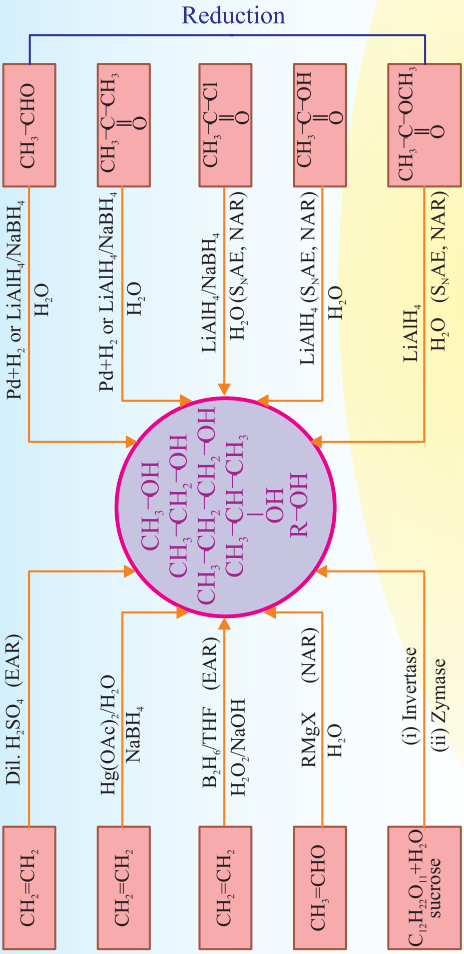
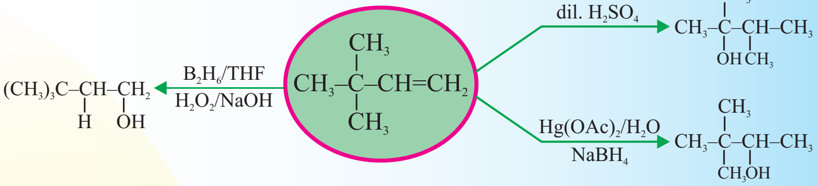
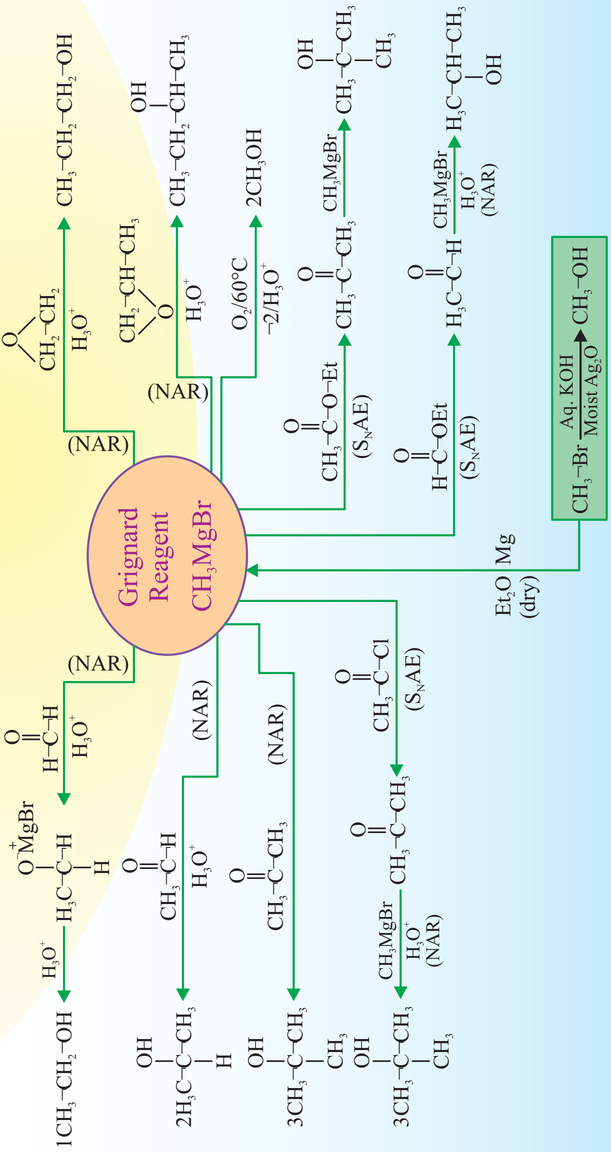
CHAPTER 17

Alcohols, Phenols and Ethers





CH_3
$CH_3–C–CH=CH_2$
CH_3
B_2H_6/THF
$H_2O_2/NaOH$
$(CH_3)_3C–CH–CH_2$
H OH
dil. H_2SO_4
CH_3
$CH_3–C–CH–CH_3$
OH CH_3
$Hg(OAc)_2/H_2O$
$NaBH_4$
CH_3
$CH_3–C–CH–CH_3$
CH_3OH



Grignard Reagent CH_3MgBr
$CH_3–Br \xrightarrow[\text{Moist }Ag_2O]{\text{Aq. KOH}} CH_3–OH$
Mg
Et_2O (dry)
(NAR)
$CH_2–CH_2$ (O)
H_3O^+
$CH_3–CH_2–CH_2–OH$
$CH_2–CH–CH_3$ (O)
H_3O^+
$CH_3–CH_2–CH–CH_3$
OH
$O_2/60°C$
$–2/H_3O^+$
$2CH_3OH$
$CH_3–C(=O)–O–Et$
(S_NAE)
$CH_3–C(=O)–CH_3$
CH_3MgBr
$CH_3–C(OH)(CH_3)–CH_3$
$H–C(=O)–OEt$
(S_NAE)
$H_3C–C(=O)–H$
CH_3MgBr
H_3O^+
(NAR)
$H_3C–CH(OH)–CH_3$
$H–C(=O)–H$
H_3O^+
$H_3C–C(O^-\overset{+}{M}gBr)(H)–H$
H_3O^+
$1CH_3–CH_2–OH$
$CH_3–C(=O)–H$
H_3O^+
$2H_3C–C(OH)(H)–CH_3$
$CH_3–C(=O)–CH_3$
$3CH_3–C(OH)(CH_3)–CH_3$
$CH_3–C(=O)–Cl$
(S_NAE)
$CH_3–C(=O)–CH_3$
CH_3MgBr
H_3O^+
(NAR)
$3CH_3–C(OH)(CH_3)–CH_3$

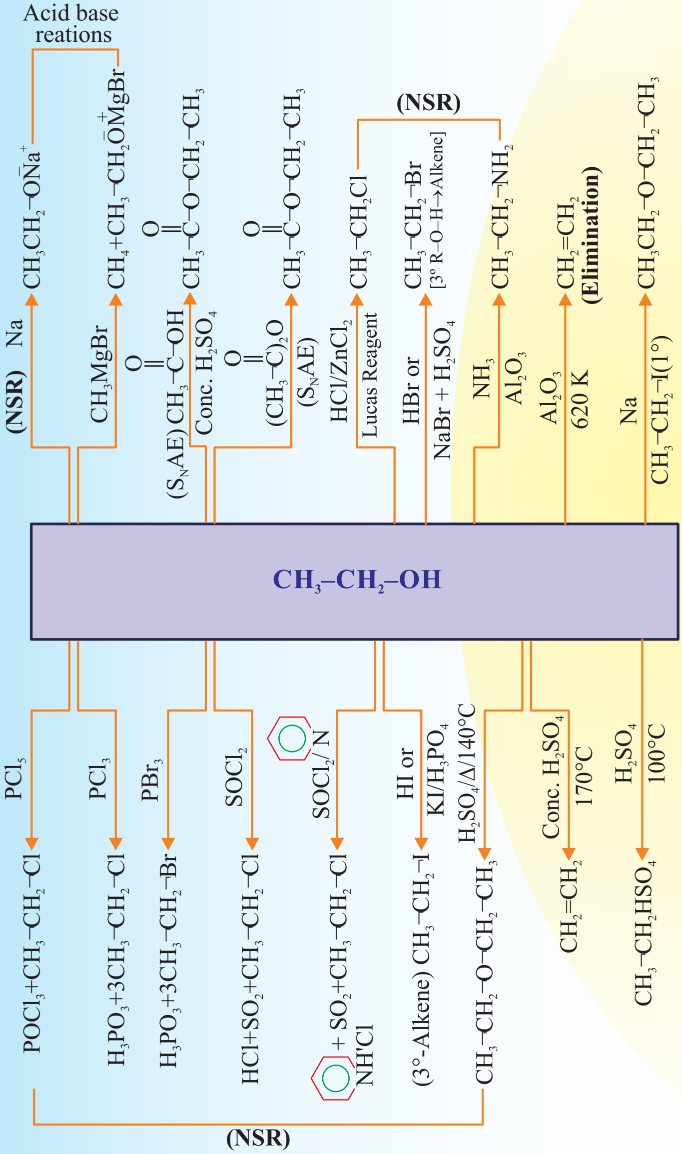
Solubility of alcohol increase in branching n < iso < neo (Isomeric).

Relative order of reactivity

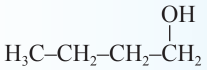
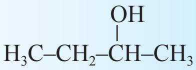
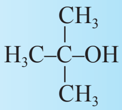
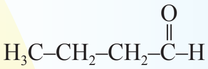
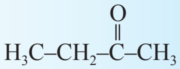
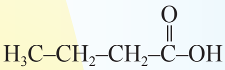
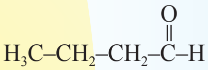
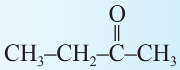
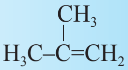
(i) 1° > 2° > 3° (O–H bond fission)

(ii) 3° > 2° > 1° > (C–O bond fission)

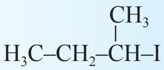
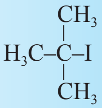
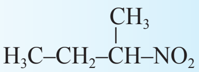
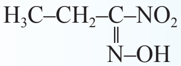
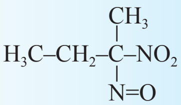
(iii) 3° > 2° > 1° (Dehydration)

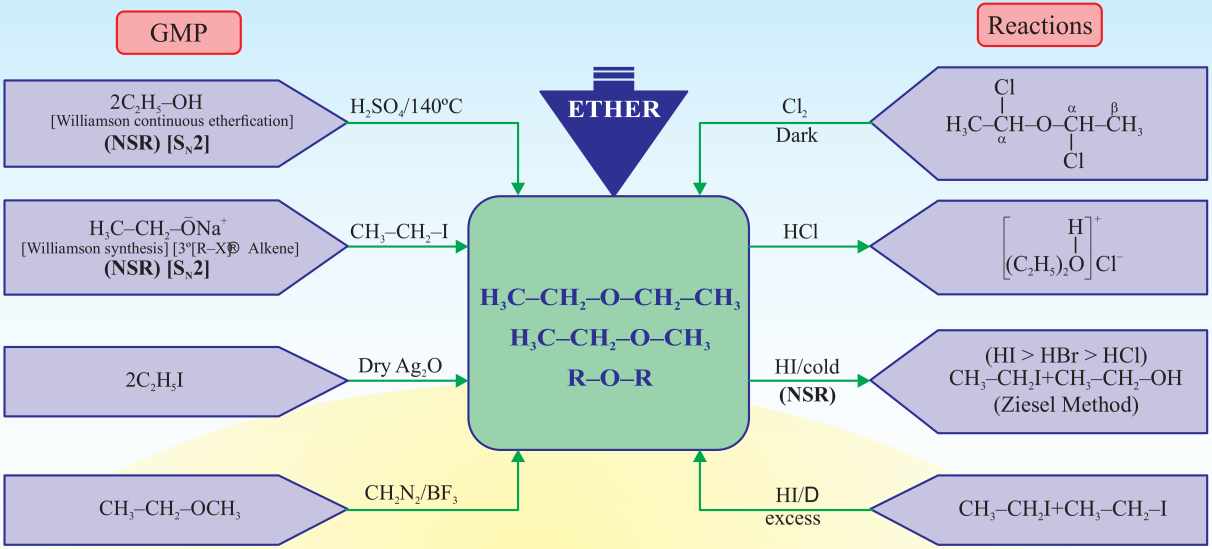


DEHYDROGENATIONS

Reagent	 $H_3C-CH_2-CH_2-\overset{\overset{OH}{\mid}}{CH_2}$ 1° Alcohol	 $H_3C-CH_2-\overset{\overset{OH}{\mid}}{CH}-CH_3$ 2°Alcohol	 $H_3C-\overset{\overset{CH_3}{\mid}}{\underset{\underset{CH_3}{\mid}}{C}}-OH$ 3° Alcohol
PCC/PDC Anhy. CrO_3	 $H_3C-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-H$	 $H_3C-CH_2-\overset{\overset{O}{\|}}{C}-CH_3$	No reaction
$K_2Cr_2O_7/H^{\oplus}$ $KMnO_4/H^+/^-OH/\Delta$ Jones Reagent	 $H_3C-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-OH$	 $H_3C-\overset{\overset{O}{\|}}{C}-OH+CH_3-\overset{\overset{O}{\|}}{C}-OH$	No reaction
Cu/500°C	 $H_3C-CH_2-CH_2-\overset{\overset{O}{\|}}{C}-H$	 $CH_3-CH_2-\overset{\overset{O}{\|}}{C}-CH_3$	 $H_3C-\overset{\overset{CH_3}{\mid}}{C}=CH_2$
Lucas Reagent $HCl/ZnCl_2$	Cloudiness appear upon heating after 30 mins.	within five min.	Immediately

VICTOR MEYER'S TEST

P/I_2	$CH_3-CH_2-CH_2-CH_2-I$	 $H_3C-CH_2-\overset{\overset{CH_3}{\mid}}{CH}-I$	 $H_3C-\overset{\overset{CH_3}{\mid}}{\underset{\underset{CH_3}{\mid}}{C}}-I$
$AgNO_2$	$CH_3-CH_2-CH_2-NO_2$	 $H_3C-CH_2-\overset{\overset{CH_3}{\mid}}{CH}-NO_2$	$(CH_3)_3C-NO_2$
HNO_2	 $H_3C-CH_2-\underset{\underset{N-OH}{\|}}{C}-NO_2$ Nitrolic acid	 $H_3C-CH_2-\overset{\overset{CH_3}{\mid}}{\underset{\underset{N=O}{\mid}}{C}}-NO_2$ Blue colour	No reaction: Colourless
NaOH	Red Colour	No reaction	



GMP

$2C_2H_5–OH$
[Williamson continuous etherfication]
(NSR) [S_N2]

$H_2SO_4/140°C$

$H_3C–CH_2–\bar{O}Na^+$
[Williamson synthesis] [3°[R–X]® Alkene]
(NSR) [S_N2]

$CH_3–CH_2–I$

$2C_2H_5I$

Dry Ag_2O

$CH_3–CH_2–OCH_3$

CH_2N_2/BF_3

ETHER

$H_3C–CH_2–O–CH_2–CH_3$

$H_3C–CH_2–O–CH_3$

R–O–R

Reactions

Cl_2
Dark

$H_3C–\underset{\alpha}{\overset{Cl}{CH}}–O–\overset{\alpha}{\underset{Cl}{CH}}–\overset{\beta}{CH_3}$

HCl

$\left[(C_2H_5)_2\overset{H}{O}\right]^+ Cl^-$

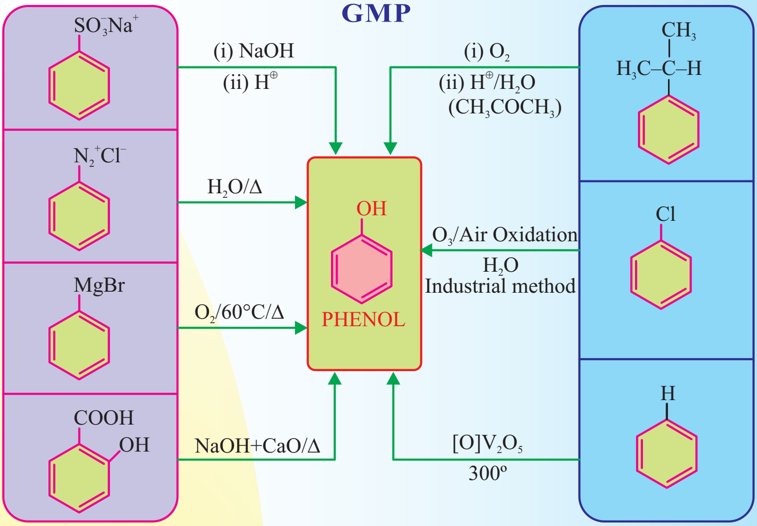
HI/cold
(NSR)

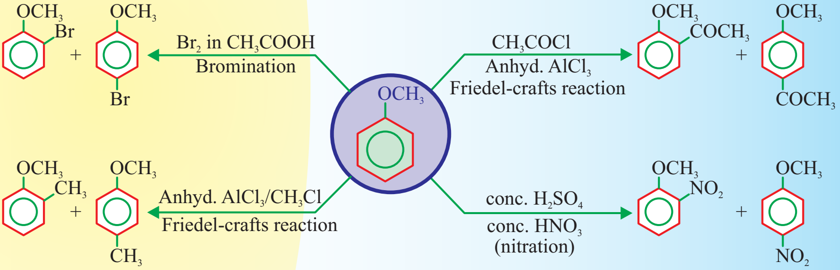
(HI > HBr > HCl)
$CH_3–CH_2I+CH_3–CH_2–OH$
(Ziesel Method)

HI/D
excess

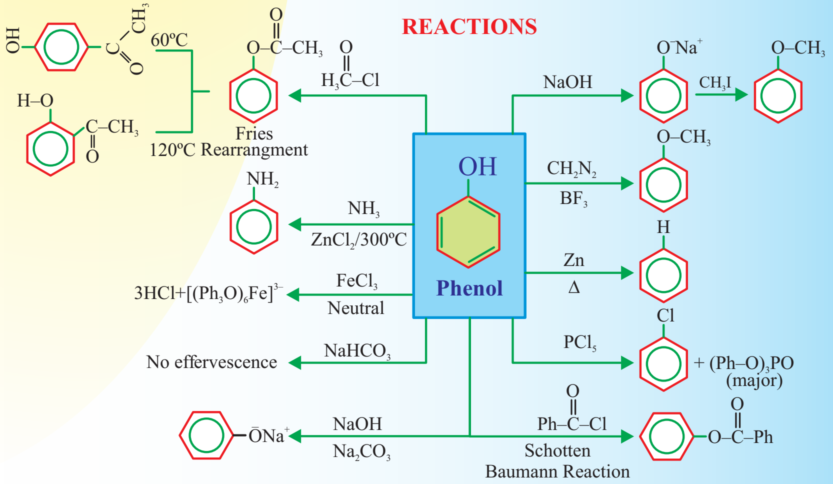
$CH_3–CH_2I+CH_3–CH_2–I$

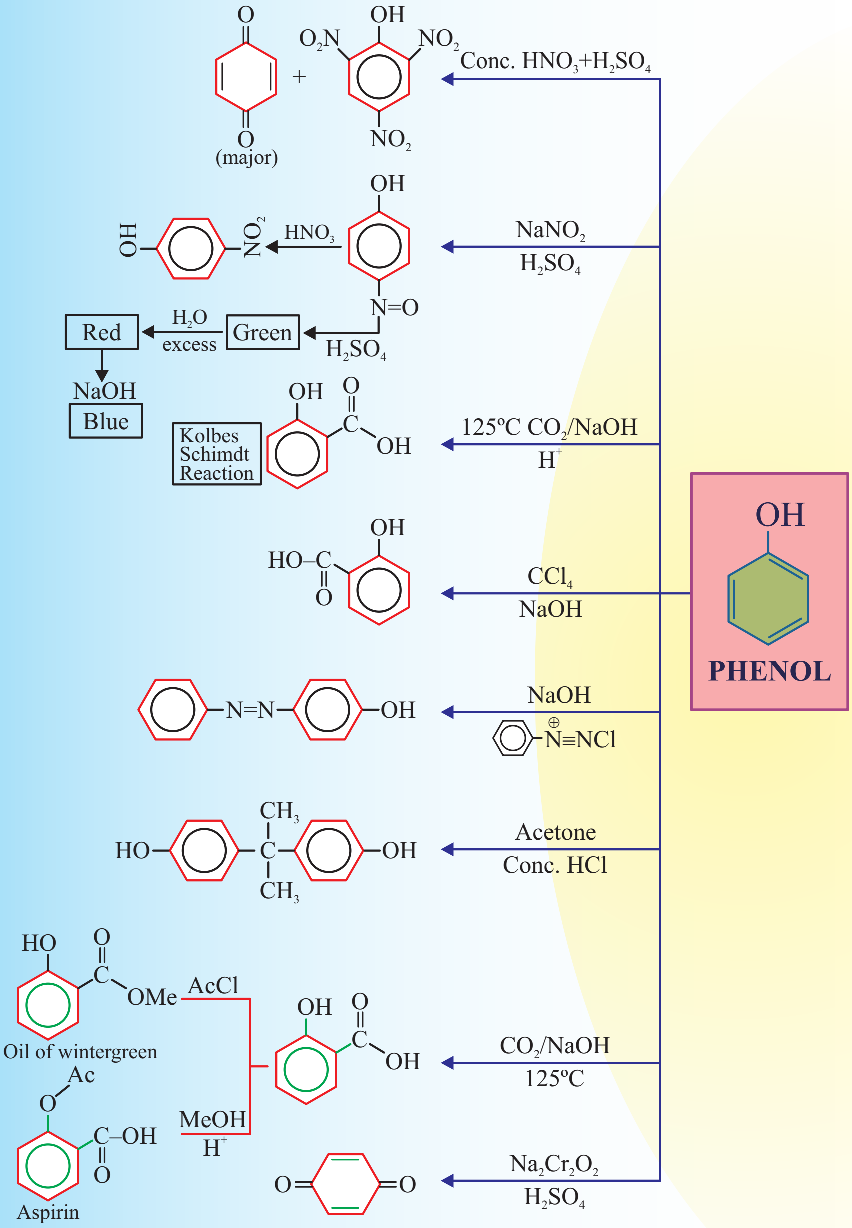
PHENOL
GMP

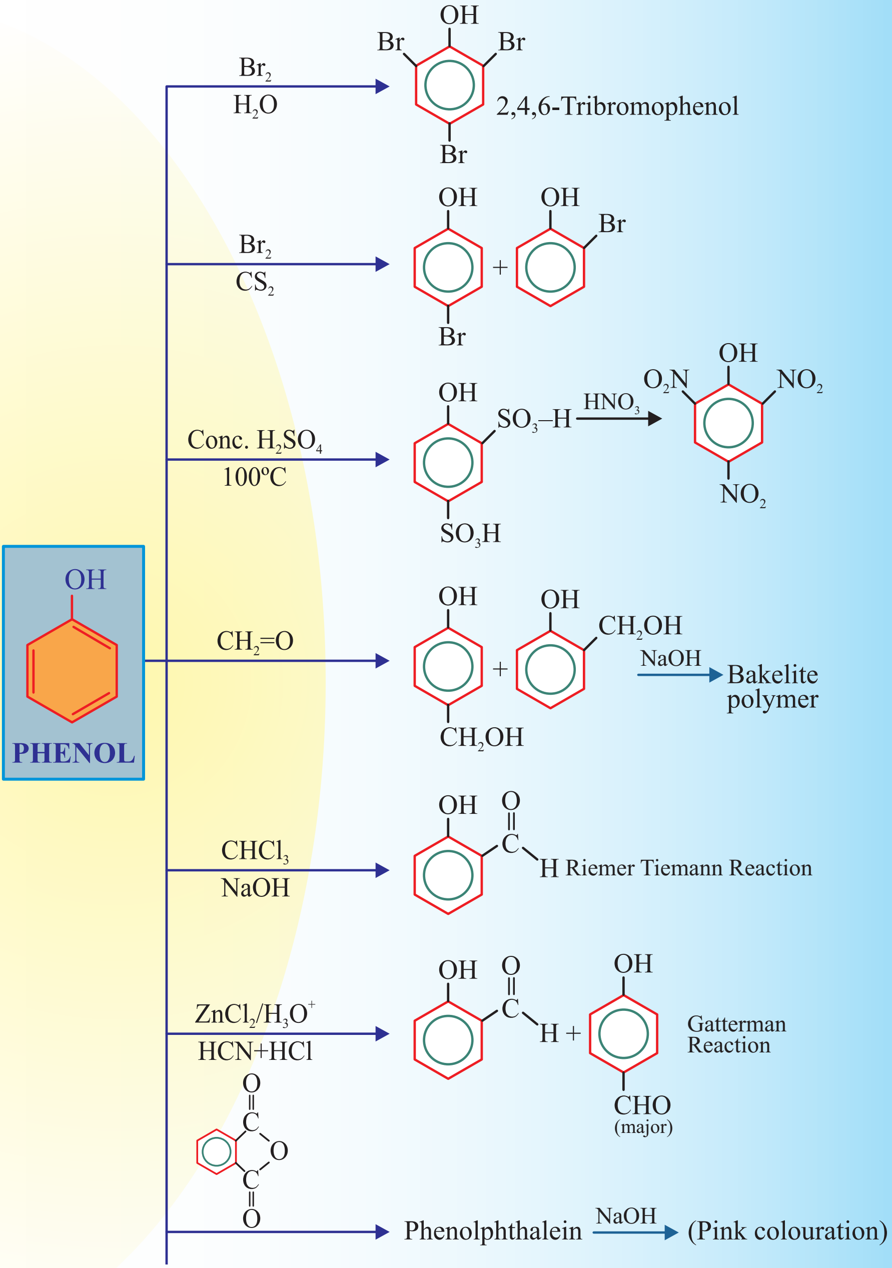




REACTIONS




PHENOL
OH
Conc. HNO$_3$+H$_2$SO$_4$
O$_2$N
NO$_2$
(major)
NaNO$_2$
H$_2$SO$_4$
HNO$_3$
N=O
H$_2$SO$_4$
Green
H$_2$O
excess
Red
NaOH
Blue
125ºC CO$_2$/NaOH
H$^+$
Kolbes Schimdt Reaction
CCl$_4$
NaOH
HO–C
NaOH
N≡NCl
N=N
Acetone
Conc. HCl
CH$_3$
CO$_2$/NaOH
125ºC
AcCl
OMe
Oil of wintergreen
Ac
C–OH
MeOH
H$^+$
Aspirin
Na$_2$Cr$_2$O$_2$
H$_2$SO$_4$


OH
PHENOL
Br2
H2O
OH
Br
Br
Br
2,4,6-Tribromophenol
Br2
CS2
OH
Br
+
OH
Br
Conc. H2SO4
100ºC
OH
SO3–H
SO3H
HNO3
OH
O2N
NO2
NO2
CH2=O
OH
CH2OH
+
OH
CH2OH
NaOH
Bakelite
polymer
CHCl3
NaOH
OH
O
C
H Riemer Tiemann Reaction
ZnCl2/H3O+
HCN+HCl
OH
O
C
H +
OH
CHO
(major)
Gatterman
Reaction
O
C
O
C
O
Phenolphthalein
NaOH
(Pink colouration)

Comparison of S_N1 and S_N2

Reactions		S_N1	S_N2
A	Kinetics	1st order	2nd order
B	Rate	k[RX]	k[RX] [$Nu:^{\ominus}$]
C	Stereochemistry	Racemisation	Inversion
D	Substrate (reactivity)	3° > 2° > 1° > MeX	MeX > 1° > 2° > 3°
E	Nucleophile	Rate Independent	Needs Strong Nu
F	Solvent	Good ionizing	Faster in aprotic
G	Leaving Group	Needs Good LG	Needs Good LG
H	Rearrangement	Possible	Not Possible

Comparison of E_1 and E_2

Reactions		E_1	E_2
A	Kinetics	1st order	2nd order
B	Rate	k[RX]	k[RX] [$B:^{-}$]
C	Stereochemistry	No special geometry	Anti-periplanar
D	Substrate	3° > 2° >>> 1°	3° > 2° > 1°
E	Base Strength	Rate Independent	Needs Strong bases
F	Solvent	Good ionizing	Polarity not import
G	Leaving Group	Needs Good LG	Needs Good LG
H	Rearrangement	Possible	Not Possible

Summary of S_N1, S_N2, E_1 and E_2 Reactions

RX	Mechanism	$\overset{\ominus}{Nu}/\overset{\ominus}{B}$	Solvent	Temp.
1°	S_N2	Better $\overset{\ominus}{O}H, C_2H_5\overset{\ominus}{O}$	Polar aprotic	Low
	E_2	Strong & bulky base $(CH_3)_3C\overset{\ominus}{O}$		High
2°	S_N2	$H\overset{\ominus}{O}; C_2H_5\overset{\ominus}{O}$	Polar aprotic	Low
	E_2	$(CH_3)_3C\overset{\ominus}{O}$		High
	(S_N1)	(Solvent)	Polar protic	(Low)
	(E_1)	(Solvent)		(High)
3°	S_N1	Solvent	Protic	Low
	E_1	Solvent	Protic	High

	Primary (1°)	**Secondary (2°)**	**Tertiary (3°)**
Strong nucleophile	$S_N2 >> E_2$	S_N2+E_2 (if weak base, S_N2 favored)	E_2
Weak nucleophile weak base	Mostly S_N2	Mostly S_N2/S_N1	Mostly S_N1 at low T mostly E_1 at high T
Weak nucleophile strong base	Mostly E_2	Mostly E_2	E_2

Order of reactivity of Allylic Halide towards

$S_N1 \propto$ Benzylic > Allylic > $3^\circ > 2^\circ > 1^\circ$

$S_N1 \propto$ Stability of carbocation

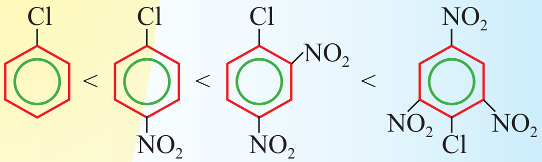
$S_N2 \propto 1^\circ > 2^\circ > 3^\circ$

$$S_N2 \propto \frac{1}{\text{Steric hindrance}}$$

Reactivity order towards S_N1 or S_N2 and E_1 or E_2

$$R–I > R–Br > R–Cl > R–F$$

With increase in number of strong electron withdrawing group at ortho and para position, reactivity of X towards aromatic nucleophilic substitution increases.



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