SLT INSTITUTE OF PHARMACEUTICAL SCIENCES

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MODEL ANSWER

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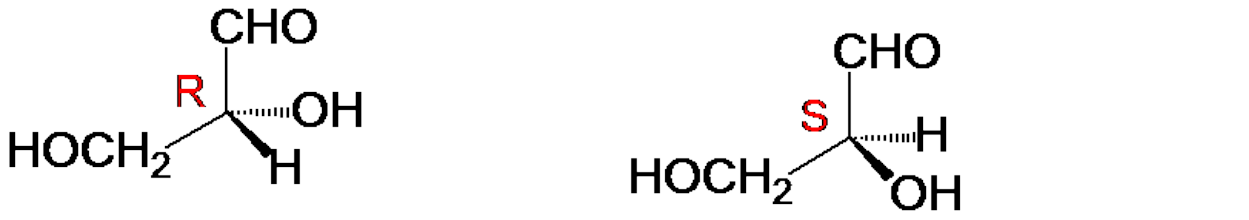
STEREOCHEMISTRY and REACTION MECHANISM

Paper: Fourth (Elective)

SECTION A

1.(i)The structures of enantiomers differ only in 'handedness' are being left handed and the other being right handed. Any molecule which is not superimposible to its mirror images and having different groups or atoms attached is said to posses chiralty (Gk Kher, hand). Thus the term chiralty means 'having handleness'.

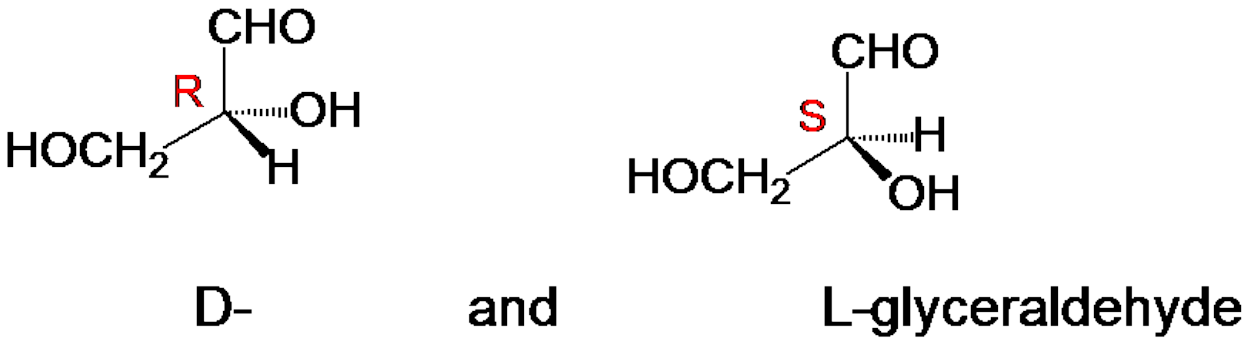
Example includes Glyceraldehyde (structure), Glucose (Structure).



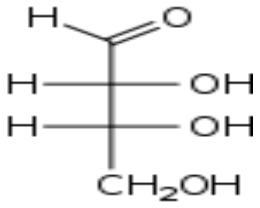
D- and L-glyceraldehyde

(ii) Configuration is the arrangement in space of the atoms or groups around the disymmetric or rigid part of a molecule –in the simplest case around an asymmetric carbon. For example the formulas for (+) and (-) lactic acid represent molecules of identical structure but different configuration. It should not have restricted rotation about single bond. It may be absolute and relative configuration.

Configuration of Glyceraldehyde: D-Glyceraldehyde(Structure) and LGlyceraldehyde (Structure)

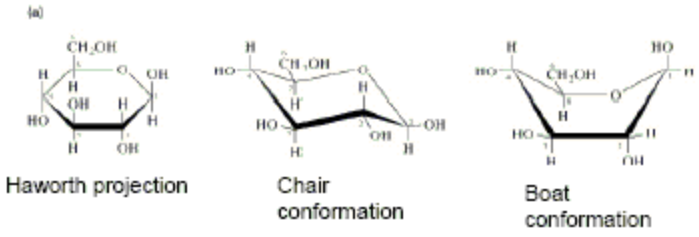


(iii)



Erythreo form of aldotetrose

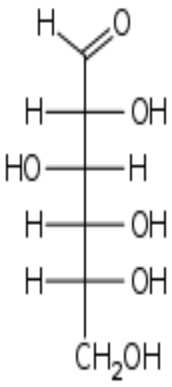
(iv) Conformation is used to denote any one of the infinite number of momentary arrangements of the atoms in space that result from rotation about single bonds. Different types of conformations are “gauche” or “skew”; “trans” or “anti”. Conformation influences physical properties.

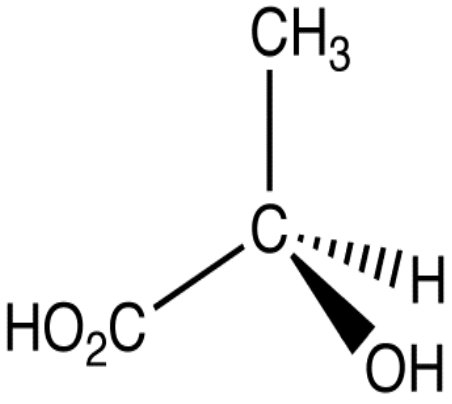


(v) In the configuration of asymmetric carbon atom containing compound, the four groups are ordered as per the sequence rule. According this rule, the groups are arranged in decreasing

atomic number of the atoms by which they are bound to the asymmetric carbon atom. If two or more of these atoms have the same atomic number, then the relative priority of the groups is determined. The order of priority sequence as: I, Br, Cl, OH, NO_2, NH_2, COOH, CHO, $CH_{3, etc}$.

(vi) The dimensional presentation of a stereochemical compound as originally invented by Scientist Fischer. This formula uses two wedge, one is solid wedge which is outside the plane.





lactic acid

Fischer projection of D Glucose

(vii) Stereoselective synthesis is meant a synthesis that produces one diastereoisomer of a given structure in considerable predominance over all the other possible diastereoisomers of the same structure. It is usually concerned with the synthesis of optically active molecules. Example includes the synthesis of ephedrine from alpha methylaminopropiophenone.

Stereospecific synthesis is the property of a reaction that leads to different stereoisomeric reaction products from different stereoisomeric reactants, or which operates on only one (or a subset) of the stereoisomers. For example, dibromocarbene and *cis*-2-butene yield *cis*-2,3-dimethyl-1,1-dibromocyclopropane, whereas the *trans* isomer exclusively yields the *trans* cyclopropane.

(viii) The rule states that when the asymmetric carbon is so oriented that the carbonyl function is flanked by the two smaller groups (M and S) attached to C, the reagent (RX) preferentially approaches the carbonyl group from the side of the smallest group S. The rule applies only to

reactions that are kinetically controlled process, not the more stable product formed in a subsequent equilibrium.

(ix)Elimination reactions are the reverse of addition reactions and consists of removing the two groups (generally one being a proton) from one or two carbon atoms of a molecule to form an unillustrated linkage or centre.

$$RCH_2CH_2X \xrightarrow{OH^-} RCH{=}CH_2 + H_2O + X^-$$

(X) The rule states that the arrangement of the groups in the starting material must be specified first, since there are several bonds around which the molecule may rotate. By convention, the molecule is so oriented that the two carbonyl groups are antiparallel and that the smallest group in the alcohol portion is eclipsed with the ketone carbonyl.

(xi) The addition of conjugated diene to a second unsaturated molecule generally know as a "dienophile" resulting in the formation of a cyclic compound i.e., adduct. This reaction is known as Diels-Alder reaction. Example of dienophile includes acraldehyde, vinylmethylketone, cinnamaldehyde.

(xii) Beta-elimination: when the two groups or atoms are removed from the two adjacent carbon atoms, the process is known as beta-elimination. Alpha-elimination: when the two groups are eliminated from the same carbon atom, the process is known as alpha elimination.

SECTION B

2. Configuration is the arrangement in space of the atoms or groups around the disymmetric or rigid part of a molecule –in the simplest case around an asymmetric carbon. For example the formulas for (+) and (-) lactic acid represent molecules of identical structure but different configuration. It should not have restricted rotation about single bond. It may be absolute and relative configuration.

   The original method of indicating enantiomers was to prefix each one by d and l according as it was dextrorotatary or laevorotatary. Van't Hoff introduced as ' + 'and '-' notations for designating the configuration of an asymmetric carbon atom. Fischer

proposed that the prefixes d and l should refer to stereochemical relation ships and not to the direction of rotation of the compound. More recently the symbols d and l have been replaced by D and L for configuration relationships, eg, L (+) Lactic acid.

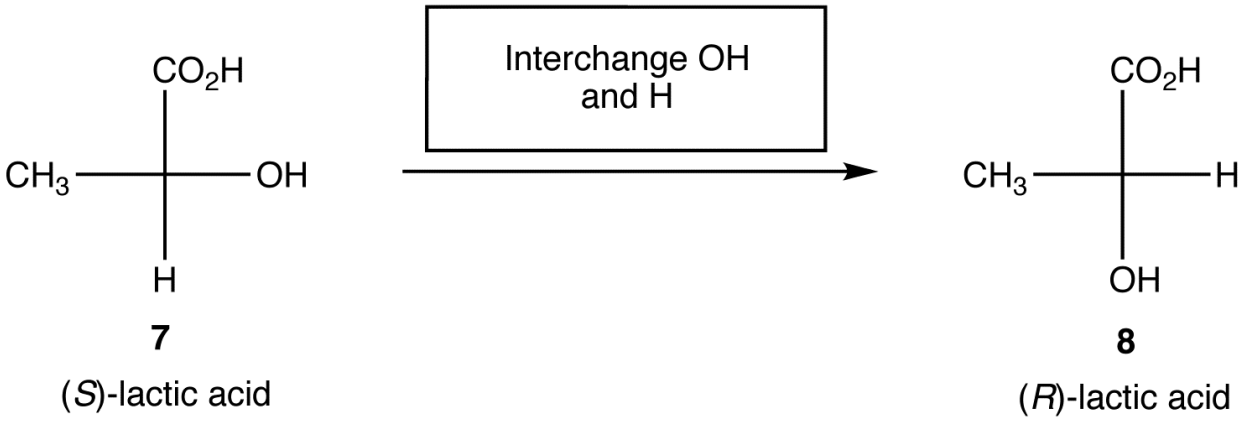
Since the configuration of (+) tartaric acid has been related to that of (+) glyceraldehydes, it is now possible to assign absolute configurations of many compounds whose relative configurations to (+) glyceraldehydes are known.
Cash et al (1964) have proposed such a system and this is now widely used. Let us consider the procedure for a molecule containing one asymmetric carbon atom (one chiral Centre).

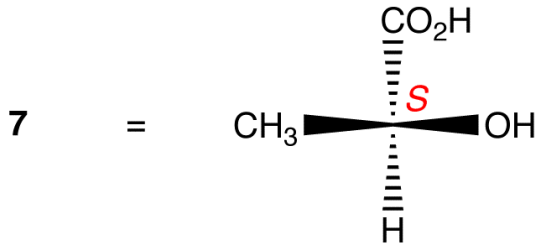
In the configuration of asymmetric carbon atom containing compound, the four groups are ordered as per the sequence rule. According this rule, the groups are arranged in decreasing atomic number of the atoms by which they are bound to the asymmetric carbon atom. If two or more of these atoms have the same atomic number, then the relative priority of the groups is determined by a similar comparison of the atomic numbers of the next atoms in the groups (The atoms joined to the atom joined to the asymmetric carbon atom). If this fails, then the next atom of the groups are considered. When multiple bonds or rings are present, the procedure for determining priority is as followings: Both atoms attached to the multiple bond are considered to be duplicated (for a double bond) or triplicate (for a triple bond). The priority sequence is then determined by consideration of the duplicated or triplicate structure in which there are phantom atoms.

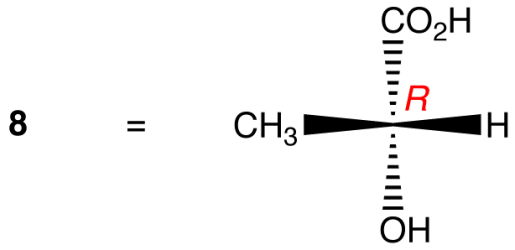
Ring systems are treated as branched chains and if unsaturated, then duplication is used for a double bond or triple bond. By using these rules, it can be shown that the order of priorty sequence as: I, Br, Cl, OH, NO_2, NH_2, COOH, CHO, $CH_{3,\ etc}$.

Next is determined whether the sequence describes a right or left handed pattern on the molecular model as viewed according to the conversion rule. When the four groups in the molecule Cabcd have been ordered in the priority a,b,c,d the conversion rule states that their spatial pattern should be described as right or left handed according as sequence a-b-

c-d is clockwise or anticlockwise when viewed from an external point on the side remote from d (the group with the lowest priority).







Absolute configurations labels are assigned under the sequence and conversion rules to a right and left handed pattern as R and S respectively (R for rectus, right; S for sinister, left). Let us consider bromochloroacetic acid. The priority of the groups according to the sequence rule is Br (a), Cl(b), COOH (c), H (d). Hence, by the conversion rule, where –COOH group is right side it is R form (a-b-c-d is clockwise).

There are different methods for determining the Configurations, like

(i) Method of cyclization

(ii) Methods of conversion of compounds with known configuration

(iii) Method of conversion in less symmetric compounds

(iv) Methods of optical activity

(v) Method of dipole moments

(vi) X-ray analytical method

(vii) Spectroscopic method-IR, NMR, Mass spectroscopy

(viii) Method of surface films

(ix) Method of formation in solid solution

(x) Method based on observations of generalized physical properties

(xi) Method of stereoselective and stereospecific reactions

(xii) Methods of different addition and elimination reactions

(xiii) Methods of chemical treatment

(xiv) Misc.

Discussion of each method in short

3. Properties of racemic modification: The racemic modification may exist in three different forms in the solid state:

(a) Racemic Mixture: This is also known as (±) conglomerate and is a mechanical mixture of two types of crystals, the (+) and (-) forms; there are two phases present. The physical properties of the racemic mixture are mainly the same as those of its constituent enantiomers. The most important difference is the melting point.

(b) Racemic compound: This consists of a pair of enantiomers in combination as a molecular compound; Only one solid phase is present. The physical properties of a racemic compound are different from those of the constituent enantiomers, but in solution racemic compounds dissociate into the (+) and (-) forms.

© Racemic solid solution: This is also known as pseudo-racemic compound and is a solid solution (one phase system) formed by a pair of enantiomers crystallizing together due to their

being isomorphous. The properties of the racemic solid solution are mainly the same as those of its constituent enantiomer, the melting points differ.

Methods for determining the nature of racemic modification: One simple method of examination is to estimate the amounts of water of crystalisation in the enantiomers and in the racemic modification; if these are different, then the racemic modification is a racemic compound. Another simple method is to measure the densities of the enantiomers and the racemic modification; again, if these are different, the racemic modification is a racemic compound; e.g., tartaric acid.

	D Tartaric Acid	L Tartaric acid	Racemic tartaric acid
Melting point	170^0C	170^0C	206^0C
Water of crystallization	None	None	1 H_2O
Density	1.7598	1.7598	1.697
Solubility in H_2O (at 20^0C)	139 g/100 ml	139 g/100 ml	20.6 g/100 ml

There are, however, two main methods for determining the nature of a racemic modification: a study of the freezing point curves and a study of the solubility curves.

Freezing point curves: These are obtained by measuring the melting points of mixtures containing different amounts of the racemic modification and its corresponding enantiomers. Various types of curves are possible according to the nature of racemic modification. The melting points of all mixtures are higher than that of the racemic modification alone.

Solubility Curves: The interpretation of solubility curves is feasible but in practice, the following simple scheme based on solubility may be used. A small amount of one of the enantiomers is added to a saturated solution of the racemic modification and the resulting solution is then examined in a polarimeter. If the solution exhibits a rotation, then the racemic modification is a compound, but if the solution has a zero rotation, the racemic modification is a mixture or a solid solution.

Infrared spectroscopy is also being used to distinguish a racemic compound from a racemic mixture or a racemic solid solution. In the latter, the spectra are identical, but are different in the former. These observations are also true for X-ray powder diagram and so X-ray analysis in the solid state may also be used.

4. Resolution of Racemic modification:

Resolution is the process whereby a racemic modification is separated into its two enantiomers. In practice, the separation may be far from quantitative and in some cases only one form may be obtained. Furthermore, the form isolated need not be optically pure, ie, it may consist of the (+) and (-) forms in unequal amounts, but in this case the process is usually refereed to as partial resolution. A large variety of methods for resolution have now been developed and the method used in a particular case depends largely on the chemical nature of the compound under consideration.

a. Mechanical separation: This method is also known as spontaneous resolution by crystallization and was introduced by Pasteur (1848). It depends on the crystallization of the two forms separately, which are then separated by hand. The method is applicable only for racemic mixtures where the crystal forms of the enantiomers are themselves enantiomorphous. Pasteur separated sodium ammonium racemate in this way. The transition temp of sodium ammonium racemate is 28^0C; above this temp the racemic compound crystalises out and below this temp the racemic mixture. Now Pasteur crystallized his sodium ammonium racemate from a conc solution at room temp, which must have been below 28^0C, since, had the temp been above this, he would have obtained the racemic compound, which cannot be separated mechanically. Actually, Staedel (1878) failed to repeat Pasteur's separation since he worked at a temp above 28^0C.
b. Preferential crystallization by inoculation: A supersaturated solution of the racemic modification is treated with a crystal of one enantiomer (or an isomorphous substance) , whereupon this form is precipitated. The resolution of glutamic acid by inoculation has been perfected for industrial use. Harada et al have also resolved the copper complex of DL aspartic acid by inoculation. Resolution was effected by seeding the supersaturated aqueous solution with pure crystals of L or D isomer of the amino acid.

c. Biochemical separation: Certain bacteria and moulds, when they grow in a dilute solution of a racemic modification, destroy one enantiomer more rapidly than the other, eg, *Penicillium glaucum* (a mould), when grow in a solution of racemic ammonium tartrate, attacks the (+) form and leaves the (-) form.

   The biochemical method of separation has some disadvantages:

   a. Dilute solution must be used and so the amounts obtained will be small.
   b. One form is always destroyed and the other form is not always obtained in 50% yield since some of this may also be destroyed.
   c. It is necessary to find a microorganism which will attack only one of the enantiomer.
   d. Chromatography: Optically active substances may be selectively adsorbed by some optically active adsorbent, eg, Henderson and Rule (1939) partially resolved p-phenylenebisiminocamphor on lactose as adsorbent. Bradley and Easty have found that wool and casein selectively adsorb (+) mandelic acid from an aqueous solution of (±) mandelic acid. A particularly important case of resolution by chromatography is that of Troger's base.

      More recently, enzymic and chromatographic methods have been developed for the direct separation of enantiomers. GSC and GLC have been used with great success for resolving racemic modifications, eg, s-butanol and s-butyl bromide have been separated into two overlapping fractions using a column of starch or ethyltartrate as the stationary phase.
   e. Kinetic method of resolution: Mackwald and Mckemie found that (-) menthol reacts more slowly with (-) mandelic acid than with the (+) acid. Hence, if insufficient (-) menthol is used to completely esterify (±) mandelic acid, the resulting mixture of diastereomers will contain more (-) menthyl (+) mandelate than (-) menthyl (-) mandelate. Consequently, there will be more (-) mandellic acid than (+) mandelic acid in the unchanged acid, i,e., a partial resolution of (±) mandelic acid has been effected.
   f. Channel complex formation: It is also used for resolving racemic modifications. This also offers a means of carrying out a resolution without chiral reagents, eg, Schlenk added 2 chloro octane to a solution of urea and obtained on fractional crystallization, the two urea inclusion complexes urea/(+) 2 chloro octane and urea/(-) 2 chloro

octane. Baker et al (1952) have prepared tri-o-thymotide and found that it formed clathrates with ethanol, n hexane etc. Powel et al (1952) have shown that tri-o-thymotide crystalises as a racemate but that resolution takes place when it forms clathrates with n hexane, benzene or chloroform.

g. Resolution by formation of Diastereoisomers (Second order asymmetric transformation): When a racemic modification is allowed to interact with an optically active material to give a derivative (such as a salt), in actual fact two diastereoisomeric derivatives result.In this case two types of salt molecule are evidently no longer enantiomers, but diastereoisomers. Although distillation and chromatographic separation have been employed , the most efficient methods of separating such diastereoisomers is by crystallization.

Acids: The alkaloids brucine, strychnine, ephedrine, quinine, quinidine, cinchonidine and morphine have been frequently used to resolve optically active acids.

Bases: The camphorderivatives camphor-10-sulphonic acid, hydroxymethylene camphor and camphoric acid; the naturally occurring active form of tartaric acid and malic acid have been used for resolution.

Amino acids: Because of their dipole character, amino acids cannot usually be resolved as such using either optically active acids or active bases as resolving agents. Some basic amino acids, which contain a free as well as a zwitterionic amine function, have been resolved by means of organic acids: thus (+)tartaric acid has been employed to resolve (±) histidine and (±)tyrosine may be resolved by means of (+) glutamic acid. Commonly, however, amino acids are resolved in the form of their acyl derivatives.

Alcohols: Alcohols are most often resolved by prior conversion to their acid phthalate or succinate esters, formed by treating the alcohol with phthalic or succinate anhydride and pyridine. These half esters are then resolved on typical acids, eg, by means of the alkaloids brucine and cinchonidine. The pure diastereoisomers salts, obtained after repeated recrystalisation are decomposed in the usual way. The half ester is then either saponified by treatment with hot aq NaOH.

Aldehyde and ketone: A few derivatives of naturally active substances, such as menthylsemicarbazide, menthylhydrazine have been used to resolve carbonyl

compounds that these reagents form with carbonyl compounds are all of the hydrazone type.

Miscellaneous: Compounds devoid of functional groups such as saturated hydrocarbons or possessing only weakly reactive functional groups such as unsaturated and aromatic hydrocarbons, ethers, allyl, halides and a variety of sulphur compounds require special methods for resolution.

5. Physical properties of substituted cyclohexanes: The rule summarizes the relationship between certain physical properties and conformation was first developed by Von Auwers and by Skita and in generally known as the "Van Auwers Skita rule" or "Conformational rule". An up-to-date statement of this rule is that among alicyclic epimers not differing in dipole moment the isomer of highest heat content (enthalpy) has the higher density, index of refraction and boiling point. An application of the rule to the dimethylcyclohexane is shown in the following table.

Isomer	conformation	BP^0C	n_D^{25}	D^{25}_4
Cis 1,2	e,a	129.7	1.4336	0.7922
Trans 1,2*	e,a	123.4	1.4247	0.7720
Cis 1,2	e,a	120.1	1.4206	0.7620
Trans 1,2	e,a	124.5	1.4284	0.7806

The relation of molecular volume to heat content and boiling point is less obvious but may be rationalized as follows: Increased molecular volume means increased distance both between non-bonded atoms within the same molecule and also between adjacent molecules in a liquid or gas. The former results in lesser intramolecular crowding and therefore lesser heat content, the latter in diminished van der Waaals attraction and therefore lower boiling point.

A few exceptions to the Von Auwer-Skita rule are known. For example, it does not apply to the boiling points of the alkylcyclohexanols, here the e,e isomers, while having the lower enthalpy, refractive index and density are more strongly hydrogen bonded than the e,a isomers (the axial hydroxyl group being less well disposed for hydrogen bonding) and therefore boil at a higher temp. Also, the rule does not apply to

isomers differing appreciably in dipole moments. Such isomers follow the "Van Arkel Rule" or "Dipole Rule" according to which the isomer of higher dipole moment has the higher physical constants, regardless of heat content.

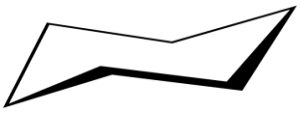
Evidently the conformational rule may be used to assign configurations to epimers when the more reliable methods cannot be readily applied. Physical properties other than those summarized in the conformational rule have been studied as a function of conformation and these, also may be used to make tentative configurationally assignments to epimers. For example, equatorial substituent usually shows typical infrared absorption at higher frequencies (shorter wavelength) than axial substituents. Thus the C=O stretching frequency of a number of equatorial steroid alcohols is found around $1040cm^{-1}$, whereas the corresponding stretching frequency for axial alcohols occurs at about $1000cm^{-1}$ at least when tha A/B ring junction is trans.

Conclusions as to configuration based on dipole moment studies or measurements of acid strength are usually more reliable, since they are based on more clear cut theoretical aspects. The 1,2 dibromocyclohexanones may be cited as an example of dipole studies. The moment for the diaxial isomer is assumed to be zero, the calculated moment for either the diequatorial or the equatorial axial isomer is 3.09D. The observed moments for the two known isomers are 3.12 and 2.11D respectively.

Turning now to acid strength measurements, the difference between the first and 2^{nd} ionization constants in cyclohexane-cis-1,2-dicarboxylic acid (aq solution) compared to 2.42pk units, whereas the corresponding difference for the trans isomer is 1.75pk units.

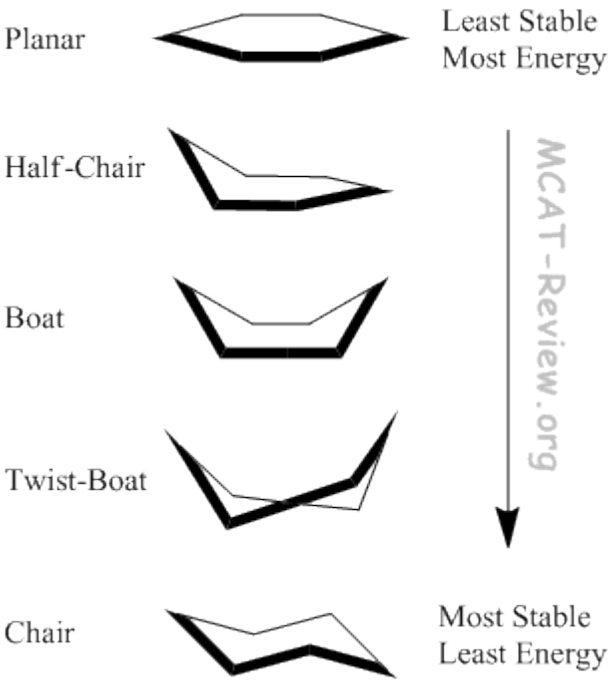
A more subtle difference is found between the acid strength of cis and trans 4-t-butylcyclohexanecarboxylic acid. The trans acid is stronger because the corresponding anion is more readily solvated than that of the cis acid which being axial encounters some steric hindrance to salvation.

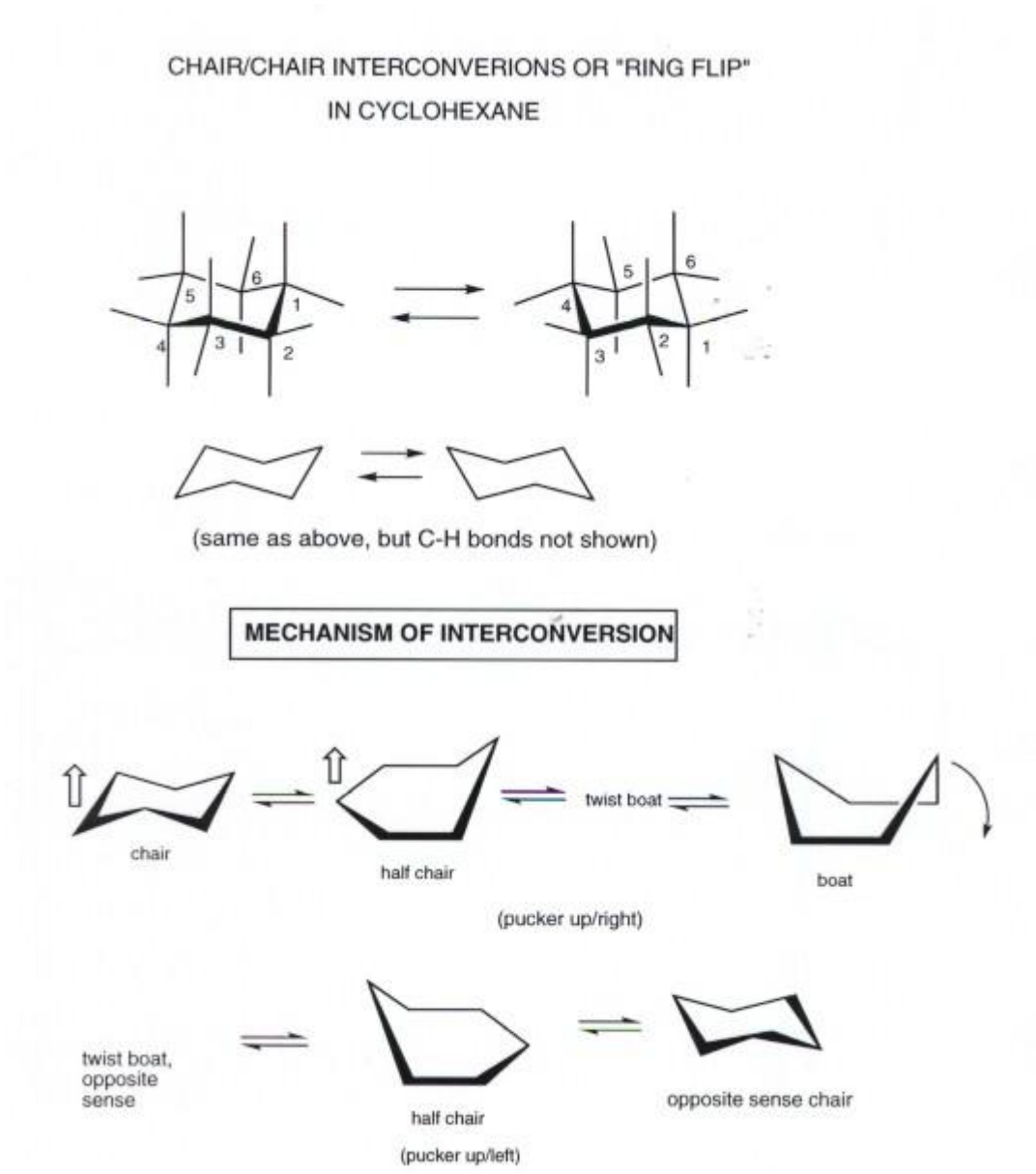
planar conformation



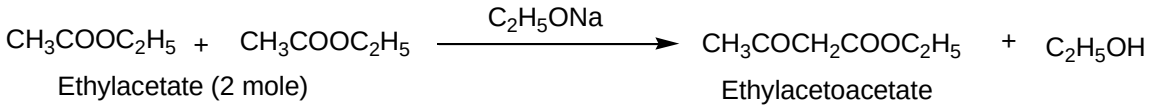
chair conformation

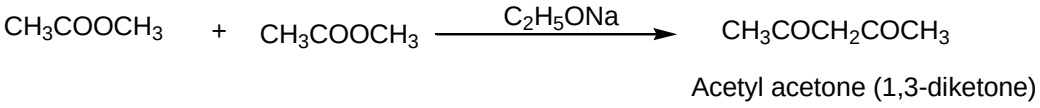
boat conformation





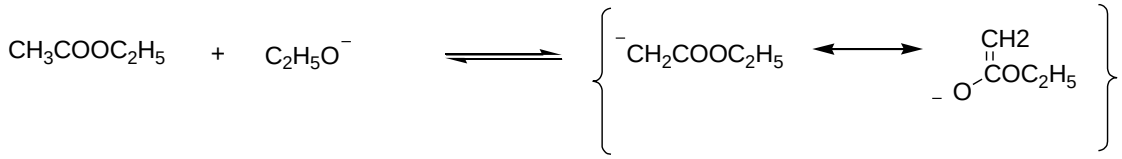
6. The condensation of ester and α-hydrogen containing ester, ketone and nitrile to form α β-ketoester, ketone or nitrile repectively is known as Claisen Condensation. The condensation is catalysed by sodium ethoxide, sodamide, triphenylmethyl sodium, etc. The most common and simplest example is the condensation of ethyl acetate in the presence of ethoxide ion to form ethyl acetoacetate.



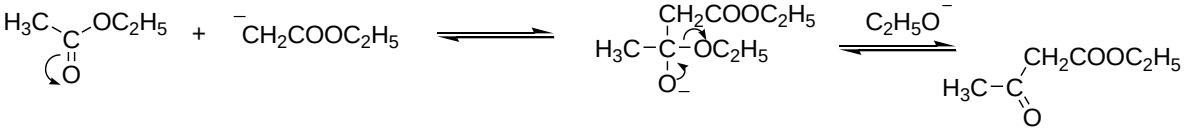


Mechanism: The ethoxide ion from sodium ethoxide remove a proton from a molecule of ethyl acetate two give a carbanion I. The carbonion adds to the carbonyl group of the second molecule of the ester or ketone and forms anion II, which loss ethoxide ion two yield β-keto ester, have a CH2 group between two carbonyl groups, ionizes evan more readily than ethyl acetate (the ethoxide ion present facilitates this) and thus enolate anion III, which is stabilized by mesomerism, is formed. Acidification of III regenerates the β-keto ester.

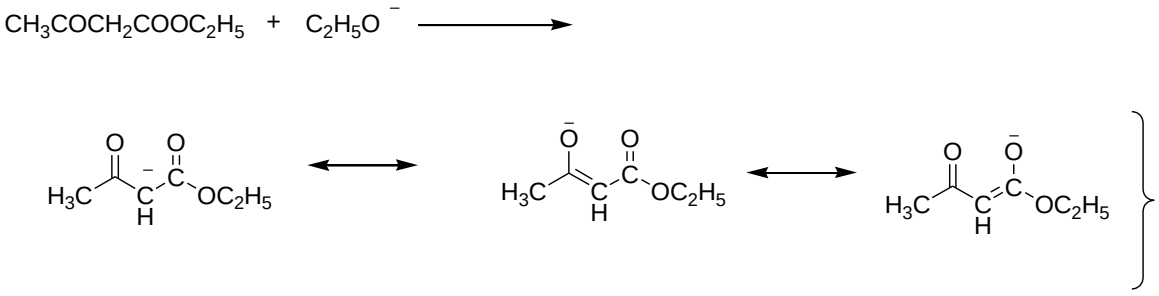
Step I



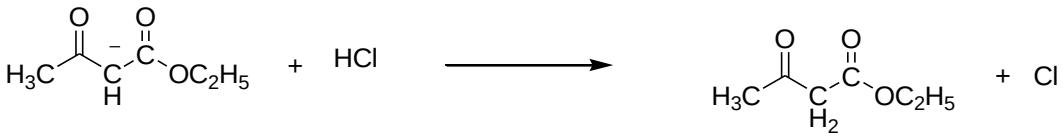
Step II



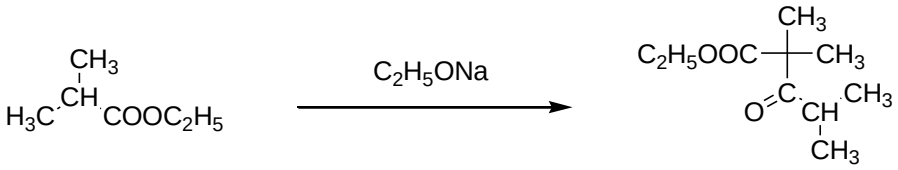
Step III

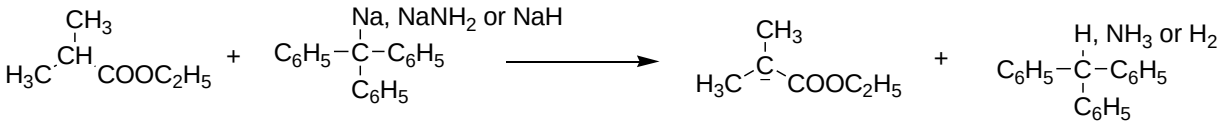


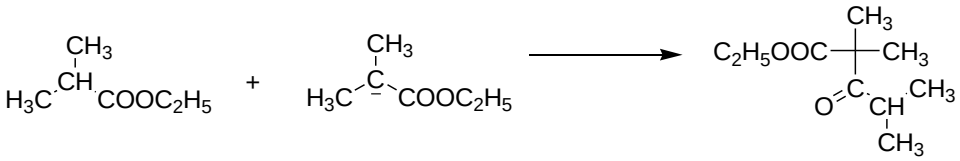
Acidification



The last step (III) ia an essential feature of the reaction as it helps to force the equilibrium of the first step to the right. The importance of the step can be proved by the fact that condensation can't affected by with sodium ehoxide when the expected product (β-keto ester) does not contain a C-H bond adjacent to both ethylisobutyrate (or ester without two α hydrogen atoms) does not goes Claisen Condensation in the presence of C2H5ONa because the β-keto ester does not contain a C-H bond, of the above mentioned type, necessary to displace the equilibrium to right.







However, ethylisobutyrate can also be made to undergo Claisen condensation in presence of either very strong base or a base that reacts irreversibly, viz sodium triphynylmethyl, mesityl magnesium bromide, NaH, in place of C2H5ONa because in the former case the second product of the acid base reaction escapes as a gas and thus the first condensation proceeds only to right.

7. Oxidation and reduction reactions occur in pairs: if one species is oxidized, another must be reduced at the same time - thus the term 'redox reaction'.

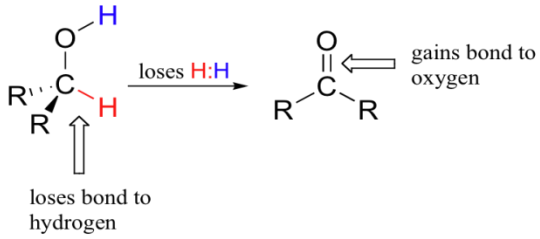
Most of the redox reactions involved the flow of electrons from one metal to another, such as the reaction between copper ion in solution and metallic zinc:

$Cu^{+2}_{(aq)} + Zn_{(s)} \rightarrow Cu_{(s)} + Zn^{+2}_{(aq)}$

In organic chemistry, redox reactions look a little different. Electrons in an organic redox reaction often are transferred in the form of a hydride ion - a proton and two electrons. Because they occur in conjunction with the transfer of a proton, these are commonly referred to as **hydrogenation** and **dehydrogenation** reactions: a hydride plus a proton adds up to a hydrogen (H_2) molecule. Do not confuse the terms hyd**rogen**ation and dehy**drogen**ation with hydration and dehydration - the latter refer to the gain and loss of a *water* molecule (and are *not* redox reactions), while the former refer to the gain and loss of a *hydrogen* molecule.

When a carbon atom in an organic compound loses a bond to hydrogen and gains a new bond to a heteroatom (or to another carbon), the compound has been dehydrogenated, or oxidized. A very common biochemical example is the oxidation of an alcohol to a ketone or aldehyde:

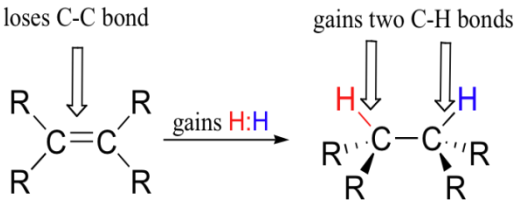
Dehydrogenation (oxidation) of an alcohol



When a carbon atom loses a bond to hydrogen and gains a bond to a heteroatom (or to another carbon atom), it is considered to be an oxidative process because hydrogen, of all the elements, is the least electronegative. Thus, in the process of dehydrogenation the carbon atom undergoes an overall loss of electron density - and loss of electrons is oxidation.

Conversely, when a carbon atom in an organic compound gains a bond to hydrogen and loses a bond to a heteroatom (or to another carbon atom), the compound has been hydrogenated, or reduced. The hydrogenation of a ketone to an alcohol, for example, is overall the reverse of the alcohol dehydrogenation shown above. Illustrated below is another common possibility, the hydrogenation (reduction) of an alkene to an alkane.

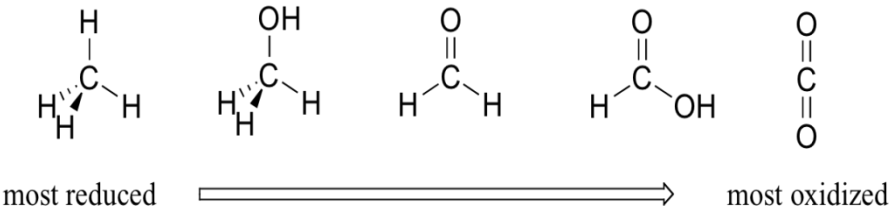
Hydrogenation (reduction) of an alkene



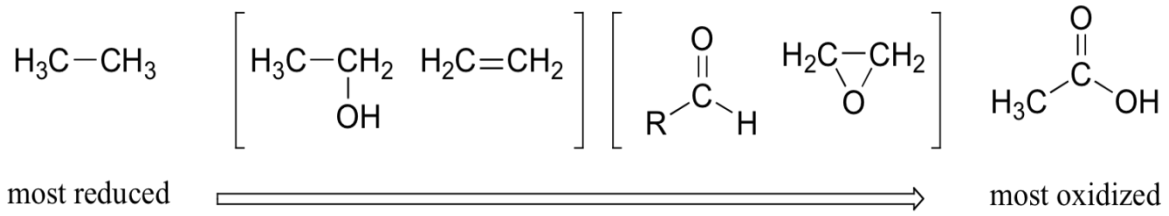
Hydrogenation results in *higher* electron density on a carbon atom(s), and thus we consider process to be one of reduction of the organic molecule.

Neither hydrogenation nor dehydrogenation involves the gain or loss of an oxygen *atom*. Reactions which *do* involve gain or loss of one or more oxygen atoms are usually referred to as 'oxygenase' and 'reductase' reactions.

For the most part, about redox reactions in organic chemistry means a small set of very recognizable functional group transformations. It is therefore very worthwhile to become familiar with the idea of 'oxidation states' as applied to organic functional groups. By comparing the relative number of bonds to hydrogen atoms, we can order the familiar functional groups according to oxidation state. A series of single carbon compounds can be considered as an example. Methane, with four carbon-hydrogen bonds, is highly reduced. Next in the series is methanol (one less carbon-hydrogen bond, one more carbon-oxygen bond), followed by formaldehyde, formate, and finally carbon dioxide at the highly oxidized end of the group.



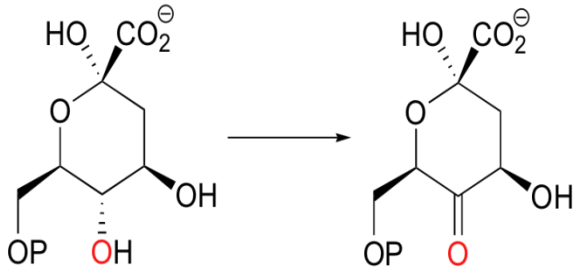
This pattern holds true for the relevant functional groups on organic molecules with two or more carbon atoms:



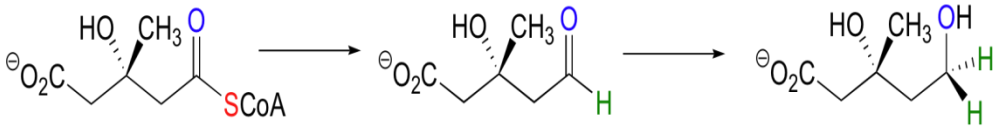
Alkanes are highly reduced, while alcohols - as well as alkenes, ethers, amines, sulfides, and phosphate esters - are one step up on the oxidation scale, followed by aldehydes/ketones/imines and epoxides, and finally by carboxylic acid derivatives (carbon dioxide, at the top of the oxidation list, is specific to the single carbon series).

Notice that in the series of two-carbon compounds above, ethanol and ethene are considered to be in the same oxidation state. We knows that alcohols and alkenes are interconverted by way of addition or elimination of water. When an alcohol is dehydrated to form an alkene, one of the two carbons loses a C-H bond and gains a C-C bond, and thus is oxidized. However, the other carbon loses a C-O bond and gains a C-C bond, and thus is considered to be reduced. Overall, therefore, there is no change to the oxidation state of the molecule.

Example, of oxidation: an alcohol functional group is converted to a ketone, which is one step up on the oxidation ladder.

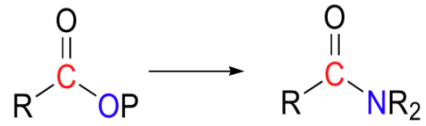


Likewise, this next reaction involves the transformation of a carboxylic acid derivative (a thioester) first to an aldehyde, then to an alcohol: this is a *double* reduction, as the substrate loses two bonds to heteroatoms and gains two bonds to hydrogens.



thioester aldehyde alcohol

An acyl transfer reaction (for example the conversion of an acyl phosphate to an amide) is *not* considered to be a redox reaction - the oxidation state of the organic molecule is does not change as substrate is converted to product, because a bond to one heteroatom (oxygen) has simply been traded for a bond to another heteroatom (nitrogen).



carbon is in same oxidation state - not a redox reaction

It is important to recognize when an organic molecule is being oxidized or reduced. The oxidation and reduction always occur in tandem and are important part of organic reactions.