REDOX REACTIONS IN ORGANIC CHEMISTRY

Oxidation and Reduction: an atom is considered to be reduced if it gains electrons and to be oxidised if it loses electrons

This concept can be applied to carbon to decide in any reaction it has been reduced or oxidised; the following rules are important:

1. Elemental Carbon has an oxidation no of 0;

2. The oxidation state of any chemically bonded Carbon is assigned as -1 for each more electropositive atom which is attached, and +1 for each more electronegative atom. In practice, this means:

$$-1 \quad \text{for H, B, Na, Li, Mg}$$
$$+1 \quad \text{for O, N, S, X}$$
$$0 \quad \text{for C}$$

3. In compounds with multiple bonds, each atom is counted as often as the multiple bond dictates, e.g.

Oxidation Numbers of Common Functional Groups

Compound Class					Oxidation Number				
	-4	-3	-2	-1	0	+1	+2	+3	+4
Hydrocarbons (saturated)	CH_4	RCH_3	R_2CH_2	R_3CH	R_4C				
Hydrocarbons (unsaturated)			$CH_2=CH_2$	$HC\equiv CH$					
Alkyl Halides			CH_3X	RCH_2X	CH_2X_2	$RCHX_2$	CHX_3	RCX_3	CX_4
Alcohols			CH_3OH	RCH_2OH	R_2CHOH	R_3COH			
Carbonyl Compounds					H_2CO $(H_2C(OR')_2)$	$RCHO$ $(RCH(OR')_2)$	$HC(O)OH$ R_2CO $(RCH_2(OR')_2)$	$RC(O)OH$	CO_2

Notes: R = alkyl or aryl
(b) A horizontal interconversion necessarily involves a redox reaction
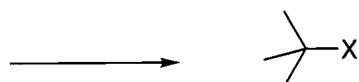(c) A vertical interconversion is **not** a redox reaction

Selective Oxidations

SUBSTRATE		REAGENT

Non-activated Carbon Atoms

$\rightarrow$ ─OH

Bugs, enzymes

$\rightarrow$ ─X

X_2 / hv

$\rightarrow$
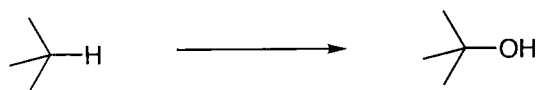
X_2 / hv or $ArICl_2$

Activated Non-functionalized Carbon Atoms

─H $\rightarrow$ ─OH

SeO_2

$\rightarrow$ =O

SeO_2, PDC

$\rightarrow$

SeO_2

$\rightarrow$ ─OH
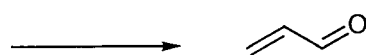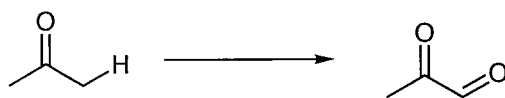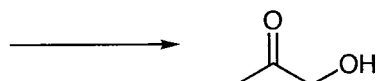
KO^tBu / $(EtO)_3P$ / O_2
or
LDA / $Mo(VI)O(O_2)_2$ / $HMPA$ /
py
(MoOOPH)

─Z $\rightarrow$ =Z
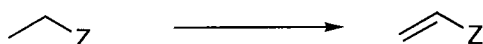
SeO_2
or (i) LDA / $PhSeBr$ (ii) H_2O_2
/$NaIO_4$

Carbon Atoms of C-C Double Bonds

$\rightarrow$
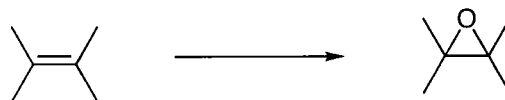
(i) HOX (ii) OH^-
or $RC(O)O\text{-}OH$
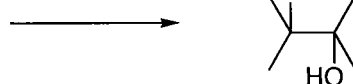
$\rightarrow$ *trans*

(i) $RC(O)O\text{-}OH$ (ii) OH^-
or (i) $AgOAc$ / I_2 (ii) OH^- or LAH

	cis	(i) AgOAc / I_2 / H_2O / AcOH

Reactions (left to right with reagents on right):

$$\longrightarrow \quad \text{(OH, OH — cis diol)} \quad cis$$

(i) AgOAc / I_2 / H_2O / AcOH
(ii) OH⁻ or LAH
or OsO_4

$$\longrightarrow \quad \text{(OH, X)}$$

HOX
or (i) (i) RC(O)O–OH (ii) HX

$$\longrightarrow \quad \text{(OH, X)}$$

CrO_2Cl_2

$$\longrightarrow \quad \text{(X, X)}$$

X_2 X = Cl, Br, I

$$\longrightarrow \quad \text{(H, OH)}$$

(i) B_2H_6 (ii) H_2O, OH⁻
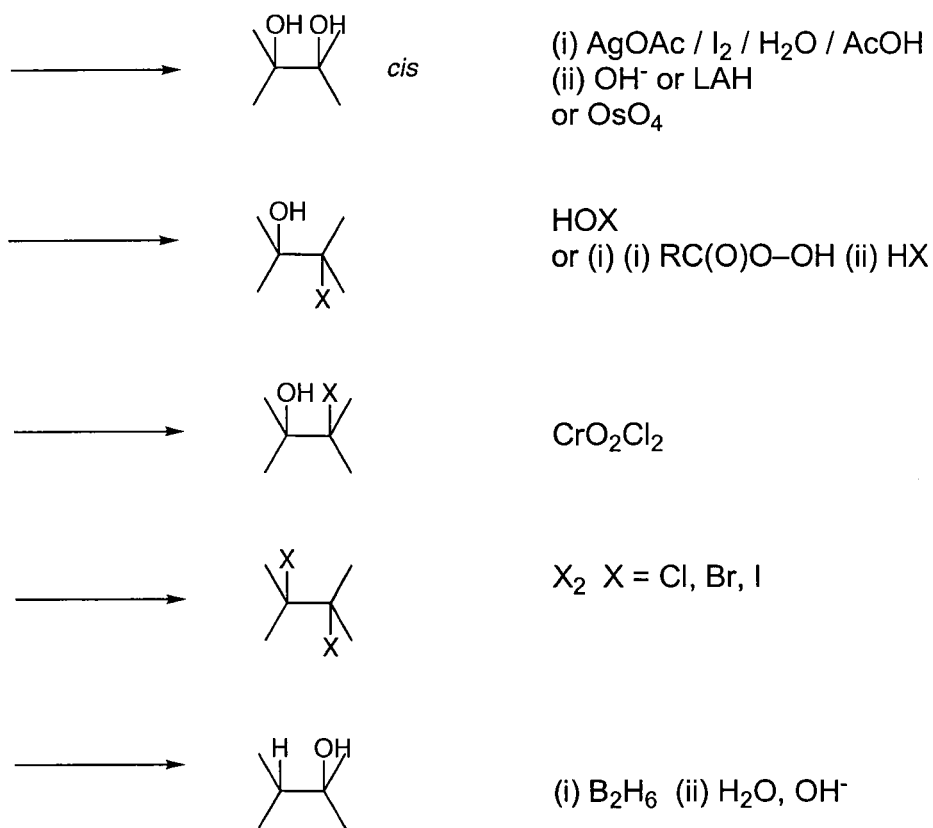
Carbon Atoms of C-C TripleBonds

$$R\!-\!\!\equiv\!\!-\!H \longrightarrow R\text{CH}_2\text{CHO}$$

(i) R_2BH (ii) H_2O_2 / OH⁻

$$\longrightarrow R\text{-C(=O)-CH}_3$$

Hg(II) / H⁺ / H_2O

$$R\!-\!\!\equiv\!\!-\!R' \longrightarrow R\text{-C(=O)-C(=O)-}R'$$

$KMnO_4$ or $Ru\,O_4$

$$R\!-\!\!\equiv\!\!-\!H \longrightarrow R\text{-COOH}$$
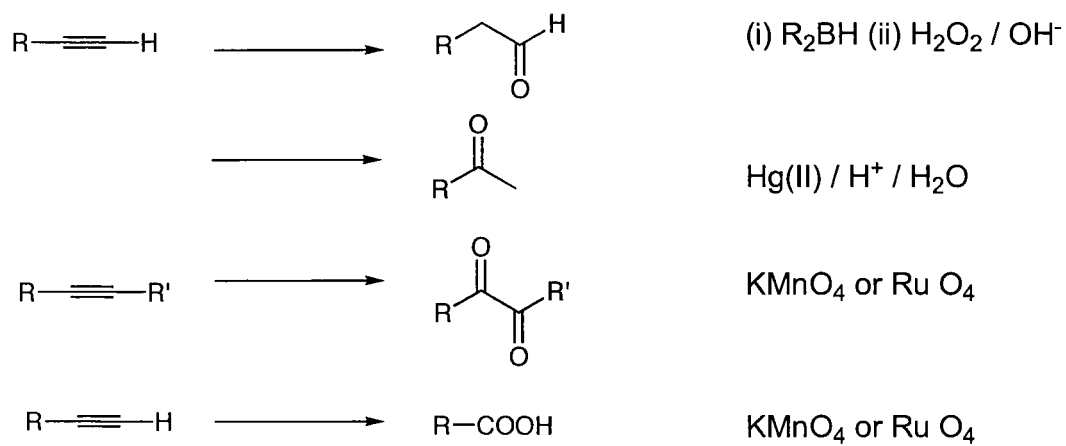
$KMnO_4$ or $Ru\,O_4$

Oxygen Containing Functional Groups

PDC or PCC
or Me_2CO / $Al(OiPr)_3$
or DMSO + E^+
E^+ = DCC or Ac_2O or SO_3 or P_4O_{10}
or $COCl_2$ or $(COCl)_2$

Ag_2CO_3 or $Pb(OAc)_4$

R—COOH   Most strong [O]

RuO_4
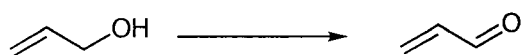
MnO_2 or DDQ
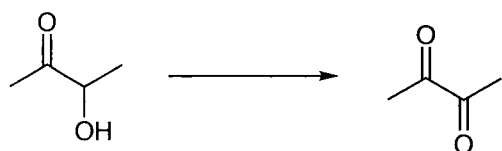
$Cu(OAc)_2$

Rearrangements & Cleavages
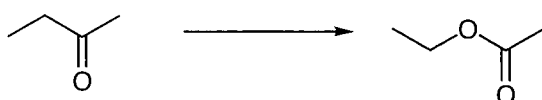
RC(O)OOH
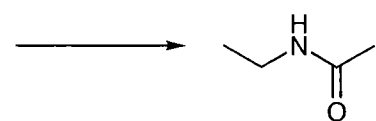
(i) NH_2OH (ii) H^+

CrO_3 or $KMnO_4$
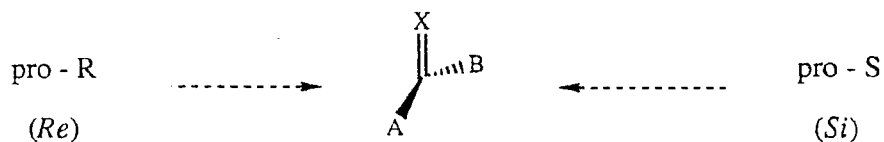or
(i) SeO_2 (ii) HIO_4

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REDUCTION

One of the most important Functional Group Interconversions which is very frequently performed in organic synthesis is that of reduction. Modern organic synthesis depends very heavily on a range of reducing agents, amongst the most useful of which are the hydride-donor reducing reagents. A selection of the more commonly used reagents are shown below, along with the substrates with which they react, and the products which are obtained.

REDUCING AGENT \ SUBSTRATE	$R\text{-}COCl$	$RCHO$	$R\text{-}CO\text{-}R$	$R\text{-}CO\text{-}OR$	$R\text{-}CO\text{-}NHR$	$RCOO^{\ominus}$
$LiAlH_4$	RCH_2OH	RCH_2OH	$R\text{-}CH(OH)\text{-}R$	RCH_2OH	RCH_2NHR	RCH_2OH
$LiAl[O\text{-}t\text{-}Bu]_3$	$RCHO$	RCH_2OH	$R\text{-}CH(OH)\text{-}R$	RCH_2OH	$RCHO$	NR
$NaBH_4$	—	RCH_2OH	$R\text{-}CH(OH)\text{-}R$	NR	NR	NR
$NaBH_3CN$	—	RCH_2OH	NR	NR	RCH_2NHR	NR
B_2H_6	—	RCH_2OH	$R\text{-}CH(OH)\text{-}R$	NR	RCH_2NHR	RCH_2OH
AlH_3	RCH_2OH	RCH_2OH	$R\text{-}CH(OH)\text{-}R$	RCH_2OH	RCH_2NHR	RCH_2OH
$\searrow\!\!\nearrow BH$	—	RCH_2OH	$R\text{-}CH(OH)\text{-}R$	NR	$RCHO$	NR
$\searrow\!\!\nearrow AlH$ (DIBAL)	—	RCH_2OH	$R\text{-}CH(OH)\text{-}R$	$RCHO$	$RCHO$	RCH_2OH

Another particularly important aspect of reductions is that of selectivity, i.e. the ability to reduce one functional group in preference to another within the same molecule (this is sometimes called CHEMOSELECTIVITY). The Table below gives a general outline of the relative reactivity of different reducing agents with different functional groups.

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REACTIVITY	CATALYTIC HYDROGENATION	COMPLEX HYDRIDES	BORANES
HIGH	$-C\equiv C-$ $>C=C<$ $-COCl$, $-CN$	$-COCl$, $-CHO$ $>C=O$, $>C=N-$	$-C\equiv C-$, $>C=C<$ $COOH$, $CONR_2$, $-C\equiv N$
MEDIUM	$-CHO$ $>C=O$ $-NO_2$ $Ar-\wedge OR$ $\sim OR$ (ketone) $>C-X$ (epoxide) HETEROARENES	(epoxide) $\sim OR$ $Ar-\wedge OR$ $COOR$, $CONHR$ CN $>C-X$ NO_2 $COO^{\ominus}$	CHO $>C=O$ $-CONR_2$ $C\equiv N$ (epoxide)
LOW	$-COOR$ $-CONR_2$ ARENES		
VERY LOW	$-COOH$ $-COO^{\ominus}$	$-C\equiv C-$ $>C=C<$	ARENES

In reactions of this type, there is an additional element of complication, in that the approach of any reducing agent to an sp^3 centre can approach, in principle, from one of two faces, to give enantiomeric products:

$$
\begin{array}{ccccc}
\text{pro - R} & \dashrightarrow & \overset{X}{\underset{A}{\overset{\|}{\big|}}}{\cdots}B & \dashleftarrow & \text{pro - S} \\
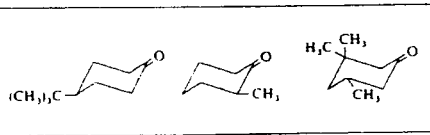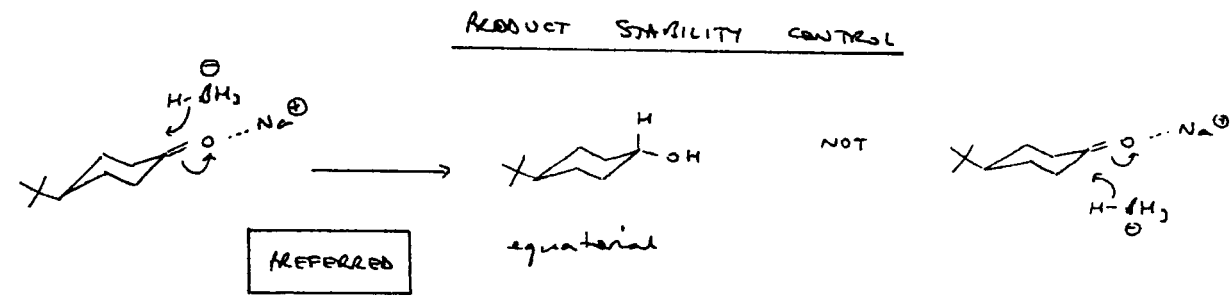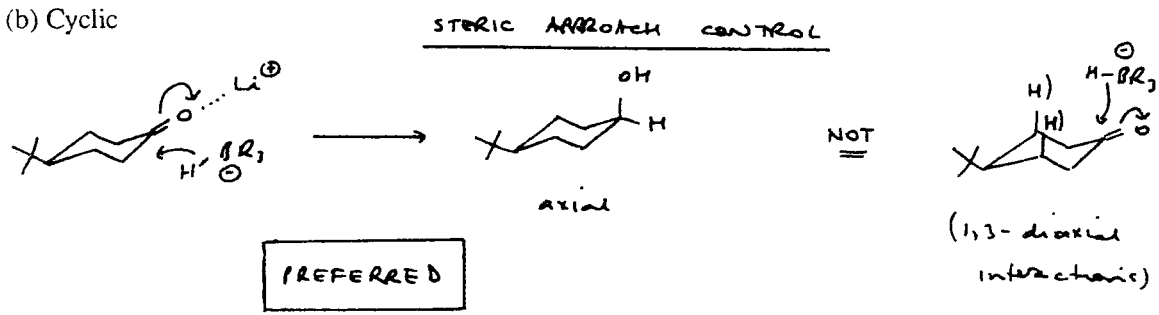(Re) & & & & (Si)
\end{array}
$$

Cahn-Ingold-Prelog Priority A > B > C

(atomic number sequence)

performed on a chiral substrate, then diastereomeric products are possible. There are two important reaction classes:

(a) Acyclic - Cram's Rule

(b) Cyclic

STERIC APPROACH CONTROL

PREFERRED

axial

NOT

(1,3- diaxial interactions)

PRODUCT STABILITY CONTROL

PREFERRED

equatorial

NOT

Reducing agent	% axial	% axial	% axial
NaBH₄	20[b]	25[c]	58[c]
LiAlH₄	8	24	83
LiAl(OMe)₃H	9	69	
LiAl(t-BuO)₃H	9[c]	36[f]	95
(CH₃CH₂CH—)₃BH Li⁺ (CH₃)	93[g]	98[g]	99.8[g]
[(CH₃)₂CHCH(CH₃)]₃BH Li⁺	>99[h]	>99[h]	