depends on the chemical comparison.

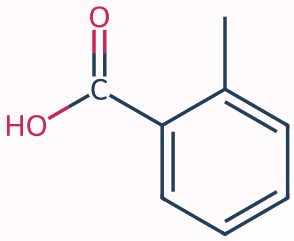
- Electron donation raises ring electron density; electron withdrawal lowers it. The effects of +M and −M are most directly represented at ortho and para positions.

21 Ortho effect and steric inhibition of resonance

- Ortho-substituted benzoic acids are often more acidic than benzoic acid. Bulky ortho substituents can cause steric inhibition of resonance (SIR): twisting the  group changes its conjugation with the ring. Steric, field, hydrogen-bonding and solvation effects all contribute to the observed ortho effect.



Benzoic acid



An ortho-substituted benzoic acid

Ortho crowding can change the orientation and environment of –COOH.

General Organic Chemistry

Ortho effect and steric inhibition of resonance · Acidity: resonance and hydrogen bonding

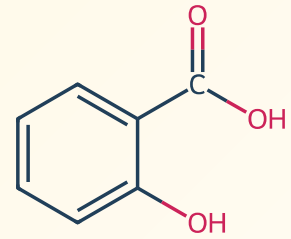
21 Ortho effect and steric inhibition of resonance

continued

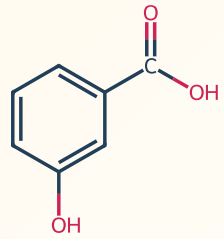
- H, D, T, OH, NH_2, CN and F are relatively small in this steric comparison. Increasing substituent size or the number of ortho substituents can strengthen steric effects; compare number before size in their comparison.

22 Acidity: resonance and hydrogen bonding

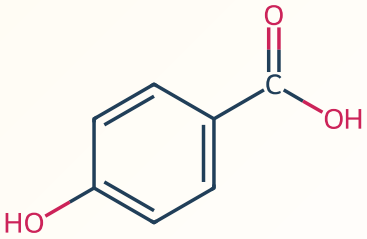
- Electron-withdrawing −M/−I groups often increase acidity by stabilizing the conjugate base. +M/+I often decrease it. Hydrogen bonding can increase or decrease acidity depending on whether it stabilizes the acid or its conjugate base more.



o-Hydroxybenzoic acid

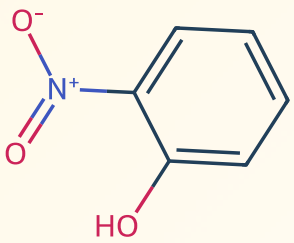


m-Hydroxybenzoic acid

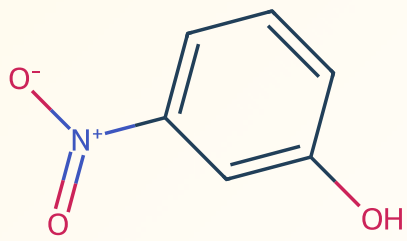


p-Hydroxybenzoic acid

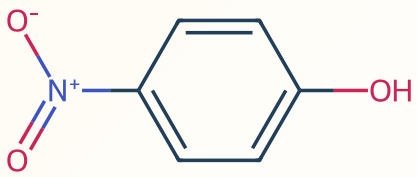
Hydroxybenzoic-acid order in this guide: ortho > meta > para. The ortho case has an intramolecular hydrogen-bond effect; meta is mainly −I; para includes +M.



o-Nitrophenol



m-Nitrophenol



p-Nitrophenol

Nitrophenol acidity in ordinary aqueous comparison: para > ortho > meta. Ortho hydrogen bonding affects the neutral acid; ortho/para allow −M, while meta lacks that direct resonance path.

23 Acid-strength map

- Read this as a revision guide for representative compounds, not an invariant ranking of entire families. Solvent, substitution and the particular acid matter.

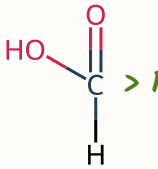
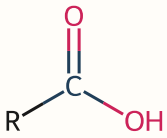
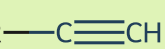
Approximate order / comparison in this guide
Sulfonic acids > picric acid > squaric acid > dinitrophenols > typical carboxylic acids > carbonic acid
Mononitrophenols (p > o > m) > phenol > representative alkylammonium ions
Methanol ≳ water > many higher simple alcohols > terminal alkynes > ammonia > alkene C–H > alkane C–H

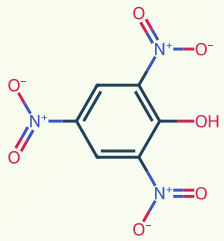
General Organic Chemistry

Acid-strength map · Acid–base reactions favour the weaker acid/base pair

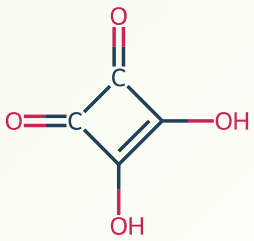
23 Acid-strength map

continued

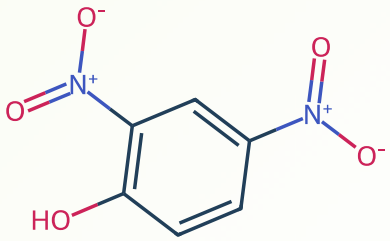
Additional comparison	Meaning / condition
$PhSO_3H$ > RSO_3H	Listed aromatic/aliphatic sulfonic-acid guide; substituents and medium matter
 > PhCOOH > simple 	Formic > benzoic > representative alkanoic acids
HC≡CH > 	Alkyl donation tends to reduce terminal-alkyne acidity in this simple comparison



Picric acid / 2,4,6-trinitrophenol



Squaric acid



2,4-Dinitrophenol

The three specifically drawn polyfunctional acids in the comparison chart.

- *Memory line: "Salman ne pic kiya Sakera ko; din mein aur car hai car mein; mono ko phir khilai aam ki mithai; paani alcohol ke saath Alka boli; ammonia, alkene, alkane." Use the chemical names and conditions above to interpret the mnemonic.*

24 Acid–base reactions favour the weaker acid/base pair

Acid–base neutralization

$$HA + NaOH \longrightarrow NaA + H_2O$$

Compare HA with water: an example HA of $pK_a \approx 1$ is much stronger than H_2O ($pK_a \approx 15.7$ under the stated convention).

- *Larger pK_a means smaller K_a and a weaker acid. Equilibrium generally favours formation of the weaker acid and weaker base; gas evolution or precipitation may additionally drive the reaction.*

General Organic Chemistry

Sodium, sodium hydride and sodamide tests · NaOH and bicarbonate tests

25 Sodium, sodium hydride and sodamide tests

Sodium metal

Heat where required

$$HA + Na \longrightarrow NaA + \tfrac{1}{2} H_2\uparrow$$

Active hydrogen can be replaced by sodium with hydrogen evolution; actual reactivity depends on the compound and conditions.

Sodium hydride

$$HA + NaH \longrightarrow NaA + H_2\uparrow$$

Hydride removes protons from sufficiently acidic substrates; do not interpret "all acids" as every C–H compound.

Sodamide

$$HA + NaNH_2 \longrightarrow NaA + NH_3$$

Favourable for acids stronger than NH_3 under comparable conditions.

- *Na / heat, NaH and $NaNH_2$ are useful active-hydrogen reagents. Sodium-metal reaction is a redox process, whereas NaH and $NaNH_2$ comparisons are conveniently explained by conjugate-acid strength.*

26 NaOH and bicarbonate tests

Sodium hydroxide

$$HA + NaOH \longrightarrow NaA + H_2O$$

Acids sufficiently stronger than water are deprotonated under suitable conditions.

Sodium bicarbonate

$$HA + NaHCO_3 \longrightarrow NaA + H_2CO_3$$

H_2CO_3 then gives $CO_2\uparrow + H_2O$; brisk effervescence is the usual positive observation.

General Organic Chemistry

NaOH and bicarbonate tests · Mesomeric effects and basic strength

26 NaOH and bicarbonate tests

continued

- The bicarbonate test normally detects carboxylic acids and stronger suitable acids. Ordinary phenol and p-nitrophenol are not standard positive bicarbonate-effervescence examples. Highly electron-withdrawing phenols can be more acidic, so distinguish the actual phenol.

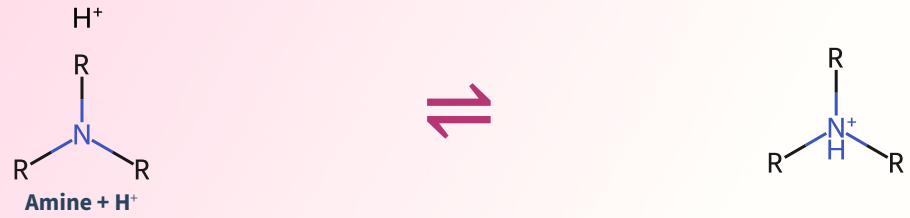
$$H_2CO_3 \longrightarrow CO_2\uparrow + H_2O$$

This gas-producing step explains effervescence.

27 Mesomeric effects and basic strength

Protonation

Reversible

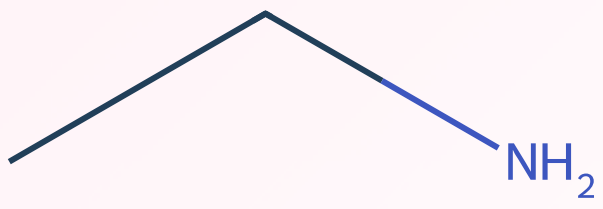


Amine + H⁺

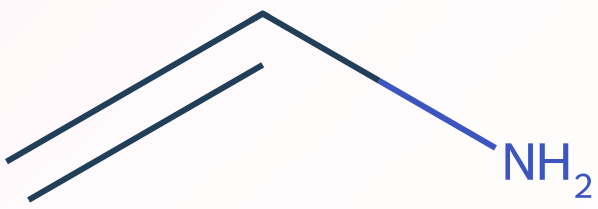
The nitrogen lone pair forms the new bond.

- Greater availability of the N lone pair generally increases basicity. +M/+I donation may help; −M/−I withdrawal may oppose it. Always identify the atom accepting the proton and compare stabilization of the conjugate acid.

- A localized lone pair is normally more available than a lone pair delocalized into a neighbouring π system. Example: ethylamine is more basic than vinylamine in the intended lone-pair comparison.



Ethylamine: localized N lone pair



Vinylamine: N lone pair conjugated with C=C

Lone-pair availability matters more than merely counting alkyl groups.

Broad nitrogen-base guide in this guide

Guanidines > amidines > amines > imines > amides > nitriles (called cyanides in this guide)

General Organic Chemistry

Mesomeric effects and basic strength · Steric effects on acidity and basicity

27 Mesomeric effects and basic strength

continued

- The simple donation sequence $RNH_2 < R_2NH < R_3N$ is a gas-phase/induction guide; the aqueous methyl/ethyl orders and solvation qualifications were given earlier.

28 Steric effects on acidity and basicity

- SIR = steric inhibition of resonance. Ortho crowding can increase acidity in substituted benzoic-acid examples by altering conjugation. In suitable sterically crowded aromatic amines, twisting N away from the aromatic π system can free its lone pair and increase basicity; an example is aromatic tertiary > secondary in this restricted SIR comparison.

- SIP = steric inhibition of protonation. Crowding near the basic nitrogen can obstruct proton approach or solvation and lower basicity; this is important this for aromatic primary-amine comparisons. The final result is the balance of SIR, SIP and solvation.

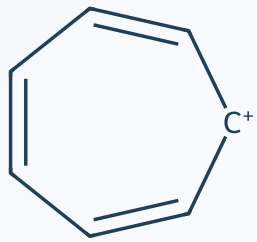
29 Aromatic, antiaromatic or non-aromatic?

- Check in order: cyclic → planar → a continuous conjugated system → count π electrons. If any of the first three conditions is missing, the compound is non-aromatic. The conjugated atoms need suitable overlapping p orbitals.

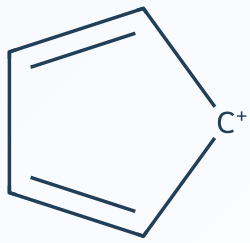
π-electron rule	Counts	Classification
$4n + 2$; $n = 0, 1, 2...$	2, 6, 10...	Aromatic (A)
$4n$; $n = 1, 2, 3...$	4, 8, 12...	Antiaromatic (AA)

Stability: A > NA > AA

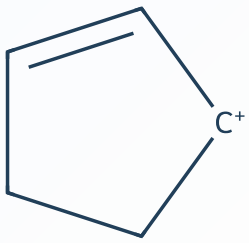
30 Application 1 · stability of intermediates



1 · Tropylium: aromatic



2 · Cyclopentadienyl cation: antiaromatic



3 · Interrupted conjugation: non-aromatic

Comparison: 1 > 3 > 2.

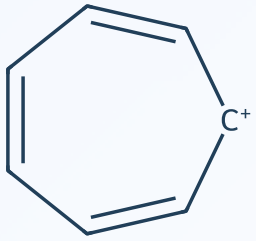
General Organic Chemistry

Application 1 · stability of intermediates · Applications 2–3 · carbonyls and rotational barrier

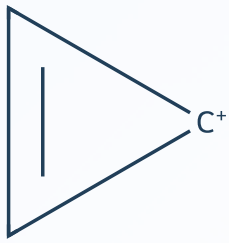
30 Application 1 · stability of intermediates

continued

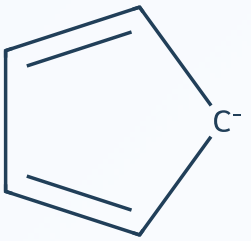
- *In this comparison, aromatic stabilisation is considered before ordinary resonance, hyperconjugation and inductive effects.*



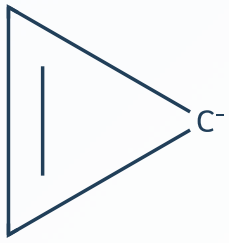
Tropylium cation



Cyclopropenyl cation



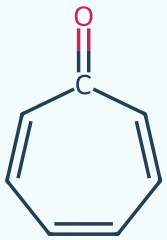
Cyclopentadienyl anion



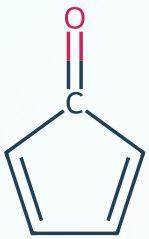
Cyclopropenyl anion

Comparisons: tropylium cation > cyclopropenyl cation; cyclopentadienyl anion > cyclopropenyl anion.

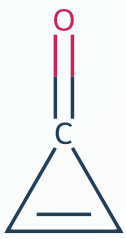
31 Applications 2–3 · carbonyls and rotational barrier



1 · Tropone



2 · Cyclopentadienone



3 · Cyclopropenone

Dipole moment, C=O bond length and rate of protonation: 1 > 3 > 2 (for the structures shown).

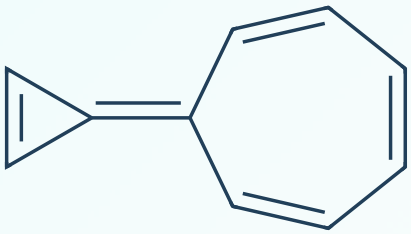
- *Rotational-barrier example: x has a cycloheptatriene ring connected by an exocyclic double bond to a cyclopropene ring; y has a cyclopentadiene ring similarly joined to a cyclopropene ring. Charge separation in y gives an aromatic cyclopentadienyl anion plus an aromatic cyclopropenyl cation. The charge-separated state of y is more stable; rotational barrier x > y.*

General Organic Chemistry

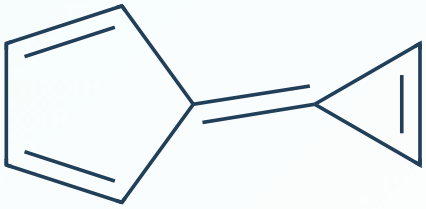
Applications 2–3 · carbonyls and rotational barrier · Applications 4–7 · reactivity, acidity and basicity

31 Applications 2–3 · carbonyls and rotational barrier

continued



x · seven-membered / three-membered rings

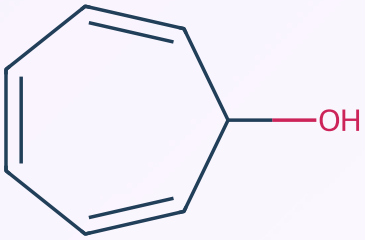


y · five-membered / three-membered rings

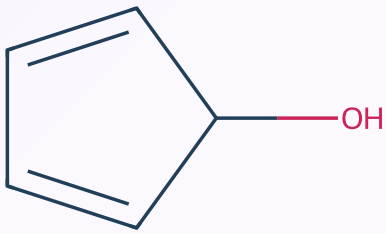
Exocyclic double-bond rotation: x > y.

32 Applications 4–7 · reactivity, acidity and basicity

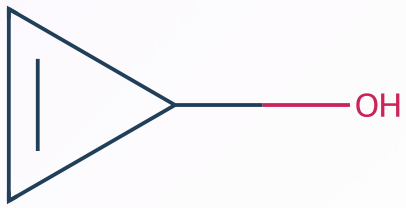
- *For alcohol reaction with HX or H_2SO_4, the rate follows the stability of the carbocation produced after protonated OH leaves. Cycloheptatrienol (1) > cyclopropenol (3) > cyclopentadienol (2). The corresponding carbocations are aromatic, aromatic and antiaromatic respectively.*



1



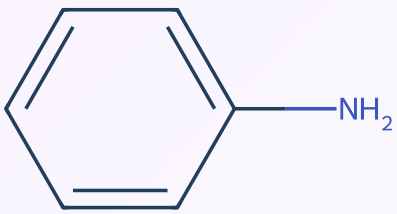
2



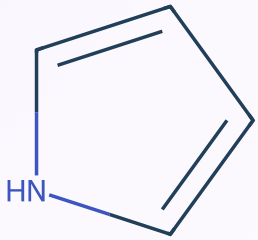
3

Alcohol reactivity: 1 > 3 > 2.

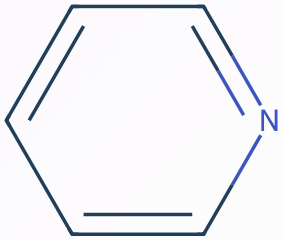
- *Reactivity towards $AgNO_3$ and $SbCl_5$ also follows carbocation stability in the illustrated ionisation comparisons: aromatic cation formation is favoured over antiaromatic cation formation. Acidity increases when deprotonation produces an aromatic conjugate base rather than an antiaromatic one.*



1 · Aniline



2 · Pyrrole



3 · Pyridine

Basic strength: pyridine (3) > aniline (1) > pyrrole (2).

General Organic Chemistry

Carbocation stability · decision rules

33 Carbocation stability · decision rules

- α-effect/back bonding: an adjacent atom A with a lone pair can donate into the empty p orbital of C^+: $C^+–A \leftrightarrow C=A^+$. Smaller size mismatch between C and A gives better overlap. This stabilisation applies for carbocations and free radicals.

$$\text{BBS} > \text{aromaticity} > M > H > I$$

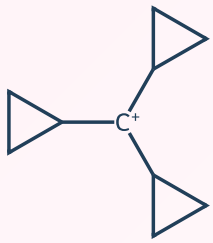
BBS = back-bonding stabilisation; M = mesomeric/resonance; H = hyperconjugation; I = inductive effect.

- Electron donation (+M, +H, +I) stabilises C^+; electron withdrawal (−M, −I) destabilises it.

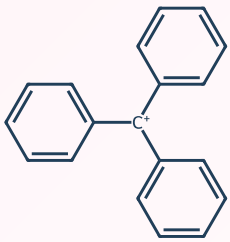
$$CH \equiv C^+ < CH_2 = CH^+ < CH_3CH_2^+$$

Higher s character means greater electronegativity, which makes positive charge less stable.

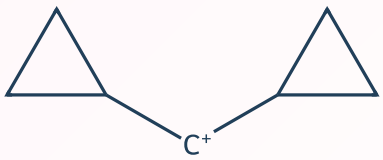
- For comparable alkyl carbocations: 3° > 2° > 1°. Extended comparison: tris(cyclopropyl)methyl cation > tropylium > triphenylmethyl cation > bis(cyclopropyl)methyl cation > diphenylmethyl cation > cyclopropylmethyl cation > tert-butyl cation > benzyl cation > allyl cation. Compare these under similar conditions; medium can change relative stabilities.



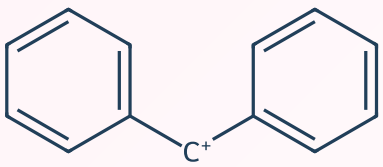
Tris(cyclopropyl)methyl



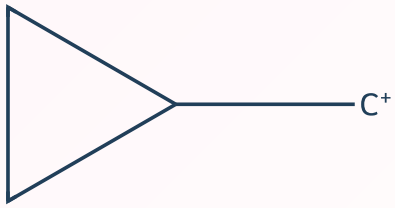
Triphenylmethyl



Bis(cyclopropyl)methyl



Diphenylmethyl



Cyclopropylmethyl

Distinct stabilised carbocations in this order.

General Organic Chemistry

Properties of carbocations · Carbanion stability

34 Properties of carbocations

Property	Localised and delocalised carbocations (ordinary planar examples)
Hybridisation	sp^2
Shape	Trigonal planar
Orbital	Vacant p orbital
Behaviour	Lewis acid
Magnetism	Diamagnetic; magnetic moment = 0

$$\mu = \sqrt{n(n+2)}\ \text{BM}$$

n = number of unpaired electrons. For the closed-shell carbocations here, $n = 0$.

35 Carbanion stability

- Consider an α/back-bonding effect for a carbanion next to an atom with an available orbital, with the comparison priority BBS > aromaticity > mesomeric > hyperconjugation > inductive effects. Electron-withdrawing −M and −I groups stabilise C^-; electron-donating +M and +I groups destabilise it.

$$CH \equiv C^- > CH_2 = CH^- > CH_3CH_2^-$$

Corresponding hybridisation: $sp > sp^2 > sp^3$ for carbanion stability. Greater s character increases electronegativity and stabilises negative charge.

- Acidic strength comparison in the notes: $CHCl_3 > CHF_3$. Their conjugate bases are CCl_3^- and CF_3^-. A historical explanation uses C(2p)–Cl(3d) back bonding and no such back bonding for F; this is a historical simplified explanation.

- For otherwise comparable delocalised anions, compare 3 resonance contributors > 2 > 1. Evaluate the quality and equivalence of contributors as well as their number.

Property	Localised carbanion	Delocalised carbanion
Hybridisation	Usually sp^3	Usually sp^2
Shape	Trigonal pyramidal	Trigonal planar
Behaviour	Lewis base	Lewis base
Magnetism	Diamagnetic; $\mu = 0$	Diamagnetic; $\mu = 0$

36 Bond energy and radical stability

$$\text{C–H bond energy} \propto \frac{1}{\text{stability of the radical formed}}$$

- Compare the marked terminal C–H bonds: x = $CH_2{=}CH{-}CH_2{-}H$, y = $CH_3{-}CH_2{-}CH_2{-}H$. The allylic radical from x is resonance-stabilised, so bond energy x < y.

General Organic Chemistry

Keto–enol equilibrium

37 Keto–enol equilibrium

equilibrium



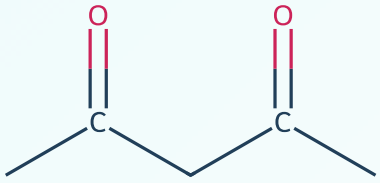
Keto: acetone **Enol**

An α-H transfers to oxygen while the carbonyl double bond shifts to the α-carbon.

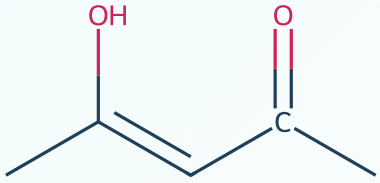
$$K_{eq} = \frac{[\text{enol}]}{[\text{keto}]}$$

Higher Keq means a greater enol proportion. This ratio itself is not the percentage enol.

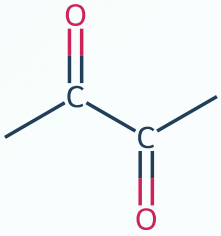
- *Usually the keto form is more stable. Enol stability rises with aromaticity, resonance, intramolecular H bonding and favourable alkene substitution.*



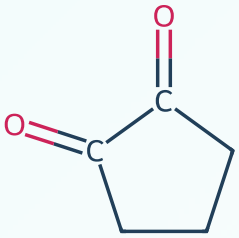
Acyclic β-diketone



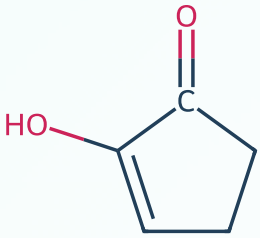
Chelated enol



Acyclic α-diketone



Cyclic α-diketone



Cyclic enol

Three cases: acyclic β-diketone, acyclic α-diketone, cyclic α-diketone.

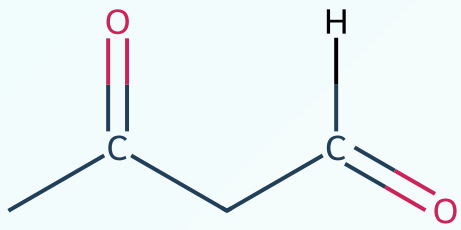
- *Enol-content comparison: β-diketone > keto-aldehyde > dialdehyde > keto-ester > diester > ketone > aldehyde. Memory note: dicarbonyl > monocarbonyl; ketone > aldehyde > ester. These comparisons assume the representative systems drawn and are not universal for every substituent.*

General Organic Chemistry

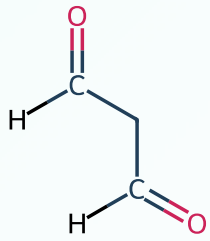
Keto–enol equilibrium · Electrophiles with vacant orbitals

37 Keto–enol equilibrium

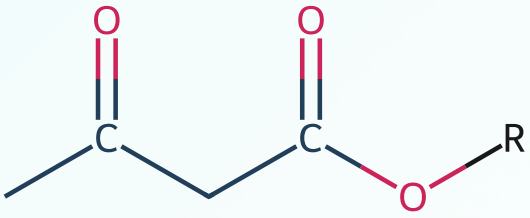
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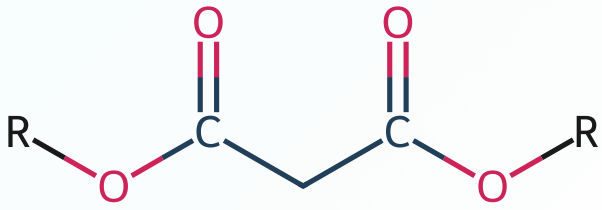
Keto-aldehyde



Dialdehyde



Keto-ester



Diester

Representative structures used in the enol-content order.

38 Electrophiles with vacant orbitals

- Electrophiles are electron-pair acceptors. They may have an empty orbital or become electrophilic through bond polarisation.

Category	Examples
Vacant s or p orbital	H^+, CH_3^+, BH_3
Other Lewis-acid examples listed under "vacant d"	$TiCl_3$, SO_3, $FeCl_3$, $SbCl_5$

39 Electrophiles without a vacant orbital

- π-polarisation examples: the central carbon in O=C=O and the nitrogen in the nitrosonium ion NO^+ are electrophilic. σ-polarisation examples: Xδ+–Xδ− induced in a halogen molecule, and Iδ+–Clδ−, Brδ+–Clδ−, Iδ+–Brδ−. In X–X′, the more electronegative X′ becomes δ−.

40 Nucleophiles

- Nucleophiles donate an electron pair: electron-rich species containing a lone pair, or a π bond capable of donating electron density.

General Organic Chemistry

Nucleophiles · Five reaction families

40 Nucleophiles

continued

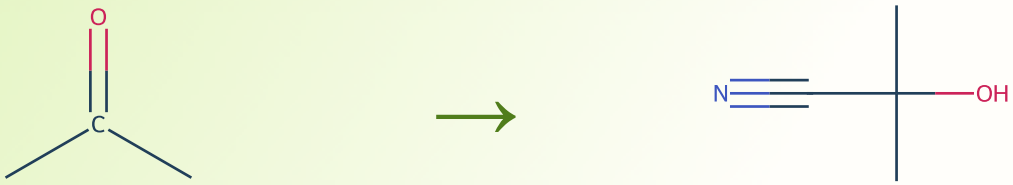
Type	Examples
Lone-pair donors	H^-, H_2O, NH_3, X^-, ROH, CN^-
π-electron donors	$CH_2{=}CH_2$, $HC{\equiv}CH$, benzene

Remember: NH_4^+ and H_3O^+ are not ordinary nucleophiles. H_3O^+ and NH_4^+ act as proton donors; BH_4^- is a hydride donor.

41 Five reaction families

Family	Example / meaning
Acid–base	Acid + base → salt + H_2O (aqueous neutralisation example)
Electrophilic addition	$C{=}C + Br_2 \rightarrow$ vicinal dibromide
Nucleophilic addition	Acetone + HCN → acetone cyanohydrin
Free-radical addition	Alkene + HBr / peroxide → bromoalkane
Electrophilic substitution	$Ar{-}H + E^+ \rightarrow Ar{-}E + H^+$
Nucleophilic substitution	$R{-}X + Nu^- \rightarrow R{-}Nu + X^-$
Free-radical substitution	$R{-}H + X_2, h\nu \rightarrow R{-}X + HX$
Elimination	Adjacent C–H and C–X groups lose HX to form C=C; E1, E2, E1cB and Ei pathways
Rearrangement	A group and/or multiple bond changes position within a molecule

HCN



Acetone → Cyanohydrin

Nucleophilic addition at the carbonyl carbon.

schematic rearrangement



Allylic starting arrangement → Rearranged arrangement

Rearrangement pattern: $C{-}C(CH_3){=}C{-}C{-}X \rightarrow C{-}C(CH_3)(X){-}C{=}C$; X is illustrated as Br.

General Organic Chemistry

Heat of hydrogenation (HOH) · Heat of combustion (HOC)

42 Heat of hydrogenation (HOH)

- Heat of hydrogenation is the energy released when an unsaturated compound is hydrogenated. Example: C=C + H_2/Ni → C–C + heat. Here, compare the positive magnitude of heat released.

- Comparison: alkynes release more heat on complete hydrogenation than corresponding alkenes because they contain more π bonds. For the illustrated alkynes: $HC{\equiv}CH$ > $CH_3C{\equiv}CH$ > $CH_3C{\equiv}CCH_3$ in heat released. Steric hindrance generally rises with the number of alkyl groups.

$$|\Delta H_{hyd}| \propto \text{number of } \pi \text{ bonds}$$

$$|\Delta H_{hyd}| \propto \frac{1}{\text{stability}} \quad (\text{same number of } \pi \text{ bonds})$$

- Resonance and hyperconjugation (more suitable α-H atoms) increase stability, so they lower the heat released when comparable unsaturated compounds give the same hydrogenated product. Steric hindrance can affect addition rates; these remain reagent- and mechanism-dependent.

43 Heat of combustion (HOC)

- Heat of combustion is the energy released on complete combustion. Combustion is exothermic: ΔHcomb < 0.

$$C_xH_y + \left(x + \frac{y}{4}\right) O_2 \longrightarrow xCO_2 + \frac{y}{2}H_2O + \text{heat}$$

- Within comparable series, heat released generally rises with carbon count. For isomers, lower stability means larger heat of combustion. Alkene stability increases with suitable α-H/hyperconjugation; alkane stability generally increases with branching. The illustrated cycloalkane stability order is six-membered > five-membered > four-membered rings.

44 Resonance energy

- With a signed-energy convention, resonance energy is the energy difference between the resonance hybrid and the most stable contributing structure. The hybrid is more stable and lies lower in energy.

$$\Delta E_{res} = E_{hybrid} - E_{best\ contributor} < 0$$

With this sign convention, resonance stabilisation is negative. The magnitude of resonance energy is often quoted as a positive number.

- It may be estimated from hydrogenation enthalpy data: write R.E. = x − y with x < y. Stability: resonance hybrid > individual contributor; energy: hybrid < contributor.

NEW CHAPTER ORGANIC CHEMISTRY

Organic Analysis

Element tests · quantitative estimation

05

01 Carbon and hydrogen detection

- Heat the organic compound with CuO. Carbon gives CO_2, which turns limewater milky by forming $CaCO_3$. Excess CO_2 and water dissolve the precipitate as $Ca(HCO_3)_2$. Hydrogen gives H_2O, which turns anhydrous $CuSO_4$ blue by forming $CuSO_4{\cdot}5H_2O$ (blue vitriol).

$$CO_2 + Ca(OH)_2 \rightarrow CaCO_3 \downarrow + H_2O$$

$$CaCO_3 + CO_2 + H_2O \rightarrow Ca(HCO_3)_2$$

02 Lassaigne's sodium-fusion test

- Nitrogen, sulphur, halogens and phosphorus are converted from covalent forms into water-soluble ionic compounds. Mnemonic: P–S–N–X: "Pankaj Sir Nikle holiday par".

Element combination	Fusion product
Na + C + N	NaCN
2Na + S	Na_2S
Na + X (X = Cl, Br, I)	NaX
3Na + P + 4O (schematic)	Na_3PO_4

03 Test for nitrogen

$$6NaCN + FeSO_4 \rightarrow Na_4[Fe(CN)_6] + Na_2SO_4$$

Fresh ferrous sulphate; sodium hexacyanidoferrate(II).

- After treatment and acidification, Fe^{3+} reacts with ferrocyanide to form Prussian blue: ferric ferrocyanide, also called iron(III) hexacyanidoferrate(II).

$$4Fe^{3+} + 3[Fe(CN)_6]^{4-} \rightarrow Fe_4[Fe(CN)_6]_3 \downarrow$$

- The test can fail for diazo-type compounds (–N=N– as drawn) and hydrazine, $NH_2–NH_2$. Hydrazine contains no carbon, so NaCN is not formed in the ordinary test; diazo compounds may lose nitrogen during heating.

04 Test for sulphur; nitrogen and sulphur together

- Na_2S in the sodium extract gives black PbS with lead acetate in acetic acid. Fresh sodium nitroprusside gives a violet colour.

Organic Analysis

Test for sulphur; nitrogen and sulphur together · Test for halogens

04 Test for sulphur; nitrogen and sulphur together

continued



$$Na_2S + Na_2[Fe(CN)_5NO] \rightarrow Na_4[Fe(CN)_5NOS]$$

Violet thionitroprusside complex.

$$Na + C + N + S \rightarrow NaSCN$$

$$3NaSCN + FeCl_3 \rightarrow Fe(SCN)_3 + 3NaCl$$

Blood-red ferric thiocyanate in this schematic notation.

$$NaSCN + 2Na \rightarrow NaCN + Na_2S$$

Excess sodium converts thiocyanate into separate cyanide and sulphide.

05 Test for halogens

- *Acidify the sodium extract with HNO_3, then add $AgNO_3$. Compare the silver-halide precipitates and their solubility in aqueous ammonia.*

Halide	Precipitate	Colour	Aqueous ammonia
Cl^-	$AgCl$	White	Soluble; $[Ag(NH_3)_2]^+$ forms
Br^-	$AgBr$	Pale yellow / cream	Sparingly soluble in dilute, soluble in concentrated ammonia
I^-	AgI	Yellow	Insoluble

- *If nitrogen is present, CN^- can otherwise give white $AgCN$; if sulphur is present, S^{2-} can give black Ag_2S. Nitric-acid treatment removes these interferences (HCN and H_2S are removed).*

06 Test for phosphorus

- *Oxidise the organic compound with Na_2O_2 to form sodium phosphate. Treat with HNO_3 and ammonium molybdate; a canary-yellow precipitate of ammonium phosphomolybdate confirms phosphorus.*

Organic Analysis

Test for phosphorus · Carbon and hydrogen · Liebig combustion method

06 Test for phosphorus

continued

$$(NH_4)_3PO_4 \cdot 12MoO_3$$

Ammonium phosphomolybdate (APM), the yellow test product.

07 Carbon and hydrogen · Liebig combustion method

$$\%C = \frac{12}{44}\frac{w_{CO_2}}{w} \times 100$$

$$\%H = \frac{2}{18}\frac{w_{H_2O}}{w} \times 100$$

- w = mass of organic compound; wCO_2 = mass of CO_2 obtained; wH_2O = mass of H_2O obtained. Use the same mass unit throughout.

08 Halogens · Carius method

- Halogens are estimated as AgX precipitates (AgCl, AgBr or AgI).

$$\%Cl = \frac{35.5}{143.5}\frac{w_{AgCl}}{w} \times 100$$

$$\%Br = \frac{80}{188}\frac{w_{AgBr}}{w} \times 100$$

$$\%I = \frac{127}{235}\frac{w_{AgI}}{w} \times 100$$

- wAgX = mass of the corresponding silver-halide precipitate; w = mass of organic compound taken.

09 Sulphur and phosphorus

- In the Carius method, sulphur is oxidised to sulphate and precipitated using $BaCl_2$ as $BaSO_4$.

$$\%S = \frac{32}{233}\frac{w_{BaSO_4}}{w} \times 100$$

Organic Analysis

Sulphur and phosphorus · Nitrogen · Dumas method

09 Sulphur and phosphorus

continued

- Phosphorus can be weighed as $Mg_2P_2O_7$ or ammonium phosphomolybdate (APM).

$$\%P = \frac{62}{222}\frac{w_{Mg_2P_2O_7}}{w} \times 100$$

$$\%P = \frac{31}{1877}\frac{w_{APM}}{w} \times 100$$

- APM = $(NH_4)_3PO_4{\cdot}12MoO_3$. Each w-product is the mass of precipitate obtained.

10 Nitrogen · Dumas method

- Heat the organic compound with CuO: carbon and hydrogen are converted to CO_2 and H_2O; nitrogen is collected as N_2. Correct the measured moist-gas volume to standard conditions.

$$\frac{(P - P_1)V_1}{T_1} = \frac{P_2V_2}{T_2}$$

Symbol	Meaning
P	Pressure of moist gas
P_1	Aqueous tension (water-vapour pressure)
V_1	Measured gas volume at T_1
T_1	Measured absolute temperature in K
P_2	1 atm or 760 mm Hg (same pressure units as P)
V_2	Dry N_2 volume at STP, in mL
T_2	273 K (rounded convention)

$$\%N = \frac{28}{224}\frac{V_2\ (\text{mL})}{w\ (\text{g})}$$

11 Nitrogen · Kjeldahl method

- Nitrogen in the organic compound is converted to ammonium sulphate by digestion with H_2SO_4 ($CuSO_4$ catalyst). Alkali liberates NH_3, which is absorbed in a measured amount of standard acid and estimated by titration.

Organic Analysis

Nitrogen · Kjeldahl method

II Nitrogen · Kjeldahl method

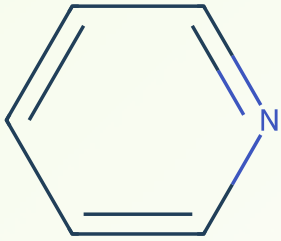
continued

$$\text{Organic compound} \xrightarrow[\text{digestion}]{H_2SO_4 / CuSO_4} (NH_4)_2SO_4$$

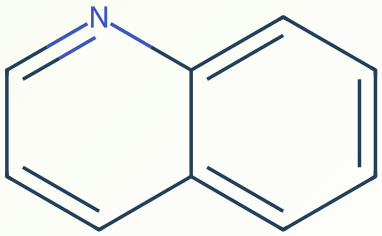
$$(NH_4)_2SO_4 + 2NaOH \rightarrow Na_2SO_4 + 2NH_3 + 2H_2O$$

$$2NH_3 + H_2SO_4 \rightarrow (NH_4)_2SO_4$$

- *Not applicable to nitro (–NO_2), nitroso (–NO), azo (–N=N–), azoxy groups, or ring nitrogen such as pyridine and quinoline: their nitrogen is not quantitatively converted to ammonium sulphate under the ordinary method.*



Pyridine



Quinoline

Ring-nitrogen examples that are unsuitable for the ordinary Kjeldahl method.

$$\text{equivalents} = N\,V_{\text{L}} = M\,n_f\,V_{\text{L}}$$

- *At neutralisation, acid equivalents consumed = ammonia equivalents. For H_2SO_4, nf = 2 and N = Mnf. If V is in mL, NV is milliequivalents.*

$$\%N = \frac{1.4\,N\,V_{\text{mL}}}{w_{\text{g}}}$$

N = acid normality; V = volume of acid actually consumed by NH_3; w = mass of organic compound. Use acid consumed after correcting for the back-titration.

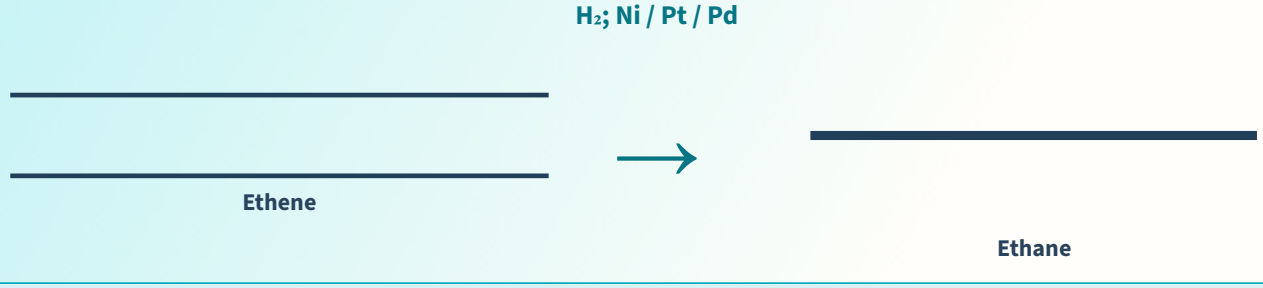
Hydrocarbons

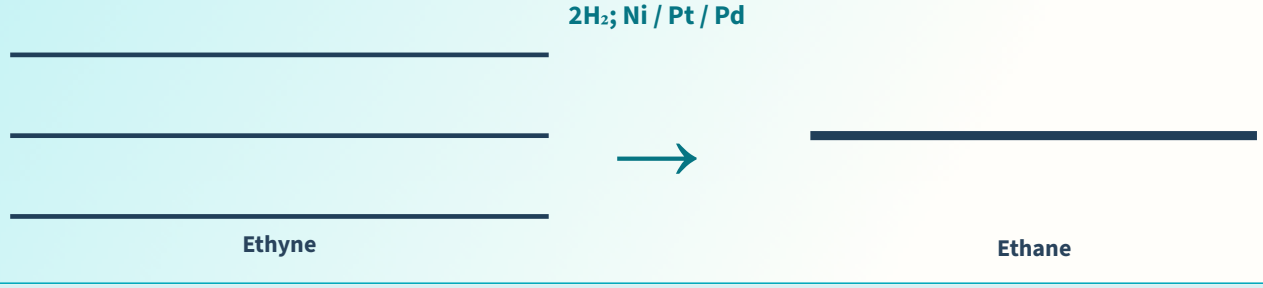
Alkanes · alkenes · alkynes · arenes

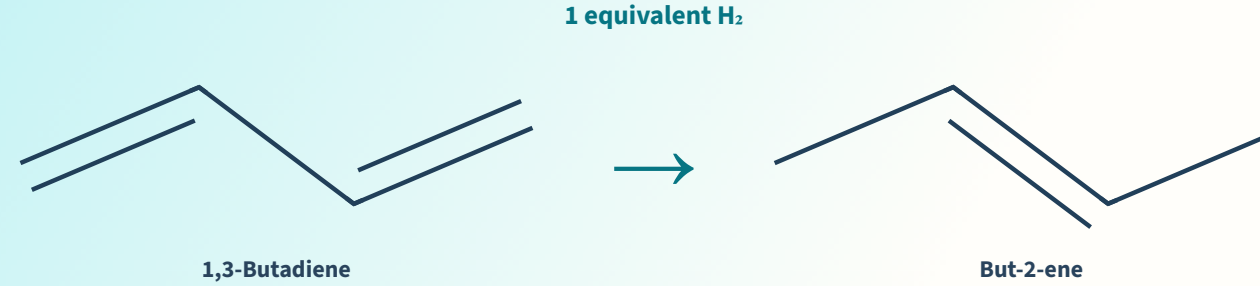
06

01 Hydrogenation of unsaturated hydrocarbons

- Sabatier–Senderens hydrogenation: add H_2 across each π bond using Ni, Pt or Pd. An alkene consumes one H_2; an alkyne consumes two H_2 to form an alkane.







Illustrated 1,4-addition: the two terminal C atoms and H_2 form a six-membered schematic arrangement. Product selectivity depends on catalyst and conditions.

02 Reduction of alkyl halides

- Alkyl halides other than fluorides can be reduced: replace X by H. Use Zn/H^+ (Zn with dilute HCl).

$$Zn + 2HCl \rightarrow ZnCl_2 + H_2$$

Hydrocarbons

Reduction of alkyl halides · Wurtz reaction

02 Reduction of alkyl halides

continued

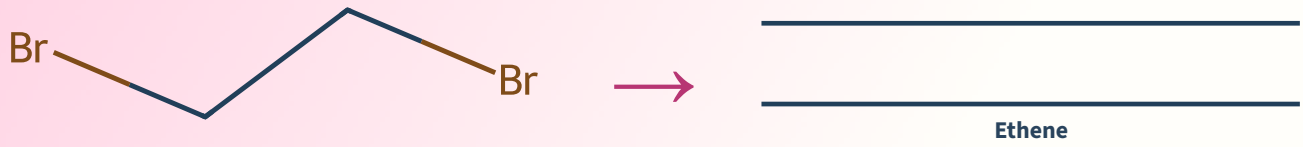


Hydrogen replaces the halogen.

03 Wurtz reaction

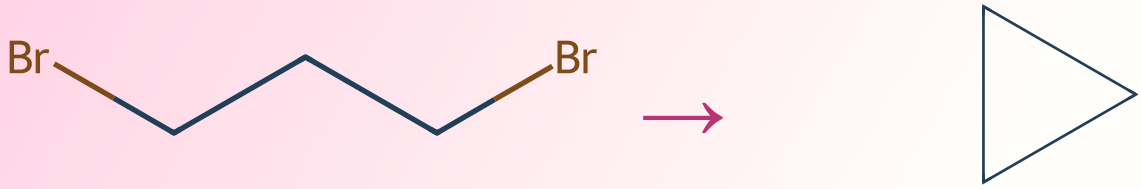
$$2R{-}X + 2Na \xrightarrow{\text{dry ether}} R{-}R + 2NaX$$

- *Coupling is illustrated through alkyl-radical formation. Methane cannot be prepared this way. One alkyl halide gives a higher, symmetrical alkane with an even number of carbon atoms.*
- *Two different halides $R_1{-}X$ and $R_2{-}X$ give a mixture: $R_1{-}R_1$, $R_1{-}R_2$ and $R_2{-}R_2$. Radical combinations are $R_1{\cdot}$ + $R_1{\cdot}$, $R_1{\cdot}$ + $R_2{\cdot}$ and $R_2{\cdot}$ + $R_2{\cdot}$.*



Vicinal dihalide example

Intramolecular removal of the two halogens gives an alkene.



1,3-Dihalide

1,3-, 1,4-, 1,5-... dihalides can undergo intramolecular cyclisation when the ring product is favourable.

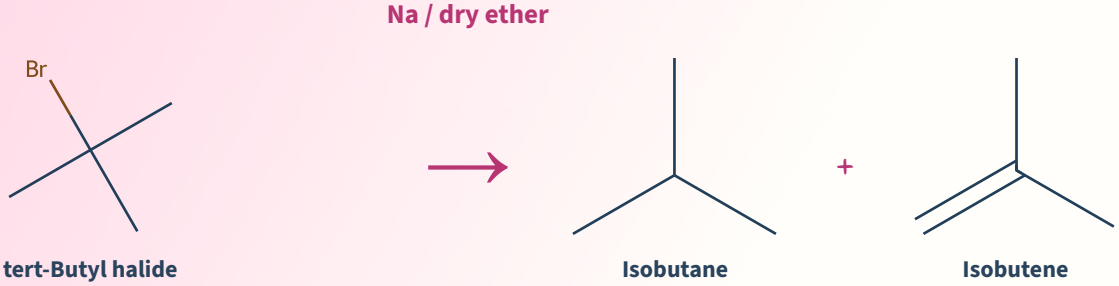
- *Intramolecular reaction is favoured when the product is sufficiently stable; a favourable aromatic or non-aromatic product is preferred over an antiaromatic one.*
- *Primary halides work best; secondary halides may couple but give more side reactions. Tertiary halides favour elimination/disproportionation rather than clean Wurtz coupling.*

Hydrocarbons

Wurtz reaction · Soda-lime decarboxylation

03 Wurtz reaction

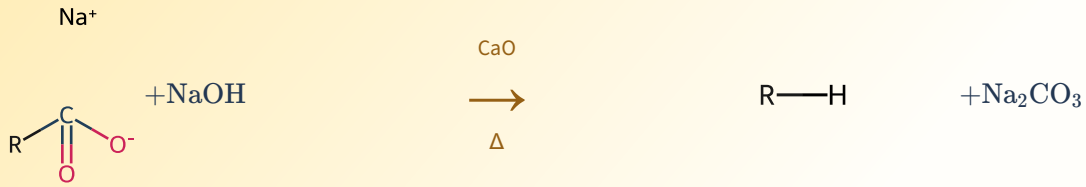
continued



tert-Butyl halide → Isobutane + Isobutene

Disproportionation products.

04 Soda-lime decarboxylation



- *Remove COOH/COONa and replace it with H; the hydrocarbon has one fewer carbon atom. A carboxylic acid first forms its sodium salt. Decarboxylation tendency is related to the stability of the developing carbanion.*

05 Kolbe electrolysis



Anodic decarboxylation and radical coupling.

- *Electrolyse an aqueous sodium or potassium carboxylate. R· + R· → R–R. Cathode: H_2. Anode: alkane and CO_2. The solution becomes more basic (pH rises).*

06 Free-radical halogenation

$$R{-}H + X_2 \xrightarrow{h\nu} R{-}X + HX$$

Halogenation	Relative reactivity of 1° : 2° : 3° H
Bromination	1 : 82 : 1600
Chlorination	1 : 3.8 : 5

Hydrocarbons

Free-radical halogenation · Isomerisation and aromatisation

06 Free-radical halogenation

continued

$$\%\text{primary product} = \frac{n_p r_p}{n_p r_p + n_s r_s + n_t r_t} \times 100$$

n = number of H atoms of that type; r = relative reactivity. These are approximate comparison values.

- *Free-radical substitution forms R–X during chain propagation. General halogen reactivity: F_2 > Cl_2 > Br_2 > I_2. Chlorination is more reactive and less selective; bromination is less reactive and more selective. Radical inhibitors such as O_2 can interrupt the chain.*
- *Further substitution produces di-, tri- and tetrahalo products: $CH_4 \rightarrow CH_3Cl \rightarrow CH_2Cl_2 \rightarrow CHCl_3 \rightarrow CCl_4$ with successive $Cl_2/h\nu$. Use excess methane relative to chlorine to favour the monochloro product.*
- *Iodination is reversible: R–H + $I_2 \rightleftharpoons$ R–I + HI. An oxidising agent such as HNO_3 or HIO_3 consumes HI and can drive the reaction forward.*

$$2HI + 2HNO_3 \rightarrow I_2 + 2NO_2 + 2H_2O$$

$$5HI + HIO_3 \rightarrow 3I_2 + 3H_2O$$

07 Isomerisation and aromatisation

Anhydrous $AlCl_3$ / HCl

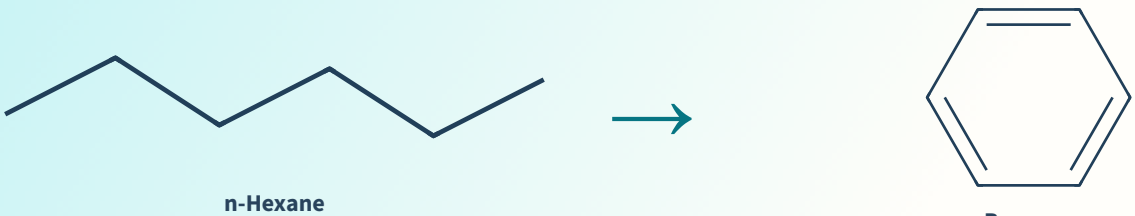


n-Butane → **Isobutane**

Straight-chain alkanes form branched-chain isomers.

Cr_2O_3 / V_2O_5 / Mo_2O_3

773 K; 10–20 atm



n-Hexane → **Benzene**

Aromatisation of n-hexane or higher alkanes.

Hydrocarbons

Isomerisation and aromatisation · Controlled oxidation

07 Isomerisation and aromatisation

continued

same catalyst conditions

773 K; 10–20 atm



n-Heptane → Toluene

08 Controlled oxidation

$$2CH_4 + O_2 \xrightarrow[100\ atm]{Cu,523\ K} 2CH_3OH$$

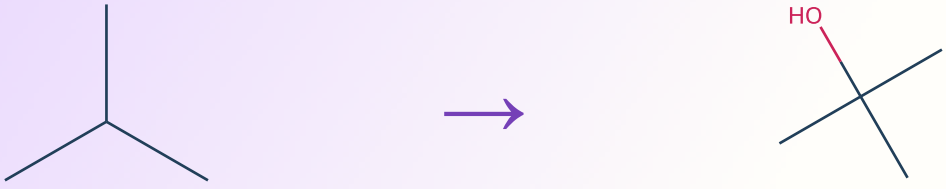
Methanol.

$$CH_4 + O_2 \xrightarrow[\Delta]{Mo_2O_3} \text{H–C(=O)–H} + H_2O$$

Methanal.

$$2CH_3CH_3 + 3O_2 \xrightarrow[\Delta]{Mn(CH_3COO)_2} 2\ CH_3COOH + 2H_2O$$

$KMnO_4$ / [O]



Isobutane: tertiary C–H → tert-Butyl alcohol

Illustrates selective replacement of a tertiary H by OH under controlled conditions.

09 Combustion, steam reforming and pyrolysis

$$C_xH_y + \left(x + \frac{y}{4}\right) O_2 \xrightarrow{\Delta} xCO_2 + \frac{y}{2}H_2O$$

Hydrocarbons

Combustion, steam reforming and pyrolysis · Alkenes from alkynes · cis reduction

09 Combustion, steam reforming and pyrolysis

continued

$$CH_4 + 2O_2 \rightarrow CO_2 + 2H_2O \quad (\Delta H < 0)$$

$$CH_4 + H_2O \xrightarrow{Ni,1273\ K} CO + 3H_2$$

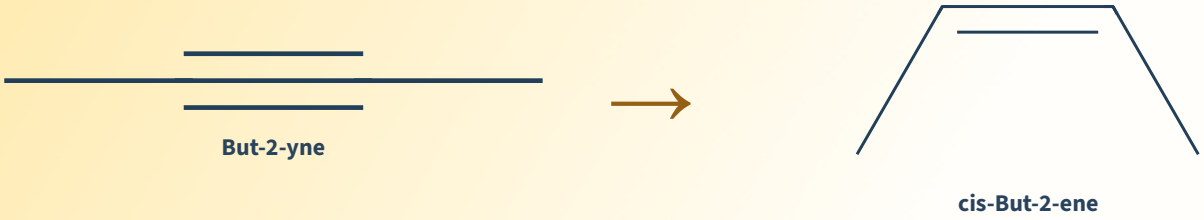
Synthesis gas: CO + H₂.

- *Pyrolysis/cracking converts higher alkanes into smaller alkanes and alkenes. Examples at 773 K:*

Reactant	Possible product set
C_6H_{14}	$C_6H_{12} + H_2$
C_6H_{14}	$C_4H_8 + C_2H_6$
C_6H_{14}	$C_3H_6 + C_2H_4 + CH_4$

10 Alkenes from alkynes · cis reduction

H₂ / Lindlar catalyst

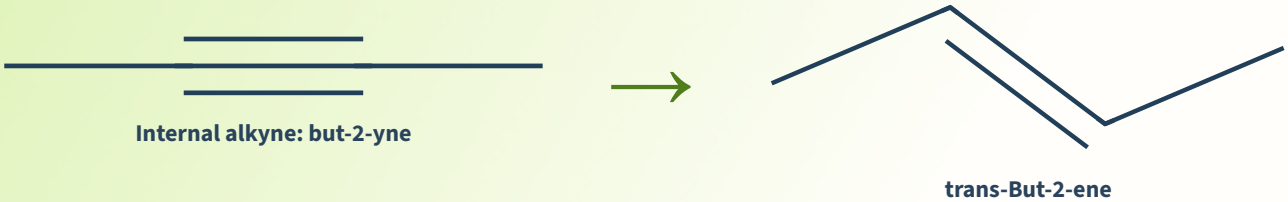


Syn addition: the two added H atoms lie on the same side. A poisoned palladium catalyst stops reduction at the alkene.

- *Lindlar catalyst uses poisoned Pd (commonly Pd/CaCO₃ with lead compounds and quinoline). Poisoned Pd/BaSO₄ is another selective-hydrogenation system; ordinary unpoisoned Pd/C can continue to the alkane.*

11 Alkenes from alkynes · trans reduction

Na or Li / liquid NH₃



Dissolving-metal reduction gives the trans alkene from an internal alkyne. Also described as a Birch-type dissolving-metal reduction in introductory notes.

12 Dehydrohalogenation · E2

- Alcoholic KOH removes X from the α-carbon and H from an adjacent β-carbon to form C=C. This is a one-step, bimolecular E2 reaction with a transition state and no discrete intermediate; the favoured geometry is anti-periplanar.

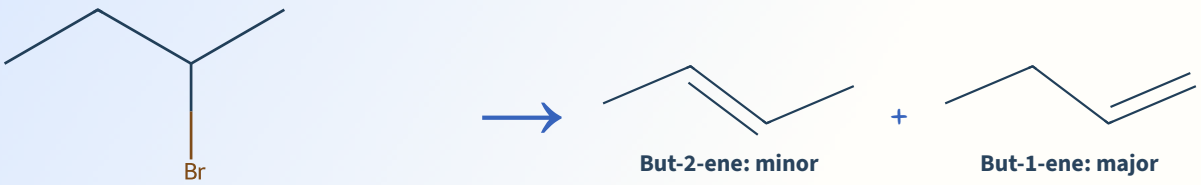
$$v = k[\mathrm{R{-}X}][\mathrm{base}]$$

Overall second order.

- For comparable substrates: leaving-group order $I^- > Br^- > Cl^- > F^-$; usual rate comparison R–I > R–Br > R–Cl. The usual substrate order is 3° > 2° > 1° under elimination-favouring conditions.

Product	Alkene substitution
Saytzeff/Zaitsev	More substituted; usually more stable
Hofmann	Less substituted; less hindered

Potassium tert-butoxide, $(CH_3)_3COK$



2-Bromobutane

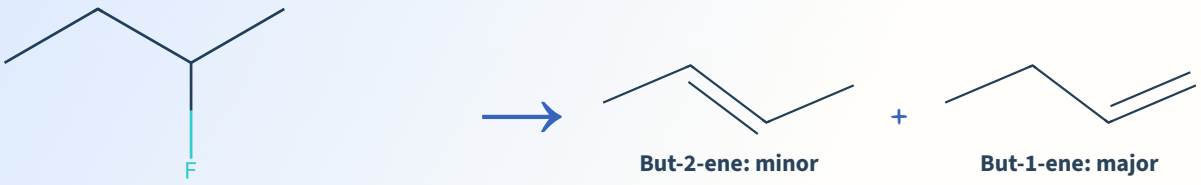
But-2-ene: minor

But-1-ene: major

A bulky base removes the less hindered β-H and favours the Hofmann product.

- For alkyl fluorides, the strong C–F bond gives an E2 transition state with increased carbanion character (often labelled E2a in these notes). Carbanion stability can favour the less substituted alkene. Bond strength: C–F > C–Cl > C–Br > C–I.

Alcoholic KOH



2-Fluorobutane

But-2-ene: minor

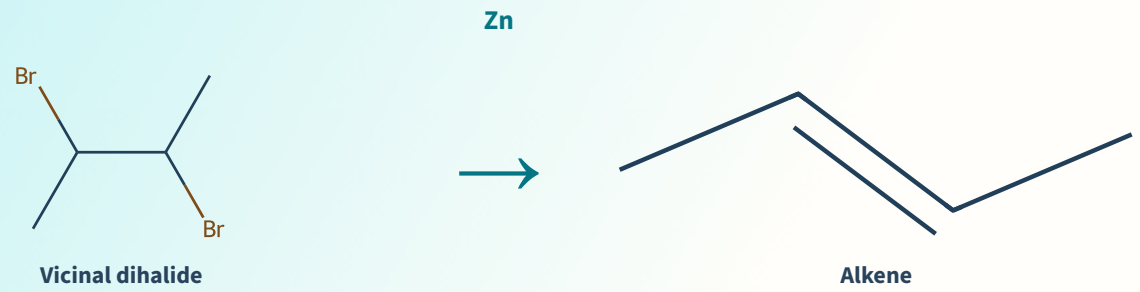
But-1-ene: major

Alkyl-fluoride example.

Hydrocarbons

Dehalogenation of vicinal dihalides · Acid-catalysed dehydration of alcohols

13 Dehalogenation of vicinal dihalides



Vicinal dihalide → **Alkene**

Two neighbouring halogens are removed; ZnX_2 is the by-product.

14 Acid-catalysed dehydration of alcohols

- *Reagents: concentrated H_2SO_4 with heat, concentrated H_3PO_4, or H^+/heat. Protonate OH to form ROH_2^+; water leaves; β-deprotonation gives an alkene. Secondary/tertiary substrates commonly follow E1 with a carbocation; rearrangement may occur.*

$$\mathrm{ROH} \xrightarrow{\mathrm{H^+}} \mathrm{ROH_2^+} \rightarrow \mathrm{R^+} + \mathrm{H_2O} \rightarrow \text{alkene} + \mathrm{H^+}$$

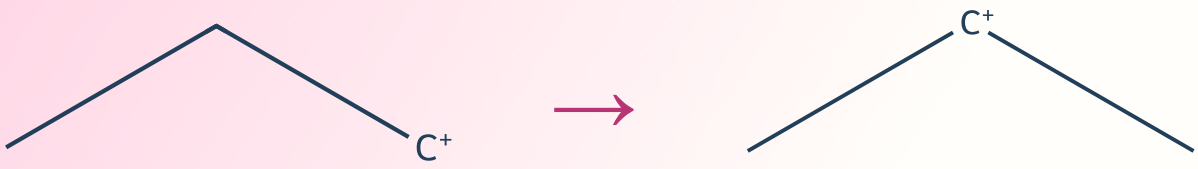
$$v = k[\mathrm{ROH_2^+}]$$

E1 description: first order in the protonated alcohol.

- *Rate follows the stability of the initially formed carbocation; the more stable alkene is generally the major product. Primary alcohols need not form a free primary carbocation.*

15 Carbocation rearrangement · hydride and methyl shifts

1,2-hydride shift



Primary propyl cation → **Secondary isopropyl cation**

Move H with its bonding pair from the adjacent carbon to C^+; the positive charge moves to the carbon that lost H. α-H count: 2 → 6.

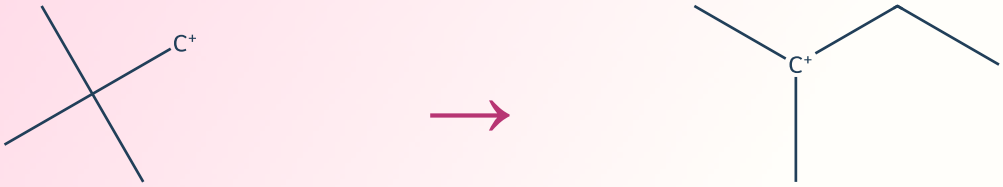
Hydrocarbons

Carbocation rearrangement · hydride and methyl shifts · Ring expansion

15 Carbocation rearrangement · hydride and methyl shifts

continued

1,2-methyl shift



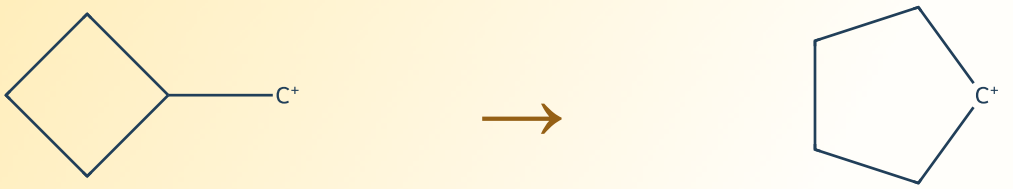
Neopentyl cation → **tert-Amyl cation**

A methyl group migrates with its bonding pair; α-H count: 0 → 8.

- *Migration preference: hydride > methyl when otherwise comparable; the stability of the final cation and structural constraints determine the actual rearrangement.*

16 Ring expansion

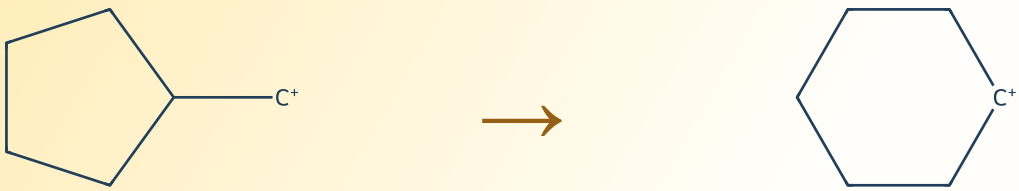
1,2-C–C bond shift



Cyclobutylmethyl cation → **Cyclopentyl cation**

Break the adjacent ring bond and reconnect it to the external C⁺; positive charge moves to the ring carbon.

ring expansion



Cyclopentylmethyl cation → **Cyclohexyl cation**

- *Preference: ring expansion > hydride shift > methyl shift when expansion relieves strain and gives a favourable cation. The cyclopropylmethyl cation is unusually stabilised by σ-delocalisation ("dancing resonance" in the notes), so it is not treated as a simple isolated primary cation.*

Hydrocarbons

Hydrogenation and halogenation · Halohydrin, interhalogen and nitrosyl-chloride additions

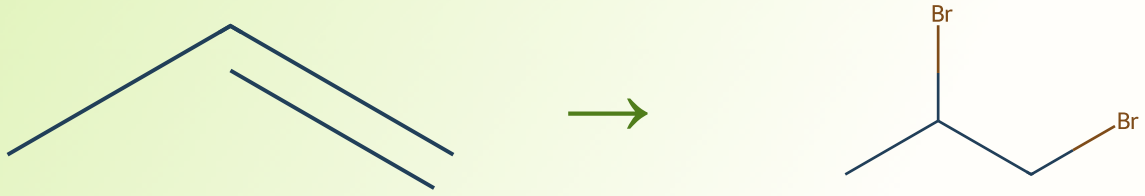
17 Hydrogenation and halogenation

H_2 / Ni, Pt or Pd



Propene → **Propane**

Br_2 / CCl_4



Propene → **1,2-Dibromopropane**

Electrophilic anti addition in a non-polar solvent; CS_2 or $CHCl_3$ are other solvent examples.

- *Halogen addition forms a cyclic halonium intermediate rather than a free carbocation, so ordinary carbocation rearrangement is absent. Alkene nucleophilicity increases with electron-donating groups and decreases with electron-withdrawing groups.*

- *Test for unsaturation: reddish-orange Br_2 solution is decolourised on addition across C=C. Bromine water can also be used.*

18 Halohydrin, interhalogen and nitrosyl-chloride additions

Br_2 / H_2O



Propene → **Bromohydrin**

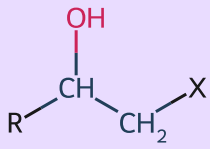
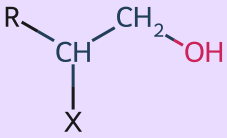
OH usually occupies the more substituted carbon and Br the less substituted carbon; anti addition. HO–X summarises the net groups added.

Hydrocarbons

Halohydrin, interhalogen and nitrosyl-chloride additions · Hydrogen halide addition · Markovnikov rule

18 Halohydrin, interhalogen and nitrosyl-chloride additions

continued

Electronic comparison: an electron-donating R group favours  *; a strongly electron-withdrawing R group can alter regiochemistry towards*  *. Evaluate the actual substrate.*

BrCl (Brδ+–Clδ–)



Propene → **1-Bromo-2-chloropropane**

The more negative chlorine component attacks the more substituted centre in the illustrated example.

NOCl (Tilden reagent)



Propene → **Nitrosochloride adduct**

Product: $CH_3–CH(Cl)–CH_2–NO$.

19 Hydrogen halide addition · Markovnikov rule

HBr



Propene → **2-Bromopropane**

Protonation gives the more stable carbocation; X^- then attacks. Rearrangement is possible.

Hydrocarbons

Hydrogen halide addition · Markovnikov rule · Hydration and sulphuric-acid addition

19 Hydrogen halide addition · Markovnikov rule

continued

- *Markovnikov rule for the usual unsymmetrical alkene: the negative part of HX attaches to the alkene carbon bearing fewer H atoms; H attaches to the carbon bearing more H atoms.*

20 Hydration and sulphuric-acid addition

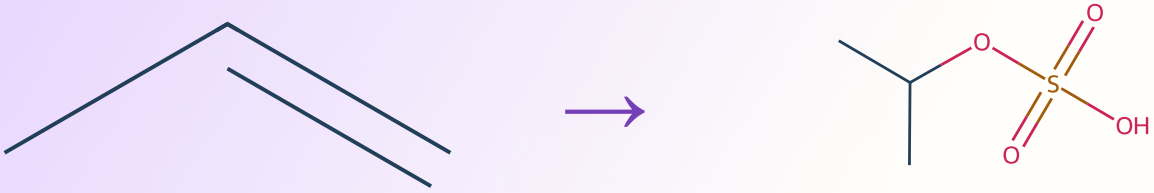
H_3O^+ / dilute H_2SO_4



Propene → **Propan-2-ol**

Carbocation formation → water attack → loss of H^+. Rearrangement is possible.

H_2SO_4

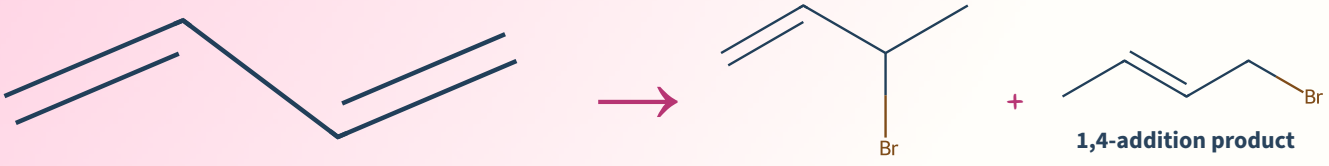


Propene → **Isopropyl hydrogen sulphate**

H_2SO_4 supplies H^+ and HSO_4^-; Markovnikov addition gives the alkyl hydrogen sulphate.

21 HX addition to a conjugated diene

HBr



1,3-Butadiene → **1,2-addition product** + **1,4-addition product**

The allylic carbocation has two resonance contributors: $CH_2{=}CH{-}CH^+{-}CH_3 \leftrightarrow {}^+CH_2{-}CH{=}CH{-}CH_3$.

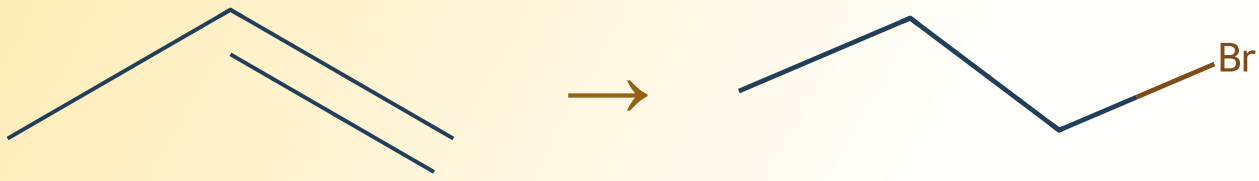
- *1,2-addition is the faster kinetic-control product (KCP); 1,4-addition gives the more stable internal double bond and is the thermodynamic-control product (TCP) under equilibrating conditions.*

Hydrocarbons

HBr / peroxide · anti-Markovnikov addition · Mild oxidation · Baeyer reagent

22 HBr / peroxide · anti-Markovnikov addition

HBr / peroxide



Propene → **1-Bromopropane**

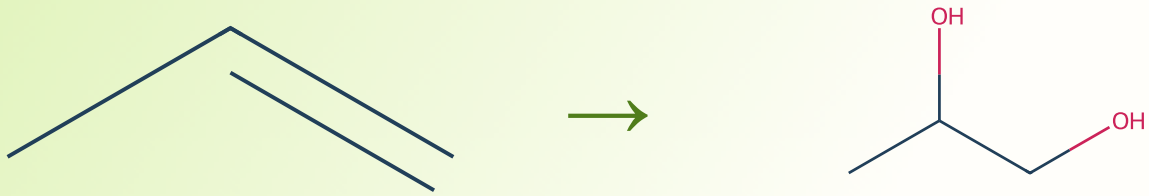
Free-radical addition; Br attaches so that the more stable carbon radical is formed. No carbocation rearrangement.

- *This peroxide effect works with HBr, not ordinarily HCl or HI, because an unfavourable/endothermic propagation step prevents the analogous efficient radical chain for HCl/HI. The first chain-addition step is commonly the slower propagation step.*

- *Free-radical initiator mnemonic "HELP R": Heat (high temperature), Energy, Light, Peroxide → Radicals.*

23 Mild oxidation · Baeyer reagent

Cold dilute alkaline $KMnO_4$



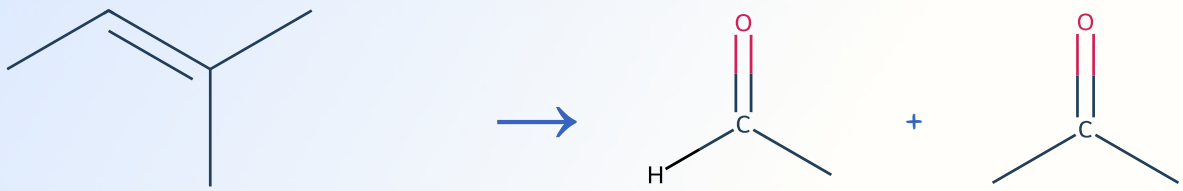
Propene → **Propane-1,2-diol**

Syn hydroxylation gives a vicinal diol (glycol). Decolourisation of $KMnO_4$ is used as a test for unsaturation.

24 Reductive ozonolysis

- *Cleave C=C and put oxygen on both carbons. O_3 is followed by a reducing work-up: Zn/H_2O, Zn, or dimethyl sulphide (Me_2S). O_3/CCl_4 is one initial solvent notation; O_3/Me_2S and O_3/Zn abbreviate the two-stage process.*

1. O_3; 2. Zn/H_2O or Me_2S



2-Methylbut-2-ene → **Ethanal** + **Acetone**

Aldehydes and/or ketones are retained under reductive work-up.

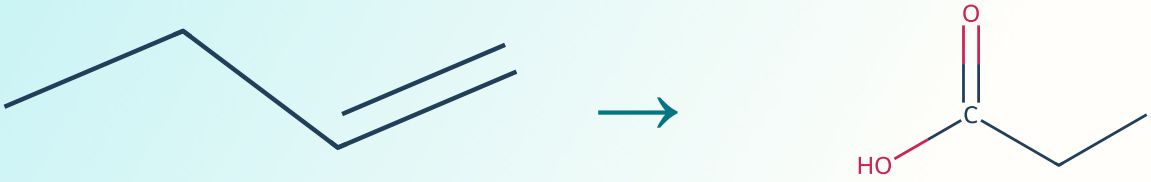
Hydrocarbons

Oxidative cleavage · Alkynes by carbide hydrolysis

25 Oxidative cleavage

- Ozonolysis followed by H_2O_2 gives oxidative cleavage. Aldehyde-derived fragments become carboxylic acids, while ketone fragments remain ketones; a terminal $=CH_2$ carbon is fully oxidised to CO_2 (via carbonic/formic products in the schematic). O_3/H_2O without a reductant may also allow oxidation of aldehyde fragments.

1. O_3; 2. H_2O_2



But-1-ene → **Propanoic acid**

The terminal carbon gives CO_2 and H_2O.

- Other cleavage reagents: hot/strong $KMnO_4$ in acidic, alkaline or heated conditions; $K_2Cr_2O_7/H^+$ and dichromate/heat are also listed. Product formation depends on oxidation conditions; alkaline products are carboxylate salts before acid work-up.

26 Alkynes by carbide hydrolysis

$$CaCO_3 \xrightarrow{\Delta} CaO + CO_2$$

$$CaO + 3C \rightarrow CaC_2 + CO$$

$$CaC_2 + 2H_2O \rightarrow HC \equiv CH + Ca(OH)_2$$

$$Mg_2C_3 + 4H_2O \rightarrow CH_3C \equiv CH + 2Mg(OH)_2$$

$$Al_4C_3 + 12H_2O \rightarrow 3CH_4 + 4Al(OH)_3$$

$$Be_2C + 4H_2O \rightarrow CH_4 + 2Be(OH)_2$$

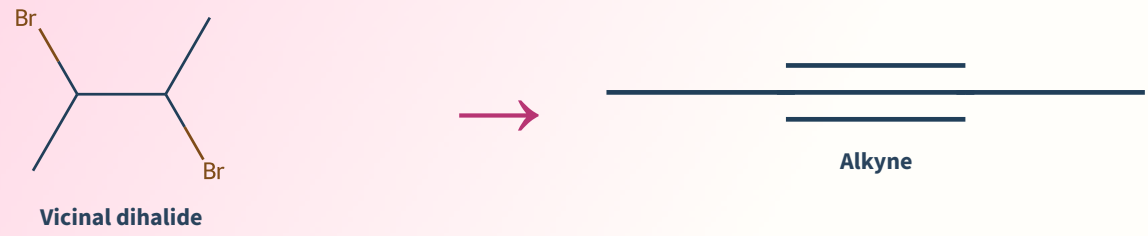
The last two carbides give methane, not an alkyne—compare the carbide carbon unit.

Hydrocarbons

Alkynes by double dehydrohalogenation · Lower to higher alkynes · acetylide alkylation

27 Alkynes by double dehydrohalogenation

1. alcoholic KOH; 2. $NaNH_2$



Vicinal dihalide

First elimination gives a vinyl halide; the second needs a stronger base. Basicity: NH_2^- > OH^-.

- *Two dehydrohalogenations are needed: a strong-base sequence such as two $NaNH_2$, or alcoholic KOH followed by $NaNH_2$. Alcoholic KOH alone is generally insufficient for the difficult vinyl-halide elimination.*

28 Lower to higher alkynes · acetylide alkylation

$$CH_3C \equiv CH + NaNH_2 \rightarrow CH_3C \equiv C^-Na^+ + NH_3$$

SN2 alkylation

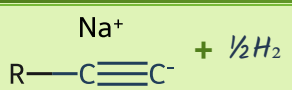
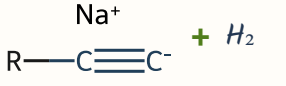
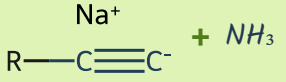


Methyl or primary alkyl halides work best; bulky halides favour elimination.

29 Acidic nature of terminal alkynes

$$HC \equiv CH > CH_3C \equiv CH > CH_3C \equiv CCH_3$$

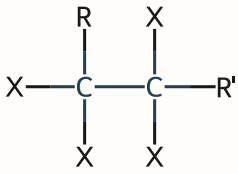
Acidity comparison: an internal alkyne has no terminal acetylenic H.

Reagent for RC≡CH	Products
Na / heat	
NaH	
$NaNH_2$	

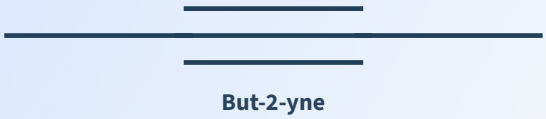
Hydrocarbons

Addition reactions of alkynes · Kucherov hydration and hydrohalogenation

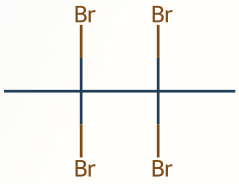
30 Addition reactions of alkynes

Reagent	Product / outcome
H_2 / poisoned Pd (Lindlar)	cis alkene
Na or Li / liquid NH_3	trans alkene from internal alkyne
$2H_2$ / Ni	Alkane
$2X_2$ / CCl_4	 tetrahalide
$2Br_2$ / CCl_4	Tetrabromide; bromine is decolourised

$2Br_2$ / CCl_4



But-2-yne

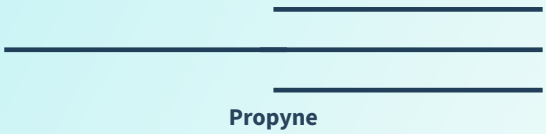


2,2,3,3-Tetrabromobutane

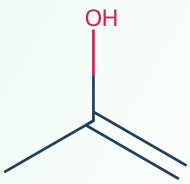
Unsaturation test.

31 Kucherov hydration and hydrohalogenation

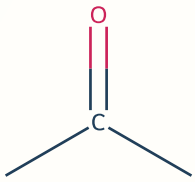
Dilute H_2SO_4 / $HgSO_4$ / H_2O



Propyne



Enol



Ketone after tautomerisation

Hydration first forms an enol, which changes into the more stable keto form. General terminal alkyne

 *gives* *; ethyne gives ethanal.*

Hydrocarbons

Kucherov hydration and hydrohalogenation · Oxidation and ozonolysis

31 Kucherov hydration and hydrohalogenation

continued

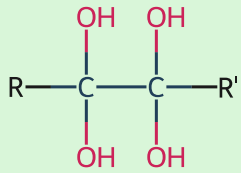
2HBr



Propyne → **Geminal dihalide**

Both X atoms end on the same carbon in the ordinary Markovnikov addition.

32 Oxidation and ozonolysis

- *A schematic representation of mild Baeyer oxidation shows reaction of* R—C≡C—R' *through a transient tetraol,*  *, followed by loss of water to an α-dicarbonyl compound.*

Decolourisation is a test for unsaturation.

Mild oxidation / reductive ozonolysis



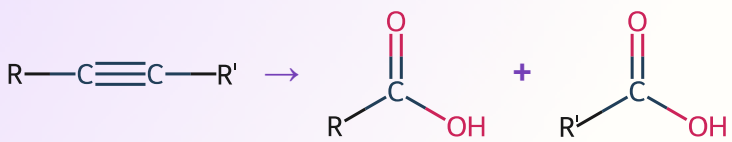
But-2-yne → **Butane-2,3-dione**

An α-diketone is shown for reductive alkyne ozonolysis.

Oxidative cleavage



But-2-yne → **Ethanoic acid (2 equivalents)**



. The schematic passes through hydroxylated carbonyl fragments before cleavage.

Hydrocarbons

Cyclic trimerisation · red-hot tube · Tests for terminal alkynes

33 Cyclic trimerisation · red-hot tube

Red-hot iron tube



Red-hot tube



1,3,5-Trimethylbenzene as the illustrated product.

Red-hot tube



Red-hot tube



34 Tests for terminal alkynes

Reagent	Product	Observation
Ammoniacal $AgNO_3$ (Tollens-type reagent)	R—C≡C—Ag	White precipitate
Ammoniacal cuprous chloride (CuCl / NH_4OH)	R—C≡C—Cu	Red precipitate

Hydrocarbons

Tests for terminal alkynes · Preparation of benzene

34 Tests for terminal alkynes

continued

- These tests distinguish terminal alkynes, which have an acidic ≡C–H, from internal alkynes.

35 Preparation of benzene

- Method I: cyclic trimerisation of ethyne in a red-hot tube, as shown above.

Zn dust / heat



Phenol → **Benzene**

ZnO is formed.

NaOH / CaO / heat

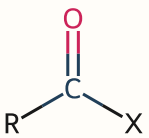
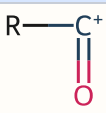


Benzoic acid / sodium benzoate → **Benzene**

Soda-lime decarboxylation.

36 Electrophilic aromatic substitution (EAS)

$$\mathrm{Ar{-}H + E^+ \rightarrow Ar{-}E + H^+}$$

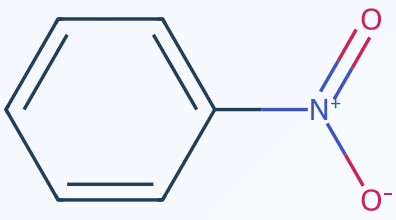
Reaction	Reagent	Electrophile
Nitration	Concentrated HNO_3 + concentrated H_2SO_4	NO_2^+
Halogenation	X_2 + anhydrous FeX_3	Electrophilic halogen (formally X^+)
Friedel–Crafts alkylation	R—X + anhydrous AlX_3	R^+-like electrophile; rearrangement possible
Friedel–Crafts acylation	 + anhydrous AlX_3	Acylium ion  ; no ordinary rearrangement
Sulphonation	Oleum (SO_3/H_2SO_4, $H_2S_2O_7$) or concentrated H_2SO_4	SO_3 / protonated SO_3 depending on medium

Hydrocarbons

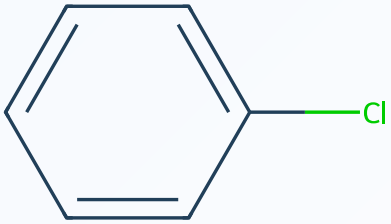
Electrophilic aromatic substitution (EAS) · Mechanism · lose aromaticity, then restore it

36 Electrophilic aromatic substitution (EAS)

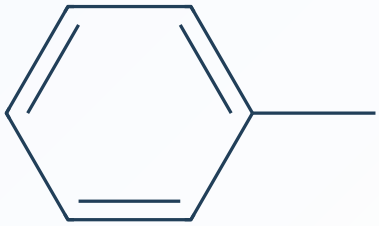
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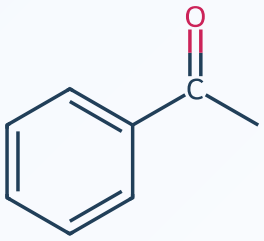
Nitrobenzene



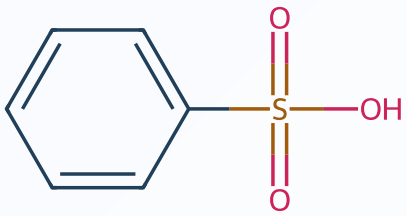
Chlorobenzene



Alkylbenzene example



Acylbenzene example

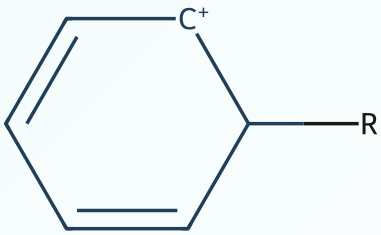


Benzenesulphonic acid

Benzene products for the five electrophilic substitution families.

37 Mechanism · lose aromaticity, then restore it

- *Step 1 (usually slow/rate-determining): benzene π electrons attack E^+. The attacked carbon becomes sp^3 and retains H; a non-aromatic carbocation (σ-complex/Wheland intermediate) forms. Its positive charge is delocalised over three ring positions.*



σ-complex: one resonance contributor

The ring carbon bonded to E and H is sp^3; the ring is temporarily non-aromatic.

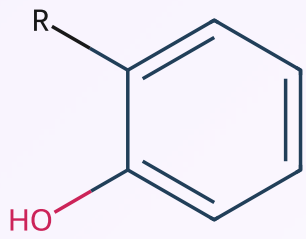
- *Step 2: loss of H^+ from the attacked carbon restores the aromatic π system, giving Ar–E. Electron-donating +M and +I groups generally accelerate EAS by stabilising the σ-complex.*

Hydrocarbons

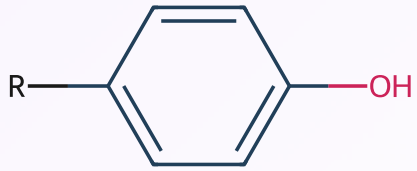
Directive influence of substituents · Addition reactions of benzene

38 Directive influence of substituents

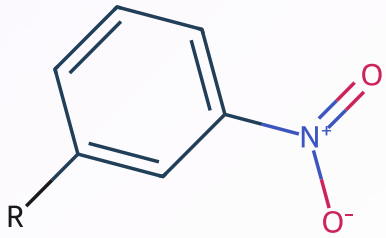
A group donating by +M increases electron density most at ortho and para positions and directs incoming E^+ there. A group withdrawing by −M generally directs to meta, avoiding the least stable σ-complex contributors. Halogens are a familiar exception: deactivating overall but ortho/para directing.



Ortho substitution beside a +M donor



Para substitution beside a +M donor



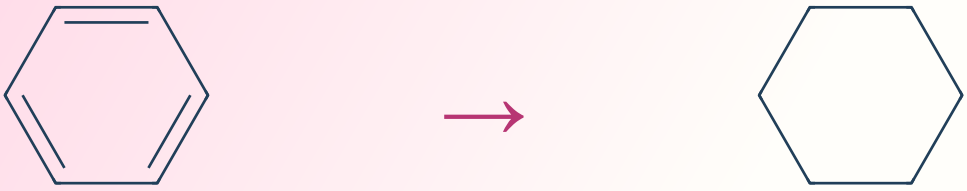
Meta substitution beside a −M group

Direction map: electron donation → ortho/para; resonance withdrawal → meta.

39 Addition reactions of benzene

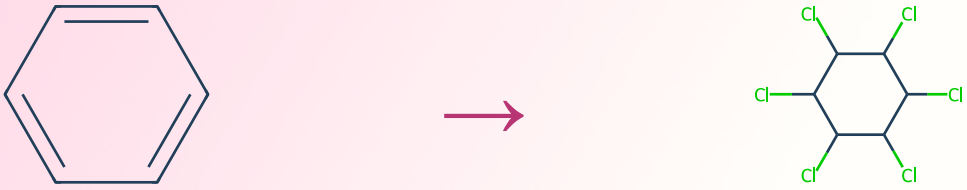
$3H_2$ / Ni

High temperature and pressure



Benzene → **Cyclohexane**

$3Cl_2$ / hv



Benzene → **Hexachlorocyclohexane (BHC)**

$C_6H_6Cl_6$. The γ-isomer is lindane / gammexane (γ-BHC; also written γ-666), historically used as an insecticide.

Haloalkanes & Haloarenes

Substitution · elimination · Grignard reagents

07

01 From alcohols with HX

- HX provides H^+ and X^-. Protonation converts poor leaving group OH into water: $ROH \rightarrow ROH_2^+$. For alcohols reacting by SN1, water leaves to give R^+, followed by X^- attack. Rearrangement is possible; rate follows stability of the initially formed carbocation.



Primary alcohols often react through substitution without a free primary carbocation.

02 Lucas test for alcohols

- Lucas reagent = concentrated HCl + anhydrous $ZnCl_2$. Turbidity comes from the insoluble alkyl chloride.

Ordinary alcohol (no special resonance stabilisation)	Observation at room temperature
1°	No immediate turbidity; very slow
2°	Turbidity in minutes
3°	Turbidity in seconds

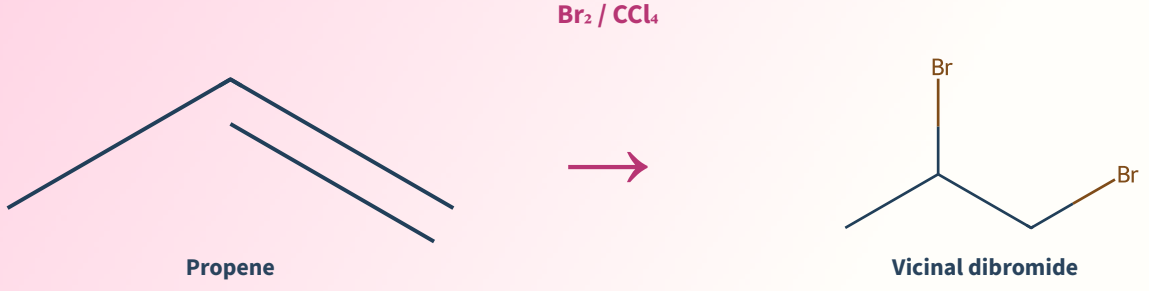
- Resonance-stabilised substrates such as benzylic/allylic alcohols can react quickly even when primary.

03 2–4 · From alkanes and alkenes



Free-radical substitution. Count distinct H environments to count monohalogenated constitutional products.

- For chlorination, product proportions follow nprp, nsrs and ntrt with rp:rs:rt = 1:3.8:5. Bromination is more selective: 3° > 2° > 1°.



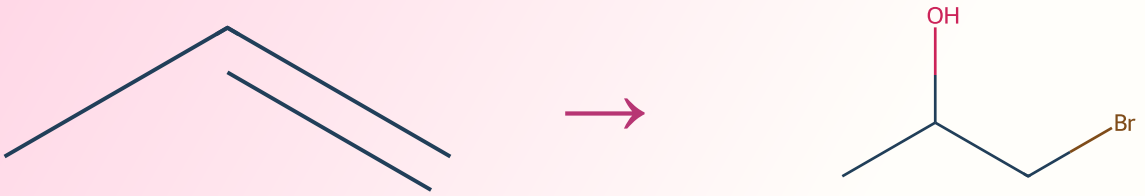
Haloalkanes & Haloarenes

2–4 · From alkanes and alkenes · Halogen-exchange reactions

03 2–4 · From alkanes and alkenes

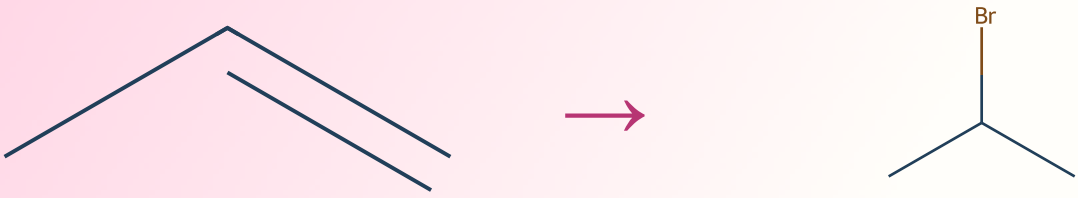
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Br_2 / H_2O



Propene → Bromohydrin

HBr



Propene → 2-Bromopropane

Markovnikov hydrohalogenation; carbocation rearrangement is possible.

04 Halogen-exchange reactions

Name	Transformation	Reagent / medium
Swarts	R–Cl or R–Br → R–F	Inorganic fluorides: AgF, SbF_3, Hg_2F_2, CoF_2
Finkelstein	R–Cl or R–Br → R–I	NaI in dry acetone (DMSO is also an aprotic medium)

- Swarts replaces the original halogen by F. Finkelstein replaces it by I; NaCl/NaBr precipitation in acetone helps drive the exchange.

05 Alcohol to halide without carbocation rearrangement

$$ROH + SOCl_2 \rightarrow RCl + SO_2\uparrow + HCl\uparrow$$

Darzens method. Thionyl chloride is useful because the by-products are gases.

$$3ROH + PX_3 \rightarrow 3RX + H_3PO_3$$

X = Cl or Br; PX_3 can be generated from red phosphorus and X_2.

Haloalkanes & Haloarenes

Alcohol to halide without carbocation rearrangement · Allylic and benzylic substitution

05 Alcohol to halide without carbocation rearrangement

continued

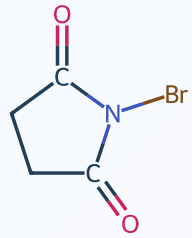
$$ROH + PX_5 \rightarrow RX + POX_3 + HX$$

X = Cl or Br; PCl_5 is the familiar example.

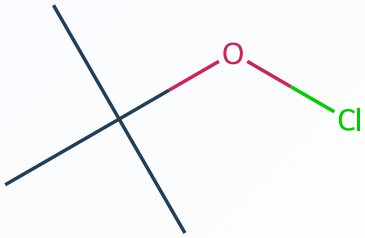
06 Allylic and benzylic substitution

- *Replace an H on the carbon beside C=C (allylic) or beside a benzene ring (benzylic). Resonance stabilises the radical intermediate.*

Chlorination options in this comparison	Bromination options
Cl_2 / hν	Br_2 / hν
Cl_2 / 500 °C	NBS (N-bromosuccinimide) / radical conditions
tert-Butyl hypochlorite, t-BuOCl	Low-concentration Br_2 / hν
Low-concentration Cl_2 / hν	



N-Bromosuccinimide (NBS)



tert-Butyl hypochlorite

Reagents used for allylic or benzylic halogenation.

07 Allylic substitution example

Cl_2 / hν

Allylic substitution conditions



Propene → **Allyl chloride**

The allyl radical $\cdot CH_2-CH=CH_2$ is resonance-stabilised.

Haloalkanes & Haloarenes

Nucleophilic substitution · SN1 · two steps

08 Nucleophilic substitution

$$\mathrm{R{-}X + Nu^- \rightarrow R{-}Nu + X^-}$$

- *SN1 = substitution with a unimolecular rate-determining step. SN2 = substitution through a bimolecular elementary step.*

09 SN1 · two steps

$$\mathrm{R{-}X \xrightarrow{slow} R^+ + X^-}$$

$$\mathrm{R^+ + Nu^- \xrightarrow{fast} R{-}Nu}$$

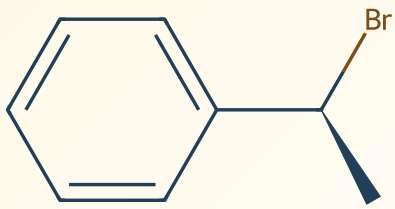
- *A carbocation intermediate forms; rearrangement may occur. The first ionisation step is slow. For comparable halides: R–F < R–Cl < R–Br < R–I. Substrate reactivity follows stability of the initially formed carbocation.*

$$v = k[\mathrm{R{-}X}]$$

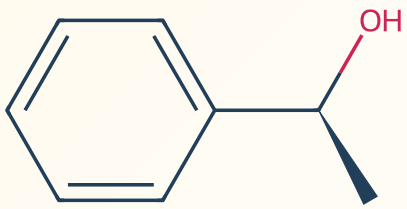
First order; the slow elementary step is unimolecular.

- *Polar protic solvents favour ionisation, and a weak/neutral nucleophile can react once the carbocation forms.*

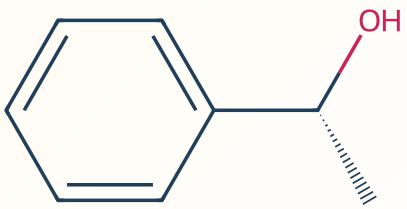
10 SN1 stereochemistry



Chiral 1-bromo-1-phenylethane



One alcohol enantiomer



Opposite alcohol enantiomer

Attack on the planar carbocation can occur from either face.

Haloalkanes & Haloarenes

SN1 stereochemistry · SN2 · one concerted step

10 SN1 stereochemistry

continued

- An ideal equal 50:50 retention/inversion mixture is racemic. Ion pairing often gives a small excess of inversion; an example is 49% retention and 51% inversion. These percentages are illustrative, not a universal ratio.

11 SN2 · one concerted step

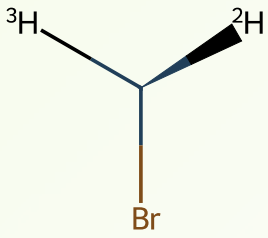
$$\mathrm{Nu^- + R{-}X \rightarrow [Nu\cdots R\cdots X]^{\ddagger} \rightarrow Nu{-}R + X^-}$$

- Bond formation and bond breaking occur together through a transition state. Backside attack gives Walden inversion at the attacked stereocentre; no carbocation intermediate or ordinary carbocation rearrangement.

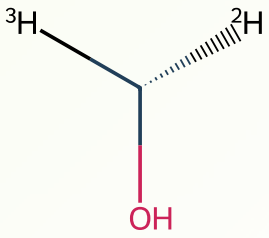
$$v = k[\mathrm{R{-}X}][\mathrm{Nu^-}]$$

Second order; bimolecular elementary step.

- Rate rises as steric hindrance falls: methyl > 1° > 2° ≫ 3°. Comparable leaving-group order: R–F < R–Cl < R–Br < R–I. A strong nucleophile and a suitable polar aprotic solvent favour SN2.



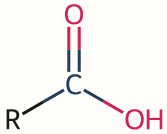
Isotope-labelled starting centre



Inverted substitution product

Stereochemical idea: T, D, H and X around C; backside Nu attack gives 100% inversion.

12 Solvent comparison

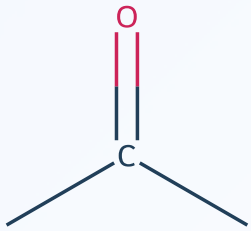
Solvent class	Examples	Effect
Non-polar	CS_2, benzene, CCl_4	Very small/zero permanent molecular dipole in these examples
Polar protic (PPS)	H_2O, ROH, 	O–H donors strongly solvate anions and help stabilise ions; commonly favour SN1
Polar aprotic (PAS)	Acetone, DMF, DMSO; source also lists ethers	No O–H/N–H donor; cations are solvated while anions remain more available for SN2

Haloalkanes & Haloarenes

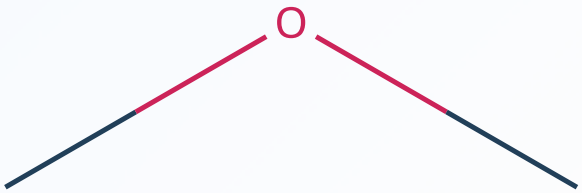
Solvent comparison · Four important substitutions

12 Solvent comparison

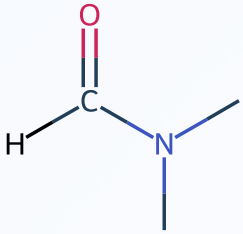
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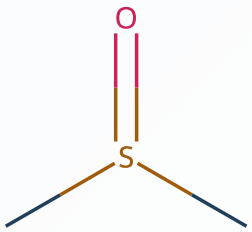
Acetone



Dimethyl ether



DMF

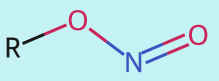
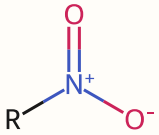


DMSO

Solvent structures shown in the notes.

- *Solvation lowers the effective availability of a nucleophile; less strongly solvated anions are more reactive. For the same donor atom, the negatively charged species is generally more nucleophilic than its neutral conjugate acid. Ether is aprotic but less polar than DMF/DMSO.*

13 Four important substitutions

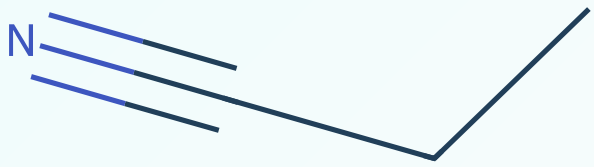
Reagent with R–X	Main product	Bond formed
KCN	R—C≡N (nitrile)	C–C
AgCN	R—N⁺≡C⁻ (isocyanide)	C–N
KNO_2	 (alkyl nitrite)	C–O
$AgNO_2$	 (nitroalkane)	C–N

Haloalkanes & Haloarenes

Four important substitutions · Nucleophilicity · charge, solvent and size

13 Four important substitutions

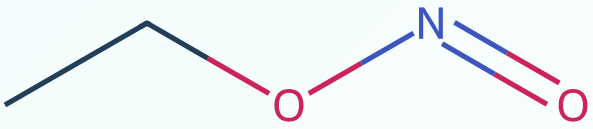
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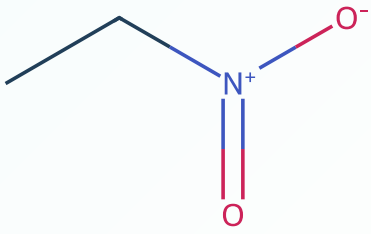
Nitrile example



Isocyanide example



Alkyl nitrite example



Nitroalkane example

Ambident nucleophiles attack through different atoms.

14 Nucleophilicity · charge, solvent and size

- Nucleophilicity is the tendency/rate of electron-pair donation to an electrophile. For the same donor atom: $OH^- > H_2O$; $HS^- > H_2S$; $NH_2^- > NH_3$; $RO^- > ROH$.

- Across a period, electronegativity generally increases from C to N to O to F while atomic size falls. Common same-period comparison: $CH_3^- > NH_2^- > OH^- > F^-$. These strongly basic species cannot all persist unchanged in a protic solvent; the useful general rule for comparable same-period donors is that nucleophilicity often parallels basicity.

Halide comparison	Polar protic solvent	Polar aprotic solvent
Nucleophilicity	$F^- < Cl^- < Br^- < I^-$	$F^- > Cl^- > Br^- > I^-$
Size (independent of solvent)	$F^- < Cl^- < Br^- < I^-$	Same size order
Charge density / strong protic solvation	$F^- > Cl^- > Br^- > I^-$	Anion H-bond solvation is greatly reduced

- Do not automatically reverse the across-period order in aprotic solvent; solvent reversal is most clearly illustrated by the halide series above.

Haloalkanes & Haloarenes

Nucleophilicity · charge, solvent and size · Choosing SN1 or SN2

14 Nucleophilicity · charge, solvent and size

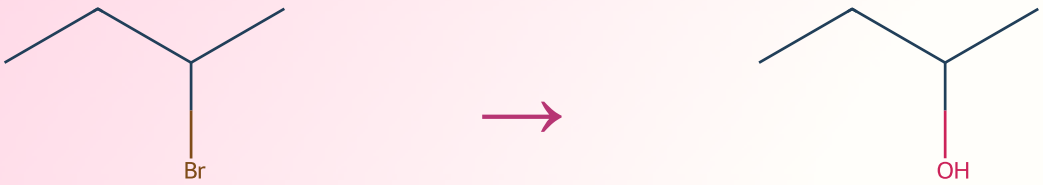
continued

- α-effect: a donor atom next to another lone-pair-bearing atom can be especially nucleophilic. Comparisons: NH_2NH_2 > NH_3 and H_2O_2 > H_2O. Steric hindrance reduces nucleophilicity: CH_3O^- is less hindered and commonly more nucleophilic in SN2 than $(CH_3)_3CO^-$.

15 Choosing SN1 or SN2

Situation	Usual preference
3° halide	SN1 under solvolysis conditions; strong base may give elimination
1° halide	SN2
2° + strong nucleophile such as OH^-	SN2 can compete; consider elimination
2° + weak neutral nucleophile such as H_2O	SN1 if ionisation is feasible
Lewis acid assists ionisation	SN1 favoured
Solvolysis	SN1 often favoured

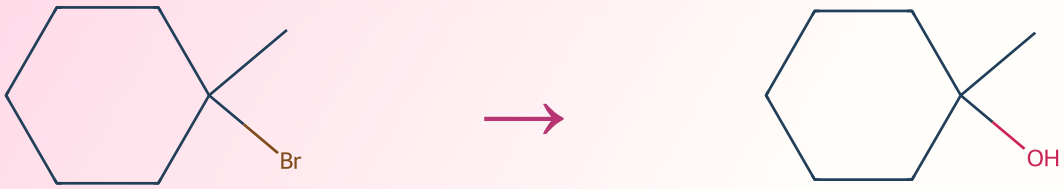
Aqueous KOH



2-Bromobutane → **Butan-2-ol**

Strong-nucleophile substitution example.

H_2O / solvolysis



1-Bromo-1-methylcyclohexane → **1-Methylcyclohexan-1-ol**

SN1: loss of Br^- gives a tertiary carbocation, water attacks, then H^+ is removed.

16 E1 dehydration example

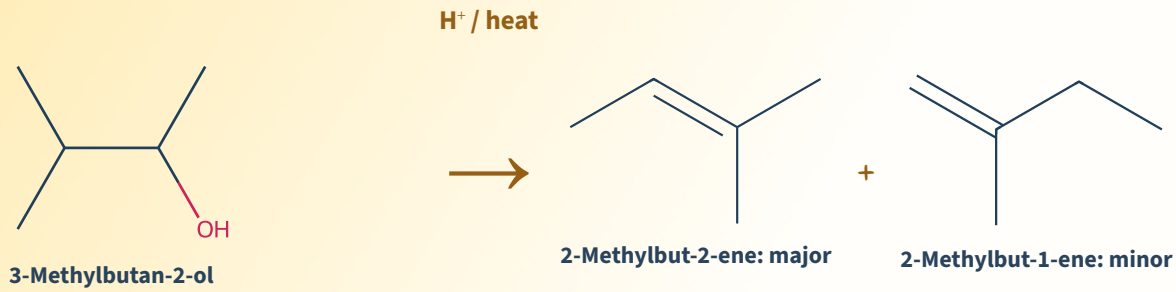
- Reagents: H^+/heat, concentrated H_2SO_4/heat or concentrated H_3PO_4/heat. Protonate OH → water leaves → carbocation; rearrange if favourable → remove β-H to form the more stable alkene. Rate depends on initial carbocation formation.

Haloalkanes & Haloarenes

E1 dehydration example · E1 versus SN1 in water

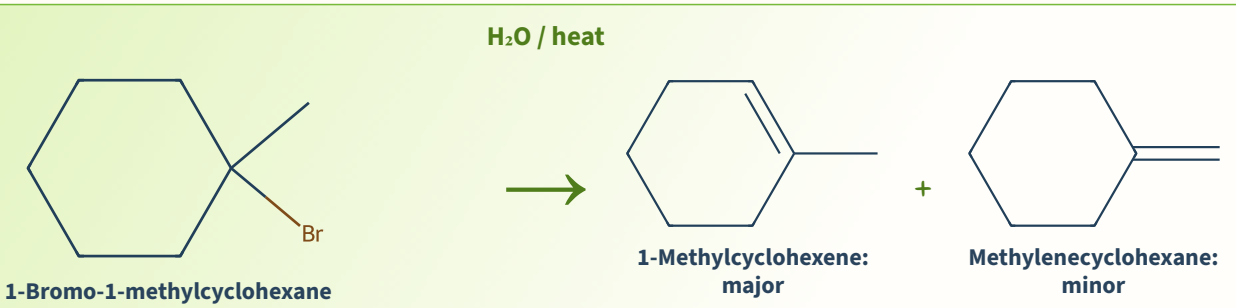
16 E1 dehydration example

continued



The initial secondary cation undergoes a 1,2-hydride shift to a tertiary cation. Hyperconjugating H counts: major 9; minor 5.

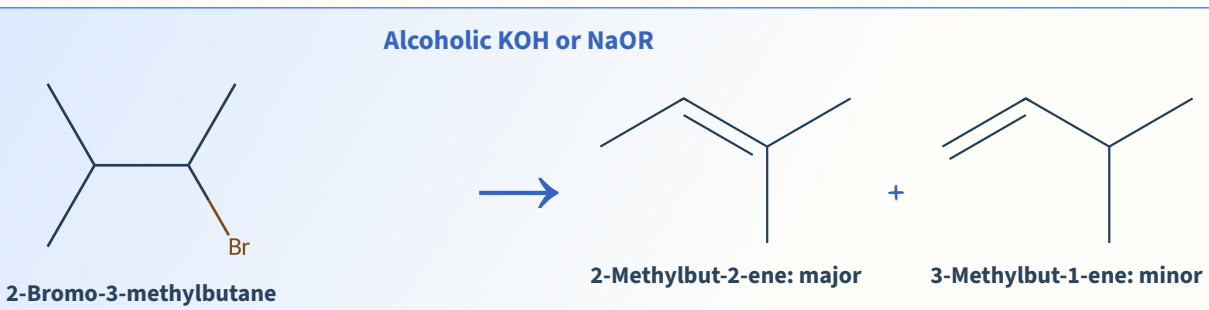
17 E1 versus SN1 in water



E1 elimination via a carbocation; α-H counts: major 7, minor 4.

- *The same substrate in water can give 1-methylcyclohexan-1-ol by SN1. Heating generally increases the importance of elimination.*

18 E2 and bulky-base product control



No rearrangement. Compare 9 hyperconjugating H in the more substituted alkene with 1 in the less substituted alkene.

Haloalkanes & Haloarenes

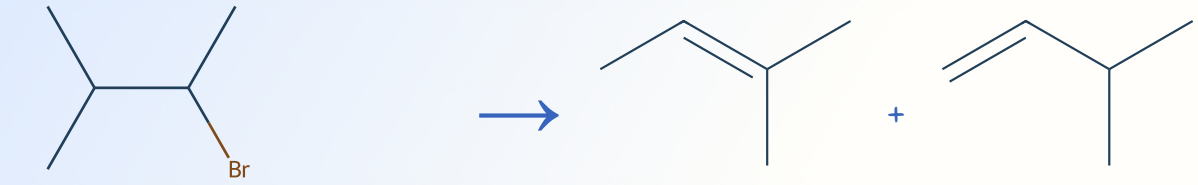
E2 and bulky-base product control · E2 with anion character and E1cB

18 E2 and bulky-base product control

continued

- *Under comparable elimination conditions: 3° > 2° > 1°. Small base usually favours the more stable Zaitsev alkene.*

Potassium tert-butoxide

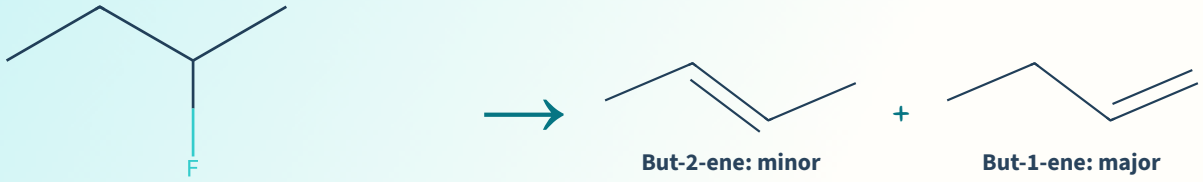


2-Bromo-3-methylbutane → **Zaitsev: minor** + **Hofmann: major**

The bulky base removes the more accessible β-H; the less hindered β-site gives the major product.

19 E2 with anion character and E1cB

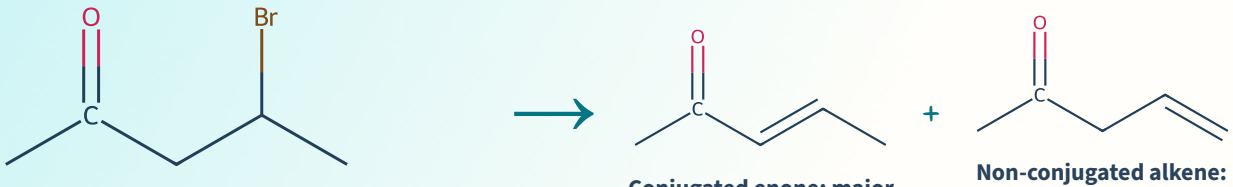
Alcoholic KOH



2-Fluorobutane → **But-2-ene: minor** + **But-1-ene: major**

Strong C–F bond: E2 transition state has greater anion character (E2a notation). Developing primary carbanion character is more favourable than secondary.

Base; E1cB scheme



4-Bromopentan-2-one → **Conjugated enone: major** + **Non-conjugated alkene: minor**

The β-carbanion/conjugate base is stabilised by resonance with C=O, favouring elimination to the conjugated enone.

Haloalkanes & Haloarenes

E2 with anion character and E1cB · Coupling reactions with metals

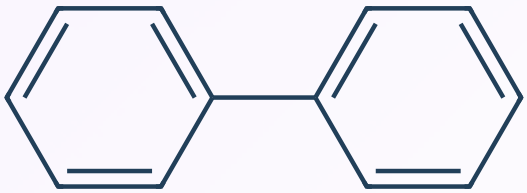
19 E2 with anion character and E1cB

continued

Mechanism	Rate expression / key species
E1	v = k[substrate] (RX or protonated alcohol under fixed acid conditions)
E2	v = k[RX][base]
E2a (notation used here)	Same bimolecular form; anion-like transition state
E1cB	Leaving-group loss can depend on the concentration of the conjugate-base carbanion; the observed law depends on which step is slow

20 Coupling reactions with metals

Reaction	Transformation	Reagent
Wurtz	$2R\text{–}X \rightarrow R\text{—}R$	Na / dry ether
Wurtz–Fittig	$R\text{—}X + Ph\text{–}X \rightarrow R\text{–}Ph$	Na / dry ether
Fittig	$2Ph\text{–}X \rightarrow Ph\text{–}Ph$	Na / dry ether
Ullmann	$2Ph\text{–}I \rightarrow Ph\text{–}Ph$	Cu / heat



Biphenyl

Aryl–aryl coupling product in Fittig and Ullmann reactions.

21 Grignard reagent · preparation and nature

$$R\text{–}X + Mg \xrightarrow{\text{dry ether}} R\text{–}MgX$$

- The C–Mg bond is strongly polarised $R\delta^{-}\text{–}Mg\delta^{+}X$. Carbon behaves as a strong base and a nucleophile. A Grignard reagent is organometallic: carbon is directly bonded to a metal.

- Formation-reactivity order: R–I > R–Br > R–Cl > R–F. Dry ether coordinates to magnesium and stabilises the reagent. Moisture destroys it and forms an alkane.

$$RMgX + H_2O \rightarrow RH + Mg(OH)X$$

Haloalkanes & Haloarenes

Acid–base reaction · Zerewitinoff principle · Active-hydrogen checklist · N A C O N S Q

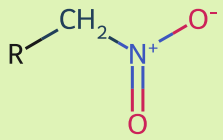
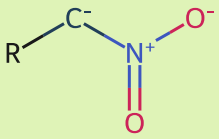
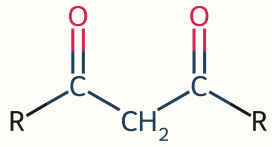
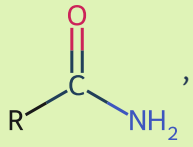
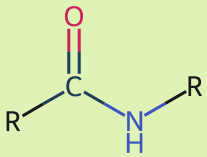
22 Acid–base reaction · Zerewitinoff principle

$$RMgX + H{-}A \rightarrow RH + A{-}MgX$$

- An acidic/active hydrogen protonates the carbon of the Grignard reagent. With CH_3MgX, methane evolution is used in the Zerewitinoff method for active hydrogen. Acid–base reaction can take priority over nucleophilic addition.

23 Active-hydrogen checklist · N A C O N S Q

- Mnemonic: N = nitroalkane; A = active methylene; C = terminal alkyne carbon; O = oxygen; N = nitrogen; S = sulphur; Q = a system that becomes aromatic after deprotonation.

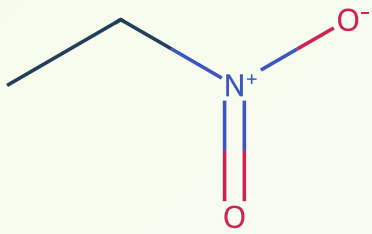
Active-H class	Source example	Why deprotonation is favoured
Nitroalkane	 →  / nitronate	Resonance stabilises the anion
Active methylene	 → delocalised β-dicarbonyl anion	Negative charge spreads over both carbonyl groups
Terminal alkyne	R—C≡CH → R—C≡C⁻	sp carbon has high s character
O–H	H_2O, ROH	Oxygen stabilises negative charge
N–H	NH_3, RNH_2, , 	An N-bound H can react with the strong base; amides also have resonance stabilisation
S–H	H_2S, RSH	Large/polarisable sulphur stabilises the anion
Quasi-aromatic precursor	Cyclopentadiene → cyclopentadienyl anion	Deprotonation creates a 6π aromatic ring

Haloalkanes & Haloarenes

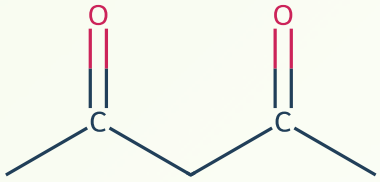
Active-hydrogen checklist · N A C O N S Q · Carbonyl addition · build the alcohol

23 Active-hydrogen checklist · N A C O N S Q

continued



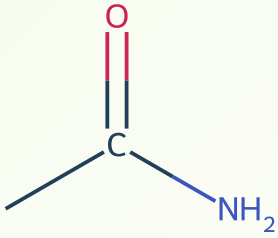
Nitroalkane



Active methylene



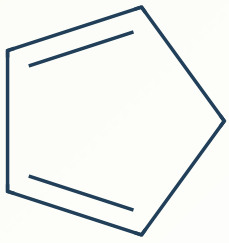
Terminal alkyne



Primary amide



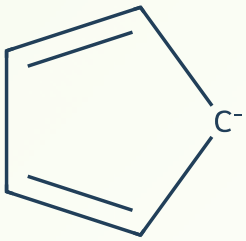
Thiol



Cyclopentadiene

Examples for the active-H checklist.

- *Counting caution: when several H atoms are on the same atom, count one readily removed H in the illustrated first deprotonation; the notes separately depict both terminal H atoms of ethyne as removable. Such shortcuts do not replace reagent stoichiometry and successive-acidity checks.*



Cyclopentadienyl anion

Cyclopentadiene loses H^+ and becomes aromatic.

24 Carbonyl addition · build the alcohol

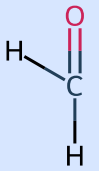
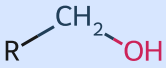
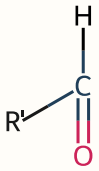
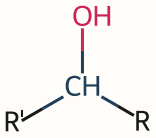
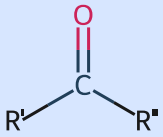
- *The R group of RMgX attacks the carbonyl carbon; C=O becomes an alkoxide bonded to MgX. Acidic or NH_4Cl/H_2O work-up protonates the alkoxide to give an alcohol.*

Haloalkanes & Haloarenes

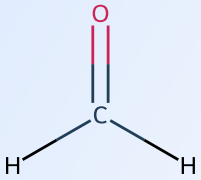
Carbonyl addition · build the alcohol

24 Carbonyl addition · build the alcohol

continued

Carbonyl starting material	After $RMgX$ then H_3O^+
	 : primary alcohol
	 : secondary alcohol
	 : tertiary alcohol

1. CH_3MgBr; 2. H_3O^+

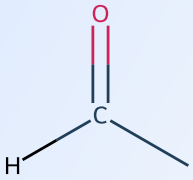


Methanal

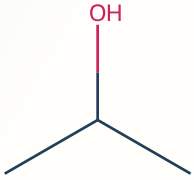


Ethanol: 1°

1. CH_3MgBr; 2. H_3O^+

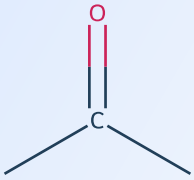


Ethanal

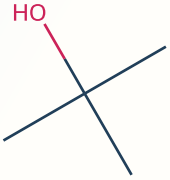


Propan-2-ol: 2°

1. CH_3MgBr; 2. H_3O^+



Acetone

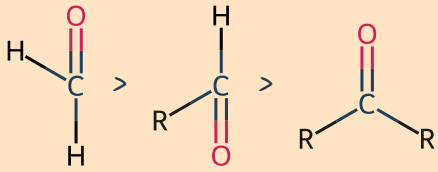


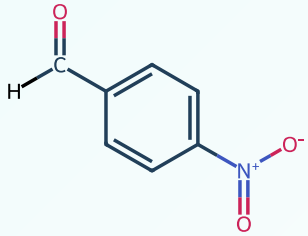
tert-Butyl alcohol: 3°

Haloalkanes & Haloarenes

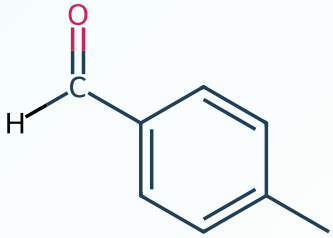
What controls carbonyl reactivity? · Nitrile addition

25 What controls carbonyl reactivity?

Less steric hindrance gives faster addition:  *for comparable carbonyls. Electron-withdrawing groups increase carbonyl electrophilicity; electron-donating groups reduce it.*



p-Nitrobenzaldehyde: more reactive



p-Methylbenzaldehyde: less reactive

−M nitro substitution increases electrophilicity; methyl donation lowers it.

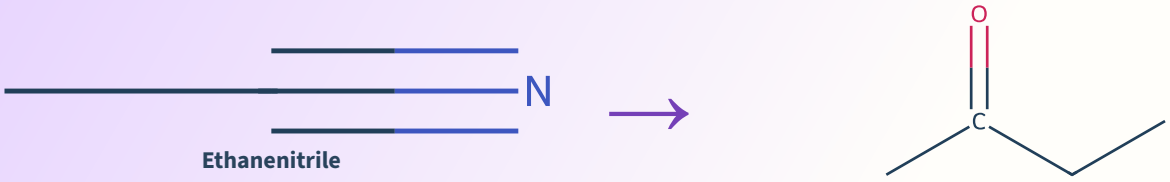
26 Nitrile addition

1. R′MgX; 2. H_3O^+



The Grignard R′ group attaches to nitrile carbon; hydrolysis of the imine magnesium salt gives a ketone.

1. C_2H_5MgBr; 2. H_3O^+



Ethanenitrile

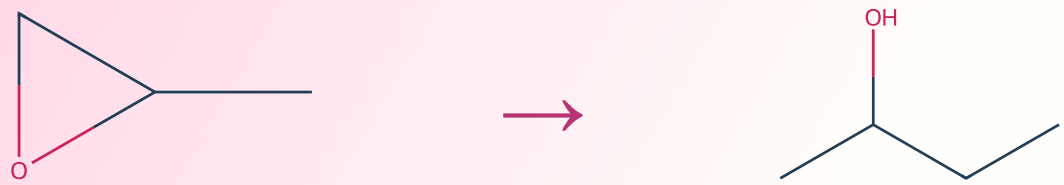
Butan-2-one

Haloalkanes & Haloarenes

Strained cyclic ethers · Reactions with oxides and sulphides

27 Strained cyclic ethers

1. CH_3MgBr; 2. H_3O^+

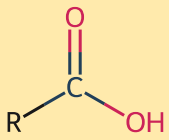
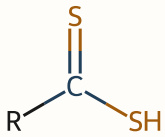
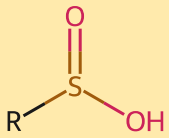
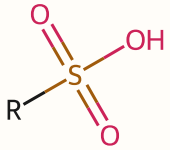


Propylene oxide → **Butan-2-ol**

The Grignard carbon attacks the less hindered epoxide carbon; oxygen remains at the other carbon and becomes OH after work-up.

- *Three- and four-membered cyclic ethers (epoxides and oxetanes) can open because of ring strain. Ordinary acyclic ethers and five-membered or larger cyclic ethers generally serve as unreactive solvent/ligands under normal Grignard conditions.*

28 Reactions with oxides and sulphides

Electrophile	After RMgX then acid work-up	Product class
CO_2		Carboxylic acid; adds one carbon
CS_2		Dithiocarboxylic acid
SO_2		Sulphinic acid
SO_3		Sulphonic acid

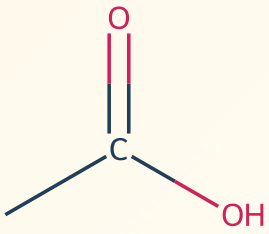
- *Attach the Grignard R group to the central atom; the anionic O/S-bearing intermediate is protonated on work-up. A magnesium salt forms before the final acid.*

Haloalkanes & Haloarenes

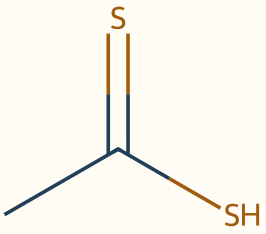
Reactions with oxides and sulphides · Nucleophilic acyl addition–elimination (SNAE)

28 Reactions with oxides and sulphides

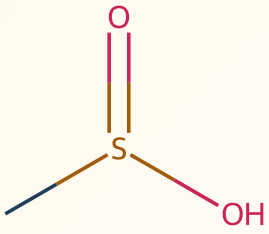
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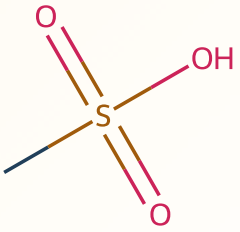
$CH_3MgX + CO_2 \rightarrow$ ethanoic acid



$CH_3MgX + CS_2 \rightarrow$ dithio acid



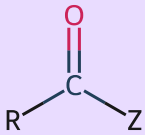
$CH_3MgX + SO_2 \rightarrow$ sulphinic acid

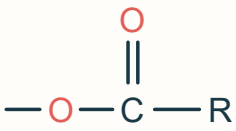
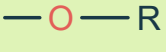
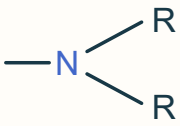


$CH_3MgX + SO_3 \rightarrow$ sulphonic acid

Four oxide/sulphide addition products.

29 Nucleophilic acyl addition–elimination (SNAE)

Acid derivatives have the form  *. The Grignard nucleophile adds to C=O; the tetrahedral intermediate eliminates Z. The first acyl-substitution product is a ketone.*

Acid derivative	Z group
Acid chloride	Cl
Anhydride	
Ester	
Tertiary amide	

Haloalkanes & Haloarenes

Nucleophilic acyl addition–elimination (SNAE) · Acyl reactivity and leaving-group ability

29 Nucleophilic acyl addition–elimination (SNAE)

continued

R′MgX



This is the first addition–elimination stage.

- *For acid chlorides, anhydrides and esters, the ketone usually reacts further with another equivalent of Grignard reagent; after work-up the usual final product is a tertiary alcohol. Tertiary amides can yield ketones after hydrolysis because their intermediate behaves differently.*

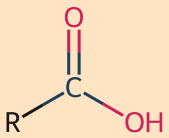
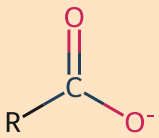
1. 2 equivalents CH_3MgBr; 2. H_3O^+

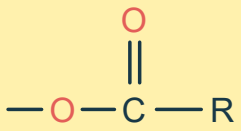


Methyl ethanoate → **tert-Butyl alcohol**

Shows the complete ester outcome beyond the first ketone stage.

30 Acyl reactivity and leaving-group ability

- *A weaker base is a better leaving group; its conjugate acid is stronger. Acid-strength order: HCl >*  *> ROH > R_2NH. Hence leaving ability: Cl^- >*  *> RO^- > R_2N^-.*

- *Donation into the carbonyl reduces electrophilicity. +M donation order: NR_2 > OR >*  *. Acid-derivative reactivity: acid chloride > anhydride > ester > amide.*

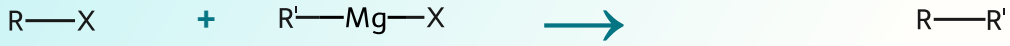
- *Acid–base reactions of Grignard reagents are very fast. A broader qualitative comparison is acid chloride > anhydride > aldehyde > ketone > ester > amide; treat it as a qualitative guide across the depicted nucleophilic-addition/acyl-substitution families, not a universal measured rate sequence.*

Haloalkanes & Haloarenes

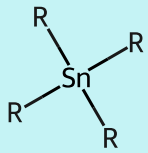
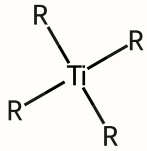
Coupling and transfer to other metals · Cyanogen, sulphur, oxygen and halogens

31 Coupling and transfer to other metals

Coupling scheme



Direct alkyl-halide/Grignard coupling can have side reactions; efficient controlled coupling commonly needs suitable substrates and catalysts.

Electrophile	Organometallic product
$SnCl_4$ + 4RMgX	
$TiCl_4$ + 4RMgX	 (schematic organotitanium formation)
$CdCl_2$ + 2RMgX	R—Cd—R

- *Shortcut: replace each halogen on the metal by R. These are stoichiometric reaction maps, not detailed preparative instructions.*

32 Cyanogen, sulphur, oxygen and halogens

Reagent / work-up	Product from RMgX
Cyanogen, N≡C—C≡N	R—C≡N (nitrile); cyanide is displaced
S, then H_2O / acid work-up	R—SH
O_2, then appropriate work-up	ROH (overall map)
X_2	R—X

- *Cyanogen mechanism: attack on one nitrile carbon gives an anionic imine-type intermediate, then loss of CN^- leaves R—C≡N .*

- *For CH_3MgBr, the reaction map gives: $CdCl_2 \rightarrow Cd(CH_3)_2$; $Br_2 \rightarrow CH_3Br$; $(CN)_2 \rightarrow CH_3CN$; $S/H_2O \rightarrow CH_3SH$; $O_2/H_2O \rightarrow CH_3OH$.*

Haloalkanes & Haloarenes

Cyanogen, sulphur, oxygen and halogens · Haloarenes by electrophilic substitution

32 Cyanogen, sulphur, oxygen and halogens

continued



Bromomethane



Ethanenitrile



Methanethiol

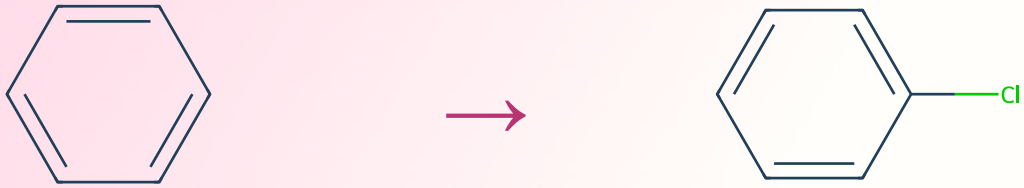


Methanol

Products branching from CH_3MgBr in the reaction map.

33 Haloarenes by electrophilic substitution

Cl_2 / Fe or anhydrous $FeCl_3$



Benzene → **Chlorobenzene**

Similarly Br_2/$FeBr_3$ gives bromobenzene. Replace ring H by X; HX is formed.

34 Aniline to benzenediazonium chloride

$NaNO_2$ + HCl

0–5 °C



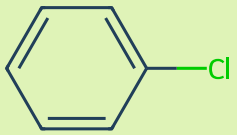
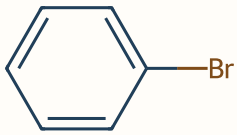
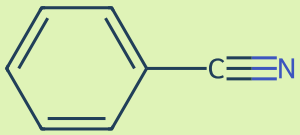
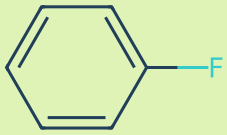
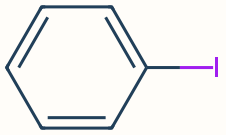
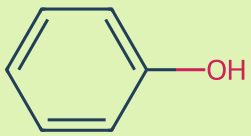
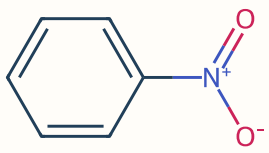
Aniline → **Benzenediazonium ion**

Product salt: $PhN_2^+Cl^-$ (BDC).

Haloalkanes & Haloarenes

Diazonium replacement map

35 Diazonium replacement map

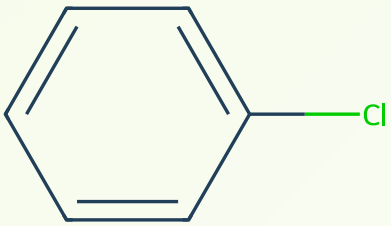
Reaction / reagent	Product from $PhN_2^+Cl^-$	Notes
Sandmeyer: CuCl/HCl		Also written Cu_2Cl_2
Sandmeyer: CuBr/HBr		Also written Cu_2Br_2
Sandmeyer: CuCN/KCN		Cyanide substitution
Gattermann: Cu/HCl or Cu/HBr	PhCl or PhBr	Copper powder with corresponding acid
Balz–Schiemann: HBF_4, then heat		Isolate/form $PhN_2^+BF_4^-$, then thermal decomposition
KI (source "Sizzi" heading)		N_2 and KCl formed
H_3PO_2		H_3PO_2 oxidises to H_3PO_3
Ethanol		Ethanol oxidises to ethanal
Warm H_2O		N_2 and HCl formed
$NaNO_2$, Cu / heat		Nitro-substitution route

Haloalkanes & Haloarenes

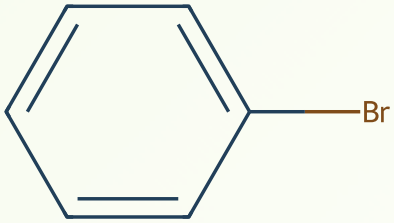
Diazonium replacement map · Azo coupling

35 Diazonium replacement map

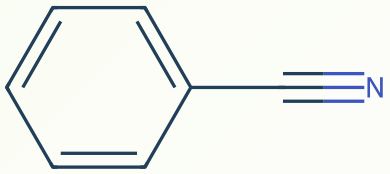
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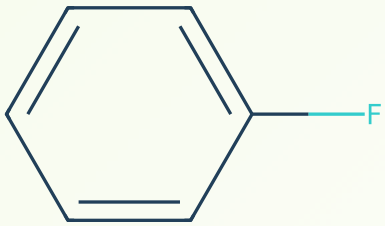
PhCl



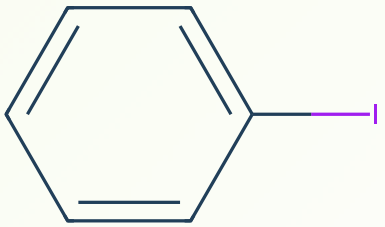
PhBr



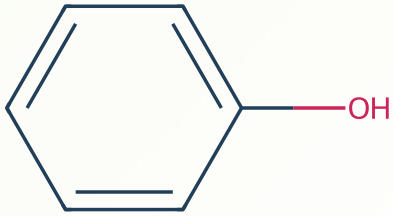
PhCN



PhF



PhI

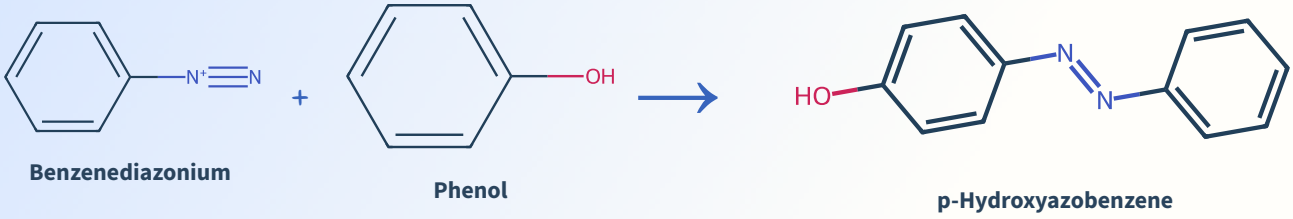


PhOH

Diazonium chemistry provides several substituted benzenes.

36 Azo coupling

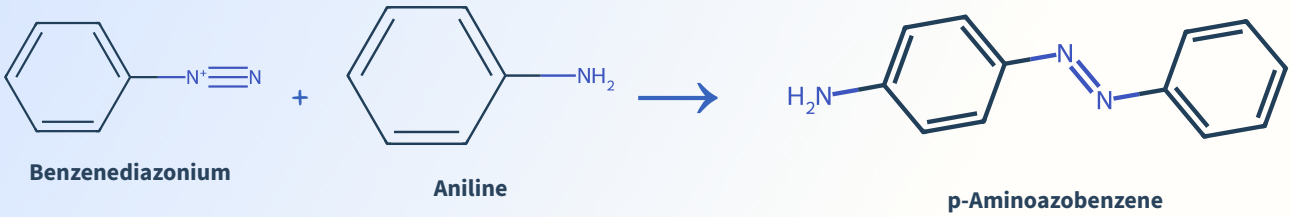
Azo coupling



Benzenediazonium + **Phenol** → **p-Hydroxyazobenzene**

Electrophilic aromatic substitution; gives an orange dye.

Azo coupling



Benzenediazonium + **Aniline** → **p-Aminoazobenzene**

Yellow dye.

Haloalkanes & Haloarenes

Related nitro reductions · Why ordinary haloarenes resist nucleophilic substitution

37 Related nitro reductions

Sn/HCl or Fe/HCl or H_2/catalyst



Nitrobenzene → Aniline

$(NH_4)_2S$



m-Dinitrobenzene → m-Nitroaniline

Selective partial reduction.

Sn/HCl, Fe/HCl or H_2/Pd



m-Dinitrobenzene → m-Phenylenediamine

Both nitro groups are reduced.

38 Why ordinary haloarenes resist nucleophilic substitution

- *1. Halogen lone-pair donation into the ring gives the aryl C–X bond partial double-bond character. 2. A phenyl cation is highly unstable, so ordinary SN1 ionisation is difficult. 3. The bonded ring carbon is sp^2, with more s character than an alkyl sp^3 carbon; the C–X bond is shorter/stronger. 4. The electron-rich aromatic π system is unfavourable for direct nucleophile approach; backside SN2 attack at aryl sp^2 carbon is geometrically difficult.*

- *These points concern unactivated haloarenes under ordinary conditions. Strong electron-withdrawing substituents or forcing conditions open other aromatic-substitution pathways.*

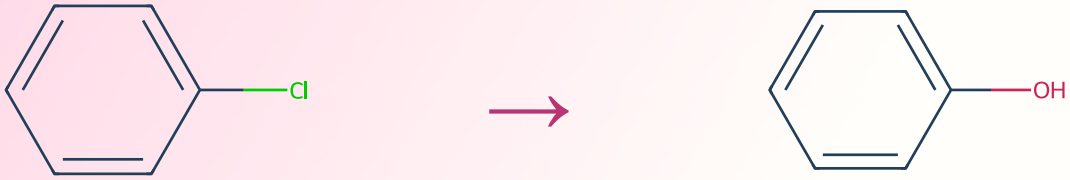
Haloalkanes & Haloarenes

Dow process · Activated aromatic nucleophilic substitution (SNAr)

39 Dow process

1. NaOH; 2. H⁺

623 K; 300 atm



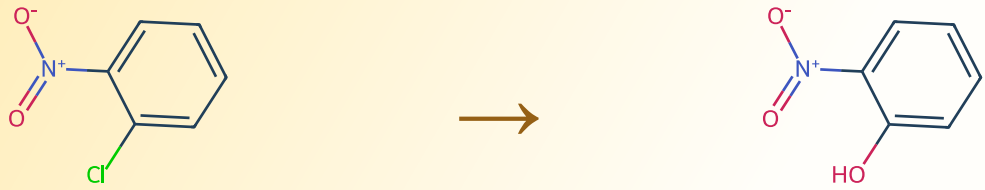
Chlorobenzene → **Phenol**

Sodium phenoxide forms first, then acidification gives phenol.

40 Activated aromatic nucleophilic substitution (SNAr)

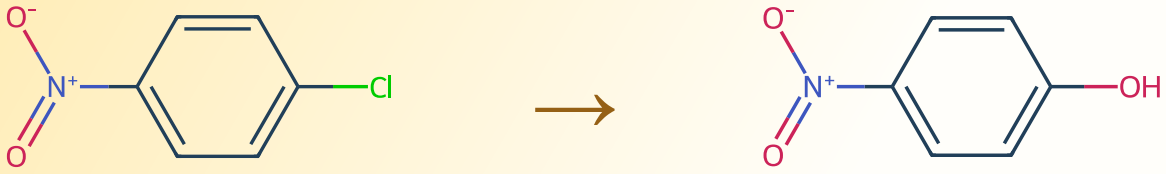
- *An electron-withdrawing nitro group ortho or para to the leaving group stabilises the anionic addition intermediate. A meta nitro group does not provide the same resonance stabilisation.*

1. OH⁻; 2. H⁺



o-Nitrochlorobenzene → **o-Nitrophenol**

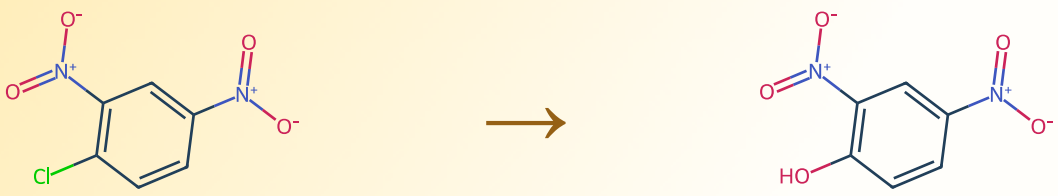
1. OH⁻; 2. H⁺



p-Nitrochlorobenzene → **p-Nitrophenol**

- *m-Nitrochlorobenzene: no analogous easy substitution in the comparison conditions. A second ortho/para nitro group increases activation.*

1. OH⁻; 2. H⁺



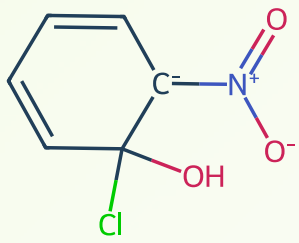
2,4-Dinitrochlorobenzene → **2,4-Dinitrophenol**

Haloalkanes & Haloarenes

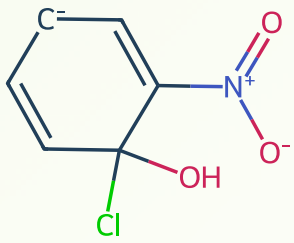
Meisenheimer intermediate · ortho and para nitro cases · SNAr rate and activation

41 Meisenheimer intermediate · ortho and para nitro cases

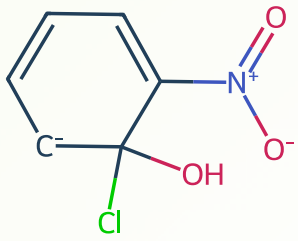
- Step 1: Nu^- adds at the carbon bearing X; this carbon becomes sp^3 while both Nu and X remain attached. The negative charge is delocalised around the ring and into an ortho/para nitro group. This anionic σ-complex is the Meisenheimer intermediate. Step 2: X^- leaves and aromaticity returns.



Ortho case: charge beside NO_2

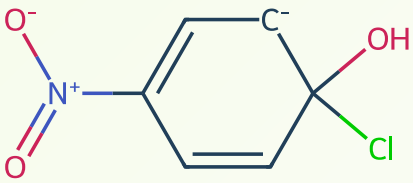


Ortho case: para ring contributor

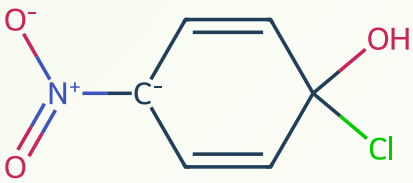


Ortho case: opposite ortho contributor

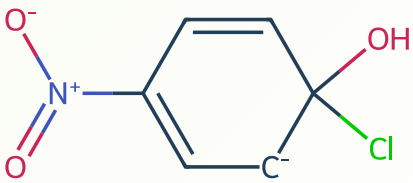
Three ring-localised contributors for the ortho-nitro Meisenheimer complex.



Para case: ortho charge



Para case: charge beside NO_2



Para case: other ortho charge

Three ring-localised contributors for the para-nitro Meisenheimer complex.

Electrophilic aromatic substitution	Activated nucleophilic aromatic substitution
Cationic Wheland / σ-complex	Anionic Meisenheimer complex
Electrophile adds, then H^+ leaves	Nucleophile adds, then X^- leaves

42 SNAr rate and activation

$$v = k[\text{activated aryl halide}][\text{Nu}^-]$$

Common addition-limited case: first addition step is rate-determining; overall second order.

- Sometimes abbreviated ArSN2, this is a two-step addition–elimination pathway rather than concerted alkyl SN2. More ortho/para nitro groups generally increase the rate. An ortho > para comparison can apply to particular examples, but equal nitro-group count alone does not fix the rate: steric and substrate effects matter.

$$\text{ArF} > \text{ArCl} > \text{ArBr} > \text{ArI}$$

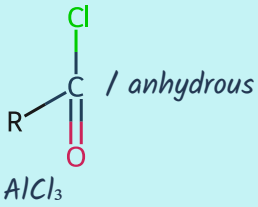
Typical leaving-group trend for activated addition-limited SNAr, where the strong −I effect of F accelerates nucleophilic addition.

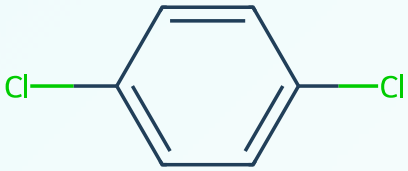
Haloalkanes & Haloarenes

Electrophilic substitution of haloarenes

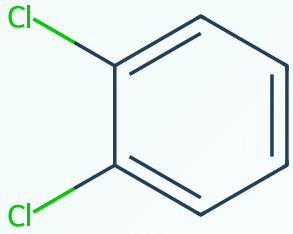
43 Electrophilic substitution of haloarenes

- Halogens deactivate the ring overall but direct incoming electrophiles to ortho and para positions by resonance donation. The illustrated reactions give para as major and ortho as minor due to steric effects; exact ratios depend on reaction conditions.

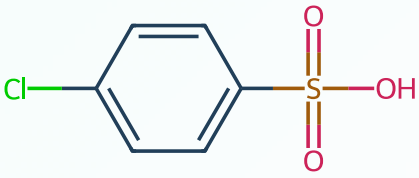
Reaction on chlorobenzene	Reagent	Illustrated products
Chlorination	Cl_2 / Fe	1,4-Dichlorobenzene major; 1,2-isomer minor
Nitration	Concentrated HNO_3 / H_2SO_4	p-Nitrochlorobenzene major; o-isomer minor
Sulphonation	Concentrated H_2SO_4	p-Chlorobenzenesulphonic acid major; o-isomer minor
Friedel–Crafts alkylation (schematic)	RCl / anhydrous $AlCl_3$	o-/p-Alkylchlorobenzene; alkyl rearrangement possible
Friedel–Crafts acylation (schematic)	 / anhydrous $AlCl_3$	o-/p-Acylchlorobenzene



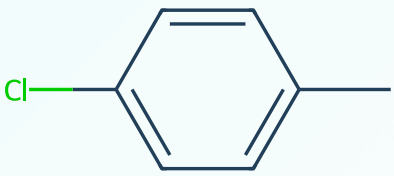
Para chlorination product



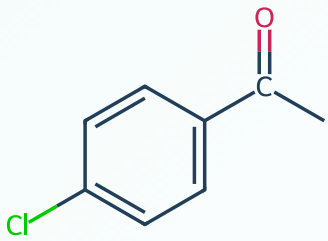
Ortho chlorination product



Para sulphonation product



Para alkylation example



Para acylation example

Substituted haloarene products.

- Friedel–Crafts reactions are harder on deactivated haloarenes than on benzene, and Lewis-acid complexation can suppress reaction. The schemes indicate substitution direction where reaction is feasible; the catalyst and substrate still determine whether substitution proceeds.

Alcohols, Phenols & Ethers

Preparations · reactions · distinguishing tests

08

01 Alcohols from alkenes

H_2O / H_3O^+ (dilute acid)

Markovnikov addition



Protonation gives a carbocation; rearrangement is possible before water attacks and H^+ is lost.

1. B_2H_6 / THF 2. H_2O_2 / OH^-

Hydroboration–oxidation



Anti-Markovnikov hydration.

1. $Hg(OAc)_2$ / H_2O 2. $NaBH_4$

Oxymercuration–demercuration



Markovnikov hydration.

02 Reduction routes

- *LAH = lithium aluminium hydride, $LiAlH_4$. SBH = sodium borohydride, $NaBH_4$. Both supply hydride, H^-. Catalytic H_2 is another reduction route.*

$LiAlH_4$, $NaBH_4$ or H_2 / catalyst



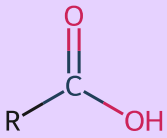
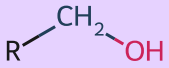
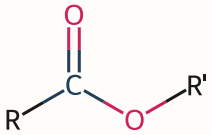
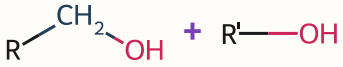
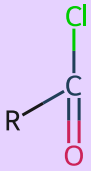
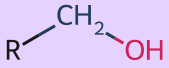
Replace the carbonyl π bond by C–H and O–H bonds.

Alcohols, Phenols & Ethers

Reduction routes

02 Reduction routes

continued

Starting compound	Reagent routes	Alcohol product
	$LiAlH_4$; suitable catalytic hydrogenation	
	$LiAlH_4$; suitable catalytic hydrogenation	
	$LiAlH_4$ or $NaBH_4$; suitable catalytic hydrogenation	

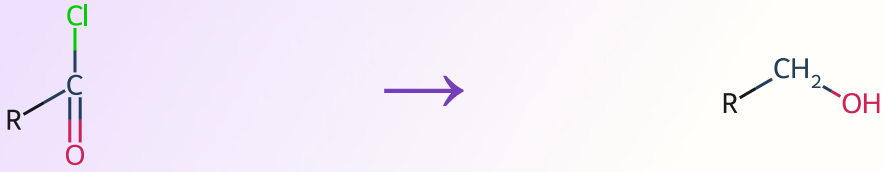
$LiAlH_4$; then work-up



$LiAlH_4$; then work-up



$LiAlH_4$ or $NaBH_4$; then work-up



1. Grignard addition 2. H_2O



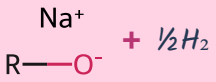
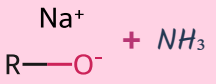
Grignard preparation was also discussed in Haloalkanes.

Alcohols, Phenols & Ethers

Acidic nature of alcohols · Esterification

03 Acidic nature of alcohols

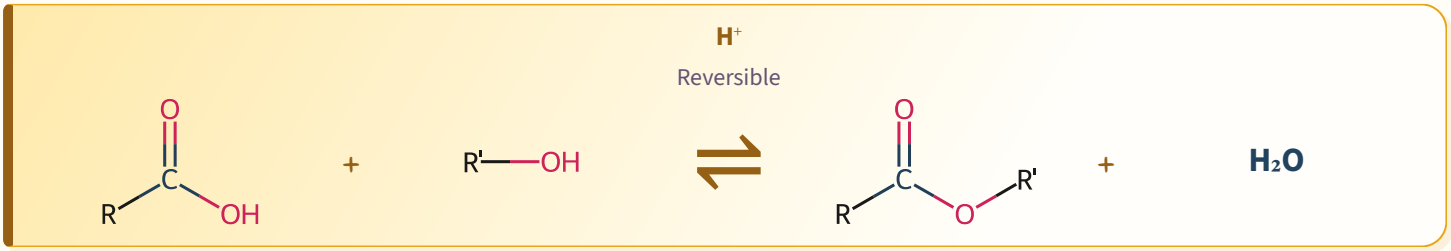
$$ROH \rightleftharpoons RO^- + H^+$$

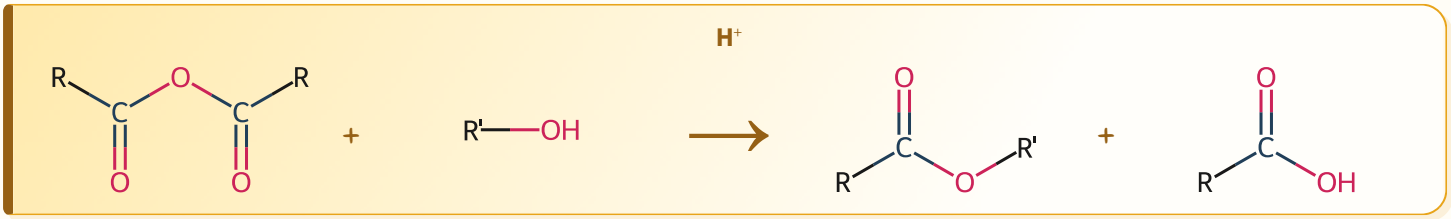
Reagent	Products / observation
Na / heat	
NaH	
$NaNH_2$	
NaOH	Ordinary alcohols: no useful net conversion in water
$NaHCO_3$	No reaction

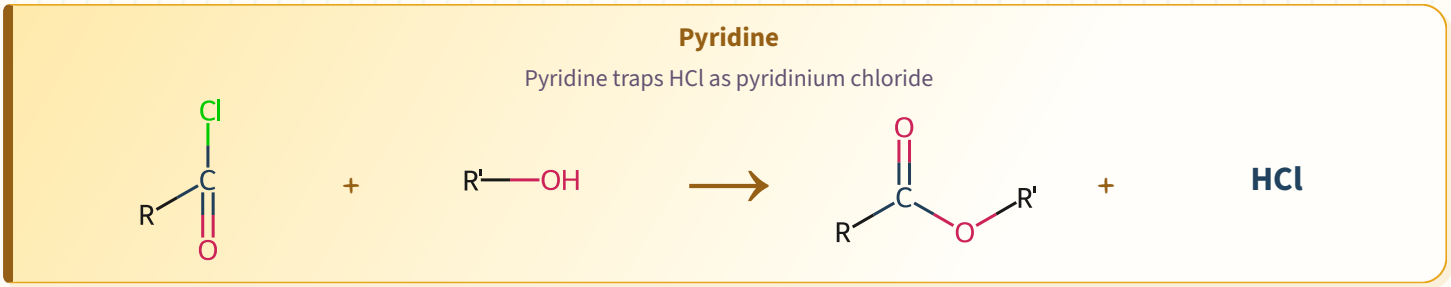
$$CH_3OH + NaOH \rightleftharpoons CH_3ONa + H_2O$$

For methanol, this is an acid–base equilibrium, not complete methoxide formation in aqueous NaOH.

04 Esterification







Steric hindrance in the alcohol usually lowers the rate: 1° > 2° > 3° in comparable cases. Acid-side effects depend on the acyl substrate and mechanism; do not use a general carbocation-stability rule.

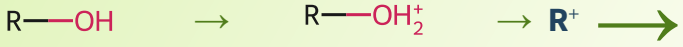
Alcohols, Phenols & Ethers

Dehydration: acid route · Dehydration without rearrangement

05 Dehydration: acid route

Conc. H_2SO_4 or conc. H_3PO_4

H^+ / heat; E1 for suitable alcohols



Water leaves; rearrangement may occur. Loss of H^+ gives the more stable alkene as major product.

06 Dehydration without rearrangement

Anhydrous $ZnCl_2$; P_2O_5 / heat; $POCl_3$ / heat; Al_2O_3 / heat

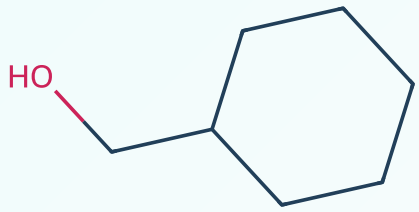
Dehydrating agents



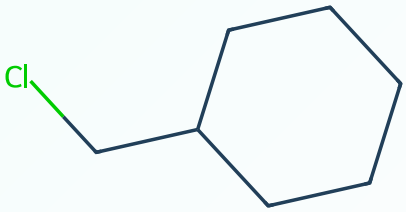
β-H and α-OH are removed; the more stable alkene is generally major. $POCl_3$/pyridine is the standard non-rearranging E2 example; mechanism depends on conditions.

07 Replacing OH by halogen

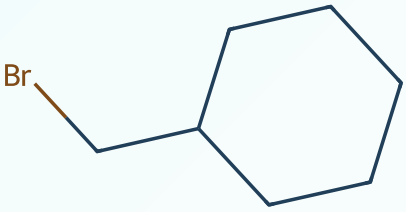
Reagent / pathway	Stereochemical note
HX; SNI for suitable substrates	Racemisation may occur
PX_3 (or red P + X_2), PX_5, $SOCl_2$ / pyridine	Inversion is common in SN2 routes; reagent and substrate matter
$SOCl_2$ without pyridine; SNi	Retention in the usual SNi case



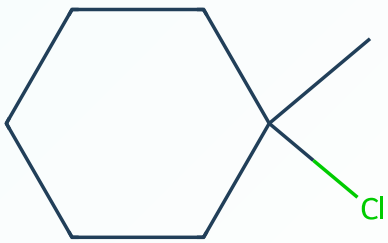
Cyclohexylmethanol



With $SOCl_2$: chloromethylcyclohexane



With red P / Br_2: bromomethylcyclohexane



With HCl: rearranged 1-chloro-1-methylcyclohexane

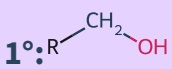
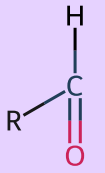
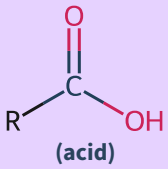
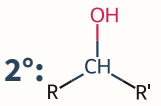
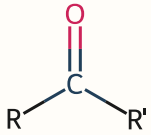
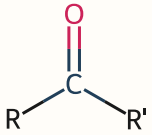
Rearrangement contrast

Alcohols, Phenols & Ethers

Oxidation of alcohols

08 Oxidation of alcohols

- MOA = mild oxidising agent; SOA = strong oxidising agent.

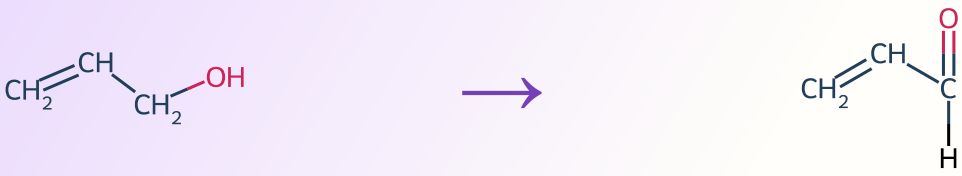
Alcohol	Mild oxidation	Strong oxidation
1°: 	 (aldehyde)	 (acid)
2°: 	 (ketone)	 initially
3° alcohol	No ordinary oxidation without C–C cleavage	Resists ordinary conditions; harsh conditions may cleave C–C bonds

Mild reagent	Identity / note
PCC	Pyridinium chlorochromate; pyridine + CrO_3 + HCl
PDC	Pyridinium dichromate, $(C_5H_6N)_2Cr_2O_7$
Anhydrous CrO_3	Dry CrO_3 / acetone
Collins reagent	CrO_3·2 pyridine in CH_2Cl_2
Cu or Ag / 300 °C	Dehydrogenates 1° / 2° alcohols; a 3° alcohol instead dehydrates to an alkene

Strong oxidising agents	Alternative conditions
$KMnO_4$	Acidified; or hot alkaline $KMnO_4$ followed by acidification
$K_2Cr_2O_7$	Acidified / heated conditions
Concentrated HNO_3	Strong oxidation
Aqueous CrO_3	$CrO_3 + H_2O$, i.e. H_2CrO_4
Jones reagent	$CrO_3 + H_2SO_4$, generally in acetone

MnO_2

Selective allylic oxidation



Alcohols, Phenols & Ethers

Oxidation of alcohols · Methods of preparation of phenol

08 Oxidation of alcohols

continued

MnO_2

Selective benzylic oxidation

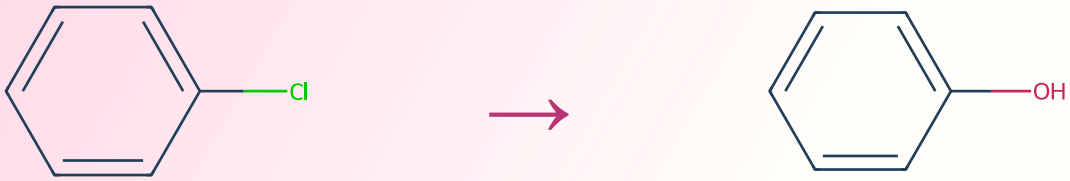


Benzyl alcohol → **Benzaldehyde**

09 Methods of preparation of phenol

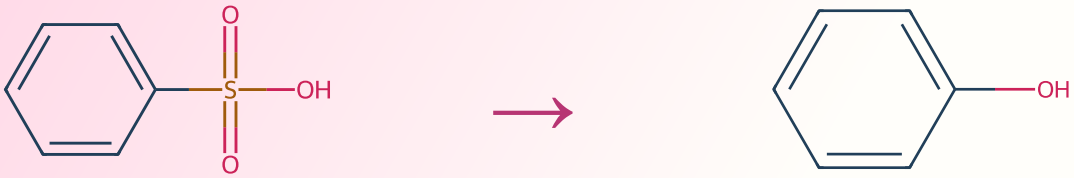
1. NaOH, 623 K, 320 atm 2. H^+

Dow process



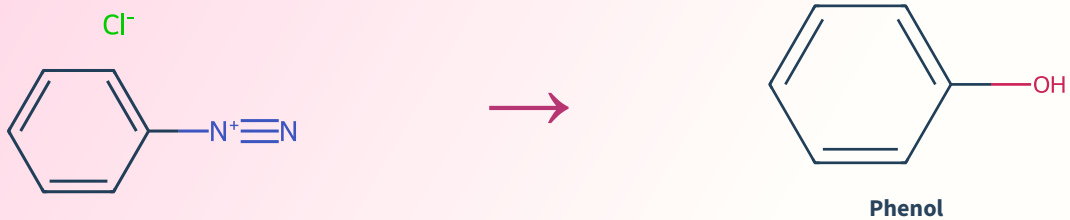
Chlorobenzene → **Phenol**

1. Fused NaOH 2. H^+



Benzenesulphonic acid → **Phenol**

Warm water or dilute acid



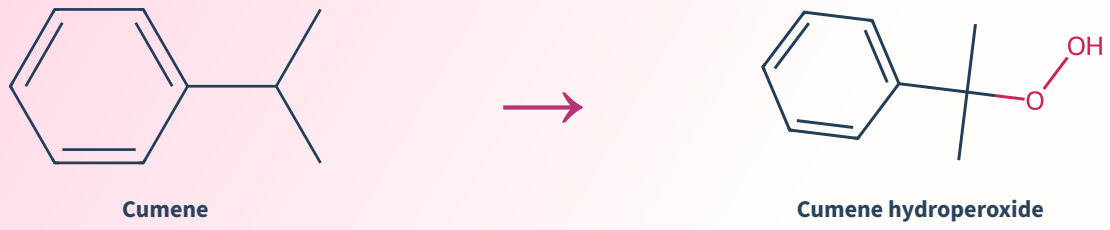
Phenol

Alcohols, Phenols & Ethers

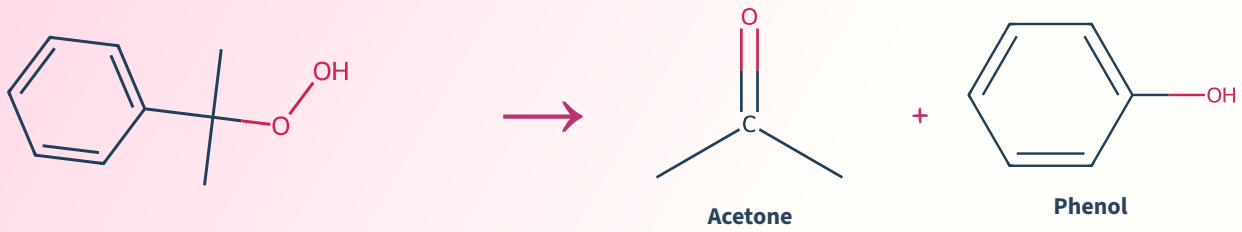
Methods of preparation of phenol · Phenol: electrophilic substitution with dilute HNO_3

09 Methods of preparation of phenol

continued

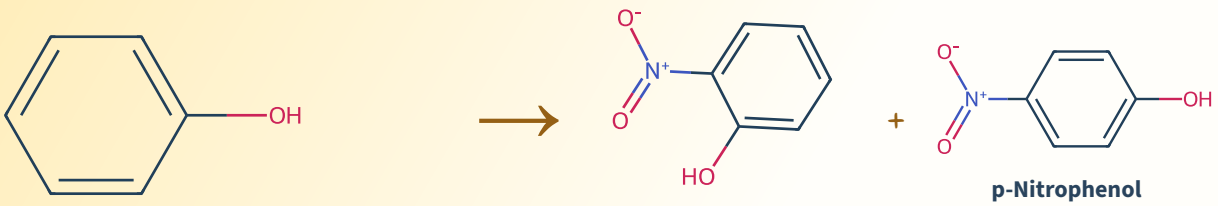


Cumene → Cumene hydroperoxide



Cumene hydroperoxide → Acetone + Phenol

10 Phenol: electrophilic substitution with dilute HNO_3



Phenol → o-Nitrophenol + p-Nitrophenol

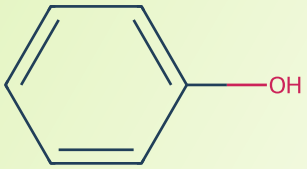
Property	Ortho versus para
Hydrogen bonding	Ortho: intramolecular; para: intermolecular
Boiling point	ortho < para
Volatility	ortho > para
Separation	The isomers can be separated by steam distillation

Alcohols, Phenols & Ethers

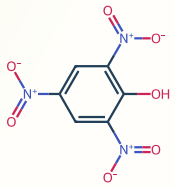
Nitration and nitro replacement reactions

11 Nitration and nitro replacement reactions

Concentrated HNO_3



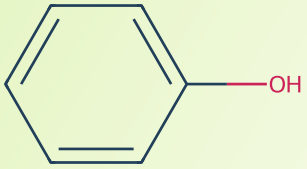
Phenol

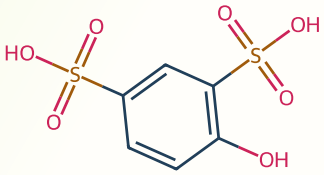


2,4,6-Trinitrophenol (picric acid)

Concentrated H_2SO_4 / SO_3

Sulphonation

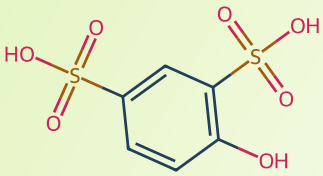


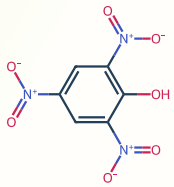


Phenol-2,4-disulphonic acid

Concentrated HNO_3

Nitro-desulphonation

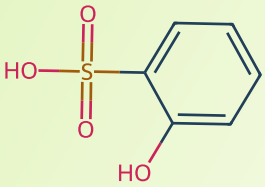




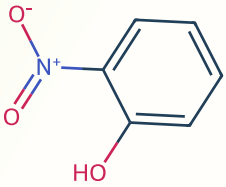
Picric acid

Concentrated HNO_3

NO_2 replaces SO_3H



o-Phenolsulphonic acid



o-Nitrophenol → further nitration to picric acid

Alcohols, Phenols & Ethers

Nitration and nitro replacement reactions · Bromination of phenol

11 Nitration and nitro replacement reactions

continued

Concentrated HNO_3

Nitro-decarboxylation: NO_2 replaces COOH

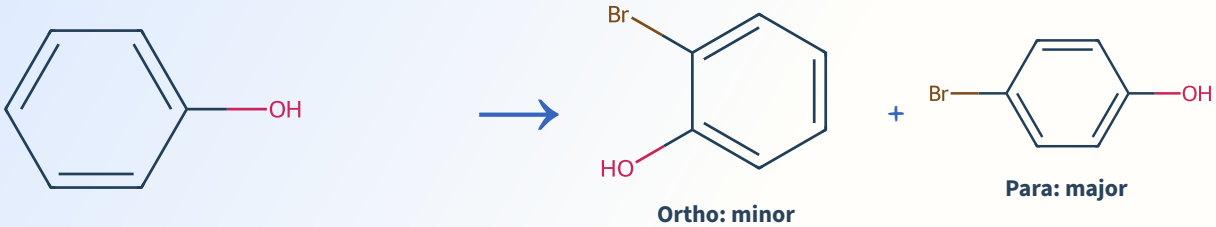


Salicylic acid → **o-Nitrophenol → further nitration to picric acid**

12 Bromination of phenol

Br_2 in CS_2 or $CHCl_3$

Low-polarity solvent; monobromination



Ortho: minor **Para: major**

Br_2 / H_2O

White precipitate



2,4,6-Tribromophenol

13 Acidic nature of phenol

$$PhOH \rightleftharpoons PhO^- + H^+$$

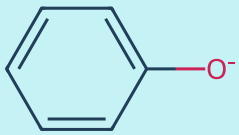
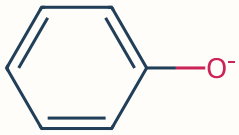
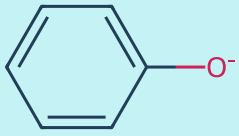
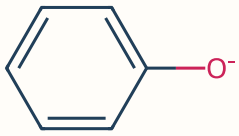
Phenoxide is resonance stabilised.

Alcohols, Phenols & Ethers

Acidic nature of phenol · Phenolic esters and aspirin

13 Acidic nature of phenol

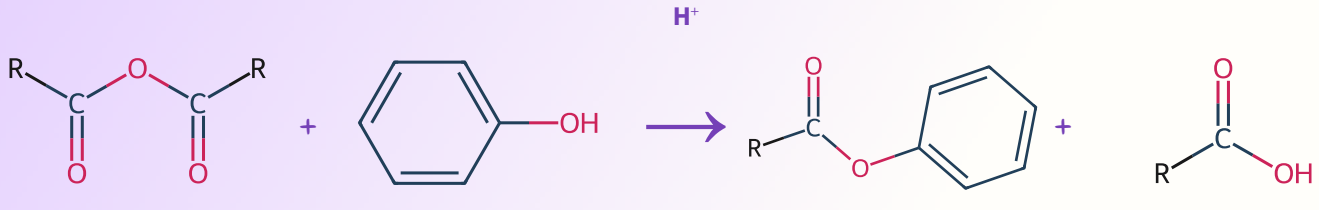
continued

Reagent	Products
Na / heat	Na^+  + ½H_2
NaH	Na^+  + H_2
$NaNH_2$	Na^+  + NH_3
NaOH	Na^+  + H_2O
$NaHCO_3$	No reaction

- Phenol behaves as a weak acid.

14 Phenolic esters and aspirin

- Phenolic esters are readily prepared with acid anhydrides or acyl chlorides. Direct Fischer esterification of phenol with a carboxylic acid is not an effective ordinary preparation, although a formal acid + phenol condensation can be written.



Alcohols, Phenols & Ethers

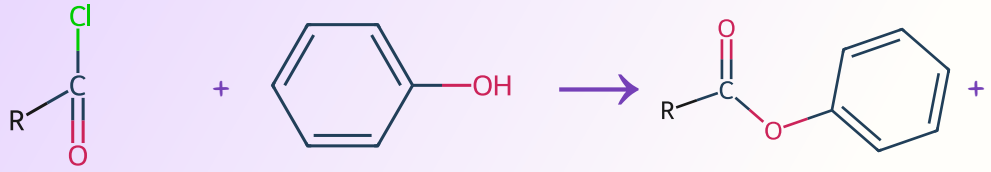
Phenolic esters and aspirin · Kolbe–Schmitt reaction

14 Phenolic esters and aspirin

continued

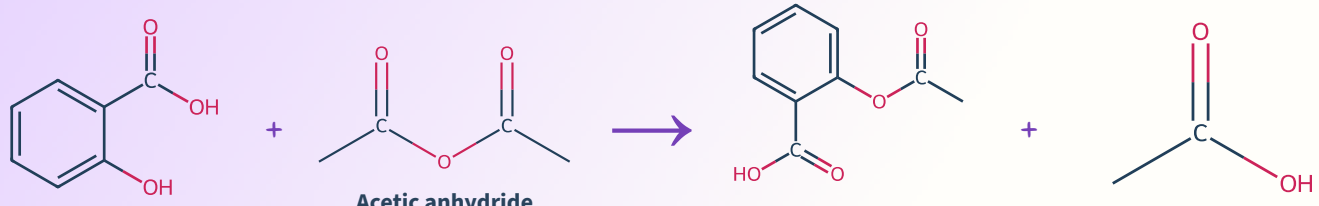
Pyridine

HCl captured as pyridinium chloride



H^+

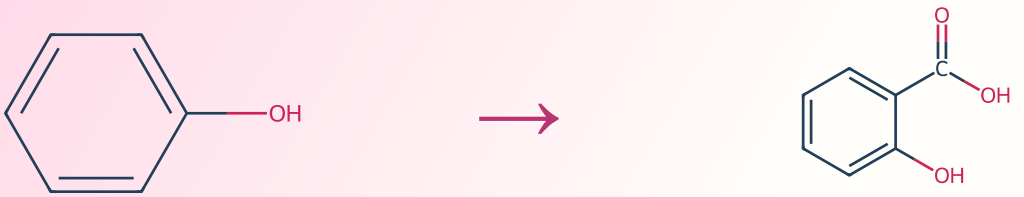
Acetylation of the phenolic OH



Salicylic acid + Acetic anhydride → Aspirin / o-acetylsalicylic acid + Acetic acid

15 Kolbe–Schmitt reaction

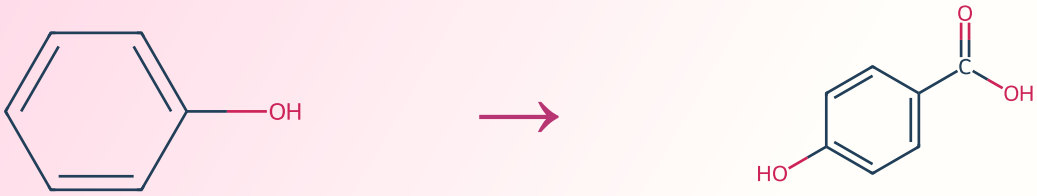
1. NaOH 2. CO_2 3. H^+



Salicylic acid: ortho product

1. KOH 2. CO_2 3. H^+

Potassium phenoxide route under suitable conditions



p-Hydroxybenzoic acid

- *Na^+ has greater charge density than K^+; this can help stabilise an ortho arrangement. Temperature and counter-ion influence orientation.*

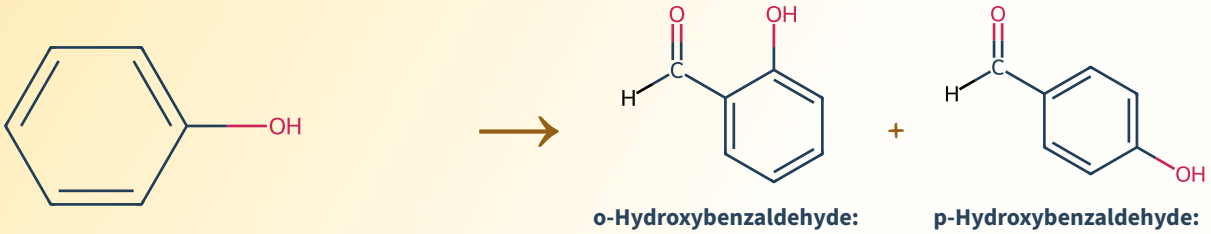
Alcohols, Phenols & Ethers

Reimer–Tiemann reaction · Reduction and oxidation of phenol

16 Reimer–Tiemann reaction

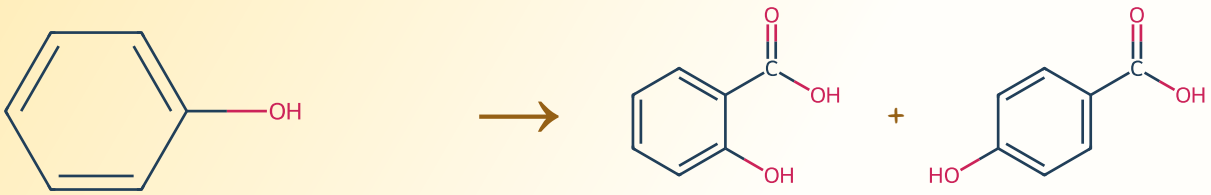
- Reagents: $CHCl_3$ + NaOH or KOH. The attacking species is dichlorocarbene, $:CCl_2$.

$CHCl_3$ / NaOH or KOH; then work-up



o-Hydroxybenzaldehyde: major | **p-Hydroxybenzaldehyde: minor**

CCl_4 / NaOH or KOH; then acidification

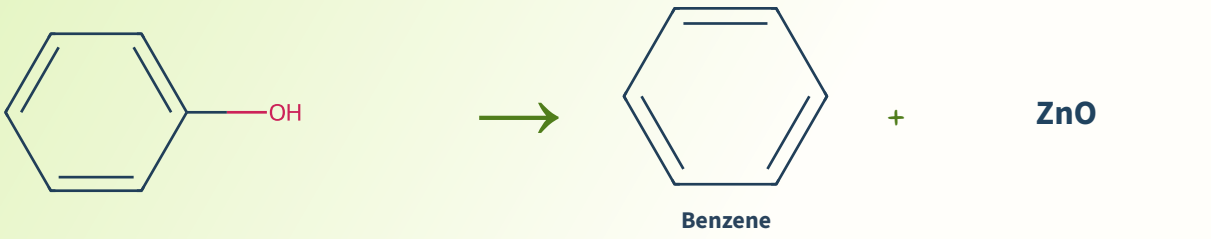


Ortho acid: major | **Para acid: minor**

17 Reduction and oxidation of phenol

Zinc dust

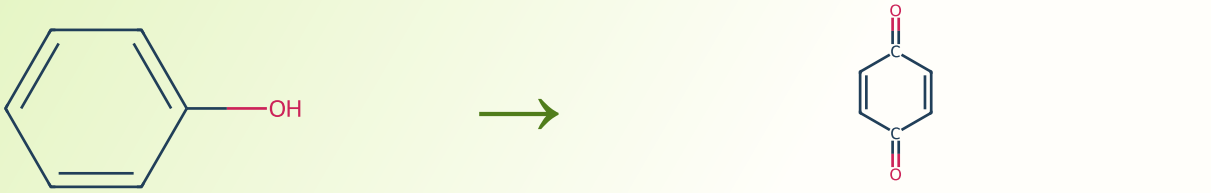
Heat



Benzene

$Na_2Cr_2O_7$ / H_2SO_4

Oxidation; air oxidation may also occur



p-Benzoquinone

Alcohols, Phenols & Ethers

Tests for phenol · Preparation of ethers

18 Tests for phenol

$$6PhOH + FeCl_3 \longrightarrow [Fe(OPh)_6]^{3-} + 3H^+ + 3HCl$$

Violet ferric-phenolate complex.

Bromine water

2,4,6-Tribromophenol



White precipitate

19 Preparation of ethers

$$2ROH \xrightarrow[413\ K]{conc.\ H_2SO_4} ROR + H_2O$$

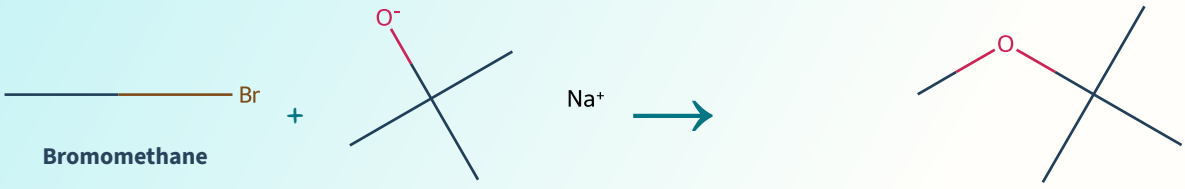
Intermolecular dehydration. Competing elimination gives an alkene; conditions and alcohol structure matter.

Williamson ether synthesis

SN2



SN2



Bromomethane + **Sodium tert-butoxide** → **Methyl tert-butyl ether**

E2

Elimination dominates



tert-Butyl bromide + **Sodium methoxide** → **2-Methylpropene**

Alcohols, Phenols & Ethers

Preparation of ethers · Cleavage of ethers by HX

19 Preparation of ethers

continued

- Secondary and especially tertiary alkyl halides with alkoxides tend to give elimination instead of useful Williamson ether synthesis.

Unsuitable halide in Williamson synthesis	Reason
$CH_2=CH-X$ (vinyl halide)	sp^2 C–X bond has partial double-bond character; ordinary SN2 is not feasible
Ph–X (aryl halide)	sp^2 C–X bond with resonance / partial double-bond character
Bridgehead halide in a small bicyclic system	Backside approach / geometric constraint prevents ordinary SN2

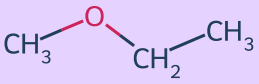
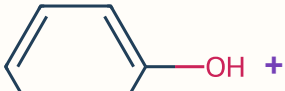
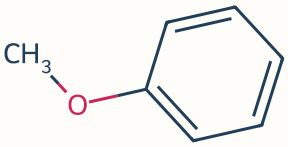
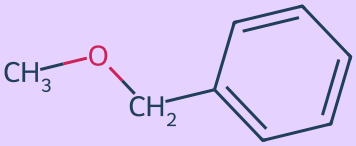
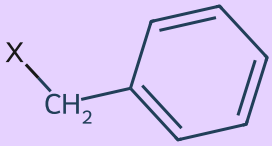
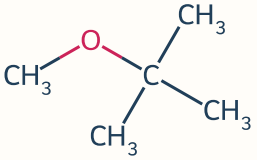
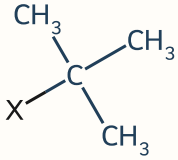
20 Cleavage of ethers by HX

- Protonate the ether oxygen first: $R-O-R' \rightarrow R-OH^+-R'$. X^- then cleaves a C–O bond. Ordinary methyl/primary groups favour SN2; tertiary, benzylic or allylic groups can favour SN1. The mechanism depends on substrate, not simply on whether HX is anhydrous.

Anhydrous HX

SN2 attack at methyl



Ether + excess HX	Final products
	 + CH_3CH_2X (+ H_2O)
	+ CH_3X; aryl–O bond remains
	 + CH_3X (+ H_2O)
	 + CH_3X (+ H_2O)

- Vicinal diiodides are unstable because C–I bonds are weak; iodine loss produces an alkene.

$$-C(I)-C(I)- \longrightarrow -C=C- + I_2$$

Alcohols, Phenols & Ethers

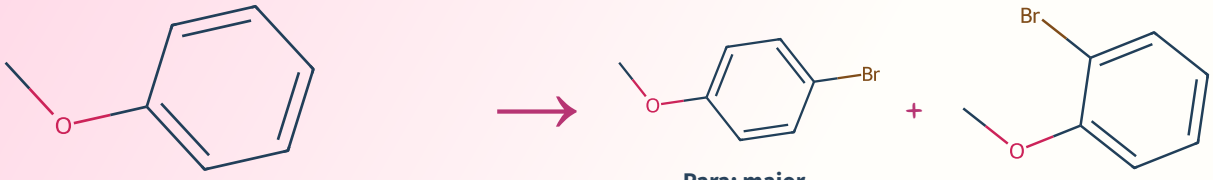
Electrophilic substitution of anisole

21 Electrophilic substitution of anisole

- *The methoxy group directs substitution to ortho and para. Para is generally favoured because it is less crowded.*

Br_2 / CH_3COOH

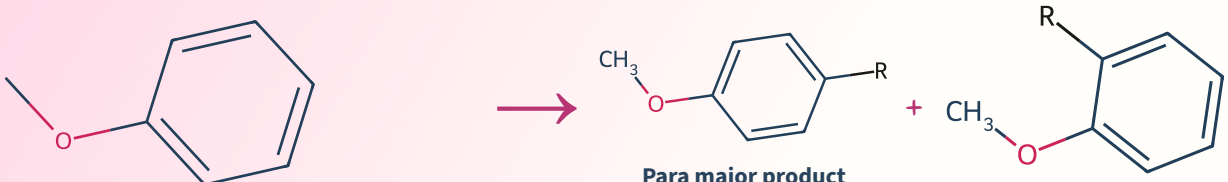
Halogenation



Anisole → **Para: major** + **Ortho**

RCl / anhydrous $AlCl_3$

Friedel–Crafts alkylation

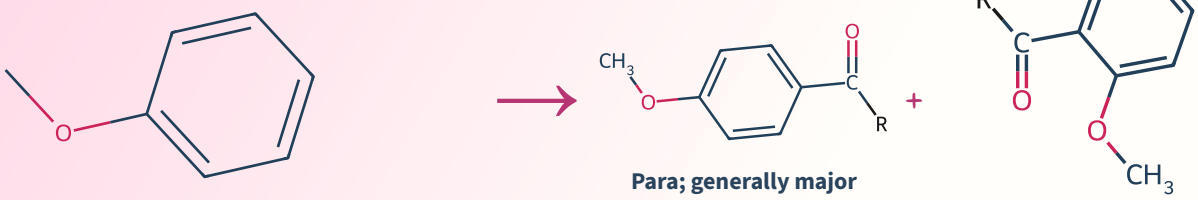


Para major product + **Ortho product**

Carbocation rearrangement is possible.

RCOCl / anhydrous $AlCl_3$

Friedel–Crafts acylation

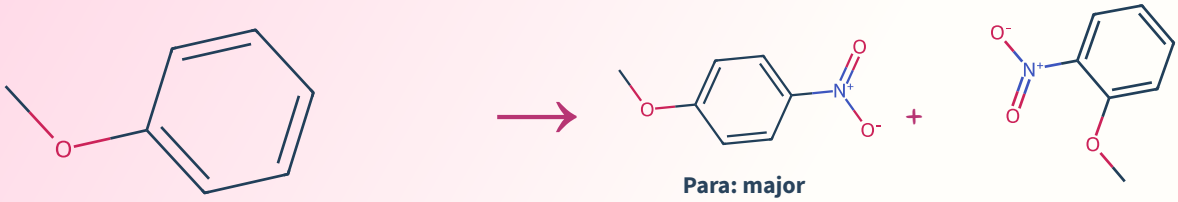


Para; generally major + **Ortho product**

No acylium-ion rearrangement.

Concentrated HNO_3 + H_2SO_4

Nitration; electrophile NO_2^+



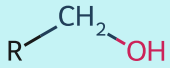
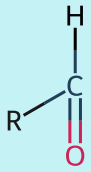
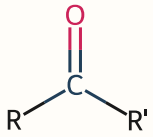
Para: major + **Ortho**

Carbonyls & Carboxylic Acids

Additions · oxidations · named reactions

09

01 From alcohols

Alcohol	Oxidation outcome
1°  + mild oxidant	
2° RCH(OH)R′ + mild or strong oxidant	
3° alcohol	No ordinary oxidation without bond cleavage

Cu or Ag at 300 °C	Product
1° alcohol: dehydrogenation	Aldehyde + H_2
2° alcohol: dehydrogenation	Ketone + H_2
3° alcohol: dehydration	Alkene + H_2O

- Removal of H_2 is oxidation.

02 From unsaturated hydrocarbons

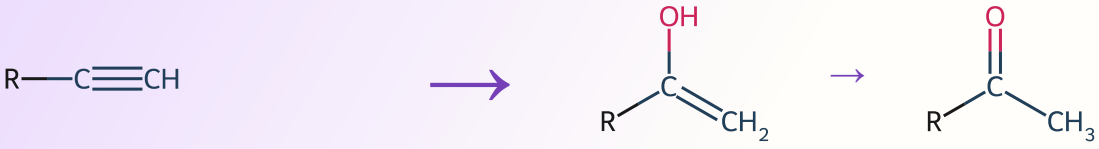
1. O_3 / CCl_4 2. Zn / H_2O or $(CH_3)_2S$

Reductive ozonolysis



Dilute H_2SO_4 / $HgSO_4$

Kucherov reaction; hydration then enol–keto tautomerism



Water adds once. Acetylene gives acetaldehyde.

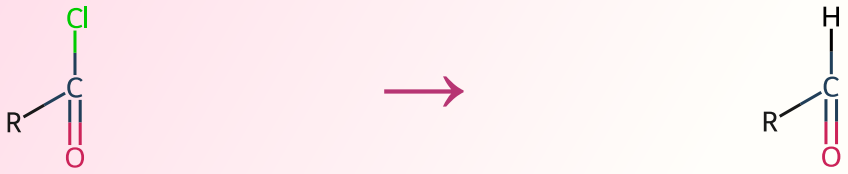
Carbonyls & Carboxylic Acids

Aldehydes from acid chlorides and nitriles

03 Aldehydes from acid chlorides and nitriles

H_2 / poisoned Pd–$BaSO_4$

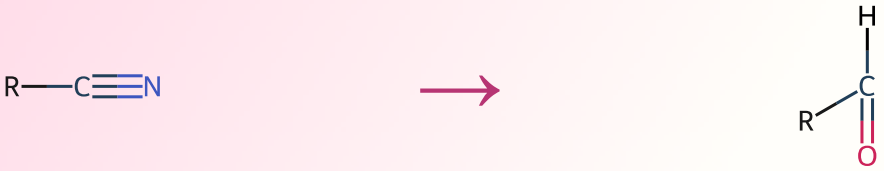
Rosenmund reduction



Replace Cl by H. Rosenmund uses poisoned Pd/$BaSO_4$; distinguish this from Lindlar partial alkyne hydrogenation.

1. $SnCl_2$ / HCl 2. H_3O^+ or steam

Stephen reduction



Replace CN by CHO after iminium hydrolysis.

- *DIBAL-H = diisobutylaluminium hydride, $(i\text{-}Bu)_2AlH$; controlled reduction followed by water gives aldehydes.*

1. DIBAL-H 2. H_2O

C=C remains

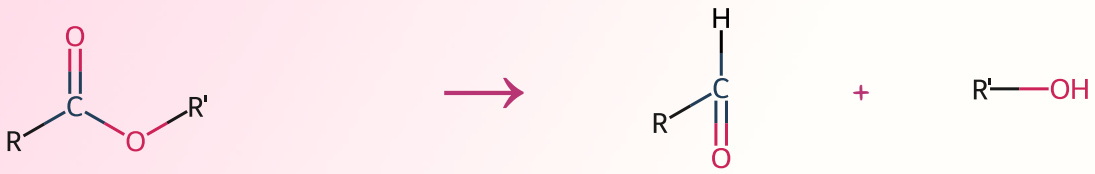


Unsaturated nitrile example

Corresponding unsaturated aldehyde

1. DIBAL-H 2. H_2O

Controlled low-temperature ester reduction



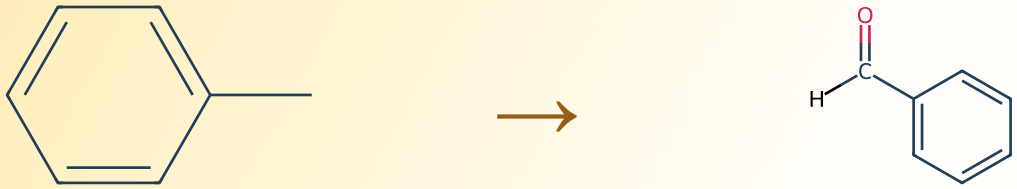
Carbonyls & Carboxylic Acids

Aromatic aldehydes from hydrocarbons

04 Aromatic aldehydes from hydrocarbons

1. CrO_2Cl_2 / CS_2 2. H_3O^+

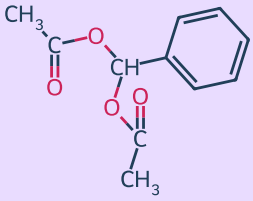
Etard reaction



Toluene → **Benzaldehyde**

Chromium-complex intermediate: $PhCH[OCr(OH)Cl_2]_2$. Replace CH_3 by CHO.

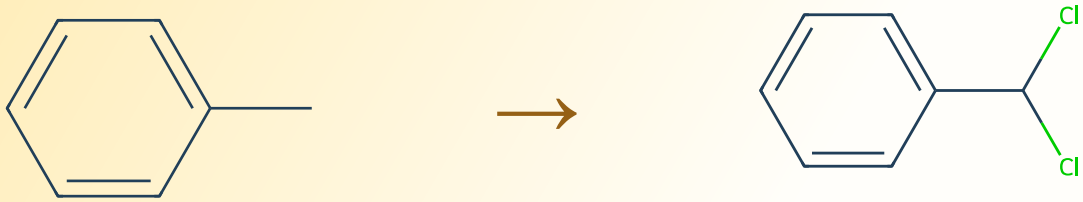
- *Alternative controlled oxidation: CrO_3 + acetic anhydride forms benzylidene diacetate,*



; hydrolysis gives benzaldehyde.

Cl_2 / hv

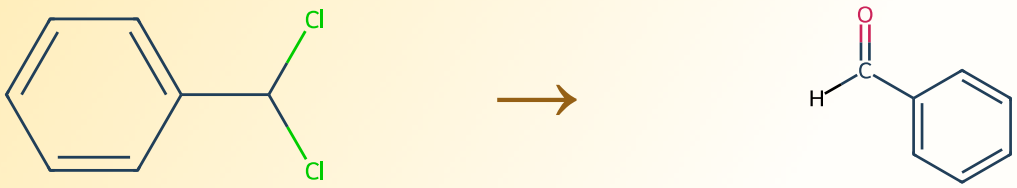
Two side-chain chlorinations



Benzal chloride

H_2O or aqueous KOH

Hydrolysis



Carbonyls & Carboxylic Acids

Aromatic aldehydes from hydrocarbons · Ketones from acyl chlorides

04 Aromatic aldehydes from hydrocarbons

continued

CO + HCl; anhydrous $AlCl_3$ / CuCl

Gattermann–Koch reaction



Benzene → **Benzaldehyde**

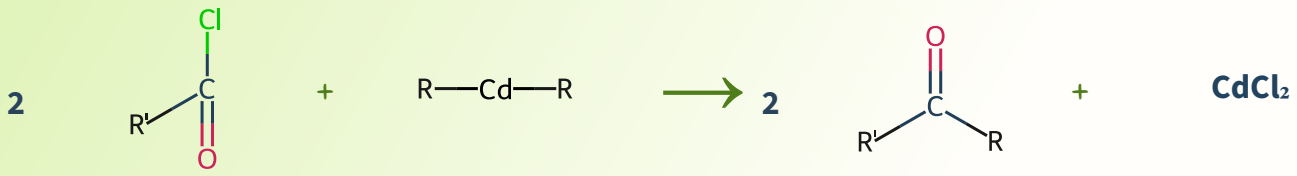
Replace a ring H by CHO.

05 Ketones from acyl chlorides

$$2RMgCl + CdCl_2 \longrightarrow R_2Cd + 2MgCl_2$$

Dialkylcadmium

Stops at the ketone stage

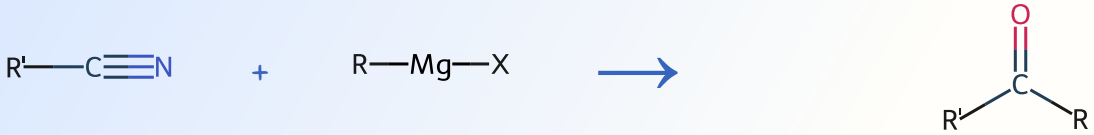


06 More routes to ketones

- *In the acid-chloride / dialkylcadmium route, replace the acyl Cl by the alkyl group from R_2Cd.*

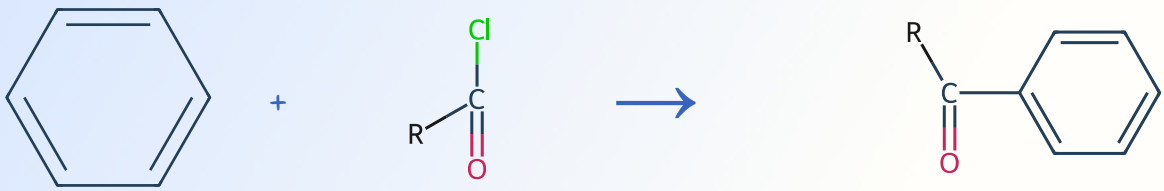
1. Grignard reagent 2. H_3O^+

Join the Grignard alkyl group to the nitrile carbon



Anhydrous $AlCl_3$

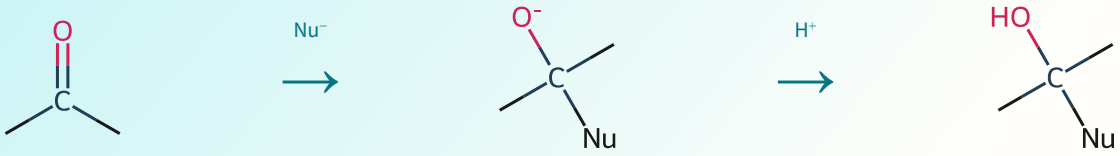
Friedel–Crafts acylation; replace ring H by COR



Carbonyls & Carboxylic Acids

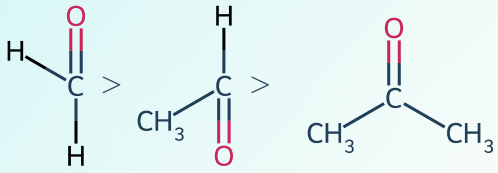
Nucleophilic addition: mechanism and reactivity · HCN addition and cyanohydrin chemistry

07 Nucleophilic addition: mechanism and reactivity



The planar sp² carbonyl carbon becomes tetrahedral sp³; an alkoxide intermediate is formed.

- *Aldehydes generally react faster than ketones. Rate rises as steric hindrance falls and carbonyl electrophilicity rises. Electron-withdrawing −I / −M groups promote attack.*



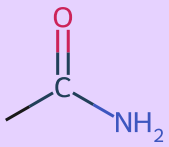
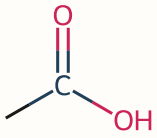
Typical nucleophilic-addition reactivity order.

08 HCN addition and cyanohydrin chemistry

HCN with NaCN or KCN / H_2O

Cyanohydrin formation



Hydrolysis of −CN	Product
Partial hydrolysis	
Complete acid hydrolysis, H_3O^+	

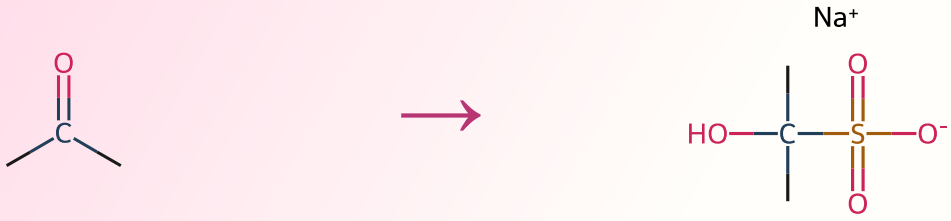
Carbonyls & Carboxylic Acids

Bisulphite addition · Addition of alcohols

09 Bisulphite addition

$NaHSO_3$

Crystalline bisulphite addition compound



- Aldehydes and suitable methyl ketones give this addition. Formation is favoured by low steric hindrance; it is not universal for every aldehyde or ketone.

10 Addition of alcohols

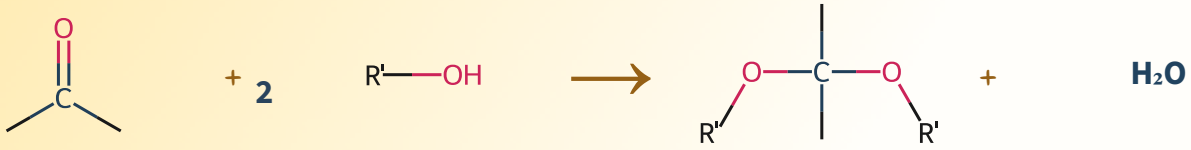
H^+

Hemiacetal or hemiketal



H^+

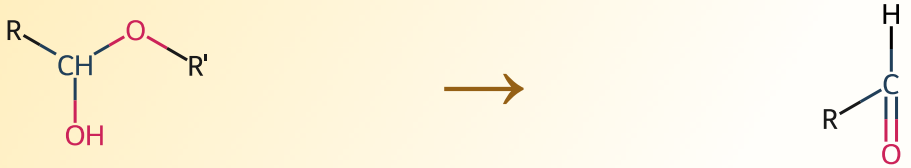
Acetal or ketal



- Acidic hydrolysis of hemiacetals, hemiketals, acetals and ketals regenerates the parent carbonyl compound.

H_3O^+

Hemiacetal hydrolysis



11 Ammonia derivatives: condensation products

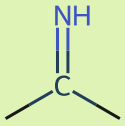
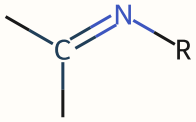
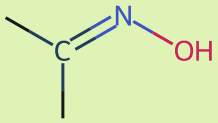
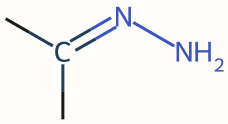
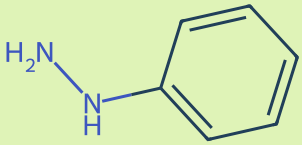
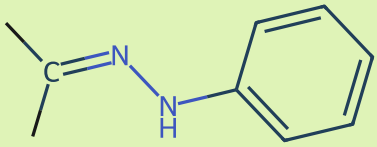
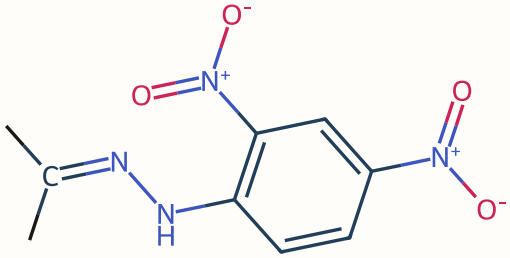
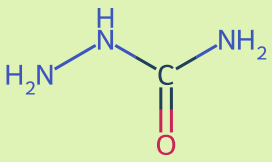
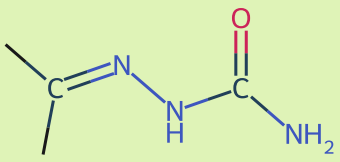


Carbonyls & Carboxylic Acids

Ammonia derivatives: condensation products · Reduction of the carbonyl group

11 Ammonia derivatives: condensation products

continued

Reagent	Carbonyl derivative	Name
NH_3		Imine
$R-NH_2$		Schiff base / substituted imine
NH_2OH		Oxime
NH_2NH_2		Hydrazone
		Phenylhydrazone
2,4-Dinitrophenylhydrazine		2,4-Dinitrophenylhydrazone
		Semicarbazone

12 Reduction of the carbonyl group

$LiAlH_4$, $NaBH_4$ or H_2 / catalyst

Replace CO by CHOH



Carbonyls & Carboxylic Acids

Reduction of the carbonyl group · Choose acidic or basic deoxygenation carefully

12 Reduction of the carbonyl group

continued

Zn(Hg) / concentrated HCl

Clemmensen reduction; replace CO by CH_2



13 Choose acidic or basic deoxygenation carefully

Zn(Hg) / concentrated HCl

Worked conversion



Hydroxycyclopentanecarbaldehyde → **Chloro-methylcyclopentane**

CHO becomes CH_3; an acid-sensitive alcohol group may also be replaced by Cl.

NH_2NH_2 / KOH; ethylene glycol

Heat; Wolff–Kishner reduction



NH_2NH_2 / KOH / ethylene glycol

Heat



α-Chloro cyclopentane carbaldehyde → **1-Methylcyclopentene**

CHO → CH_3, accompanied by base-induced elimination of HCl.

14 Tollens test: silver mirror

- *Tollens reagent is ammoniacal silver nitrate, conventionally prepared from $AgNO_3$ and ammonia solution. Ag(I) is reduced to silvery metallic Ag as an aldehyde is oxidised to carboxylate.*

Carbonyls & Carboxylic Acids

Tollens test: silver mirror · Fehling test: red-brown Cu_2O

14 Tollens test: silver mirror

continued

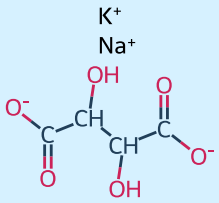


Compound	Tollens test
Aliphatic aldehyde	Positive
Aromatic aldehyde	Positive
Ordinary ketone	Negative
Hemiacetal able to open to an aldehyde	Positive
α-Hydroxy ketone	Positive under alkaline test conditions



Oxidation of an α-hydroxy ketone to a diketone.

15 Fehling test: red-brown Cu_2O

- *Fehling A = aqueous $CuSO_4$. Fehling B = alkaline sodium potassium tartrate (Rochelle salt). Tartrate has the skeleton* 

.

Compound	Fehling test
Aliphatic aldehydes	Positive: red-brown Cu_2O precipitate
Aromatic aldehydes	Generally negative
Ordinary ketones	Negative
Reducing hemiacetals	Positive
α-Hydroxy ketones	Positive

Carbonyls & Carboxylic Acids

Fehling test: red-brown Cu_2O · Haloform test

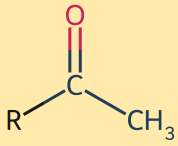
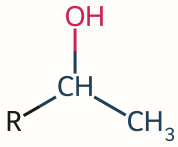
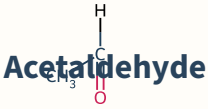
15 Fehling test: red-brown Cu_2O

continued

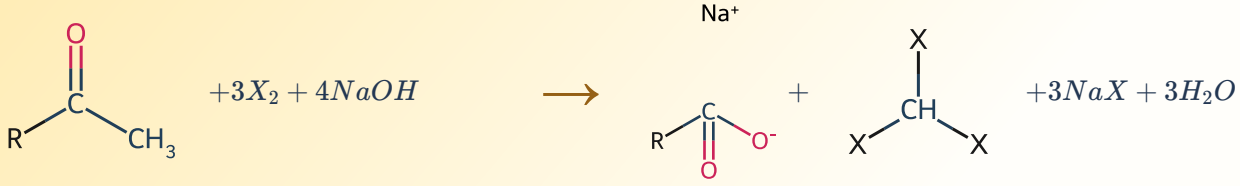


16 Haloform test

- *Reagents: X_2 + NaOH / KOH, or NaOX / KOX; bleaching powder is a chlorine-source alternative. The useful haloform reactions use Cl_2, Br_2 or I_2; the iodoform test gives yellow CHI_3.*

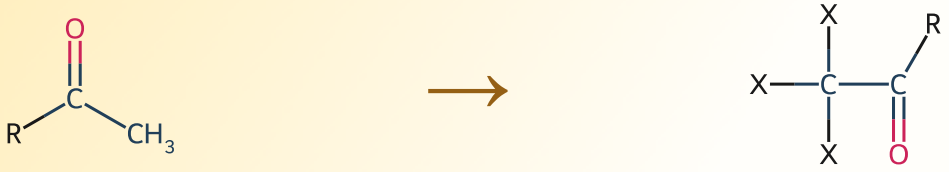
Positive class	Required group / example
Methyl ketones	
Suitable secondary alcohols	 , oxidised first to methyl ketones
Primary alcohol	Ethanol only
Aldehyde	 Acetaldehyde

- *An enolate / carbanion intermediate enables repeated α-halogenation. Replace the three methyl H atoms by X, then alkaline cleavage releases CHX_3.*



3 X_2 / base

Repeated α-halogenation



Carbonyls & Carboxylic Acids

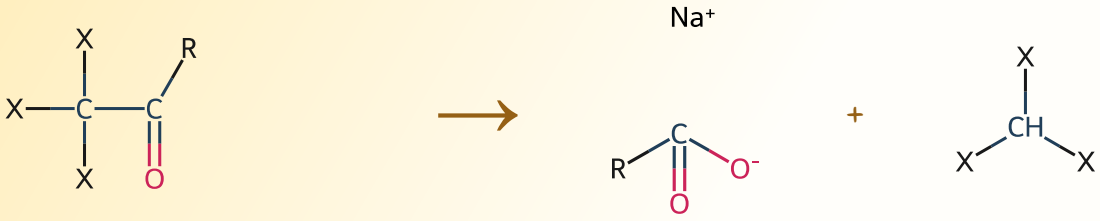
Haloform test · Oxidation under vigorous conditions

16 Haloform test

continued

NaOH

Alkaline cleavage

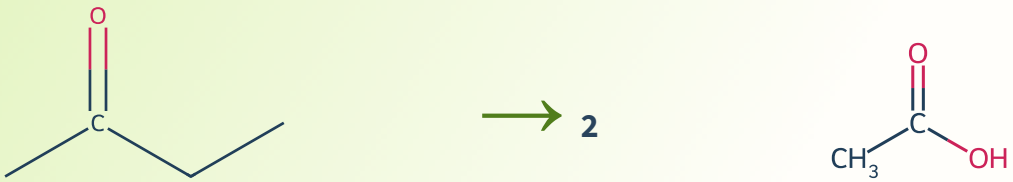


17 Oxidation under vigorous conditions

- *Popoff's rule is an empirical guide for oxidative cleavage of unsymmetrical ketones: the carbonyl carbon tends to remain with the smaller alkyl group.*

Hot $KMnO_4$ or acidified $KMnO_4$

Oxidative cleavage example



Butan-2-one

Strong oxidising agent

Aldehyde → carboxylic acid



18 Aldol condensation

- *A carbonyl compound with at least one α-H can undergo aldol reaction with dilute NaOH, KOH or $Ba(OH)_2$. The first product is a β-hydroxy carbonyl; heating gives an α,β-unsaturated carbonyl by dehydration.*

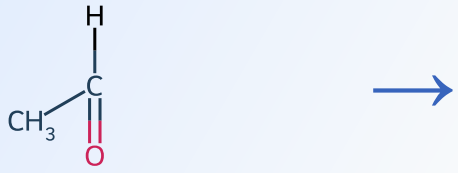
Carbonyls & Carboxylic Acids

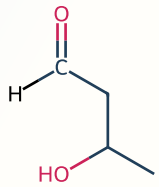
Aldol condensation · Cross aldol: acetaldehyde + propanal

18 Aldol condensation

continued

Dilute NaOH

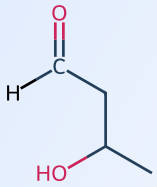
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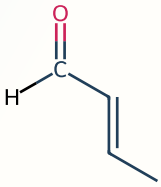


3-Hydroxybutanal: aldol

Heat

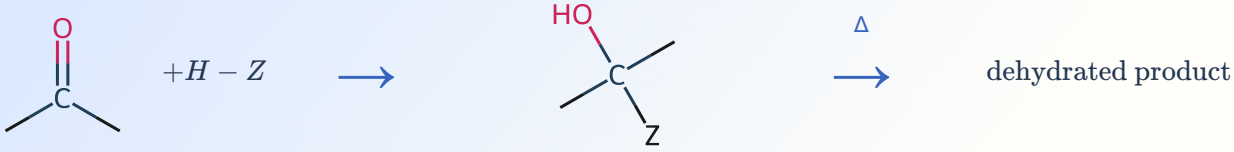
Loss of H_2O



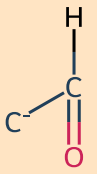
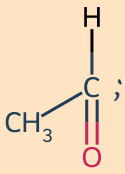


But-2-enal / crotonaldehyde

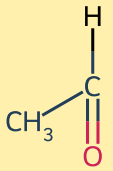
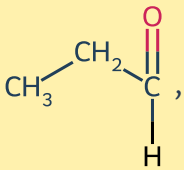
- *Enolate (carbanion) formation enables attack on another carbonyl. Enolate formation can be the slow step; the detailed rate law depends on conditions. Intramolecular hydrogen bonding can stabilise suitable aldol conformations.*



A memory aid for addition followed by dehydration. The reacting H is α to a carbonyl.

- *For acetaldehyde, its enolate fragment*  *attacks*  *; dehydration then joins the carbonyl carbon of one molecule to the α-carbon of the other.*

19 Cross aldol: acetaldehyde + propanal

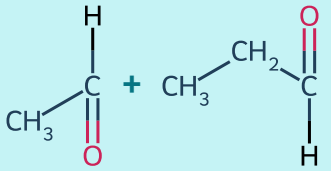
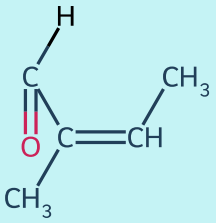
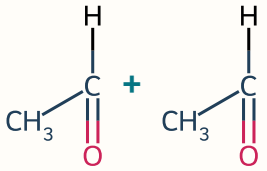
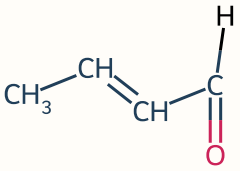
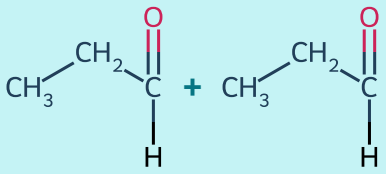
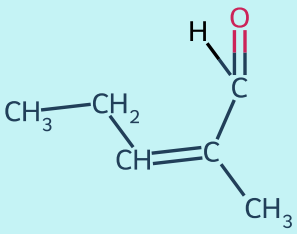
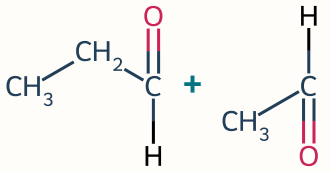
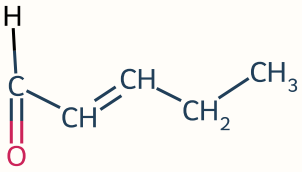
- *With*  *and*  *, both compounds have α-H. Dilute base followed by heating can give two self-condensation products and two crossed products: four constitutional products, before counting stereoisomers.*

Carbonyls & Carboxylic Acids

Cross aldol: acetaldehyde + propanal · Cannizzaro reaction

19 Cross aldol: acetaldehyde + propanal

continued

Electrophile + enolate donor	Dehydrated product	Type
		Cross
		Self
		Self
		Cross

20 Cannizzaro reaction

- *Aldehydes without α-H undergo disproportionation with concentrated NaOH or KOH (about 50% solution). One molecule is oxidised to carboxylate; another is reduced to alcohol.*



Self-Cannizzaro of formaldehyde.

- *Hydride transfer is the key slow step in the usual mechanism; proton transfers also occur. Think: alcohol ⇄ aldehyde ⇄ acid, with simultaneous reduction and oxidation of aldehyde molecules.*

Carbonyls & Carboxylic Acids

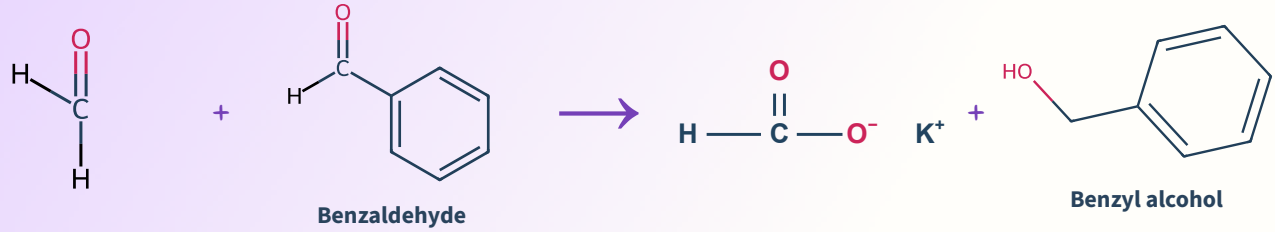
Cannizzaro reaction · Electrophilic substitution of benzaldehyde

20 Cannizzaro reaction

continued

50% KOH

Cross-Cannizzaro



Formaldehyde is preferentially oxidised; benzaldehyde is reduced. Formaldehyde undergoes nucleophilic addition faster than benzaldehyde.

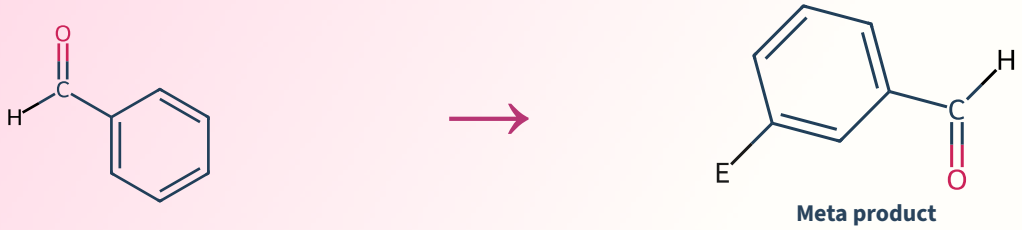
21 Electrophilic substitution of benzaldehyde



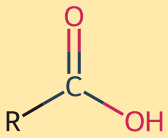
withdraws by the −M effect and directs electrophilic aromatic substitution to meta.

E^+

Meta substitution



22 Carboxylic acids from oxidation

Starting compound	Oxidation route
Primary alcohol	Strong oxidant → 
Aldehyde	Strong oxidant or Tollens / Fehling / Benedict oxidation gives acid or carboxylate according to medium
Ketone	Vigorous oxidative cleavage; Popoff guide

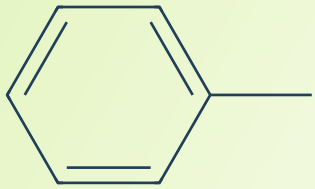
Carbonyls & Carboxylic Acids

Preparation routes

23 Preparation routes

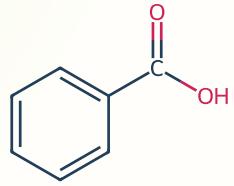
1. $KMnO_4$ / KOH / heat 2. H^+

Side-chain oxidation

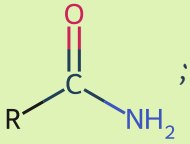
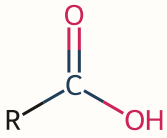
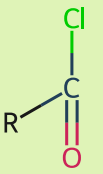
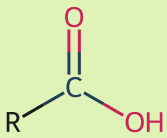
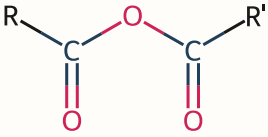
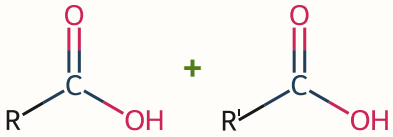
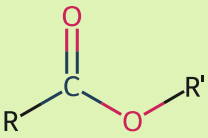
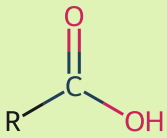
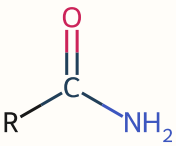
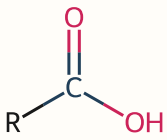


Alkylbenzene with at least one benzylic H





Benzoic acid

Acid derivative	Hydrolysis product / memory aid
R—C≡N, *partial hydrolysis, H_3O^+ / heat*	 ; *CN → $CONH_2$*
R—C≡N, *complete hydrolysis, H_3O^+ / heat*	 ; *CN → COOH*
 *+ water*	 ; *Cl → OH*
 *+ water*	
 *+ water / H^+*	 *+ R'OH; OR' → OH*
 *+ water / H^+*	 *+ ammonium ion; NH_2 → OH*

Carbonyls & Carboxylic Acids

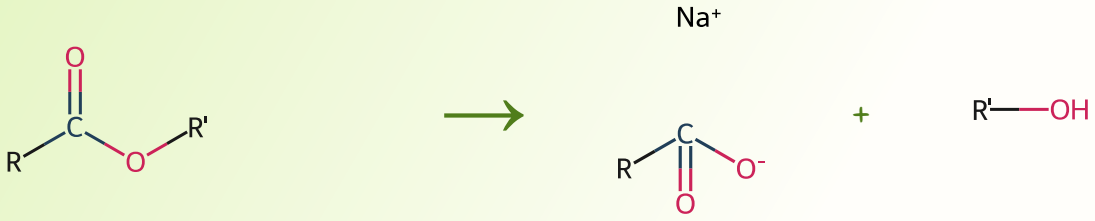
Preparation routes · Acid strength

23 Preparation routes

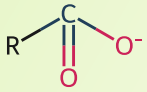
continued

NaOH / H_2O

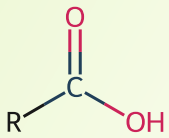
Saponification = alkaline ester hydrolysis



Acidify



to obtain



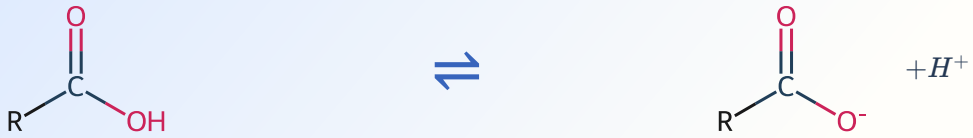
.

1. CO_2 2. H^+

Grignard carboxylation; adds one carbon



24 Acid strength



- *Electron withdrawal by −I / −M increases acidity by stabilising carboxylate. Larger K_a means stronger acid and smaller pK_a. At equal analytical concentration, stronger acid generally gives larger $[H^+]$ and lower pH. These are trends, not literal inverse-proportionality equations.*

Carbonyls & Carboxylic Acids

Reactions at the COOH group · Hell–Volhard–Zelinsky reaction

25 Reactions at the COOH group

PCl_3, PCl_5 or $SOCl_2$

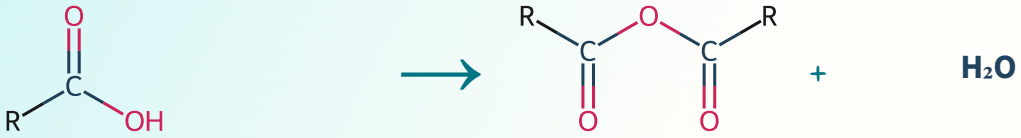
OH → Cl



P_2O_5 / P_4O_{10} or suitable dehydrating conditions

Anhydride formation; concentrated H_2SO_4 / heat is another listed dehydrating condition

2



H^+

Reversible esterification



Heat

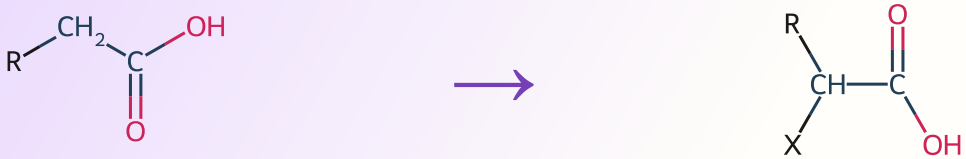
Ammonium carboxylate forms first, then dehydrates to an amide



26 Hell–Volhard–Zelinsky reaction

1. Red P + X_2 2. H_2O

Acid must have at least one α-H; α-halo acid forms



Carbonyls & Carboxylic Acids

Hell–Volhard–Zelinsky reaction · Decarboxylation and coupling

26 Hell–Volhard–Zelinsky reaction

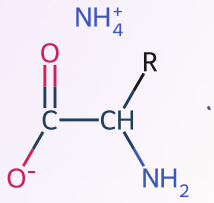
continued

Excess NH_3; then work-up

α-Amino acid preparation



The intermediate is an ammonium carboxylate,

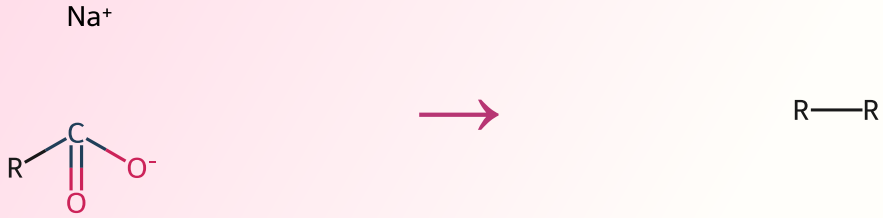


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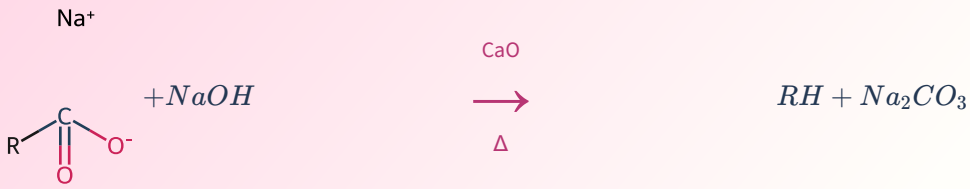
27 Decarboxylation and coupling

Electrolysis

Kolbe electrolysis



Two carboxylate units couple with loss of CO_2; R–R has twice the R fragment.

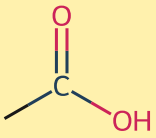


Soda-lime decarboxylation: one carbon fewer. The acid may first be converted to its sodium salt.

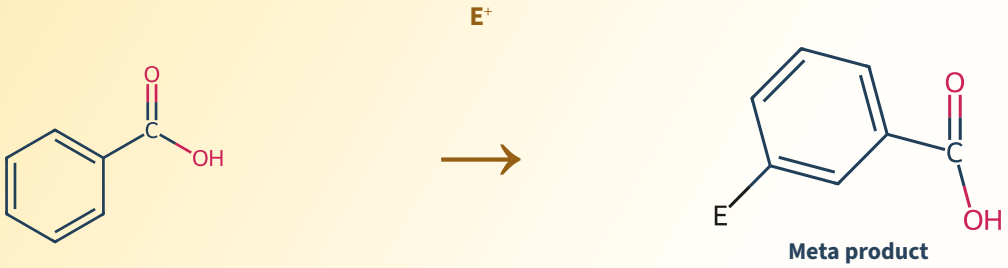
Carbonyls & Carboxylic Acids

Aromatic substitution and reduction

28 Aromatic substitution and reduction



is a deactivating, meta-directing group (–M).

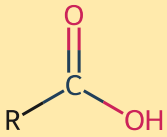
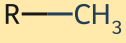
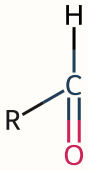
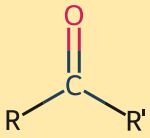
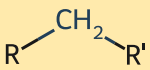


Meta product

$LiAlH_4$ or BH_3 / diborane; then work-up

Borane is particularly useful for selective carboxylic-acid reduction



HI / red P, strong reduction	Product
	
	
	
	*RH*

Amines

Basicity · preparations · diazonium chemistry

10

01 Reduction routes to amines

H_2 / Pd in alcohol; or Sn / HCl; or Fe / HCl

$NO_2 \longrightarrow NH_2$



Nitrobenzene → Aniline

$LiAlH_4$

Aliphatic nitro-compound reduction



- *For aromatic nitro compounds, use the standard catalytic hydrogenation or metal / acid routes. $LiAlH_4$ reduction of nitroarenes can give different nitrogen products, depending on conditions.*

1. $LiAlH_4$, then H_2O; or H_2 / Ni; or Na(Hg) / ROH

$CN \longrightarrow CH_2NH_2$



$LiAlH_4$

Isocyanide reduction gives a secondary N-methylamine



$LiAlH_4$

Amide reduction: $CO \longrightarrow CH_2$



Amines

Ammonolysis and successive alkylation · Gabriel phthalimide synthesis

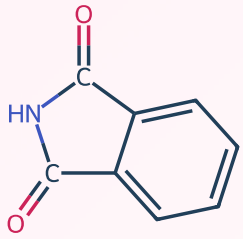
02 Ammonolysis and successive alkylation

- NH_3 attacks an alkyl halide (ordinary primary RX by SN2). The first alkylammonium salt is deprotonated to the primary amine. Further alkylation gives secondary and tertiary amines, then a quaternary ammonium salt.

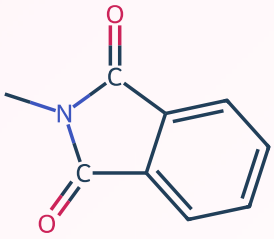
$$NH_3 \xrightarrow{RX} RNH_2 \xrightarrow{RX} R_2NH \xrightarrow{RX} R_3N \xrightarrow{RX} R_4N^+X^-$$

$$NH_3 \xrightarrow{CH_3Cl} CH_3NH_2 \xrightarrow{CH_3Cl} (CH_3)_2NH \xrightarrow{CH_3Cl} (CH_3)_3N \xrightarrow{CH_3Cl} (CH_3)_4N^+Cl^-$$

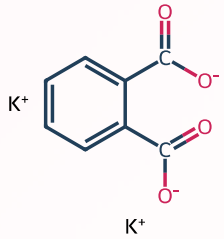
03 Gabriel phthalimide synthesis



Phthalimide



N-alkylphthalimide (methyl shown)



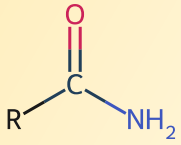
Potassium phthalate

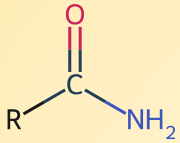
Primary aliphatic amine synthesis

04 Hofmann bromamide degradation

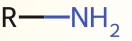
Br_2 / KOH

One carbon fewer; remove the carbonyl carbon





$+Br_2 + 4KOH \longrightarrow$



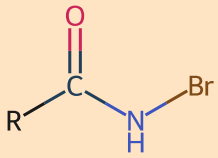
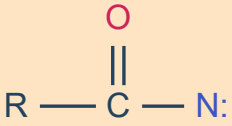
$+2KBr + K_2CO_3 + 2H_2O$

Amines

Hofmann bromamide degradation · Basic strength of amines

04 Hofmann bromamide degradation

continued

- *N-Bromoamide,  , is an intermediate. A nitrene-like  sketch is sometimes used as a memory aid; the standard pathway proceeds via deprotonated N-bromoamide and rearrangement to an isocyanate before hydrolysis.*

05 Basic strength of amines

- *Electron-donating +I / +M effects generally raise basicity; electron withdrawal and delocalisation of the nitrogen lone pair lower it. Solvation and steric effects matter in water.*

Medium / series	Basicity order / caution
Gas phase, comparable alkyl groups	$R_3N > R_2NH > RNH_2$
Water, methylamines	2° > 1° > 3°
Water, ethylamines	2° > 3° > 1°
Water, propylamines	No universal aqueous 3° > 2° > 1° rule; use measured pKa/pKb values for the actual compounds

06 Acylation and carbylamine test

Acylation

Replace an N–H by an acetyl group; amide is much less nucleophilic



$CHCl_3$ / alcoholic KOH

Carbylamine (isocyanide) test for primary amines



Both primary aliphatic and primary aromatic amines respond.

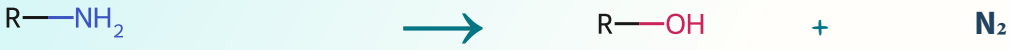
Amines

Primary aliphatic amines with nitrous acid · Reaction with nitrous acid: compare amine classes

07 Primary aliphatic amines with nitrous acid

HNO_2, or $NaNO_2$ + HCl

Unstable aliphatic diazonium intermediate



RN_2^+ loses N_2 to give a carbocation; rearrangement may occur before water gives alcohol.

08 Reaction with nitrous acid: compare amine classes

Amine	Reaction / product
Primary aromatic, $ArNH_2$	$NaNO_2$ / HCl at 0–5 °C → $ArN_2^+Cl^-$
Secondary aliphatic or aromatic, R_2NH	$R_2N–N=O$ (N-nitrosamine), commonly yellow oily product
Tertiary aliphatic, R_3N	Forms an ammonium nitrite salt in cold nitrous acid; no N–H for ordinary nitrosamine formation
Tertiary aromatic, e.g. N,N-dimethylaniline	Electrophilic ring nitrosation, usually at para

HNO_2 / acid

Electrophilic NO^+ substitution



N,N-Dimethylaniline → **p-Nitroso-N,N-dimethylaniline**

09 Hinsberg test

- Hinsberg reagent = benzenesulphonyl chloride, $PhSO_2Cl$. It distinguishes 1°, 2° and 3° amines.

Amine	Product with $PhSO_2Cl$	Behaviour in aqueous KOH
1° RNH_2	$PhSO_2NHR$; retains N–H	Soluble after deprotonation
2° R_2NH	$PhSO_2NR_2$; no N–H	Insoluble
3° R_3N	No sulphonamide under test conditions	No reaction; can dissolve on acidification as ammonium salt

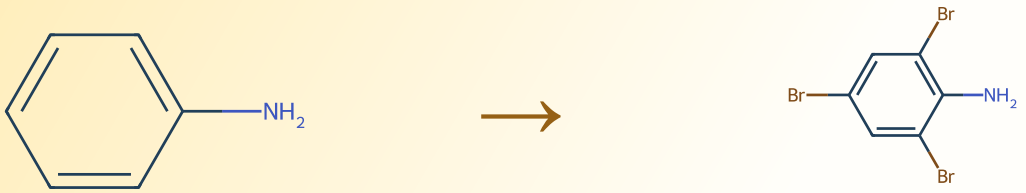
Amines

Aniline bromination and protection · Aniline nitration

10 Aniline bromination and protection

Bromine water

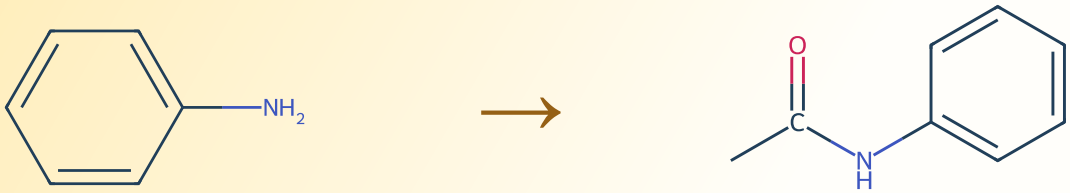
Strong activation; Br_2 / CS_2 is also listed as a bromination medium



2,4,6-Tribromoaniline

CH_3COCl

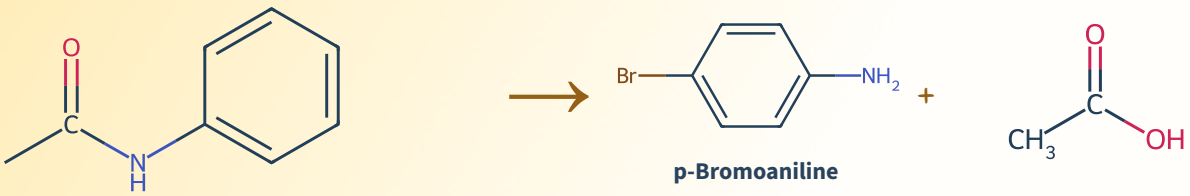
Protect NH_2 by acetylation



Acetanilide

1. Br_2 / CH_3COOH 2. H_3O^+

Controlled monobromination followed by deprotection

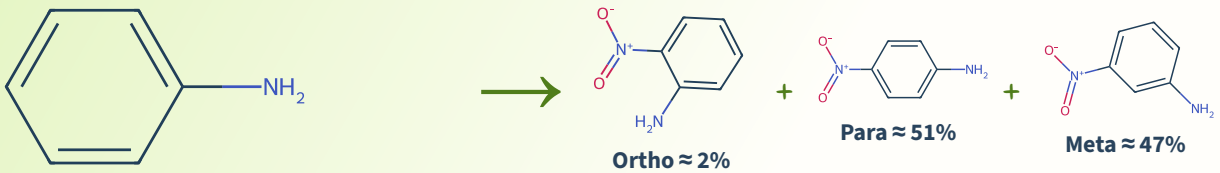


p-Bromoaniline

11 Aniline nitration

HNO_3 / H_2SO_4

Approximate isomer distribution



Ortho ≈ 2% **Para ≈ 51%** **Meta ≈ 47%**

- *Neutral NH_2 is ortho/para-directing, but strong acid forms anilinium, $PhNH_3^+$, which is meta-directing.*

Amines

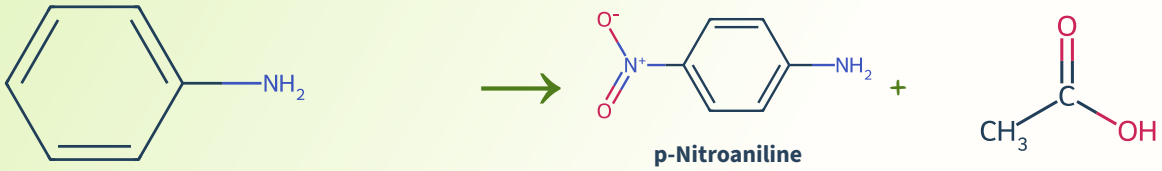
Aniline nitration · Sulphonation and aniline limitations

11 Aniline nitration

continued

1. CH_3COCl 2. Controlled nitration in acetic acid 3. H_3O^+

Protection → nitration → hydrolysis



p-Nitroaniline

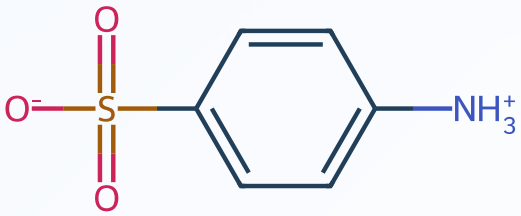
12 Sulphonation and aniline limitations

H_2SO_4; then 453–473 K

Sulphanilic acid



$PhNH_3^+\ HSO_4^- \rightarrow p\text{-}H_2N\text{–}C_6H_4\text{–}SO_3H$



Sulphanilic acid zwitterion

A bipolar internal salt

- *Aniline does not undergo ordinary Friedel–Crafts reactions because its basic NH_2 group complexes with Lewis-acid catalysts.*

13 Preparation of aromatic diazonium salt

$NaNO_2$ + HCl

0–5 °C; diazotisation

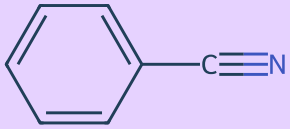
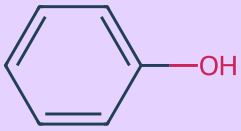
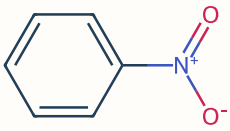
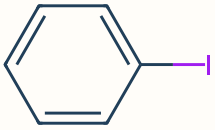


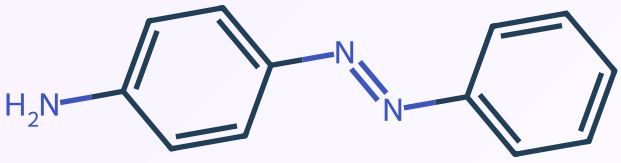
Aniline

Amines

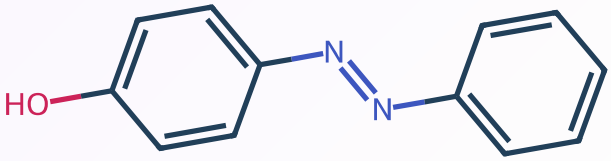
Diazonium conversion map

14 Diazonium conversion map

Reagent for $PhN_2^+Cl^-$	Product
Aniline; coupling conditions	p-H_2N–C_6H_4–N=N–Ph
Phenol; alkaline coupling conditions	p-HO–C_6H_4–N=N–Ph
CuCl / HCl (also written Cu_2Cl_2)	PhCl; Sandmeyer
CuBr / HBr (also written Cu_2Br_2)	PhBr; Sandmeyer
CuCN / KCN	
Cu / HCl	PhCl; Gattermann
Cu / HBr	PhBr; Gattermann
H_3PO_2 or ethanol	
Warm H_2O	
$NaNO_2$, Cu, heat	
HBF_4, then heat	PhF; Balz–Schiemann
KI	



p-Aminoazobenzene



p-Hydroxyazobenzene

Azo coupling products

Biomolecules

Carbohydrates · proteins · vitamins · nucleic acids

11

01 What is a carbohydrate?

- The old name means "hydrate of carbon", suggesting $C_x(H_2O)_y$. This formula alone is not a definition.

Compound	Formula / hydrate form	Carbohydrate?
Glucose	$C_6H_{12}O_6 = C_6(H_2O)_6$	Yes
Acetic acid	$C_2H_4O_2 = C_2(H_2O)_2$	No
Rhamnose	$C_6H_{12}O_5$	Yes, although it does not fit $C_x(H_2O)_y$

- Carbohydrates are polyhydroxy aldehydes or ketones, or compounds that yield such units on hydrolysis. Most are optically active, but optical activity is not universal.

02 Classification by hydrolysis

Class	Hydrolysis result	Examples
Monosaccharides	Cannot be hydrolysed into simpler carbohydrate units	Glucose, fructose, galactose
Oligosaccharides	2–10 monosaccharide units	Disaccharides and trisaccharides
Polysaccharides	Many monosaccharide units, conventionally more than 10	Starch, cellulose, glycogen, gums

Oligosaccharide	Units released
Sucrose (disaccharide)	Glucose + fructose
Maltose (disaccharide)	2 glucose
Lactose (disaccharide)	Glucose + galactose
Raffinose (trisaccharide)	3 monosaccharide units

- Polysaccharides are generally not sweet and are commonly called non-sugars.

03 Reducing and non-reducing sugars

Feature	Reducing	Non-reducing
Tollens reagent	Positive	Negative
Fehling solution	Positive	Negative
Benedict reagent	Positive	Negative
Examples	All ordinary monosaccharides, including glucose and fructose; maltose and lactose	Sucrose; starch/cellulose/glycogen usually show no appreciable ordinary reducing test

Biomolecules

Reducing and non-reducing sugars · Classification by carbon count and carbonyl type

03 Reducing and non-reducing sugars

continued

- A free anomeric hemiacetal / hemiketal permits ring opening. Polysaccharides may have a reducing end, but its contribution is negligible compared with the large polymer.

04 Classification by carbon count and carbonyl type

Carbon atoms	General name	Aldose	Ketose
3	Triose	Aldotriose	Ketotriose
4	Tetrose	Aldotetrose	Ketotetrose
5	Pentose	Aldopentose	Ketopentose
6	Hexose	Aldohexose	Ketohexose

05 Preparation and identity of glucose

$$\text{Sucrose} + H_2O \xrightarrow{H_3O^+} \text{Glucose} + \text{Fructose}$$

Sucrose is dextrorotatory; the hydrolysis mixture is levorotatory and is called invert sugar.

$$(C_6H_{10}O_5)_n + nH_2O \xrightarrow{H_3O^+} nC_6H_{12}O_6$$

Hydrolysis of starch or cellulose gives glucose.

- D-(+)-Glucose is called dextrose and is an aldohexose. In a standard Fischer projection, the OH on the lowest stereocentre is on the right for D and on the left for L. D/L does not determine the +/− direction of optical rotation.

06 Open-chain D-glucose



D-glucose: OH pattern right–left–right–right

Biomolecules

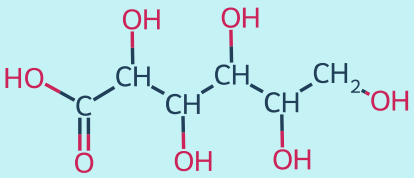
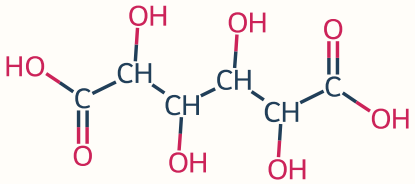
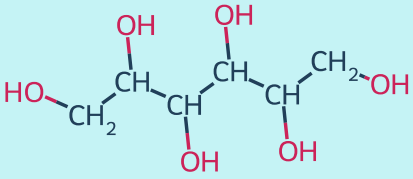
Open-chain D-glucose · Reactions establishing functional groups

06 Open-chain D-glucose

continued

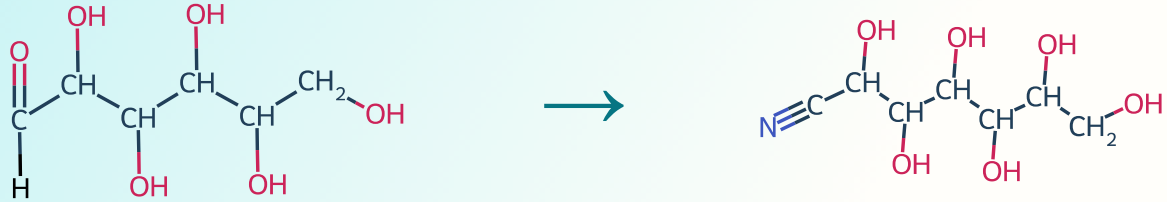
- Molecular formula: $C_6H_{12}O_6$. The open chain has four stereocentres, so the aldohexose family has $2^4 = 16$ stereoisomers.

07 Reactions establishing functional groups

Reagent	Product / structural evidence
HCN	Glucose cyanohydrin; confirms a carbonyl group
HI / red P	n-Hexane; confirms a straight six-carbon chain
NH_2OH	Glucose oxime, CH=N–OH at C1
Excess acetic anhydride / acid	Glucose pentaacetate; five OH groups are acetylated
Br_2 / H_2O	Gluconic acid, 
Concentrated HNO_3	Glucaric (saccharic) acid, 
Na(Hg) / ROH, $NaBH_4$ / MeOH or H_2 / catalyst	Sorbitol, 

HCN

Cyanohydrin



Five stereocentres are present; $2^5 = 32$ is the family maximum, but a fixed D-glucose reactant gives only two new-C1 epimers.

Biomolecules

Reactions establishing functional groups · Osazone formation

07 Reactions establishing functional groups

continued

HI / red P



NH_2OH

Oxime formation

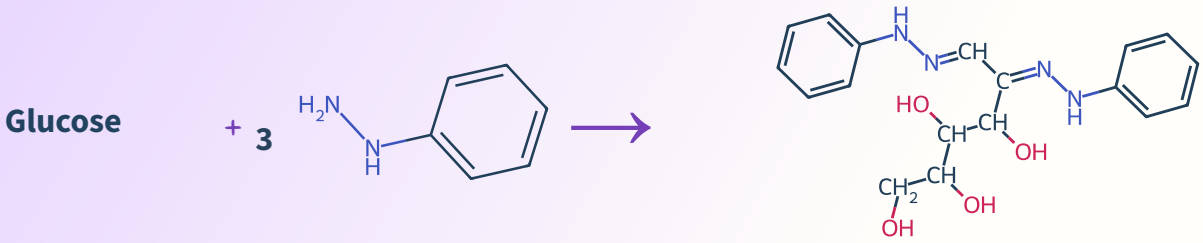


- *Acetylation is often abbreviated using OAc = $OCOCH_3$. Glucose pentaacetate is cyclic; an open-chain "CHO–$(CHOAc)_4$–CH_2OAc" sketch is only an OH-counting shorthand, not its correct structure.*

08 Osazone formation

Mildly basic medium

Glucosazone



The first two carbon atoms are transformed. The other phenylhydrazine equivalents participate in oxidation / by-product formation.

09 Why the cyclic form is needed

- *Glucose does not give the usual Schiff test or a $NaHSO_3$ addition product. It also fails the ordinary 2,4-DNP test. Glucose pentaacetate does not react with NH_2OH: it has no free aldehyde.*

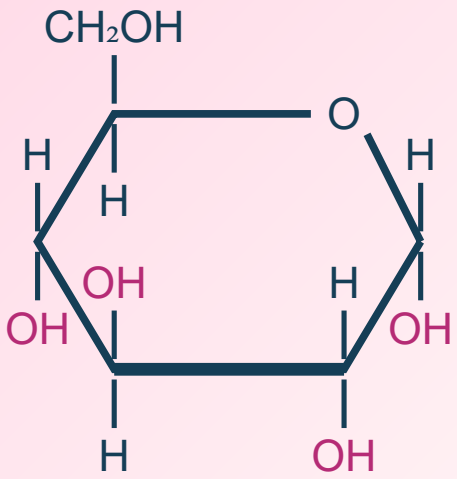
Biomolecules

Why the cyclic form is needed

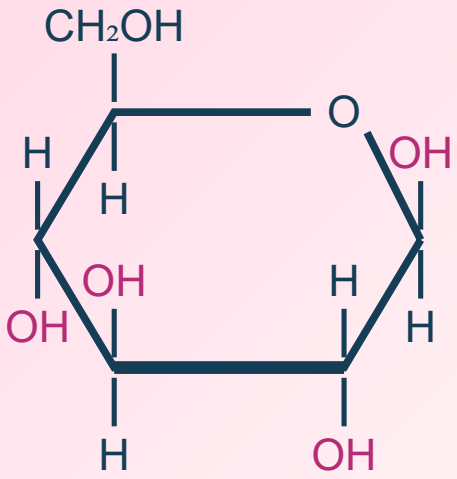
09 Why the cyclic form is needed

continued

- The C5 OH attacks the C1 aldehyde, forming a six-membered cyclic hemiacetal. The new C1 stereocentre gives α and β forms. A pyran-type six-membered ring gives the name glucopyranose.



α-D-glucopyranose



β-D-glucopyranose

Biomolecules

Why the cyclic form is needed · Mutarotation

09 Why the cyclic form is needed

continued

- α- and β-D-glucopyranose are C1 anomers, a special pair of diastereomers; they are not mirror images.

10 Mutarotation

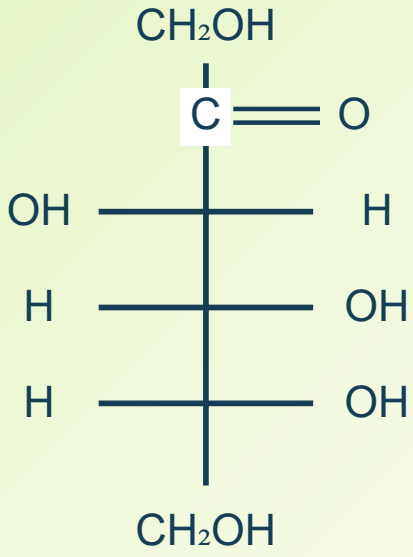
$$\alpha\text{-form} \rightleftharpoons \text{open chain} \rightleftharpoons \beta\text{-form}$$

- Mutarotation is the change of optical rotation as anomers equilibrate in solution through the open chain. Acid or base catalyses the process; the free hemiacetal enables it.

Glucose form	Approximate abundance / rotation
α-D-glucopyranose	About 36%; [α] ≈ +112°
β-D-glucopyranose	About 63.8%; [α] ≈ +19°
Equilibrium mixture	[α] ≈ +52.4°

- α/β forms are anomers and diastereomers (special epimers). L-glucose is the mirror image of D-glucose.

11 Fructose: open chain and furanose anomers



D-fructose: ketohexose; carbonyl at C2

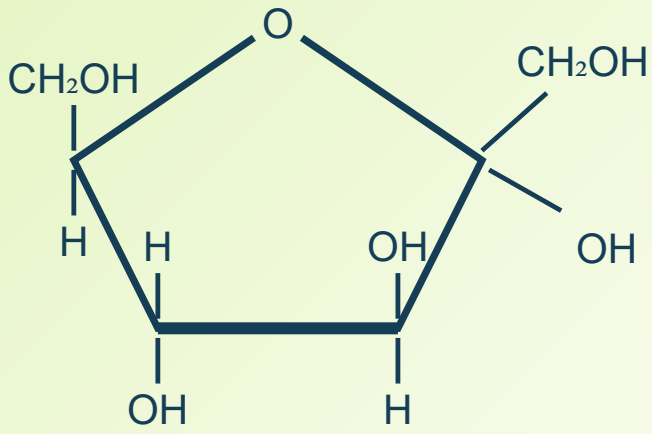
Biomolecules

Fructose: open chain and furanose anomers

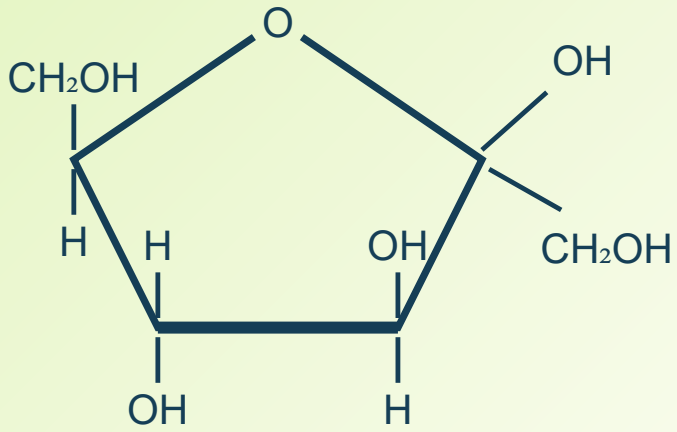
11 Fructose: open chain and furanose anomers

continued

- D-fructose is levorotatory. Ring formation between C2 and C5 gives a five-membered hemiketal, fructofuranose. α and β differ at C2.



α-D-fructofuranose



β-D-fructofuranose

Biomolecules

Aldose family tree and epimers · Osazone, periodic acid and reduction

12 Aldose family tree and epimers

Starting family	Next level
Glyceraldehyde (aldotriose)	Erythrose, threose (aldotetroses)
Erythrose	Ribose, arabinose (aldopentoses)
Threose	Xylose, lyxose (aldopentoses)
Ribose	Allose, altrose
Arabinose	Glucose, mannose
Xylose	Gulose, idose
Lyxose	Galactose, talose

- Memory order: ribose–arabinose–xylose–lyxose; allose–altrose–glucose–mannose–gulose–idose–galactose–talose. Hinglish cues: "Rekha Amitabh ka ladka" and "AAG main GiGiT".

Epimer pair	Single differing stereocentre
Glucose and mannose	C2
Glucose and galactose	C4

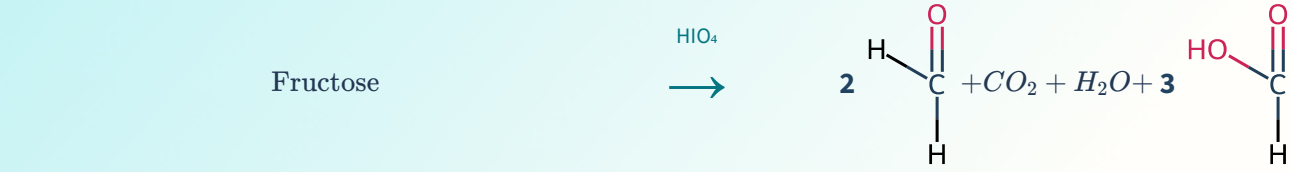
- Epimers have the same molecular formula and differ at one stereocentre; they are diastereomers.

13 Osazone, periodic acid and reduction

- Glucose, mannose and fructose give the same osazone because their differences at C1/C2 are erased. Their configurations from C3 onward match.



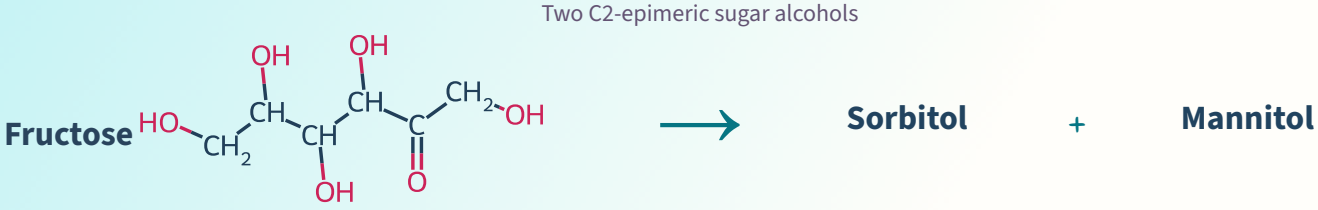
Exhaustive periodic-acid oxidation of the open-chain form; products shown.



Exhaustive periodic-acid oxidation: product pattern.

Reduction

Two C2-epimeric sugar alcohols

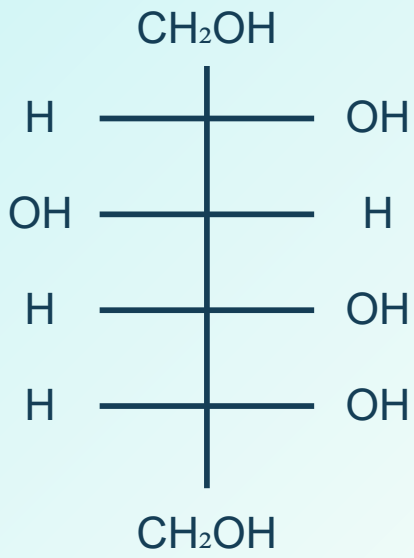


Biomolecules

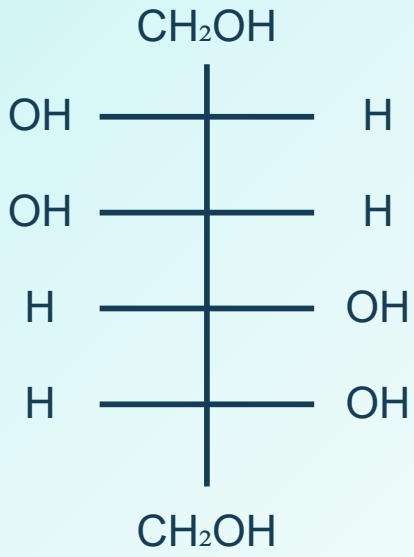
Osazone, periodic acid and reduction · Quick distinctions

13 Osazone, periodic acid and reduction

continued



Sorbitol



Mannitol

14 Quick distinctions

- *Bromine water distinguishes glucose (oxidised) from fructose (not oxidised under neutral conditions). Tollens, Fehling and Benedict tests do not distinguish them: fructose tautomerises in alkaline medium and also responds.*

- *Hydrogen-bond interactions help stabilise the osazone system.*

Biomolecules

Fermentation · Disaccharide structures and hydrolysis

15 Fermentation

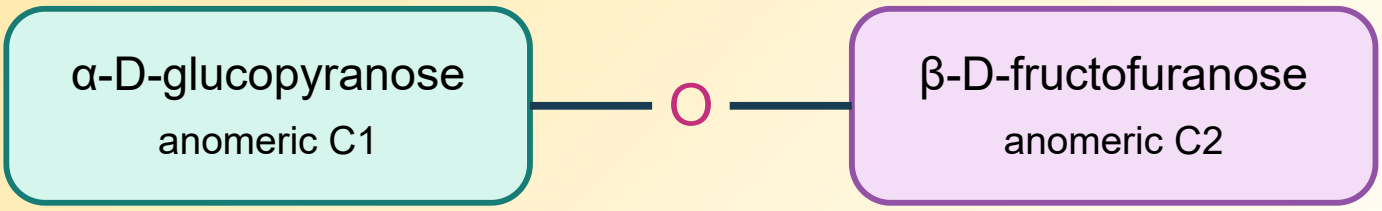
$$C_6H_{12}O_6 \xrightarrow{\text{zymase}} 2C_2H_5OH + 2CO_2$$

Glucose or fructose can give ethyl alcohol by fermentation.

16 Disaccharide structures and hydrolysis

Sugar	Constituent units	Glycosidic bond	Reducing?
Sucrose	α-D-glucopyranose + β-D-fructofuranose	α(1→2)β; both anomeric carbons linked	No
Maltose	Two D-glucopyranose units	α(1→4); one free anomeric carbon	Yes
Lactose	β-D-galactopyranose + D-glucopyranose	β(1→4); one free anomeric carbon	Yes

- Hydrolysis releases the component monosaccharides. The free reducing-end glucose of maltose/lactose can mutarotate, so it need not remain one fixed α or β form.



Sucrose linkage map

17 Polysaccharides

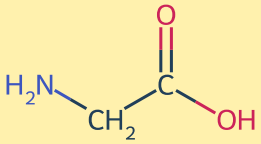
Polymer	Monomer / linkage	Feature
Cellulose	β-D-glucose; β(1→4)	Plant cell-wall structural polymer
Starch: amylose	α-D-glucose; α(1→4)	Linear; about 15–20% of starch; water-soluble
Starch: amylopectin	α-D-glucose; α(1→4), branches α(1→6)	Branched; about 80–85%; insoluble in water
Glycogen	α-D-glucose; α(1→4), branches α(1→6)	Highly branched storage polysaccharide

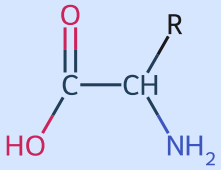
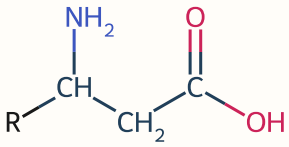
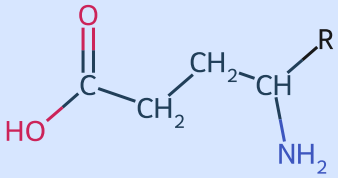
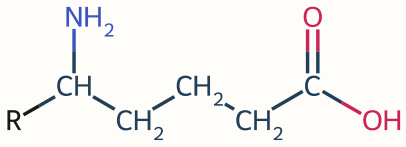
- Acid hydrolysis of cellulose or starch yields glucose. These large polymers show no appreciable ordinary reducing test.

Biomolecules

Amino acids · Important α-amino acids: side-chain table

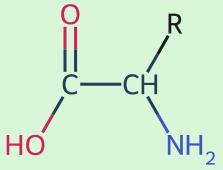
18 Amino acids

- Proteins are polymers of α-amino acids. Most protein amino acids have L configuration. Glycine, , is achiral and optically inactive. Twenty common amino acids form the standard school-level set; selenocysteine and pyrrolysine extend genetically encoded amino acids to 22 in appropriate organisms.

Position of NH_2 relative to COOH	General structure
α-Amino acid	
β-Amino acid	
γ-Amino acid	
δ-Amino acid	

Side-chain character	Simple classification
Extra carboxyl group	Acidic amino acid
Extra basic amino / nitrogen group	Basic amino acid
Neither extra acidic nor strongly basic group	Neutral amino acid

19 Important α-amino acids: side-chain table

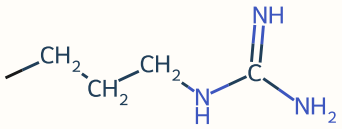
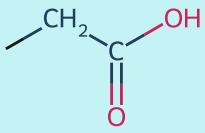
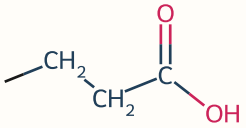
- Every row uses the common framework . The R group below supplies the individual side chain.

Biomolecules

Important α-amino acids: side-chain table · Zwitterion and pH

19 Important α-amino acids: side-chain table

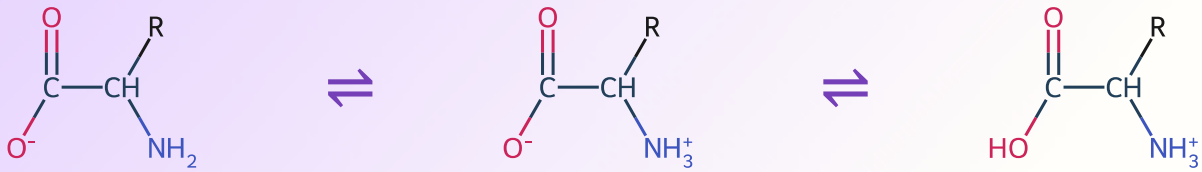
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Symbol	Name	R group	Classification
Tyr	Tyrosine	p-HO–C_6H_4–CH_2–	Neutral
Ser	Serine	HO–CH_2–	Neutral
Gly	Glycine	H–	Neutral; achiral
Ala	Alanine	CH_3–	Neutral
Phe	Phenylalanine	Ph–CH_2–	Essential
Val	Valine	$(CH_3)_2CH$–	Essential
Leu	Leucine	$(CH_3)_2CH$–CH_2–	Essential
Ile	Isoleucine	CH_3CH_2–$CH(CH_3)$–	Essential
Lys	Lysine	H_2N–$(CH_2)_4$–	Basic; essential
Arg	Arginine		Basic; conditionally essential
Asp	Aspartic acid		Acidic
Glu	Glutamic acid		Acidic

- Memory cues: "Tere shehar gaye aaj phir wale lene aaye" maps Tyr–Ser–Gly–Ala–Phe–Val–Leu–Ile. "LAGAN" groups Lys (basic), Asp (acidic), Glu (acidic), Arg (basic).

- Essential amino acids must be supplied adequately by diet because the body cannot make enough. Non-essential amino acids can be synthesised. Arginine is conditionally essential, especially during growth.

20 Zwitterion and pH



Left: anionic at high pH; middle: zwitterion (bipolar ion); right: cationic at low pH. Adding H^+ moves right; OH^- moves left.

- Memory cue: "AAJ katreena hill station par hai" / A–Z–Cat at high–intermediate–low pH: Anion → Zwitterion → Cation.

Biomolecules

Isoelectric point, pI · Important physical and stereochemical points

21 Isoelectric point, pI

- pI is the pH at which the average net charge is zero, so there is no net migration in an electric field. For a simple α-amino acid, the zwitterionic form predominates.

$$pI = \frac{pK_{a,\,below} + pK_{a,\,above}}{2}$$

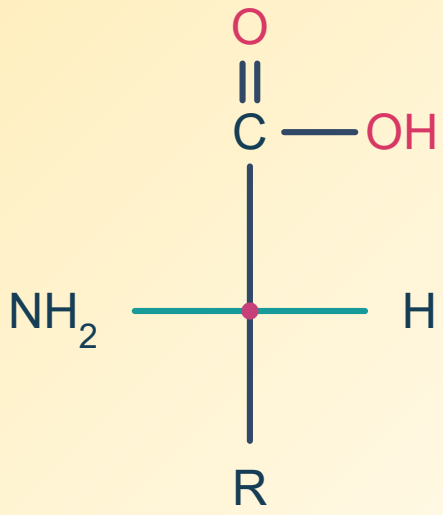
Average the two pKa values that bracket the neutral (net-zero) species.

Amino-acid type	Which pKa values to average?	Typical pI guide
Neutral side chain	α-COOH and α-NH_3^+	Around 6
Acidic side chain	The two carboxylic-acid pKa values	Low pI, commonly around 3
Basic side chain	The two higher pKa values, usually amino / basic side-chain groups	High pI, often around 9–11

- With labels pKa_1 = NH_3^+, pKa_2 = α-COOH and pKa_3 = ionisable R: neutral pI = $(pKa_1+pKa_2)/2$; acidic pI = $(pKa_2+pKa_3)/2$; basic pI = $(pKa_1+pKa_3)/2$. Always identify the groups rather than memorising index numbers.

22 Important physical and stereochemical points

- Most naturally occurring protein α-amino acids belong to the L family. Among the common α-amino acids, glycine alone is optically inactive. They are salt-like, generally water-soluble crystalline solids with high melting/decomposition temperatures; they usually decompose before boiling.



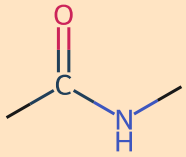
L-α-amino acid Fischer convention

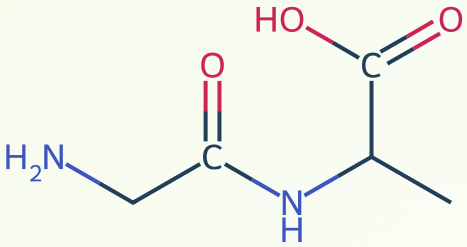
- α-Amino acids are the monomers of proteins.

Biomolecules

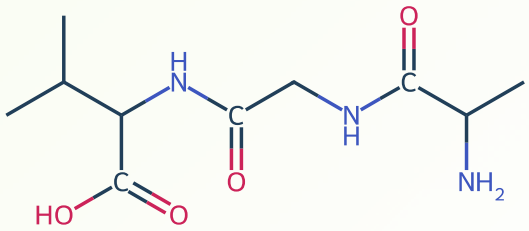
Peptide linkage and peptide examples · Fibrous versus globular proteins

23 Peptide linkage and peptide examples

- Proteins are polymers of α-amino acids. Condensation joins a carboxyl group to an amino group through , the peptide linkage. Every peptide linkage is an amide linkage, but every amide linkage is not necessarily a peptide bond.



Gly–Ala dipeptide



Ala–Gly–Val tripeptide

Count the peptide bonds

- Long chains are polypeptides.

24 Fibrous versus globular proteins

Property	Fibrous	Globular
Shape	Extended / fibre-like	Folded into compact three-dimensional form
Water solubility	Usually insoluble	Often soluble
Stabilising interactions	Hydrogen bonds; disulphide links where present	Hydrogen bonds, disulphide links, dipole interactions, van der Waals and hydrophobic interactions
Examples	Keratin (hair), myosin (muscle)	Insulin, albumin

25 Four levels of protein structure

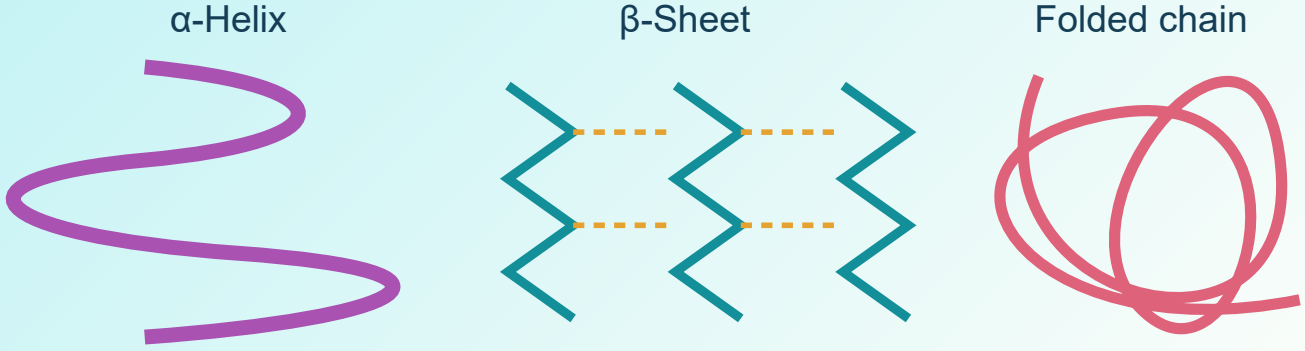
Level	Meaning / example
Primary	Amino-acid sequence; changing the residue order changes the protein. Compare G–A–V–L–I–G–A–V with G–A–V–L–I–A–G–V.
Secondary: α-helix	Coiled backbone stabilised by intrachain hydrogen bonds
Secondary: β-pleated sheet	Extended strands joined by hydrogen bonds; strands can be from one folded chain or different chains
Tertiary	Overall folding of one chain; van der Waals, dipole interactions, H bonds and disulphide links
Quaternary	Arrangement of two or more polypeptide subunits

Biomolecules

Four levels of protein structure · Denaturation

25 Four levels of protein structure

continued



Protein folding at a glance

26 Denaturation

- A native protein has a characteristic shape and biological function. Heating or chemical changes disrupt the interactions holding its folded structure. Secondary and tertiary structure are disturbed (and quaternary organisation may be lost), while the primary peptide sequence usually remains intact.

- Examples: coagulation of egg white; curdling of milk.

27 Enzymes

- Enzymes are biological catalysts: they lower activation energy and increase reaction rate. Most are globular proteins; many names end in "-ase". Oxidoreductases catalyse oxidation–reduction reactions.

Substrate	Enzyme	Products / action
Urea	Urease	Ammonia + CO_2
Maltose	Maltase	Glucose
Sucrose	Invertase	Glucose + fructose
Starch	Amylase	Maltose and shorter saccharides
Protein	Trypsin	Peptides; complete digestion later yields amino acids
Ascorbic acid	Ascorbic-acid oxidase	Dehydroascorbic acid

28 Vitamins

- Vitamins are required in small dietary amounts for normal growth and biological functions. Their deficiency produces characteristic disorders.

Biomolecules

Vitamin classes · Vitamin deficiency table

29 Vitamin classes

- Fat-soluble vitamins: A, D, E, K (memory cue "KEDA"). Water-soluble vitamins: B group and C ("BC").

30 Vitamin deficiency table

Vitamin	Name where given	Deficiency effects
A	Retinol	Xerophthalmia (dryness / damage of eye surface) and night blindness
B_1	Thiamine	Beriberi; loss of appetite and impaired growth
B_2	Riboflavin	Cheilosis: fissures at mouth corners / lips; may also involve digestive disturbance and burning skin sensation
B_6	Pyridoxine	Convulsions
B_{12}	Cobalamin	Megaloblastic anaemia; pernicious anaemia involves impaired B_{12} absorption
C	Ascorbic acid	Scurvy; bleeding gums
D	—	Rickets in children; osteomalacia (soft bones / pain) in adults
E	—	Increased red-cell fragility and muscle weakness
K	—	Increased blood-clotting time

31 DNA and RNA

Feature	DNA	RNA
Full name	Deoxyribonucleic acid	Ribonucleic acid
Pentose sugar	β-D-2-Deoxyribose	β-D-Ribose
Bases	C, G, A, T	C, G, A, U
Main role	Genetic information / control	Protein synthesis
Usual strand form	Double-stranded	Single-stranded

- Each nucleic acid contains nitrogenous bases, a pentose sugar and phosphate groups. Purines: adenine (A), guanine (G). Pyrimidines: cytosine (C), thymine (T), uracil (U).

32 Nucleoside, nucleotide and bonds

$$\text{Nucleoside} = \text{base} + \text{sugar}$$

$$\text{Nucleotide} = \text{base} + \text{sugar} + \text{phosphate}$$

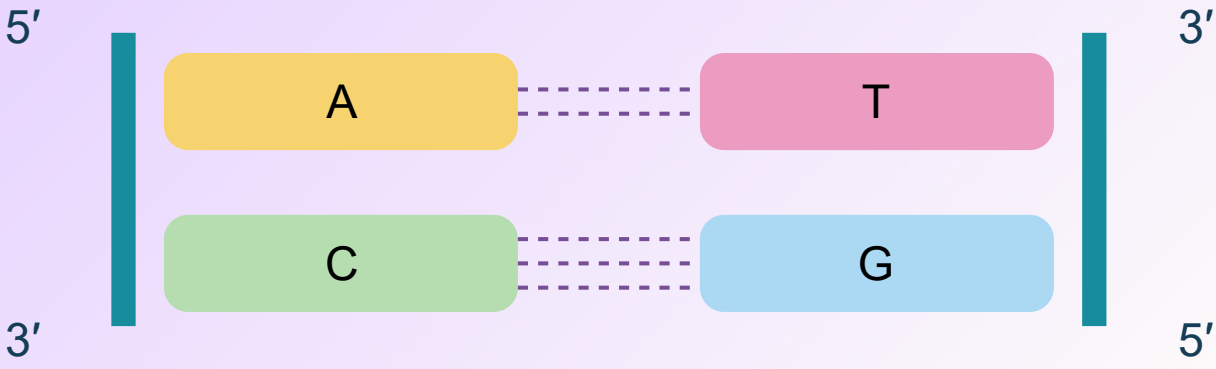
- Many nucleotides form a nucleic-acid chain. Adjacent nucleotides within a strand are joined by 3′–5′ phosphodiester bonds. Complementary bases between DNA strands are hydrogen-bonded: A–T has two H bonds; C–G has three.

Biomolecules

Nucleoside, nucleotide and bonds · Biological functions of nucleic acids

32 Nucleoside, nucleotide and bonds

continued



DNA: two complementary antiparallel strands

33 Biological functions of nucleic acids

- DNA stores hereditary information and transmits it during reproduction and cell division. It can replicate, so daughter cells receive copies of the genetic information.
- Nucleic acids direct protein synthesis. DNA contains the information for a particular protein; RNA participates in carrying and translating that information into a polypeptide in the cell.

34 Chemical messengers

- Hormones act as intercellular messengers. Endocrine glands release them directly into the bloodstream, which carries them to target tissues.

35 Types of hormones

Chemical class	Examples
Steroids	Estrogens and androgens
Polypeptides	Insulin and endorphins
Amino-acid derivatives	Epinephrine and norepinephrine

36 Important functions

- Hormones help balance biological activities in the body. Growth hormone and sex hormones contribute to growth and development.
- Insulin helps lower and regulate blood glucose. Glucagon tends to raise blood glucose. Together, they help maintain glucose within the physiological range.
- Epinephrine and norepinephrine mediate responses to external stimuli, including the rapid stress response.