Karpagam Academy of Higher Education

(Deemed University Established Under Section 3 of UGC Act 1956)

Coimbatore-21

Department of Chemistry

B.Sc Chemistry

Semester - V

15CHU501 ORGANIC CHEMISTRY 5H-5C

Instruction Hours/week:L: 5 T:0 P:0 Marks: Internal:40 External: 60 Total:100

Scope

This paper presents the basic principles of Organic Chemistry. It enables the students to learn about the fundamental aspects of stereochemistry, rearrangements, carbohydrates, proteins and heterocyclic compounds. It will help the students to work in pharmaceutical and food industries.

Programme Outcome

The course enables the students to

1. To understand the basics of stereochemistry.
2. To understand the mechanism of different molecular rearrangement reactions.
3. To understand about the isolation, synthesis and structure elucidation of proteins and aminoacids.
4. To understand the preparation and uses of heterocyclic compounds.

Programme Learning outcome

After the completion of the course, the students know about basics of stereochemistry, a versatile knowledge about different molecular rearrangement reactions. In addition to that the he knows about the isolation, synthesis and structure elucidation of proteins and aminoacids.

UNIT-I

Optical activity: compounds with asymmetric carbon- racemisation-Resolution- Asymmetric synthesis-Configuration –DL and RS nomenclature for compounds containing one asymmetric carbon. Walden inversion. Optical activity of Biphenyls, Allenes. Geometrical isomerism for olefin compounds. E-Z nomenclature.

UNIT-II

Mechanism of molecular rearrangement reaction: Pinacol-Pinacolone, Wagner-Meerwein, Beckmann, Hofmann, Curtius, Benzilic acid and Claisen rearrangements, Fries rearrangement and Cope rearrangement.

UNIT-III

Carbohydrates: Chemistry of monosaccharide- Glucose and Fructose. Chemistry of disaccharide- Sucrose and Maltose. Chemistry of polysaccharide - Starch and Cellulose - an elementary account (Elucidation of structure not necessary).

Inter conversion of Sugars – Muta rotation – Epimerization.

UNIT-IV

Amino acids– Classification, Preparation and properties –Peptides and synthesis of Polypeptides. Proteins- classification based on physical properties and biological functions, colour reactions – Primary, Secondary and tertiary structure.

UNIT-V

Heterocyclic compounds: Preparation, properties and use of Furan, Pyrrole, Thiophene, Pyridine, Quinoline, α and β-Flavones.

TEXT BOOKS:

1. Finar, I.L., 2013. "Organic Chemistry",Vol. I, Pearson Education, Singapore .
2. Finar, I.L., 2011. "Organic Chemistry", Vol. II, Pearson Education, Singapore.
3. Agarwal, O.P., 2014. "Natural Product Chemistry", Vol . I, Goel publishing House, Meerut.
4. Agarwal, O.P., 2014. "Natural Product Chemistry", Vol . II, Goel publishing House, Meerut.

REFERENCES :

1. Bahl, B.S. & Arun bahl, 2015. Advanced Organic Chemistry, S.Chand & Co., New Delhi.
2. Morrison, R.T. and Boyd, 2013. Organic Chemistry, 6th Edition, Pearson Education, Singapore.
3. Soni, P.L., 2014. A textbook of Organic Chemistry, S.Chand & Co., New Delhi.
4. Jerry March, 2012. "Advanced Organic Chemistry'', 4th Edition, Wiley, New York.
5. Pillai, C.N. 2010, Text book of Organic Chemistry, University press, New Delhi.
6. Michael B. Smith and Jerry March, 2015, Advanced Organic Chemistry, 6th edn, John Wiley & sons, New York.

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COIMBATORE-21

DEPARTMENT OF CHEMISTRY

LECTURE PLAN

Name of the Staff : Dr. K. Sundaram
Department : Chemistry
Title of the Paper : Organic Chemistry
Paper Code : 15CHU501
Class : III B.Sc. Chemistry
Year and Semester : III Year and V Semester
Total Hours : 75 Hours

UNIT-I

Stereochemistry **Hour's required-15**

S.No	Lecture Hour	Topics	Support Material
1	1	Optical isomerism- chiral and achiral molecules	T1:1.196-1.200
2	1	Optical Isomers of Lactic acids, Malic acid, tartaric acids	T1:1.-203-1.206
3	1	Racemisation	T1:1.223,R2:118-124
4	1	Resolution	T1:1.221-1.223,R2:124-129
5	1	Asymmetric synthesis	T1:1.226-1.227
6	1	Configuration – DL Nomenclature	T1:1.207-1.209
7	1	RS Nomenclature, Sequence rule	T1:1.209-1.213
8	1	Elements of symmetry	T1:1.200-1.202,R2:107-111
9	1	Walden Inversion	T1:1.223-1.226,R:147-150
10	1	Optical activity of Biphenyl's	R1:175,R:230-237
11	1	Allenes	R1:175-176,R2:247-252
12	1	Spiranes	R1:176
13	1	Geometrical isomerism for olefin compounds,	T1:1.190,R2:170-176
14	1	E-Z nomenclature.	T1:1.190,R2:170-176
15	1	Recapitulation and discussion of important questions	

SUPPORTING MATERIALS:

TEXT BOOKS

T1. Soni, P.L., 2014, A Textbook of Organic Chemistry, S. Chand & Co., New Delhi

REFERANCE BOOKS

R1. M.K. Jain and S.C. Sharma, 2015, Modern Organic Chemistry, 4th Edition, Vishal Publishing Co, NewDelhi

R2. Finar. I.L., 2013, Organic Chemistry, Vol.I, 5th Edition, Pearson Education, Singapore

UNIT-II

Mechanism of molecular Rearrangement reaction: Hours required-15

S.No	Lecture Hour	Topics	Support Material
1.	1	Mechanism of molecular Rearrangement reaction-Introduction	T2:1-10
2	1	Pinacol-Pinacolone rearrangement	T2:158-161,R3:1072-1073
3	1	Beckmann rearrangement	T2:91-94,R3:1095-1097
4	1	Hofmann rearrangement	T2:136-139,R3:1090-1091
5	1	Schmidt rearrangement	R1:622,773
6	1	Lossen rearrangement	R1:1305-1306
7	1	Benzilic acid rearrangements	T2:112-114,R3-1080
8	1	Curtius rearrangement	T2:105-107,R3:1091-1092
9	1	Mechanism of Curtius rearrangement	T2:105-107,R3:1091-1092
10	1	Claisen rearrangements	T2:94-96,R3:1136-1141
11	1	Fries rearrangement	T2:131-133,R3:555-556
12	1	Cope rearrangement	T2:303-306,R3:1130-1136
13	1	Benzidine rearrangement	T3:284-286,R3:1144-1146
14	1	Recapitulation and discussion of important questions	
15	1	Revision and discussion of previous year questions	

SUPPORTING MATERIALS:

TEXT BOOKS

T2: Somendranath Sanyal, 2013, Reaction and Mechanism, Rearrangement, Reagents,4th Edition, Bharathi Bhawan, New Delhi

T3: V.K.Ahluvalia, R.K. Parashar, 2013, Organic Chemistry Reaction and Mechanism

REFERANCE BOOKS

R1. M.K.Jain, S.C.Sharma-2015, Modern Organic Chemistry, 4th Edition, Vishal Publishing Co NewDelhi

R3. Jerry March, 2014 Advanced Organic Chemistry, 4th Edition John Wiley, New York

UNIT-III

Carbohydrates: **Hours required-15**

S.No	Lecture Hour	Topics	Support Material
1	1	Chemistry of monosaccharide	T4:768-769,T1:3.93-3.95
2	1	Glucose – Structure	T4:785-797,T1:3.95-3.97
3	1	Reactions of glucose	T4:797-804,T1:3.97-3.108
4	1	Fructose – structure	T4:804-812,T1:3.112-3.120
5	1	Reactions of fructose	T4:804-812,T1:3.112-3.120
6	1	Sucrose – structure – reactions	T4:813-819,T1:3.123-3.130
7	1	Maltose – structure – reactions	T4:-822—824,T1:3.130-3.131
8	1	Starch	T4:825-826,T1:3.132-3.133
9	1	Properties of Starch	T4:-826-827, T1:3.133-3.135
10	1	Cellulose	T4828-830,T1:3.136-3.137
11	1	Inter conversion of sugars killiani fisher cyanohydrine synthesis swanden fisher nitro methane	T4:778-782,T1:3.109-3.112
12	1	Aldose to ketose, Ketose to Aldose	T4:782,T1:3.120-3.121
13	1	Mutarotation	T4:784,790-793
14	1	Epimerisation	T1-3.111-3.112
15	1	Recapitulation and discussion of important questions	

SUPPORTING MATERIALS:

TEXT BOOKS

T1: Soni, P.L., 2014, A Textbook of Organic Chemistry, S. Chand & Co., New Delhi

T4: Bahl, B.S. & Arun Bahl, 2015. Advanced Organic Chemistry, S.Chand & Co., New Delhi

UNIT-IV

Hour's required-15

S.No	Lecture Hour	Topics	Support Material
1.	1	Amino acids– Classification, Nomenclature	T4:838-841,R2:652
2	1	Synthesis of α-amino acids	T4:842-845,R2:652-660
3	1	Properties- Reaction of the carboxyl group	T4:845-848,R2:660-669
4	1	Properties- Reaction of the amino group	T4:848-851
5	1	reaction of the both carboxyl and amino group	T4:848-851
6	1	Peptides- Nomenclature and variations	T4:851-852,R2:674-682
7	1	N-terminal and C- terminal amino acid residues	T4:851,R2:674-682
8	1	End group analysis	T4:853-855,R2-:82-687
9	1	Synthesis of peptides	T4:853-855,R2:682-687
10	1	Proteins classification	T4:855-856,R2:672-675
11	1	Structure of proteins	T4:856-857
12	1	Properties of proteins	T4:857-859
13	1	Color reactions – Primary reactions, Secondary and tertiary reactions	T4:859-860,R2:692-697
14	1	Structure – properties and uses of color reactions	R2:670-671
15	1	Recapitulation and discussion of important questions	

SUPPORTING MATERIALS:

TEXT BOOK

T4: Bahl, B.S. & Arun Bahl, 2015, Advanced Organic Chemistry, S. Chand & Co., New Delhi

REFERANCE BOOK

R2. Finar. I.L., 2013, Organic Chemistry, Vol.I, 5th Edition, Pearson Education, Singapore

UNIT-V

Heterocyclic compounds: **Hours required-15**

S.No	Lecture Hour	Topics	Support Material
1	1	Heterocyclic compounds	T4:1201-1202,R2:826-828
2	1	Preparation , properties and uses of furan	T4:1209-1214,R2:828-832
3	1	Pyrrole	T4:1202-1209,R2:836-841
4	1	Thiophene	T4:1219-1222,R2:834-836
5	1	Pyridine	T4:1229-1239,R2:848-854
6	1	Reactions of Pyridine	T4:1229-1239,R2:848-854
7	1	Quinoline	T4:1241-1245,R2:857-860
8	1	Isoquinoline	T4:1245-1246,R2860-861
9	1	Benzofuran, Indole	R2:833& R1:1223-1228,R2:841-843
10	1	Indigo	R1:1214-1216,R2:895-897
11	1	Isatin	T4:1228-1229,R2:844-845
12	1	Recapitulation and discussion of important questions	
13	1	Previous year ESE question paper discussion	
14	1	Previous year ESE question paper discussion	
15	1	Previous year ESE question paper discussion	

SUPPORTING MATERIALS:

TEXT BOOK

T4: Bahl, B.S. & Arun bahl, 2015. Advanced Organic Chemistry, S.Chand & Co., New Delhi

REFERANCE BOOKS

R1: M.K.Jain, S.C.Sharma-2014, Modern Organic Chemistry, 4th Edition, Vishal publishing co NewDelhi

R2: Finar. I.L., 2013, Organic Chemistry, Vol.I, 5th Edition, Pearson Education, Singapore

UNIT-1

Stereo Isomerism

Optical activity: compounds with asymmetric carbon- racemisation-Resolution- Asymmetric synthesis-Configuration –DL and RS nomenclature for compounds containing one asymmetric carbon. Walden inversion. Optical activity of Biphenyls, Allenes. Geometrical isomerism for olefin compounds. E-Z nomenclature.

Isomerism

The phenomenon in which two or more,different compounds have the same molecular formula is called isomerism.

Eg, i) Ethyl alcohol C2H5OH

II) Dimethyl ether CH3OCH3

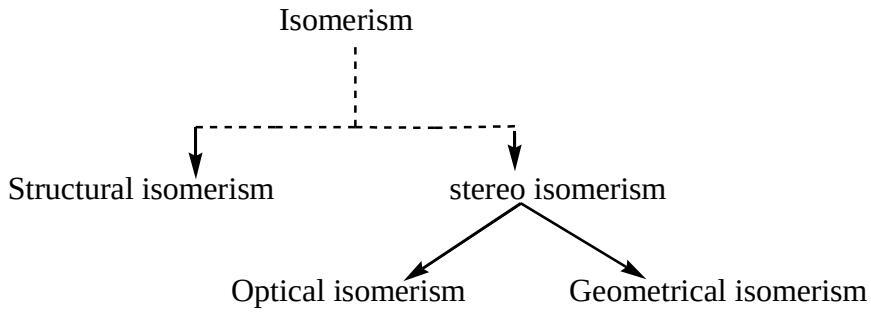
The Two are entirely different compounds. But they have the same molecular formula, viz C2H6O

Isomerism is dividedin totwo parts

i) Structural isomerism

ii) Stereoisomerism

You musthave studied about structural isomerism in your earlier classes. We shall readabout stereoisomerism here.



What is Stereoisomerism?

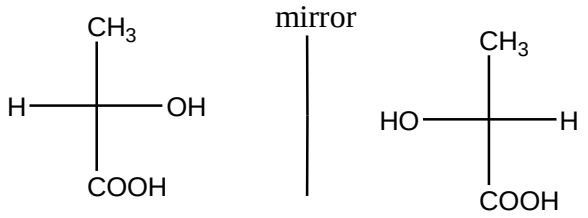
The Phenomenon in which differentcompounds have the same molecular and structural formulae but have different configuration, i.e., different arrangement of atoms and groups in space, is called stereoisomerism.

Eg., i)d and l lactic acids and

ii) Maleic and fumaric acids

Explanation

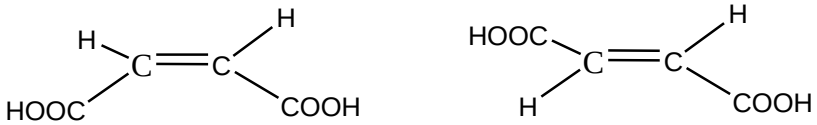
i). d and l lactic acids are two different compounds. Both have the same molecular formula, viz., C3H6O3. Both have the same structuralformula, viz., CH3 CH (OH) COOH. But they have different configurations. Thatis, the arrangement of various atoms and groups in space, of the two acids are different. The sstructure of one compound is the mirror image of the other.



d-lacti acids l-lactic acids

Thus d and l lactic acids are a pair of stereoisomers.

ii). Maleic and fumaric acids are two different compounds. Bothhave the same molecular formula, viz., C4H4O4. Both have the same structuralformula, viz., CH 9COOH)=CH(COOH). But they havedifferent configurations. That is , The arrangement of various atoms and groups in space, of the two acids, are different as shown.



maleic acid fumaric acid

Thus maleic and fumaric acids are another pair of stereo isomers. Stereoisomerism is divided in to two types.

i) Optical isomerism and

ii) Geometrical isomerism

OPTICAL ISOMERISM

Definition:

Optical isomerism is the phenomenon in which differentcompounds have the same molecular formula, same structural formula bur have different configurations, I.e., the arrangement of atoms and group in them aredifferent. They route the plane of the plane polarized light in different directions.

The two compounds which have the same molecular and structural formula and have different configurationsand which rotate the plane of plane polarized light in different directions are called optical isomers. Eg., d and l lactic acids.

Optical activity:

Solutionsof some organic compoundshave an unique property of rotating the plane of the plane polarized light. This propertyiscalled optical activity. Such subtancesare called optically active substances. It they rotate the plane of the plane polarized light towards the right (clock wise) they are called dextro-rotatory. If they rotate the plane polarized light towards the left (anti clock wise) they are called laevorotatory.

The amount of rotation depends, for a given substance, one number of factors like

i). the thickness of the layer traversed

ii). the nature of the solvent

iii). the temperature and

iv). the wave length of the light used

If [a] represents the specific rotation, l the thickness of the layers in decimeters, C, the number of grams of substance (per 100 ml of solution) and the determination is carried out at temperature t°C using light with wave length l, then if q is the observed rotation (+ or -).

$$[\alpha]^{t}_{\lambda} = \frac{100\theta}{lC}$$

If we use sodium light (the D line)

$$[\alpha]^{t}_{\lambda} = \frac{100\theta}{lC}$$

Since the value of rotation depends on the solvent, this should also be given.

Conditions for optical activity

The molecule must be chiral i.e. it must have two structureswhich are mirror images and which cannot be super imposed on one another.

Asymmetric centre

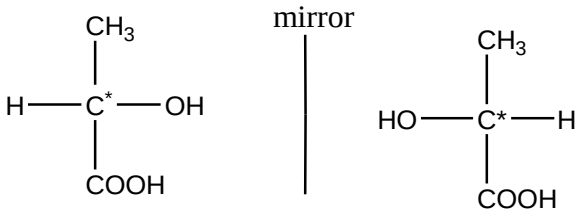
Any structural feature of a molecule which gives rise to optical activity may be called an asymmetric center. In many reactions a asymmetric center is created, for example,

$$CH_3CH_2COOH \xrightarrow{Br_2} CH_3{*}CHBrCOOH$$

Chiral and Achiral molecules

Chiral molecule

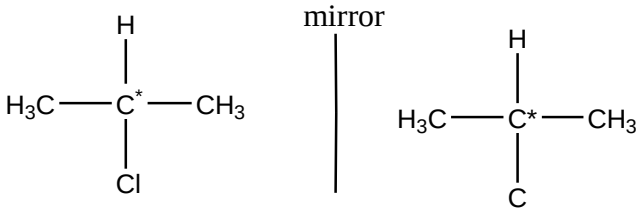
According to Vant Hoff and Le Bel Theory in a moleculelike methane the carbon atom is at the centre of a regulartetrahedron and the four atoms or groups are presentat thefour corners. If the four gropsattached to a control carbon atom of a molecule are different, then the molecule is not superimposable on its mirror image such amolecule called chiral molecule and that carbon is called chiral carbon or asymmetric carbon. The phenomenonis called chirality. Chirality is the necessary condition for the existence of enentiomers. Eg. Lactic acid



Lactic acid chiral (not superimposable)

Achiral molecule

Molecules that are superimposable or their mirror images are called achiral. Achiral molecules cannot exist as enantiomers. Achiral molecules possess symmetry. Eg. Isopropyl chloride.

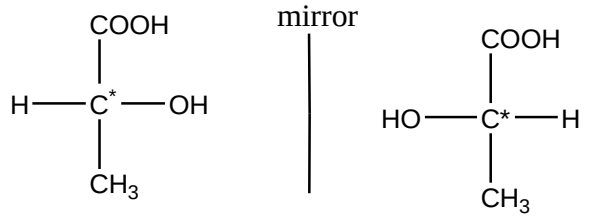


Isopropyl chloride- Achiral (Superimposable

Meaningof (+) and (-), and D and L notations:

(+) and (-) Signs:

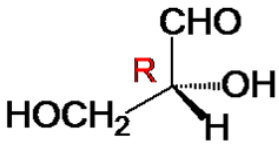
An enantiomer can be named by the direction in which it rotates the plane of polarized light. If it rotates the light clockwise (as seen by a viewer towards whom the light is traveling), that enantiomer is labeled (+). Its mirror-image is labeled (−). The (+) and (−) isomers have also been termed *d*- and *l*-, respectively (for *dextrorotatory* and *levorotatory*). Naming with *d*- and *l*- is easy to confuse with D- and L- labeling and is therefore strongly discouraged by IUPAC.

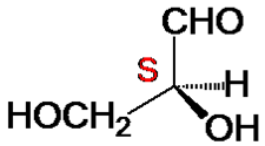


Dextro(+)-lacti acids Laevo(-)lactic acids

By configuration: D- and L:

An optical isomer can be named by the spatial configuration of its atoms. The D/L system (named after Latin dexter and laevus, right and left), not to be confused with the *d*- and *l*-system, see above, does this by relating the molecule to glyceraldehyde. Glyceraldehyde is chiral itself, and its two isomers are labeled D and L (typically typeset in small caps in published work). Certain chemical manipulations can be performed on glyceraldehyde without affecting its configuration, and its historical use for this purpose (possibly combined with its convenience as one of the smallest commonly used chiral molecules) has resulted in its use for nomenclature. In this system, compounds are named by analogy to glyceraldehyde, which, in general, produces unambiguous designations, but is easiest to see in the small biomolecules similar to glyceraldehyde. One example is the chiral amino acid alanine, which has two optical isomers, and they are labeled according to which isomer of glyceraldehyde they come from. On the other hand, glycine, the amino acid derived from glyceraldehyde, has no optical activity, as it is not chiral (achiral).





D- and L-glyceraldehyde

The D/L labeling is unrelated to (+)/(−); it does not indicate which enantiomer is dextrorotatory and which is levorotatory. Rather, it says that the compound's stereochemistry is related to that of the dextrorotatory or levorotatory enantiomer of glyceraldehyde—the dextrorotatory isomer of glyceraldehyde is, in fact, the D- isomer. Nine of the nineteen L-amino acids commonly found in proteins are dextrorotatory (at a wavelength of 589 nm), and D-fructose is also referred to as levulose because it is levorotatory.

A rule of thumb for determining the D/L isomeric form of an amino acid is the "CORN" rule. The groups:

COOH, **R**, **N**H_2 and H (where R is the side-chain)

are arranged around the chiral center carbon atom. With the hydrogen atom away from the viewer, if the arrangement of the **CO→R→N** groups around the carbon atom as center is counter-clockwise, then it is the L form.[14] If the arrangement is clockwise, it is the D form. The L form is the usual one found in natural proteins. For most amino acids, the L form corresponds to an *S* absolute stereochemistry, but is *R* instead for certain side-chains.

Elements of symmetry:

Presence of asymmetric carbon atom is not sufficient to decide whether themolecule is optically active or not. The molecule as a whole must be asymmetric. A simple device to decide whether a molecule is symmetric or not, is to ascertain whether it contains the elements of symmetry. The following are the elements of symmetry.

1. Plane of symmetry.

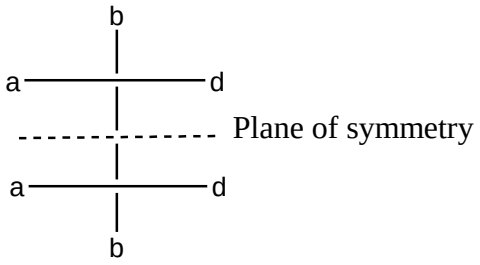
2. Centre of symmetry.

3. Alternating axis of symmetry.

If any one of the elements of symmetry is presentin the molecule, then the molecule is symmetrical, That is, the molecule becomes superimposable on its mirror image. So it will NOT be optically active.

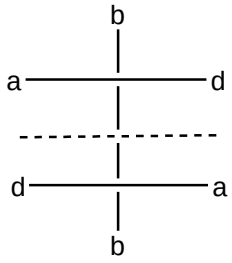
1. Plane of symmetry:

A plane which devides an object in to two identical halves is called plane of symmetry. A ball can be divided in to two identical halves. It is a non chiral object i.e., it possesses a plane of symmetry. A plane of symmetry divides a molecule in such a way that points (atoms or groups of atoms) on the side of the plane form mirror images of those on the other side. The following molecule possesses a plane of symmetry. It is a meso form.

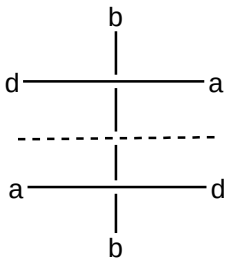


E.g., meso tartaric acid

Whereas the d and *l* forms of the above compound do not possess plane of symmetry.



d-form

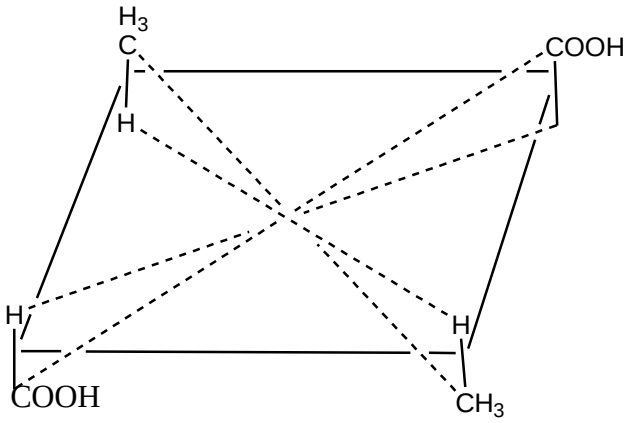


l-form

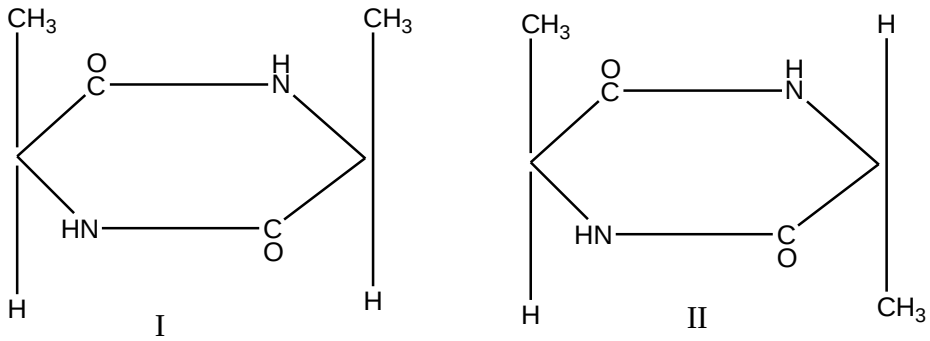
E .g., d and *l* tartaric acids

2. Centre of symmetry:

A centre of symmetry is a point from which lines, when drawn on one side and produced an equal distance on the other side, will meet identical points in the molecule. This test is possible only to three dimensional formula, particularly those of ring systems. The following molecule possesses a centre of symmetry.



In the following example dimethyldiketopiperazine exists in two geometrical forms namely ***cis*** and ***trans*** forms.



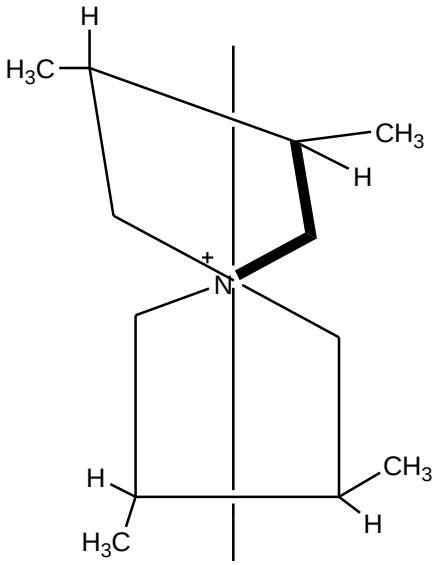
I
Cis

II
Trans

Structure I has neither a plan nor a centre of symmetry. So it is optically active. Structure II has a centre of symmetry. So it is optically active.

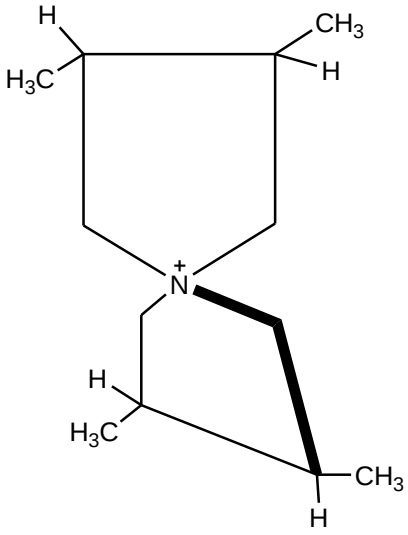
3. Alternating axis of symmetry:

A molecule possesses an n fold alternating axis of symmetry if, when rotated through an angle of 360/n about this axis and then followed by reflection in a plane perpendicular to the axis, the molecule is the same as it was in the starting position. The following molecule possesses alternating axis of symmetry.



axis

III



IV

RACEMIZATION:

Definition:

Racemization is the process of converting an optically active compound into the racemic modifications.

Racemic modifications are also called racemic mixtures or racemates.

Methods to bring about racemization:

i) **Action of heat:**

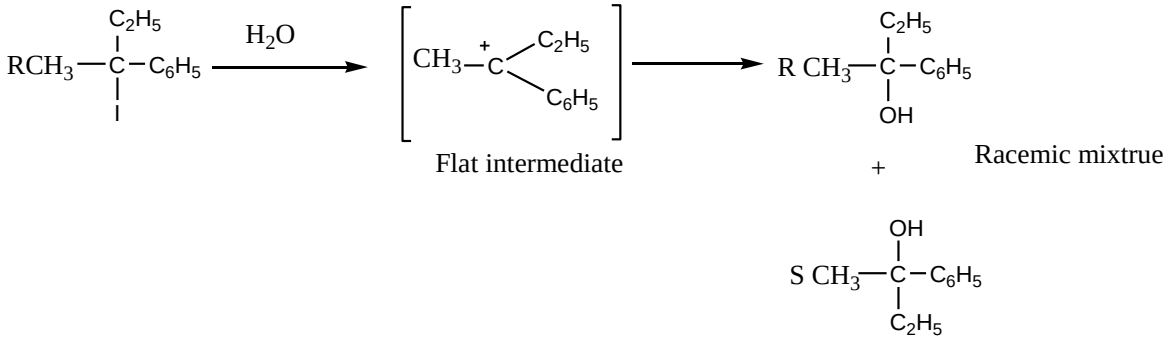
When d or l isomer is heated we get the dl mixture.

ii) **Treatment with chemical reagents:**

Many substances undergo racemization when treated with chemical reagents. E.g., mandelic acid ($C_6H_5CHOHCOOH$) forms (±) bromo acid when treated with hydrobromic acid.

iii) **Substitution and rearrangements**:

Substitution and rearrangements reactions which take place via S_N^1 type stepwise mechanisms end up in racemised products.E.g.,

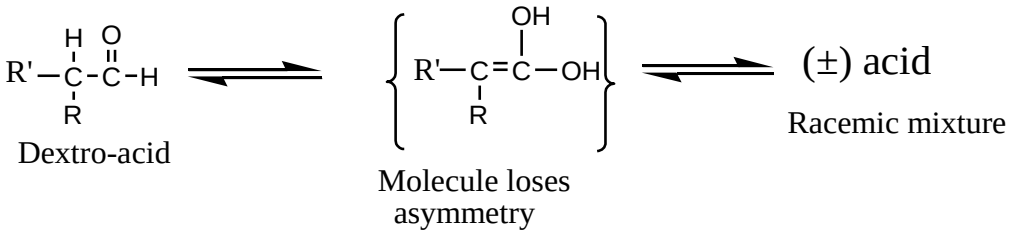


iv) Auto-racemization:

In some cases racemization occurs spontaneously at room temperature, e.g., dimethyl bromo sucinate undergoes racemization on standing at room temperature. This type of racemization is termed as auto racemization.

Mechanism of racemization:

Compound which racemise readily are found to contain an asymmetric carbon atom joined to a hydrogen atom and a negative group. Such compounds readily undergo tautomeric change and racesation occurs via enolisation. For example

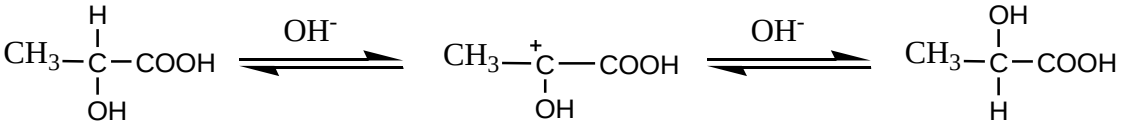


The intermediate enol form is nor asymmetric. When it reverts to the stable form, there are equal chances to produce the dextro and laevo forms. So it gives a racemic mixture.

In the case of a compound which cannot udergo tautometic change, mechanism of racemisation is uncertain. Howeverthe racemization is said to take place via the formation of planar

intermediate which when reverts to the stable form, there are equal changes to produce the dextro and laevo forms. So it gives a racemic mixture.

This can be illustrated by taking the base catalysed racemization of (-) lactic acid.



(-) FORM (+) form

RESOLUTON:

Defination: "The separation of a racemic mixture into its enantiomers(dextro and laevo components) is termed as resolution".

Explanation: Any attempt to prepare an optically active form of a compound ends up in a racemic mixture only. So they have to be separated into d and l forms. The process of such separation is called resolution.

Methods used for resolving racemic compounds:

i) Mechanical separation:

When the enantiomers(+) and (-) forms of the optically active compound or their salts form well-defined crystals, showing hemihedral faces, they can be separated by simple hand-picking. Pasteur separates in this manner crystals of sodium ammonium racemate. $Na.NH_4.C_4O_6.2H_2O$.

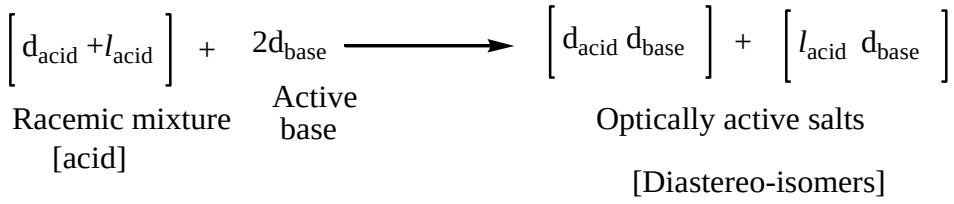
ii) Bio-chemical separation:

Certain bacteria or fungi when allowed to grow in a solution of the racemic compounds destroy one of the optical isomers at much quicker rate than the other due to selective assimilation. For example, when penicillium glaucum is allowed to grow in a solution of ammonium racemate, it destroys the d-tartrate by assimilation leaving behind the *l*-tartrate practically unaffected.

However, the separation is not always complete and one component is always lost. Some other side-products may also be formed and the sample may be difficult to purify.

iii) **By means of salt formation**:

This method is best of all methods of resolution. In this method the active constituents of a racemic mixture are conerted in to diastereo isomers [salts] with another active base or acid.

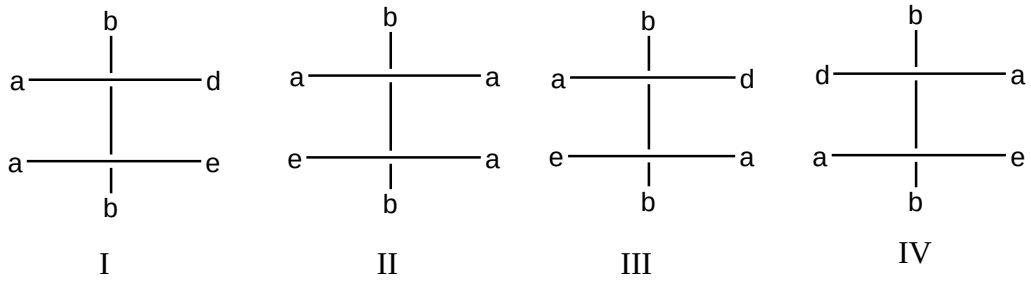


The two salts thus obtained often differ in their solubilities and can be separated by fractional crystallization. The salts can be hydrolysed with inorganic acids or alkalis to get the original active compounds. For example, racemic tartaric acid is separated by this method. The optically active bases used for this purpose are mainly alkaloids like quinine, brucine, cinchonine and morphine. Similarly racemic bases can be separated by using optically activeacids like tartaric acids, camphor sulphonic acid, etc.

Diastereo Isomers:

A compound may exist in several forms with various configurations. Two such forms may be optical isomers, with different configurations but not mirror images. Such a pair is called diastereo isomers. Thus optical isomers which are mirror images are called enantiomers which arenot mirror images are called diastereo isomers.

E.g., in the following four compounds I and III are diastereoisomers. But II and IV are enantiomers.



ASYMMETRIC SYNTHESIS:

Whenever an optically active compound is synthesized in the laboratory, the product is alwaysa racemic mixture which has to be resolved to get optically active isomer in the laboratory using special methods without the necessity of resolution.

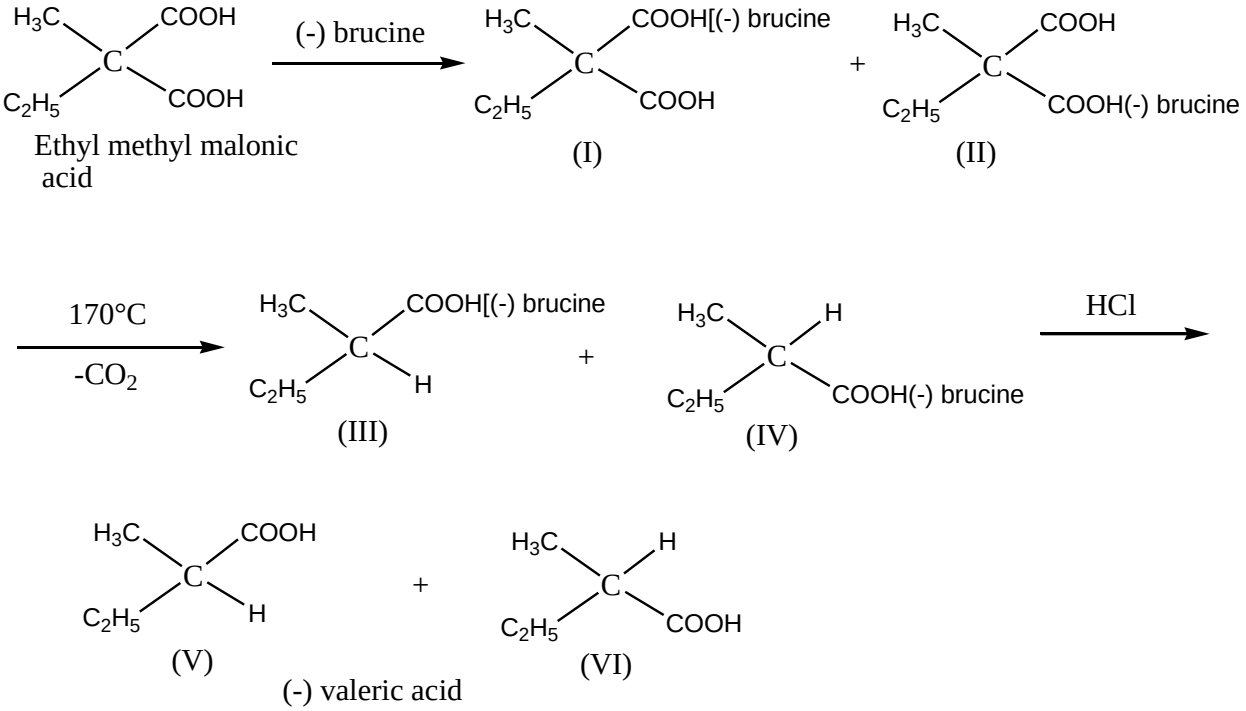
Definition:

The production of an optically active compound from a symmetric molecule without the necessity of resolution is called asymmetric synthesis.

Partial Asymmetric synthesis:

In ordinary laboratory preparation of active compounds, the racemic modification is always obtained. By special means, however, it is possible to prepare optically active compounds from symmetrical compounds (i.e., not optically active) without the necessity of resolution. The method involves the use of optically active compounds, and is known as partial asymmetric synthesis.

The first partial asymmetric synthesis was carried out by Marchwald (1904), who prepared an active (-) valeric acid by heating the half brucine salt of ethyl methyl malonic acid at 170°C. (I) and (II) are diastereo isomers, so are (III) and (IV) (V) and (VI) are enantiomers, and since the mixture is optically active, they must be present in unequal amounts. This was believed to be due to the different rates of decomposition of diastereo isomers (I) and (II).



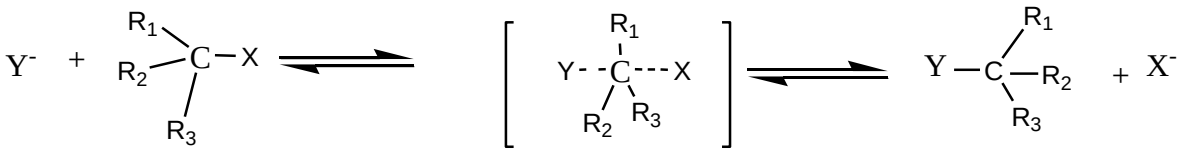
Absolute asymmetric synthesis:

The other type of asymmetric synthesis is absolute asymmetric synthesis. This is preparation of optically active compound without intermediate use of optically active reagents. The first conclusive evidence for an absolute asymmetric synthesis was obtained by Kuhn and Knopf. Who irradiated (±) α- azidopropionic dimethylamide, $CH_3CH(N_3)CON(CH_3)_2$, with right circularly polarized light and obtained a product that was slightly dextorotatory. When the amide was irradiated with left circularly polarized light, the product was slightly laevorotatory.

WALDEN INVERSION:

Transformation of an optically active compound in to a compound opposite configuration is called Walden Inversion or optical inversion.This phenomenon was discovered by P. Walden is 1893 and hence the name.

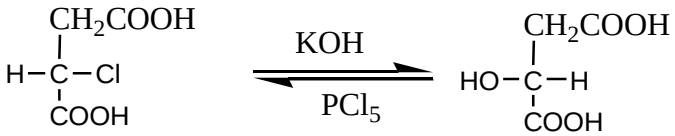
When an alkyl halide isattacked by a nucleophile (Y)from the back side there is substitution of the leaving group (X) by the nucleophile. Since two species are taking part in this substitution it is a bimolecular reaction represented as S_N^2 reaction.



Transition state

As the nucleophile approaches the carbon atom,the bond C-X is stretched. At aparticular stage both Y and X are partially attached to the carbon atom. This is called trasition state. In transition state, the three substituents namely, R_1,R_2, and R_3 lie in a single plane which is perpendicular to the Y-C-X plane. As the leaving group X leaves the bond between. Y and C in completely formed. The central atom undergoes a type of flipping. It inverts just like an umbrella turning inside out in a windstorm. This type of inversion is called Walden Inversion.

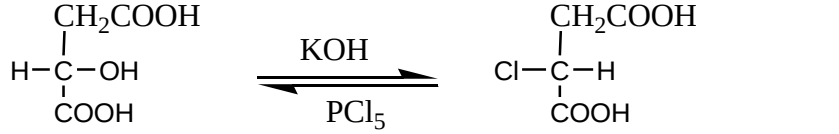
It must be noted that in Walden inversion there is a change in the sign of rotation as well as inversion of configuration. For example, when D(-) ChloroSuccinic acid is hydrolysed, it undergoes,Walden inversion to give L (+) malic acid and vice versa.



D(-)Chloro succinic acid

L-Malic acid

Similarly D (-) malic acid on treatment with PCl_5 gives L (+) Chlorosuccinic acid and vice versa.



D-Malic acid

L (+) Chloro succinic acid

Naming Chiral Centers—The *R,S* System

So far, we have discussed the fact that enantiomers exist. We have not considered the question of which isomer is which, that is, the absolute confi guration, or which is the right-handed enantiomer is and which is the left is. For a given sample of a pure enantiomer, the correct arrangement must be determined by experiment.Experimental determination of absolute confi guration can be accomplished byusing x-ray analysis of a derivative that has a chiral center with a known absolute configuration. In biological molecules,many absolute configurations weredetermined by comparison to absolute configurations of the chiral center inglyceraldehyde.

A system for designating the absolute confi guration of a chiral center was devisedin the late1950s by R. S. Cahn and C. K. Ingold in England and V. Prelogin Switzerland and is named after them. The system, also called the ***R,S* system**,has been incorporated into the IUPAC rules of nomenclature. The orientation ofgroups about a chiral center is specifi ed using a set of priority rules.

Priority Rules

1. Each atom bonded to the chiral center is assigned a priority. Priority is based on atomic number; the higher the atomic number, the higher the priority. Following are several substituents arranged in order of increasing priority. The atomic number of the atom determining priority is shown in parentheses.

,(1) (6) (7) (8) (16) (17) (35) (53)

-H, -CH_3, -NH_2, -OH, -SH, -Cl, -Br, -I

……increasing priority……..>

2. If priority cannot be assigned on the basis of the atoms bonded directly to the chiral center (because of a tie, that is, the same first atom on more than one substituent), look at the next set of atoms and continue until a priority can be assigned. Priority is assigned at the fi rst point of difference. Following is a series of groups arranged in order of increasing priority. The atomic number of the atom on which the assignment of priority is based is shown above it.

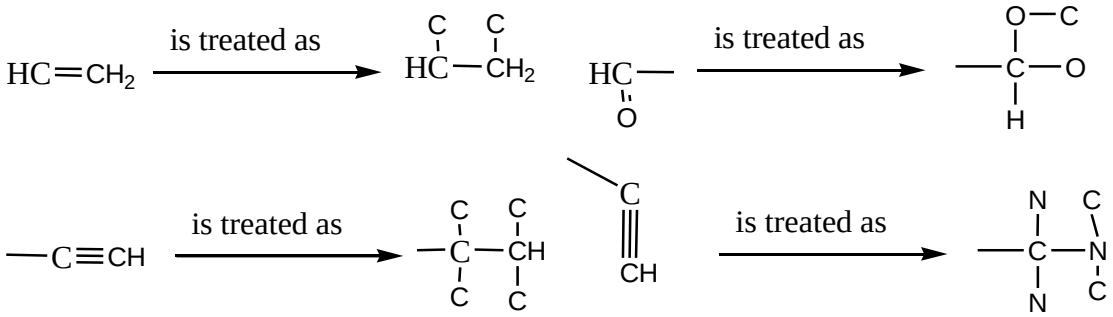
(1) (6) (7) (8) (17)

-CH_2-H, -CH_2-CH_3 ,CH_2NH_2 , -CH_2-OH ,-CH_2-Cl

……increasing priority……..>

If two carbons have substituents of the same priority, priority is assigned to the carbon that has more of these substituents. Thus, -CHCl2 > -CH2Cl.

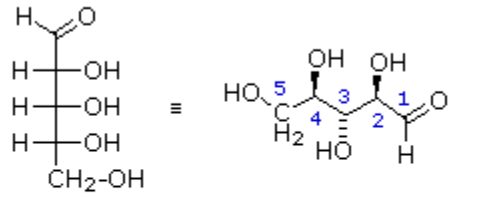
4. Atoms participating in a double or triple bond are considered to be bonded to an equivalent number of similar "phantom" atoms (shown here highlighted) by single bonds; that is, atoms of the double bond are duplicated, and atoms of a triple bond are triplicated. The phantom atoms are bonded to no other atoms.



Note: priority assignment is made at the *fi rst point of difference* between groups. A common mistake is to assume that larger groups must always have higher priority, but this might not necessarily be the case. For example, a -CH_2Cl group has priority over a-$CH_2CH_2CH_2CH_3$ group because the Cl atom is the *fi rst point of difference.*

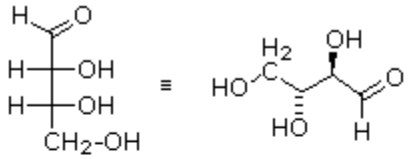
ERYTHRO AND THREO REPRESENTATIONS

Fischer projection formulas are particularly useful for comparing configurational isomers within a family of related chiral compounds, such as the carbohydrates. However, the eclipsed conformations implied by these representations are unrealistic. When describing acyclic compounds incorporating two or more chiral centers, many chemists prefer to write zig-zag line formulas for the primary carbon chain. Here, the zig-zag carbon chain lies in a plane and the absolute or relative configurations at the chiral centers are then designated by wedge or hatched bonds to substituent groups. This is illustrated for D-(-)-ribose and the diastereoisomeric D-tetroses erythrose and threose in the following diagram.

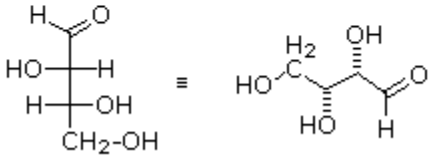


D-(-)-Ribose

2(R),3(R),4(R),5-tetrahydroxypentanal

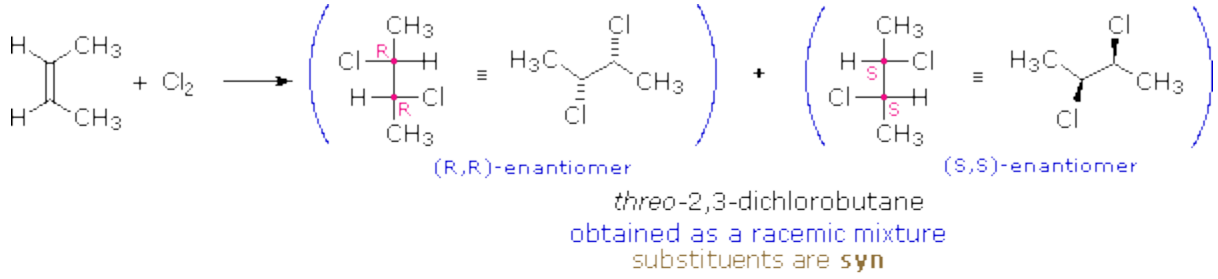


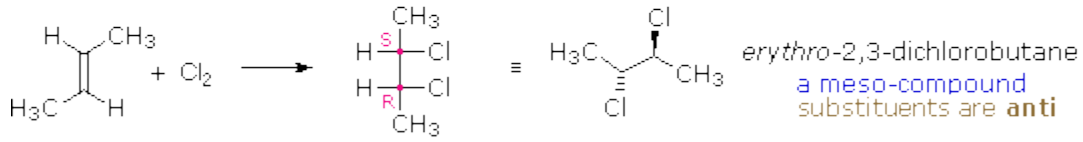
D-(-)-Erythrose

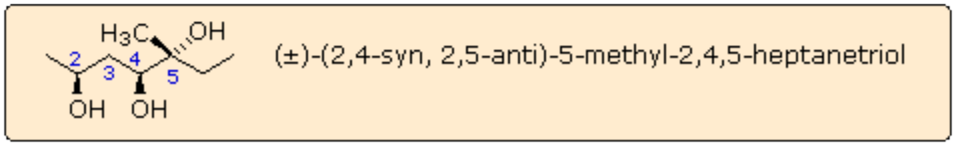


D-(-)-Threose

These compounds are all chiral and only one enantiomer is drawn (the D-family member). Many times, however, we must refer to and name diastereoisomers that are racemic or achiral. For example, addition of chlorine to cis-2-butene yields a stereoisomer of 2,3-dichlorobutane different from the one obtained by chlorine addition to trans-2-butene. In cases having two adjacent chiral centers, such as this, the prefixeserythro and threo may be used to designate the relative configuration of the centers. These prefixes, taken from the names of the tetroses erythrose and threose (above), may be applied to racemic compounds, as well as pure enantiomers and meso compounds, as shown in the following diagram. In the commonly used zig-zag drawings substituents may lie on the same side of the carbon chain, a synorientation, or on opposite sides, an anti orientation. For adjacent (vicinal) substituents this is opposite to their location in a Fischer formula. Thus, the substituents in the erythro isomer have an anti orientation, but are syn in the threo isomer.





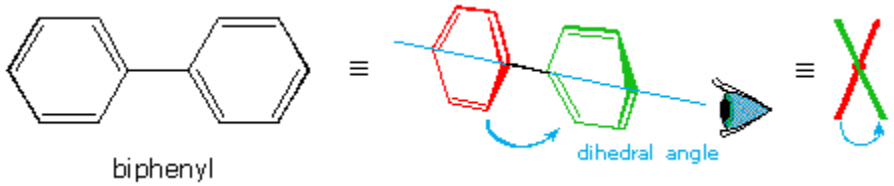


The syn-anti nomenclature may be applied to acyclic compounds having more than two chiral centers, as illustrated by the example in the colored box. The stereogenic center nearest carbon #1 serves as a reference. At sites having two substituents, such as carbon #5, the terms refer to the relative orientation of the highest order substituent, as determined by the C.I.P. sequence rules.

OPTICAL ACTIVITY OF BIPHENYL

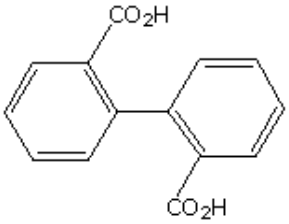
Conformations of Biphenyls

Another class of compounds that display conformational enantiomorphism are the substituted biphenyls. As shown in the following diagram, biphenyl itself is not planar, one benzene ring being slightly twisted or canted in relation to the other as a consequence of steric crowding. This crowding will be demonstrated by clicking on the diagram. The resulting chiral conformation, having a dihedral angle of about 45º, equilibrates rapidly with its enantiomer by rotation about the connecting single bond. Note that a conformation having a 90º dihedral angle is achiral, as a consequence of a plane of symmetry.

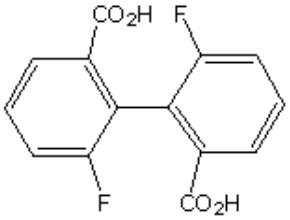


biphenyl

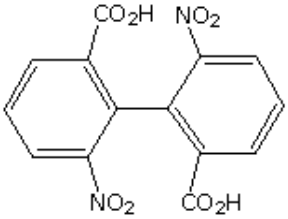
If each of the phenyl rings of a biphenyl has two different ortho or meta substituents (one may be hydrogen), even the twisted 90º dihedral angle conformer becomes chiral. In order to interconvert such conformers with their mirror image structures, a rotation through the higher energy coplanar form must be made. The ease with which this interconversion occurs will depend on the size of the ortho substituents, since these groups must slide past each other. The 2,2'-dicarboxylic acid on the left below cannot be resolved at room temperature, since thermal (kinetic) energy is sufficient to provide the necessary activation energy for racemization. The two additionally substituted diacids to its right have a higher activation energy for racemization, and can be resolved if care is taken to avoid heating them. As a rule, an activation energy barrier of 16 to 19 kcal/mole is required to prevent spontaneous room temperature racemization of substituted biphenyls. Since fluorine is smaller than a nitro group, the center compound racemizes more rapidly on heating than does the nitro compound to its right. Conformational isomers that are isolable due to high energy barriers are called atropisomers.



not resolved at room temperature



resolved at room temperature
racemizes easily



resolved at room temperature
racemizes slowly

By clicking on the diagram, three additional examples of resolvable biphenyls will be displayed. The 2,2'-disulfonic acid (compound A) can be resolved with care, confirming the larger size of SO_3H compared with CO_2H. Compounds B and C provide additional insight into the racemization of biphenyls. Although these biphenyls have identical ortho substituents, the meta nitro substituent adjacent to the methoxyl group in C exerts a buttressing influence that increases the effective size of that ortho substituent. Finally, by clicking on the diagram a second time two additional examples of substituted biphenyls will be shown. The left hand compound is held in a twisted conformation by the bridging carbon chain. Racemization requires passing through a planar configuration, and the increased angle and eclipsing strain

in this structure contribute to a large activation energy. Consequently, this compound is easily resolved into enantiomeric stereoisomers. The right hand compound is heavily ortho-substituted and most certainly resists assuming a planar configuration. However, the right benzene ring has two identical ortho substituents, so the stable 90º dihedral angle conformer has a plane of symmetry. All chiral twisted conformers are present as racemates, so this compound cannot be resolved.

OPTICAL ACTIVITY OF ALLENES

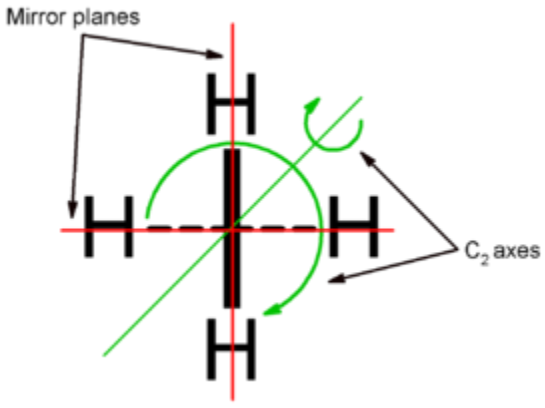
An allene is a compound in which one carbon atom has double bonds with each of its two adjacent carbon centres. Allenes are classified as polyenes with cumulated dienes. The parent compound of allene is propadiene. Compounds with an allene-type structure but with more than three carbon atoms are called cumulenes. Allenes are much more reactive than most other alkenes. For example, their reactivity with gaseous chlorine is more like the reactivity of alkynes than that of alkenes.

Structure and bonding

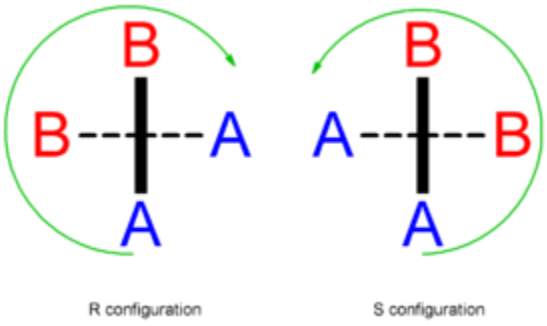
Geometry

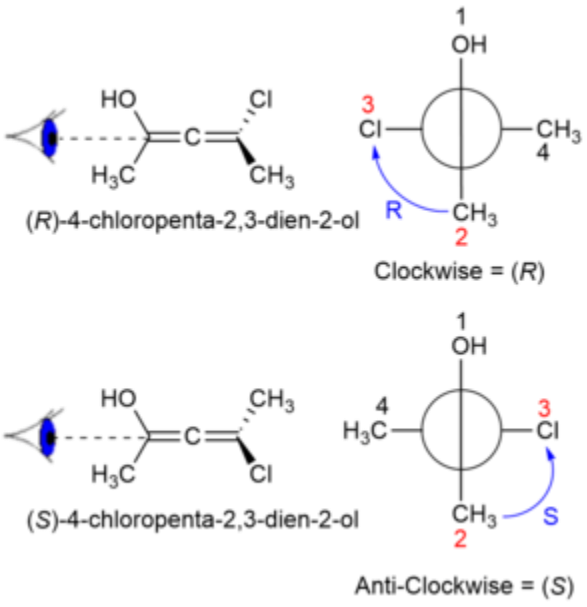
The central carbon of allene forms two sigma bonds and two pi bonds. The central carbon is sp-hybridized, and the two terminal carbons are sp^2-hybridized. The bond angle formed by the three carbons is 180°, indicating linear geometry for the carbons of allene. It can also be viewed as an "extended tetrahedral" with a similar shape to methane.

Symmetry



The symmetry and isomerism of allenes has long fascinated organic chemists. For allenes with four identical substituents, there exist two twofold axes of rotation through the center carbon, inclined at 45° to the CH_2 planes at either end of the molecule. The molecule can thus be thought of as a two-bladed propeller. A third twofold axis of rotation passes through the C=C=C bonds, and there is a mirror plane passing through both CH_2 planes. Thus this class of molecules belong to the D_{2d} point group. Because of the symmetry, an unsubstituted allene has no net dipole moment.





R and *S* configurations are determined by precedences of the groups attached to the axial section of the molecule when viewed along that axis. The front plane is given higher priority over the

other and the final assignment is given from priority 2 to 3 (i.e. the relationship between the two planes).

An allene with two different substituents on each of the two carbons will be chiral because there will no longer be any mirror planes. Where A has a greater priority than Baccording to the Cahn-Ingold-Prelog priority rule, the configuration of the axial chirality can be determined by considering the substituents on the front atom followed by the back atom when viewed along the allene axis. For the bottom, only the group of higher priority need be considered. Chiral allenes have been recently used as building blocks in the construction of organic materials with exceptional chiroptical properties. Although allenes often require specialized syntheses, the parent, propadiene is produced on a large scale as an equilibrium mixture with methylacetylene:

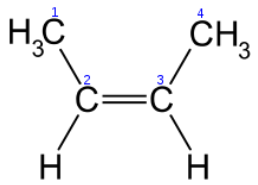
$$H_2C{=}C{=}CH_2 \rightleftharpoons CH_3C{\equiv}CH$$

This mixture, known as MAPP gas, is commercially available.

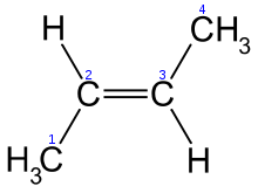
Laboratory methods for the formation of allenes include:

- from geminal dihalocyclopropanes and organolithium compounds in the Skattebøl rearrangement.
- from reaction of certain terminal alkynes with formaldehyde, copper(I) bromide and added base
- from dehydrohalogenation of certain dihalides.
- from reaction of a triphenylphosphinyl ester with an acid halide, a Wittig reaction accompanied by dehydrohalogenation

Cis–trans isomerism



cis-but-2-ene



trans-but-2-ene

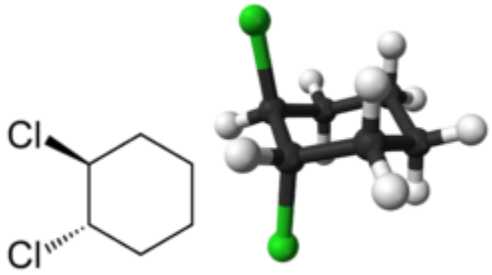
Cis/trans isomerism (*geometric isomerism*, *configurational isomerism*) is a term used in organic chemistry to refer to the stereoisomerism engendered in the *relative* orientation of functional groups within a molecule. It is not to be confused with *E*/*Z* isomerism, which is an *absolute* stereochemical description, and only to be used with alkenes. In general, such isomers contain double bonds that cannot rotate, or they may contain ring structures, where the rotation of bonds is restricted or eliminated. Cis and trans isomers occur both in organic molecules and in inorganic coordination complexes. Cis and trans descriptors are not used for cases of conformational isomerism where the two geometric forms easily interconvert, such as most open-chain single-bonded structures; instead, the terms “syn” and “anti” would be used.

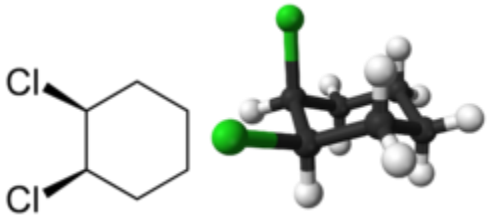
The terms “cis” and “trans” are from Latin, in which *cis* means "on this side" and *trans* means "on the other side" or "across". The term "geometric isomerism" is considered an obsolete synonym of "cis/trans isomerism" by IUPAC.

Organic chemistry

When the substituent groups are oriented in the same direction, the diastereomer is referred to as *cis*, whereas, when the substituents are oriented in opposing directions, the diastereomer is referred to as *trans*. An example of a small hydrocarbon displaying cis/trans isomerism is but-2-ene.

Alicyclic compounds can also display cis/trans isomerism. As an example of a geometric isomer due to a ring structure, consider 1,2-dichlorocyclohexane:



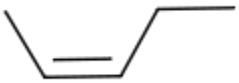


trans-1,2-dichlorocyclohexane

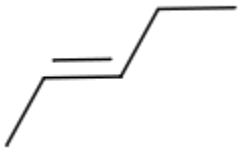
cis-1,2-dichlorocyclohexane

Comparison of physical properties

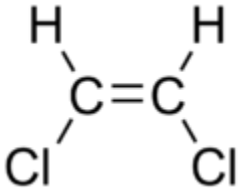
Cis and trans isomers often have different physical properties. Differences between isomers, in general, arise from the differences in the shape of the molecule or the overall dipole moment.



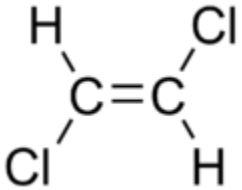
cis-2-pentene



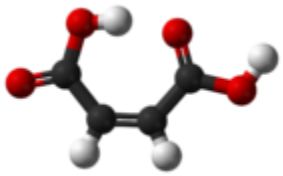
trans-2-pentene

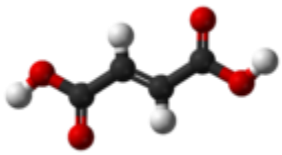


cis-1,2-dichloroethene



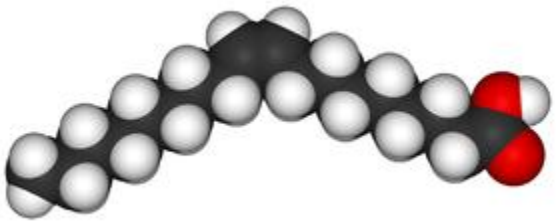
trans-1,2-dichloroethene

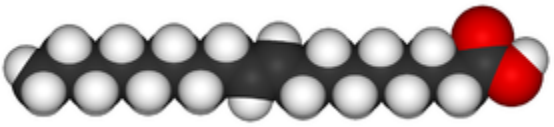




cis-butenedioic acid (maleic acid)

trans-butenedioic acid (fumaric acid)





Oleic acid

Elaidic acid

These differences can be very small, as in the case of the boiling point of straight-chain alkenes, such as pent-2-ene, which is 37 °C in the cis isomer and 36 °C in the trans isomer. The differences between cis and trans isomers can be larger if polar bonds are present, as in the 1,2-dichloroethenes. The cis isomer in this case has a boiling point of 60.3 °C, while the trans isomer has a boiling point of 47.5 °C. In the cis isomer the two polar C-Cl bond dipole moments combine to give an overall molecular dipole, so that there are intermolecular dipole–dipole forces (or Keesom forces), which add to the London dispersion forces and raise the boiling point. In the trans isomer on the other hand, this does not occur because the two C–Cl bond moments cancel and the molecule has a net zero dipole (it does however have a non-zero quadrupole).

The two isomers of butenedioic acid have such large differences in properties and reactivities that they were actually given completely different names. The cis isomer is called maleic acid and the trans isomer fumaric acid. Polarity is the key in determining relative boiling point as it causes increased intermolecular forces, thereby raising the boiling point. In the same manner, symmetry is the key in determining relative melting point as it allows for better packing in the solid state, even if it does not alter the polarity of the molecule. One example of this is the relationship between oleic acid and elaidic acid; oleic acid, the cis isomer, has a melting point of 13.4 °C, making it a liquid at room temperature, while the trans isomer, elaidic acid, has the much higher melting point of 43 °C, due to the straighter trans isomer being able to pack more tightly, and is solid at room temperature.

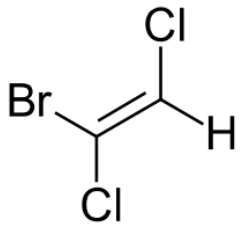
Thus, trans alkenes, which are less polar and more symmetrical, have lower boiling points and higher melting points, and cis alkenes, which are generally more polar and less symmetrical, have higher boiling points and lower melting points.

In the case of geometric isomers that are a consequence of double bonds, and, in particular, when both substituents are the same, some general trends usually hold. These trends can be attributed to the fact that the dipoles of the substituents in a cis isomer will add up to give an overall molecular dipole. In a trans isomer, the dipoles of the substituents will cancel out due to their being on opposite site of the molecule. Trans isomers also tend to have lower densities than their cis counterparts As a general trend, trans alkenes tend to have higher melting points and lower solubility in inert solvents, as trans alkenes, in general, are more symmetrical than cis alkenes. Vicinal coupling constants ($^3J_{HH}$), measured by NMR spectroscopy, are larger for trans (range: 12–18 Hz; typical: 15 Hz) than for cis (range: 0–12 Hz; typical: 8 Hz) isomers.

Stability

Usually, for acyclic systems trans isomers are more stable than cis isomers. This is typically due to the increased unfavourable steric interaction of the substituents in the cis isomer. Therefore, trans isomers have a less exothermic heat of combustion, indicating higher thermochemical stability. In the Benson heat of formation group additivity dataset, cis isomers suffer a 1.10 kcal/mol stability penalty. Exceptions to this rule exist, such as 1,2-difluoroethylene, 1,2-difluorodiazene (FN=NF), and several other halogen- and oxygen-substituted ethylenes. In these cases, the cis isomer is more stable than the trans isomer. This phenomenon is called the cis effect.

E/Z notation



Bromine has a higher CIP priority than chlorine, so this alkene is the *Z* isomer

E-Z notation

The cis/trans system for naming alkene isomers should generally only be used when there are only two different substituents on the double bond, so there is no confusion about which substituents are being described relative to each other. For more complex cases, the cis/trans designation is generally based on the longest carbon chain as reflected in the root name of the molecule (i.e. an extension of standard organic nomenclature for the parent structure). The IUPAC standard designations *E*/*Z* are unambiguous in all cases, and therefore are especially useful for tri- and tetrasubstituted alkenes to avoid any confusion about which groups are being identified as cis or trans to each other. *Z* (from the German *zusammen*) means "together". *E* (from the German *entgegen*) means "opposite". That is, *Z* has the higher-priority groups cis to each other and *E* has the higher-priority groups trans to each other. Because the cis/trans and *E*/*Z* systems compare different groups on the alkene, it is not strictly true that *Z* corresponds to cis and *E* corresponds to trans. For example, *trans*-2-chlorobut-2-ene (the two methyl groups, C1 and C4, on the but-2-ene backbone are trans to each other) is (*Z*)-2-chlorobut-2-ene (the chlorine and C4 are together because C1 and C4 are opposite).

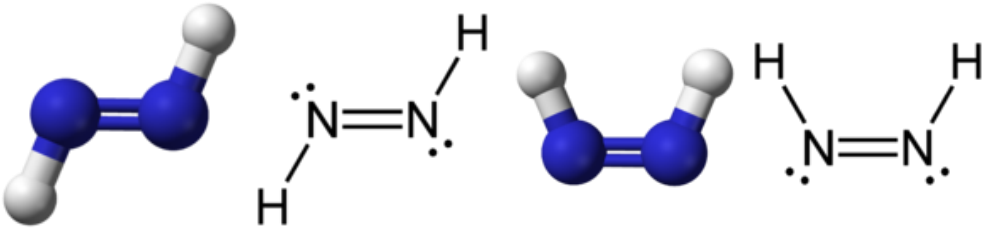
Whether a molecular configuration is designated *E* or *Z* is determined by the Cahn-Ingold-Prelog priority rules; higher atomic numbers are given higher priority. For each of the two atoms in the double bond, it is necessary to determine the priority of each substituent. If both the higher-priority substituents are on the same side, the arrangement is *Z*; if on opposite sides, the arrangement is *E*.

Inorganic chemistry

Cis/trans isomerism can also occur in inorganic compounds, most notably in diazenes and coordination compounds.

Diazenes

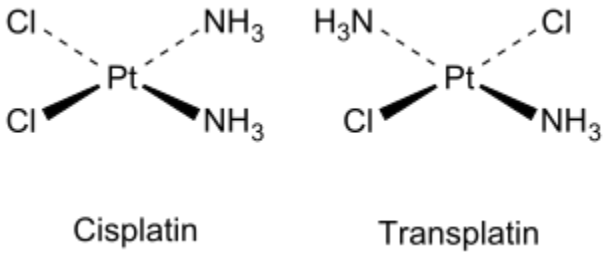
Diazenes (and the related diphosphenes) can also exhibit cis/trans isomerism. As with organic compounds, the cis isomer is generally the more reactive of the two, being the only isomer that can reduce alkenes and alkynes to alkanes, but for a different reason: the trans isomer cannot line its hydrogens up suitably to reduce the alkene, but the cis isomer, being shaped differently, can.



trans-diazene *cis*-diazene

Coordination complexes

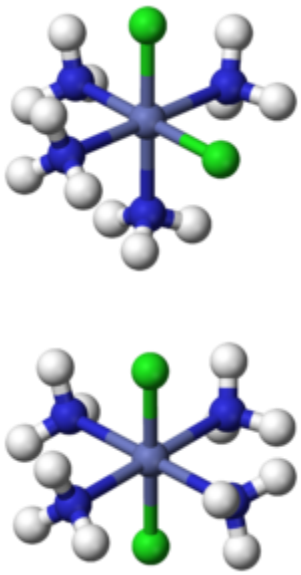
In inorganic coordination complexes with octahedral or square planar geometries, there are also cis isomers in which similar ligands are closer together and trans isomers in which they are further apart.



The two isomeric complexes, cisplatin and transplatin

For example, there are two isomers of square planar $Pt(NH_3)_2Cl_2$, as explained by Alfred Werner in 1893. The cis isomer, whose full name is *cis*-diamminedichloroplatinum(II), was shown in

1969 by Barnett Rosenberg to have antitumor activity, and is now a chemotherapy drug known by the short name cisplatin. In contrast, the trans isomer (transplatin) has no useful anticancer activity. Each isomer can be synthesized using the trans effect to control which isomer is produced.



cis-$[Co(NH_3)_4\ Cl_2]^+$ and *trans*-$[Co(NH_3)_4\ Cl_2]^+$

For octahedral complexes of formula MX_4Y_2, two isomers also exist. (Here M is a metal atom, and X and Y are two different types of ligands.) In the cis isomer, the two Y ligands are adjacent to each other at 90°, as is true for the two chlorine atoms shown in green in *cis*-$[Co(NH_3)_4Cl_2]^+$, at left. In the trans isomer shown at right, the two Cl atoms are on opposite sides of the central Co atom.

A related type of isomerism in octahedral MX_3Y_3 complexes is facial–meridional (or *fac*/*mer*) isomerism, in which different numbers of ligands are cis or trans to each other. Metal carbonyl compounds can be characterized as "fac" or "mer" using infrared spectroscopy.

POSSIBLE QUESTIONS

PART A (1 Marks Questions)

1. The R and S notation of compounds containing chiral centres is given by the priority system of the
a. Cahn-Ingold-Prelog b. Newman-Ingold-Cahn c. Cahn –Newman-Ingold
d. Cahn-Ingold-Langmuir

2. Erythrose and threose
a. are homomers b. are cis-transisomers c. **are diastereomers** d. are optimers

3. The restricted rotation around double bond in alkene is the cause of
a. **Geometrical isomerism** b. Chain isomerism c. Positional isomerism
d. Optical isomerism

4. Which of the following exhibits geometrical isomerism
a. 2-Methyl propene b. 1-butene
c. **2-butene** d. 2,3-dibromo-2-2-butene

5. The intermediate formed in Beckmann rearrangement is also the intermediate is
a.Perkin reaction b. Stobbe reaction c. Dields-Alder reaction d. **Hofmann reaction**

6. Which of the following reaction undergoes without the formation of any intermediate?
a.SN_1 reaction b.SN_i reaction c. Ar SN_1 reaction d.**SN_2 reaction**

7. Which of the following reaction gives crossed products?
a.Claisen rearrangement b. **Fries rearrangement** c.Lossen rearrangement
d. Curtius rearrangement

8. Which of the following reaction gives temperature dependence products?
a.Perkin reaction b. **Fries rearrangement** c. Beckmann rearrangement
d. Claisen rearrangement

9. Isomers differs in configuration at asymmetric carbon due to hemiacetal ring formation are known as
a.Epimers b.conformers c.**Anomers** d.Tautomers

10. Fructose is leavorotatory yet it is written as D-fructose. This 'D' indicates
a.specific rotation b.**Generic relationship to D-glyceraldehyde** c.Mutarotation
d.Resolution

11. Invert sugar is
a.Sucrose b. **Mixture of Glucose+Fructose** c.Mannose d.D-xylose

12. Hydrolysis of D-Lactosegives
a.**Glucose+Galactose** b.Galactose+Fructose c.Glucose +Fructose d.Only glucose

13. An amino acid with a hydroxyl group is
a.Alanine b.**Serine** c.Valine d.Ornithine

Serine

14. Aspartic acid contains---------- amino group/s and----------carboxyl group
a. 1,1 b.**1,2** c.2,1 d.2,0

15. The acidic group in glycine is
a. -COOH b.-COO^- c.-NH_2 d. -**$NH3^+$**

16. Towards which of the following reagents does glycine behave as an acid?
a.**ethanol** b.HCl c.acetic anhydride d.nitrous acid

17.The 'N' atom in pyridine is
a.sp^3 hybridized b.**sp^2 hybradized** c.sp hybridized d.cannot be predicted

18. Pyrrole is less basic than pyridine because the lone pair of electrons on N-atom in pyrrole
a.**is part of the delocalised π molecular orbital** b.is not part of thedelocalised π molecular orbital
c.resides in sp2 hybridized orbital d.resides in sp hybridized orbital

19. Pyridine is less basic than trimethylamine because the lone pair of electrons on N-atom in pyridine resides in
a.**sp2 hybradized orbital** b.sp hybridized orbital c.sp3 hybridized orbital d.P orbital

20. Pyridine reacts with mixture of KNO_3 and sulphuric acid at 300°C to give
a.1-Nitro pyridine b.**2-Nitro pyridine** c.3-Nitro pyridine d.4-Nitro pyridine

PART B (8 Marks Questions)

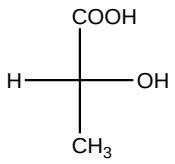
1. Explain Walden invension with suitable example.

2. Write notes on Sequence rules.

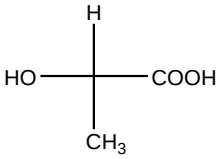
3. Write notes on Elements of symmetry? Explain with example.

4. Write notes on Racemisation.

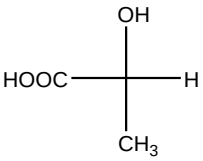
5. Discuss E-2 elimination (example: Dehydro halogenations) in cyclohexyl system?
6. Assign configuration (R) or(S) to the Fischer projection of lactic acid as shown below:



(i)



(ii)



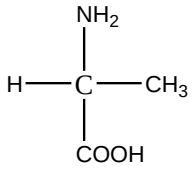
(iii)

7. Define a prochiral centre? How the Hydrogen's or any other ligands attached to a prochiral centre are designated?
8. What is the significane of Prelog's rule in asymmetric synthesis?

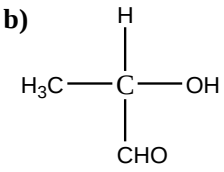
9. What is optical activity? Discuss the optical isomerism of lactic acid and malic acid and describe a method for its preparation.

10. Assign R or S configuration to the following compounds.

a)



b)



11. Define the terms (i) Plane of symmetry (ii) center of symmetry (iii) axis of symmetry

Karpagam Academy of Higher Education

(Deemed University Established Under Section 3 of UGC Act 1956)

Coimbatore-21

Department of Chemistry

III B.Sc Chemistry

Organic Chemistry

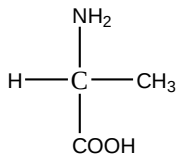
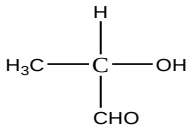
Unit I objective questions

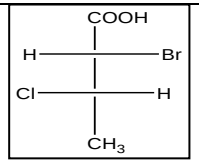
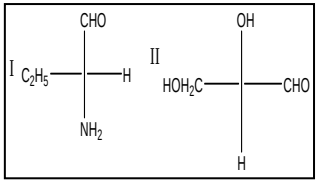
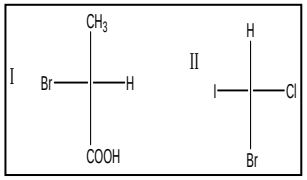
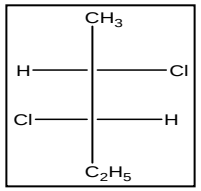
S. No	Question	Option A	Option B	Option C	Option D	Answer
1.	Optical activity is shown by a molecule which	a. Contains at least three asymmetric centres	b. is asymmetric as a whole	c. contains a double bond	d.Has a centre of symmetry	is asymmetric as a whole
2.	A chiral carbon atom has	a.1 different atom or group	b.2 different atoms or groups	c.3 different atoms or groups	d.4 different atoms or groups	4 different atoms or groups
3.	In structural representation of molecules, the prefixes Z and E stands for	Zeigler-Erythro	b. Zusammen-Estrogen	c. Zeigler-Erhard	d. Zusammen-Enteggen	Zusammen-Enteggen
4.	The R and S notation of compounds containing chiral centres is given by the priority system of the	**a.** Cahn-Ingold-Prelog	b. Newman-Ingold-Cahn	c. Cahn – Newman-Ingold	d. Cahn-Ingold-Langmuir	Cahn-Ingold-Prelog
5.	Erythrose and threose	a. are homomers	b. are cis-transisomers	c. are diastereomers	d. are optimers	are diastereomers
6.	The restricted rotation around double bond in alkene is the cause of	a. Geomentrical isomerism	b. Chain isomerism	c. Positional isomerism	d. Optical isomerism	Geomentrical isomerism
7.	Which of the following exhibits geomentrical isomerism	a. 2-Methyl propene	b. 1-butene	c. 2-butene	d. 2,3-dibromo-2-2-butene	2-butene
8.	Which of the following compounds are optically active	a. N-butanol	b. 4-hydroxy neptene	c. 2-chlorobutane	d. 3-chloropentene	2-chlorobutane
9.	Which of the following have least	a.Ethane	b.Ethylene	c. Acetylene	d.	Ethane

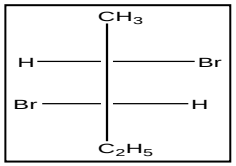
	hindered rotation about carbon bond				Hexachloroethane	
10.	The number of isomers of C_6H_{14} is	a.4	b.5	c. 6	d. 7	5
11.	The concept of stereochemistry is based on	a. VSEPR theory	b. molecular orbital theory	c. valence bond theory	d. Vant Hoff and Label's theory	Vant Hoff and Label's theory
12.	A cisoid arrangement means to	**a.** Eclipsed conformation	b. anti staggered conformation	c. skew conformation	d. gauche conformation	Eclipsed conformation
13.	Butane has	**a**. Three staggered and three eclipsed conformations	b. Two eclipsed and four staggered conformations	c. One eclipsed and five staggered conformations	d. Four eclipsed and two staggered conformations	Fout eclipsed and two staggered conformations
14.	In glyceraldehydes the order of priority for RS notation is	a. –CH2OH> -CHO>-OH>H	b. –OH>-CH2OH>-CHO>H	**c.** –OH>-CHO>-CH2OH >H	d. –CH2OH>-OH>-CHO>H	–OH>-CHO>-CH2OH >H
15.	A molecule is said to be chiral	a. if it contains plane of symmetry	b. if it contains center of symmetry	**c.** if it cannot be superimposed on its mirror image	d.if it cannot superimposed on its mirror image	if it cannot be superimposed on its mirror image
16.	Which of the statements is false regarding chiral compounds?	a.rotate the plane of polarized light	b.have cis trans isomers	c.exists as enantiomers	d.can be detected with a polarimeter	have cis trans isomers
17.	Which of the following compounds will be optically active?	a. propanoic acid	b. 3-Chloropropanoic acid	c. 2-Chloropropanoic acid	d. 3-Chloropropene	2-Chloropropanoic acid
18.	Which of the following compounds will be optically active?	a. Succinic acid	b. meso-tartaric acid	c. Lactic acid	d.Chloroacetic acid	Lactic acid
19.	Which of the following isomeric compounds showoptical isomerism?	a. 1-aminopentene	b. 2-aminopentene	c. 3-aminopentene	d.2,2-dimethylpropyl amine	2-aminopentene
20.	2-Butanol is optically active because it contains	a**.** a chiral carbon	b. a planeof symmetry	c. a hydroxyl group	d. a center of symmetry	a chiral carbon
21.	Optical isomers that are not mirror images are called	a. Diastereomers	b. Enantiomers	c. Metamers	d. Meso compounds	Diastereomers
22.	Which of the following statements is false about enantiomers?	a. rotate the plane of	b**.** are superimposablem	c. are non superimposable	d. havetha samemelting	are superimposabl

		polarized light	irror images	mirror images	point	emirror images
23.	A meso compound	a. is an achiral molecule which contains chiral carbons	b. contains a plane of symmetry or a center of symmetry	c. is optically active	d. is characterized by all of the above	is characterized by all of the above
24.	**meso-**tartaric acid is	a. sometimes optically active	b. always optically active	c. sometimes optically inactive	d. always optically inactive	always optically inactive
25.	Which of the following represents a recemic mixture?	a.75% (R) -2 – butanol,25 %(S) -2-butanol	b. 25% (R) -2 – butanol,75 %(S) -2-butanol	c. 50% (R) -2 – butanol,50 %(S) -2-butanol	d. 70% (R) -2 – butanol,30 %(S) -2-butanol	50% (R) -2 – butanol,50 %(S) -2-butanol
26.	Consider R and S -2-butanol. Which physical property distinguishes the two compounds?	a. melting point	b. Solubility in common solvents	c. Rotation of plane polarized light	d. Infrared spectrum	Rotation of plane polarized light
27.	The stereoisomer's related each other as non super imposable mirror images are called ----------	a. Enantiomers	b. Racemic mixtures	c. Diastereomers	d. Resolution	Diastereomers
28.	Reaction of the type in which one of the several possible diastereomeric products predominated are called----------	a. Stereospecific reactions	b. Stereoselective reactions	c. Racemic mixtures	d. Meso compounds	Stereoselective reactions
29.	A reaction is ---------- when a particular stereoisomeric form of the starting material reacts in such a way that it gives a specific stereoisomeric form of the product.	a.Stereospecific reactions	b. Stereoselective reactions	c.Tautomers	d. Meso compounds	Stereospecific reactions
30.	The readily inter convertible torsional structures are known as	a. Configurations	b. Conformations	c. Isomers	d. Diastereomers	Conformations
31.	The simple rotation about an axis passing through the molecule by an angle $2\pi/n$. This operation is called ----------	a. an proper rotation	b. an improper rotation	c. Isomers	d. Diastereomers	an proper rotation
32.	Reflection of atoms through a plane that passes through the molecule. This operation is called ----------	a. Reflection	b.Inversion	c. improper rotation	d. Properrotation	Reflection

33.	A symmetry element is	a. Enantiomers	b. plane	c. Diastereomers	d. Resolution	plane
34.	The molecule has an axis of three fold proper rotation; this is called----------	a. a C_4 axis	b. a C_3 axis	c. a C_2 axis	c. a C_{2v} axis	a C_3 axis
35.	The part of the science which deals with structure in three dimensions is called----------	a. Stereochemistry	b. Food technology	c. Nano chemistry	d. Physical chemistry	Stereochemistry
36.	Study of branch of stereochemistry is called----------	a. Conformational analysis	b. Chemical analysis	c. Structural analysis	d. Physical analysis	Conformational analysis
37.	Plane polarized light is light whose vibrations takes place in only ---------- of these possible planes.	a. Two	b. Three	c. One	d. Four	One
38.	An optically active substance is one that rotates the plane of ----------	a. Non polarized light	b. Luminous light	c. Polarized light	d. Sun light	Polarized light
39.	Molecules that are not super imposable on their mirror images are ----------	a. A chiral	b. Chiral	c. optival activity	d. Monomers	Chiral
40.	Mirror image isomers are called----------	a. Enantiomers	b. Diastereomers	c. Monomers	d. isomerism	Enantiomers
41.	A carbon atom to which four different groups are attached is a ----------	a.Chiral center	b.a Chiral carbon	c. Enantiomers	d. Diastereomers	Chiral center
42.	The horizontal line represent bond---------- towards is out of the plane of the paper, where as the vertical lines represent bonds---------- away from us behind the plane of the paper in Fischer-projection formula	a. Going, going	b. Coming, coming	c. Coming, going	d. Going, coming	Coming, going
43.	Enantiomers have identical ---------- expect for the direction of rotation of the plane of polarized light	a. Chemical properties	b. Physical properties	c. chemical and physical properties	d. isomerism	chemical and physical properties
44.	When the mold of pencillium glacum feeds on mixture of enantiomeric tartaric acids. It consumes only the ----------	a. (-)-tartaric acid	b. (+) –tartaric acid	c. meso-tartaric acid	d. Enantiomers	(+) –tartaric acid
45.	(-) –glucose is ----------	a. not metabolized by animals	b. fermented by yeasts	c. metabolized by animals	d.metabolized by enzymes	a. not metabolized by animals
46.	Which one of the following statement is	a. The	b. A racemic	c. The amount	d.	

	not correct?	arrangement of atoms that characterizes a particular stereoisomer is called configuration	modification is optically inactive	of rotation depends upon how many molecules the light encounters in passing through	Diastereomers have similar physical properties	
47.	Which one of the following statement is not correct?	a.Diastereomers have similar chemical properties	b. Diastereomers have different physical properties the tube	c. Stereoisomer's that are not mirror images of each other are called diastereomers	d. Diastereomers have different chemical properties	
48.	A meso compound is one whose molecules are super imposible on their mirror images even though they contain----------	a. Chiral centers	b. Asymmetric centers	c.chiral centers and asymmetric centers	d.symmericcenters	chiral centers and asymmetric centers
49.	Optically inactive reactants yield optically ----------	a. inactive products	b. Active products	c. Racemic mixtures	d. Meso compounds	inactive products
50.	  Assign the R ,S configuration of the follow	. R,S	. S,R	. R,R	. S,S	. R,R
51.	Assign the R ,S configuration of the following compound	a.2S,3R	b.2R,3S	c.2S,3S	. 2R,3R	2S,3S

						
52.	 Assign the R ,S configuration of the follow	a.R,R	b.R,S	C.S.S	d.S,R	R,R
53.	 Assign the R ,S configuration of the follow	a.R,S	b.R,R	C.S.S	d.S,R	R,S
54.	 Assign the R ,S configuration of the follow	a.2S,3S	b.2S,3R	c.2R,3S	. 2R,3R	2S,3S

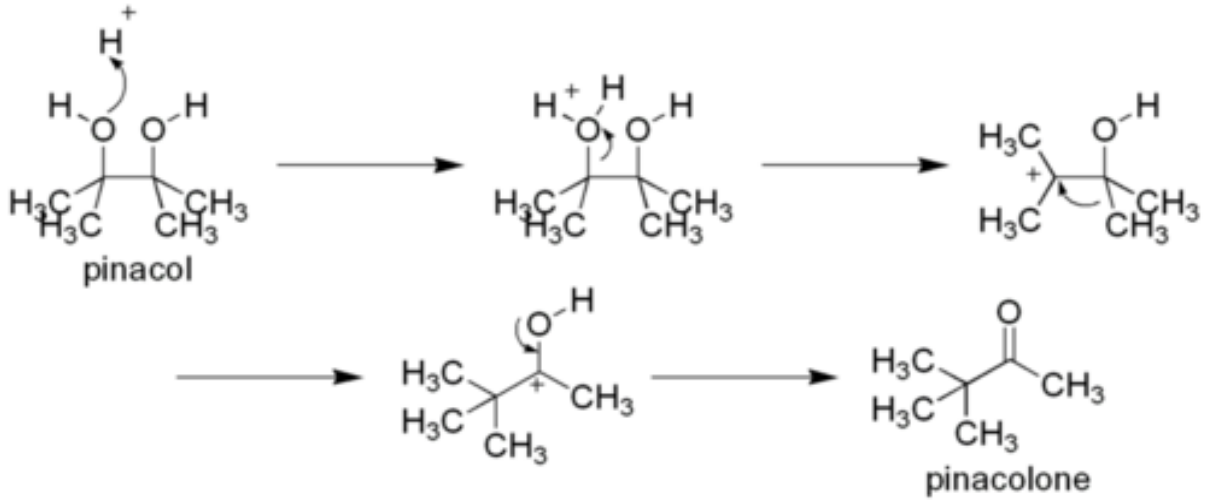
55.	 Assign the R ,S configuration of the follow	a.2S,3S	b.2S,3R	c.2R,3S	. 2R,3R	2S,3S
56.	Compounds having same molecular formula but different functional groups are called	a.Stereoisomers	b.Metamers	c.Functional isomers	d.Tautomers	Functional isomers
57.	n-Butane have several conformations given below. Which one of these is most stable-	a.Eclipsed	b.Gauche	c.Fullyeclipsed	d.Anti form	Anti form
58.	Which one form of cyclohexane is most stable	a.Chair	b.Half Chair	c.Boat	d.Twist boat	Chair
59.	Enantiomeric excess is defined as	a.% Enantiomeric excess=Observed rotation /Specificrotation rotation of pure enantiomer*100	b.% Enantiomeric excess Specific rotation of pure enantiomers/Observed specific rotation*100	c.% ofEnantiomericexcess Observed specific rotation/specific rotation ofdiastereomers *100	d.% of Enantiomeric excess= Specific rotation of diasteriomers/ Observed specific rotation*100	% Enantiomeric excess=Observed rotation /Specificrotation on rotation of pure enantiomer*100
60.	The actual arrangement in space of the atoms of a stereoisomer is	a.Configuration	b.Conformation	c.Absolute configuration	d.Absolute conformaton	Absolute configuration

UNIT-II

Mechanism of molecular rearrangement reaction: Pinacol-Pinacolone, Wagner-Meerwein, Beckmann, Hofmann, Curtius, Benzilic acid and Claisen rearrangements, Fries rearrangement and Cope rearrangement.

1. PINACOL-PINACOLONE REARRANGEMENT:

The **pinacol rearrangement** or **pinacol–pinacolone rearrangement** is a method for converting a 1, 2-diol to a carbonyl compound in organic chemistry. This 1, 2-rearrangementtakes place under acidic conditions. The name of the reaction comes from the rearrangement of pinacol to pinacolone.



This reaction was first described by Wilhelm Rudolph Fittig in 1860.

Mechanism:

In the course of this organic reaction, protonation of one of the –OH groups occurs and a carbocation is formed. If both the –OH groups are not alike, then the one which yields a more stable carbocation participates in the reaction. Subsequently, an alkyl group from the adjacent carbon migrates to the carbocation center. The driving force for this rearrangement step is believed to be the relative stability of the resultant oxonium ion, which has complete octet configuration at all centers (as opposed to the preceding carbocation). The migration of alkyl groups in this reaction occurs in accordance with their usual migratory aptitude, i.e. Aryl >>>> hydride > Phenyl > tertiary carbocation (if formed by migration) > secondary carbocation (if formed by migration) > methyl cation . The conclusion which group stabilizes carbocation more effectively is migrated.

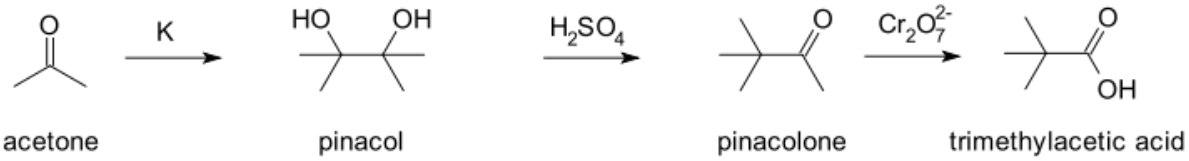
Stereochemistry:

In cyclic systems, the reaction presents more features of interest. In these reactions, the stereochemistry of the diol plays a crucial role in deciding the major product. An alkyl group which is situated trans- to the leaving –OH group alone may migrate. If otherwise, ring expansion occurs, i.e. the ring carbon itself migrates to the carbocation centre. This reveals another interesting feature of the reaction, viz. that it is largely concerted. There appears to be a connection between the migration origin and migration terminus throughout the reaction.

Moreover, if the migrating alkyl group has a chiral center as its key atom, the configuration at this center is *retained* even after migration takes place.

Although Fittig first published about the pinacol rearrangement,it was not Fittig but Aleksandr Butlerov who correctly identified the reaction products involved.

In a 1859 publication Wilhelm Rudolph Fittig described the reaction of acetone with potassium metal... Fittig wrongly assumed a molecular formula of $(C_3H_3O)_n$ for acetone, the result of a long standing atomic weight debate finally settled at the Karlsruhe Congress in 1860. He also wrongly believed acetone to be an alcohol which he hoped to prove by forming a metal alkoxide salt. The reaction product he obtained instead he called paraceton which he believed to be an acetone dimer. In his second publication in 1860 he reacted paraceton with sulfuric acid (the actual pinacol rearrangement).



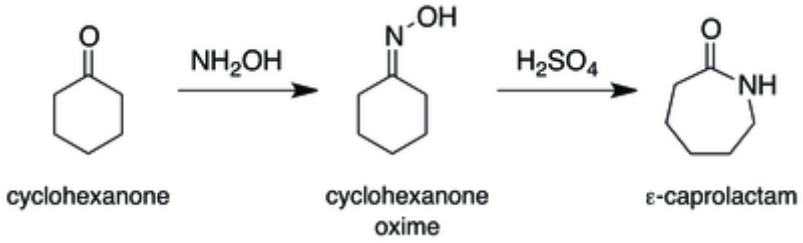
Again Fittig was unable to assign a molecular structure to the reaction product which he assumed to be another isomer or a polymer. Contemporary chemists who had already adapted to the new atomic weight reality did not fare better. One of them, Charles Friedel, believed the reaction product to be the epoxide tetramethylethylene oxide in analogy with reactions of ethylene glycol. Finally Butlerov in 1873 came up with the correct structures after he independently synthesised the compound trimethylacetic acid which Friedel had obtained earlier by oxidizing with a dichromate.

Some of the problems during the determination of the structure are because carbon skeletal rearrangements were unknown at that time and therefore the new concept had to be found.

Butlerov theory allowed the structure of carbon atoms in the molecule to rearrange and with this concept a structure for pinacolone could be found.

2. BECKMANN REARRANGEMENT:

The **Beckmann rearrangement**, named after the German chemist Ernst Otto Beckmann (1853–1923), is an acid-catalyzed rearrangement of an oxime to an amide. Cyclic oximes yield lactams.

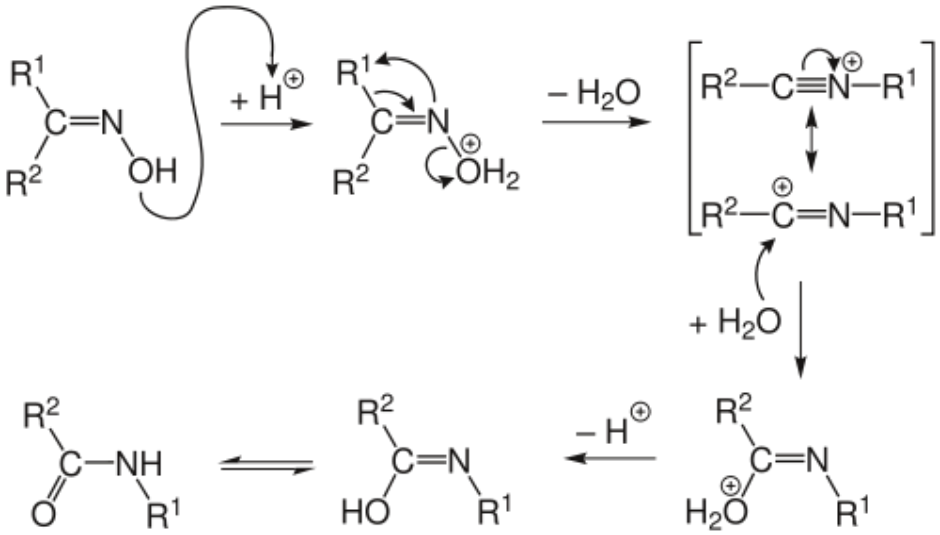


This example reaction starting with cyclohexanone, forming the reaction intermediate cyclohexanone oxime and resulting in caprolactam is one of the most important applications of the Beckmann rearrangement, as caprolactam is the feedstock in the production of Nylon 6.

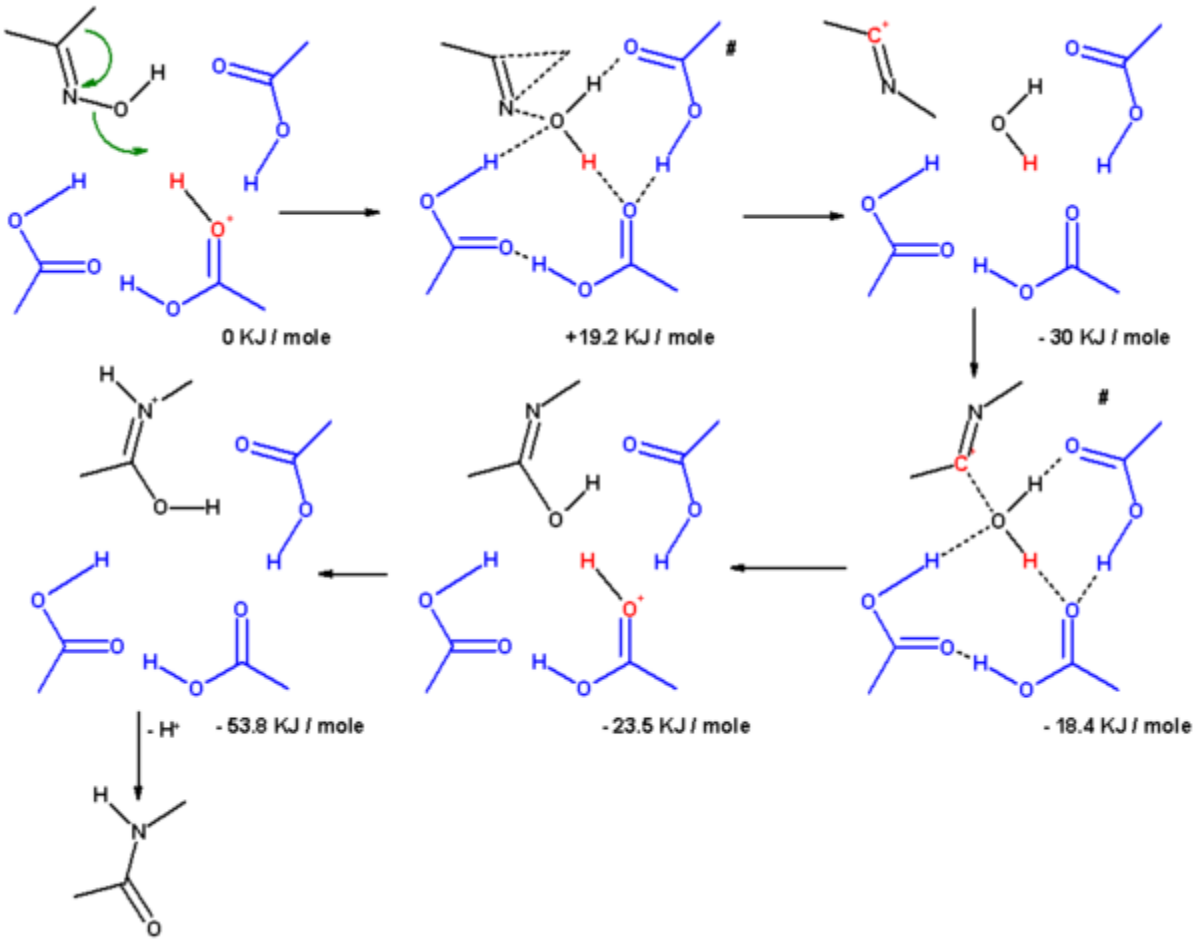
The **Beckmann solution** consists of acetic acid, hydrochloric acid and acetic anhydride, and was widely used to catalyze the rearrangement. Other acids, such as sulfuric acid orpolyphosphoric acid, can also be used. Sulfuric acid is the most commonly used acid for commercial lactam production due to its formation of an ammonium sulfate by-product when neutralized with ammonia. Ammonium sulfate is a common agricultural fertilizer providing nitrogen and sulfur.

Mechanism:

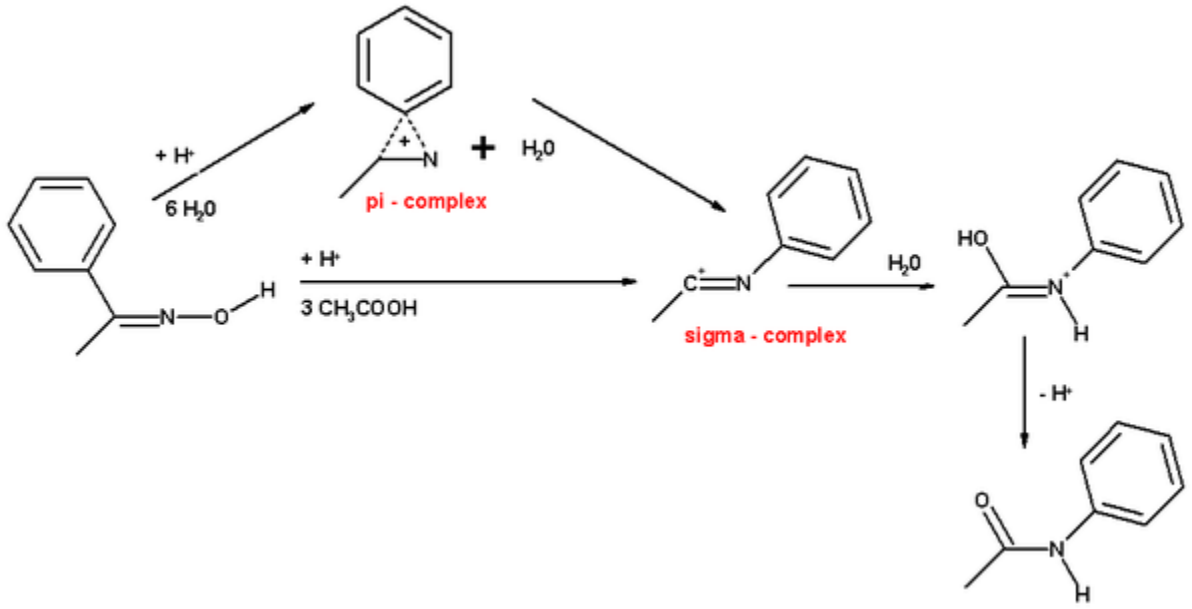
The reaction mechanism of the Beckmann rearrangement is in general believed to consist of an alkyl migration with expulsion of the hydroxyl group to form a nitrilium ion followed by hydrolysis:



In one study, the mechanism is established in silico taking into account the presence of solvent molecules and substituents. The rearrangement of acetone oxime in the Beckmann solution involves three acetic acid molecules and one proton (present as an oxonium ion). In the transition state leading to the iminium ion (σ-complex), the methyl group migrates to the nitrogen atom in a concerted reaction and the hydroxyl group is expulsed. The oxygen atom in the hydroxyl group is stabilized by the three acetic acid molecules. In the next step the electrophilic carbon atom in the nitrilium ion is attacked by water and the proton is donated back to acetic acid. In the transition state leading to the N-methyl acetimidic acid, the water oxygen atom is coordinated to 4 other atoms. In the third step, an isomerization step protonates the nitrogen atom leading to the amide.



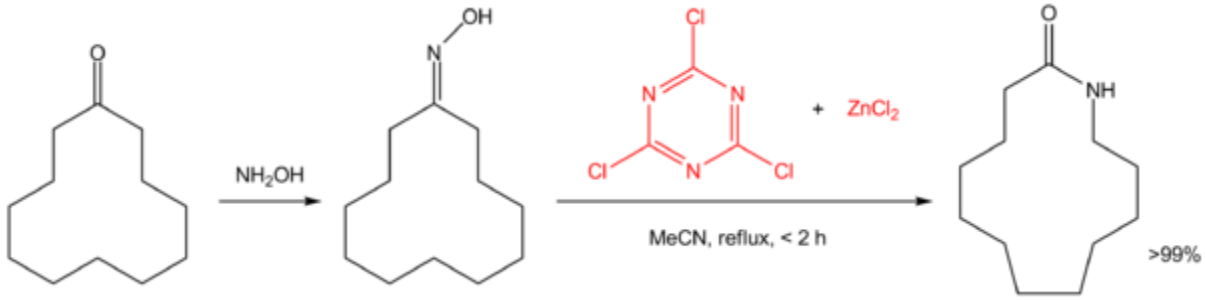
The same computation with a hydroxonium ion and 6 molecules of water has the same result, but, when the migrating substituent is phenyl in the reaction of acetophenone oxime with protonated acetic acid, the mechanism favors the formation of an intermediate three-membered π-complex. This π-complex is again not found in the H_3O^+ $(H_2O)_6$.



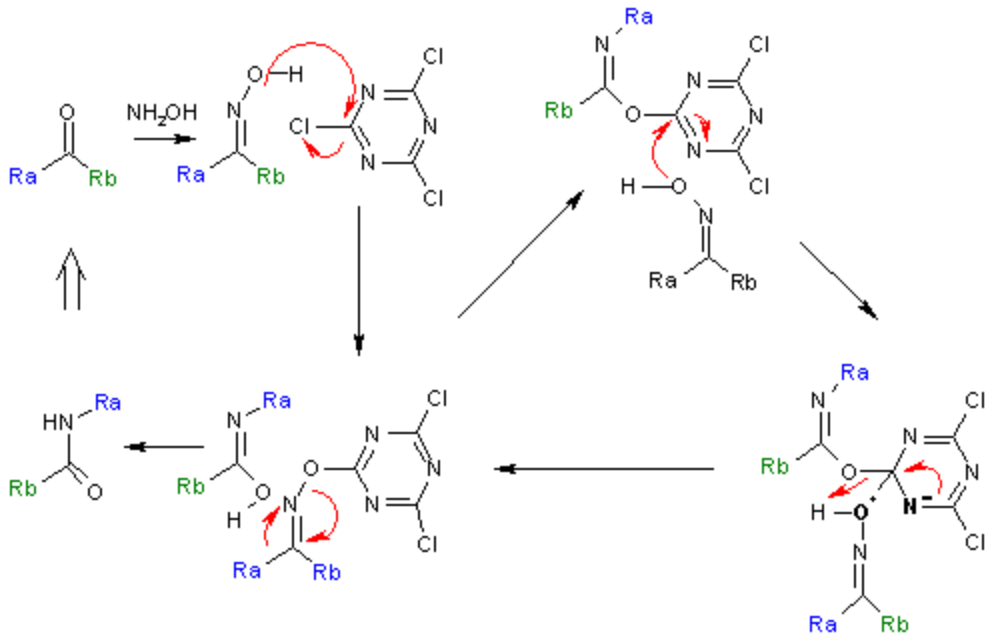
With the cyclohexanone-oxime, the relief of ring strain results in a third reaction mechanism, leading directly to the protonated caprolactam in a single concerted step without the intermediate formation of a π-complex or σ-complex.

Cyanuric Chloride Assisted Beckmann Reaction:

Beckmann reaction is known to be catalyzed by cyanuric chloride and zinc chloride co-catalyst. For example, cyclododecanone can be converted to the corresponding lactam, amonomer for the production of Nylon 12.

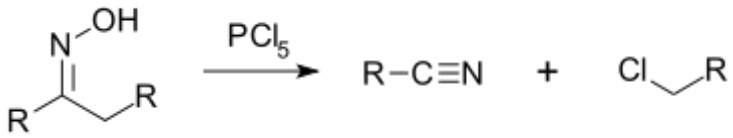


The reaction mechanism for this reaction is based on a catalytic cycle with cyanuric chloride activating the hydroxyl group via a nucleophilic aromatic substitution. The reaction product is dislodged and replaced by new reactant via an intermediate Meisenheimer complex.

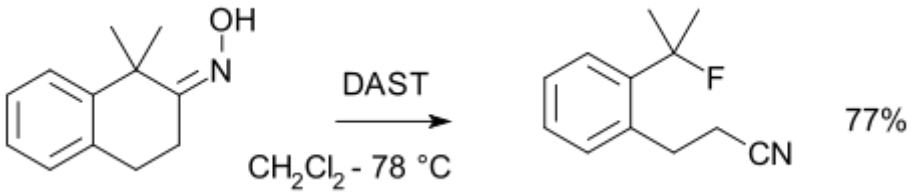


Beckmann fragmentation:

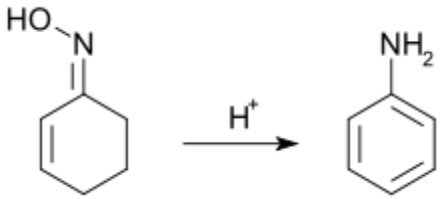
When the oxime has a quaternary carbon atom in an anti position to the hydroxyl group a fragmentation occurs forming a nitrile:



The fluorine donor in this fragmentation reaction is diethylaminosulfur trifluoride (DAST):

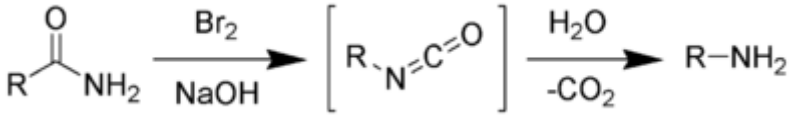


The oxime of cyclohexenone with acid forms aniline in a dehydration – aromatization reaction called the **Semmler–Wolff reaction** or **Wolff aromatization**



3. HOFMANN REARRANGEMENT:

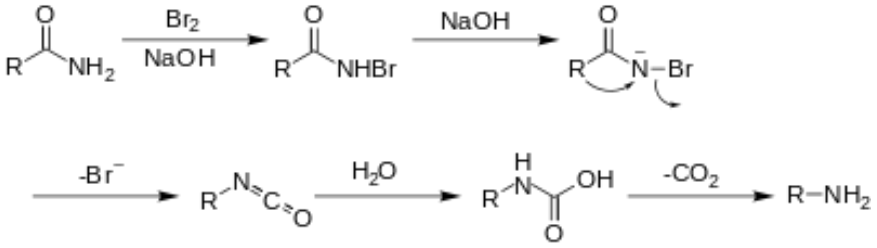
The **Hofmann rearrangement** is the organic reaction of a primary amide to a primary amine with one fewer carbon atom.



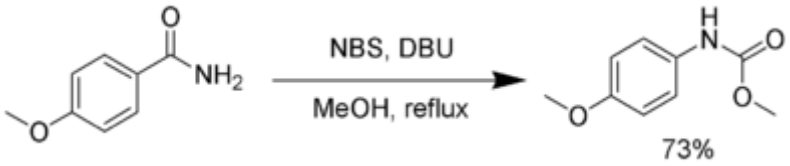
The reaction is named after its discoverer: August Wilhelm von Hofmann. This reaction is also sometimes called the **Hofmann degradation** or the **Harmon Process**, and should not be confused with the Hofmann elimination.

Mechanism:

The reaction of bromine with sodium hydroxide forms sodium hypobromite *in situ*, which transforms the primary amide into an intermediate isocyanate. The intermediate isocyanate is hydrolyzed to a primary amine, giving off carbon dioxide.



Several reagents can substitute for bromine. N-Bromosuccinimide and 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU) can effect a Hofmann rearrangement. In the following example, the intermediate isocyanate is trapped by methanol, forming a carbamate.



In a similar fashion, the intermediate isocyanate can be trapped by tert-butanol, yielding the t-butoxycarbonyl (Boc)-protected amine.

A mild alternative to bromine is also (bis(trifluoroacetoxy)iodo)benzene.

Applications:

Aliphatic & Aromatic amides are converted into aliphatic and aromatic amines, respectively

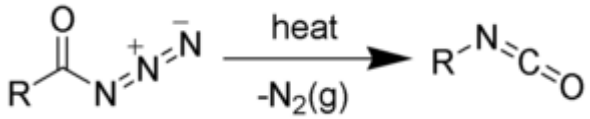
In the preparations of Anthranilic Acid from Phthalimide

Nicotinic acid is converted into 3-Amino pyridine

The Symmetrical structure of α-phenyl propanamide does not change after hofmann reaction.

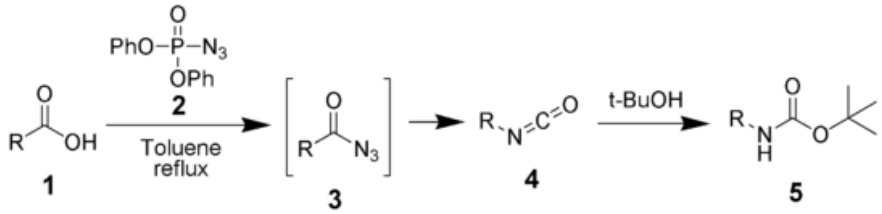
4. CURTIUS REARRANGEMENT:

The **Curtius rearrangement** (or **Curtius reaction** or **Curtius degradation**), as first defined by Theodor Curtius, is a chemical reaction that involves the rearrangement of an acyl azide to an isocyanate. Several reviews have been published.



The isocyanate can be trapped by a variety of nucleophiles. Water is often added in order to hydrolyze the isocyanate to an amine. When done in the presence of *tert*-butanol, the reaction generates Boc-protected amines, useful intermediates in organic synthesis.

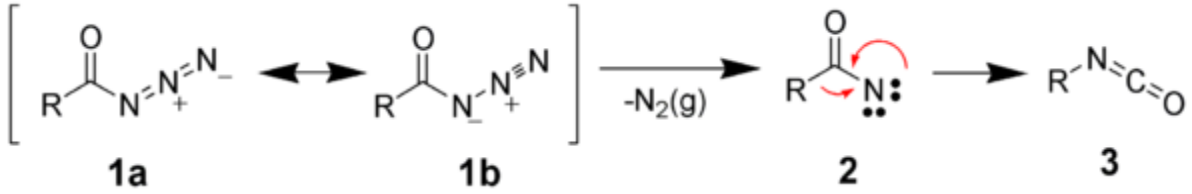
Carboxylic acids **1** can be easily converted to acyl azides **3** using diphenylphosphoryl azide **2**.



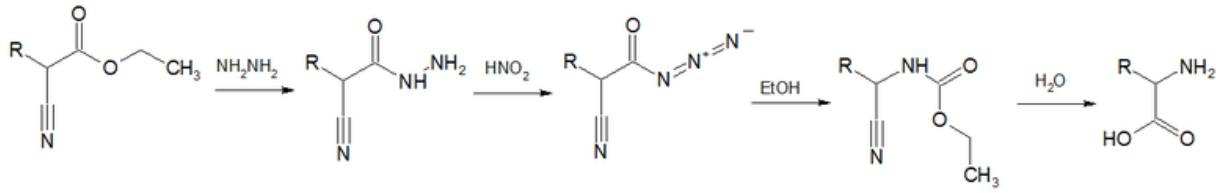
Likewise, when the Curtius reaction is performed in the presence of benzyl alcohol, Cbz-protected amines are formed.

Mechanism:

The Curtius rearrangement may be thought of as a two-step process, the first step being the loss of nitrogen gas, forming an acyl nitrene (**2**), and the second step being the rearrangement of acyl nitrenes by migration of R-group to form the desired isocyanate (**3**). However, current evidence indicates that these two steps are likely concerted (i.e., they occur at the same time), and no free nitrene intermediate is formed.

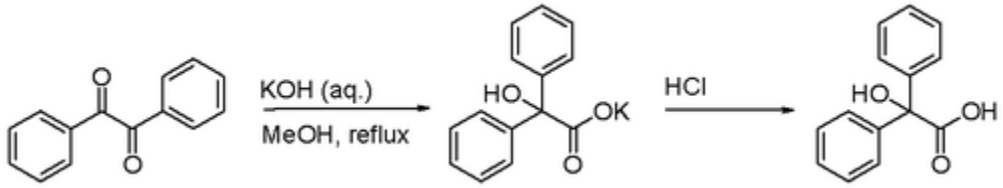


In one variation called the **Darapsky degradation** (A. Darapsky, 1936), a Curtius rearrangement takes place as one of the steps from a α-cyanoester to an amino acid.[13]



5. BENZILIC ACID REARRANGEMENT:

The **benzilic acid rearrangement** is the rearrangement reaction of benzil with potassium hydroxide to benzilic acid. First performed by Justus Liebig in 1838 this reaction type is displayed by 1, 2-diketones in general. The reaction product is a α-hydroxy-carboxylic acid.



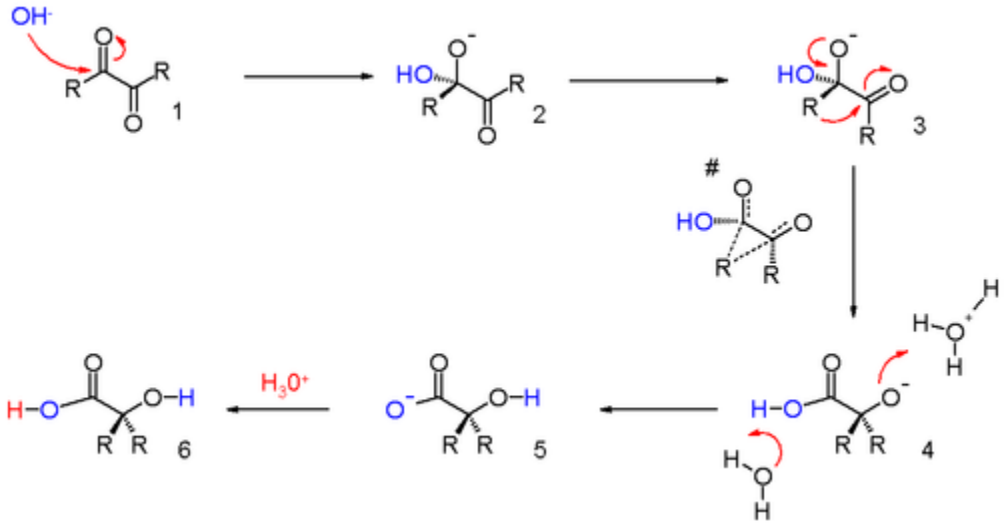
Certain acyloins also rearrange in this fashion.

This diketone reaction is related to other rearrangements: the corresponding keto-aldehyde (one alkyl group replaced by hydrogen) rearranges in a Cannizzaro reaction, the corresponding 1, 2-diol reacts in a pinacol rearrangement.

Mechanism:

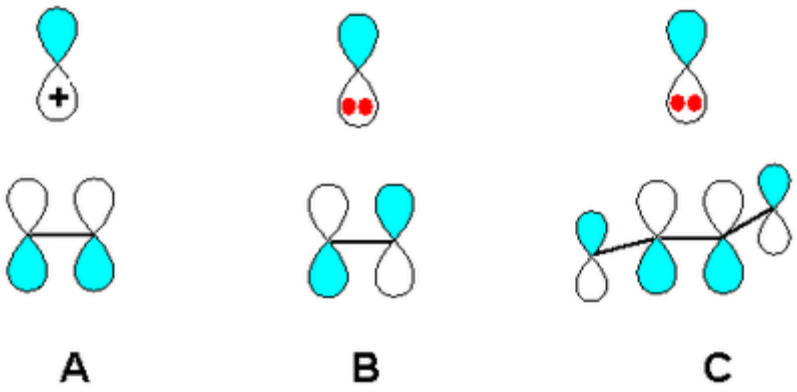
The reaction is a representative of 1, 2-rearrangements. These rearrangements usually have migrating carbocations but this reaction is unusual because it involves a migratingcarbanion. The long established reaction mechanism updated with in silico data is outlined in *scheme 2*.

A hydroxide anion attacks one of the ketone groups in **1** in a nucleophilic addition to the hydroxyl anion **2**. The next step requires a bond rotation to conformer **3** which places the migrating group R in position for attack on the second carbonyl group in a concerted step with reversion of the hydroxyl group back to the carbonyl group. This sequence resembles a nucleophilic acyl substitution. Calculations show that when R is methyl the charge build-up on this group in the transition state can be as high as 0.22 and that the methyl group is positioned between the central carbon carbon at a separation of 209 pm.



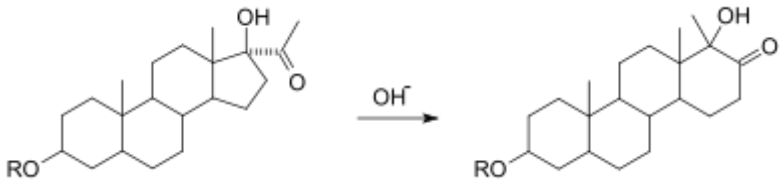
The carboxylic acid in intermediate **4** is less basic than the hydroxyl anion and therefore proton transfer takes place to intermediate **5** which can be protonated in acidic workup to the final α-hydroxy-carboxylic acid **6**. Calculations show that an accurate description of the reaction sequence is possible with the participation of 4 water molecules taking responsibility for the stabilization of charge buildup. They also provide a shuttle for the efficient transfer of one proton in the formation of intermediate 5.

From a molecular orbital point of view this rearrangement may at a first glance not obvious. Contrary to a carbocationic rearrangement as in the Wagner-Meerwein rearrangement in which the empty carbocationic orbital interacts positively and symmetry allowed with the filled pi orbital HOMO of the central C-C bond (situation **A** in *scheme 3*), a filled carbanionic orbital should not be able to escape a symmetry forbidden MO overlap with the LUMO which is the empty antibonding pi orbital having one node (situation **B**).



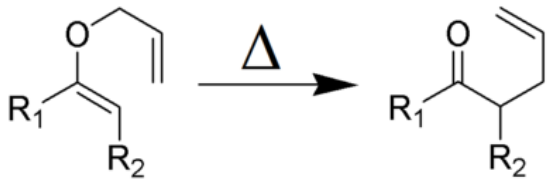
In reality a 1, 2-diketone LUMO is a 4 electron system without any nodes in the central C-C bond and symmetry allowed transition is possible (Situation **C**). In other words the transition states of both a carbocationic rearrangement and the benzilic rearrangement obey the Woodward-Hoffmann rules because the involves respectively 2 electrons and 6 electrons (n=0 and 1 in the 4n+2 Hückel's rule).

A variation of this reaction occurs in certain steroids. In the so-called **D-Homo Rearrangement of Steroids** a cyclopentane ring expands to a cyclohexane ring with added base.



6. CLAISEN REARRANGEMENT:

The **Claisen rearrangement** (not to be confused with the Claisen condensation) is a powerful carbon–carbon bond-forming chemical reaction discovered by Rainer Ludwig Claisen. The heating of an allyl vinyl ether will initiate a [3, 3]-sigmatropic rearrangement to give a γ,δ-unsaturated carbonyl.



Discovered in 1912, the Claisen rearrangement is the first recorded example of a [3,3]-sigmatropic rearrangement.

Mechanism:

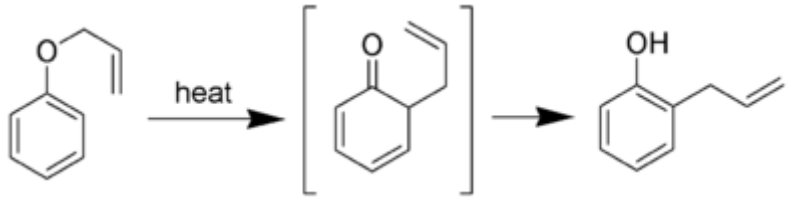
The Claisen rearrangement is an exothermic (about 84 kJ/mol), concerted pericyclic reaction which according to the Woodward–Hoffmann rules shows a suprafacial reaction pathway.

There are substantial solvent effects in the Claisen reactions. More polar solvents tend to accelerate the reaction to a greater extent. Hydrogen-bonding solvents gave the highest rate constants. For example, ethanol/water solvent mixtures give rate constants 10-fold higher than sulfolane.

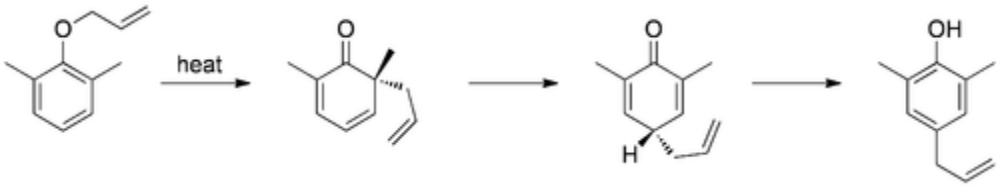
Trivalent organoaluminium reagents, such as trimethylaluminium, have been shown to accelerate this reaction.

Aromatic Claisen rearrangement

The aromatic variation of the **Claisen rearrangement** is the [3,3]-sigmatropic rearrangement of an allyl phenyl ether to an intermediate which quickly tautomerizes to an ortho-substituted phenol.

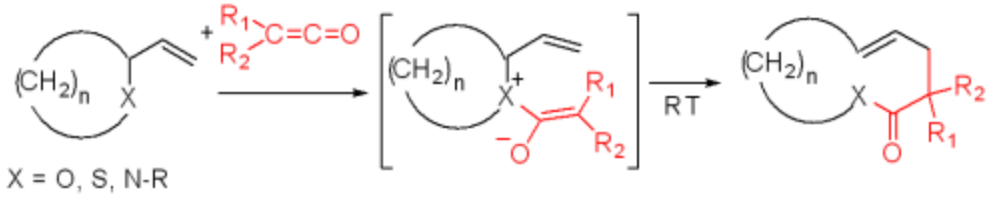


If ortho position is substituted then reaction goes to para position with retention in configuration.[10]



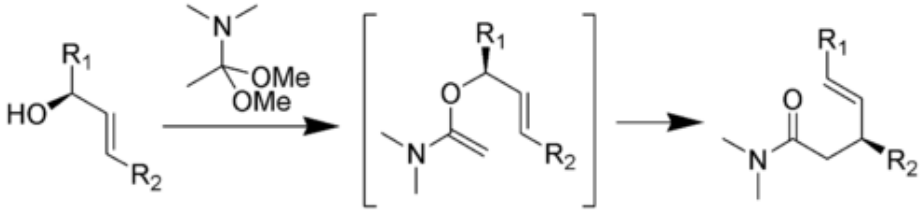
Bellus–Claisen rearrangement

The *Bellus–Claisen rearrangement* is the reaction of allylic ethers, amines, and thioethers with ketenes to give γ,δ-unsaturated esters, amides, and thioesters.



Eschenmoser–Claisen rearrangement

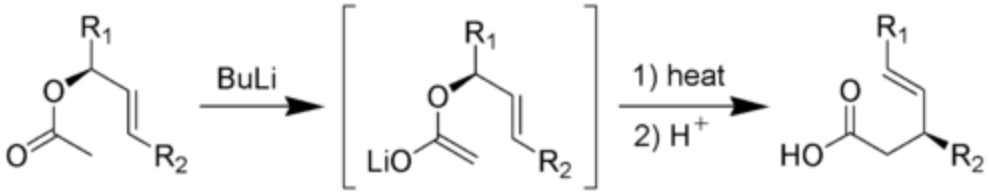
The *Eschenmoser–Claisen rearrangement* proceeds from an allylic alcohol to a γ,δ-unsaturated amide, and was developed by Albert Eschenmoser in 1964.



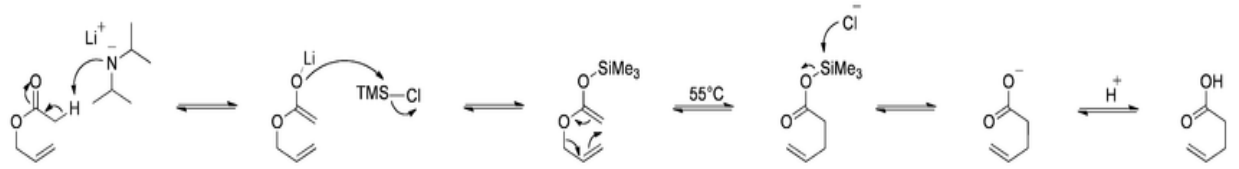
Mechanism:

Ireland–Claisen rearrangement

The *Ireland–Claisen rearrangement* is the reaction of an allylic acetate with strong base (such as Lithium diisopropylamide) to give a γ,δ-unsaturated carboxylic acid. The actual rearrangement occurs from the enolate of the ester—this is the structural analog of the simple alkene in the original Claisen rearrangement.



Mechanism:



Johnson–Claisen rearrangement

The *Johnson–Claisen rearrangement* is the reaction of an allylic alcohol with trimethyl orthoacetate to give a γ,δ-unsaturated ester.

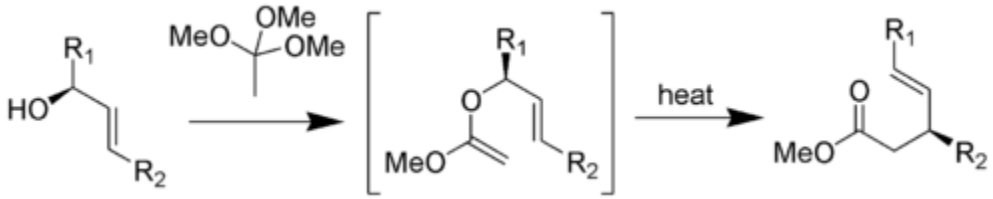
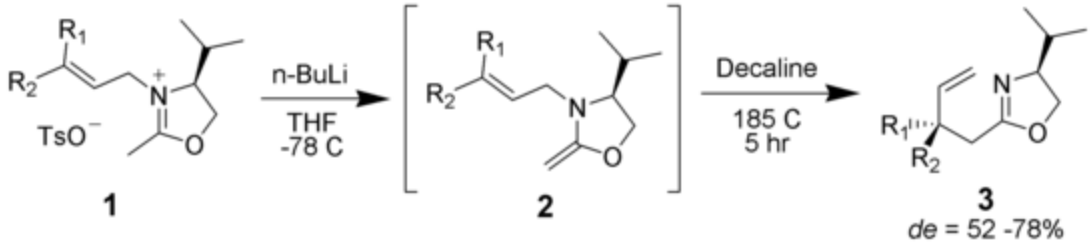


Photo-Claisen rearrangement

The *photo-Claisen rearrangement* is closely related to the photo-Fries rearrangement, proceeding by a similar mechanism. Aryl ethers undergo the photo-Claisen, while the photo-Fries are experiences by aryl esters.

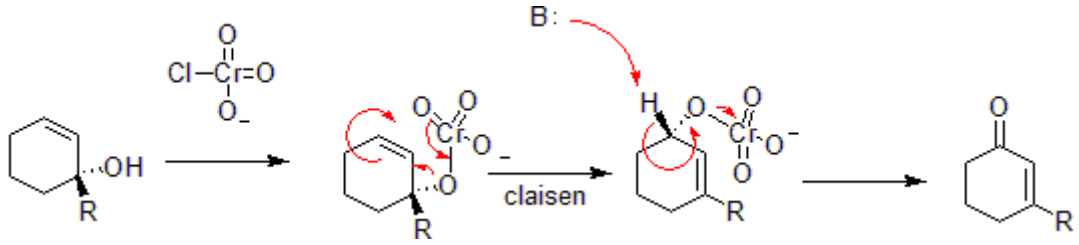
Aza–Claisen

An iminium can serve as one of the pi-bonded moieties in the rearrangement.



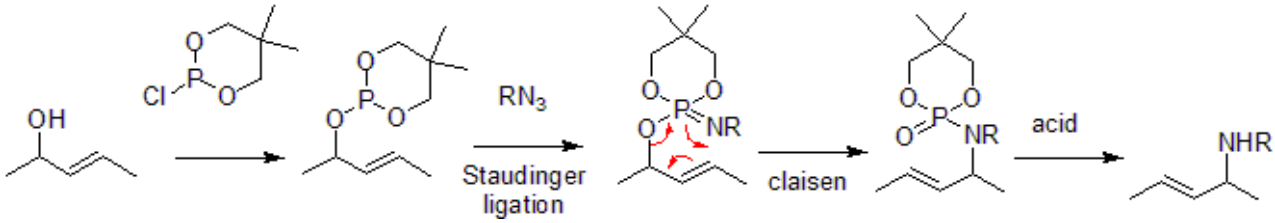
Chromium oxidation

Chromium can oxidize allylic alcohols to alpha-beta unsaturated ketones on the opposite side of the unsaturated bond from the alcohol. This is via a concerted hetero-Claisen reaction, although there are mechanistic differences since the chromium atom has access to d- shell orbitals which allow the reaction under a less constrained set of geometries.



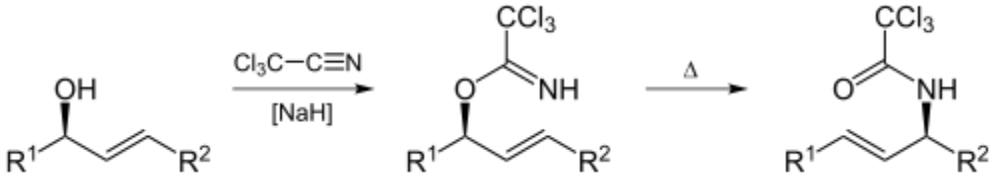
Chen–Mapp reaction

The **Chen–Mapp reaction** also known as the **[3,3]-Phosphorimidate Rearrangement** or **Staudinger–Claisen Reaction** installs a phosphite in the place of an alcohol and takes advantage of the Staudinger reduction to convert this to an imine. The subsequent Claisen is driven by the fact that a P=O double bond is more energetically favorable than a P=N double bond.



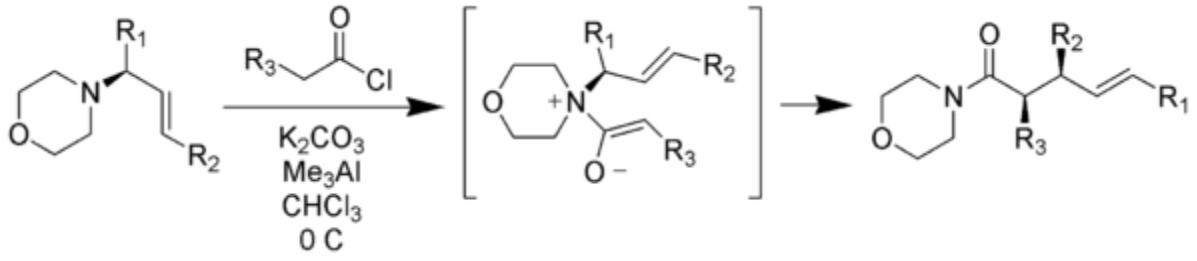
Overman rearrangement

The Overman rearrangement (named after Larry Overman) is a Claisen rearrangement of allylic trichloroacetimidates to allylic trichloroacetamides.



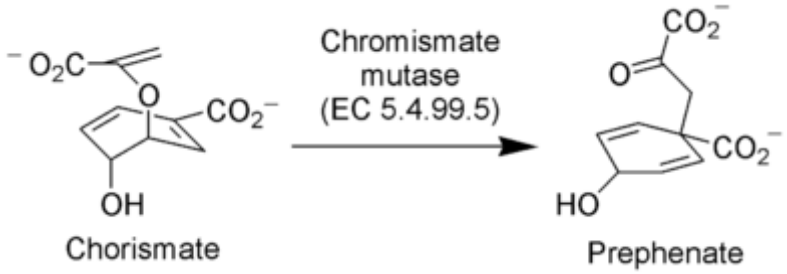
Zwitterionic Claisen rearrangement

Unlike typical Claisen rearrangements which require heating, zwitterionic Claisen rearrangements take place at or below room temperature. The acyl ammonium ions are highly selective for Z-enolates under mild conditions.



Claisen rearrangement in nature:

The enzyme Chorismate mutase (EC 5.4.99.5) catalyzes the Claisen rearrangement of chorismate ion to prephenate ion, a key intermediate in the shikimic acid pathway (thebiosynthetic pathway towards the synthesis of phenylalanine and tyrosine).



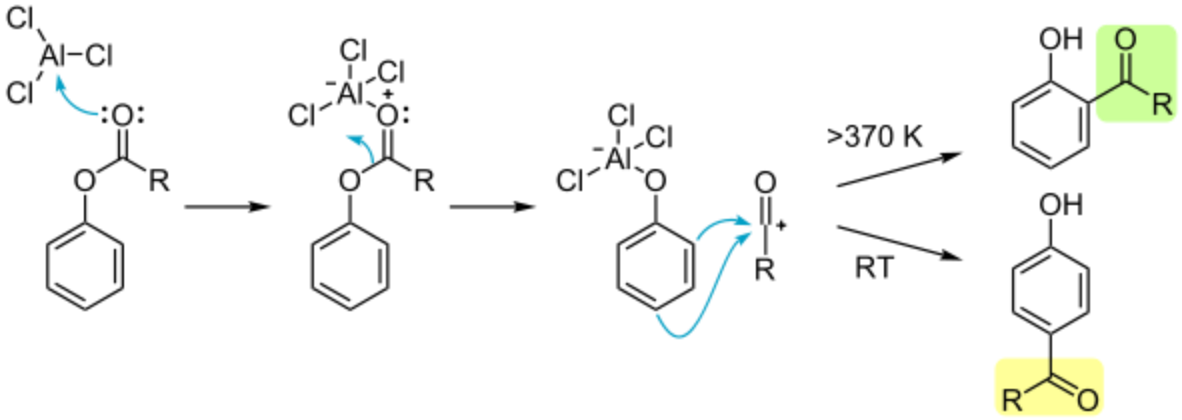
7. **FRIES REARRANGEMENT**:

The **Fries rearrangement**, named for the German chemist Karl Theophil Fries, is a rearrangement reaction of a phenyl ester to a hydroxy aryl ketone by catalysis of Lewis acids.

It involves migration of an acyl group of phenyl ester to benzene ring. The reaction is ortho and para selective and one of the two products can be favoured by changing reaction conditions, such as temperature and solvent.

Mechanism:

Despite many efforts a definitive reaction mechanism for the Fries rearrangement is not available. Evidence for inter- and intramolecular mechanisms have been obtained by so-called cross-experiments with mixed reactants. Reaction progress is not dependent on solvent or substrate. A widely accepted mechanism involves a carbocation intermediate.



In the first reaction step a Lewis acid for instance aluminium chloride AlCl 3 co-ordinates to the carbonyl oxygen atom of the acyl group. This oxygen atom is more electron rich than the phenolic oxygen atom and is the preferred Lewis base. This interaction polarizes the bond between the acyl residue and the phenolic oxygen atom and the aluminium chloride group rearranges to the phenolic oxygen atom. This generates a free acylium carbocation which reacts in a classical electrophilic aromatic substitution with the aromatic ring. The abstracted proton is released as hydrochloric acid where the chlorine is derived from aluminium chloride. The orientation of the substitution reaction is temperature dependent. A low reaction temperature favors para substitution and with high temperatures the ortho product prevails. Formation of the ortho product is also favoured in non-polar solvents; as the solvent polarity increases, the ratio of the para product also increases.

Phenols react to esters but do not react to hydroxyarylketones with acylhalogen compounds under Friedel-Crafts acylation reaction conditions and therefore this reaction is of industrial importance for the synthesis of hydroxyarylketones which are important intermediates for several pharmaceutics such as paracetamol and salbutamol. As an alternative toaluminium chloride, other Lewis acids such as boron trifluoride and bismuth triflate or strong protic acids such as hydrogen fluoride and methanesulfonic acid can also be used. In order to avoid the use of these corrosive and environmentally unfriendly catalysts altogether research into alternative heterogeneous catalysts is actively pursued.

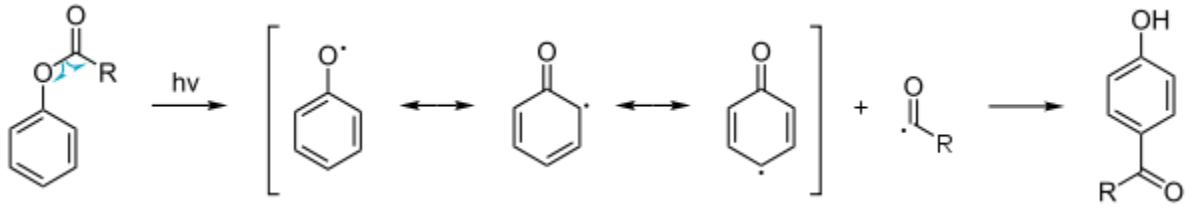
Limits:

In all instances only esters can be used with stable acyl components that can withstand the harsh conditions of the Fries rearrangement. If the aromatic or the acyl component is heavily substituted then the chemical yield will drop due to steric constraints. Deactivating meta-

directing groups on the benzene group will also have an adverse effect as can be expected for a Friedel–Crafts acylation.

Photo Fries Rearrangement:

In addition to the ordinary thermal phenyl ester reaction a so-called photochemical **Photo-Fries rearrangement** exists that involves a radical reaction mechanism. This reaction is also possible with deactivating substituents on the aromatic group. Because the yields are low this procedure is not used in commercial production. However, photo-Fries rearrangement may occur naturally, for example when a plastic bottle made of polyethylene terephthalate (PET) is exposed to the sun, particular to UV light at a wavelength of about 310 nm, if the plastic has been heated to 40 degrees Celsius or above (as might occur in a car with windows closed on a hot summer day). In this case, photolysis of the ester groups would lead to leaching of phthalate from the plastic.

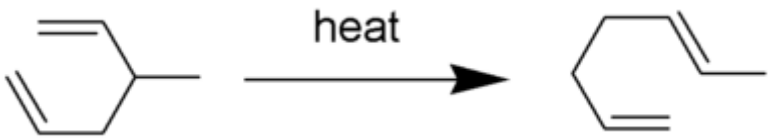


Anionic fries rearrangement:

In addition to Lewis acid and photo-catalysed Fries rearrangements, there also exists an anionic Fries rearrangement. In this reaction, the aryl ester undergoes ortho-metallation with a strong base, which then rearranges in a nucleophilic attack mechanism.

8. COPE REARRANGEMENT:

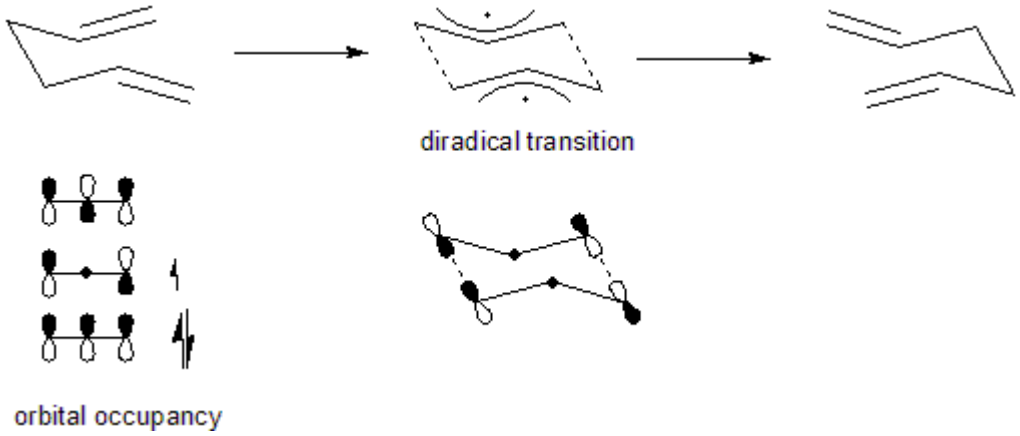
The **Cope rearrangement** is an extensively studied organic reaction involving the [3,3]-sigmatropic rearrangement of 1,5-dienes. It was developed by Arthur C. Cope. For example 3-methyl-1, 5-hexadiene heated to 300°C yields 1, 5-heptadiene.



The Cope rearrangement causes the fluxional states of the molecules in the bullvalene family.

Mechanism:

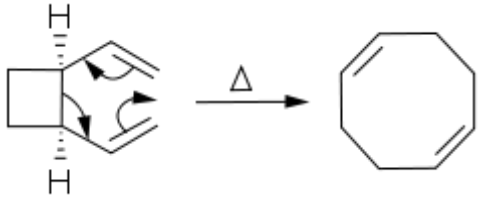
Although the Cope rearrangement is concerted and pericyclic, it can also be considered to go via a transition state that is energetically and structurally equivalent to adiradical.[*citation needed*] This is an alternative explanation which remains faithful to the uncharged nature of the Cope transition state, while preserving the principles of orbital symmetry. This also explains the high energy requirement to perform a Cope rearrangement. Although illustrated in the chair conformation, the Cope can also occur with cyclohexadienes in the "boat" conformation.



The above description of the transition state is not quite correct. It is currently generally accepted that the Cope rearrangement follows an allowed concerted route through a homoaromatic transition state and not a diradical. That is unless the potential energy surface is perturbed to favor the diradical.

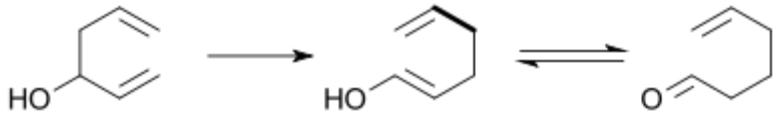
Examples:

The rearrangement is widely used in organic synthesis. It is symmetry-allowed when it is suprafacial on all components. The transition state of the molecule is passes through a boat or chair like transition state. An example of the Cope rearrangement is the expansion of a cyclobutane ring to a 1, 5-cyclooctadiene ring:

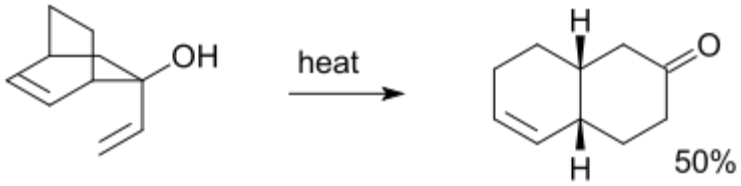


In this case, the reaction must pass through the boat transition state to produce the two cis double bonds. A trans double bond in the ring would be too strained. The reaction occurs under thermal conditions. The driving force of the reaction is the loss of strain from the cyclobutane ring.

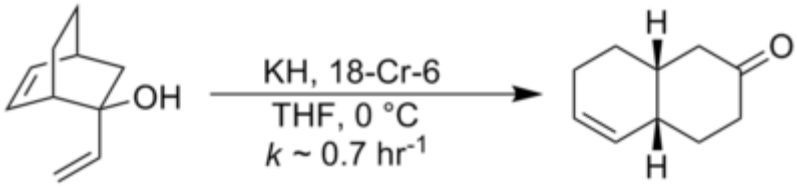
In the **oxy-Cope rearrangement** a hydroxyl group is added at C3 forming an enal or enone after Keto-enol tautomerism of the intermediate enol:



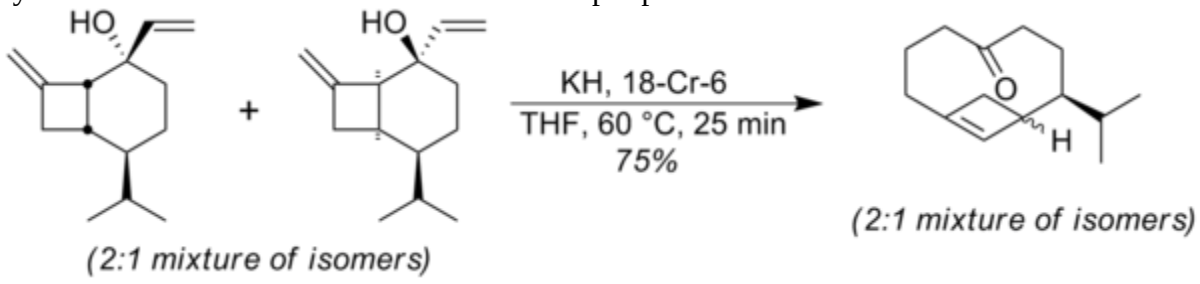
For instance in this reaction:



In 1975, Evans and Golob showed that deprotonation of oxy-Cope substrates to form the corresponding alkali metal alkoxides resulted in rate accelerations of 10^{10} to 10^{17} for the oxy-Cope rearrangement. Typically potassium hydride and 18-crown-6 are employed in order to generate a fully dissociated potassium alkoxide:



It is noteworthy that the anion-accelerated oxy-Cope reaction can proceed with high efficiency even in systems that do not permit good orbital overlap, as seen in this example from Schreiber's synthesis of periplanone B:



The authors remark that the corresponding neutral oxy-Cope and siloxy-Cope rearrangements failed, giving only elimination products at 200 °C.

Another variation of the Cope rearrangement is the heteroatom Cope reactions such as the Aza-Cope rearrangement. Another widely studied [3, 3] sigmatropic rearrangement is theClaisen rearrangement. Also see the divinylcyclopropane-cycloheptadiene rearrangement.

Possible Questions

PART A (1 Marks Questions)

1. The concept of stereochemistry is based on
a. VSEPR theory b. molecular orbital theory c. valence bond theory
d. **Vant Hoff and Label's theory**

2. A cisoid arrangement means to
a. Eclipsed conformation b. anti staggered conformation c. skew conformation
d. gauche conformation

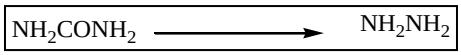
3. Butane has
a. Three staggered and three eclipsed conformations
b. Two eclipsed and four staggered conformations
c. One eclipsed and five staggered conformations
d. **Four eclipsed and two staggered conformations**

4. In glyceraldehydes the order of priority for RS notation is
a. –CH2OH> -CHO>-OH>H b. –OH>-CH2OH>-CHO>H
c. –OH>-CHO>-CH2OH >H d. –CH2OH>-OH>-CHO>H

5.The conversion of Carboxylic acid to primary amine is known as
a**. Schmidt rearrangement** b. Lossen rearrangement c. Hofmann rearrangement
d. Claisen rearrangement

6.The conversion of amide to primary amine is known as
a.Schmidt rearrangement b. Lossen rearrangement c. **Hofmann rearrangement**
d. Claisen rearrangement

7. What is the reagent used in the following reaction?



a. **Br_2+KOH** b.Br_2+NaOH c.Br_2+NH_4OH d.Br_2+NH_4Cl

8. Benzidine react with Br_2 in KOH it gives
a.**aniline** b.urea c.amide d.ammonia

9. A freshly prepared solution of glucose has specific rotation of +112° but on keeping for some time it changes to +52.7°. This phenomenon is known as
a.**Mutarotation** b.Epimerization c.Racemisation d.Resolution

10. The specific rotation for identification of carbohydrate is
a.**Molisch's test** b.Tollen's test c.Fehling's test d.Benedicts test

11. Glucose does not restore the pink colour of Schiff's reagent. It is due to
a. **aldehyde involved in hemiacetal formation** b.no aldehyde group c.-I effect of -OH group d.keto group

12. The reagent which can be used to distinguish between starch and cellulose is
a.Tollen's test b.**Iodine solution** c.acetic anhydride d.Fehling's reagent

13. Proteins have characteristic
a.Boiling point b.Melting point c.**Isoelectric point** d.pH of the solution

14. The peptides have---------- linkages
a.**CONH linkage** b. COOH linkage c.RCNR linkage d.CH2NH2 linkage

15. In IR spectra the amino acid shows absorption band at
a.**1400&1600cm-1** b. 1300-1600 cm-1 c.1200-1600cm-1 d.1350-1700 cm-1

16. The simplest amino acid is
a.Alanine b.Histidine c.Crystinine d.**Glycine**

17. Pyridine reacts with HCl to form
a. **Pyridinium Chloride** b.2-Chloropyridine c.3-Chloropyridine
d. 4-Chloropyridine

18. Pyridine undergoes electrophilic substitution with fuming sulphuric acid at 350°C to give
a.2-pyridine sulphonic acid b.**3-pyridine sulphonic acid** c.4-pyridine sulphonic acid
d.5-pyridine sulphonic acid

19. Furan reacts with ammonia in the presence of alumina at 400°C to give
a.Pyridine b.**Pyrrole** c.Furfural d.Furoic acid

20. Which of the following reagents will react with furan to form 2-furansulphonic acid
a**. SO3 in pyridine at 100°C** b. dilute sulphuric acid at 200°C c. SO at 100°C
d. dilute sulphuric acid at 100°C

PART B (8 Marks Questions)

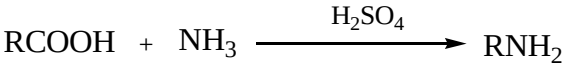
1) Explain with suitable example Hofmann Rearrangement.

2) Explain benzidine rearrangement.

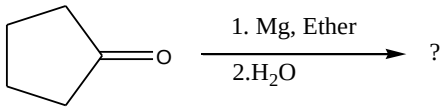
3) Explain Benzilic acid Rearrangement

4). Explain Claisen condensation.

5) i. Give the mechanism for the following reaction and explain its application.

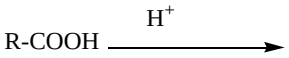


ii. Predict the product



6) Explain claisen rearrangement with suitable example?

7) Complete the following rearrangement reaction mechanism.



8) Explain the mechanism of following reactions

a) Lossen rearrangement.

b) Benzidine rearrangement.

c) Curtius rearrangement.

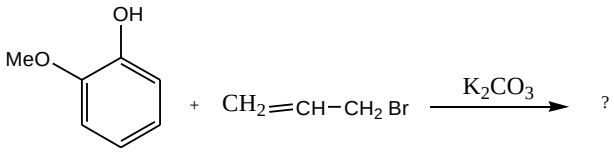
d) Benzilic acid rearrangement.

9) What are the products formed when following reaction undergo the Hoffmann rearrangement?

10) What is Pinacol-Pinacolane Rearrangement? Explain its mechanism. Give the applications of Pinacole- Pinacolane rearrangement in organic synthesis

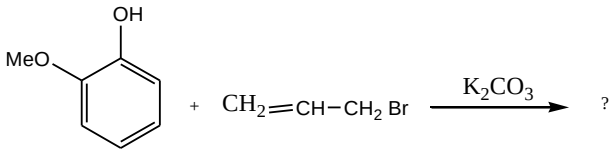
11) i. Fries Rearrangement and explain its mechanism.

ii. Predict the product?



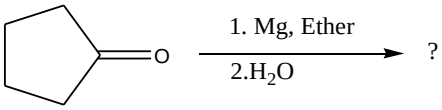
12) i. Explain Claisen Rearrangement

ii. Predict the product?



13) i. Explain Hofmann Rearrangement

ii. Predict the product



Karpagam Academy of Higher Education

(Deemed University Established Under Section 3 of UGC Act 1956)

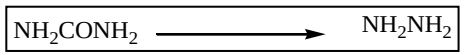
Coimbatore-21

Department of Chemistry

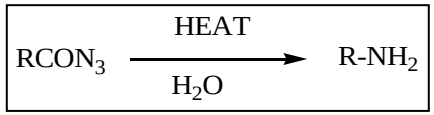
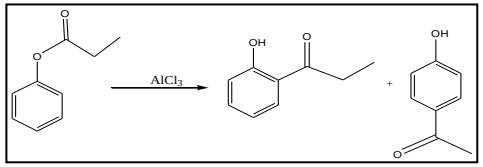
III B.Sc Chemistry

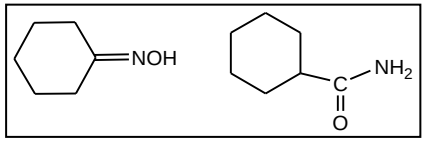
Organic Chemistry

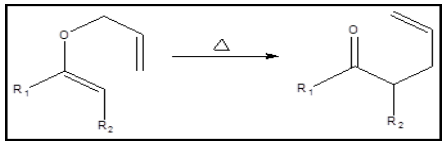
Unit II Objective Questions

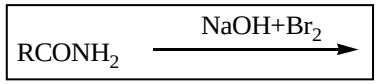
S. No	Question	Option A	Option B	Option C	Option D	Answer
1.	The intermediate formed in Beckmann rearrangement is also the intermediate is	a.Perkin reaction	b. Stobbe reaction	c. Dields-Alder reaction	d. Hofmann reaction	d. Hofmann reaction
2.	Which of the following reaction undergoes without the formation of any intermediate?	a.SN_1 reaction	b.SNi reaction	c. Ar SN1 reaction	d.SN_2 reaction	d.SN_2 reaction
3.	Which of the following reaction gives crossed products?	a.Claisen rearrangement	b. Fries rearrangement	c.Lossen rearrangement	d. Curtius rearrangement	b. Fries rearrangement
4.	Which of the following reaction gives temperature dependence products?	a.Perkin reaction	b. Fries rearrangement	c. Beckmann rearrangement	d. Claisen rearrangement	b. Fries rearrangement
5.	The conversion of Carboxylic acid to primary amine is known as	a. Schmidt rearrangement	b. Lossen rearrangement	c. Hofmann rearrangement	d. Claisen rearrangement	Schmidt rearrangement
6.	The conversion of amide to primary amine is known as	a.Schmidt rearrangement	b. Lossen rearrangement	c. Hofmann rearrangement	d. Claisen rearrangement	Hofmann rearrangement
7.	What is the reagent used in the following reaction? 	a. Br_2+KOH	b.Br_2+NaOH	c.Br_2+NH_4OH	d.Br_2+NH_4OH	a. Br_2+KOH
8.	Benzidine react with Br2 in KOH it gives	a.aniline	b.urea	c.amide	d.ammonia	aniline
9.	Hydrazo benzene when boiled with acid it gives	a. Benzidine	b.Aniline	c.Azobenzene	d.Azoxybenzene	Benzidine
10.	Hydrazo compounds, when boiled with acids, rearranges to benzidine. This	a.Claisen rearrangement	b. Fries rearrangement	c.Lossen rearrangement	d.Benzidine rearrangement	Benzidine rearrangement

	rearrangement is known as					
11.	When benzil treated with NaOH it gives	a.Benzilic acid	b.benzanilide	c.benzoic acid	d.benzyl alcohol	Benzilic acid
12.	The reaction of hydrozoic acid with a carboxylic acid in the presence of sulphuric acid to form a primary amine is known as	a.Schmidt rearrangement	b. Lossen rearrangement	c. Hofmann rearrangement	d. Claisen rearrangement	Schmidt rearrangement
13.	oxidative cleavage of C-C bond by malaprade occurs only when diol is	a.gem-diol	b.vicinal diol	c.isolated diol	d.diol	vicinal diol
14.	The migrating order of alkyl or aryl group to intermediate carbocation in pinacol pinacolone rearrangement is	a. p-anisyl>p-tolyl>phenyl>R	b. p-tolyl>p-anisyl>phenyl>R	c.phenyl> p-anisyl>p-tolyl>R	d.p-tolyl>R>p-anisyl>phenyl	p-anisyl>p-tolyl>phenyl> R
15.	Pinacol when heatedwithAl2O3 at 450°C	a.2,3-Dimethyl-2-butene	b. 2,3-Dimethyl-1,3-butadiene	c.2,3-Dimethyl-butene	d.2,3-Dimethyl-4-butene	2,3-Dimethyl-1,3-butadiene
16.	Liebermann's test is a diagnostic test for	a. Primary amine	b.Secondary amine	c.Tertiary amine	d.Quaternary ammonium salt	Secondary amines
17.	Carbylamine test is a diagonistic test for	a. Primary amine	b.Secondary amine	c.Tertiary amine	d.Quaternary ammonium salt	Primary amine
18.	Hofmann elimination is a nucleophilic reaction involving	a.α-elimination	b.β-elimination	c.ϒ-elimination	d.δ-elimination	β-elimination
19.	Sterically hinderednprimary aromatic amine can be prepared by	a.Schmidt rearrangement	b. Lossen rearrangement	c. Hofmann rearrangement	d. Claisen rearrangement	Schmidt rearrangement
20.	Hofmann degradation of benzamides if falicitated by the presence of	a.Electron releasing group	b. Electron realising group	c.Under goes diazotization	d.noteffected by any group	Electron releasing group
21.	The Hammet equationin organic chemistry relates structure to both equilibrium constants and rate constants for-------	a.Reactions of meta and para sustituted benzene	b. Free radical reactions	c. Photochemical reactions	d. Multicentered reactions	Reactions of meta and para sustituted benzene
22.	Ethyl acetoacetateis prepared from ethylacetate by the---------	a.Benzoin condensation	b.Aldol condensation	c.Claisen condensation	d.Dieckmann condensation	Claisen condensation
23.	The Hofmann rearrangement has an intermediate that is electronically similar to that in the------	a.Pinacol rearrangement	b. claisen rearrangement	c.Beckmann rearrangement	d.Cope rearrangement	Beckmann rearrangement
24.	α,β unsaturated carbonyl compounds	a.Hofmann	b. Sandmayer	c. Dield's Alder	d.Perkin	Dield's Alder

	undergo a ring closure reaction with conjugated dienes. This reaction is known as	reaction	reaction	reaction	reaction	reaction
25.	The Claisen condensation is often used in preparing	a. β-hydroxy ester	b.α-hydroxyester	c.ϒ-keto ester	d. β-keto ester	β-keto ester
26.	In the SN2reaction mechanism which one of the following is the most reactive?	a. C6H6	b. CH3X	c.C2H5X	d.R2CHX	CH3X
27.	The conversion is an example of 	a.Pinacol rearrangement	b. Claisen rearrangement	c.Curtius rearrangement	d.Hofmann rearrangement	Hofmann rearrangement
28.	Which of the following is not an electrophile?	a.NH3	b.Br+	c.H+	d.BF3	NH3
29.	The central C-atom of carbanion possesses----------	a.Duet of electrons	b.Octet of electrons	c.Sextet of electrons	d.Quartet of electrons	Octet of electrons
30.	The electrophilic aromatic substitution proceeds through a----------	a.Free radical	b.Sigma complex	c.Benzene	d.Carbene	Sigma complex
31.	Which of the following is true for the electrophilic aromatic substitution reaction?	a. Involves a single step	b.Involves a free radical intermediate	c. KH/KD>5	d.KH/KD=1	d.KH/KD=1
32.	The most stable diene among the following is-------	a.1,4-pentadiene	b.1,2-butadiene	c.1,3-butadiene	d.1,4-cyclohexadiene	1,3-butadiene
33.	The conversion of acetophenone to acetanil by using---	a.Beckmann rearrangement	b.Curtius rearrangement	c. Lossen rearrangement	d.Hofmann rearrangement	Beckmann rearrangement
34.	The conversion is an example of 	a.Fries rearrangement	b. Claisen rearrangement	c.Friedel crafts acylation	d.Reimer-Tiemann reaction	Fries rearrangement

35.	In which of the following reaction, amide is reduced to amine which has one carbon less then the starting material?	a. Lossen rearrangement	b.Beckmann rearrangement	c.Dieckmann condensation	d.Hofmann rearrangement	Hofmann rearrangement
36.	In the Beckmann reaction, migrating group is chiral. Select the true statement for it---	a.it will chage its configuration while in migration	b. It will retain its configuration while in migration	c.it can change as well a it can retain itsconfiguration	d. there is nothing todo with configuration	It will retain its configuration while in migration
37.	Claisen rearrangement is an example of	a.[1,3] sigmatropic rearrangement	b.[2,4] sigmatropic rearrangement	c.[1,5]sigmatropic rearrangement	d.[3,3] sigmatropic rearrangement	[3,3] sigmatropic rearrangement
38.	Which of the following reaction involves oxime?	a.Beckmann rearrangement	b.Favorski rearrangement	c.Riemar tiemann reaction	d.Curtius rearrangement	Beckmann rearrangement
39.	Hydrozamic acid with base is reacted in	a.Schimidt reaction	b. Lossen rearrangement	c.Beckmann rearrangement	d.Curtius rearrangement	Lossen rearrangement
40.	The following preparation of caprolactum fr cyclohexanone involves a rearrangement is 	a.Pinacol rearrangement	b. claisen rearrangement	c.Beckmann rearrangement	d.hofmann rearrangement	Beckmann rearrangement
41.	The formation of carpolactum involves	a.Pinacol rearrangement	b. claisen rearrangement	c.Beckmann rearrangement	d.hofmann rearrangement	Beckmann rearrangement
42.	Beckmann rearrangement of ketoxime gives	a. an amide	b.a ketoamine	c.an alcohol amine	d.a nitrite	an amide
43.	The conversion of acid azides to amine with lose of a carbon atom is known as	a.Pinacol rearrangement	b. claisen rearrangement	c.Curtius rearrangement	d.hofmann rearrangement	Curtius rearrangement
44.	When benzophenone treated with aqueous ammonia in the presence of sulphuric acid it gives	a.benzamide	b.benzanilide	c.benzoic acid	d.benzyl alcohol	benzanilide
45.	When acids treated with aqueous ammonia in the presence of sulphuric acid it gives	a.amine	b.amide	c.ammonia	d. alcohol	amine
46.	Isocyanates are hydrolysed by water it	a.hydroxamic	b.cyanide	c.amine	d.hydrazine	hydroxamic

	gives	acid				acid
47.	When acids on heating with NH4OH it gives	a.aniline	b.amide	c.ammonia	d. alcohol	amide
48.	When urea treated with Br2/KOH it gives	a. pyrrole	b.hydrazine	c.ammoniumhydroxide	d.ammonium bromide	hydrazine
49.	Which one of the following if isocyanate	a.RCON	b. CONR	C. CORN	D.ONCR	RCON
50.	The mechanism involved in a pinacol rearrangement is	a. 1,2-Shift	b.1,3-Shift	c. 1,4-Shift	d.1,5-Shift	1,2-Shift
51.	In a benzilic acid rearrangement,	benzaldehyde is converted intobenzoin	b. benzoin is converted into benzilic acid	c. benzilic acid is converted in to benzil	d. benzil is converted in to benzilic acid	benzil is converted into bezilic acid
52.	Claisen rearrangement always leads to a/an	a.ortho product	b.para product	c.meta product	d.both a & b arepossible	both a &b are possible
53.	A Beckmann rearrangement is effected by	a.Sulphuric acid	b.HCl	c. acetic acid	d. nitric acid	Sulphuric acid
54.	In Beckmann rearrangement, the group that generally migrates is	a. syn to hydroxyl	b.anti to hydroxyl	c.adjacent to hydroxyl	d.none of the above	anti to hydroxyl
55.	The reagent used in Hoffmann rearrangement is	a.Sodium hypobromide	b.NaOH+HBr	KOH+NaCl+Bromine	d.NaOH+Bromine	NaOH+Bromine
56.	In Hofmann rearrangement, the product is	a.primary amine	b.one carbon less than the reactant	c. obtained by the hydrolysis os isocyanate	d. all the above	all the above
57.	Pinacols formed by the bimolecular reduction of aldehydes/ketons in the presence of	a. Copper	b.Platinum	c.Magnesium	d.Palladium	Magnesium
58.	The mechanism involved in a claisen rearrangement is	a. 1,2-Shift	b.1,3-Shift	1,4-Shift	d.3,3-Shift	3,3-Shift
59.	The following reaction is 	a.Pinacol rearrangement	b. claisen rearrangement	c.Beckmann rearrangement	d.hofmann rearrangement	claisen rearrangement
60.		a.Pinacol rearrangement	b. claisen rearrangement	c.Beckmann rearrangement	d.hofmann rearrangement	hofmann rearrangement

	Complete the reaction 					

UNIT-III

Carbohydrates: Chemistry of monosaccharide- Glucose and Fructose. Chemistry of disaccharide- Sucrose and Maltose. Chemistry of polysaccharide - Starch and Cellulose - an elementary account (Elucidation of structure not necessary).

Inter conversion of Sugars – Muta rotation – Epimerization.

Introduction

The term "carbohydrates'' is used to identify a rather diverse group of materials found in nature. They are known to have important functions as constituents of both plants and animals. Carbohydrates provide a structural frame work for plants and serve as a source of energy for both plants and animals. Many industries nowadays depend on carbohydrates.

Carbohydrates, as the name implies, are composed mainly of carbon, hydrogen and oxygen, although other elements have been found in few compounds. For example *chitin*, *glucosamine* contain nitrogen. Although many of the simpler compounds have the empirical formula CH_2O as that of carbohydrates, are polyfunctional compounds. They have two kinds of functional groups- the alcoholic (hydroxyl) group and the carbonyl group. Thus, they are *polyhydroxy ketones or aldehydes.*

Classification

The behavior of carbohydrates materials towards acid hydrolysis provides the basis for an initial separation into groups.

1) The simplest of these which do not hydrolysis into smaller unit are known as "*monosaccharides"*.
   Examples: Glucose, fructose, mannose and galactose.
2) Compounds which undergo hydrolysis to liberate two or more, but fewer than eleven monosaccharide molecules are designed as *"oligosaccharide"*
3) If the oligosaccharide, upon hydrolysis yields two monosaccharide units, then it is termed as *disaccharide* (with molecular formula ($C_{12}H_{22}O_{11}$).
   Examples: Maltose and lactose.

4) If more than ten molecules of monosaccharides result during hydrolysis, the compound is referred to as a *polysaccharide.*

   Examples: Starch and cellulose.

5) Generally the monosaccharides and oligosaccharides are crystalline solids, soluble in water and sweet to taste. They are known as *sugars.*

6) Polysaccharides are non-sugars which are amorphous, tasteless and insoluble in water.

7) The carbohydrates may further be classified as either *reducing* or *non-reducing* sugar. All those carbohydrates which reduce *Fehling's solution* and *Tollen's reagent* are reducing sugars while others are non-reducing sugar. All monosaccharides and disaccharides (expect sucrose) are reducing sugar.

8) Then term *tetrose, pentose* and *hexose* are used to indicate those carbohydrates having four, five and six carbon atoms respectively.

   Example: Glucose has six carbon atoms and is a hexose.

9) If the monosaccharide posseses an aldehyde group, it is an *aldose* and that with a keto group, is a *ketose*.

10) The number of carbon atoms in conjugation with the type of carbonyl group in a sugar is indicated as *aldopentose* and *ketohexose.* The glucose, mannose and galactose are aldohexoses and fructose is a ketohexose.

1. GLUCOSE

Glucose, *dextrose* (grape sugar) is the central carbohydrate of living organisms of all types, the major source of energy. It is widely distributed in nature as the monosaccharides in ripe grapes. Honey,sweet fruit and as a component of disaccharides-lactose, maltose, sucrose and cellobiose. It is the building unit from which the polysaccharides like starch, cellulose and glycogen are formed. It is also normal constituent of blood and occurs in urine of diabetics.

1) Commercially pure D(+) glucose is manufactured by heating starch with dilute hydrochloric acid under pressure:

$$(C_6H_{10}O_5)_n + n\ H_2O \xrightarrow{\text{dil.HCl}} n\ C_6H_{12}O_6$$

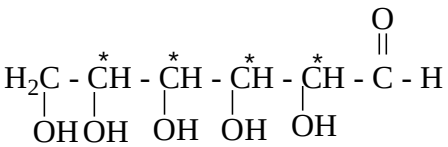
2) It is formed as an intermediate product in the fermentation of starch for the manufacture of ethyl alcohol.

3) Glucose is made by the hydrolysis of sucrose by boiling with dilute hydrochloric acid in alcoholic solution. Glucose and fructose are obtained in equal amounts. On cooling the resulting solution, glucose being less soluble than fructose, separates out.

$$\underset{\textbf{sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{\text{dil.HCl}} \underset{\textbf{glucose}}{C_6H_{12}O_6} + \underset{\textbf{fructose}}{C_6H_{12}O_6}$$

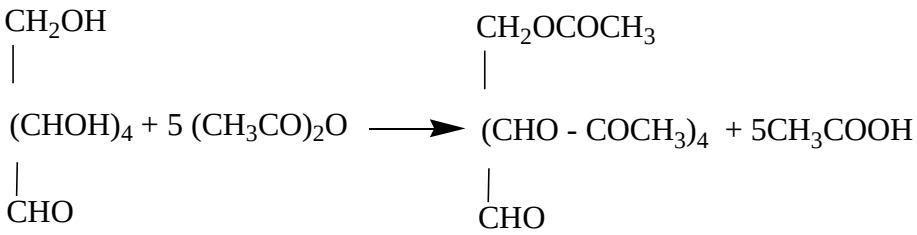
Properties

Glucose is a white crystalline solid (m.p 419 K), sweet to taste. It is readily soluble in water. Naturally occurring glucose is *dextro-rotatory* (hence, the name Dextrose) and it has four asymmetric carbon atom (marked by *).

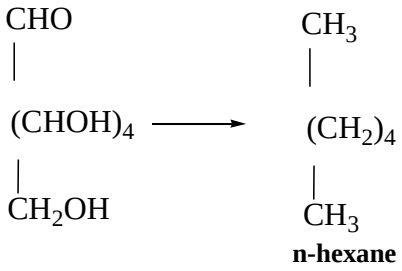


Structural formula of glucose indicates the presence of one aldehydic group, one primary alcoholic group and four secondary alcoholic groups. Chemical properties of glucose are, therefore, the properties of the above functional groups. The structural elucidation very easily follows from its reactions:

1) Quantitative analysis establishes the empirical formula as CH_2O.
2) The molecular weight of glucose determined from a study of the depression of freezing point of glucose solution, shows a value of 180. When this is compared with the empirical formula weight, the conclusion reached is that the molecular formula is $(CH_2O)_6$ or $C_6H_{12}O_6$.
3) The presence of the five alcoholic groups is indicated by its reaction with 5 moles of acetyl chloride or acetic anhydride.

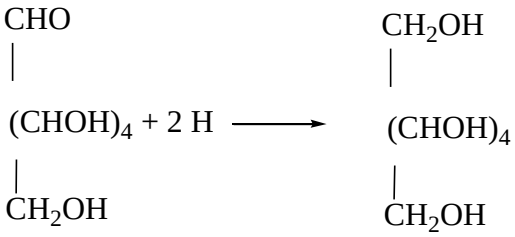


4) Reduction of glucose with concentrated hydriodic acid and red phosphorus at 373 K yields 2-iodohexane. Prolonged heating produces n-hexane. This would mean that glucose is a straight chain compound of six carbon atoms.

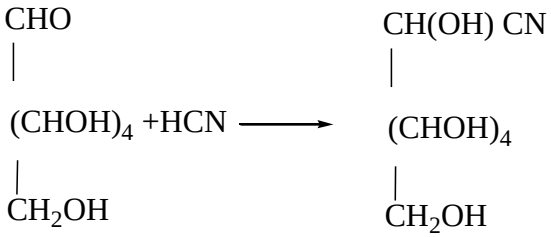


n-hexane

5) The nature of the carbonyl group is indicated by its reaction with mild reducing agent. When reduced with sodium amalgam in aqueous solution, the aldehyde group is reduced to a primary alcoholic group to yield a hexahydric alcohol, called sorbitol.

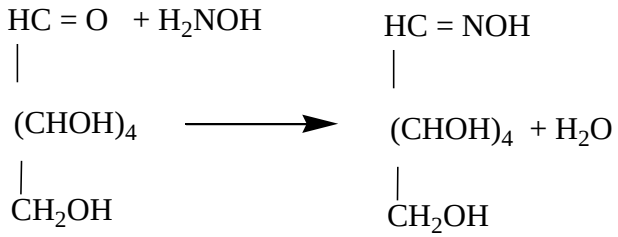


6) Glucose gives addition product with hydrogen cyanide *(but not with ammonia or sodium bisulphite).* This reaction indicates the presence of a carbonyl group.

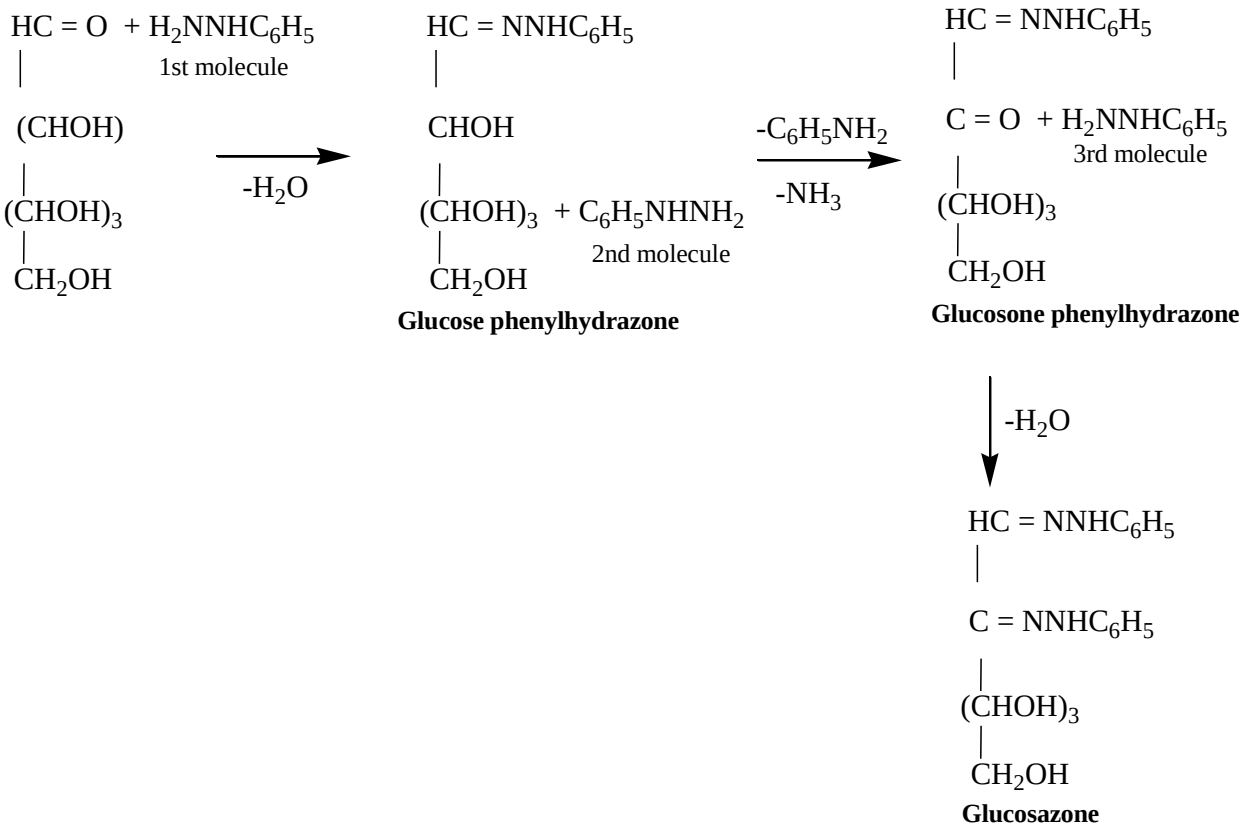


glucose cyanohydrin

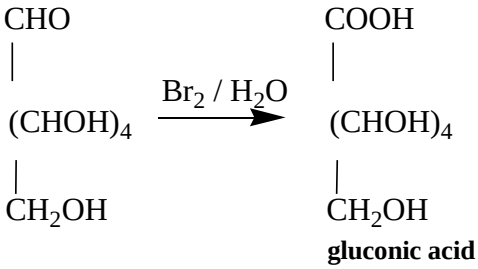
7) Glucose condenses with hydroxylamine to yield the oxime with the elimination of a water molecule.



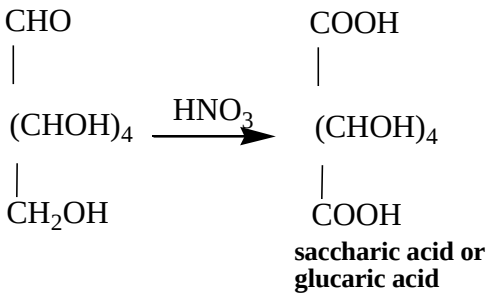
8) Glucose reacts with one molecule of phenylhydrazine in acetic acid which condenses with the aldehyde group to give *phenylhydrazone*. When warmed with excess phenylhydrazine, the secondary alcoholic group, adjacent to the aldehyde group, is next oxidised to a keto group. With this keto group, third molecule of phenylhydrazine condenses to yield *glucosazone:*



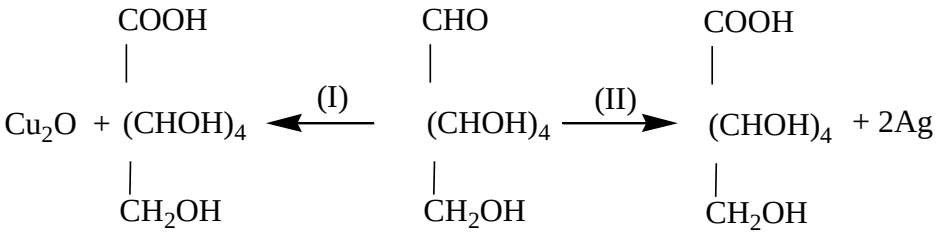
9) With mild oxidising agents like bromine water, glucose is oxidised to gluconic acid, an acid with the same number of carbon atoms. In this reaction, the aldehyde group alone gets oxidised.



10) With strong oxidising agents like nitric acid, it is oxidised to a dicarboxylic acid, saccharic acid. Nitric acid is able to oxidise the primary alcohol group also to an acid group.



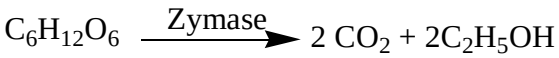
11) Because glucose is readily oxidised, it acts as a strong reducing agent. It reduces both Fehling's solution (I) and Tollen's reagent [ammoniacal silver nitrate, (II)]



The above reactions (5 to 11) confirm the presence of an aldehyde group in glucose.

Other Reactions of Glucose

12) Glucose on fermentation yields ethyl alcohol.

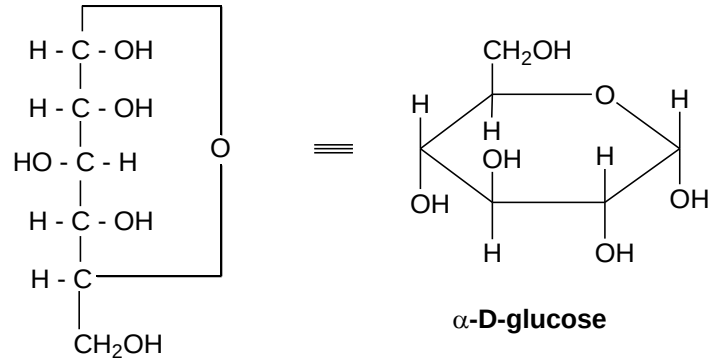


13) A dilute solution of glucose when warmed with dilute alkali solution, gives a mixture of glucose, fructose and mannose.

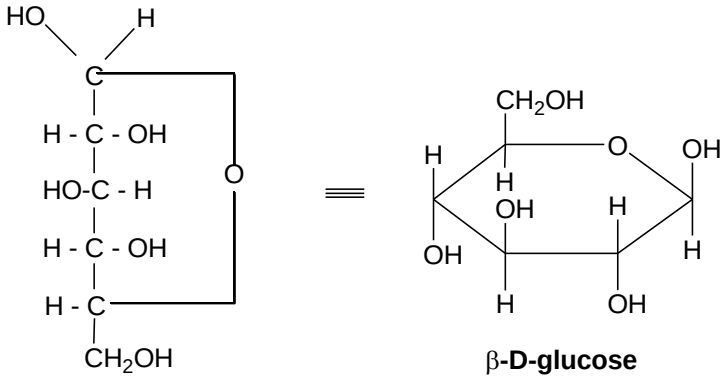
14) When heated with concentrated hydrochloric acid, it gives laevulic acid and hydroxymethyl furfural.

All the above reactions of glucose indicate that glucose is a polyhydric alcohol with a terminal aldehyde group and that it is a straight chain compound.

As mentioned earlier, glucose does not react with ammonia or sodium bisulphite. Further, it exists in two isomeric forms, *α*- and *β* – glucose. The evidence for these forms is *muta rotation.* *α* – glucose with specific rotation +110^o is obtained by crystallizing glucose form alcoholic or acetic acid solution whereas *β* – glucose with specific rotation +19.7^o is obtained by crystallizing glucose form pyridine solution. An aqueous solution of glucose shows muta roration *(meaning, a change of rotation)* i.e., its specific rotation gradually falls from +110^o to +52.5^o in the case of *α* – glucose and increases from +19.7^o to +52.5^o in the case of *β* – glucose. To account for these facts satisfactorily, Tollen suggested a ring formula with no free aldehyde group. The ring structure for glucose is best representing by a hexagonal formula base on *pyran.*



α-D-glucose



β-D-glucose

Uses

1) It is used as a sweetening agent in confectionery.
2) It is utilised in the manufacture of ascorbic acid (Vitamin C).
3) It serves as food for invalids and as food preservatives.

2. FRUCTOSE

D (-) Fructose, (Laevulose or Fruit Sugar) $C_6H_{12}O_6$

The only important ketohexose is D (-) fructose, m.p. 368 K. In the course of its degradation in cells and tissues, glucose is converted into fructose derivatives.

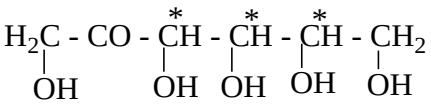
Preparation

1) Fructose is prepared in the laboratory by the hydrolysis of sucrose by boiling with dilute acids. It is formed along with glucose.
2) Fructose is obtained commercially by the hydrolysis of *inulin* with oxalic acid or dilutes sulphuric acid.

$$\underset{\textbf{inulin}}{(C_6H_{10}O_5)_n} + nH_2O \xrightarrow{\text{dil.}H_2SO_4} n\,C_6H_{12}O_6$$

Properties

Fructose is a white crystalline solid. It is the sweetest of all sugars. It is readily soluble in water. It is laevorotatory and therefore called *laevulose.* Structural formula of fructose indicates



The presence of a keto group, two primary and three secondary (* marked, asymmetric carbons) alcoholic groups. The structure of fructose has been derived from a consideration of facts and conclusion such as the following:

1) Elemental analysis and molecular weight determination show that the molecular formula of fructose is $C_6H_{12}O_6$.
2) Complete reduction of fructose with HI and red phosphorus give n-hexane as the major products, suggesting a straight chain formula.

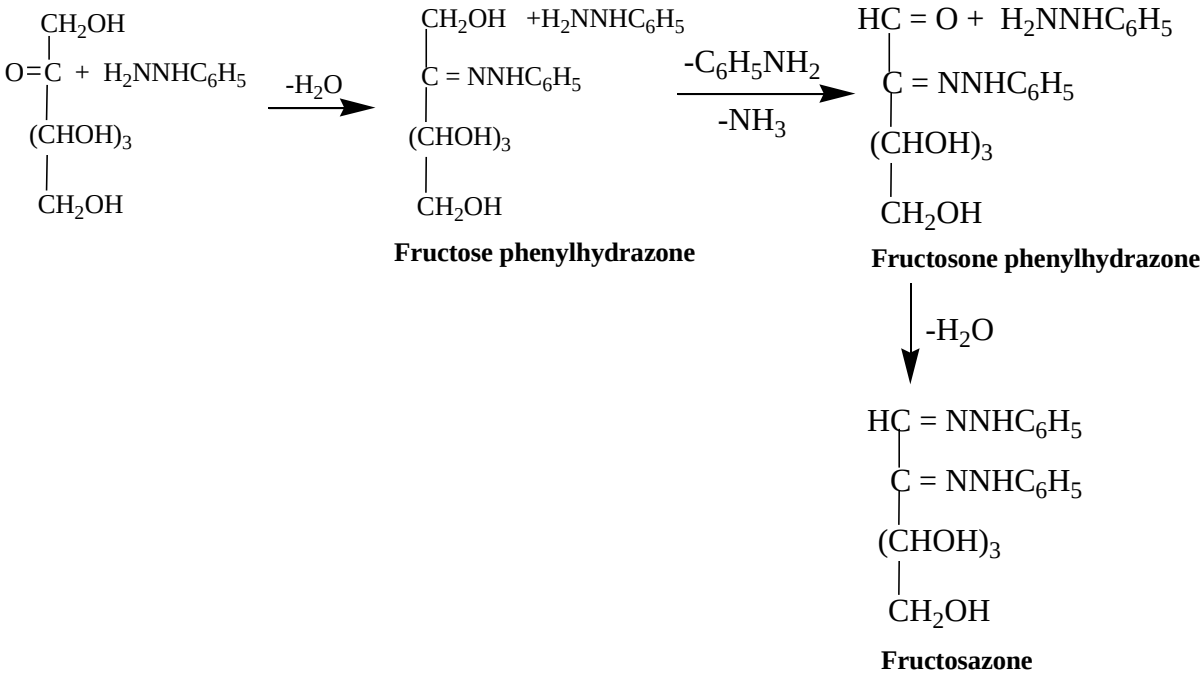
3) Fructose reacts with 5 moles of acetyl chloride or acetic anhydride to form a penta-acetate. This indicates the presence of five hydroxyl group in a fructose molecule. Since fructose is a stable compound, the five hydroxyl groups must be present on separate carbon atoms.

4) (a) Fructose reacts with hydroxylamine to form an oxime

(b) It adds with only one mole of HCN to give a cyanohydrin.

These reactions indicate the presence of a carbonyl group.

5) Fructose condenses with phenylhydrazine and yields fructosazone similar to glucose. Here again the reaction proceeds in stages:

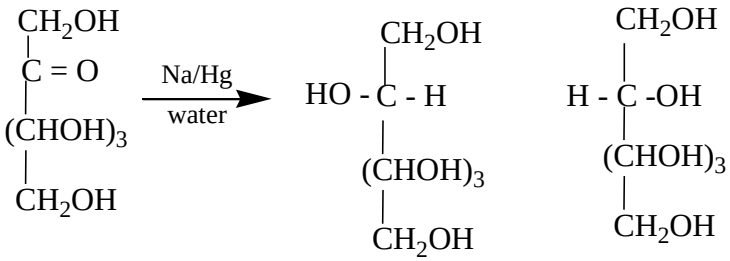


Fructose phenylhydrazone

Fructosone phenylhydrazone

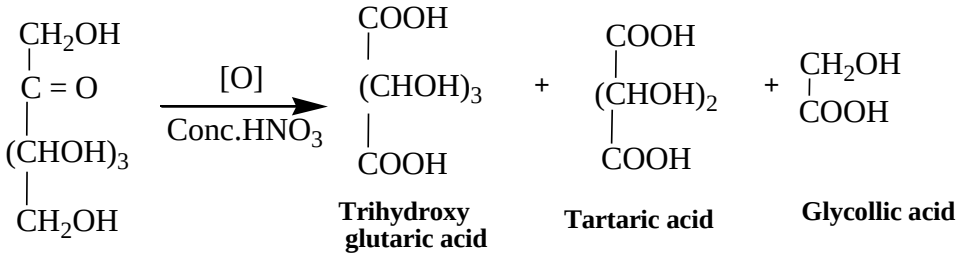
Fructosazone

6) Reduction of fructose with sodium amalgam and water produces a mixture of two epimeric alcohols, sorbital and mannitol because a new asymmetric carbon has been created at C_2. This indicates the presence of keto group.



Mannitol **Sorbitol**

7) Fructose is not affected by mild oxidising agents. But strong oxidising agents, like nitric acid, oxidise fructose to a mixture of trihydroxy glutaric acid, tartaric acid and glycollic acid:

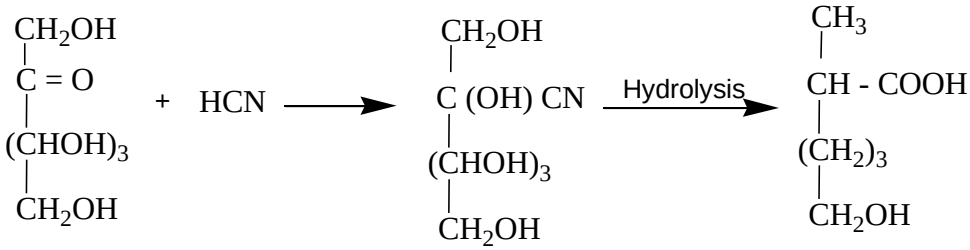


Trihydroxy glutaric acid **Tartaric acid** **Glycollic acid**

Since this oxidation occurs with the rupture of the carbon chain, the carbonyl group must be present as a keto group in fructose.

8) Fructose is a reducing sugar like glucose. Hence, it reduces both Tollen's reagent and Fehling's solution. Usually ketones do not reduce above reagents but hydroxy ketones possess reducing properties.

9) When fructose is treated with HCN it forms a cyanohydrin which upon hydrolysis and subsequent reduction gives 2-methyl-hexanoic acid. This indicates that the keto group is adjacent to one of the terminal carbon atom.



2-methylhexanoic acid

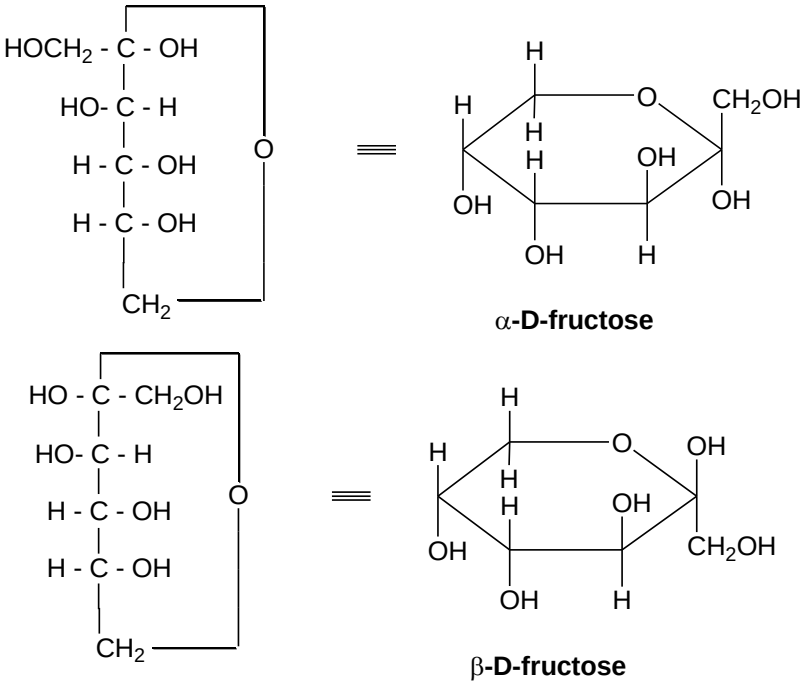
10) Fructose is fermented by yeast to ethyl alcohol.

$$C_6H_{12}O_6 \xrightarrow{\text{Zymase}} 2\,CO_2 + 2C_2H_5OH$$

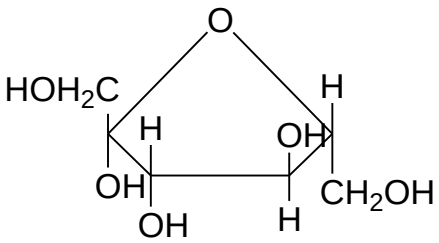
11) Fructose when warmed with dilute alkali forms a mixture of glucose, fructose and mannose like glucose.

12) When heated with Conc. hydrochloric acid, fructose gives laevulic acid. They yield is better than glucose.

13) Fructose does not react with ammonia and sodium bisulphite like glucose. Moreover, it exhibits muta rotation which suggests that it exists in two isomeric forms. So, a cyclic ring formula was suggested for fructose. As in the case of glucose, the hexagonal formula based on pyran is given for fructose.



Γ-fructose is also known which exists in a five membered furan ring structure:

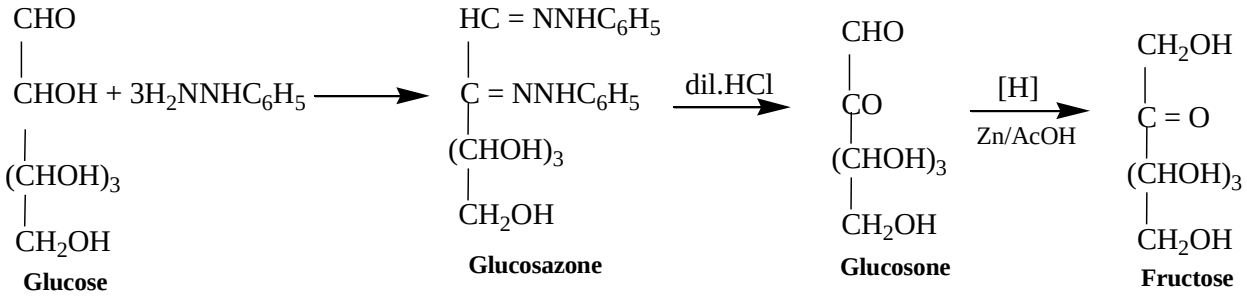


Uses

1) Fructose finds use as sweetening agent.
2) It is used by diabetic patients in the place of cane sugar.

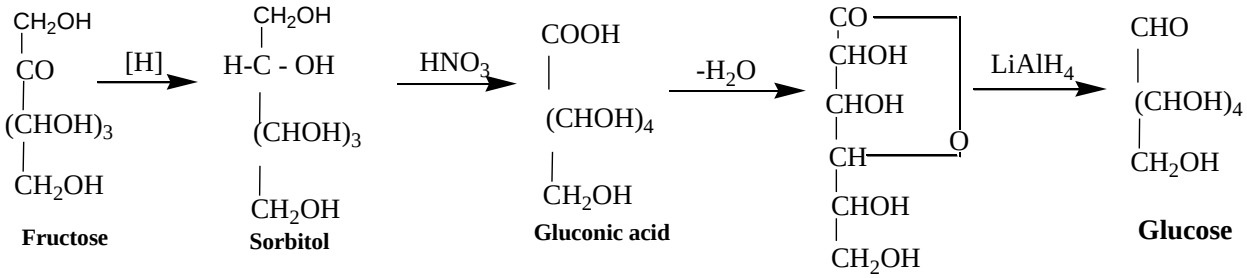
Conversion of Glucose into Fructose

Glucose is first treated with excess phenylhydrazine in acetic acid to form glucosazone which is next hydrolysed with dil.HCl to give *glucosone.* This is then reduced with zinc and glacial acetic acid to yield fructose:



Conversion of Fructose into Glucose

Fructose is first reduced with sodium amalgam to give hexitols. These are next oxidised with nitric acid to yield the corresponding mono-carboxylic acids which on treatment with dil.HCl give γ- lactones. The individual lactones are reduced with $LiAlH_4$ to obtain the corresponding aldohexoses. In this conversion, both mannose and glucose are obtained but the route for the conversion of fructose to glucose alone is give below:

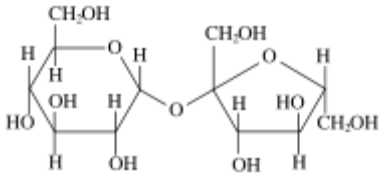


Comparative study of Glucose and Fructose:

No.	Properties	Glucose	Fructose
1.	Nature	(i) Aldohexose (ii) Dextro rotatory	(i) Ketohexose (ii) Laevo rotatory
2.	Osazone	Forms	Forms
3.	Muta rotation	Exhibits	Exhibits
4.	With HNO_3	Saccharic acid	Meso tartaric acid, glycollic acid
5.	With Bromine water	Gluconic acid	No reaction
6.	Fehling solution and Tollen's reagent	Reduces	Reduces
7.	With NaOH	Forms epimer	Forms epimer
8.	In Ether	Insoluble	soluble

3. SUCROSE: $C_{12}H_{22}O_{11}$

Sucrose (common name: **table sugar**, also called **saccharose**) is a disaccharide (glucose + fructose) with the molecular formula $C_{12}H_{22}O_{11}$. Its systematic name is Î±-D-glucopyranosyl-(1â†'2)-Î²-D-fructofuranose. It is best known for its role in human nutrition and is formed by plants but not by higher animals.



Physical and chemical properties

Pure sucrose is most often prepared as a fine, colorless, odorless crystalline powder with a pleasing, sweet taste. Large crystals are sometimes precipitated from water solutions of sucrose onto a string (or other nucleation surface) to form rock candy, a confection.

Like other carbohydrates, sucrose has a hydrogen to oxygen ratio of 2:1. It consists of two monosaccharides, Î±-glucose and fructose, joined by a glycosidic bond between carbon atom 1 of the glucose unit and carbon atom 2 of the fructose unit. What is notable about sucrose is that unlike most polysaccharides, the glycosidic bond is formed between the reducing ends of both glucose and fructose, and not between the reducing end of one and the nonreducing end of the other. The effect of this inhibits further bonding to other saccharide units. Since it contains no free anomeric carbon atom, it is classified as a nonreducing sugar.

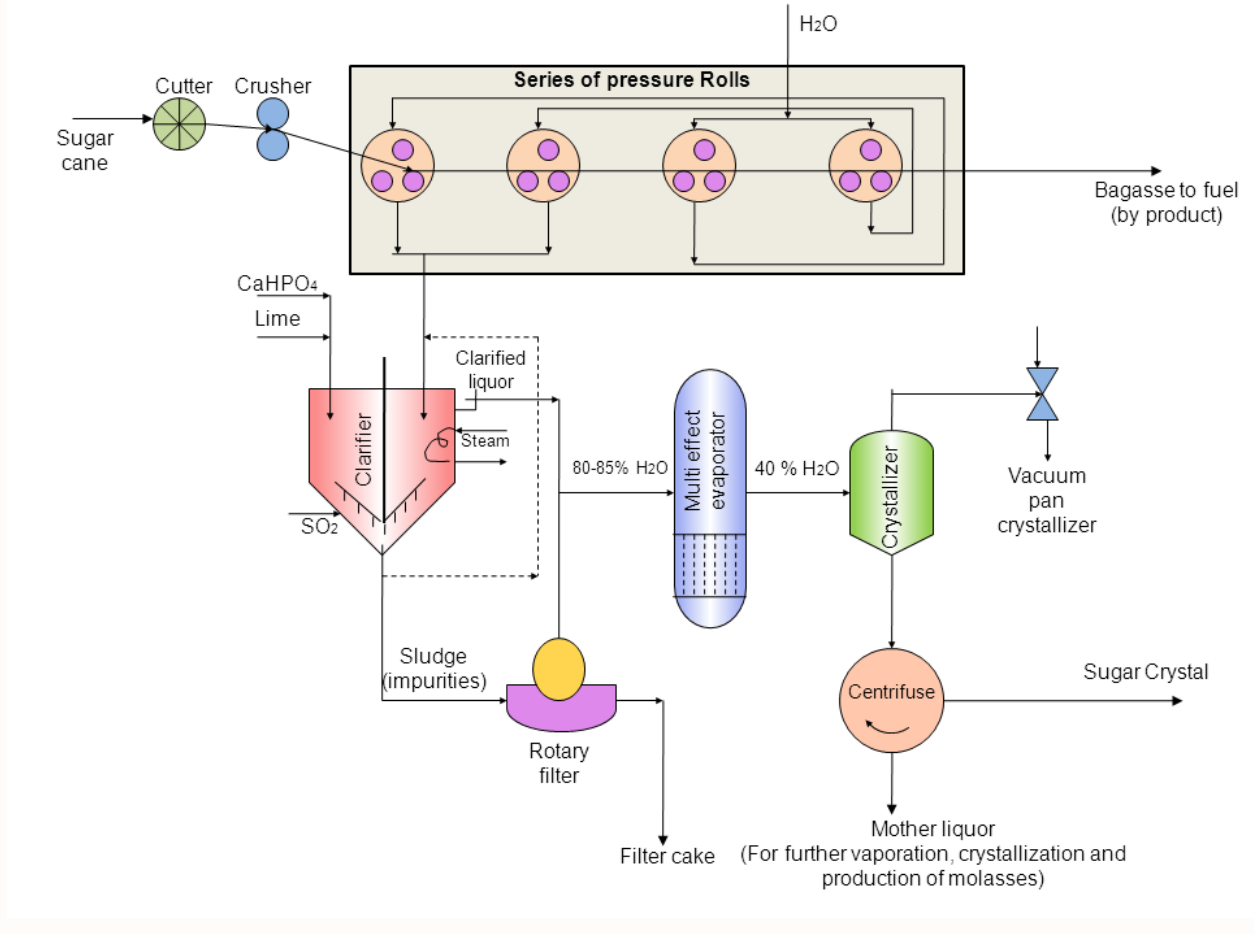
Sucrose melts and decomposes at 186 °C to form caramel, and when combusted produces carbon, carbon dioxide, and water. Water breaks down sucrose by hydrolysis, however the process is so gradual that it could sit in solution for years with negligible change. If the enzyme sucrase is added however, the reaction will proceed rapidly.

Reacting sucrose with sulfuric acid dehydrates the sucrose and forms elemental carbon, as demonstrated in the following equation:

$C_{12}H_{22}O_{11} + H_2SO_4$ catalyst --->12 C + 11 H_2O

Sugar Manufacture Process

Juice extraction from cane



Flow sheet of manufacture of sugar from sugarcane

Sugar cane

The cane plant consists of a stalk, roots, growing leaves, the remains of dead leaves, and a growing leafy top. The typical composition of cane is as follows:

- 15% dissolved matter (13% sucrose; 2% are other sugars -mainly glucose and fructose)
- 15% fibre (insoluble), and
- 70% water.

For every 100 tons cane crushed, 30 tons of fibrous residue (bagasse), and about 12 tons sugar and 4 tons molasses are made.

The farmers transport the cane *stalks* (i.e. cane without roots, without leaves and without tops) to the sugar mill in specially designed vehicles that facilitate easy loading and offloading.

Cane preparation

Juice can be removed from cane either by repeated crushing and washing (milling) or by washing alone, with a final squeezing simply to dry the spent fibre (diffusion). Better sucrose extraction can be obtained by crushing finely shredded cane rather than intact stalks and "Preparation" refers to that step in which cane is finely shredded before juice is extracted either by milling or diffusion. Cane is prepared by passing it through one or two sets of cane knives and then through a shredder.

Milling

A basic cane mill consists of three grooved rollers. Prepared cane is squeezed between the rollers, thus forcing the juice out of the fibre.

The basic work of a mill is the separation of juice from fibre. Fibre, however, has the natural property of always retaining approximately its own weight of juice regardless of the pressure applied to it. To displace retained juice, water is poured onto the cane fibre before crushing. This is called imbibition.

A single milling unit would give an unacceptably low extraction. Typically, six mills are set in tandem and cane is passed in series from Mill 1 to Mill 6.

Diffusion

A diffuser is an enclosed carrier through which a bed of prepared cane is slowly dragged, while copious quantities of water and juice percolate through the bed to wash out the sucrose -bearing juice.

The fibre leaving the diffuser is saturated with liquid and has to be dewatered in a mill before being sent either to the boilers or to by-product processes.

Purification of juice

Juice from a milling tandem contains a large amount of cane fibre that falls out with the juice between the rollers of the mills. To remove the fibre, juice is poured over a wire-mesh screen, or cascaded over an inclined wedge-wire screen). Diffuser juice, because of the screening effect of the cane bed itself, is generally not screened.

The juice is heated and lime is added to neutralise the natural acidity. It is then placed in a large settling tank called a clarifier The purpose of clarification is to produce a clear juice that is light in colour and free of suspended matter. To improve the precipitate formation, flocculent is added.

The settled precipitate, referred to as mud, is pumped out of the trays of the clarifier and sent to the filtration station where the juice it contains will be recovered. If a diffuser is used, it is sent to the diffuser and filtered through the bed of bagasse.

Crystal growth

Evaporation

Before crystal growth can take place the clear juice must be concentrated to syrup by the removal of water by evaporation. To improve the efficiency of the water removal step a process known as multiple effect evaporation is used. Multiple effect evaporation is the scheme where juice is boiled in series in several vessels, with steam fed to vessel 1 only. Vapour from vessel 1 boils the juice in vessel 2, vapour from 2 boils the juice in 3, and so on until vapour from the final vessel goes to waste.

Sugar boiling

The syrup produced by the evaporators is concentrated further in specially designed vessels known as pans. As the concentration rises the dissolved sugar crystallises and the work of the

pans is to grow sugar crystals (from the sucrose in syrup) in several steps to maximise the amount of sucrose recovered in raw sugar.

This is typically done in three boiling steps; each step producing, after crystal/molasses separation, A-sugar and A-molasses, B-sugar and B-molasses, and C-sugar and C-molasses or final molasses.

Supersaturation is the "driving force" in all sugar boiling. Supersaturation is controlled by adding water or syrup to massecuite (crystal / molasses mixture) and by controlling the temperature.

When the massecuite is discharged from the pans it is retained in stirred tanks called crystallisers, where the sugar crystals continue to grow through cooling rather than boiling.

Separation of crystals from molasses

Massecuite leaving the crystallisers has now to be separated into crystals and molasses. The more efficient this separation, the more sucrose will be recovered as sugar and the less sucrose will be lost in molasses. A centrifugal is a machine that separates crystals from molasses. Centrifugation involves spinning massecuite in a perforated basket; centrifugal force acts on the molasses, forcing it through the perforations while the sugar remains on the basket wall. Water and steam may then be sprayed onto the crystals to wash off the remaining molasses.

Sugar drying

Sugar leaving the centrifugals has excess moisture which has an extremely detrimental effect on the keeping quality of the raw sugar and drying is therefore important. In a drier, the moisture is driven off from the surface of the liquor layer covering the crystal by passing heated air around the sugar crystals.

The product from the process described so far is a raw sugar (Brown sugar) that can be used as is, or sent to a refinery to be converted to a white (refined) sugar.

Sugar refining

The purpose of the refinery is to remove impurities from sugar crystals. The refinery accepts raw sugar as its feed material. The sugar is dissolved (melted) and the colour is removed by various clarification processes.

Re-crystallisation (from a higher purity mother liquor) is alone responsible for a considerable amount of colour removal but other techniques must be employed to obtain the low colour levels of white sugar. Tongaat Hulett uses two colour removal processes before the crystallisation and these are carbonatation and ion exchange.

In carbonatation lime and CO^2 (carbon dioxide) gas are added to the melt to form a calcium carbonate precipitate. This precipitate absorbs colour, is removed by filtration. Further colour is then removed by ion exchange. Resin beads are held in tanks through which the liquor is allowed to percolate under pressure.

The purified melt is evaporated and up to 4 crops of crystals are boiled from this. These crystals are combined to form the refined sugar product.

4. MALTOSE (MALT SUGAR) $C_{12}H_{22}O_{11}$

Preparation:

Maltose does not occur in free state in nature.

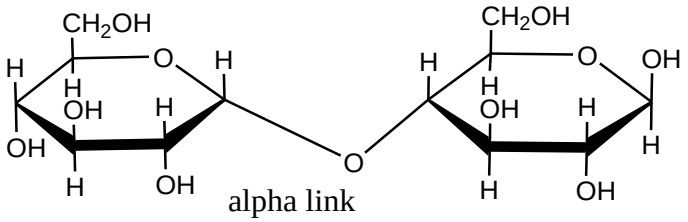
$(C_6H_{10}O_5)_n + H_2O \xrightarrow{\text{diastase}} C_{12}H_{22}O_{11}$

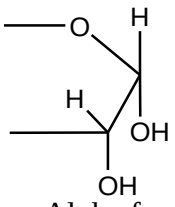
Starch maltose

Structure

Maltose $\xrightarrow[\text{With dilute acids}]{\text{Hydrolysis}}$ D-Glucose

This indicates that the maltose molecule is made up of 2 glucose units.





,β- Maltose

Maltose exists in α- and β- forms each of which exhibits mutarotation.

The values specific rotations are +168° for α- maltose and + 136° for the equilibrium mixture.

Properties:- (physical)

Maltose (β-form) is a colourless, odourless crystalline solid, mp : 160°-165°C.

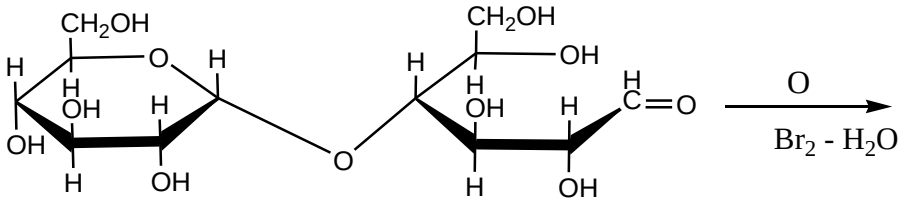
It is soluble in water, but insoluble in alcohol or ether.

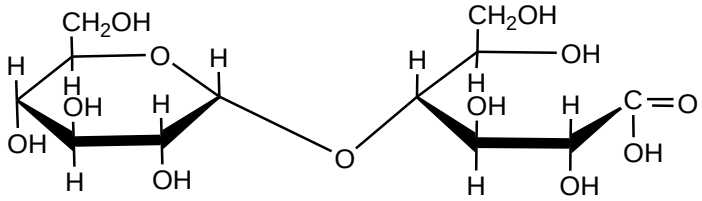
An aqueous solution of maltose is dextrorotatory and exhibits mutarotation.

Chemical Properties:-

Maltose is a reducing sugar, Like lactose. Its reactivity is also due mainly to the presence of a free hemiacetal group in one of the glucose units of its reactivity is also due mainly to the presense of a free lemiactel group in one of the glucose units of its molecule.

1. <u>Oxidation</u>





2. Hydrolysis

$$\text{Maltose} \xrightarrow[\text{or enzyme maltose}]{\text{hot dil. acids}} \text{D-glucose}$$

3. Reaction with Phenyl hydrazine (Osazone formation)

$$\text{Maltose} \xrightarrow[CH_3COOH]{\text{excess } C_6H_5NHNH_2} \text{Maltosazone mp 206°C}$$

4. Reaction with acetic anhydride (Acetylation)

$$\text{Maltose} \xrightarrow[ZnCl_2 \text{ or } CH_3COONa]{\text{acetic anhydride}} \text{alpha- maltose octaacetate (mp 125°C)} \quad [\text{alpha}]_D = +123°$$

and

beta- MaltoseOctaacetate (mp 160°C) $[\alpha]_D = +63°$

5. Fermentation :-

$$C_{11}H_{22}O_{11} + H_2O \xrightarrow{\text{Maltose}} C_6H_{12}O_6 \text{ glucose}$$

$$C_6H_{12}O_6 \xrightarrow{\text{Zyma}} 2C_2H_5OH + 2CO_2$$

Uses

Maltose used in infant food and in malted milk.

Polysaccharides are polymers of simple sugars

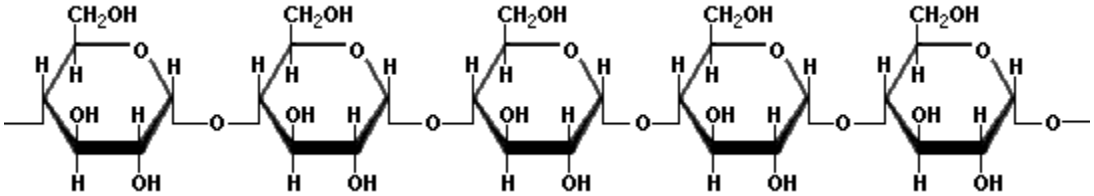
Many polysaccharides, unlike sugars, are insoluble in water. Dietary fiber includes polysaccharides and oligosaccharides that are resistant to digestion and absorption in the human small intestine but which are completely or partially fermented by microorganisms in the large intestine. The polysaccharides described below play important roles in nutrition, biology, or food preparation.

6. STARCH

Starch is the major form of stored carbohydrate in plants. Starch is composed of a mixture of two substances: *amylose*, an essentially linear polysaccharide, and *amylopectin*, a highly branched polysaccharide. Both forms of starch are polymers of **α-D-Glucose**. Natural starches contain 10-

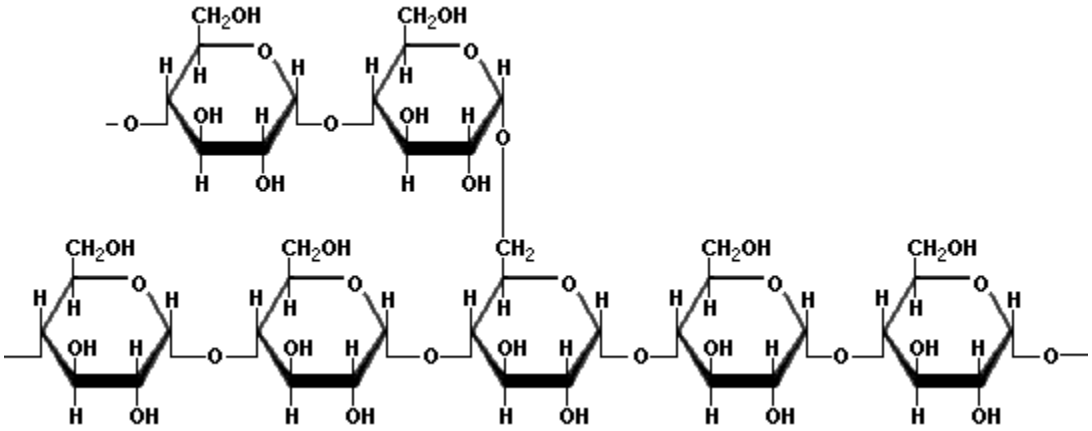
20% amylose and 80-90% amylopectin. Amylose forms a colloidal dispersion in hot water (which helps to thicken gravies) whereas amylopectin is completely insoluble.

Amylose molecules consist typically of 200 to 20,000 glucose units which form a helix as a result of the bond angles between the glucose units.



Amylose

Amylopectin differs from amylose in being highly branched. Short side chains of about 30 glucose units are attached with 1α→6 linkages approximately every twenty to thirty glucose units along the chain. Amylopectin molecules may contain up to two million glucose units.



Amylopectin

The side branching chains are clustered together within the amylopectin molecule

Starches are transformed into many commercial products by hydrolysis using acids or enzymes as catalysts. Hydrolysis is a chemical reaction in which water is used to break long polysaccharide chains into smaller chains or into simple carbohydrates. The resulting products are assigned a Dextrose Equivalent (DE) value which is related to the degree of hydrolysis. A DE value of 100 corresponds to completely hydrolyzed starch, which is pure glucose (dextrose). Dextrins are a group of low-molecular-weight carbohydrates produced by the hydrolysis of starch. Dextrins are mixtures of polymers of D-glucose units linked by 1α→4 or 1α→6 glycosidic bonds. Maltodextrin is partially hydrolyzed starch that is not sweet and has a DE value less than 20. Syrups, such as corn syrup made from corn starch, have DE values from 20 to 91. Commercial dextrose has DE values from 92 to 99. Corn syrup solids, which may be labeled as soluble corn fiber or resistant maltodextrin, are mildly sweet semi-crystalline or powdery amorphous products with DEs from 20 to 36 made by drying corn syrup in a vacuum or in spray driers. Resistant maltodextrin or soluble corn fiber are not broken down in the digestive system, but they are partially fermented by colonic bacteria thus providing only 2 Calories per gram instead of the 4 Calories per gram in corn syrup. High Fructose Corn Syrup (HFCS), commonly used to sweeten soft drinks, is made by treating corn syrup with enzymes to convert a portion of the glucose into fructose. Commercial HFCS contains from 42% to 55% fructose, with the remaining percentage being mainly glucose. There is an effort underway to rename High Fructose Corn Syrup as Corn Sugar because of the negative public perception that HFCS contributes to obesity. Modified starch is starch that has been changed by mechanical processes or chemical treatments to stabilize starch gels made with hot water. Without modification, gelled starch-water mixtures lose viscosity or become rubbery after a few hours. Hydrogenated glucose syrup (HGS) is produced by hydrolyzing starch, and then hydrogenating the resulting syrup to produce sugar alcohols like maltitol and sorbitol, along with hydrogenated oligo- and polysaccharides. Polydextrose (poly-D-glucose) is a synthetic, highly-branched polymer with many types of glycosidic linkages created by heating dextrose with an acid catalyst and purifying the resulting water-soluble polymer. Polydextrose is used as a bulking agent because it is tasteless and is similar to fiber in terms of its resistance to digestion. The name resistant starch is

applied to dietary starch that is not degraded in the stomach and small intestine, but is fermented by microflora in the large intestine.

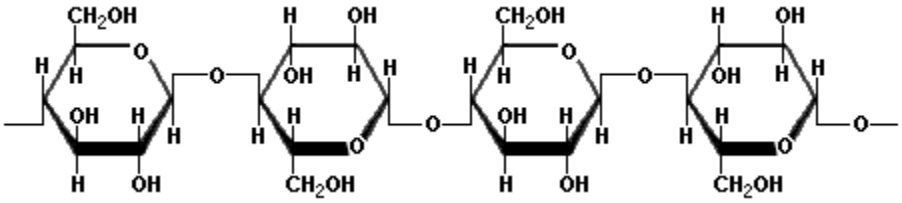
Relative sweetness of various carbohydrates

Fructose	173
Invert sugar*	120
HFCS (42% fructose)	120
Sucrose	100
Xylitol	100
Tagatose	92
Glucose	74
High-DE corn syrup	70
Sorbitol	55
Mannitol	50
Trehalose	45
Regular corn syrup	40
Galactose	32
Maltose	32
Lactose	15

* Invert sugar is a mixture of glucose and fructose found in fruits.

7. CELLULOSE

Cellulose is a polymer of β-D-Glucose, which in contrast to starch, is oriented with -CH_2OH groups alternating above and below the plane of the cellulose molecule thus producing long, unbranched chains. The absence of side chains allows cellulose molecules to lie close together and form rigid structures. Cellulose is the major structural material of plants. Wood is largely cellulose, and cotton is almost pure cellulose. Cellulose can be hydrolyzed to its constituent glucose units by microorganisms that inhabit the digestive tract of termites and ruminants. Cellulose may be modified in the laboratory by treating it with nitric acid (HNO_3) to replace all the hydroxyl groups with nitrate groups (-ONO_2) to produce cellulose nitrate (nitrocellulose or guncotton) which is an explosive component of smokeless powder. Partially nitrated cellulose, known as pyroxylin, is used in the manufacture of collodion, plastics, lacquers, and nail polish.



Cellulose

MUTAROTATION

Mutarotation can be defined as the change in optical rotation that is observed when a reducing sugar is dissolved in water, due to the formation of different tautomeric forms. A sugar crystal will consist of molecules having a specific anomeric ring form (furanose or pyranose with _- or _-configuration). Upon dissolution, ring opening (hydrolysis) and subsequent ring closure will occur, producing the _- and _-pyranose and _- and _-furanose forms. These forms have different chemical and physical properties (e.g., optical rotation, solubility, chemical reactivity, relative sweetness, etc.). Figure 3.1 shows the five forms of D-glucose that will theoretically exist in solution. For glucose, only the _- and _-pyranose forms exist in significant amounts. _-D-Glucopyranose has an "initial" optical rotation of +112◦, whereas _-D-glucopyranose has an "initial" rotation of free energy. _-D-Glucopyranose has the greatest stability and predominates

by being present at 63.6% at equilibrium at 20◦C. Glucose is classified as undergoing "simple" mutarotation since,for practical purposes, only two tautomers are present.

INTERCONVENTION OF SUGARS:

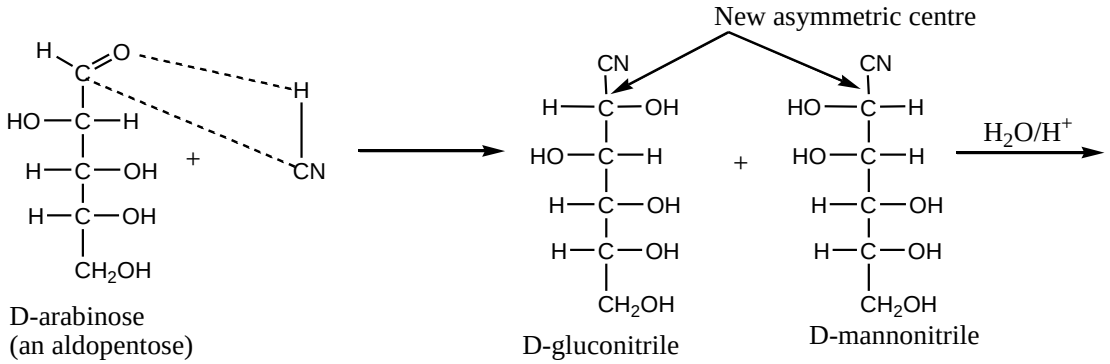
SYNTHESIS AND INTERCONVERSIONS OF MONOSACCHARIDES:

By means of the following methods it is possible to convert one monosaccharide into another. These interconversions are important for two main reasons.: they are used in determining the relative configurations of monosaccharides, and they also provide routes to compounds which are unknown or very rare in nature.

(1) Conversion of an Aldose in to the next higher Aldose:

(a). Killiani-Fisher Cyanohdrin Synthesis:

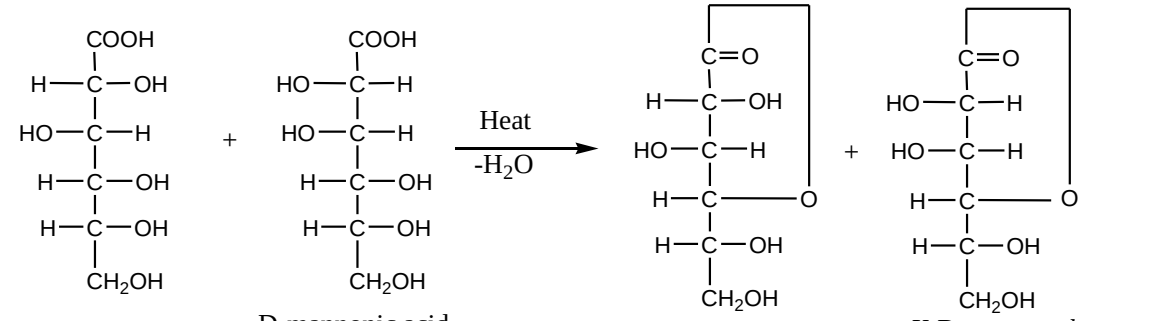
The aldose is first allowed to react with HCN. This process introduces a new asymmetric centre and results in the formation of two cyanohydrins (aldononitriles). It should be noted that these cyanohydrins differ only inconfigurationabout the newly introduced asymmetric carbon atom (carbon number 2), and are therefore, epimers. These cyanohydrins are next hydrolysed with dilute acid to give the corresponding aldonic acids. The aldonic acids on heating lose a molecule of water to give γ-lactones (1,4-aldonolactones). These γ-lactones are solids and are separated by fractional crystallization. The individual lactonescan then be reduced with lithium aluminium hydride or sodium amalgam in a weakly acidic solution to give aldoses which contain one more carbon atoms than the original aldose. Thus D-arabinose may be converted into D-glucose and D-mannose as follows.



D-arabinose
(an aldopentose)

D-gluconitrile

D-mannonitrile

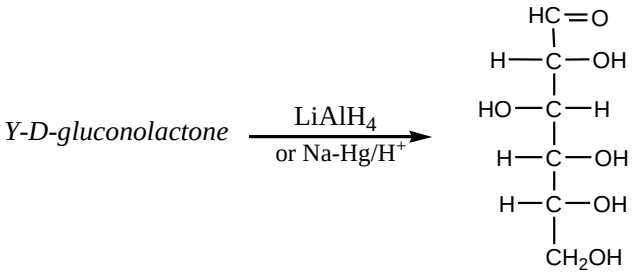


D-gluconic acid

D-mannonic acid

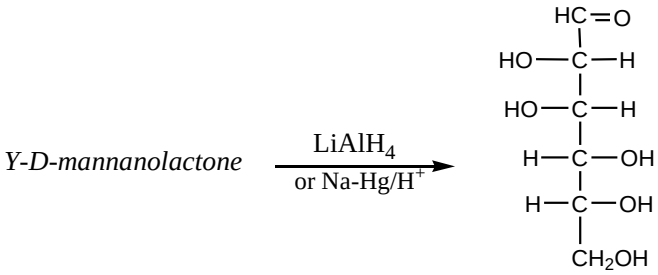
Y-D-gluconolactone

Y-D-mannanolactone



Y-D-gluconolactone

D-glucose(aldohexose)

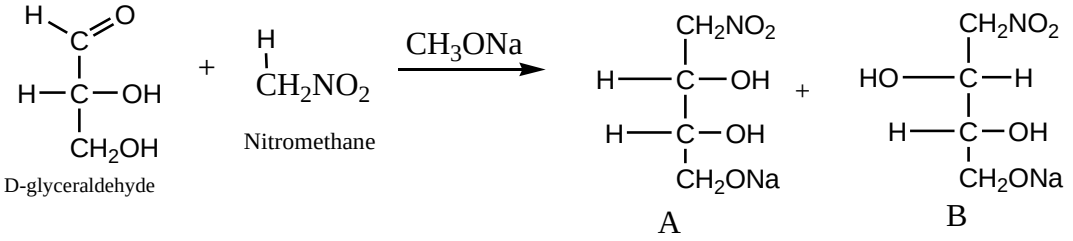


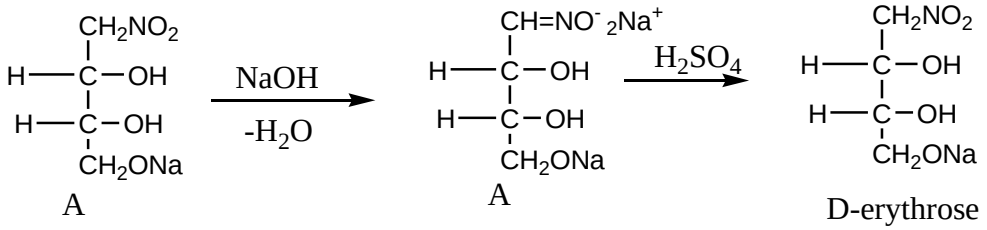
Y-D-mannanolactone

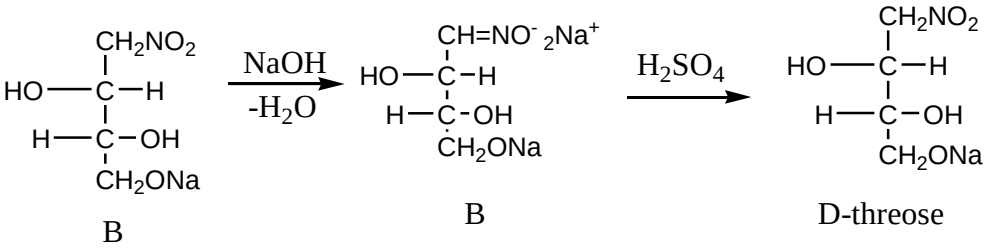
D-mannose(aldohexose)

(b). Swoden-Fischer Nitromethane Synthesis:

This is a more recent method and involvesthe reaction of an aldose with nitromethane in the presence of a base. This process introduces a new asymmetric centre and results in the formaton of two different nitroalcohols, which are separated by fractional crystallization. The individual nitroalcohola are next treated with NaOH solution to give the corresponding sodium salts, which may then be decomposed to givethe higher aldoses. Thus , D-glyceraldehyde may be converted in to D-erythrose and D-threose





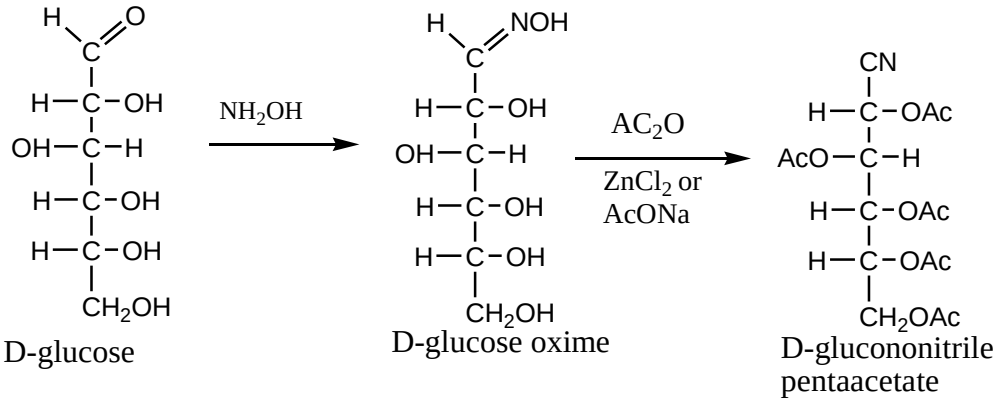


(2).Conversion of the Aldose in to the next lower Aldose:

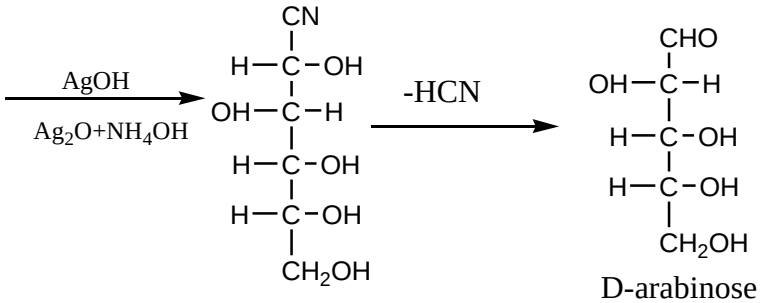
(a). Wohl's Method:

In this method the aldose is first treated with hydroxylamine to give the corresponding aldoxime. The aldoxime is next warmed with acetic anhydride in the presence of zinc chloride or sodium acetate, so that the oxime group is dehydrated and the hydroxyl groups esterified to give the acetylated aldononitrile. This is next warmed with ammoniacal silver oxide, so that the acetyl

groups are removed by hydrolysis and a molecule of hydrogencyanide is eliminated to give an aldose having one carbon atom less than the original aldose. Thus D-glucose may be converted into D-arabinose as indicated below.



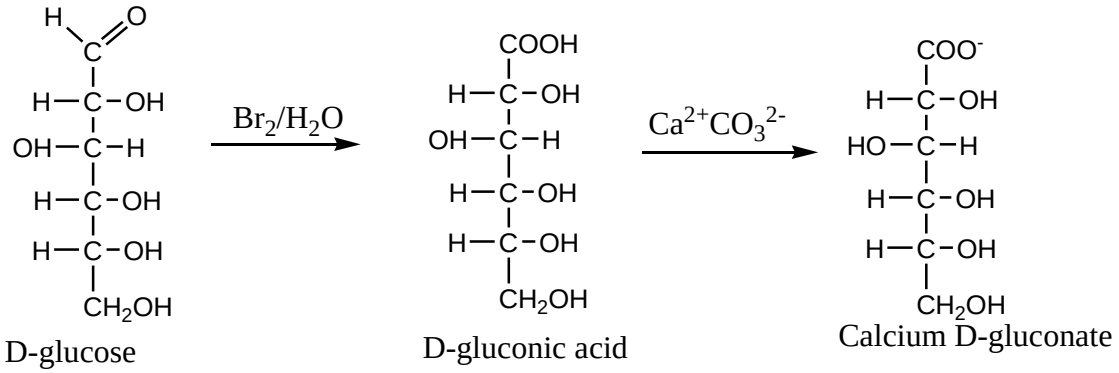
D-glucose D-glucose oxime D-gluconononitrile pentaacetate

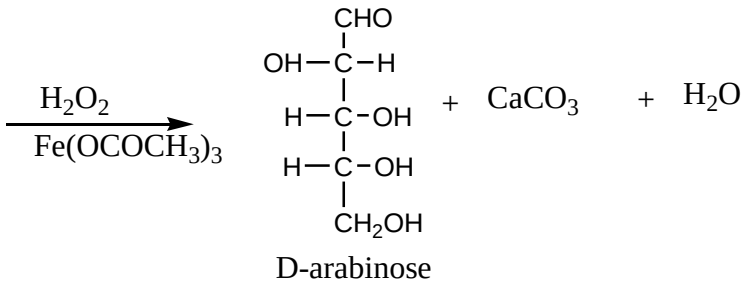


D-arabinose

(b). Ruff's Method:

In this method the aldose is first oxidized with bromine water to give the corresponding aldonic acid. The aldonic acid is next treated with calcium carbonate to givethe calcium salt of acid. This is ten treated with hydrogen peroxide and ferric acetate (Fentons's reagent), so that CO_2 and H_2O are eliminated to give the next lower aldose. Thus D-glucose may be converted into D-arabinose as shown below.

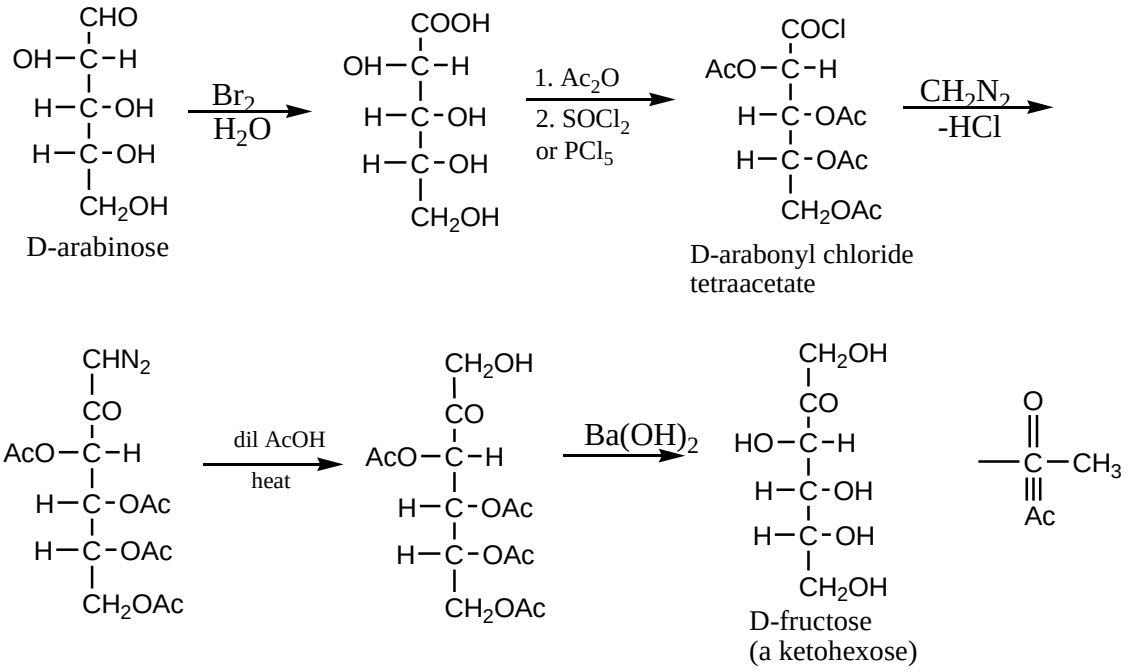




(3). Conversion of Aldose in to next higher Ketose:

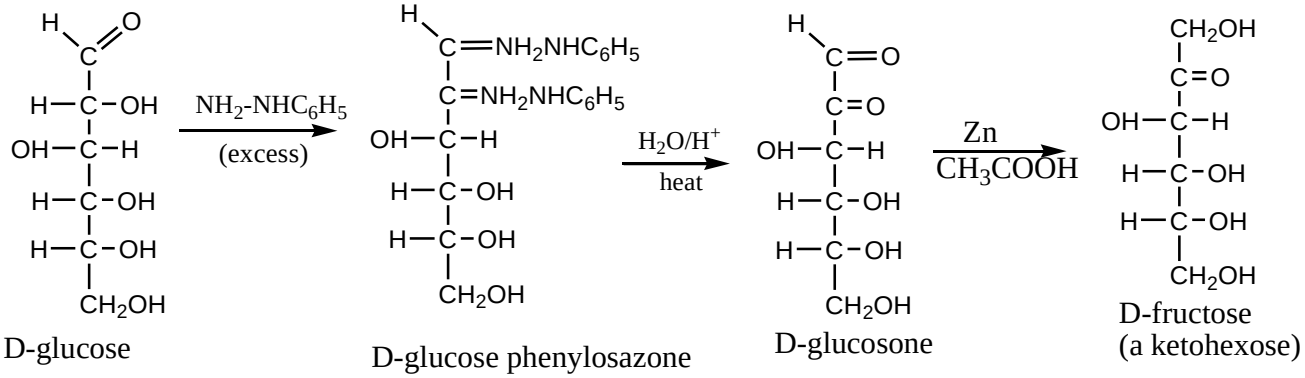
Wolfrom's Method:

In this method the aldose is oxidisedto the corresponding aldonic acid, which is acetylated with acetic anhydride. The acetylated aldonic acid is then treated with thionylchloride or PCl_5 to give the corresponding acid chloride. Treatment of this with diazomethane followed by heating with aqueous acetic acid and, finally, deacetylation by alkaline hydrolysis to gives next higher ketose. Thus, D-arabinose may be converted in to D-fructose as follows.



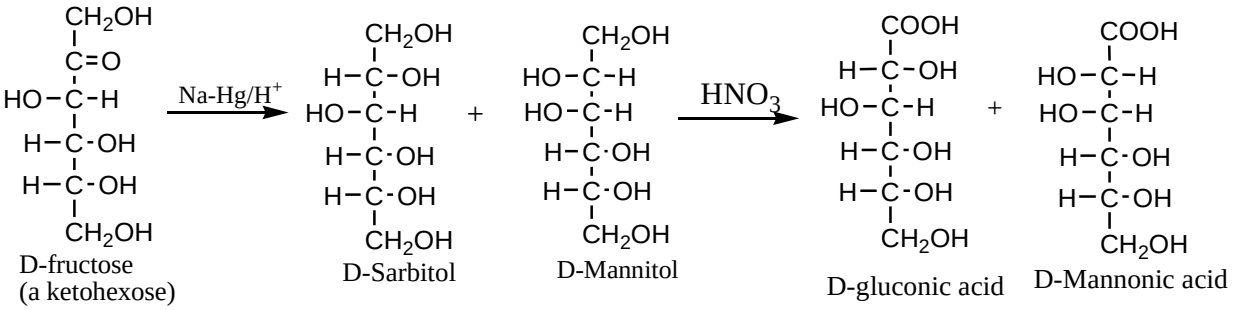
(4). Conversion of Aldose in to corresponding Ketose:

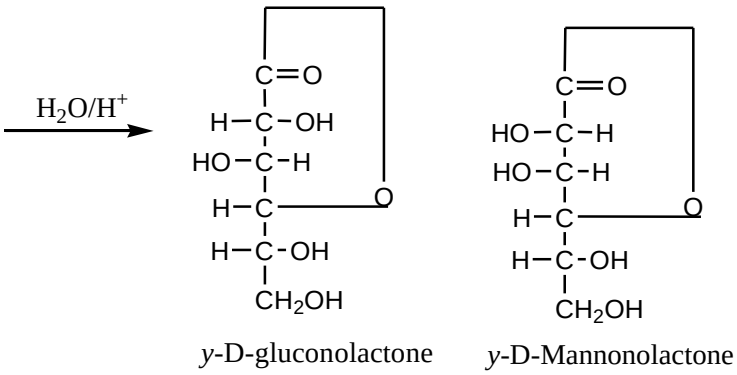
The aldose is first allowed to react with excess phenylhydrazine to give the corresponding osazone. The osazone is next hydrolysed with dilute hydrochloride acid to give the ozone. This is then redused with zinc and glacial acetic acid to give ketose which is isomeric with the original aldose. It should be noted that in glacial acetic acid , zinc reduces the aldehyde group in preference to the ketone group. Thus D-glucose may beconverted into D-fructose as follows.

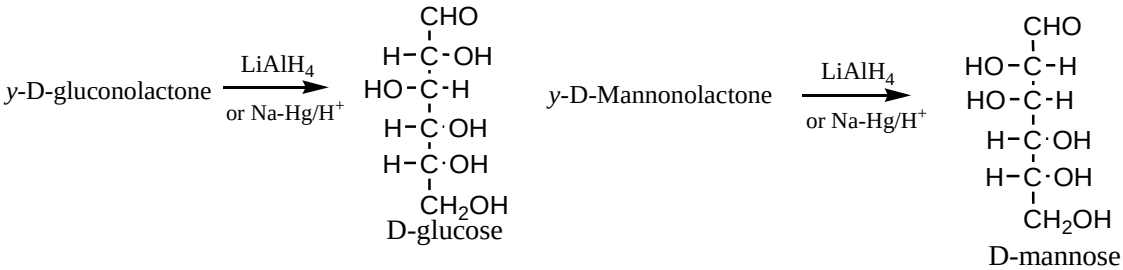


(5). Conversion of Ketose into the corresponding Aldose:

The ketose is first reduced with sodium amalgam in the presence of a trace of acid. This process introduces a new asymmetric centre and results in the formation of two different polyhydric alcohols. These alcohols are next oxidized with nitric acid to give the corresponding monobasic aldonic acids. The aldonic acids on treatment with dilute HCl give γ-lactones. These lactones are solids, and are separated by fractional crystallization. The individual lactones are then reduced with lithium aluminium hydride or sodium amalgam in a weakly acidic solution to yield aldoses which are isomeric with original ketose. The D-fructose may be converted in to D-glucose and D-mannose as shown below.

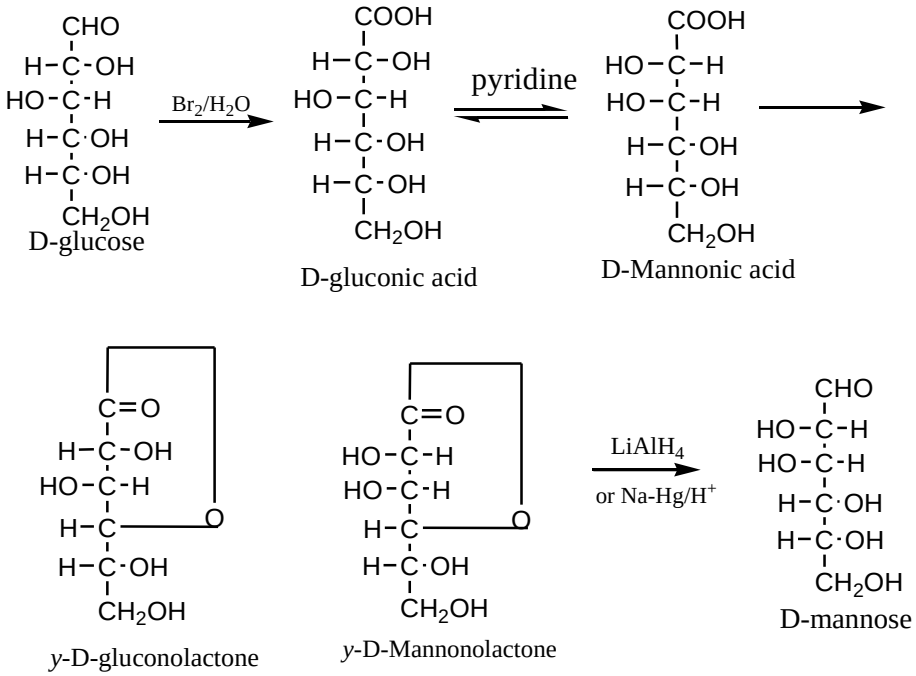






(6). Conversion of Aldose in to its Epimeric Aldose: (Epimerisation)

The aldose is first oxidized with bromine water to give the corresponding aldonic acid, which is then heated in aqueous pyridine or quinoline to give an equilibrium mixture of the original acid and its isomer. These isomeric aldonic acids are identical in all respects expect for the configuration about the asymmetric carbon number 2. They are, therefore, epimers (or more precisely C-2-epimers). These acids are next converted in to lactones. Separated and reduced to the original aldose and its C-2-epimer. Thus D-glucose may be converted into D-mannose as shown below.



This change of configuration of one asymmetric carbon atom in a compound containing two or more asymmetric carbon atoms is known as epimerization.

Possible Questions

PART A (1 Marks Questions)

1. A molecule is said to be chiral
a. if it contains plane of symmetry b. if it contains center of symmetry
c. if it cannot be superimposed on its mirror image d. **if it cannot superimposed on its mirror image**

2. Which of the following compounds will be optically active?
a. Succinic acid b. meso-tartaric acid c**. Lactic acid** d.Chloroacetic acid

3. Which of the following isomeric compounds show optical isomerism?
a. 1-aminopentene b. **2-aminopentene** c. 3-aminopentene d.2,2-dimethylpropylamine

4. 2-Butanol is optically active because it contains
a. **a chiral carbon** b. a plane of symmetry c. a hydroxyl group d. a center of symmetry

5. Hydrazo benzene when boiled with acid it gives
a. **Benzidine** b.Aniline c.Azobenzene d.Azoxybenzene

6. Hydrazo compounds, when boiled with acids, rearranges to benzidine. This rearrangement is known as
a.Claisen rearrangement b. Fries rearrangement c.Lossen rearrangement
d.**Benzidine rearrangement**

7. When benzil treated with NaOH it gives
a.**Benzilic acid** b.benzanilide c.benzoic acid d.benzyl alcohol

8. The Claisen condensation is often used in preparing
a. β-hydroxy ester b.α-hydroxyester c.ϒ-keto ester d. **β-keto ester**

9. Method used to ascend the aldoses series is known as
a.Ruff degradation b.Wolf's degradation c.**Killiani synthesis** d.Zemplen's modification

10. Monosaccharides undergo reversible isomerisation in the presence of dilute alkali.This reaction is
a.Mutarotation b.**Lobry de-Bruynand Albedra Van Ekenstein rearrangement**
c.Killiani synthesis d.wood's synthesis

11. Which one of the following is not a polysaccharide?
a.cellulose b.**sucrose** c.Amylose d.Inulin

12. Epimers differ in configuration at
a. C-1carbon b.**C-2 carbon** c.C-3 carbon d.C-3 carbon

13. Which one of the following test is not shown by proteins?
a.**Mulliken -Baker** b.Xanthoproteic test c.Hoopin's-cole reaction

d.Ninhydrin

14. Primary structure of protein shows
a. orientation of amino acids b. arrangement of peptides c. **amino acid sequence**
d. α or β-helix space structure

15. Spatial arrangement of peptides in protein to give helical structureis known as
a.**Secondary** b.Primary c.Tertiary d.Quaternery

16. Coagulation of protein on heating with heavy metal salts is known as
a.**Sedimentation** b.Decolourization c.Denaturation d.Precipitation

17. IUPAC name of pyrrole is
a.Azine b.Azolidine c.**Azole** d.Diazine

18. IUPAC name of pyrimidine is
a. Azolidine b.Azine c.**1,3-Diazine** d.Triazine

19. Which one of the following is not a five membered heterocyclic compounds?
a.Pyrrole b.Furan c.Thiophene d.**pyridine**

20. Which one of the following is most basic?
a.Aniline b.Pyrrole c.**pyridine** d.Thiophene

PART B (8 Marks Questions)

1) Give the conversion of the Ketose in to the corresponding Aldose.

2) Explain Epimerization.

3).(i) Methyl-α-D glucoside react with 1:2 ratio mole with HIO_4 to give a molase HCOOH and B. The compound B is also obtained when methyl glycoside, C reacts in equimolar ratio with HIO_4 and with no formic acid formation. Identify the structure of A, B, C.?
(ii)How can be verified that maltose, cellobiose and lactose are not composed of L-monosaccharides? Are L-sugars observed in nature?

4) Give the conversion of an Aldose in to the next lower Aldose by (1) Wohl's Method (2) Ruff's Method.

5) An unknown carbohydrate formula $C_{12}H_{22}O_{11}$ reacts with tollens reagent to form a silver mirror. An α-glycosidase as no effect on the carbohydrate, but a β-galactosides hydrolysis it to D-galactose and D-mannose. When the carbohydrate is methylated and then hydrolysed with HCl , the products are 2,3,4,6-tetra-O-methyl galactose and 2,3,4-tri-O-methyl mannose. Propose the structure of this unknown carbohydrate?

6). Discuss the structure of D-Fructose.

7**)** (i) Compound A, $C_5H_{10}O_4$ on oxidation with Br_2-H_2O gives B, $C_5H_{10}O_8$. A forms a tri acetate and is reduced by HI to n-pentane. Oxidation of A with HIO_4 gives, among other products one molecule of HCHO and 1 mole of HCOOH. What is possible structure of A and how could you distinguish between them?

(ii).How can the sequence,

Sugar $\xrightarrow{HIO_4}$ $\xrightarrow{aq\ Br_2}$ $\xrightarrow{H_3O^+}$ show if a methyl gulcoside has a pyranose or furanose ring?

8).Explain the following:

(i) Killiani synthesis

(ii)Epimerization

(iii)Sucrose does not show mutarotation

9). Describe the manufacture of Sugar beet. How does Sucrose react with (i) lime water (ii) acetic anhydride (iii) yeast (iv) Conc. HNO_3 and (v) Conc. and hot H_2SO_4?

10). Discuss the Structure of D- Glucose.

11). What happens when Fructose is treated with (i) Mettalic Hydroxides (ii) Na/Hg (iii)Semicarbazide (iv) Phenylhydrazine.

12).(i) Compound A is D-Aldopentose and on oxidation yields an optically inactive dibasic acid B. A on ruff's degradation gives an aldotetrose C whose oxidation product is mesotataric acid. Deduce the correct configuration of the compound A to C?

(ii)Suggest a mechanism of the acid catalysed muta rotation of D(+) glucose ?

UNIT-III		Subject: Organic Chemistry			Subject code:15CHU501	
1.	On warming with glucose, a silver mirror is formed by	a.Fehling's solution	b.Benedict's solution	c.Barfoed's reagent	d.Tollen's reagent	Fehling's solution
2.	Fehling's solution and Benedict's solution are reduced by glucose to form	a.CuO	b.Cu_2O	c.$Cu(OH)_2$	d.CuO_2	Cu_2O
3.	The sugar which will not reduce Fehling's solution is	a. maltose	b.lactose	c.sucrose	d.glucose	sucrose
4.	Glucose on oxidation with bromine ater gives	a.tartaric acid	b.glutaric acid	c.gluconic acid	d.glycollic acid	gluconic acid
5.	The number of asymmetric carbon atom in glucose is	a.2	b.3	c.4	d.5	4
6.	Which of the following statement concerning glucose is incorrect	a.it has 4 asymmetric c-atoms	b.it is an aldehyde	c.itisoptically active	d. it is a disaccharide	it is a disaccharide
7.	Which one the following compounds is different from the rest?	a.sucrose	b.maltose	c.lactose	d.glucose	glucose
8.	The fact that(+) glucose and (+)mannose yield the same osazone shows that	a.they are optical isomers	b. both are aldoses	c.(+) mannose is same as (+) glucose	d.they are epimers	they are epimers
9.	Common sugar is	a.glucose	b.fructose	c.sucrose	d.a mixture of glucose and fructose	sucrose
10	Sucrose on hydrolysis gives	a.2 molecules of glucose	b.2 molecules of fructose	c. 1molecule each of glucose and fructose	d. 1 molecule each of glucose and mannose	one molecule each of glucose and fructose
11	Common table sugar is disaccharide of	a. glucose and mannose	b.glucose and fructose	c.fructose and mannose	d. glucose and lactose	glucose and fructose
12	An example of atrisaccharide is	a.starch	b.cellulose	c.raffinose	d.maltose	raffinose
13	An organic compound insoluble in water is	a.glucose	b.cellulose	c.sucrose	d.fructose	cellulose
14	The carbohydrate which has an extremely high molecular weight (macomolecule) is	a.cellulose	b.maltose	c.cellobiose	d.lactose	cellulose
15	Which one othe following is	a.lactose	b.maltose	c.sucrose	d.glucose	sucrose

	non reducing carbohydrate?					
16	Carbohydrates are characterized by thepresence of	a.OH group	b.C=O group	c.Asymmetric carbon	d.all of these	all of these
17	How many isomeric aldohexoses are possible for the molecular formula C6H12O6?	a.2	b.4	c.8	d.16	16
18	Both glucose and mannose can be prepared byKilliani synthesis from	a.D-ribose	b.D-lyxose	c. D-arabinose	d.D-xylose	D-arabinose
19	Method used to ascend the aldoses series is known as	a.Ruff degradation	b.Wolf's degradation	c.Killiani synthesis	d.Zemplen's modification	Killiani synthesis
20	Monosaccharides undergo reversible isomerisation in the presence of dilute alkali.This reaction is	a.Mutarotation	b.Lobry de-Bruynand Albedra Van Ekenstein rearrangement	c.Killiani synthesis	d.wood's synthesis	Lobry de-Bruynand Albedra Van Ekenstein rearrangement
21	Which one of the following is not a polysaccharide?	a.cellulose	b.sucrose	c.Amylose	d.Inulin	Sucrose
22	Epimers differ in configuration at	a.C-1carbon	b.C-2 carbon	c.C-3 carbon	d.C-3 carbon	C-2 carbon
23	A freshly prepared solution of glucose has specific rotation of +112° but on keeping for some time it changes to +52.7°. This phenomenon is known as	a.Mutarotation	b.Epimerization	c.Racemisation	d.Resolution	Mutarotation
24	The specific rotation for identification of carbohydrate is	a.Molisch's test	b.Tollen's test	c.Fehling's test	d.Benedicts test	Molisch's test
25	Glucose does not restore the pink colour of Schiff's reagent. It is due to	a. aldehyde involvedin hemiacetal formation	b.no aldehyde group	c.-I effect of -OH group	d.keto group	aldehyde involvedin hemiacetal formation
26	The reagent which can be used to distinguish between starch and cellulose is	a.Tollen's test	b.Iodine solution	c.acetic anhydride	d.Fehling's reagent	Iodine solution
27	Isomers differs in configuration at asymmetric carbon due to hemiacetal ring formation are	a.Epimers	b.conformers	c.Anomers	d.Tautomers	Anomers

	known as					
28	Fructose is leavorotatoryyet it is written as D-fructose. This 'D' indicates	a.specific rotation	b.Generic relationship to D-glyceraldehyde	c.Mutarotation	d.Resolution	Generic relationship to D-glyceraldehyde
29	Invert sugar is	a.Sucrose	b. Mixture of Glucose+Fructose	c.Mannose	d.D-xylose	Mixture of Glucose+Fructose
30	Hydrolysis of D-Lactosegives	a.Glucose+Galactose	b.Galactose+Fructose	c.Glucose +Fructose	d.Only glucose	Glucose+Galactose
31	Synthetic silk known as viscose rayon is	a.Cellulose acetate	b.Regenerated cellulose	c.Cellulose nitrate	d.Nitrated starch	Regenerated cellulose
32	Which one of the following disaccharideon hydrolysis gives only glucose units.	a. maltose	b.sucrose	c.lactose	d.Amylose	maltose
33	Which product derived form of cellulose is nick named skin	a.Cellulose nitrate	b.Pyroxyline	c.Cellulose xanthate	d.Cellulose acetate	Pyroxyline
34	Methylation of sucrose gives	a.Tetramethyl derivative	b.Octamethyl derivative	c.Monomethyl derivative	d.Dimethylderivative	Octamethyl derivative
35	Acetylation of fructose gives	a.Monoacetyl derivative	b.Diacetyl derivative	c.Triacetyl derivative	d.Pentaacetyl derivative	Pentaacetyl derivative
36	The conversion of aldohexose into aldopentose is	a.Ruff degradation	b.Wolf's degradation	c.Killiani synthesis	d.wood's synthesis	Wolf's degradation
37	The molecular formula of sucrose is	a. C10 H22 O11	b.C12 H22 O11	c.C6 H12O6	d.C11 H22 012	C12 H22 O11
38	Which one of the following aldopentoses yield a mixture of glucose and mannose in killiani hologation?	a.D-ribose	b.D-lyxose	c.D-xylose	d. D-arabinose	D-xylose
39	Which one of the following compound is leavorotatory compound?	a.Fructose	b.glucose	c.Mannose	d.cellulose	Fructose
40	Acetylation of glucose gives	a.Monoacetyl derivative	b.Diacetyl derivative	c.Triacetyl derivative	d.Pentaacetyl derivative	Pentaacetyl derivative
41	When fructose heated with conc.HCl, it gives	a.Tartaric acid	b.Glycollic acid	c.Trihydroxyglutaric acid	d.Laevulinic acid	Tartaric acid
42	Which one of the following tests is used to distinguish	a.Pinoff's test	b. Selivanoff's test	c.furfural test	d.Xanthoprotic test	Selivanoff's test

	fructose from glucose?					
43	The digesion of proteins involves their	a.Tartaric acid	b.Succinic acid	c.Oxalic acid	d.Laevulinic acid	Oxalic acid
44	The disaccharide present in milk is	a.Maltose	b.Lactose	c.sucrose	d.cellbiose	Lactose
45	Which one gives positive silver mirror test?	a.sucrose	b.glucose	b.glucose	d.Fructose	Fructose
46	Glucose react with X number of molecules of phenylhydrazinento yield osazone. The value of 'X' is	a.Three	b. Two	c.One	d.Four	Three
47	Glucose forms many derivatives.The derivative which will help to prove the furanose structure is	a.Osazone	b.benzoyl	c.acetyl	d. isopropylidine	isopropylidine
48	Which enzyme breaks sucrose into glucose and fructose?	a.Zymase	b.Maltase	c.Diastase	d.Invertase	Invertase
49	A sugar that is not a disaccharide among the following is	a.Lactose	b.Galactose	c.Sucrose	a.Maltose	Galactose
50	α-D(+) glucose and β-D(+) glucose are	a.Enantiomers	b.Geometrical isomers	c.Epimers	d.Anomers	Anomers
51	Mutarotation does not occur in	a.sucrose	b.D-glucose	b.glucose	b.L-glucose	sucrose
52	Complete hydrolysis of cellulose gives	a.L-glucose	b.D-fructose	c.D-ribose	d.D-glucose	D-glucose
53	How many stereoisomers can an aldotetrose have?	a.2	b.4	c.6	d.8	4
54	How many stereoisomers can an aldopentose have?	a.12	b.8	c.6	d.4	8
55	How many stereoisomers are possible for a ketohexose	a.8	b.16	c.10	d.6	8
56	In the fischer projection of D-glyceraldehyde,the-OH on thechiral carbon is drawn	a.to the left	b.above	c.below	d.to the right	to the right
57	What is the	a. 2%	b.20%	c.90%	d.0.02%	0.02%

	approximateequilibrium concentration of the open chain formof D-glucose in an aqueous solution?					
58	What is the structural relationship between the osazones of D-glucose and D-fructose?	a. They are epimers	b.They are enantiomers	c.They are anomers	d.They are identical	They are identical
59	In maltose, the glucose molecules are connected by	a.β-1,4-glycosidic bond	b.α-1,6-glcosidic bond	c.1,2 -glycosidic bond	d.α-1,4-glcosidic bond	α-1,4-glcosidic bond
60	In amylopectin, the glucose molecules are connected by	a.β-1,4-glycosidic bond	b.α-1,6-glcosidic bond	c.α-1,4-glcosidic bond	d.α-1,4-glcosidic bond and α-1,6-glycosidic bonds	α-1,4-glcosidic bond and α-1,6-glycosidic bonds

UNIT-IV

Amino acids– Classification,Preparation and properties –Peptides and synthesis of Polypeptides. Proteins- classification based on physical properties and biological functions, colour reactions – Primary, Secondary and tertiary structure.

1. Introduction

Proteins, from the Greek *proteios*, meaning first, are a class of organic compounds which are present in and vital to every living cell. In the form of skin, hair, callus, cartilage, muscles, tendons and ligaments, proteins hold together, protect, and provide structure to the body of a multi-celled organism. In the form of enzymes, hormones, antibodies, and globulins, they catalyze, regulate, and protect the body chemistry. In the form of hemoglobin, myoglobin and various lipoproteins, they effect the transport of oxygen and other substances within an organism.

Proteins are generally regarded as beneficial, and are a necessary part of the diet of all animals. Humans can become seriously ill if they do not eat enough suitable protein, the disease *kwashiorkor* being an extreme form of protein deficiency. Protein based antibiotics and vaccines help to fight disease, and we warm and protect our bodies with clothing and shoes that are often protein in nature (e.g. wool, silk and leather).
The deadly properties of protein toxins and venoms is less widely appreciated. Botulinum toxin A, from *Clostridium botulinum*, is regarded as the most powerful poison known. Based on toxicology studies, a teaspoon of this toxin would be sufficient to kill a fifth of the world's population. The toxins produced by tetanus and diphtheria microorganisms are nearly as poisonous. A list of highly toxic proteins or peptides would also include the venoms of many snakes, and ricin, the toxic protein found in castor beans.

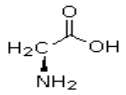
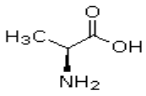
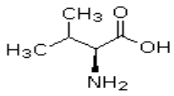
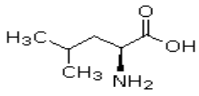
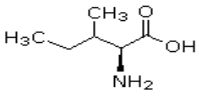
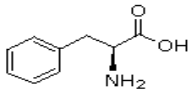
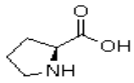
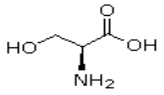
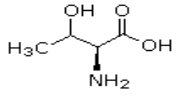
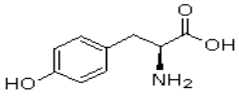
Despite the variety of their physiological function and differences in physical properties--silk is a flexible fiber, horn a tough rigid solid, and the enzyme pepsin water soluble crystals--proteins are sufficiently similar in molecular structure to warrant treating them as a single chemical family.

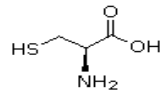
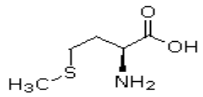
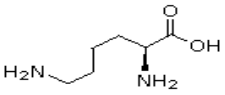
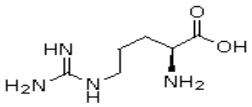
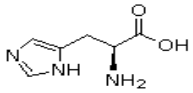
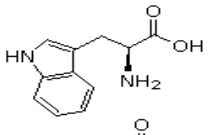
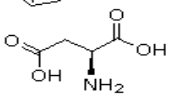
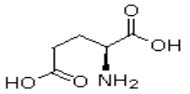
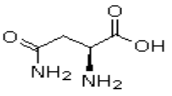
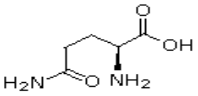
When compared with carbohydrates and lipids, the proteins are obviously different in fundamental composition. The lipids are largely hydrocarbon in nature, generally being 75 to 85% carbon. Carbohydrates are roughly 50% oxygen, and like the lipids, usually have less than 5% nitrogen (often none at all). Proteins and peptides, on the other hand, are composed of 15 to 25% nitrogen and about an equal amount of oxygen. The distinction between proteins and peptides is their size. Peptides are in a sense small proteins, having molecular weights less than 10,000.

2. Natural α-Amino Acids

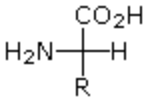
Hydrolysis of proteins by boiling aqueous acid or base yields an assortment of small molecules identified as α-aminocarboxylic acids. More than twenty such components have been isolated, and the most common of these are listed in the following table. Those amino acids having green colored names are **essential** diet components, since they are not synthesized by human metabolic processes. The best food source of these nutrients is protein, but it is important to recognize that not all proteins have equal nutritional value. For example, peanuts have a higher weight content of protein than fish or eggs, but the proportion of essential amino acids in peanut protein is only a third of that from the two other sources. For reasons that will become evident when discussing the structures of proteins and peptides, each amino acid is assigned a one or three letter abbreviation.

Natural α-Amino Acids

Name	Formula	Abbreviations	
Glycine		Gly	G
Alanine		Ala	A
Valine		Val	V
Leucine		Leu	L
Isoleucine		Ile	I
Phenylalanine		Phe	F
Proline		Pro	P
Serine		Ser	S
Threonine		Thr	T
Tyrosine		Tyr	Y

Name	Formula	Abbreviations	
Cysteine		Cys	C
Methionine		Met	M
Lysine		Lys	K
Arginine		Arg	R
Histidine		His	H
Tryptophan		Trp	W
Aspartic Acid		Asp	D
Glutamic Acid		Glu	E
Asparagine		Asn	N
Glutamine		Gln	Q

Some common features of these amino acids should be noted. With the exception of proline, they are all 1°-amines; and with the exception of glycine, they are all


L-Amino Acid

chiral. The configurations of the chiral amino acids are the same when written as a Fischer projection formula, as in the drawing on the right, and this was defined as the **L-configuration** by Fischer. The R-substituent in this structure is the remaining structural component that varies from one amino acid to another, and in proline R is a three-carbon chain that joins the nitrogen to the alpha-carbon in a five-membered ring. Applying the Cahn-Ingold-Prelog notation, all these natural chiral amino acids, with the exception of cysteine, have an **S**-configuration.For the first seven compounds in the left column the R-substituent is a hydrocarbon. The last three entries in the left column have hydroxyl functional groups, and the first two amino acids in the right column incorporate thiol and sulfide groups respectively. Lysine and arginine have basic amine functions in their side-chains; histidine and tryptophan have less basic nitrogen heterocyclic rings as substituents. Finally, carboxylic acid side-chains are substituents on aspartic and glutamic acid, and the last two compounds in the right column are their corresponding amides.

The formulas for the amino acids written above are simple covalent bond representations based upon previous understanding of mono-functional analogs. **The formulas are in fact incorrect**. This is evident from a comparison of the physical properties listed in the following table. All four compounds in the table are roughly the same size, and all have moderate to excellent water solubility. The first two are simple carboxylic acids, and the third is an amino alcohol. All three compounds are soluble in organic solvents (e.g. ether) and have relatively low melting points. The carboxylic acids have pK_a's near 4.5, and the conjugate acid of the amine has a pK_a of 10. The simple amino acid alanine is the last entry. By contrast, it is very high melting (with decomposition), insoluble in organic solvents, and a million times weaker as an acid than ordinary carboxylic acids.

Physical Properties of Selected Acids and Amines

Compound	Formula	Mol.Wt.	Solubility in Water	Solubility in Ether	Melting Point	pK_a
isobutyric acid	$(CH_3)_2CHCO_2H$	88	20g/100mL	complete	-47 ºC	5.0
lactic acid	$CH_3CH(OH)CO_2H$	90	complete	complete	53 ºC	3.9
3-amino-2-butanol	$CH_3CH(NH_2)CH(OH)CH_3$	89	complete	complete	9 ºC	10.0
alanine	$CH_3CH(NH_2)CO_2H$	89	18g/100mL	insoluble	ca. 300 ºC	9.8

These differences all point to internal salt formation by a proton transfer from the acidic carboxyl function to the basic amino group. The resulting ammonium carboxylate structure, commonly referred to as a**zwitterion**, is also supported by the spectroscopic characteristics of alanine.

$$CH_3CH(NH_2)CO_2H \rightleftharpoons CH_3CH(NH_3)^{(+)}CO_2^{(-)}$$

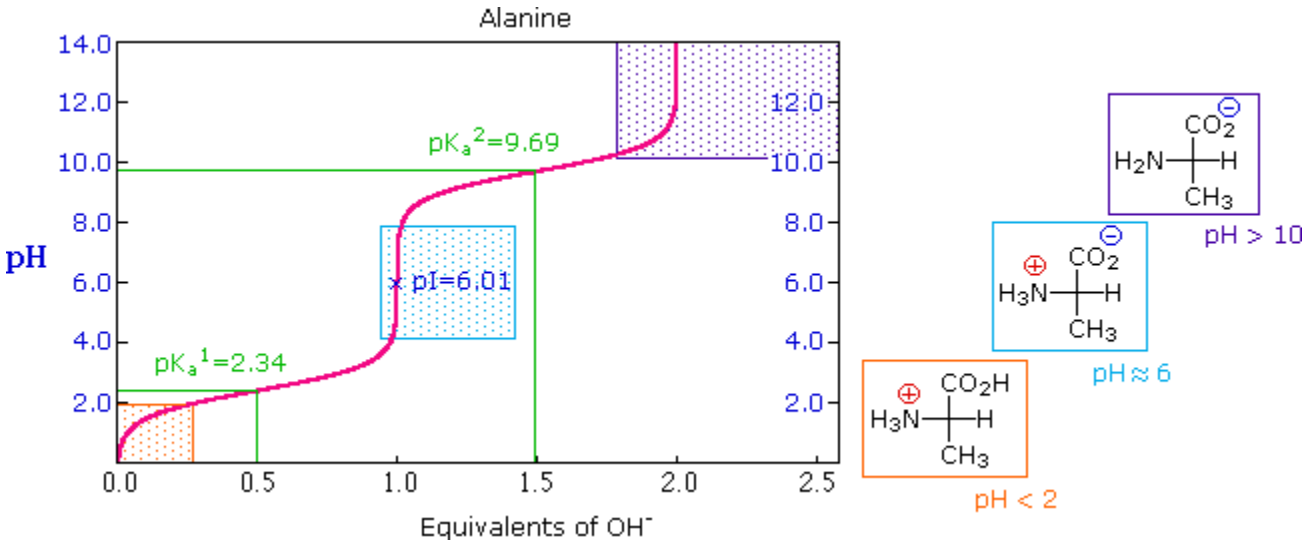
As expected from its ionic character, the alanine zwitterion is high melting, insoluble in nonpolar solvents and has the acid strength of a 1º-ammonium ion. To the right above is a Jmol display of an L-amino acid. The model will change to its zwitterionic form by clicking the appropriate button beneath the display. Examples of a few specific amino acids may also be viewed in their favored neutral zwitterionic form. Note that in lysine the amine function farthest from the carboxyl group is more basic than the alpha-amine. Consequently, the positively charged ammonium moiety formed at the chain terminus is attracted to the negative carboxylate, resulting in a coiled conformation.

Since amino acids, as well as peptides and proteins, incorporate both acidic and basic functional groups, the predominant molecular species present in an aqueous solution will depend on the pH of the solution. In order to determine the nature of the molecular and ionic species that are

present in aqueous solutions at different pH's, we make use of the **Henderson - Hasselbalch Equation**, written below. Here, the pK_a represents the acidity of a specific conjugate acid function (HA). When the pH of the solution equals pK_a, the concentrations of HA and $A^{(-)}$ must be equal (log 1 = 0).

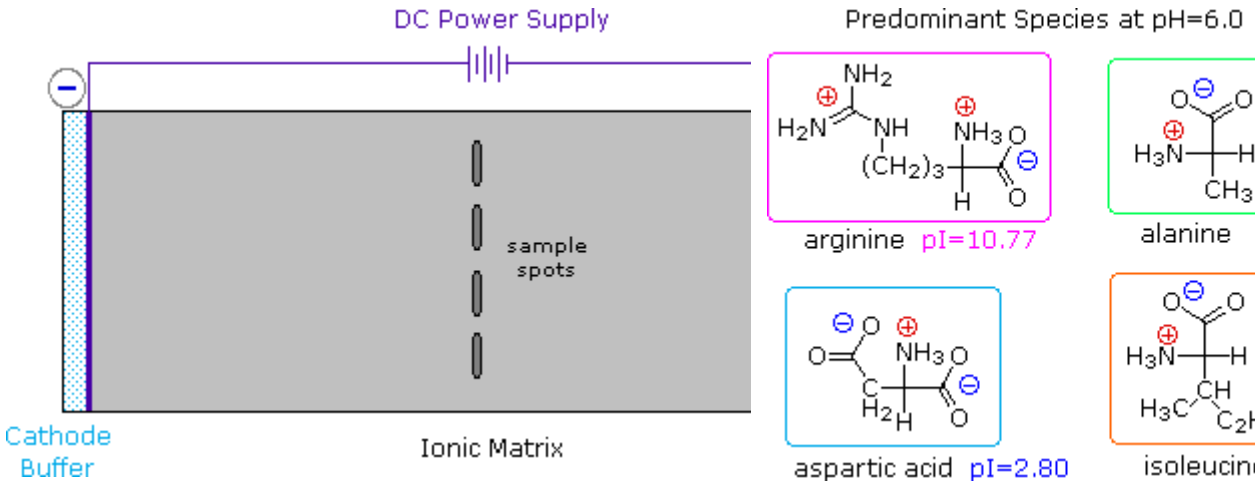
Henderson-Hasselbalch Equation: $$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

The titration curve for alanine, shown below, demonstrates this relationship. At a pH lower than 2, both the carboxylate and amine functions are protonated, so the alanine molecule has a net positive charge. At a pH greater than 10, the amine exists as a neutral base and the carboxyl as its conjugate base, so the alanine molecule has a net negative charge. At intermediate pH's the zwitterion concentration increases, and at a characteristic pH, called the **isoelectric point** (**pI**), the negatively and positively charged molecular species are present in equal concentration. This behavior is general for simple (difunctional) amino acids. Starting from a fully protonated state, the pK_a's of the acidic functions range from 1.8 to 2.4 for $-CO_2H$, and 8.8 to 9.7 for $-NH_3^{(+)}$. The isoelectric points range from 5.5 to 6.2. Titration curves show the neutralization of these acids by added base, and the change in pH during the titration.



Titration curves for many other amino acids may be examined at a useful site provided by The University of Virginia in Charlottesville. (Click this name)

The distribution of charged species in a sample can be shown experimentally by observing the movement of solute molecules in an electric field, using the technique of **electrophoresis**. For such experiments an ionic buffer solution is incorporated in a solid matrix layer, composed of paper or a crosslinked gelatin-like substance. A small amount of the amino acid, peptide or protein sample is placed near the center of the matrix strip and an electric potential is applied at the ends of the strip, as shown in the following diagram. The solid structure of the matrix retards the diffusion of the solute molecules, which will remain where they are inserted, unless acted upon by the electrostatic potential. In the example shown here, four different amino acids are examined simultaneously in a pH 6.00 buffered medium. To see the result of this experiment, click on the illustration. Note that the colors in the display are only a convenient reference, since these amino acids are colorless.



At pH 6.00 alanine and isoleucine exist on average as neutral zwitterionic molecules, and are not influenced by the electric field. Arginine is a basic amino acid. Both base functions exist as "onium" conjugate acids in the pH 6.00 matrix. The solute molecules of arginine therefore carry an excess positive charge, and they move toward the cathode. The two carboxyl functions in aspartic acid are both ionized at pH 6.00, and the negatively charged solute molecules move toward the anode in the electric field. Structures for all these species are shown to the right of the display.

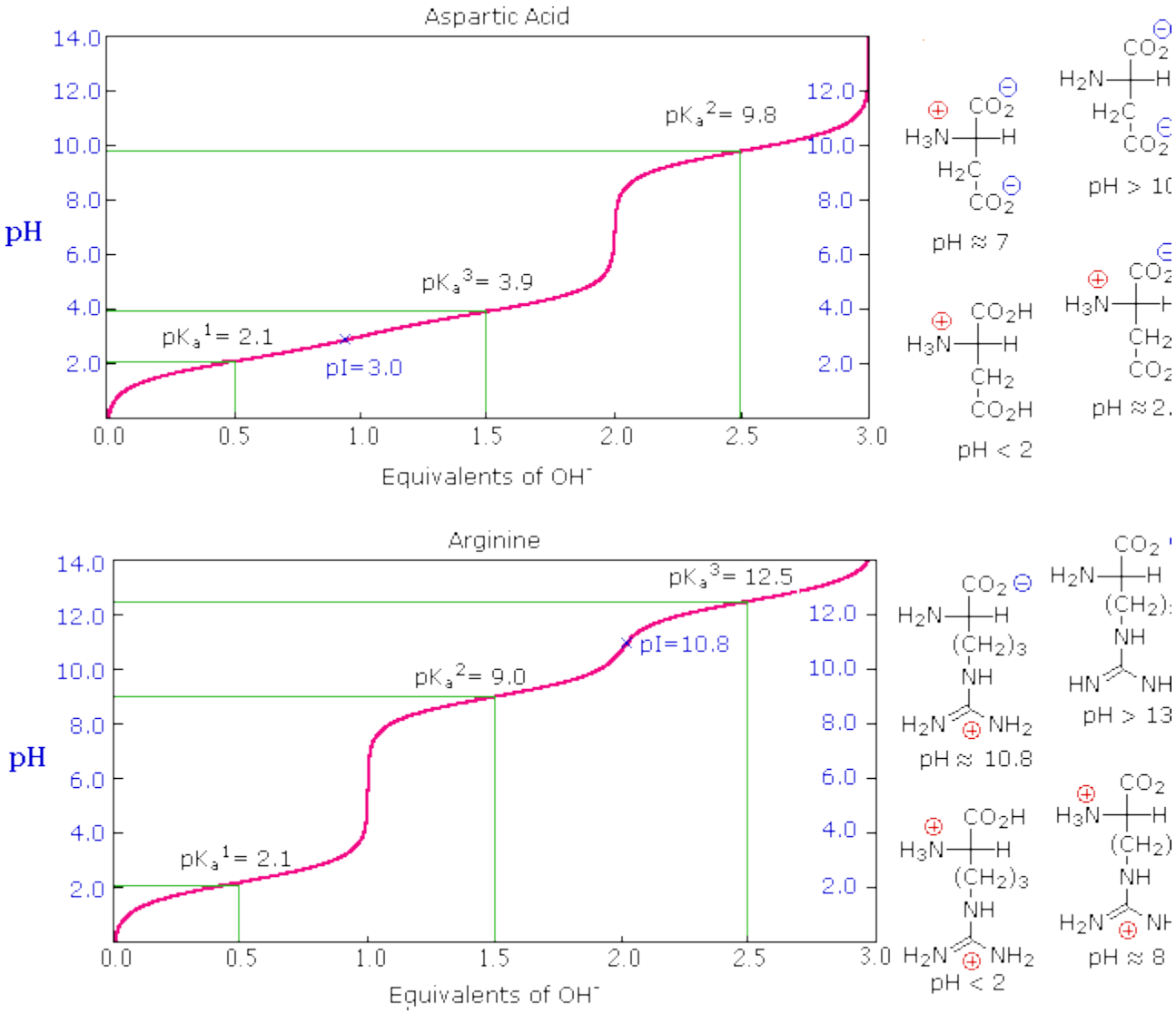
It should be clear that the result of this experiment is critically dependent on the pH of the matrix buffer. If we were to repeat the electrophoresis of these compounds at a pH of 3.80, the aspartic acid would remain at its point of origin, and the other amino acids would move toward the cathode. Ignoring differences in molecular size and shape, the arginine would move twice as fast as the alanine and isoleucine because its solute molecules on average would carry a double positive charge.

pK_a Values of Polyfunctional Amino Acids

Amino Acid	α-CO_2H pK_a^1	α-NH_3 pK_a^2	Side Chain pK_a^3	pI
Arginine	2.1	9.0	12.5	10.8
Aspartic Acid	2.1	9.8	3.9	3.0
Cysteine	1.7	10.4	8.3	5.0
Glutamic Acid	2.2	9.7	4.3	3.2
Histidine	1.8	9.2	6.0	7.6
Lysine	2.2	9.0	10.5	9.8
Tyrosine	2.2	9.1	10.1	5.7

As noted earlier, the titration curves of simple amino acids display two inflection points, one due to the strongly acidic carboxyl group (pK_a^1 = 1.8 to 2.4), and the other for the less acidic ammonium function (pK_a^2 = 8.8 to 9.7). For the 2º-amino acid proline, pK_a^2 is 10.6, reflecting the greater basicity of 2º-amines. Some amino acids have additional acidic or basic functions in their side chains. These compounds are listed in the table on the right. A third pK_a, representing the acidity or basicity of the extra function, is listed in the fourth column of the table. The pI's of these amino acids (last column) are often very different from those noted above for the simpler members. As expected, such compounds display three inflection points in their titration curves, illustrated by the titrations of arginine and aspartic acid shown below. For each of these compounds four possible charged species are possible, one of which has no overall charge. Formulas for these species are written to the right of the titration curves, together with the pH at which each is expected to

predominate. The very high pH required to remove the last acidic proton from arginine reflects the exceptionally high basicity of the guanidine moiety at the end of the side chain.

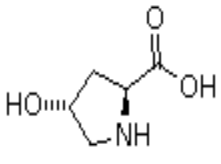


3. The Isoelectric Point

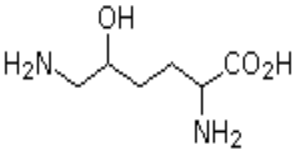
As defined above, the isoelectric point, **pI**, is the pH of an aqueous solution of an amino acid (or peptide) at which the molecules on average have no net charge. In other words, the positively charged groups are exactly balanced by the negatively charged groups. For simple amino acids such as alanine, the pI is an average of the pK_a's of the carboxyl (2.34) and ammonium (9.69) groups. Thus, the pI for alanine is calculated to be: (2.34 + 9.69)/2 = 6.02, the experimentally determined value. If additional acidic or basic groups are present as side-chain functions, the pI is the average of the pK_a's of the two most similar acids. To assist in determining similarity we define two classes of acids. The first consists of acids that are neutral in their protonated form (e.g. CO_2H & SH). The second includes acids that are positively charged in their protonated state (e.g. $-NH_3^+$). In the case of aspartic acid, the similar acids are the alpha-carboxyl function (pK_a = 2.1) and the side-chain carboxyl function (pK_a = 3.9), so pI = (2.1 + 3.9)/2 = 3.0. For arginine, the similar acids are the guanidinium species on the side-chain (pK_a = 12.5) and the alpha-ammonium function (pK_a = 9.0), so the calculated pI = (12.5 + 9.0)/2 = 10.75.

4. Other Natural Amino Acids

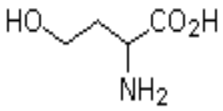
The twenty alpha-amino acids listed above are the primary components of proteins, their incorporation being governed by the genetic code. Many other naturally occurring amino acids exist, and the structures of a few of these are displayed below. Some, such as hydroxylysine and hydroxyproline, are simply functionalized derivatives of a previously described compound. These two amino acids are found only incollagen, a common structural protein. Homoserine and homocysteine are higher homologs of their namesakes. The amino group in beta-alanine has moved to the end of the three-carbon chain. It is a component of pantothenic acid, $HOCH_2C(CH_3)_2CH(OH)CONHCH_2CH_2CO_2H$, a member of the vitamin B complex and an essential nutrient. Acetyl coenzyme A is a pyrophosphorylated derivative of a pantothenic acid amide. The gamma-amino homolog GABA is a neurotransmitter inhibitor and antihypertensive agent.



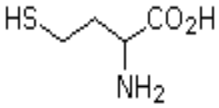
4-hydroxyproline



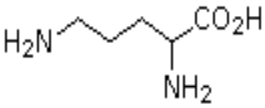
5-hydroxylysine



homoserine



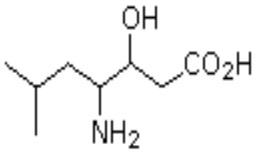
homocysteine



ornithine

β-alanine

γ-aminobutyric acid (GABA)



statine

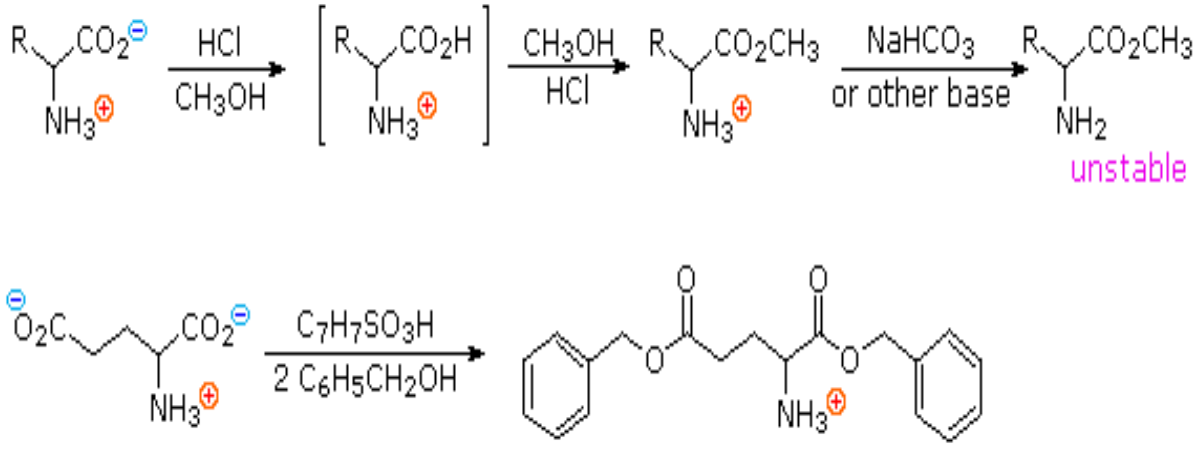
Many unusual amino acids, including D-enantiomers of some common acids, are produced by microorganisms. These include ornithine, which is a component of the antibiotic bacitracin A, and statin, found as part of a pentapeptide that inhibits the action of the digestive enzyme **pepsin**.

Reactions of α-Amino Acids

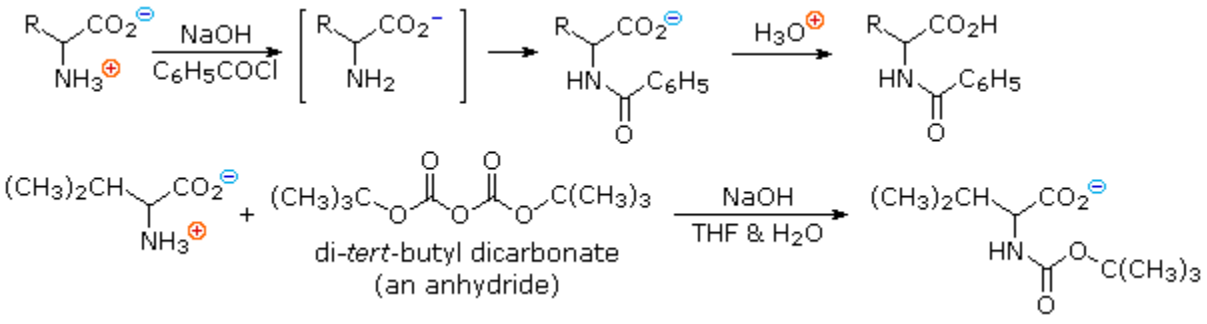
1. Carboxylic Acid Esterification

Amino acids undergo most of the chemical reactions characteristic of each function, assuming the pH is adjusted to an appropriate value. Esterification of the carboxylic acid is usually conducted under acidic conditions, as shown in the two equations written below. Under such conditions, amine functions are converted to their ammonium salts and carboxyic acids are not dissociated. The first equation is a typical Fischer esterification involving methanol. The initial product is a stable ammonium salt. The amino ester formed by neutralization of this salt is unstable, due to acylation of the amine by the ester function.
The second reaction illustrates benzylation of the two carboxylic acid functions of aspartic acid, using p-toluenesulfonic acid as an acid catalyst. Once the carboxyl function is esterified, zwitterionic species are no longer possible and the product behaves like any 1°-amine.

2. Amine Acylation

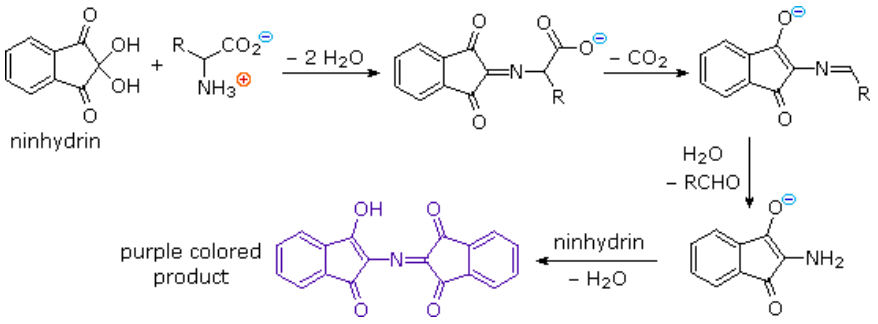


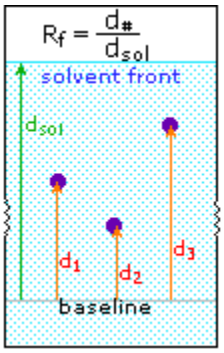
In order to convert the amine function of an amino acid into an amide, the pH of the solution must be raised to 10 or higher so that free amine nucleophiles are present in the reaction system. Carboxylic acids are all converted to carboxylate anions at such a high pH, and do not interfere with amine acylation reactions. The following two reactions are illustrative. In the first, an acid chloride serves as the acylating reagent. This is a good example of the superior nucleophilicity of nitrogen in acylation reactions, since water and hydroxide anion are also present as competing nucleophiles. A similar selectivity favoring amines was observed in the Hinsberg test. The second reaction employs an anhydride-like reagent for the acylation. This is a particularly useful procedure in peptide synthesis, thanks to the ease with which the t-butylcarbonyl (**t-BOC**) group can be removed at a later stage. Since amides are only weakly basic (pK_a~ -1), the resulting amino acid derivatives do not display zwitterionic character, and may be converted to a variety of carboxylic acid derivatives.



3. The Ninhydrin Reaction

In addition to these common reactions of amines and carboxylic acids, common alpha-amino acids, except proline, undergo a unique reaction with the triketohydrindene hydrate known as ninhydrin. Among the products of this unusual reaction (shown on the left below) is a purple colored imino derivative, which provides as a useful color test for these amino acids, most of which are colorless. A common application of the ninhydrin test is the visualization of amino acids in **paper chromatography**. As shown in the graphic on the right, samples of amino acids or mixtures thereof are applied along a line near the bottom of a rectangular sheet of paper (the baseline). The bottom edge of the paper is immersed in an aqueous buffer, and this liquid climbs slowly toward the top edge. As the solvent front passes the sample spots, the compounds in each sample are carried along at a rate which is characteristic of their functionality, size and interaction with the cellulose matrix of the paper. Some compounds move rapidly up the paper, while others may scarcely move at all. The ratio of the distance a compound moves from the baseline to the distance of the solvent front from the baseline is defined as the retardation (or retention) factor $\mathbf{R_f}$. Different amino acids usually have different R_f's under suitable conditions. In the example on the right, the three sample compounds (1, 2 & 3) have respective R_f values of 0.54, 0.36 & 0.78. To animate this diagramClick on It.



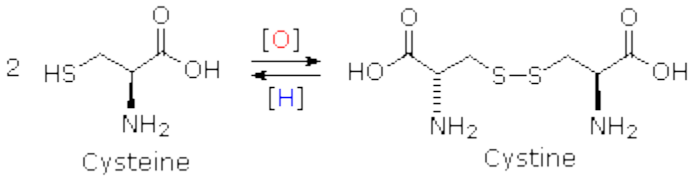


Paper Chromatography

4. Oxidative Coupling

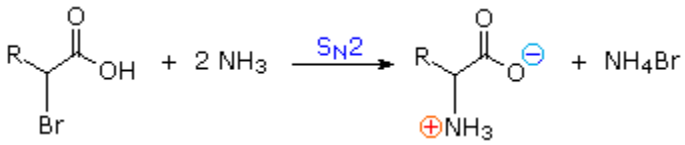
The mild oxidant iodine reacts selectively with certain amino acid side groups. These include the phenolic ring in tyrosine, and the heterocyclic rings in tryptophan and histidine, which all yield products of electrophilic iodination. In addition, the sulfur groups in cysteine and methionine are also oxidized by iodine. Quantitative measurement of iodine consumption has been used to determine the number of such residues in peptides. The basic functions in lysine and arginine are onium cations at pH less than 8, and are unreactive in that state. Cysteine is a thiol, and like most thiols it is oxidatively dimerized to a disulfide, which is sometimes listed as a distinct amino acid under the name **cystine**. Disulfide bonds of this kind are found in many peptides and proteins. For example, the two peptide chains that constitute insulin are held together by two disulfide links. Our hair consists of a fibrous protein called keratin, which contains an unusually large proportion of cysteine. In the manipulation called "permanent waving", disulfide bonds are first broken and then created after the hair has been reshaped. Treatment with dilute aqueous iodine oxidizes the methionine sulfur atom to a sulfoxide.

Cysteine-Cystine Interconversion

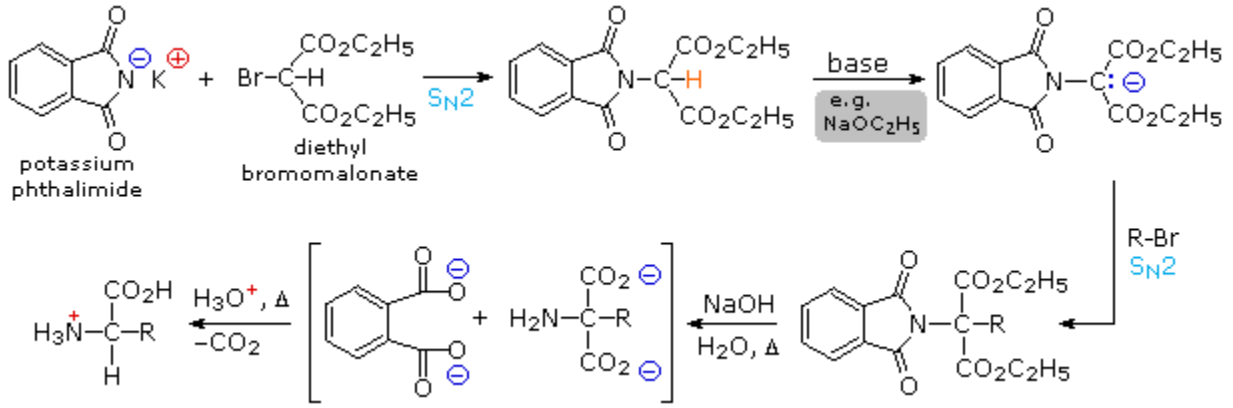


Synthesis of α-Amino Acids

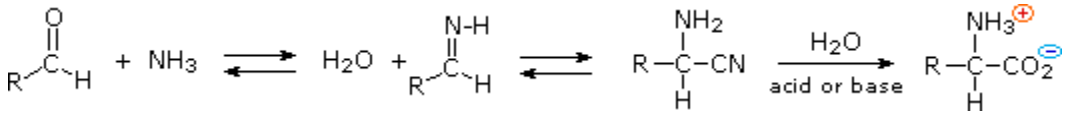
1) Amination of alpha-bromocarboxylic acids, illustrated by the following equation, provides a straightforward method for preparing alpha-aminocarboxylic acids. The bromoacids, in turn, are conveniently prepared from carboxylic acids by reaction with Br_2 + PCl_3. Although this direct approach gave mediocre results when used to prepare simple amines from alkyl halides, it is more effective for making amino acids, thanks to the reduced nucleophilicity of the nitrogen atom in the product. Nevertheless, more complex procedures that give good yields of pure compounds are often chosen for amino acid synthesis.



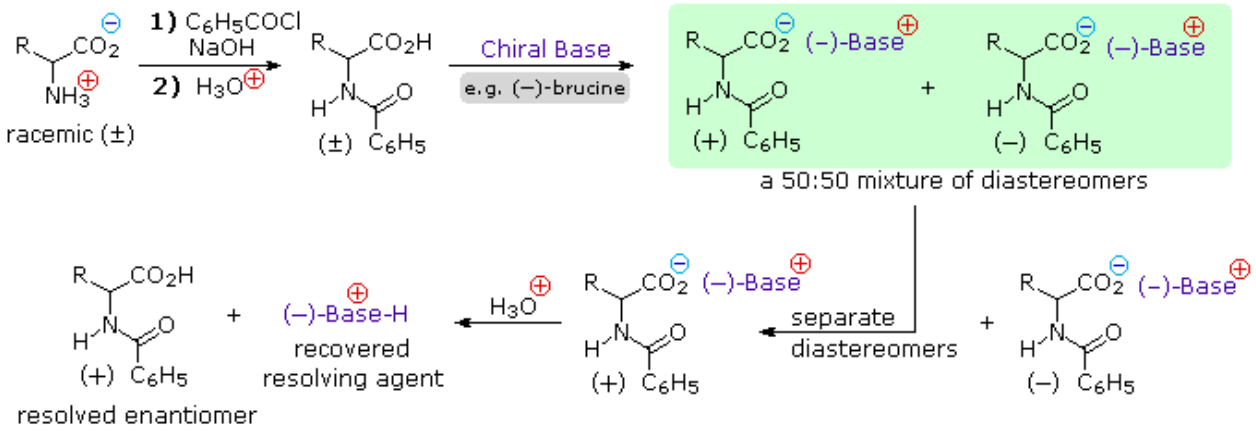
2) By modifying the nitrogen as a phthalimide salt, the propensity of amines to undergo multiple substitutions is removed, and a single clean substitution reaction of 1º- and many 2º-alkylhalides takes place. This procedure, known as the Gabriel synthesis, can be used to advantage in aminating bromomalonic esters, as shown in the upper equation of the following scheme. Since the phthalimide substituted malonic ester has an acidic hydrogen (colored orange), activated by the two ester groups, this intermediate may be converted to an ambident anion and alkylated. Finally, base catalyzed hydrolysis of the phthalimide moiety and the esters, followed by acidification and thermal decarboxylation, produces an amino acid and phthalic acid (not shown).



3) An elegant procedure, known as the **Strecker synthesis**, assembles an alpha-amino acid from ammonia (the amine precursor), cyanide (the carboxyl precursor), and an aldehyde. This reaction (shown below) is essentially an imino analog of cyanohydrin formation. The alpha-amino nitrile formed in this way can then be hydrolyzed to an amino acid by either acid or base catalysis.



4) Resolution The three synthetic procedures described above, and many others that can be conceived, give racemic amino acid products. If pure **L** or **D** enantiomers are desired, it is necessary to resolvethese racemic mixtures. A common method of resolving racemates is by diastereomeric salt formation with a pure chiral acid or base. This is illustrated for a generic amino acid in the following diagram. Be careful to distinguish charge symbols, shown in colored circles, from optical rotation signs, shown in parenthesis.
In the initial display, the carboxylic acid function contributes to diastereomeric salt formation. The racemic amino acid is first converted to a benzamide derivative to remove the basic character of the amino group. Next, an ammonium salt is formed by combining the carboxylic acid with an optically pure amine, such as brucine (a relative of strychnine). The structure of this amine is not shown, because it is not a critical factor in the logical progression of steps. Since the amino acid moiety is racemic and the base is a single enantiomer (levorotatory in this example), an equimolar mixture of diastereomeric salts is formed (drawn in the green shaded box). Diastereomers may be separated by crystallization, chromatography or other physical manipulation, and in this way one of the isomers may be isolated for further treatment, in this illustration it is the (+):(-) diastereomer. Finally the salt is broken by acid treatment, giving the resolved (+)-amino acid derivative together with the recovered resolving agent (the optically active amine). Of course, the same procedure could be used to obtain the (-)-enantiomer of the amino acid.



Since amino acids are amphoteric, resolution could also be achieved by using the basic character of the amine function. For this approach we would need an enantiomerically pure chiral acid such as tartaric acid to use as the resolving agent. By clicking on the above diagram, this alternative resolution strategy will be illustrated. Note that the carboxylic acid function is first esterified, so that it will not compete with the resolving acid. Resolution of aminoacid derivatives may also be achieved by enzymatic discrimination in the hydrolysis of amides. For example, an aminoacylase enzyme from pig kidneys cleaves an amide derivative of a natural L-amino acid much faster than it does the D-enantiomer. If the racemic mixture of amides shown in the green shaded box above is treated with this enzyme, the L-enantiomer (whatever its rotation) will be rapidly converted to its free zwitterionic form, whereas the D-enantiomer will remain largely unchanged. Here, the diastereomeric species are transition states rather than isolable intermediates. This separation of enantiomers, based on very different rates of reaction, is called **kinetic resolution**.

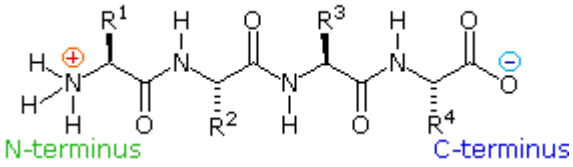
Peptides & Proteins

1. The Peptide Bond

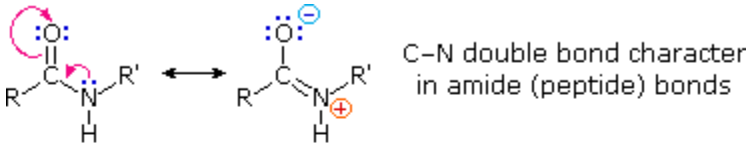
If the amine and carboxylic acid functional groups in amino acids join together to form amide bonds, a chain of amino acid units, called a **peptide**, is formed. A simple tetrapeptide structure is shown in the following diagram. By convention, the amino acid component retaining a free amine group is drawn at the left end (the N-terminus) of the peptide chain, and the amino acid

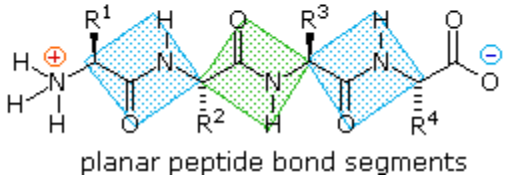
retaining a free carboxylic acid is drawn on the right (the C-terminus). As expected, the free amine and carboxylic acid functions on a peptide chain form a zwitterionic structure at their isoelectricpH.

By clicking the "Grow Peptide" button, an animation showing the assembly of this peptide will be displayed. The "Show Structure" button displays some bond angles and lengths that are characteristic of these compounds.

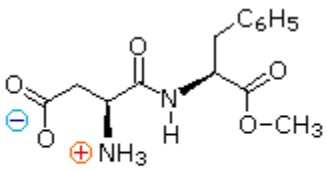


The conformational flexibility of peptide chains is limited chiefly to rotations about the bonds leading to the alpha-carbon atoms. This restriction is due to the rigid nature of the amide (peptide) bond. As shown in the following diagram, nitrogen electron pair delocalization into the carbonyl group results in significant double bond character between the carbonyl carbon and the nitrogen. This keeps the peptide links relatively planar and resistant to conformational change. The color shaded rectangles in the lower structure define these regions, and identify the relatively facile rotations that may take place where the corners meet (i.e. at the alpha-carbon). This aspect of peptide structure is an important factor influencing the conformations adopted by proteins and large peptides.





2. The Primary Structure of Peptides



Asp-Phe-OCH_3
Aspartame

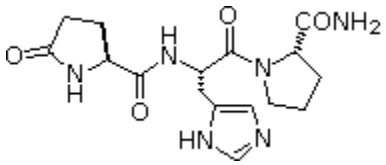
Because the N-terminus of a peptide chain is distinct from the C-terminus, a small peptide composed of different aminoacids may have a several constitutional isomers. For example, a dipeptide made from two different amino acids may have two different structures. Thus, aspartic acid (Asp) and phenylalanine (Phe) may be combined to make Asp-Phe or Phe-Asp, remember that the amino acid on the left is the N-terminus. The methyl ester of the first dipeptide (structure on the right) is the artificial sweetener **aspartame**, which is nearly 200 times sweeter than sucrose. Neither of the component amino acids is sweet (Phe is actually bitter), and derivatives of the other dipeptide (Phe-Asp) are not sweet.

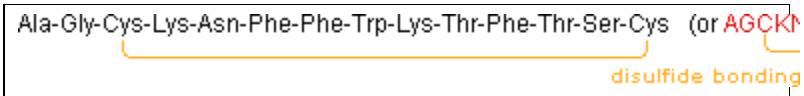
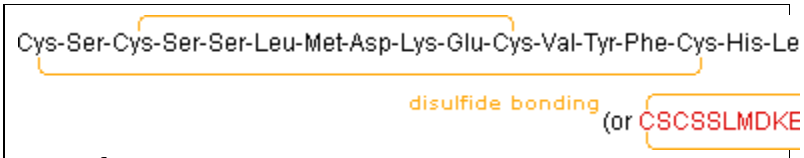
A tripeptide composed of three different amino acids can be made in 6 different constitutions, and the tetrapeptide shown above (composed of four different amino acids) would have 24 constitutional isomers. When all twenty of the natural amino acids are possible components of a peptide, the possible combinations are enormous. Simple statistical probability indicates that the decapeptides made up from all possible combinations of these amino acids would total 20^{10}!

Natural peptides of varying complexity are abundant. The simple and widely distributed tripeptide glutathione (first entry in the following table), is interesting because the side-chain carboxyl function of the N-terminal glutamic acid is used for the peptide bond. An N-terminal glutamic acid may also close to a lactam ring, as in the case of TRH (second entry). The abbreviation for this transformed unit is pGlu (or pE), where p stands for "pyro" (such ring closures often occur on heating). The larger peptides in the table also demonstrate the importance of amino acid abbreviations, since a full structural formula for a nonapeptide (or larger) would prove to be complex and unwieldy. The formulas using single letter abbreviations are colored red.

The ten peptides listed in this table make use of all twenty common amino acids. Note that the C-terminal unit has the form of an amide in some cases (e.g. TRH, angiotensin & oxytocin). When two or more cysteines are present in a peptide chain, they are often joined by disulfide

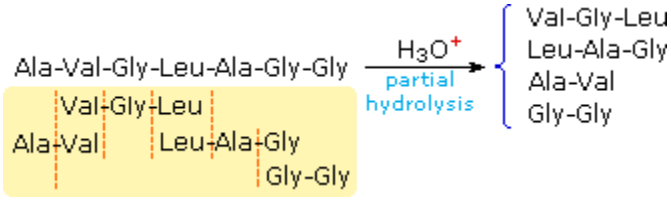
bonds (e.g. oxytocin & endothelin); and in the case of insulin, two separate peptide chains (A & B) are held together by such links.

Some Common Natural Peptides		
Name (residues)	**Source or Function**	**Amino Acid Sequence**
Glutathione (3)	Most Living Cells (stimulates tissue growth)	$^{(+)}H_3NCH(CO_2^{(-})CH_2CH_2CONHCH(CH_2SH)CONHCH_2CO_2H$ γ-Glu-Cys-Gly (or γECG)
TRH (3)	Hypothalmic Neurohormone (governs release of thyrotropin)	 pGlu-His-ProNH$_2$ (or pEHPNH$_2$)
Angiotensin II (8)	Pressor Agent (acts on the adrenal gland)	Asp-Arg-Val-Tyr-Ile-His-Pro-PheNH$_2$ (or DRVYIHPFNH$_2$)
Bradykinen (9)	Hypotensive Vasodilator (acts on smooth muscle)	Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg (or RPPGFSPFR)
Oxytocin (9)	Uterus-Contracting Hormone (also stimulates lactation)	 Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-GlyNH$_2$ (or CYIQNCPLGNH$_2$) disulfide bonding

Somatostatin (14)	Inhibits Growth Hormone Release (used to treat ulcers)	
Endothelin (21)	Potent Vasoconstrictor (structurally similar to some snake venoms)	 <=”” td=””>
Melittin (26)	Honey Bee Venom (used to treat rheumatism)	Gly-Ile-Gly-Ala-Val-Leu-Lys-Val-Leu-Thr-Thr-Gly-Leu-Pro~ ~Ala-Leu-Ile-Ser-Trp-Ile-Lys-Arg-Lys-Arg-Gln-GlnNH_2 (or GIGAVLKVLTTGLPALISWIKRKRQQNH_2)
Glucagon (29)	Hyperglycemic Factor (used as an anti-diabetic)	His-Ser-Gln-Gly-Thr-Phe-Thr-Ser-Asp-Tyr-Ser-Lys-Tyr-Leu-Asp~ ~Ser-Arg-Arg-Ala-Gln-Asp-Phe-Val-Gln-Trp-Leu-Met-Asn-Thr (or HSQGTFTSDYSKYLDSRRAQDFVQWLMNT)
Insulin (51)	Pancreatic Hormone (used in treatment of diabetes)	 <=”” td=””>

The different amino acids that make up a peptide or protein, and the order in which they are joined together by peptide bonds is referred to as the **primary structure**. From the examples shown above, it should be evident that it is not a trivial task to determine the primary structure of

such compounds, even modestly sized ones. Complete hydrolysis of a protein or peptide, followed by amino acid analysis establishes its gross composition, but does not provide any bonding sequence information.

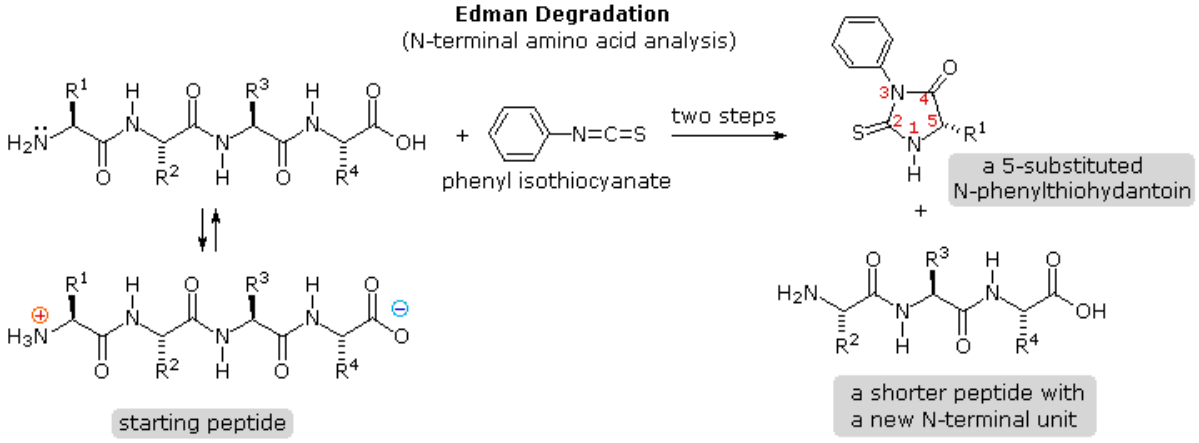


Partial hydrolysis will produce a mixture of shorter peptides and some amino acids. If the primary structures of these fragments are known, it is sometimes possible to deduce part or all of the original structure by taking advantage of overlapping pieces. For example, if a heptapeptide was composed of three glycines, two alanines, a leucine and a valine, many possible primary structures could be written. On the other hand, if partial hydrolysis gave two known tripeptide and two known dipeptide fragments, as shown on the right, simple analysis of the overlapping units identifies the original primary structure. Of course, this kind of structure determination is very inefficient and unreliable. First, we need to know the structures of all the overlapping fragments. Second, larger peptides would give complex mixtures which would have to be separated and painstakingly examined to find suitable pieces for overlapping. It should be noted, however, that modern mass spectrometry uses this overlap technique effectively. The difference is that bond cleavage is not achieved by hydrolysis, and computers assume the time consuming task of comparing a multitude of fragments.

3. N-Terminal Group Analysis

Over the years that chemists have been studying these important natural products, many techniques have been used to investigate their primary structure or amino acid sequence. Indeed, commercial instruments that automatically sequence peptides and proteins are now available. A few of the most important and commonly used techniques will be described here. Identification of the N-terminal and C-terminal aminoacid units of a peptide chain provides helpful information. N-terminal analysis is accomplished by the **Edman Degradation**, which is outlined in the following diagram. A free amine function, usually in equilibrium with zwitterion species, is necessary for the initial bonding to the phenyl isothiocyanate reagent. The products of

the Edman degradation are a thiohydantoin heterocycle incorporating the N-terminal amino acid together with a shortened peptide chain. Amine functions on a side-chain, as in lysine, may react with the isothiocyanate reagent, but do not give thiohydantoin products.



Repeated clicking of the "Next Diagram" button displays the mechanism of this important analytical method.

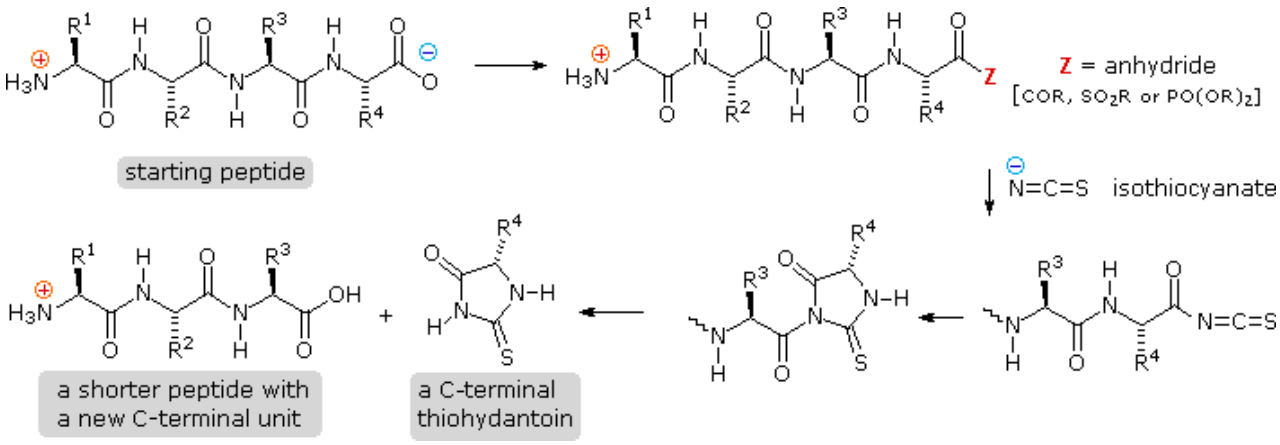
A major advantage of the Edman procedure is that the remaining peptide chain is not further degraded by the reaction. This means that the N-terminal analysis may be repeated several times, thus providing the sequence of the first three to five amino acids in the chain. A disadvantage of the procedure is that is peptides larger than 30 to 40 units do not give reliable results.

4. C-Terminal Group Analysis

ChemicalAnalysis

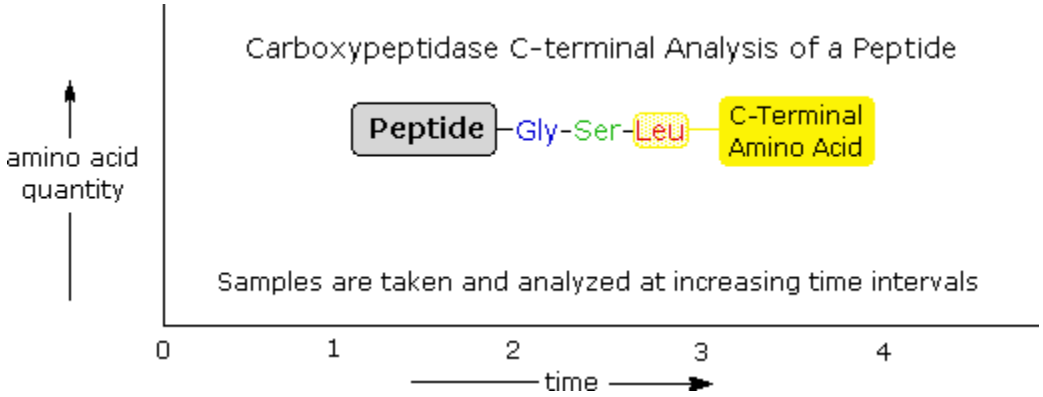
Complementary C-terminal analysis of peptide chains may be accomplished chemically or enzymatically. The chemical analysis is slightly more complex than the Edman procedure. First, side-chain carboxyl groups and hydroxyl groups must be protected as amides or esters. Next, the C-terminal carboxyl group is activated as an anhydride and reacted with thiocyanate. The resulting acyl thiocyanate immediately cyclizes to a hydantoin ring, and this can be cleaved from the peptide chain in several ways, not described here. Depending on the nature of this final

cleavage, the procedure can be modified to give a C-terminal acyl thiocyanate peptide product which automatically rearranges to a thiohydantoin incorporating the penultimate C-terminal unit. Thus, repetitive analyses may be conducted in much the same way they are with the Edman procedure.



Enzymatic Analysis:

Enzymatic C-terminal amino acid cleavage by one of several carboxypeptidase enzymes is a fast and convenient method of analysis. Because the shortened peptide product is also subject to enzymatic cleavage, care must be taken to control the conditions of reaction so that the products of successive cleavages are properly monitored. The following example illustrates this feature. A peptide having a C-terminal sequence: ~Gly-Ser-Leu is subjected to carboxypeptidase cleavage, and the free aminoacids cleaved in this reaction are analyzed at increasing time intervals. By clicking on the diagram, the results of this experiment will be displayed. The leucine is cleaved first, the serine second, and the glycine third, as demonstrated by the sequential analysis. Of course, fourth and fifth units will also be released as time passes, but these products are not shown.

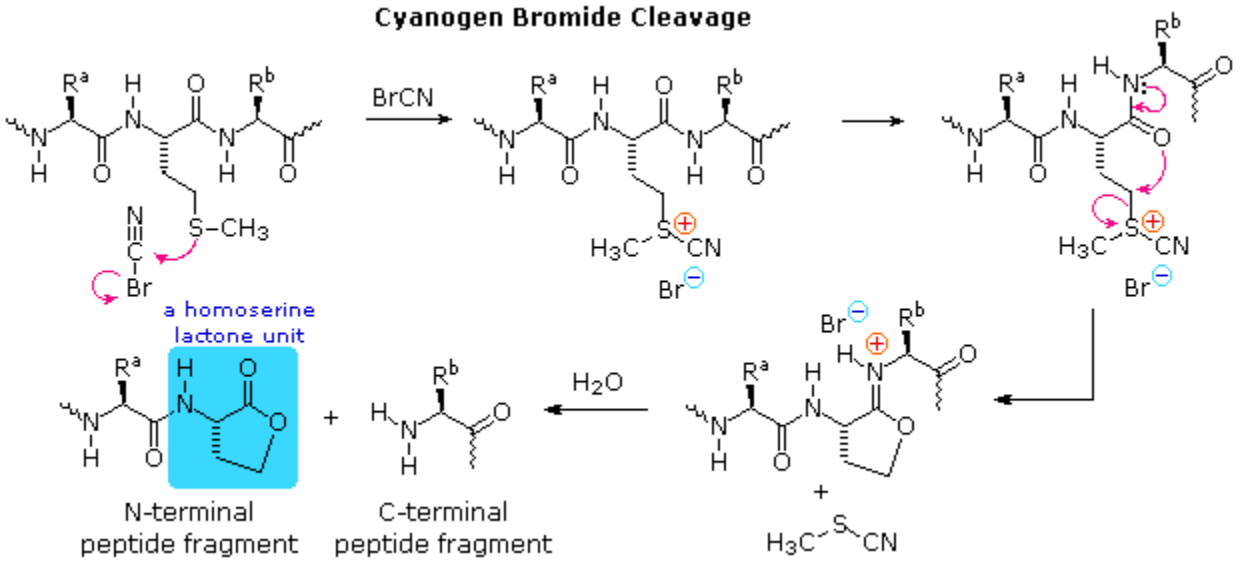


5. Selective Peptide Cleavage

Name	Type	Specificity
Cyanogen Bromide	Chemical	Carboxyl Side of Methionine
Trypsin	Enzymatic	Carboxyl Side of Basic Amino Acids e.g. Lys & Arg
Chymotrypsin	Enzymatic	Carboxyl Side of Aryl Amino Acids e.g. Phe, Tyr & Trp

Since end group analysis of large peptides and proteins is of limited value, methods of selectively cleaving such macromolecules into smaller peptide fragments are commonly employed as a major step in structure elucidation. Three selective cleavage methods are outlined in the table on the left. These procedures all cleave peptide chains at designated locations, and at the carboxyl side of the targeted amino acid. A plausible mechanism for the cyanogen bromide cleavage is outlined below. The C-terminal side of the methionine is obtained as a smaller peptide, which can be examined by any of the preceding techniques. The N-terminal side is characterized by a homoserine lactone at its C-terminus.

Mechanisms for the enzymatic reactions are not as easily formulated. Other enzymatic cleavages have been developed, but the two listed here will serve to illustrate their application.



An Example of Primary Structure Analysis

To see how these procedures can be combined to elucidate the primary structure of a peptide, consider the melanocyte stimulating hormone isolated from pigs. This octadecapeptide (18 amino acid units) has the composition: $Arg,Asp_2,Glu_2,Gly_2,His,Lys_2,Met,Phe,Pro_3,Ser,Tyr_2$, and is abbreviated $\mathbf{P^{18}}$. The following diagram, which begins with the results of terminal unit analysis, illustrates the logical steps that could be used to solve the structural problem. By clicking the "Next Stage" button the results and conclusions from each step will be displayed. Comments about each stage are presented under the diagram.

Pig β-Melanocyte Stimulating Hormone (P^{18})

Amino Acid Analysis: $P^{18} = Arg,Asp_2,Glu_2,Gly_2,His,Lys_2,Met,Phe,Pro_3,Ser,Tyr_2$

N-Terminal Analysis: Asp–Glu–Gly~~~~

C-Terminal Analysis: ~~~~Pro–Lys–Asp

a) Cyanogen bromide cleavage gives two peptide fragments, the longer of which has all the units on the C-terminal side of methionine.

b) N-terminal analysis of the undecapeptide fragment, $\mathbf{P^{11}}$, locates the three amino acids to the right of methionine.

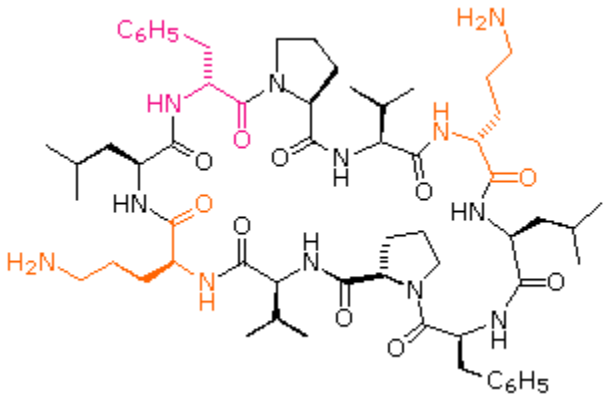
c) Trypsin cleavage of $\mathbf{P^{11}}$ shows the location of the single arginine, which is found as the C-terminal unit of the tetrapeptide fragment. One of the two lysines was known to be next to the C-terminus. The other must be part of the smaller peptide from the cyanogen bromide reaction.

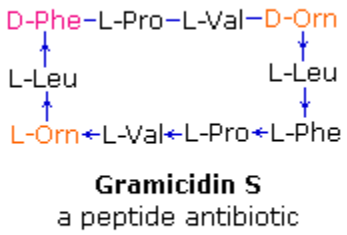
d) With only four amino acids remaining to be located, the position of the second tyrosine may be pursued by chymotrypsin cleavage of $\mathbf{P^{18}}$ itself. Four fragments are obtained, and the final structure might have been solved by these alone. However, selective terminal group analysis of the two pentapeptides serves to locate the tyrosine and a second proline next to the left most glycine, as well as identifying the units on each side of the methionine. The one remaining amino acid, a proline, is then placed at the last vacant site (yellow box).

6. Cyclic Peptides

If the carboxyl function at the C-terminus of a peptide forms a peptide bond with the N-terminal amine group a cyclic peptide is formed. Carboxyate and amine functions on side chains may also combine to form rings. Cyclic peptides are most commonly found in microorganisms, and often incorporate some D-amino acids as well as unusual amino acids such as ornithine (Orn). The decapeptide antibiotic gramacidin S, produced by a strain of *Bacillus brevis*, is one example of this interesting class of natural products. The structure of gramicidin S is shown in the following diagram. The atypical amino acids are colored. When using a shorthand notation for cyclic structures, the top line is written by the usual convention (N-group on the left), but vertical and lower lines must be adjusted to fit the bonding. Arrows on these bonds point in the CO-N direction of each peptide bond.

Fibrous Proteins	As the name implies, these substances have fiber-like structures, and serve as the chief structural material in various tissues. Corresponding to this structural function, they are relatively insoluble in water and unaffected by moderate changes in temperature and pH. Subgroups within this category include: Collagens & Elastins, the proteins of connective tissues. tendons and ligaments. Keratins, proteins that are major components of skin, hair, feathers and horn. Fibrin, a protein formed when blood clots.





Gramicidin S
a peptide antibiotic

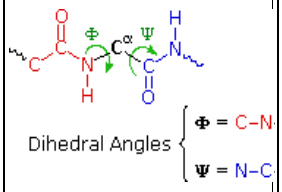
To see a model of another cyclic peptide, having potentially useful medicinal properties Click Here.

Structure-Property Relationships The compounds we call proteins exhibit a broad range of physical and biological properties. Two general categories of simple proteins are commonly recognized.

Globular Proteins	Members of this class serve regulatory, maintenance and catalytic roles in living organisms. They include hormones, antibodies and enzymes. and either dissolve or form colloidal suspensions in water. Such proteins are generally more sensitive to temperature and pH change than their fibrous counterparts. More Information

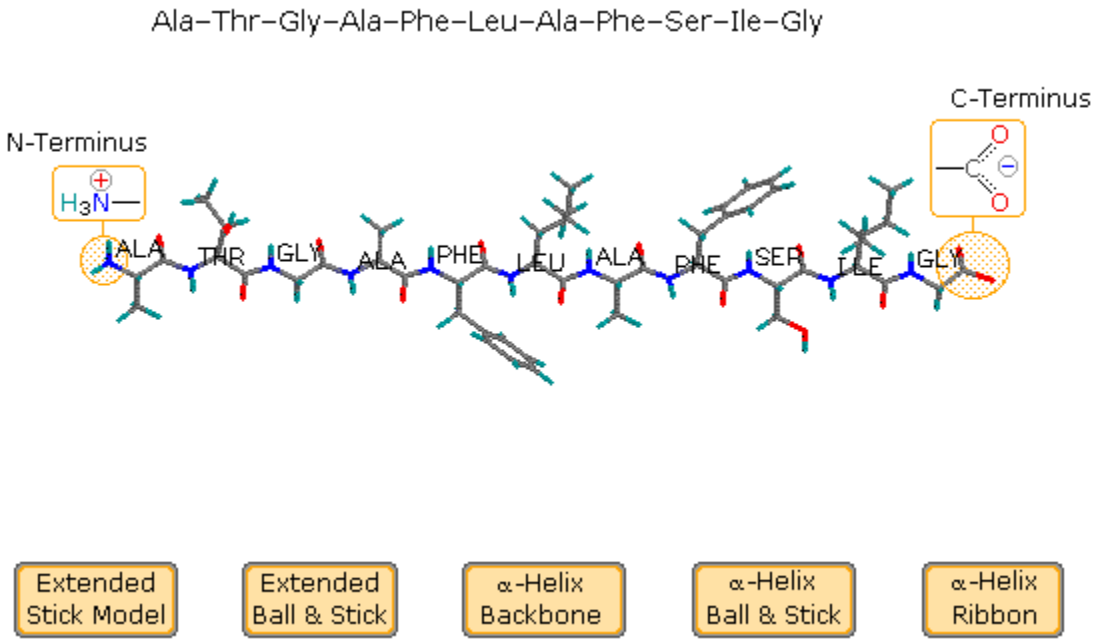
1. The Secondary and Tertiary Structure of Large Peptides and Proteins

The various properties of peptides and proteins depend not only on their component amino acids and their bonding sequence in peptide chains, but also on the way in which the peptide chains are stretched, coiled and folded in space. Because of their size, the orientational options open to these macromolecules might seem nearly infinite. Fortunately, several factors act to narrow the structural options, and it is possible to identify some common structural themes or **secondary structures** that appear repeatedly in different molecules. These conformational segments are sometimes described by the dihedral angles Φ & Ψ, defined in the diagram on the right below. Most proteins and large peptides do not adopt completely uniform conformations, and full descriptions of their preferred three dimensional arrangements are defined as **tertiary structures**.

Five factors that influence the conformational equilibria of peptide chains are: • The planarity of peptide bonds. Conformations are defined by dihedral angles Φ & Ψ. • Hydrogen bonding of amide carbonyl groups to N-H donors. • Steric crowding of neighboring groups. • Repulsion and attraction of charged groups. • The hydrophilic and hydrophobic character of substituent groups.	

A. Helical Coiling

The relatively simple undecapeptide shown in the following diagram can adopt a zig-zag linear conformation, as drawn. A ball & stick model of this peptide will be displayed by clicking the appropriate button. However, this molecule prefers to assume a coiled helical conformation, displayed by clicking any of the three buttons on the right. The middle button shows a stick model of this helix, with the backbone chain drawn as a heavy black line and the hydrogen bonds as dashed maroon lines. The other buttons display a ball & stick model and a ribbon that defines this **α-helix**. Seven hydrogen bonds, that together provide roughly 30 kcal/mol stability, help to maintain this conformation.

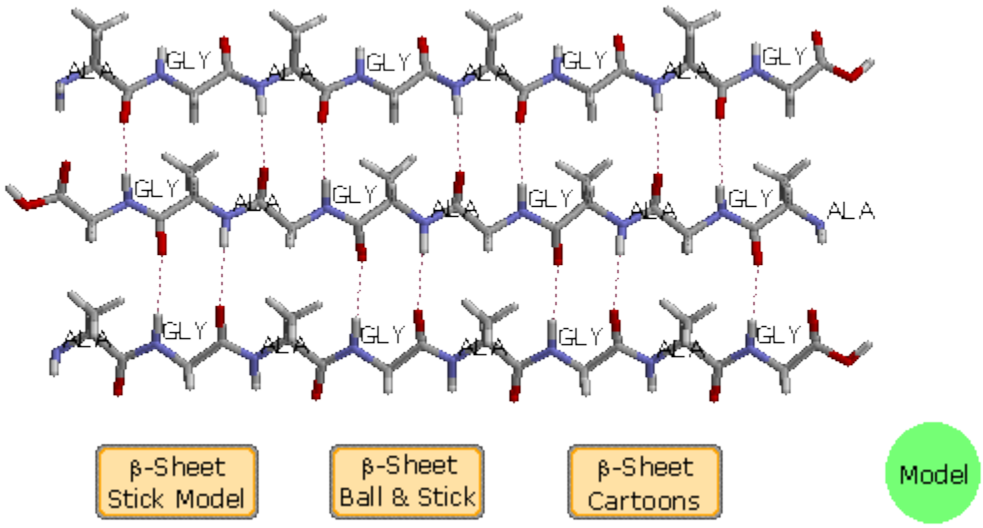


Examine the drawing activated by the middle button. The N-terminal residue (Ala) is on the left, and the C-terminal Gly on the right. The alpha-helix is right-handed, which means that it rotates clockwise as it spirals away from a viewer at either end. Other structural features that define an alpha-helix are: the relative locations of the donor and acceptor atoms of the hydrogen bond, the number of amino acid units per helical turn and the distance the turn occupies along the helical axis. The first hydrogen bond (from the N-terminal end) is from the carbonyl group of the alanine to the N-H group of the phenylalanine. Three amino acids, Thr, Gly & Ala, fall entirely

within this turn. Parts of the N-terminal alanine acceptor and the phenylalanine donor also fall within this helical turn, and careful analysis of the structure indicates there are 3.6 amino acid units per turn. The distance covered by the turn is 5.4 Å. Using the dihedral angle terminology noted above, a perfect α-helix has Φ = -58º and Ψ = -47º. In natural proteins the values associated with α-helical conformations range from -57 to -70º for Φ, and from -35 to -48º for Ψ. To examine a model of this alpha-helix, click on the green circle. Once this display is activated, the important hormone **insulin** may be shown by clicking the appropriate button in the blue-shaded rows.Helical conformations of peptide chains may also be described by a two number term, $\mathbf{n_m}$, where **n** is the number of amino acid units per turn and **m** is the number of atoms in the smallest ring defined by the hydrogen bond. Using this terminology, the alpha-helix is a 3.6_{13} helix. Other common helical conformations are 3_{10} and 4.4_{16}. The alpha helix is the most stable of these, accounting for a third of the secondary structure found in most globular (non-fibrous) proteins.

B. β-Pleated Sheets

The linear zig-zag conformation of a peptide chain may be stabilized by hydrogen bonding to adjacent parallel chains of the same kind. Bulky side-chain substituents destabilize this arrangement due to steric crowding, so this **beta-sheet** conformation is usually limited to peptides having a large amount of glycine and alanine. Steric interactions also cause a slight bending or contraction of the peptide chains, and this results in a puckered distortion (the pleated sheet). As shown in the following diagram, the adjacent chains may be oriented in opposite N to C directions, termed **antiparallel**. Using the dihedral angle terminology, an antiparallel β-sheet has Φ = -139º and a Ψ = 135º. Alternatively, the adjacent peptide chains may be oriented in the same direction, termed **parallel**. By convention, beta-sheets are designated by broad arrows or cartoons, pointing in the direction of the C-terminus. In this diagram, these cartoons (colored violet) are displayed by clicking on the appropriate button. A model of a two-antiparallel-chain structure may be examined by clicking on the green circle.



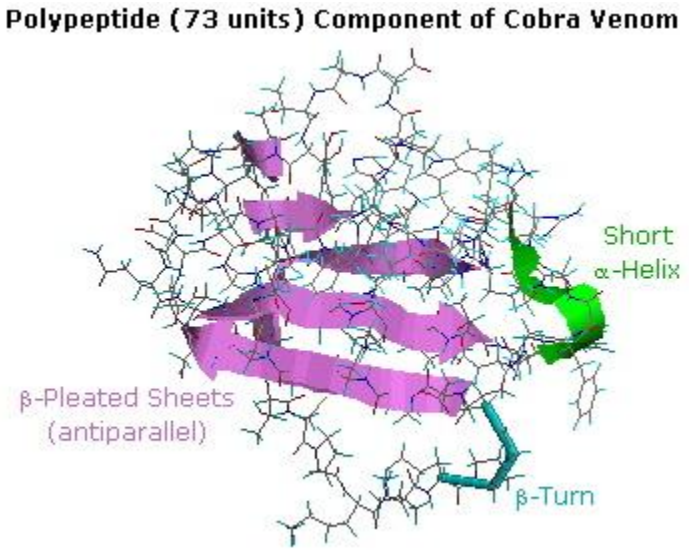
Some proteins have layered stacks of β-sheets, which impart structural integrity and may open to form a cavity (a beta barrel). An example is human retinol binding protein, which has a cavity formed by eight β-sheet strands. A model of this interesting protein may be displayed by clicking the upper button in the blue-shaded rows.When beta-sheets are observed as secondary structural components of globular proteins, they are twisted by about 5 to 25º per residue; consequently, the planes of the sheets are not parallel. The twist is always of the same handedness, and is usually greater for antiparallel sheets. Examples will be found in the following structures.

C. Other Structures

Although most proteins and large peptides may have alpha-helix and beta-sheet segments, their tertiary structures may consist of less highly organized turns, strands and coils. **Turns** reverse the direction of the peptide chain, and are considered to be a third common secondary structure motif. Approximately a third of all the residues in globular proteins are found in turns. Turns occur chiefly on the protein surface, often incorporate polar and charged residues, and have been classified in three sub-groups. As noted earlier, several factors perturb the organization of peptide chains. One that has not yet been cited is the structural influence of proline. Unlike the other common amino acids, rotation about the α C-N bond in proline is not possible due to the structural constraint of the five-membered ring. Consequently, the presence of a proline in a peptide chain introduces a bend or kink that disrupts helices or sheets. Also, prolines that are part

of a peptide chain have no N-H hydrogen bonding donors to contribute to conformer stabilization.

With the exception of silk fibroin and certain synthetically engineered peptides, significant portions of most proteins adopt conformations that resist simple description or categorization. For example, the following diagram shows the tertiary structure of a polypeptide neurotoxin found in cobra venom. A large section of antiparallel beta-sheets is colored violet, and a short alpha-helix is green. The remaining peptide chain seems disorganized, but certain features such as a 180º turn (called a beta-turn) and five disulfide bonds can be identified. A Chime model of this compound may be examined by clicking on the diagram.



Additional Examples

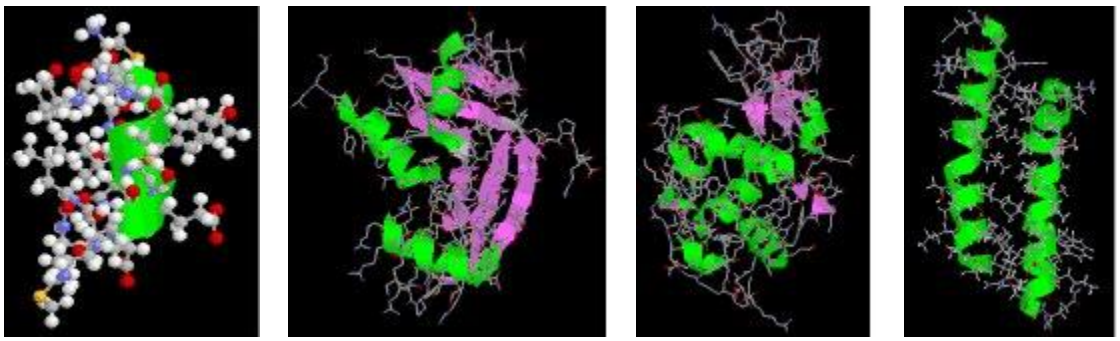
A full description and discussion of protein structure is beyond the scope of this text, but a few additional examples will be instructive. In addition to the tertiary structures that will be displayed, attention must also be given to the way in which peptide structures may aggregate to form dimeric, trimeric and tetrameric clusters. These assemblies, known as **quaternary structures**, have characteristic properties different from their monomeric components. The examples of mellitin, collagen and hemoglobin, shown below demonstrate this feature. Some proteins incorporate nonpeptide molecules in their overall structure, either bonded covalently or positioned by other forces. These are called **conjugated proteins**, and the non-

peptide components are referred to as **prosthetic groups**. Examples of conjugated proteins include:

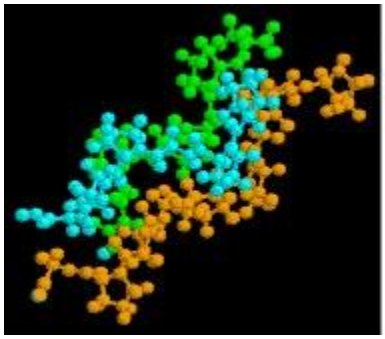
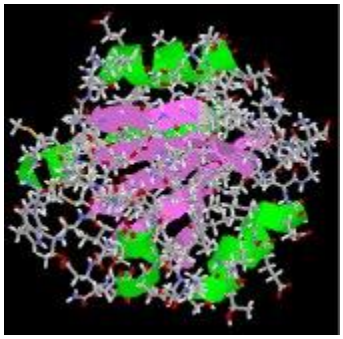
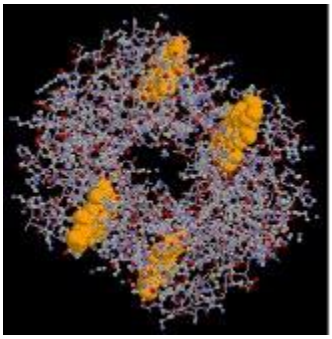
Glycoproteins, incorporating polysaccharide prosthetic groups (e.g. collagen and mucus).
Lipoproteins, incorporating lipid prosthetic groups (e.g. HDL and LDL).
Chromoproteins, incorporating colored prosthetic groups (e.g. hemoglobin).

The seven illustrations shown below identify a set of peptides and proteins that may be examined as Jmol models by clicking on a selected picture.

Endothelin & Angiogenin are small peptides that have important and selective physiological properties.
Lysozyme a typical globular protein, incorporating many identifiable secondary structures.
Mellitin, from honey bee venom, has a well-defined quaternary structure, half of which is shown here.
Collagen is a widely distributed fibrous protein with a large and complex quaternary structure. Only a small model segment is shown here.
Thioredoxin is a relatively small regulatory protein serving an important redox function.
Hemoglobin, the most complex of these examples, is a large conjugated protein that transports oxygen. A 170 pound human has about a kilogram of hemoglobin distributed among some five billion red blood cells. A liter of arterial blood at body temperature can transport over 200 mL of oxygen, whereas the same fluid stripped of its hemoglobin will carry only 2 to 3 mL. The supramolecular assembly of four subunits exemplifies a **quaternary structure**.



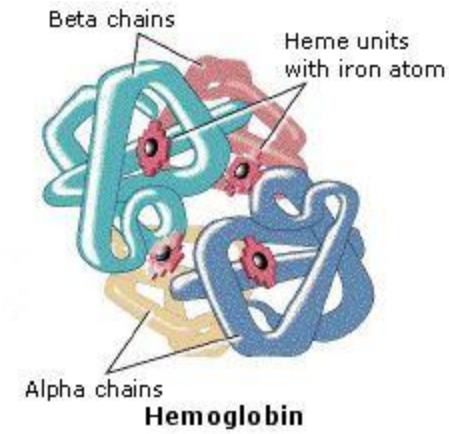
endothelin **angiogenin** **lysozyme** **mellitin**

collagen **thioredoxin** **hemoglobin**

2. Quaternary Structures of Proteins

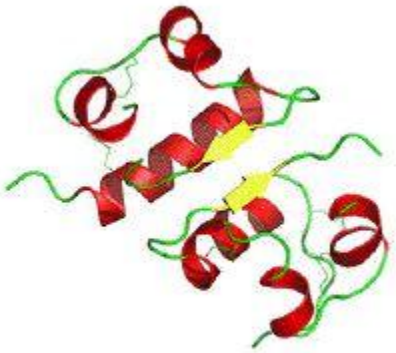
Many proteins are actually assemblies of several polypeptides, which in the context of the larger aggregate are known as protein subunits. Such multiple-subunit proteins possess a **quaternary structure**, in addition to the tertiary structure of the subunits. The subunits of a quaternary structure are held together by the same forces that are responsible for tertiary structure stabilization. These include hydrophobic attraction of nonpolar side chains in contact regions of the subunits, electrostatic interactions between ionic groups of opposite charge: hydrogen bonds between polar groups; and disulfide bonds. Examples of proteins having a quaternary (or quartary) structure include hemoglobin, HIV-1 protease and the insulin hexamer.

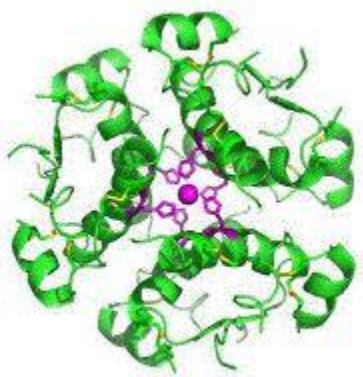


Hemoglobin

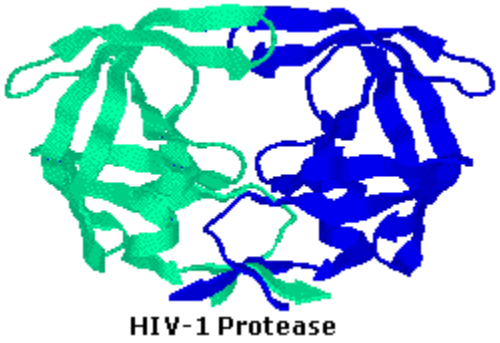
The hemoglobin molecule is an assembly of four protein subunits, two alpha units and two beta units. Each protein chain folds into a set of alpha-helix structural segments connected together in a globin arrangement, so called because this arrangement is the same folding motif used in other heme/globin proteins such as myoglobin. This folding pattern contains a pocket which strongly binds the heme group. The four polypeptide chains are bound to each other by salt bridges, forming a tetrameric quaternary structure. A model of hemoglobin was shown above, and may also be examined by clicking the image on the left.

In animals, hemoglobin transports oxygen from the lungs or gills to the rest of the body, where it releases the oxygen for cell use. Hemoglobin's oxygen-binding capacity is decreased in the presence of carbon monoxide because both gases compete for the same binding sites on hemoglobin. The binding affinity of hemoglobin for CO is 200 times greater than its affinity for oxygen. When hemoglobin combines with CO, it forms a very bright red compound called carboxyhemoglobin, which may cause the skin of CO poisoning victims to appear pink in death. In heavy smokers, up to 20% of the oxygen-active sites can be blocked by CO. Similarly, hemoglobin has a competitive binding affinity for cyanide, sulfur monoxide, nitrogen dioxide and sulfides including hydrogen sulfide . All of these bind to the heme iron without changing its oxidation state, causing grave toxicity.


Insulin Dimer


Insulin Hexamer

Insulin is a peptide hormone composed of 51 amino acids, with a molecular weight of 5808 Da. Insulin has a strong effect on metabolism and other body functions, causing cells in the liver, muscle, and fat tissue to take up glucose from the blood, storing it as glycogen in the liver and muscle. Insulin is formed in the islets of Langerhans in the pancreas. The molecular structure of insulin varies slightly between species of animals. Porcine (pig) insulin is especially close to the human version. Insulin molecules have a tendency to form dimers in solution due to hydrogen-bonding between the C-termini of B chains. In the presence of zinc ions, insulin dimers associate into hexamers. Insulin is stored in the body as a hexamer, whereas the active form is the monomer. These interactions have important clinical ramifications. Monomers and dimers readily diffuse into blood; hexamers diffuse poorly. By clicking the image on the far left, a model of the insulin monomer will be displayed . A model of the hexamer will be shown by clicking its image.



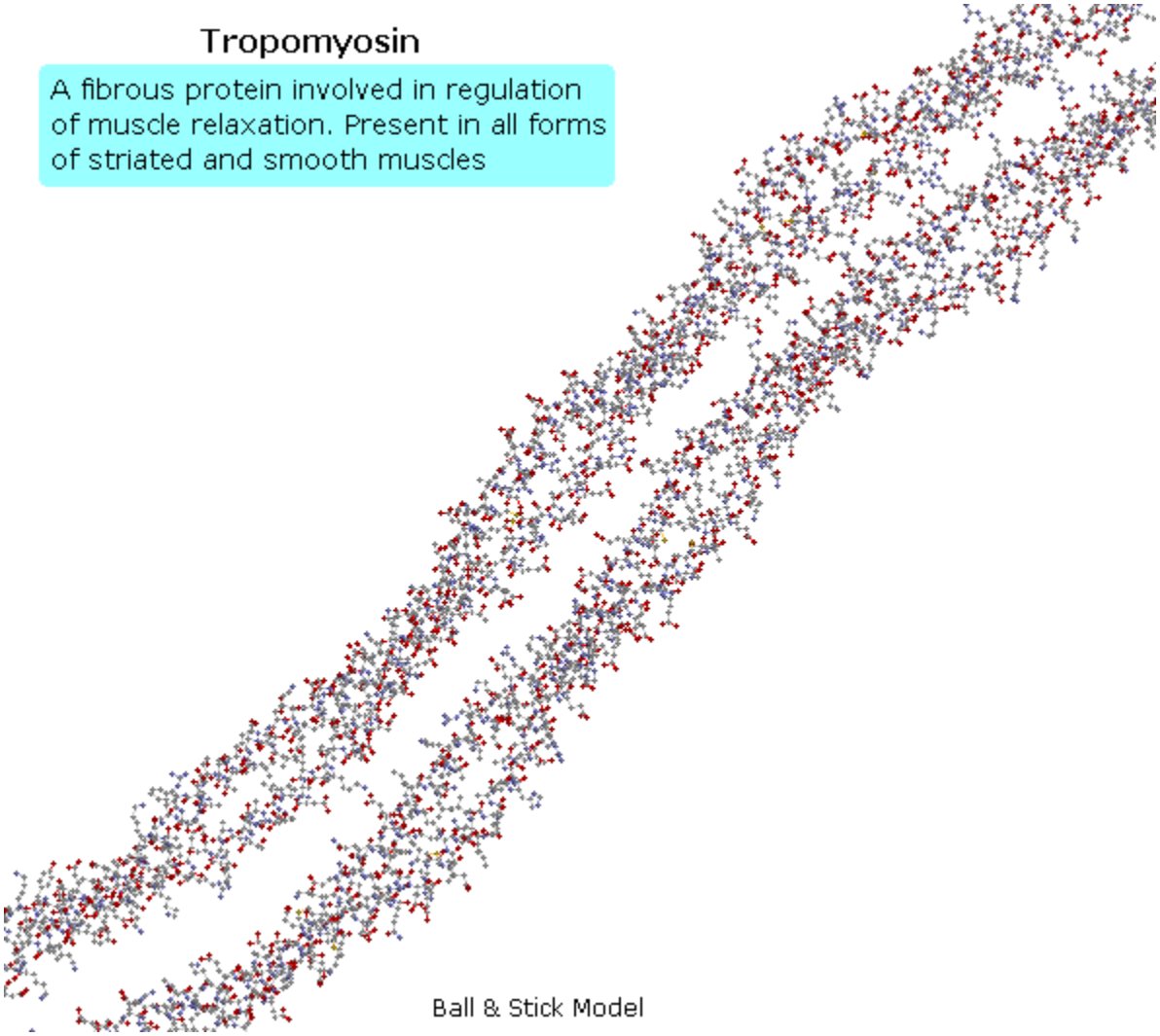
HIV-1 protease is an enzyme made by the HIV virus that is essential for it's life-cycle. The virus makes certain proteins that need to be cleaved or cut, in order to transform into functional proteins that enable the virus to infect new cells. HIV-1 protease cleaves the nascent proteins into their functional form. The enzyme is composed of two symmetrically related subunits, shown here in cartoon backbone representation to highlight the secondary structure. Each subunit consists of the same small chain of 99 amino acids, which come together in such as way as to form a tunnel where they meet. The protein to be cleaved sits in this tunnel, which houses the active site of the enzyme. Two Asp-Thr-Gly catalytic triads, one on each chain, compose the active site. The two Asp's act as the main catalytic agents, and together with a water molecule cleave the protein chain bound in the tunnel. Without effective HIV-1 protease, HIV virions remain uninfectious.

Because of its role in HIV replication, HIV-1 protease has been a target for antiviral drugs. Such drugs function as inhibitors, binding to the active site by mimicking the tetrahedral intermediate of its substrate, thus disabling the enzyme. The structure of one such inhibitor, BEA388, will be displayed on the left by clicking here.

Tropomyosin

The following animation shows a segment of the fibrous protein tropomyosin, a common muscle regulator. The peptide chains are largely alpha-helices. These are wrapped in superhelix pairs, which are then aligned in a parallel array.

If animation is not occurring, click on the drawing or reload.



Two excellent resources of additional information are:

First Glance Motivated Proteins

Also, The Protein Data Bank provides a large collection of protein structures obtained by Xray and NMR.

Peptide Synthesis

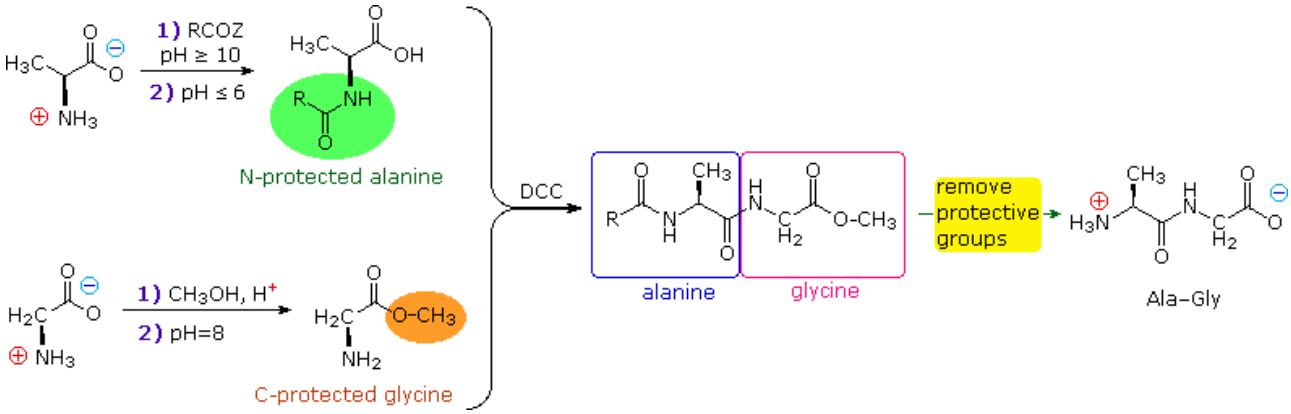
In order to synthesize a peptide from its component amino acids, two obstacles must be overcome. The first of these is statistical in nature, and is illustrated by considering the dipeptide Ala-Gly as a proposed target. If we ignore the chemistry involved, a mixture of equal molar amounts of alanine and glycine would generate four different dipeptides. These are: **Ala-Ala, Gly-Gly, Ala-Gly & Gly-Ala**. In the case of tripeptides, the number of possible products from these two amino acids rises to eight. Clearly, some kind of selectivity must be exercised if complex mixtures are to be avoided.The second difficulty arises from the fact that carboxylic acids and 1º or 2º-amines do not form amide bonds on mixing, but will generally react by proton transfer to give salts (the intermolecular equivalent ofzwitterion formation).

From the perspective of an organic chemist, peptide synthesis requires selective acylation of a free amine. To accomplish the desired amide bond formation, we must first deactivate all extraneous amine functions so they do not compete for the acylation reagent. Then we must selectively activate the designated carboxyl function so that it will acylate the one remaining free amine. Fortunately, chemical reactions that permit us to accomplish these selections are well known.

First, the basicity and nucleophilicity of amines are substantially reduced by amide formation. Consequently, the acylation of amino acids by treatment with acyl chlorides or anhydrides at pH > 10, as described earlier, serves to protect their amino groups from further reaction. Second, acyl halide or anhydride-like activation of a specific carboxyl reactant must occur as a prelude to peptide (amide) bond formation. This is possible, provided competing reactions involving other carboxyl functions that might be present are precluded by preliminary ester formation. Remember, esters are weaker acylating reagents than either anhydrides or acyl halides, as noted earlier.

Finally, dicyclohexylcarbodiimide (DCC) effects the dehydration of a carboxylic acid and amine mixture to the corresponding amide under relatively mild conditions. The structure of this reagent and the mechanism of its action have been described. Its application to peptide synthesis will become apparent in the following discussion.

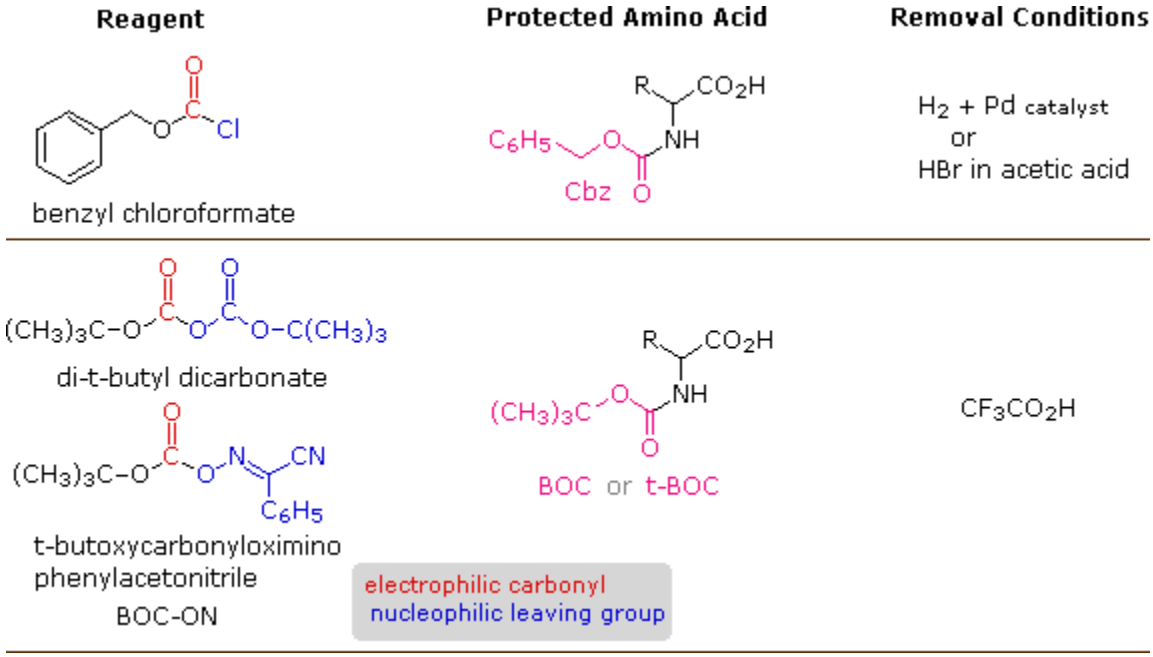
The strategy for peptide synthesis, as outlined here, should now be apparent. The following example shows a selective synthesis of the dipeptide Ala-Gly.



An important issue remains to be addressed. Since the N-protective group is an amide, removal of this function might require conditions that would also cleave the just formed peptide bond. Furthermore, the harsh conditions often required for amide hydrolysis might cause extensive racemization of the amino acids in the resulting peptide. This problem strikes at the heart of our strategy, so it is important to give careful thought to the design of specific N-protective groups. In particular, three qualities are desired:

1) The protective amide should be easy to attach to amino acids.
2) The protected amino group should not react under peptide forming conditions.
3) The protective amide group should be easy to remove under mild conditions.

A number of protective groups that satisfy these conditions have been devised; and two of the most widely used, **carbobenzoxy** (Cbz) and **t-butoxycarbonyl** (BOC or t-BOC), are described here.

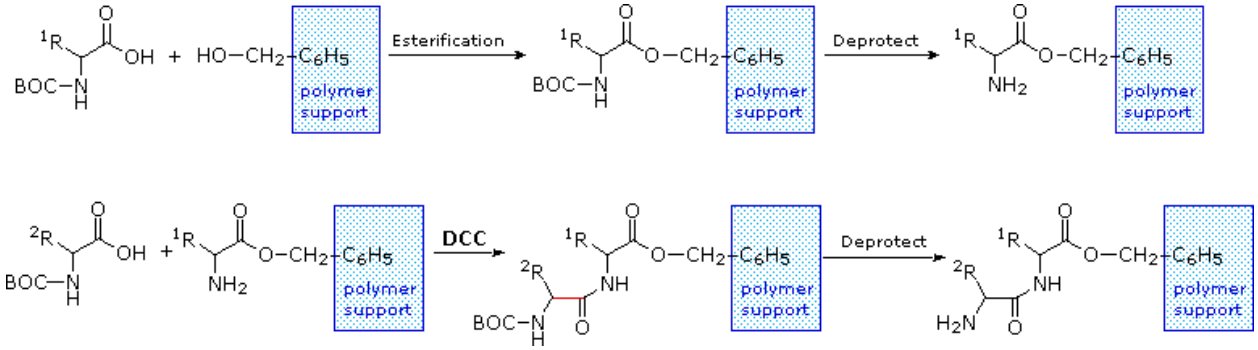


The reagents for introducing these N-protective groups are the acyl chlorides or anhydrides shown in the left portion of the above diagram. Reaction with a free amine function of an amino acid occurs rapidly to give the "protected" amino acid derivative shown in the center. This can then be used to form a peptide (amide) bond to a second amino acid. Once the desired peptide bond is created the protective group can be removed under relatively mild non-hydrolytic conditions. Equations showing the protective group removal will be displayed above by clicking on the diagram. Cleavage of the reactive benzyl or tert-butyl groups generates a common carbamic acid intermediate (HOCO-NHR) which spontaneously loses carbon dioxide, giving the corresponding amine. If the methyl ester at the C-terminus is left in place, this sequence of reactions may be repeated, using a different N-protected amino acid as the acylating reagent. Removal of the protective groups would then yield a specific tripeptide, determined by the nature of the reactants and order of the reactions.

The synthesis of a peptide of significant length (e.g. ten residues) by this approach requires many steps, and the product must be carefully purified after each step to prevent unwanted cross-reactions. To facilitate the tedious and time consuming purifications, and reduce the material losses that occur in handling, a clever modification of this strategy has been developed. This procedure, known as the **Merrifield Synthesis** after its inventor R. Bruce Merrifield, involves

attaching the C-terminus of the peptide chain to a polymeric solid, usually having the form of very small beads. Separation and purification is simply accomplished by filtering and washing the beads with appropriate solvents. The reagents for the next peptide bond addition are then added, and the purification steps repeated. The entire process can be automated, and peptide synthesis machines based on the Merrifield approach are commercially available. A series of equations illustrating the Merrifield synthesis may be viewed by clicking on the following diagram. The final step, in which the completed peptide is released from the polymer support, is a simple benzyl ester cleavage. This is not shown in the display.

The Merrifield Peptide Synthesis



Two or more moderately sized peptides can be joined together by selective peptide bond formation, provided side-chain functions are protected and do not interfere. In this manner good sized peptides and small proteins may be synthesized in the laboratory. However, even if chemists assemble the primary structure of a natural protein in this or any other fashion, it may not immediately adopt its native secondary, tertiary and quaternary structure. Many factors, such as pH, temperature and inorganic ion concentration influence the conformational coiling of peptide chains. Indeed, scientists are still trying to understand how and why these higher structures are established in living organisms.

Denaturation

The natural or native structures of proteins may be altered, and their biological activity changed or destroyed by treatment that does not disrupt the primary structure. This **denaturation** is often done deliberately in the course of separating and purifying proteins. For example, many soluble globular proteins precipitate if the pH of the solution is set at the pI of the protein. Also, addition of trichloroacetic acid or the bis-amide urea (NH_2CONH_2) is commonly used to effect protein precipitation. Following denaturation, some proteins will return to their native structures under proper conditions; but extreme conditions, such as strong heating, usually cause irreversible change.

Some treatments known to denature proteins are listed in the following table.

Denaturing Action	Mechanism of Operation
Heat	hydrogen bonds are broken by increased translational and vibrational energy. (coagulation of egg white albumin on frying.)
Ultraviolet Radiation	Similar to heat (sunburn)
Strong Acids or Bases	salt formation; disruption of hydrogen bonds. (skin blisters and burns, protein precipitation.)
Urea Solution	competition for hydrogen bonds. (precipitation of soluble proteins.)
Some Organic Solvents (e.g. ethanol & acetone)	change in dielectric constant and hydration of ionic groups. (disinfectant action and precipitation of protein.)

Agitation	shearing of hydrogen bonds. (beating egg white albumin into a meringue.)

Not all proteins are easily denatured. As noted above, fibrous proteins such as keratins, collagens and elastins are robust, relatively insoluble, quaternary structured proteins that play important roles in the physical structure of organisms. Secondary structures such as the α-helix and β-sheet take on a dominant role in the architecture and aggregation of keratins. In addition to the intra- and intermolecular hydrogen bonds of these structures, keratins have large amounts of the sulfur-containing amino acid Cys, resulting in disulfide bridges that confer additional strength and rigidity. The more flexible and elastic keratins of hair have fewer interchain disulfide bridges than the keratins in mammalian fingernails, hooves and claws. Keratins have a high proportion of the smallest amino acid, Gly, as well as the next smallest, Ala. In the case of β-sheets, Gly allows sterically-unhindered hydrogen bonding between the amino and carboxyl groups of peptide bonds on adjacent protein chains, facilitating their close alignment and strong binding. Fibrous keratin chains then twist around each other to form helical filaments.

Elastin, the connective tissue protein, also has a high percentage of both glycine and alanine. An insoluble rubber-like protein, elastin confers elasticity on tissues and organs. Elastin is a macromolecular polymer formed from tropoelastin, its soluble precursor. The secondary structure is roughly 30% β-sheets, 20% α-helices and 50% unordered. The elastic properties of natural elastin are attributed to polypentapeptide sequences (Val-Pro-Gly-Val-Gly) in a cross-linked network of randomly coiled chains. Water is believed to act as a "plasticizer", assisting elasticity.

Collagen is a major component of the extracellular matrix that supports most tissues and gives cells structure. It has great tensile strength, and is the main component of fascia, cartilage, ligaments, tendons, bone and skin. Collagen contains more Gly (33%) and proline derivatives (20 to 24%) than do other proteins, but very little Cys. The primary structure of collagen has a frequent repetitive pattern, Gly-Pro-X (where X is a hydroxyl bearing Pro or Lys). This kind of regular repetition and high glycine content is found in only a few other fibrous proteins, such as

silk fibroin (75-80% Gly and Ala + 10% Ser). Collagen chains are approximately 1000 units long, and assume an extended left-handed helical conformation due to the influence of proline rings. Three such chains are wound about each other with a right-handed twist forming a rope-like superhelical quaternary structure, stabilized by interchain hydrogen bonding.

Globular proteins are more soluble in aqueous solutions, and are generally more sensitive to temperature and pH change than are their fibrous counterparts; furthermore, they do not have the high glycine content or the repetitious sequences of the fibrous proteins. Globular proteins incorporate a variety of amino acids, many with large side chains and reactive functional groups. The interactions of these substituents, both polar and nonpolar, often causes the protein to fold into spherical conformations which gives this class its name. In contrast to the structural function played by the fibrous proteins, the globular proteins are chemically reactive, serving as enzymes (catalysts), transport agents and regulatory messengers.


Ribonuclease A

Although globular proteins are generally sensitive to denaturation (structural unfolding), some can be remarkably stable. One example is the small enzyme ribonuclease A, which serves to digest RNA in our food by cleaving the ribose phosphate bond. Ribonuclease A is remarkably stable. One procedure for purifying it involves treatment with a hot sulfuric acid solution, which denatures and partially decomposes most proteins other than ribonuclease A. This stability reflects the fact that this enzyme functions in the inhospitable environment of the digestive tract. Ribonuclease A was the first enzyme synthesized by R. Bruce Merrifield, demonstrating that biological molecules are simply chemical entities that may be constructed artificially. By clicking the cartoon image on the left, an interactive model of ribonuclease A will be displayed.

Possible Questions

PART A (1 Marks Questions)

1. meso-tartaric acid is
a. sometimes optically active b. always optically active c. sometimes optically inactive
d. **always optically inactive**

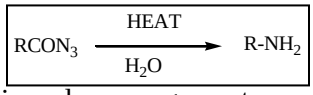
2. Which of the following represents a recemic mixture?
a.75% (R) -2 – butanol, 25 %(S) -2-butanol b. 25% (R) -2 – butanol,75 %(S) -2-butanol
c. **50% (R) -2 – butanol, 50 %(S) -2-butanol** d. 70% (R) -2 – butanol,30 %(S) -2-butanol

3. Consider R and S -2-butanol. Which physical property distinguishes the two compounds?
a. melting point b. Solubility in common solvents c. **Rotation of plane polarized light** d. Infrared spectrum

4. The stereoisomer's related each other as non super imposable mirror images are called ----------
a. Enantiomers b. Racemic mixtures c. **Diastereomers** d. Resolution

5. In the SN_2 reaction mechanism which one of the following is the most reactive?
a. C_6H_6 b. **CH_3X** c.C_2H_5X d.R_2CHX

6. The conversion is an example of



a.Pinacol rearrangement b. Claisen rearrangement c.Curtius rearrangement
d.**Hofmann rearrangement**

7. Which of the following is not an electrophile?
a. **NH_3** b.Br^+ c.H^+ d.BF_3

8. When benzil treated with NaOH it gives
a.**Benzilic acid** b.benzanilide c.benzoic acid d.benzyl alcohol

9. The carbohydrate which has an extremely high molecular weight (macromolecule) is
a.**cellulose** b.maltose c.cellobiose d.lactose

10. Which one othe following is non reducing carbohydrate?
a.lactose b.maltose c.**sucrose** d.glucose

11. Both glucose and mannose can be prepared byKilliani synthesis from
a. D-ribose b.D-lyxose c. **D-arabinose** d.D-xylose

12. How many isomeric aldohexoses are possible for the molecularformula $C_6H_{12}O_6$?
a.2 b.4 c.8 d.**16**

13. Which one of the following compound is used to protect amino group in Sheehan method of peptide synthesis

a.Carbobenzoxy chloride b.**phthalic anhydride** c.tert-Butoxyazidoformate d.Diketopiperazine

14. Which one of the following is a globular protein?
a.**Insulin** b.Collegen c.Fibroin d.Myosin

15. Which one of the following is a conjugated protein?
a.Albumins b.Globulins c.**Lipoproteins** d.Histones

16. Which one of the following test is a characteristic of proteins containing tryptophan?
a.**Hoopin's-cole reaction** b.Xanthoproteic test c.Millon's test d.Nitroprusside test

17. Which of the following is not an aromatic compound?
a.Furan b.Pyrrole c.**Piperidine** d.pyridine

18. Which one of the following has least resonance energy?
a.Thiophene b.**Furan** c.Pyrrole d.pyridine

19. In pyridine the electrophilic substitution occurs exclusively at-
a. **β-Position** b.α-position c.ϒ-Position d. at any of these position

20. The heterocyclic compound which is most reactive towards electrophilic reagent is
a.Thiophene b**.Pyrrole** c.Furan d.pyridine

PART B (8 Marks Questions)

1). Write the equation for the reaction of glycine with (i) NaOH aq. (ii) HCl aq. (iii) C_2H_5OH, H^+, Heat, (iv)Formaldehyde,(v) Ninhydrine.

2). i. Explain the synthesis of Peptides.

ii. Describe Edman's method for determining N- terminal group in a poly peptide.

3). Explain the following synthesis

(i) Gabriel Synthesis (ii) Koop Synthesis iii. By Strecker synthesis.

4).Write notes on (i) N-Terminal and C-Terminal amino acid residues (ii) End Group analysis.

5). Write the equation for the reaction of Alanine with (i) HNO_2 (ii) HCl aq (iii) Formaldehyde (iv) Ninhydrine (v) Benzyl Chloroformate.

6).i. What do you understand by primary, secondary and tertiary structure of protein? Illustrate your answer with suitable examples?

ii. How will you distinguish between glycine and acetamide?

7**)** (i). What is the mechanism for denaturation of proteins by(i) change in P^H (ii)heavy metal ion such as Pb^{2+}?

(ii)What kind of bonding is greatly responsible for the secondary structure of protein?

(iii)Describe the 3 types of secondary structure of protein?

8) i. Describe the Color tests for Protein.

ii. How will you distinguish between glycine and acetamide?

9).(i) Explain the synthesis of Peptides.

(ii). Describe the kind of bonding responsible for the tertiary, quaternary structure of proteins?

10).(i) Establish the structure of the tripeptide gly, ser, cys by terminal residue analysis?

(ii).How different peptides may be separated from each other?

(iii).Describe the types of secondary structures of protein?

UNIT-IV		Subject: Organic Chemistry				Subject code:15CHU501
1.	Which one of the following protein transport oxygen in the body	a.Keratin	b.Nucleoprotein	c.Haemoglobin	d.Inulin	Haemoglobin
2.	Which one of the following amino acid cannot be prepared by general formula $RCH(NH_2)COOH$	a.Proline	b.Glycine	c.Alanine	d.Valine	Proline
3.	Which one of the following aminoacid is not optically active	c.Alanine	b.Glycine	d.Valine	d.Isoleucine	Glycine
4.	Which one of the following aminoacid is a basic amino acid	a.Tryptophan	b.Leucine	c.Histidine	d.Glutamic acid	Histidine
5.	Which one of the following reaction canbe used for the synthesis of α-amino acids	a.Gabriel phthalimide	b.Erlenmeyer azlactone	c.Streckersynthesis	d.all of these	all of these
6.	Which one of thefollowing acid is capable of forming Zwitterion	a.Halo acid	b.Hydroxy acid	c.α-Amino acid	d.Nitro acid	α-Amino acid
7.	Isoelectric point is the pH at which a protein or amino acid has	a.Dipolar ion	b.Cation	c.Anion	d.pH of the solution	Dipolar ion
8.	Glycine boiled with barium hydroxide to give	a.Diketopiperazine	b.Amino alcohol	c.Methyl amine	d.Hyppuric acid	Methyl amine
9.	Glycine when heated alone give	a.Methyl amine	b.2-amino ethanol	c.Diketopiperazine	d.Zwitterion	Diketopiperazine
10.	Van slyke method is used for theestimation of	a.Primaryamino group	b.secondary amino group	c.alcoholic group	d.amide group	Primary amino group
11.	Which one of the following meethod is used for the synthesis of pepetides	a.Carbobenzoxy chloride	b.Sheehan	c.Merrifield	d.all of these	all of these
12.	Which one of the following compound is used to protectamino group in sheehan method of peptide synthesis	a.Carbobenzoxy chloride	b.phthalic anhydride	c.tert-Butoxyazidoformate	d.Diketopiperazine	phthalic anhydride
13.	Which one of the following is a globular protein	a.Insulin	b.Collegen	c.Fibroin	d.Myosin	Insulin
14.	Whichone of the following is a	a.Albumins	b.Globulins	c.Lipoproteins	d.Histones	Lipoprotein

	conjugated protein					
15.	Which one of the following test is characteristics of proteinscontaining tryptophan	a.Hoopin's-cole reaction	b.Xanthoproteic test	c.Millon's test	d.Nitroprusside test	Hoopin's cole reaction
16.	Sangar's reagent is	a.2,4-Difluorobenzene	b.Phenylisothiocyanate	c.2,4-Dinitrophenyl hydrazine	d.Ninhydrin	2,4-Difluorobenzene
17.	Which one of the following test is not shown by proteins	a.Mulliken -Baker	b.Xanthoproteic test	c.Hoopin's-cole reaction	d.Ninhydrin	Mulliken -Baker
18.	Primary structure of protein shows	a.oreintation of amino acids	b.arrangement of peptides	c.amino acid sequence	α or β-helix space structure	amino acid sequence
19.	Spatial arrangement of peptides in protein to give helical structureis known as	a.Secondary	b.Primary	c.Tertiary	d.Quaternery	Secondary
20.	Coagulation of protein on heating with heavy metal salts is known as	a.Sedimentation	b.Decolourization	c.Denaturation	d.Precipitation	Sedimentation
21.	Proteins have characteristic	a.Boiling point	b.Melting point	c.Isoelectric point	d.pH of the solution	Isoelectric point
22.	The peptides have---------- linkages	a.CONH linkage	COOHlinkage	c.RCNR linkage	d.CH2NH2 linkage	CONH linkage
23.	In IR spectra the amino acid shows absorption band at	a.1400&1600cm-1	b. 1300-1600 cm-1	c.1200-1600cm-1	d.1350-1700 cm-1	1400&1600cm-1
24.	The simplest amino acid is	a.Alanine	b.Histidine	c.Crystinine	d.Glycine	Glycine
25.	An amino acid with a hydroxyl group is	a.Alanine	b.Serine	c.Valine	d.Ornithine	Serine
26.	Aspartic acid contains---------- amino group/s and---------- carboxyl group	a. 1,1	b.1,2	c.2,1	d.2,0	1,2
27.	The acidic group in glycine is	a-COOH	b.-COO-	c.-NH2	d. -NH3+	d. -NH3+
28.	Towards which of thefollowing reagents does glycine behave as an acid?	a.ethanol	b.HCl	c.acetic anhydride	d.nitrous acid	ethanol
29.	Which one of the following statement is true for glycine?	a. it exists in crystalline form	ib. It is optically inactive	c.it is insoluble in water	d.it cannot form zwitterion	a. it exists in crystalline form
30.	Hyppuric acid is also calledas	a.benzoyl glycine	b.Glycollic acid	c.Oxalic acid	benzoyl alanine	benzoyl glycine

31.	Glycine treated with NaOH it gives	a.sodium acetate	b.sodium ammonium acetate	c.ammonium acetate	d.sodium nitrate	sodium ammonium acetate
32.	The optical rotation of amino acids depends upon the	a.pH of the solution	b.pKa of the solution	c.pH>7	d.pH<7	pH of the solution
33.	In neutral solution most of the amino acids are	a.Mutarotation	b.racemic mixture	c. dextrorotatory	d. leavorotatory	dextrorotatory
34.	Alanine treated with NaOH it gives	a.sodium ammonium acetate	b.sodium ammonium acetate	c. Sodium amino propionate	d.sodium ammonium oxalate	Sodium amino propionate
35.	Amino acids can be esterified byboiling with an alcohol in the presence ofanhydrous	a. HCl	b. H2SO4	c.HNO3	d.NaOH	HCl
36.	When Glycine heated with Ba(OH)2 it gives	a. methylamine	b. ethylamine	c. propyl amine	d. triethyl amine	a. methylamine
37.	When Alanine heated with Ba(OH)2 it gives	a. methylamine	b. methylamine	c. propyl amine	d. triethyl amine	ethylamine
38.	When Glycine on treated with LiAlH4 it gives	a. 2-amino ethanol	b. 2-amino propanol	c.3-amino ethanol	d. 3-amino propanol	2-amino ethanol
39.	When Alanine on treated with LiAlH4 it gives	a. 2-amino ethanol	b. 2-amino propanol	c.3-amino ethanol	d. 3-amino propanol	2-amino propanol
40.	When Alanine on treated with nitrous acid it gives	a.Glycollic acid	b.Oxalic acid	c.benzoic acid	d.lactic acid	lactic acid
41.	2,4-Diflurobenzeneis also called as	a. Felling's solution	b.Tollen's reagent	c. Sangar's reagent	d.Ninhydrine	Sangar's reagent
42.	When Glycine on treated with nitrous acid it gives	a.Glycollic acid	b.Oxalic acid	c.benzoic acid	d.lactic acid	Glycollic acid
43.	When alanine reacts with ninhydrin it gives	a.redcomplex	b. brown complex	c. purple complex	d. deep blue complex	purple complex
44.	When glycine reacts with ninhydrin it gives	a.redcomplex	b. brown complex	c. purple complex	d. deep blue complex	deep blue complex
45.	Which one of the following statement is false for glycine?	a. it exists in crystalline form	ib. It is optically active	c.it is insoluble in water	d.it can form zwitterion	it is insoluble in water
46.	An amino acid usually shows its lowest solubility	a.in acidic solution	b. in basic solution	c. in aqueous solution	d.at the isoelectric point	at the isoelectric point
47.	The arbitary standard chosen for correlating the configuration of	a.L-alanine	b.L.valine	c.D-serine	d. L-serine	L-serine

	α-amino acid is					
48.	Which one of thefollowing statement is not true?	a.peptides give α-amino acid on hydrolysis	b.peptides arenot amino acids	c.2 peptides can be producedfrom two different amino acids	d.peptides contain amide linkage	peptides arenot amino acids
49.	The protein which transport oxygen in the blood stream is	a.myoglobin	b.haemoglobin	c.insulin	d.collagen	haemoglobin
50.	Which one of the following is a protein?	a.rayon	b. natural silk	c.terycotton	d.nylon	natural silk
51.	The digesion of proteins involves their	a.Denaturation	b.Oxidation	c.reduction	d.hydrolysis	hydrolysis
52.	When a protein is subjected to denaturation	a.it is hydrolysed to its constituent aminoacids	b. electric field has no influence on its migration	c. irreversible precipitation is effected	d. constituent amino acids are seperated	irreversible precipitation is effected
53.	Which one of the following statement is false for protein	a.amino acid residue join together to form protein molecule	b.proteins are polymer	c.eggs are rich in protein	d.pules are good souces of protein	proteins are polymer
54.	The number tripeptidesformed by three different amino acids are	a. Three	b.Four	c.Five	d.Six	Six
55.	Proteins are polyamides of	a.β-amino acids	b.α-amino acids	c.α-hydroxy acids	d.β-hydroxy acids	α-amino acids
56.	The number of polypeptide chains present ina molecule of haemoglobin is	a.Four	b.One	c.Two	d.Six	Four
57.	Which fuctional group participates indisulphide bond formation in proteins?	a.Thioether	b.Thio	c.Thioester	d.Thioacetone	Thio
58.	Ninhydrine test is given by	a.Carbohydrates	b. Proteins	c.Alkanes	d.Alkenes	Protiens
59.	The α-Helix is held in a coiled conformation partially because of	a.Optical activity	b.Hydrogen bonding	c.Resonance	d.Delocalization	Hydrogen bonding

UNIT-V

Heterocyclic compounds: Preparation, properties and use of Furan, Pyrrole, Thiophene, Pyridine, Quinoline, α and β-Flavones.

Introduction

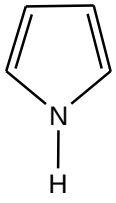
Cyclic compounds in which the ring includes only one type of atoms are called homocyclic compounds. E.g. Benzene. Cyclic compounds in which the ring includes only carbon atoms are called carbocyclic compounds. E.g Benzene, Naphthalene,etc. cyclic compounds in which the ring includes. In addition, to carbon atoms, one or morepolyvalent atoms such as O, N, S are called heterocyclic compounds. E.g.,Furan, thophene,pyrrole,pyrine etc.

A variety of such heterocyclic compounds of different ring sizes are known. In this chapter we will restrict our study to the most important ones which are made of five and six membered rings.

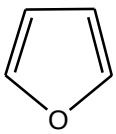
Structure:

The common names of some of the most important five and six membered heterocyclic ring compounds are given below.

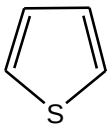
Five - Membered Rings:



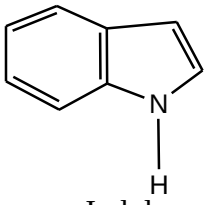
Pyrrole



Furan

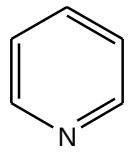


Thiophene

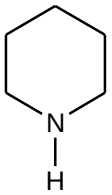


Indole

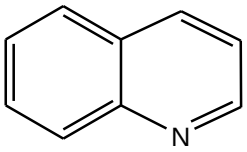
Six-Membered Rings:



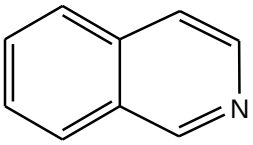
Pyridine



Piperidine



Quinoline



Isoquinoline

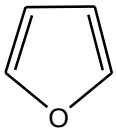
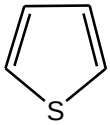
Notice: That the rings containing nitrogen usually end with –ole if five membered and with –ine if six membered. The hetero atom is always numbered as 1 (isoquinoline is an expection), and in such a way as to keep the substituent numbers as low as possible.

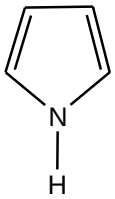
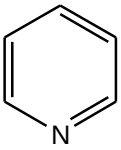
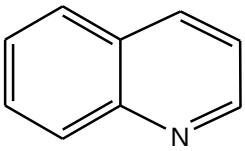
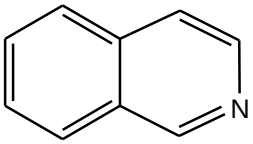
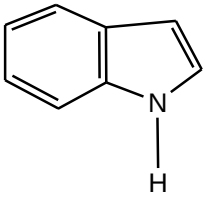
Aromatic Characteristics of Heterocyclic Compounds

The heterocyclic compounds are much more stable and possess aromatic properties.

Most of the heterocyclic compounds obey's Huckel's rule and show aromatic character. According to Huckel's rule "If a system containing $(4n+2)\pi$ electrons will be aromatic in nature". Where n= 0,1,2,……..

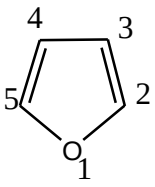
Examples of heterocyclic compounds which obey Huckel's Rule

Name	**No. of π *electrons***	**n**
 Furan	6	1
 Thiophene	6	1

 Pyrrole	6	1
 Pyridine	6	1
 Quinoline	10	2
 Isoquinoline	10	2
 Indole	10	2

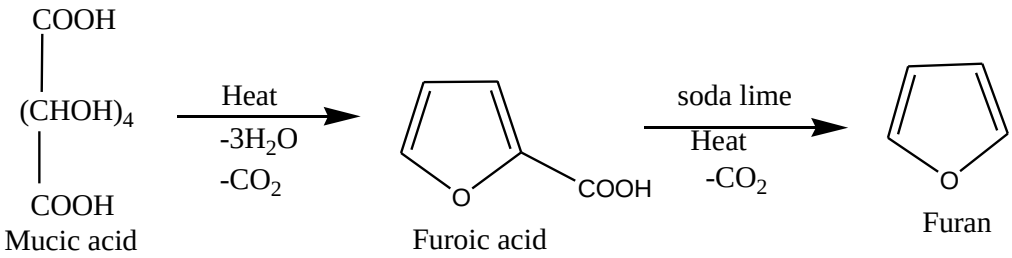
1. CHEMISTRY OF FURAN,(C_4H_4O)

Molecular Formula: C_4H_4O. It contains one oxygen atom in its ring. The positions of side-chains or substitutions are indicated by numbers or Greek letters. Number 1 is given to the Oxygen atom.(In all the heterocyclic compounds containing one hetero atom, number1 is always given to the hetero-atom).

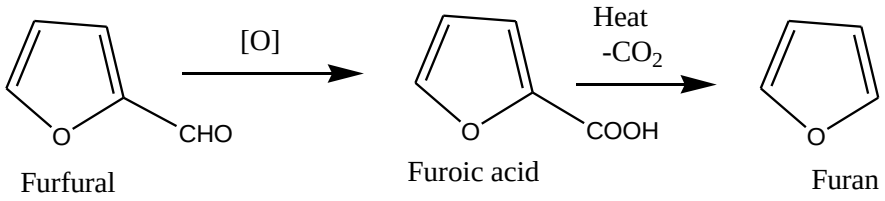


Preparation:

1. Mucic acid is heated. We get furoic acid. It is distilled with lime, we get furan.



2. When furfural undergoes Oxidation and followed by heating it gives furan.



Properties:

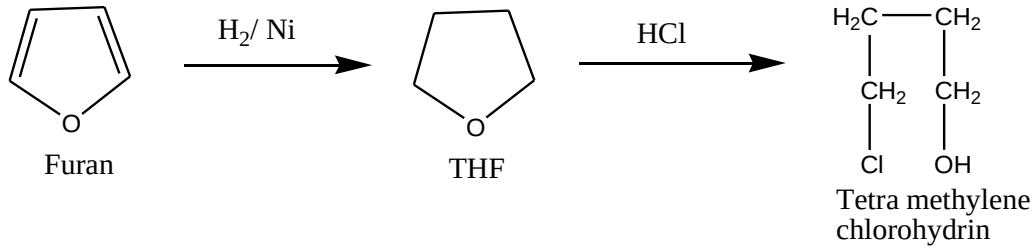
i. It is a colourless liquid.

ii. It is insoluble in water but soluble in alcohol and ether.

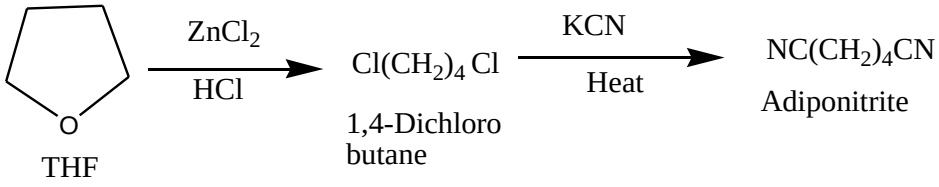
iii. It turns a pine splint moistened with hydrochloric acid green.

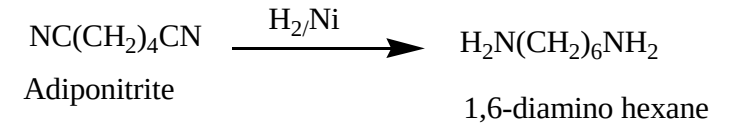
1. Reactions:

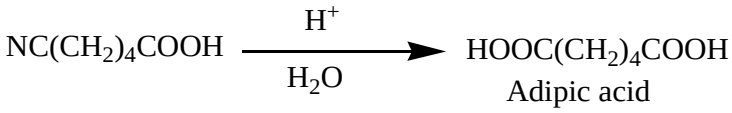
When furan is catalatically reduced with H_2 in thepresence of Ni or Pd we get tetrahydrofuran (THF) which is used as a non aqueous solvent.

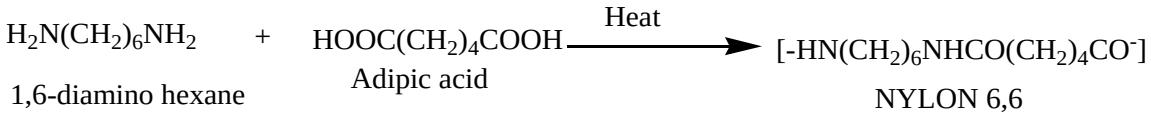


THF is used i) as a solvent in the preparation of Grignard reagents and its reactions. ii) It is used in the manufacture of nylon 6, 6. It is used as a starting material for this synthesis.



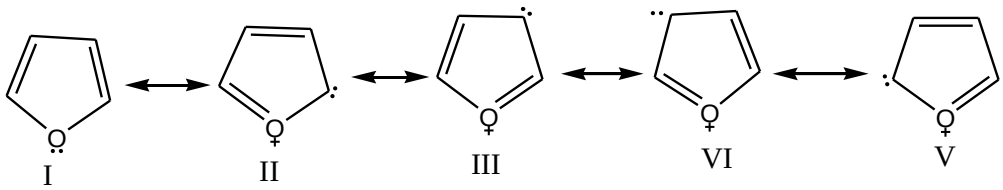




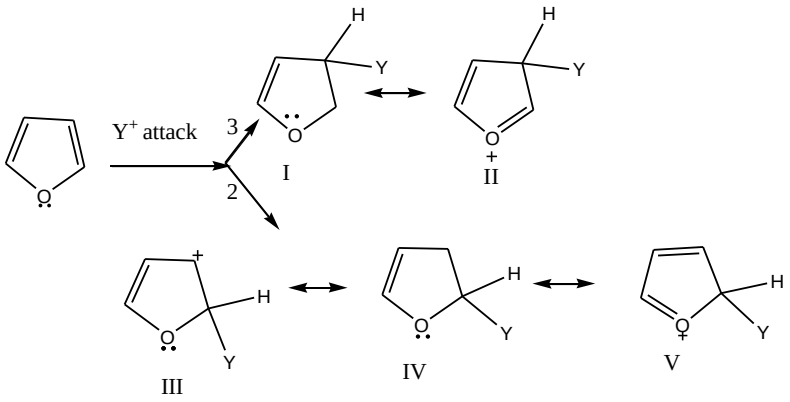


Electrophilic substitution reactions:

Furon is a resonance hybrid of the following five resonating structures (I to V).



If obey's the Huckel's rule and contains (4n+2)π *electrons* (here n=number of rings=1). The molecule is planer. Therefore it is an aromatic compound. It is less aromatic than benzene. It has a larger electron density at position 2 or 5 than at 3 or 4.

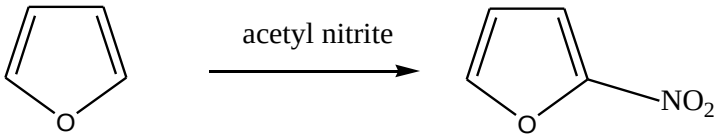


Therefore electrophilic substitution is expected to take place in position 2 or 5 i.e., α position. In practice 2-substitution is favoured. It is because attachment of the electrophilic reagent at position 2 results in the formation of a more stable carbonium ion which, is the resonance hybrid of three structures III, IV and V. on the otherhand the attachment of the electrophilic reagent at position 3 results in the formation of a less stable carbonium ion which is the resonance hybrid of only two structures I& II.

Furan is more reactive than benzene i.e, less aromatic than benzene because the lone pair on the oxygen atom is involved in resonance. There by activating the ring. Thus furan undergoes substitution reactions more readily than does benzene. We get 2 or 5 substituted products. If both positions are occupied we get 3- substituted products.

a) Nitration:

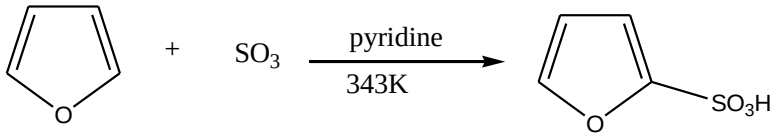
When furan is nitrated with acetyl nitrate or a hot solution of nitric acid and acetic anhydride, we get 2- nitrofuran.



Furan 2- nitro furan

b) Sulphonation:

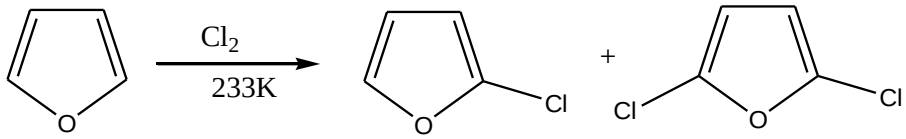
When furan is treated with pyridine and SO_3 mixture we get furan-2-sulphonic acid.



Furan Furan-2- Sulphonic acid

c) Halogenation:

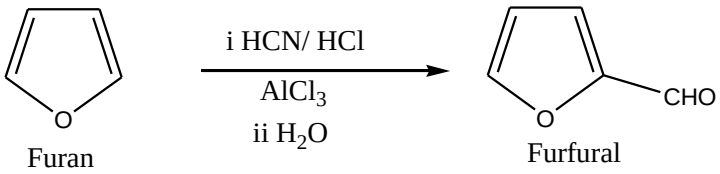
When furan is treated with chlorine at 233K we get 2-chlorofuran and 2,5-dichlorofuran.



Furan 2-Chlorofuran 2,5-dichlofuran

d) Gattermann reaction:

It undergoes Gattermann reaction to give furfural as the product.



Furan Furfural

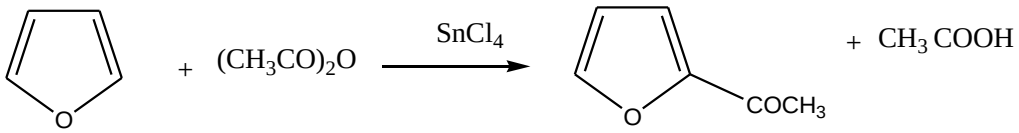
Comparison of the properties of Benzaldehyde and furan

S.No	Properties	Furfural	Benzaldehyde
	Similarities		
1	Oxidation	Furoic acid	Benzoic acid
2	Reduction	Furfuryl alcohol	Benzyl alcohol
3	Cannizaro reaction(+NaOH)	Furfuryl alcohol+ Furoic acid	Benzyl alcohol+ Benzoic acid
4	With alcoholic KCN	Furion $\xrightarrow{[O]}$ Furil	Benzoin $\xrightarrow{[O]}$ Benzil
5	Perkins reaction Sodium acetate+ aceticanhydride	Furyl acrylic acid	Cinnamic acid

	Differences		
1	Aniline+HCl	Red colour	No red colour
2	A pine splint moistened with HCl	Turns green	No reaction

e) Friedel-Crafts Acylation:

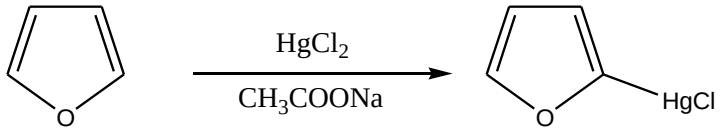
Furan can be acylated with acetic anhydride in the presence of BF_3 or $SnCl_2$ at 273K to yield 2-acetyl furan.



Furan 2-Acetyl furan

f) Mercuration:

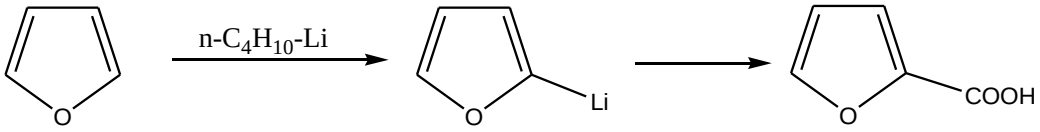
It can be mecurated to give 2- Chloromercuric furan.



Furan 2-Chloromercuric Furan

g) Reaction with n-butyl lithim:

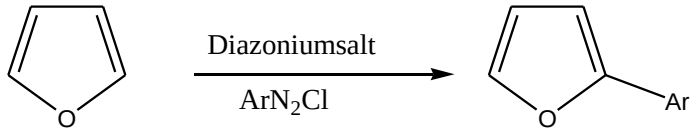
It is used in the synthesis of Furoic acid.



Furan 2-Lithium furan Furoic acid

h) Gomberg reaction)

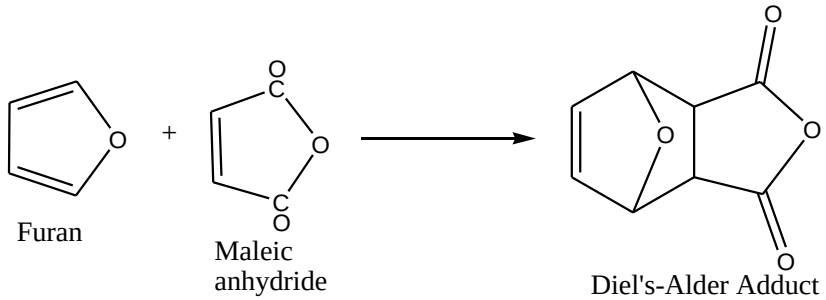
It is used in the synthesis of 2-Aryl furan.



Furan 2-Aryl furan

3) Dields – Alder reaction:

Furan is the only one offive membered heterocyclic compound to undergo theDields –Alder reaction with maleic anhydride. The addition occurs across C-2 and C-5.

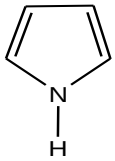


Furan Maleic anhydride Diel's-Alder Adduct

[Furan is less aromatic than thiophene and pyrrole. Thiophene and pyrrole don't give adduct. In this reaction it reacts as a 1,3 diene].

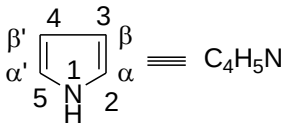
2. CHEMISTRY OF PYRROLE(C_4H_5N)

Molecular Formula: C_4H_5N. It is a five membered ring compound containing a nitrogen atom. The position of side chains or stituentsare indicated as follows.



Pyrrole

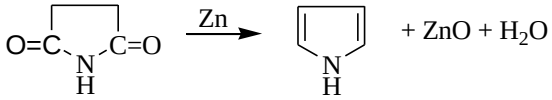
PYRROLE, C_4H_5N



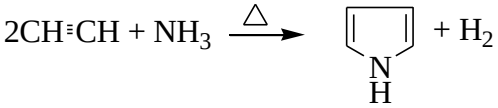
Pyrrole is an important heterocyclic compound. It is found in many natural compounds, e.g. alkaloids, chlorophyll etc. It occurs in coal tar and bone oil.

Preparation

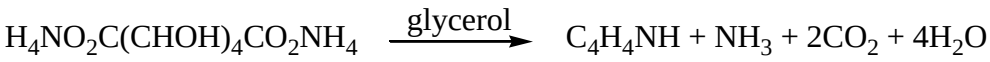
1. **Isolation from bone oil:** Bone oil is washed with dilute alkali to remove acidic impurities and then with acid to remove basic impurities. The liquid is then fractionated. Pyrrole distills over in the fraction boiling between 373 K and 423 K. This may be purified by fusing with potassium hydroxide. Solid potassio pyrrole is formed. This on steam distillation gives pure pyrrole.
2. Pyrrole is formed when succinimide is distilled with zinc dust.



3. Pyrrole may be synthesized by passing a mixture of acetylene and ammonia through a red hot tube.



4. It is conveniently prepared by distilling a mixture of ammonium mucate and glycerol at 473 K.



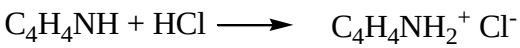
Properties

It is a colourless liquid (bp.404 K), sparingly soluble in water but readily soluble in ether and alcohol. On exposure to air, it darkens rapidly and forms a resinous mass finally.

Chemically, it shows the reactions of aromatic compounds.

Some important reactions are -

a) Basic nature : Pyrrole is a weak, secondary amine and dissolves very slowly in cold, dilute acids:

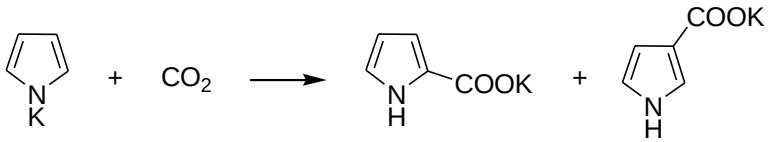


b) Substitution of imino hydrogen: The imino hydrogen of pyrrole is replaced by Grignard reagent, sodium, potassium, alkyl or acyl radicles Eg. On heating with solid potassium hydroxide, potassio pyrrole is formed (*Cf.* phenol).

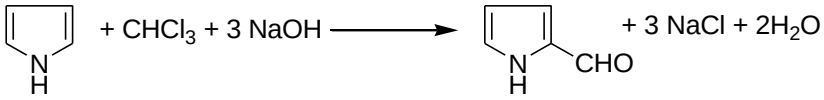
$$C_4H_4NH + KOH \longrightarrow C_4H_4N^- K^+ + H_2O$$

At 333 K pyrrole forms N-methyl pyrrole with methyl iodide. With acetyl chloride, N-acetylpyrrole is formed at 353 K.

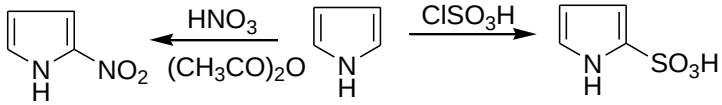
c) Substitution reactions: In many reactions, pyrrole resembles phenol. For example, potassio pyrrole reacts with carbon dioxide to form 2- and 3-pyrrole carboxylic acid (*Cf.* kolbe Schmidt reaction)



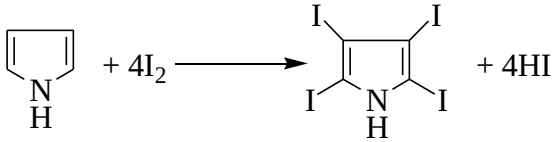
Pyrrole reacts with chloroform and sodium hydroxide to form pyrrole-2-aldehyde (*Cf.* Reimer –Tiemann reaction).



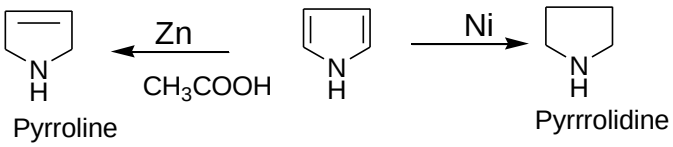
Pyrrole cannot be nitrated and sulphonated or halogenated by the methods used in the case of benzene. At 263 K, pyrrole yields 2-nitropyrrole with nitric acid in acid in acetic anhydride. With chlorosulphonic acid, pyrrole is sulphonated to form pyrrole-2-sulphonic acid.



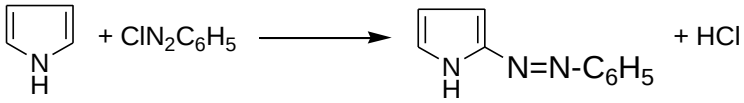
Halogenation occurs readily if the solution is alkaline. Iodine forms tetraiodopyrrole.



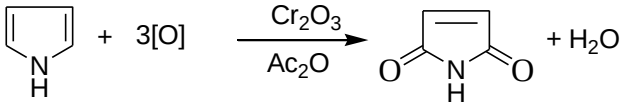
d) Reduction: With zinc dust and acetic acid, pyrrole undergoes reduction to give pyrroline (2,5-dihydropyrrole). At 473 K catalytically reducing pyrrole using nickel, pyrrolidine (tetrahydropyrrole) is formed.



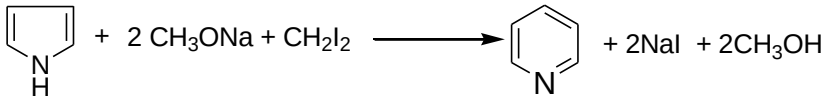
e) Coupling: Pyrrole couples with benzenediazonium chloride in a weakly acidic solution to give 2-phenyl azo pyrrole:



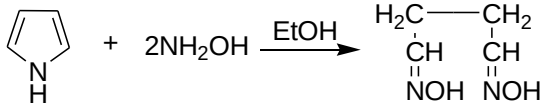
f) Oxidation : Pyrrole is oxidized by chromic acid to give maleic imide:



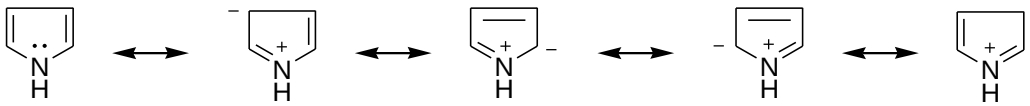
g) Ring expansion: When treated with sodium methoxide and methylene iodide, pyrrole undergoes ring expansion forming pyridine.



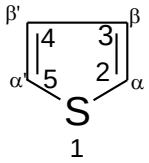
h) Ring opening reaction: When treated with ethanolic hydroxylamine, pyrrole undergoes ring opening forming succindialdoxime.



Pyrrole is a resonance hybrid with resonance energy 87.8-130 $kJmol^{-1}$ and the possible resonance hybrid are drawn below.



3. CHEMISTRY OF THIOPHENE, $C_4H_4S_4$



From Coal Tar

Benzene, obtained from coal tar, contains thiophene. It is difficult to separate them by fractional distillation as their boiling points (357 K) are close to each other. Thiophene may be separated from benzene by shaking the mixture with cold, concentrated sulphuric acid when thiophene gives thiophene-2-sulphonic acid which is dissolved out in water. Thiophene sulphonic acid is treated with superheated steam to recover thiophene.

Another method of separation is by refluxing the mixture with aqueous mercuric acetate when thiophene is mercurated and benzene remains unaffected. Thiophene can be regenerated from the organomercury compound by treating with hydrochloric acid.

The best method of removing thiophene from benzene is by shaking with Raney nickel.

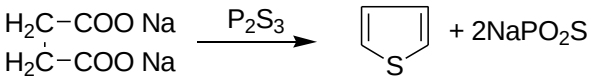
Preparation

Thiophene may be obtained –

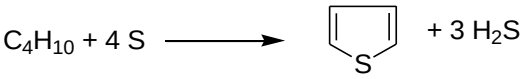
1) By passing a mixture of acetylene and hydrogen sulphide through a tube containing alumina at 673 K.

$$2\ C_2H_2 + H_2S \longrightarrow C_4H_4S + H_2$$

2) By heating sodium succinate with phosphorus trisulphide.



3) It is also obtained commercially by the reaction between n-butane and sulphur in the vapour phase:

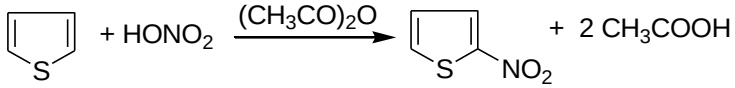


Properties

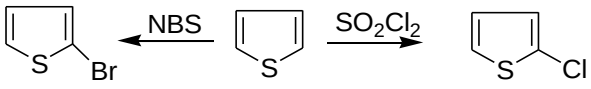
Thiophene is a colourless liquid, smelling like benzene. It is insoluble in water but soluble in organic solvents. Chemically thiophene resembles benzene rather closely. As compared with furan and pyrrole, it is comparatively more stable.

Electrophilic substitution: Thiophene undergoes electrophilic substitution reactions primarily at C-2 Substituted at C-3 occurs only when both the *α* and *α'* position are occupied.

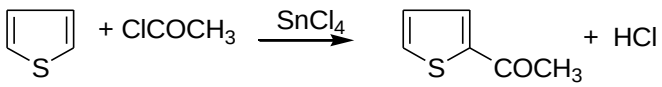
Thiophene can be nitrated by a solution of nitric acid in acetic anhydride to yield 2-nitrothiophene. Sulphonation with cold, concentrated sulphuric acid gives 2-sulphonic acid.



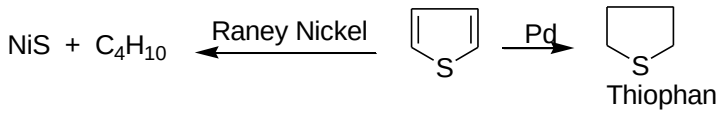
Chlorination at room temperature gives 2-chlorothiophene with SO_2Cl_2. 2-bromothiophene is obtained at room temperature when thiophene is treated with N-bromosuccinimide (NBS).



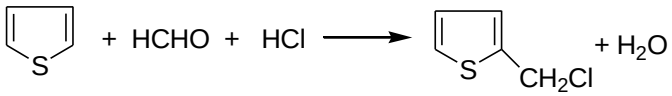
Thiophene may be acetylated with acetic anhydride in presence of phosphoric acid or with acetyl chloride in presence of stannic chloride to yield 2-acetyl thiophene.



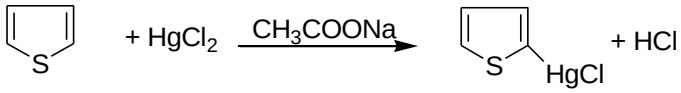
Reduction: Catalytic hydrogenation of thiophene using large amount of catalyst gives tetrahydrothiophene (**thiophan)** and using Raney nickel as catalyst thiophene is converted to n-butane, C_4H_{10}.



Chloromethylation: Thiophene reacts with formaldehyde and hydrochloric acid to give 2-chloromethyl thiophene.



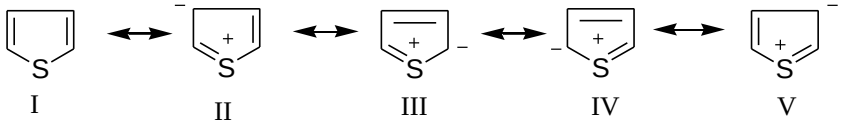
Mercuration: Thiophene undergoes mercuration with mercuric chloride in aqueous sodium acetate to produce 2-chloromercurithiophene.



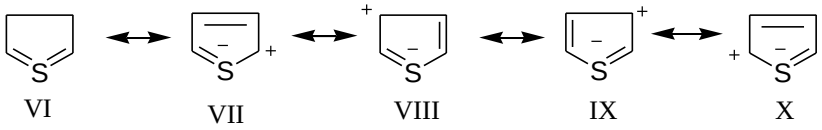
Thiophene does not react with benzenediazonium chloride.

Thiophene is a resonance hybrid with resonance energy 117-130 k. J mol^{-1}. In the resonance structures written below in **group (a)** sulphur atom uses p-orbitals and in **group (b)** sulphur uses d-orbital.

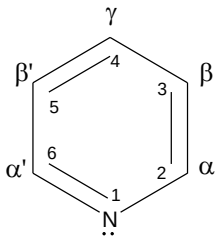
(a)



(b)



4. CHEMISTRY OF PYRIDINE, C_5H_5N



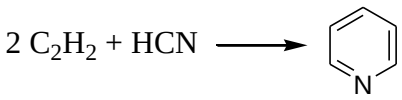
Pyridine is an important heterocyclic compound containing a six membered ring. It may be regarded as benzene in which one = CH-group has been replaced by = N-. Because of the presence of the heteroatom in the ring, three isomeric mono substituted pyridines can exist corresponding to the substituents at α ,β *or* γ (2,3 or 4) positions.

It occurs along with pyrrole in bone oil and in the light oil fraction (b.p. up to 443 K) of coal tar. It can be isolated from the latter by extracting with dilute sulphuric acid. The acid layer is separated and treated with sodium hydroxide when a dark brown liquid separates. Pyridine is obtained from this oily liquid by fractional distillation.

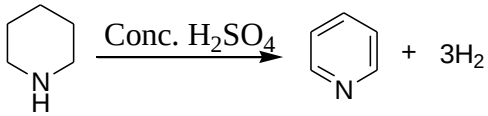
Preparation

Pyridine may be obtained-

1) By passing a mixture of acetylene and hydrogen cyanide through a red hot tube.



2) By dehydrogenization of piperidine with concentrated sulphuric acid at 573 K or with nitrobenzene at 533 K.



Properties

Pyridine is a colourless liquid (b.p 338 K) having an unpleasant odour. It is miscible with water in all proportions and is hygroscopic. Pyridine is basic in nature (pK_b = 5.2) and resembles benzene in many of its properties.

Pyridine is a strong tertiary amine which gives salts with inorganic acids and form quaternary salts when heated with alkyl halides.

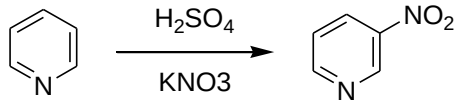
$$C_5H_5N + HCl \longrightarrow C_5H_5NH^+Cl^-$$

pyridinium chloride

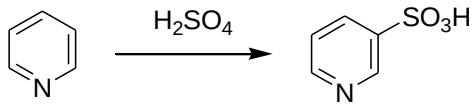
$$C_5H_5N + CH_3I \longrightarrow [C_5H_5NCH_3]^+ I^-$$

pyridine methiodide

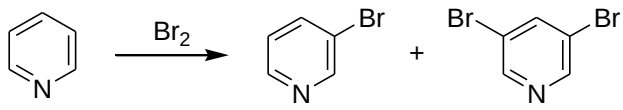
Electrophilic Sustitution: Pyridine is considerably less reactive than benzene towards electrophiles. So, it does not undergo Friedel Craft's reaction. It undergoes nitration, sulphonation and halogenations only under vigorous conditions. With conc.H_2SO_4 and KNO_3 at 573 K it gives 3-nitropyridine.



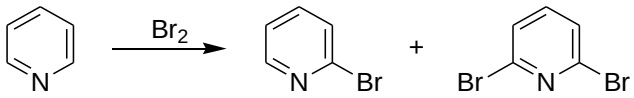
Sulphonation of pyridine is difficult. On heating with concentrated sulphuric acid at 623 K for some hours it gives pyridine-3- sulphonic acid.



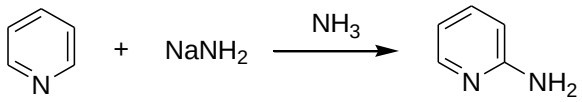
With bromine at 573 K in the presence of catalyst (pumice or charcoal) pyridine gives a mixture of 3- bromopyridine and 3, 5-dibromopyridine.



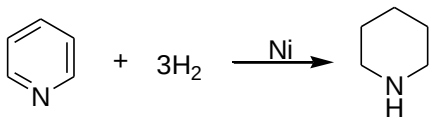
At 773 K bromination occurs at C-2 or C-2 and C-6 positions. The substitutions probably occur by a free radical mechanism.



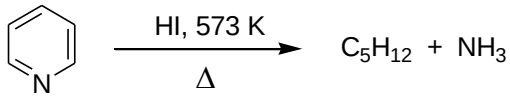
Pyridine reacts with sodamide in liquid ammonia at about 373 K to form 2-aminopyridine **(Chichibabin reaction)**. This reaction is an example of nucleophilic substitution reaction.



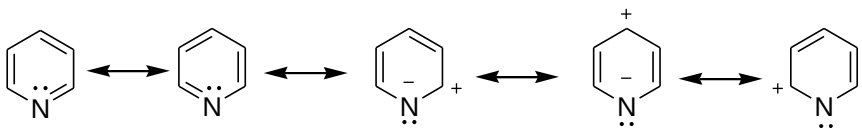
Pyridine undergoes reduction with lithium aluminum hydride or hydrogen in the presence of nickel catalyst to form piperidine.



With hydrogen iodide at 573 K, the reduction is accompanied by fission to form n-pentane and ammonia.



Pyridine has resonance energy of about 125 k.J mol^{-1}. Because pyridine has a large dipole moment of 2.23 D, it is best regarded as a resonance hybrid of the following contributing structures.



Reactivity of pyridine

A close look at the contributing structures of pyridine reveals that positions 3 and 5 will be sites for electrophilic attack. The remaining positions (2, 4 and 6) will be the sites for nucleophillic attack. Moreover, the ring is deactivated towards electrophilic reagents due to the withdrawal of

electrons from the ring carbon atoms towards the nitrogen atom. Thus pyridine resembles benzene ring in nitrobenzene. Pyridine can be protonated in strongly acid medium. At that time, the positively charged nitrogen atom deactivates the ring much more than the unprotonated nitrogen atom. This is indicated by the difficulty in nitration and sulphonation in pyridine. Thus, pyridine is less reactive than benzene.

Uses

1. Due to its strong basic property and solvent properties, pyridine is used in reactions where halogen acid is to be removed as in alkylation and benzoylation.
2. It is utilized to denature ethyl alcohol.
3. It finds use as a catalyst in many reactions.
4. Pyridine is used as starting material in the preparation of sulphapyridine and pyridoxine (Vitamin B_6).

Aromaticity and Basic nature in Pyrrole and Pyridine

The prime condition for a molecule to be aromatic is that it must obey **Huckel's** (4n + 2) **rule**. According to this rule, the molecules must possess. According to this rule, the molecules must possess π electron cloud formed by (4n +2) electrons. Here 'n' represent may the number of ring present in the molecule. Obviously, there must be 6, 10, 14 …. electrons for delocalization if the compound is made up of 1, 2, 3…. rings respectively.

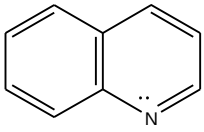
Both pyrrole and pyridine have single ring. If they were to be aromatic, then they must have six π electrons for delocalization according to Huckel's rule. Pyrrole has π electron cloud made up of six electrons. It uses the lone pair of electrons residing over nitrogen for this purpose. On the other hand, pyridine obeys Huckel,s rule without using the lone pair of electrons of nitrogen atom. In other words, pyridine, as in benzene, has three alternate double bonds which satisfy the rule.

Based on the above argument, it is clear that the lone pair of electrons of nitrogen in pyrrole is not available for donation to an acid. Consequently pyrrole is weak Lewis base (pK_b = 3.4)

and even it behaves as an acid. The lone pair of electrons on nitrogen in pyridine is available for donation. Thus, pyridine is a strong Lewis base (pK_b = 5.2).

5. QUINOLINE:

α, β- Benzopyridine,

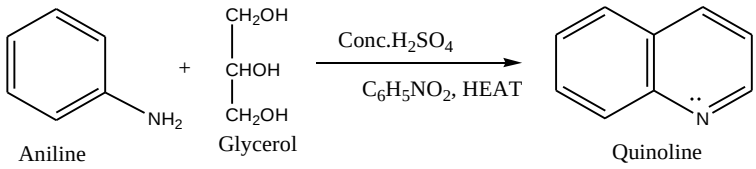


Quninoline consists of a benzene ring fused to the α,β positions of a pyridine ring. It derives its name from the fact that it was first obtained by heating the famous antimalarial alkaloid quinine, with alkali. Quinoline occurs in coal-tar, bone oil.and in angostura bark.

Preparation: Quinoline may be obtained:

(1) **By Skraup Synthesis.**

In this reaction, a mixture of aniline and glycerolis heated in the presence of sulphuric acid and a mild oxidizing agent, usually nitrobenzene or arsenic pentoxide. The reaction is exothermic and tends to become very violent. Ferrous sulphate or boric acid is generallyadded to make the reaction less violent.



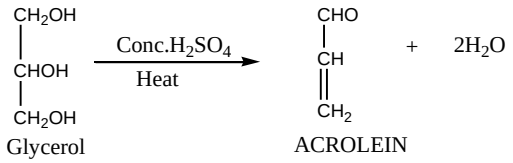
Aniline Glycerol Quinoline

Mechanism:

The mechanism of this reaction is not completely understood. However, it is believed that it proceeds by the following steps.

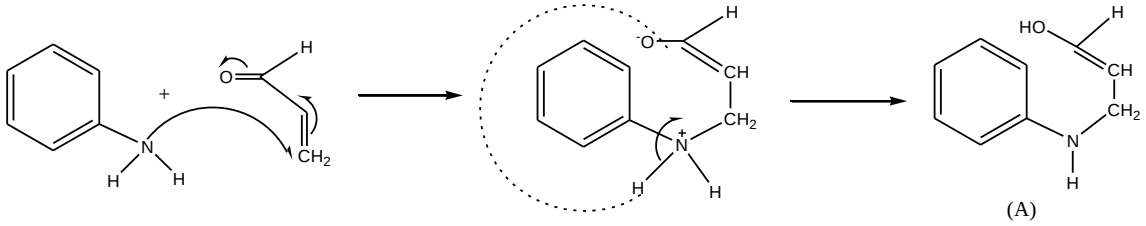
Step-1:

Glycerol undergoes dehydration with sulphuric acid to give acrolein.



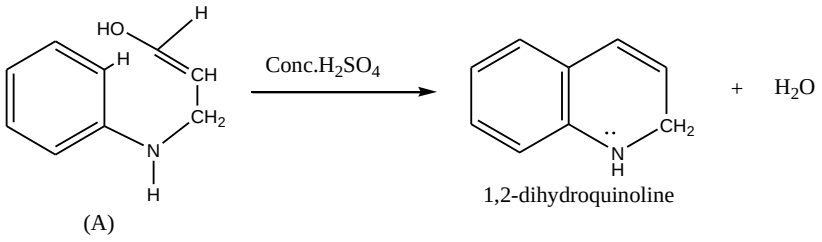
Step-2:

Aniline adds to acrolein (1,4-addition) to give (A).



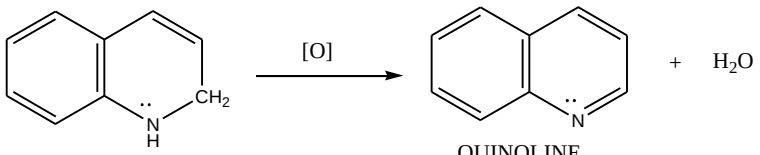
Step-3:

Compound (A) Undergoes ring closure in the presence of sulphuric acid to form 1,2-dihydroquinoline.



Step-4:

1,2-dihydroquinoline undergoes oxidation with nitrobenzene to finally yield quinoline. Nitrobenzene itself is reduced to aniline which is reused in step (2).

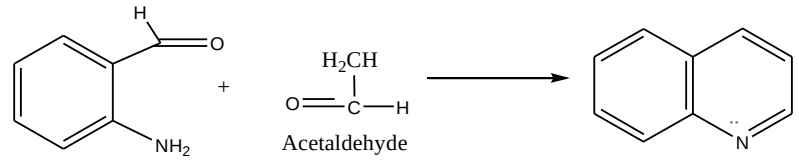


1,2-dihydroquinoline QUINOLINE

This synthesis is used for the commercial preparation of quinoline. It is also important because by starting with substituted anilines, substituted quinolines can be made.

(2). By the Friedlender Synthesis:

This involves the condensation of o-aminoenzaldehyde with acetaldehyde in the presence of an alkali.

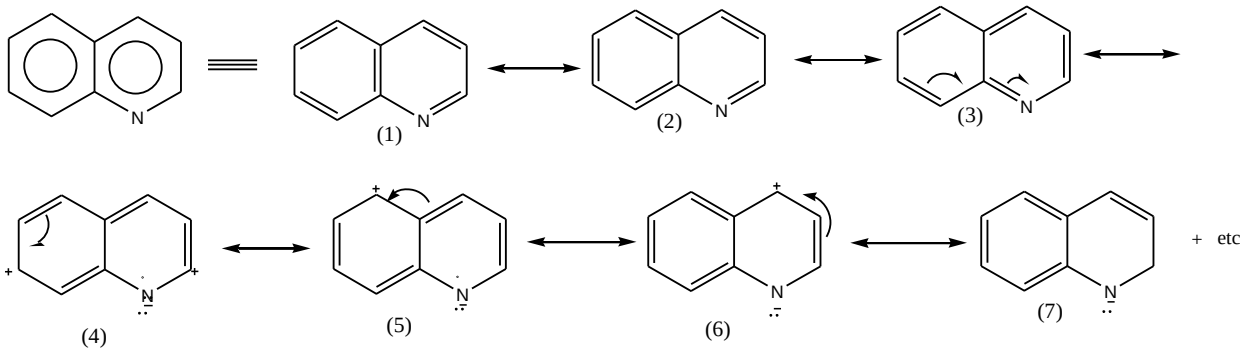


o-amino benzaldehyde Acetaldehyde QUINOLINE

Structure of Quinoline:

All ring atoms in quinoline are sp^2 hybridised. As in the case of pyridine, the nitrogen lone pair electrons reside in a sp^2 orbital, and are not involved in te formation of the delocalized π molecular orbital. It shows aromatic properties because its π orbital contains ten electrons and satisfies the Huckel's rule (n=2 in 4n+2).

Quinoline is considered to be the hybrid of the following canonical forms.



The first three structures are similar to the Kekule structures written for naphthalene. The last four, which are polar structures, show the effect of the electron attracting nitrogen atom on the molecule.

Properties:

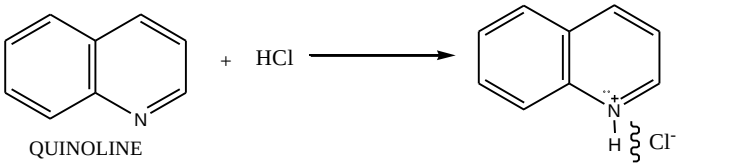
Physical properties:

Quinoline is a colourless liquid, bp 237°C. it turns yellow on standing, and has pyridine-like smell. Quinoline is miscible with most organic solvents, and dissolves in water to about 0.7 % at room temperature.

Chemical properties:

The main chemical properties of quinoline are described below.

1. Basic character: quinoline is a slightly weaker base (pK_a=4.94) than pyridine pK_a= 5.2). it reacts with acid to yield salts which are sparingly soluble in water.

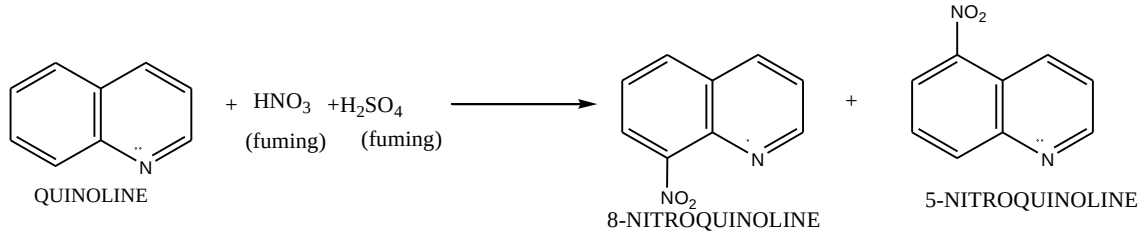


2. **Electrophilic substitutions:**

Quinoline undergoes electrophilic substitution reactions only under vigorous conditions,as was the casewith pyridine. Substitution occurs at C-8 and C-5.

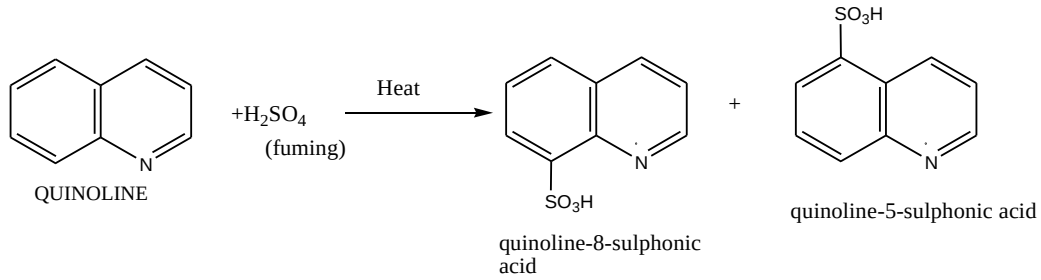
Nitration:

Quinoline undergoes nitration with fuming nitric acid in the presence of fuming sulphuric acid to give a mixture of 8-nitroquinoline and 5-nitroquinoline.



Sulphonation:

quinoline may be sulphonatedwith fuming sulphuric acid at 220°C to yield a mixtureofquinoline-8-sulphonic acid and quinoline-5-sulphonic acid.

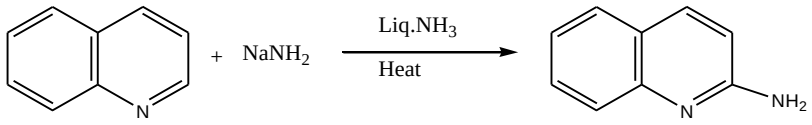


3. **Nucleophilic substitutions**:

Like pyridine, quinoline undergoes nucleophilic substitution reactions. substitution occurs at C-2 (or at C-4 if C-2 is blocked).

(a). Reaction with sodamide:

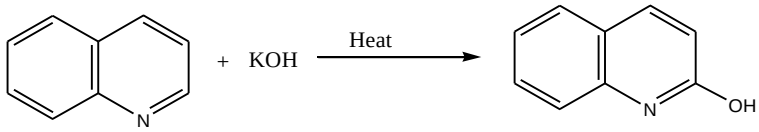
Quinoline reacts with sodamide in liquid ammonia at about 100°C to form 2-aminoquinoline.



QUINOLINE 2-aminoquinoline

(b). Reaction with potassium hydroxide:

Quinoline react with KOH at 220°C to give 2-hydroxyquinoline.



QUINOLINE 2-Hydroxyquinoline

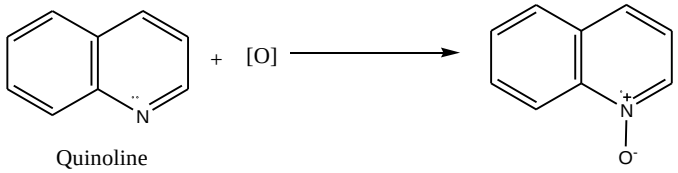
(c). Reaction with n-butyl-lithium:

Quinoline reacts with n-butyl-lithium to yield 2-n-butyl-lithium.

QUINOLINE 2-n-BUTYLQUINOLINE

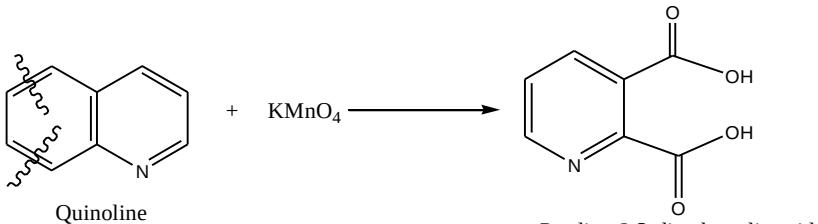
(4). Oxidation:

Quinoline is oxidized by peraceticacid to give quinoline-N-oxide.



Quinoline Quinoline-n-oxide

Oxidation with alkaline potassiumpermanganate yields pyridine-2,3-dicarboxylic acid.



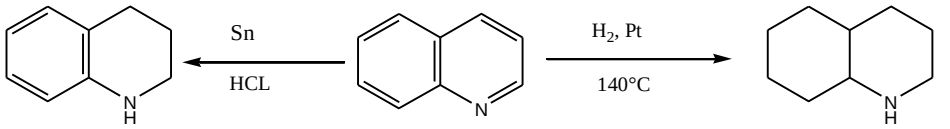
Quinoline

Prydine-2,3-dicarboxylic acid
(quinolic acid)

The above reaction provides a major clue to the structure of quinoline because it shows the position of ring fusion relative to the nitrogen atom.

(5). Reduction:

Mild reaction of quinoline with tin and hydrochloric acid gives 1,2,3,4- tetrahydroquinoline. Reduction with hydrogen and platinum catalyst produces decahydroquinoline.



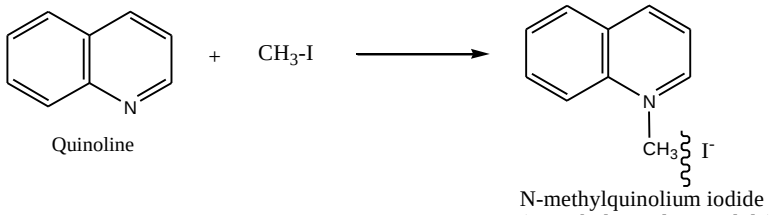
1,2,3,4-tetrahydro quinoline

Quinoline

Dehahydroquinoline

(6). Reaction with alkyl halides:

Quinoline reacts with alkyl halides to give N-alkyl-quinolium halides. For example, with methyl iodide it ields N-methylquinoliun iodide.



Quinoline

N-methylquinolium iodide
(1-methylquinolium iodide)

Uses:

Quinoline is used: (1) in organic synthesis as a high-boiling basic solvent, whereby it not only exerts a catalytic action but also can combine with acids produced in reactions; (2) in the manufacture of pharmaceuticals, dyes and insecticides.

Possible Questions

PART A (1Marks Questions)

1. The simple rotation about an axis passing through the molecule by an angle $2\pi/n$. This operation is called ----------
a**. an proper rotation** b. an improper rotation c. Isomers d. Diastereomers

2. Reflection of atoms through a plane that passes through the molecule. This operation is called ----------
a**. Reflection** b.Inversion c. improper rotation d. Proper rotation

3. A symmetry element is
a. Enantiomers b. **plane** c. Diastereomers d. Resolution

4. The molecule has an axis of three fold proper rotation; this is called----------
a. a C_4 axis b. **a C_3 axis** c. a C_{2v} axis d. a C_2 axis

5. The electrophilic aromatic substitution proceeds through a----------
a.Free radical b.**Sigma complex** c.Benzene d.Carbene

6. Which of the following is truefor the electrophilic aromatic substitutionreaction?
a. Involves a single step b. Involves a free radical intermediate c. KH/KD>5
d.**KH/KD=1**

7. The most stable diene among the following is--------
a.1,4-pentadiene b.1,2-butadiene c.**1,3-butadiene** d.1,4-cyclohexadiene

8. Pinacol when heatedwithAl2O3 at 450°C
a.2,3-Dimethyl-2-butene b. **2,3-Dimethyl-1,3-butadiene** c.2,3-Dimethyl-butene
d.2,3-Dimethyl-4-butene

9. Sucrose on hydrolysis gives
a.2 molecules of glucose b.2 molecules of fructose
c. **1molecule each of glucose and fructose** d. 1 molecule each of glucose and mannose

10. Common table sugar is disaccharide of
a. glucose and mannose b.**glucose and fructose** c.fructose and mannose d. glucose and lactose

11.Example of atrisaccharide is
a.starch b.cellulose c.**raffinose** d.maltose

12. An organic compound insoluble in water is
a.glucose b.**cellulose** c.sucrose d.fructose

13. Isoelectric point is the pH at which a protein or amino acid has
a.**Dipolar ion** b.Cation c.Anion d.pH of the solution

14. Glycine boiled with barium hydroxide to give
a.Diketopiperazine b.Amino alcohol c.**Methyl amine** d.Hyppuric acid

15. Glycine when heated alone gives
a.Methyl amine b.2-amino ethanol c.**Diketopiperazine** d.Zwitterion

16. Van slyke method is used for the estimation of
a. **Primaryamino group** b.secondary amino group c.alcoholic group d.amide group

17. Nucleophilic substitution in pyridine occurs at
a. N-atom b. **α-position** c. β-Position d. does not occur

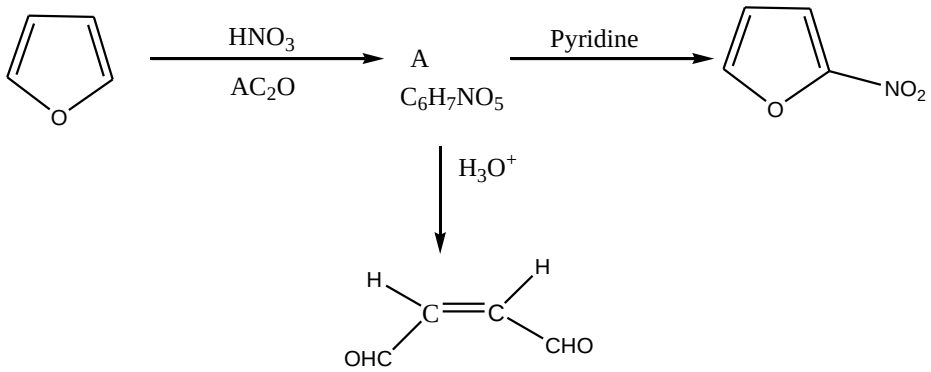
18. The hybridization of nitrogen atom in in piperidine is
a. sp b.sp^2 c.**sp^3** d.unhybridized

19. Which one of thefollowing is most basic?
a.Aniline b.Pyrrole c.pyridine d.**Piperidine**

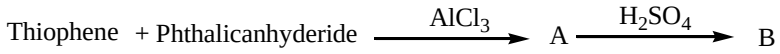
20. Peracid oxidation of pyridine gives
a.**pyridine N-oxide** b.Picolinic acid c.Cinchomeronicacid d.does notgive reaction

PART B (8 Marks Questions)

1). (i) Suggest the mechanism for the following reaction?



(ii) Provide structure for A and B



(b) i) Discuss the constitution of pyridine. Give Hantzsch synthesis of pyridine derivatives.

ii) How will you prepare from the following.

a. Pyrrole from acetylene and formaldehyde. b. 2,5-Dimethylfuran from acetonyl acetone.

2) .i. What is the role of nitrobenzene, glycerol and conc.H_2SO_4 in the synthesis of quinoline?

ii. Write suitable reasons for the following:

a. Electrophilic substitution in pyrrole takes place at 2 or α-position, where as in pyridine at 3- position.
b. Thiophene is more aromatic than furan.

3). (i) Compare the reactivities of Pyrrole and Pyridine

(ii) . How is pyridine converted to i) pyridine-3-sulphonic acid, ii) N-methyl pyridinium iodide.

iii). Describe Bischler-Napieralski synthesis.

4). i. Write the reactions of Pyridine.

ii. Explain why pyridine has low reactivity toward electrophilic substitution.

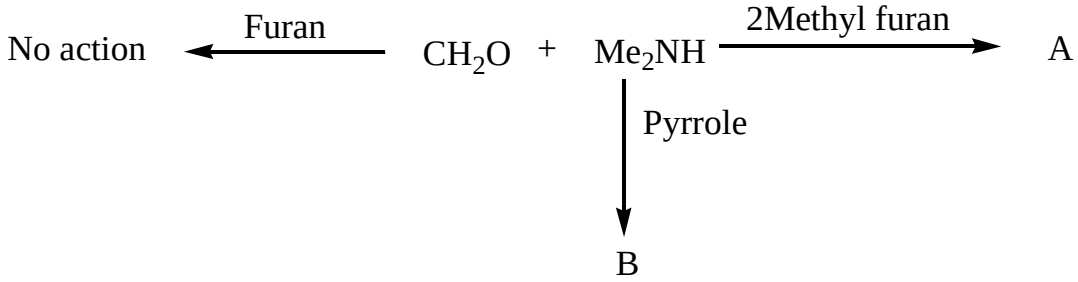
(b) Explain the reactions associated with the following

(i) Hantzsch reaction (ii) Skraup synthsis (iii) Bischer-Napieralsky reaction (iv) Paal- Knorr reaction.

5). (i) Using Skraup synthesis, prepare (a) 4- methyl quinaline,(b) ethyl quinaline

(ii) Suggest a mechanism for the Pomeranz- Fritsch synthesis for isoquinaline?

(iii)



What are A and B explain?

6) (i) How could your account for the difference in the resistance of pyrrole and pyridine rings to the action of acids?

(ii) How can you explain the instability of furan and pyrrole against the action of acidic agents?

(iii)Between pyrrole and pyridine which one is more basic? Explain.

7). Write notes on Chemistry of Indole?

8) Discuss the electrophilic substitution reactions of Thiophene.

9) How will you prepare from the following

a. Furan from furoic acid b. Pyridine from acetylene

Karpagam Academy of Higher Education

(Deemed University Established Under Section 3 of UGC Act 1956)

Coimbatore-21

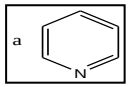
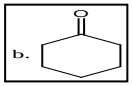
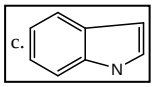
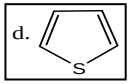
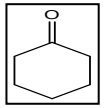
Department of Chemistry

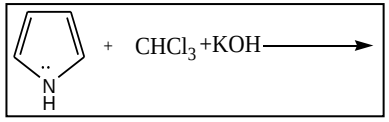
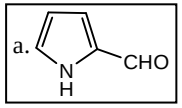
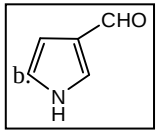
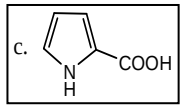
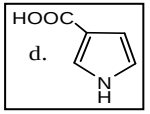
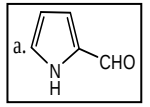
III B.Sc Chemistry

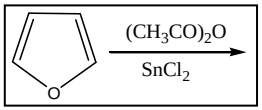
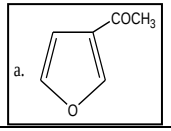
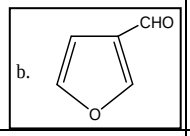
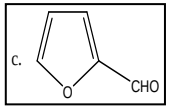
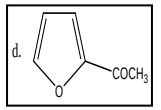
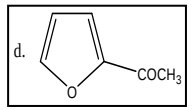
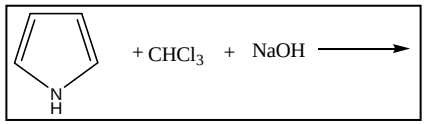
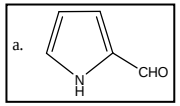
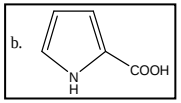
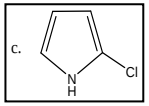
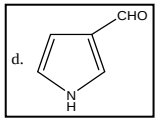
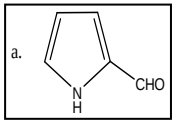
Organic Chemistry

Unit V objective questions

S. No	Question	Option A	Option B	Option C	Option D	Answer
1.	The 'N' atom in pyridine is	a.sp3 hybridized	b.sp2 hybradized	c.sp hybridized	d.cannot be predicted	sp2 hybradized
2.	Pyrrole is less basic than pyridine because the lone pair of electrons on N-atom in pyrrole	a.is part of thedelocalised π molecular orbital	b.is not part of thedelocalised π molecular orbital	c.resides in sp2 hybridized orbital	d.resides in sp hybridized orbital	is part of thedelocalised π molecular orbital
3.	Pyridine is less basic than trimethylamine because the lone pair of electrons on N-atom in pyridine resides in	a.sp2 hybradized orbital	b.sp hybridized orbital	c.sp3 hybridized orbital	d.P orbital	a.sp2 hybradized orbital
4.	Pyridine reacts with mixture of KNO_3 and sulphuric acid at 300°C togive	a.1-Nitro pyridine	b.2-Nitro pyridine	c.3-Nitro pyridine	d.4-Nitro pyridine	b.2-Nitro pyridine
5.	Pyridine undergoesnucleophilic substitution with$NaNH_2$ at 100°C to form	a. 2-amino pyridine	b. 1-amino pyridine	c. 3-amino pyridine	d. 4-amino pyridine	2-amino pyridine
6.	Which of the following reagents will react with pyrrole to form 2-formylpyrrole	a.HCOOH	b.$CHCl_3$/KOH	c.H_2O_2	d.$(CH_3CO)_2O$/ $SnCl_4$	$CHCl_3$/KOH
7.	Quinoline undergoes nucleophilic substitution on heating with NaNH2 to give	a.2-aminoquinoline	b.4-aminoquinoline	c.3-aminoquinoline	d.8-aminoquinoline	2-aminoquinoline
8.	When aniline heated with glycol in the presence of sulphuric acid and nitrobenzene, it gives quinoline. This reaction is called	a.Fischer synthesis	b. Skraup synthesis	c.Diazotization	d.Corey-house synthesis	Skraup synthesis

9.	Which of the followingis not a heterocyclic compound?					
10.	Which of the following compound is not aromatic?	a.Pyridine	b.Pyrrole	c.Furan	d.Piperidine	Pyridine
11.	Pyridinehas a delocalized π molecular orbital containing	a.4 electrons	b.6 electrons	c.8 electrons	d.12 electrons	6 electrons
12.	Pyridine react with HCl to form	a.Pyridinium Chloride	b.2-Chloropyridine	c.3-Chloropyridine	b.4-Chloropyridine	Pyridinium Chloride
13.	Pyridine undergoes electrophilic substitution with fuming sulphuric acid at 350°C to give	a.2-pyridine sulphonic acid	b.3-pyridine sulphonic acid	c.4-pyridine sulphonic acid	d.5-pyridine sulphonic acid	3-pyridine sulphonic acid
14.	Furan reacts with ammonia in the presence of alumina at 400°C to give	a.Pyridine	b.Pyrrole	c.Furfural	d.Furoic acid	Pyrrole
15.	Which of the following reagents will react with furan to form 2-furansulphonic acid	a. SO3 in pyridine at 100°C	b. dilute sulphuric acid at 200°C	c. SO at 100°C	d. dilute sulphuric acid at 100°C	SO3 in pyridine at 100°C
16.	IUPAC name ofpyrrole is	a.Azine	b.Azolidine	c.Azole	d.Diazine	Azole
17.	IUPAC name of pyrimidineis	a. Azolidine	b.Azine	c.1,3-Diazine	d.Triazine	1,3-Diazine
18.	Which one of the following is not a five membered heterocyclic compounds?	a.Pyrrole	b.Furan	c.Thiophene	d.pyridine	Pyridine
19.	Which one of the following is most basic?	a.Aniline	b.Pyrrole	c.pyridine	d.Thiophene	pyridine
20.	Which of the following is not an aromatic compound?	a.Furan	b.Pyrrole	c.Piperidine	d.pyridine	Piperidine
21.	Which one of the following has least resonance energy?	a.Thiophene	b.Furan	c.Pyrrole	d.pyridine	Furan
22.	In pyridine the electrophilic substitution occurs exclusively at-	a.β-Position	b.α-position	c.ϒ-Position	d. at any of these position	β-Position
23.	The heterocyclic compound which is most reactive towards electrophilic reagent is	a.Thiophene	b.Pyrrole	c.Furan	d.pyridine	Pyrrole
24.	Nucleophilic substitution in pyridine occurs at	a.N-atom	b.α-position	c.β-Position	d.doesnot occur	α-position

25.	The hybridization ofnitrogen atom in in piperidine is	a. sp	b.sp2	c.sp3	d.unhybridized	sp3
26.	Which one of the following is most basic?	a.Aniline	b.Pyrrole	c.pyridine	d.Piperidine	Piperidine
27.	Peracid oxidation of pyridine gives	a.pyridine N-oxide	b.Picolinic acid	c.Cinchomeroni cacid	d.does notgive reaction	pyridine N-oxide
28.	Which one of the following resembles to phenol in properties?	a.Pyridine	b.Pyrrole	c.Thiophene	d.Quinoline	Pyrrole
29.	Which one of the following does not couple with diazonium salt?	a.Furan	b.Pyrrole	c.Thiophene	d.Quinoline	Thiophene
30.	Skraup synthesis is used to prepare	a.Pyridine	b.Pyrrole	c.Quinoline	d.Isoquinoline	Quinoline
31.	A condensed ring system containing a five membered heterocyclic ring is-	a.Indole	b.Isoquinoline	c.Quinoline	d.Isoxazole	Indole
32.	Oxidation of is oquinoline with alk.KMnO4 gives	a.Quinolic acid	b.Nicotinic acid	c.Cinchomeroni cacid	d.Picolinic acid	Cinchomeroni cacid
33.	Which one of the following is not a monoacid tertiarybase?	a.Pyridine	b.Quinoline	c.Isoquinoline	d.Pyrrole	Pyrrole
34.	Nucleophilic substitution in quinoline occurs at	a.N-atom	b.α-position	c.β-Position	d.ϒ-Position	α-position
35.	Which one of the following gives Dield's-Alder reaction?	a.Thiophene	b.pyridine	c.Pyrrole	d.Furan	Pyrrole
36.	The order of reactivity of five membered heterocyclic is	a.Pyrrole>Furan > Thiophene	b. Furan> Pyrrole>Thiophene	c.Pyrrole>Thiophene>Furan	d.Furan>Thiophene>Pyrrole	Pyrrole>Furan > Thiophene
37.	Which one is the weakest base among the following?	a.Pyrimidine	b.pyridine	c.Purine	d.Piperidine	Pyrimidine
38.	Write the product of the following reaction? 					

39.	 Complete the following reaction					
40.	 Complete the following reaction					
41.	When pyrrole react with methylmegnesium iodide it gives	a.Pyrrole 2-aldehyde	b.N-PyrrylMagnesium Iodide	c.2-Pyrrole azo pyrrole	d.Pyridine	N-PyrrylMagnesium Iodide
42.	When pyrrole is nitrated with nitric acid in aceticanhydride it gives	a. 2-nitro pyrrole	b.3-nitro pyrrole	c.4-nitropyrrole	d.5-nitropyridine	2-nitro pyrrole
43.	When pyrrole is halogenated with Iodine it gives	a. 2-Iodo pyrrole	b.3-Iodopyrrole	c.2,3-diiodopyrrole	d.2,3,4,5-tetraiodopyrrole	2,3,4,5-tetraiodopyrrole
44.	When thiophene is treated with isatin and H2SO4 acid---------- is formed	a.a blue colour	b.a red colour	c. a green colour	d. aviolet colour	a blue colour
45.	Which one of the following is the molecular formula of pyridine	a.C6H5N	b.C5H5N	c.C4H4N	d.C6H6NH2	C5H5N
46.	Thiophene reacts with formaldehyde and HCl to give	a. 2-Chloromethyl thiophene	b. 3-Chloromethyl thiophene	c. 3-Chloromethyl thiophene	d. 4-Chloromethyl thiophene	2-Chloromethyl thiophene
47.	When thiophene is treated with HgCl2 in the presence of sodium acetate it gives	a. 3-Chloromercuric thiophene	b.4-Chloromercuric thiophene	c.2-Chloromercuric thiophene	d. 5-Chloromercuric thiophene	2-Chloromercuric thiophene
48.	Isoquinoline when reduced withSn/HCl it gives	a.Dihydroisoquinoline	b.Trihydroisoquinoline	c.1,2,3,4-Tetrahydroisoquinoline	d.dehahydroisoquinoline	1,2,3,4-Tetrahydroisoquinoline
49.	The conversion of furan to 2-aryl furan is called	a.Gomberg reaction	b. Skraup Synthesis	c.Lipp's synthesis	d.Fischer indole	Gomberg reaction

					synthesis	
50.	The conversion of o-amino-ω-chlorostyreneto benzopyrrole is called	a. Skraup Synthesis	b.Gomberg reaction	c.Lipp's synthesis	d.Fischer indole synthesis	Skraup Synthesis
51.	The conversion of pyridine to 2-amino pyridine isknown as	a.Gomberg reaction	b. Skraup Synthesis	c.Lipp's synthesis	d.Chichibabin reaction	Chichibabin reaction
52.	When furoicacid treated withquinoline in presence ofCu-catalyst it gives	a.Furan	b.Furfural	c.Pyrrole	d.thiophene	Furan
53.	When pyridine react withhydrazine it gives	a.Triazole	b.Diazole	c.Pyrazole	d.Tetrazole	Pyrazole
54.	The completely reduced hexahydro derivative of pyridine is called	a.pyrrole	b.Piperidine	c.Thiophene	d.Pyrimidine	Piperidine
55.	The IUPAC name of picollinic acid is	a.Pyridine -2-carboxylic acid	b. Pyridine -3-carboxylic acid	c.Pyridine -4-carboxylic acid	d.Pyridine -5-carboxylic acid	Pyridine -2-carboxylic acid
56.	The IUPAC name of Nicotine is	a.Pyridine -2-carboxylic acid	b. Pyridine -3-carboxylic acid	c.Pyridine -4-carboxylic acid	d.Pyridine -5-carboxylic acid	Pyridine -3-carboxylic acid
57.	The IUPAC name of Isonicotinic acid is	a.Pyridine -2-carboxylic acid	b. Pyridine -3-carboxylic acid	c.Pyridine -4-carboxylic acid	d.Pyridine -5-carboxylic acid	Pyridine -4-carboxylic acid
58.	When pyridine react with Hcl it gives	a.Pyridinium Chloride	b.2-Chloropyridine	c.Pyridine hydrochloride	d. 3-Chloropyridine	Pyridine hydrochloride
59.	The decreasing order of reactivity for 1.2-azole is	a.Pyrazole>Isothiazole>Isoxazole	b.Isothiozole>Isoxazole>pyrazole	c.Isoxazole>pyrazole>Isothiazole	d.Pyrazole>Isoxazole>Isothiazole	Pyrazole>Isothiazole>Isoxazole
60.	When indole undergoes mannich reaction with formaldehyde and dimethylamine to form	a.3-Dimethylamino methylindole	b.4-Dimethylaminomethylindole	c.4-Dimethylamino methylindole	d.5-Dimethylamino methylindole	3-Dimethylaminomethylindole

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Reg.No.....

[15CHU501]

KARPAGAM ACADEMY OF HIGHER EDUCATION
COIMBATORE-21
(For the candidates admitted from 2015 & onwards)
B.SC DEGREE EXAMINATION
ORGANIC CHEMISTRY
INTERNAL TEST-I

DATE:
TIME: 2 HRS

SUBJECT CODE: 15CHU501
TOTAL: 50 MARKS

PART-A (20x1=20)

ANSWER ALL THE QUESTIONS:

1. A symmetry element is
a. Enantiomers b. Plane c. Diastereomers d. Resolution

2. The molecule has an axis of three fold proper rotation; this is called----------
a. a C_4 axis b. a C_3 axis c. a C_2 axis d. a C_2 axis

3. The part of the science which deals with structure in three dimensions is called----------,
a. Stereochemistry b. Food technology c. Nano chemistry d. Physical chemistry

4. Study of branch of stereochemistry is called----------
a. Conformational analysis b. Chemical analysis c. Structural analysis d. Physical analysis

5. Plane polarized light is light whose vibrations takes place in only ---------- of these possible planes.
a. Two b. Three c. One d. Four

6. The number of isomers of C_6H_{14} is
a.4 b.5 c. 6 d. 7

7. The concept of stereochemistry is based on
a. VSEPR theory b. molecular orbital theory c. valence bond theory
d. Vant Hoff and Label's theory

8. A cisoid arrangement means to
a. Eclipsed conformation b. anti staggered conformation
c. skew conformation d. gauche conformation

9. In glyceraldehydes the order of priority for RS notation is
a. $-CH_2OH$> -CHO>-OH>H b. –OH>-CH_2OH>-CHO>H
c. –OH>-CHO>-CH_2OH >H d. –CH_2OH>-OH>-CHO>H

10. A molecule is said to be chiral
a. if it contains plane of symmetry b. if it contains center of symmetry
c. if it cannot be superimposed on its mirror image d.if it cannot superimposed on its mirror image

11. The stereoisomer's related each other as non super imposable mirror images are called ---------
a. Enantiomers b. Racemic mixtures c. Diastereomers d. Resolution

12. Reaction of the type in which one of the several possible diastereomeric products predominated are called----------
a. Stereospecific reactions b. Stereoselective reactions c. Racemic mixtures
d. Meso compounds

13. Mirror image isomers are called----------
a. Enantiomers b. Diastereomers c. Monomers d. isomerism

14. A carbon atom to which four different groups are attached is a ----------
a.Chiral center b.a Chiral carbon c. Enantiomers d. Diastereomers

15. The horizontal line represent bond---------- towards is out of the plane of the paper, where as the vertical lines represent bonds---------- away from us behind the plane of the paper in Fischer-Projection formula
a. Going, going, b. Coming, coming c. Coming, going d. Going, coming

16. Which of the following reaction gives crossed products?
a.Claisen rearrangement b. Fries rearrangement c.Lossen rearrangement
d. Curtius rearrangement

17. Which of the following reaction gives temperature dependence products?
a.Perkin reaction b. Fries rearrangement c. Beckmann rearrangement
d. Claisen rearrangement

18. In the Beckmannreaction,migrating group is chiral. Select the true statement for it---,
a.it will chage its configuration while in migration,
b. It will retain its configuration while in migration,
c.it can change as well a it can retain itsconfiguration,
d. there is nothing todo with configuration

19. The conversion of amide to primary amine is known as
a.Schmidt rearrangement b. Lossen rearrangement c. Hofmann rearrangement
d. Claisen rearrangement

20. What is the reagent used in the following reaction?

$NH_2CONH_2 \longrightarrow NH_2NH_2$

a. Br_2+KOH^- b. Br_2+NaOH c. Br_2+NH_4OH d. $Br_2+NH_4\bar{O}H$

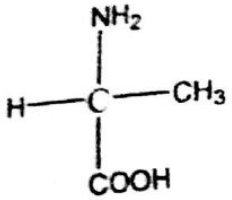
PART-B (3X10=30 MARKS)

ANSWER ALL THE QUESTIONS:

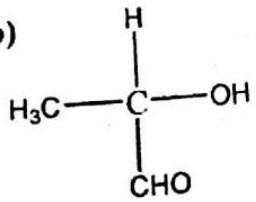
21. (a).(i). Explain Walden inversion with suitable example.

(ii) Assign R or S configuration to the following compounds.

a)



b)



(OR).

(b).(i) Define racemisation and eplain what are the methods to bring about racemisation.

(ii). Define the terms resolution.enantiomers and diastereomers

22. (a).(i).What is optical activity? Discuss the optical isomerism of lactic acid and maleic acid and describe a method for its preparation.

(ii). Discuss the geometrical isomerism of maleic and fumaric acid.

OR

(b). (i) Explain the reaction and mechanism for Hofmann rearrangement.

23. (a).What is Pinacol-Pinacolane Rearrangement? Explain its mechanism. Give the applications of Pinacole- Pinacolane rearrangement in organic synthesis.

OR

(b). (i).What is Beckmann rearrangement? Give the suitable reaction mechanism.

(ii) Explain the synthesis of nylon-6.

Reg. No……. **[15CHU501]**

KARPAGAM ACADEMY OF HIGHEREDUCATION
COIMBATORE-21
DEPARTMENT OF CHEMISTRY
I MSC CHEMISTRY
ORGANIC CHEMISTRY
INTERNAL TEST-I

DATE: **SUBJECT CODE: 15CHU501**

TIME: 2.00 HRS **TOTAL: 50 MARKS**

Answer Key

Part- A (20 x1 = 20 Marks)

ANSWER ALL THE QUESTIONS:

1.b). Plane

2. b) C_3 axis

3. a) Stereochemistry

4. a) Conformational analysis

5. c) one

6. b) 5

7. d) Vant Hoff and Label's theory

8. a)Eclipsed conformation

9.c) –OH> CHO>CH_2OH > H

10.c) If it cannot be superimposed on its mirror image

11.c) Diastereomers

12. b) Stereoselective reactions

13. a) Enantiomers

14. a) Chiral center

15. c) Coming, going

16.b) Fries rearrangement

17. b) Fries rearrangement

18. b) it will be retain its configuration while in migration

19. c) Hofmann rearrangement

20. a) Br_2 + KOH

Part B (3 X 10=30 MARKS)

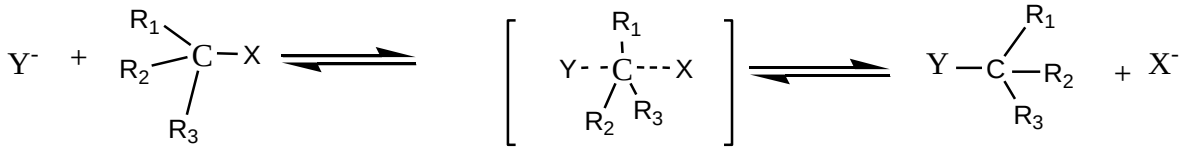
Answer all the Questions

1. 21. (a) (a). Write notes on Walden invension.

WALDEN INVERSION:

Transformation of an optically active compound in to a compound opposite configuration is called Walden Inversion or optical inversion.This phenomenon was discovered by P. Walden is 1893 and hence the name.

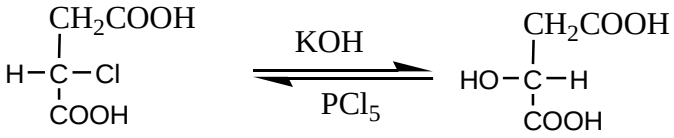
When an alkyl halide isattacked by a nucleophile (Y)from the back side there is substitution of the leaving group (X) by the nucleophile. Since two species are taking part in this substitution it is a bimolecular reaction represented as S_N^2 reaction.



Transition state

As the nucleophile approaches the carbon atom,the bond C-X is stretched. At aparticular stage both Y and X are partially attached to the carbon atom. This is called trasition state. In transition state, the three substituents namely, R_1,R_2, and R_3 lie in a single plane which is perpendicular to the Y-C-X plane. As the leaving group X leaves the bond between. Y and C in completely formed. The central atom undergoes a type of flipping. It inverts just like an umbrella turning inside out in a windstorm. This type of inversion is called Walden Inversion.

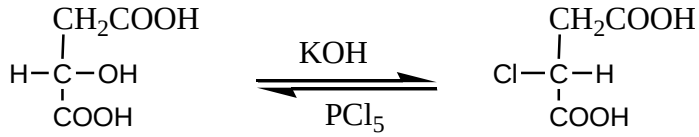
It must be noted that in Walden inversion there is a change in the sign of rotation as well as inversion of configuration. For example, when D(-) ChloroSuccinic acid is hydrolysed, it undergoes,Walden inversion to give L (+) malic acid and vice versa.



D(-)Chloro succinic acid

L-Malic acid

Similarly D (-) malic acid on treatment with PCl_5 gives L (+) Chlorosuccinic acid and vice versa.

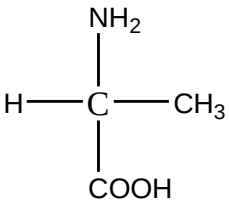


D-Malic acid

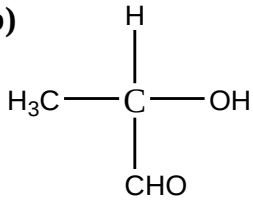
L (+) Chloro succinic acid

ii)Assign R or S configuration of the following

a)



b)



a)R configuration

b) R Configuration

OR

b)i). Define racemization and explain what are the methods to bring about racemization.

Definition:

Racemization is the process of converting an optically active compound into the racemic modifications.

Racemic modifications are also called racemic mixtures or racemates.

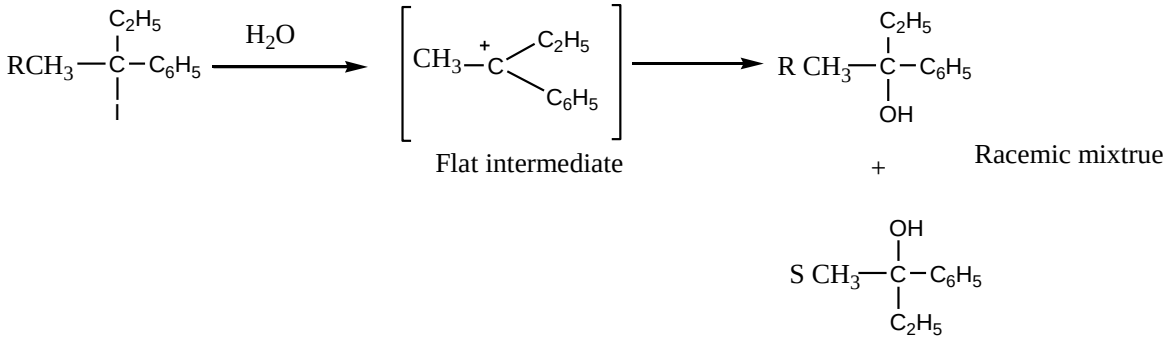
Methods to bring about racemization:

i) Action of heat:
When d or l isomer is heated we get the dl mixture.

ii) Treatment with chemical reagents:
Many substances undergo racemization when treated with chemical reagents. E.g., mandelic acid ($C_6H_5CHOHCOOH$) forms (±) bromo acid when treated with hydrobromic acid.

iii) **Substitution and rearrangements**:

Substitution and rearrangements reactions which take place via S_N^1 type stepwise mechanisms end up in racemised products.E.g.,

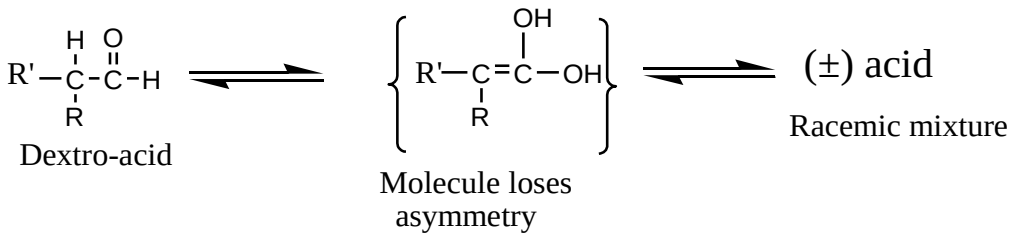


iv) Auto-racemization:

In some cases racemization occurs spontaneously at room temperature, e.g., dimethyl bromo sucinate undergoes racemization on standing at room temperature. This type of racemization is termed as auto racemization.

Mechanism of racemization:

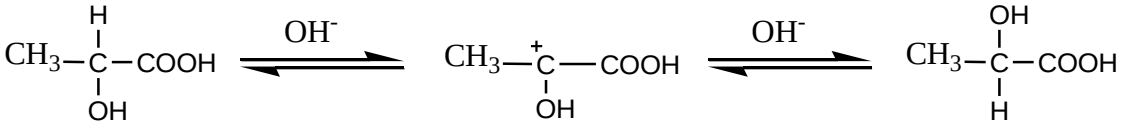
Compound which racemise readily are found to contain an asymmetric carbon atom joined to a hydrogen atom and a negative group. Such compounds readily undergo tautomeric change and racesation occurs via enolisation. For example



The intermediate enol form is nor asymmetric. When it reverts to the stable form, there are equal chances to produce the dextro and laevo forms. So it gives a racemic mixture.

In the case of a compound which cannot udergo tautometic change, mechanism of racemisation is uncertain. Howeverthe racemization is said to take place via the formation of planar intermediate which when reverts to the stable form, there are equal changes to produce the dextro and laevo forms. So it gives a racemic mixture.

This can be illustrated by taking the base catalysed racemization of (-) lactic acid.



(-) FORM (+) form

ii) Define the term resolution, enentiomers and diastereomers

Defination: "The separation of a racemic mixture into its enantiomers(dextro and laevo components) is termed as resolution".

An enantiomer is one of the two molecules that are mirror images of each other and are non-superposable.

Enantiomers have identical chemical and physical properties except for their ability to rotate plane-polarized light (+/-) by equal amounts but in opposite directions. Enantiomers interact differently with other chiral molecules i.e. biologically active molecules as aminoacids, sugars, steroids etc. This means that some molecules have, for example, different odours. Limonene is just such a case.

Diastereomers (sometimes called diastereoisomers) are a type of a stereoisomer. Diastereomerism occurs when two or more stereoisomers of a compound have different configurations at one or more (but not all) of the equivalent (related) stereocenters and are not mirror images of each other. When two diastereoisomers differ from each other at only one stereocenter they are epimers. Each stereocenter gives rise to two different configurations and thus increases the number of stereoisomers by a factor of two.

22. a) i). What is Optical activity? Discuss the optical isomerism of lactic acid and maleic acid and describe its preparation.

The angle of rotation by which the plane polarised light is rotated, can be measured by an analyzer in a polarimeter. A diagram of the polarimeter is shown in Figure 6.36.

A polarimeter consists of a light source, two nicol prisms and a sample table to hold the substance. The sample tube is placed between two nicol prisms. The prism placed near the source of light is called **polarizer** while the other placed near the eye is called **analyzer**. The aqueous solution of the substance is placed between the polarizer and analyzer. The analyzer can be rotated by certain angle to compensate for the rotation of the plane-polarized light by the optically active sample. The observed rotation ($\alpha_{observed)}$ is expressed in degrees.

If the substance rotates plane polarised light *to the right (clock wise),* it is called **dextro rotatory** (Greek for right rotation) or the *d*-form and it is indicated by placing a (+) sign before the degrees of rotation. If light is rotated *towards left (anti clock wise),* the substance is said to be **laevo rotatory** (Greek for left rotating) or the *l*-form and a negative (-) sign is placed before

the degrees of rotation. The dextro rotatory and laevo rotatory compounds are called **optically active compounds.**

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For example, lactic acid, $CH_3CH(OH)COOH$ (Figure 6.39). However, the presence of chiral carbon atoms is not a guarantee that the molecule will be optically active, and many molecules even if do not contain any chiral carbon, can still be optically active.

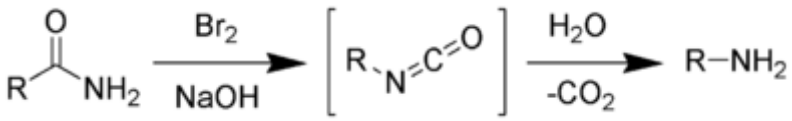
ii). Discuss the geometrical isomerism of maleic anf fumaric acid

Maleic acid or **cis-butenedioic acid** is an organic **compound** that is a **dicarboxylic**acid, a molecule with two **carboxyl groups**. Its chemical formula is $HO_2CCHCHCO_2H$. Maleic acid is the **cis-isomer** of **butenedioic** acid, whereas fumaric acid is the **trans-isomer**.

OR

b).i). Explain the reaction and mechanism of hofmannrearrangement.

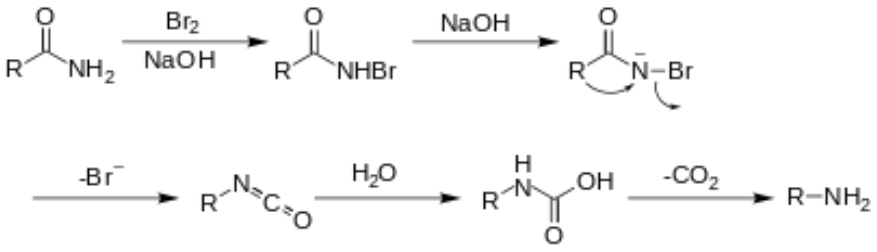
The **Hofmann rearrangement** is the organic reaction of a primary amide to a primary amine with one fewer carbon atom.



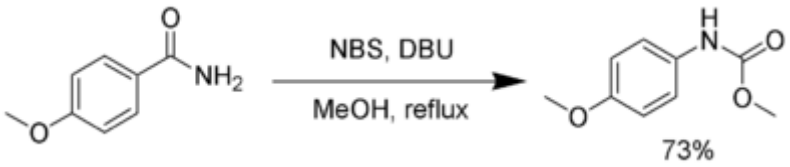
The reaction is named after its discoverer: August Wilhelm von Hofmann. This reaction is also sometimes called the **Hofmann degradation** or the **Harmon Process**, and should not be confused with the Hofmann elimination.

Mechanism:

The reaction of bromine with sodium hydroxide forms sodium hypobromite *in situ*, which transforms the primary amide into an intermediate isocyanate. The intermediate isocyanate is hydrolyzed to a primary amine, giving off carbon dioxide.



Several reagents can substitute for bromine. N-Bromosuccinimide and 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU) can effect a Hofmann rearrangement. In the following example, the intermediate isocyanate is trapped by methanol, forming a carbamate.



In a similar fashion, the intermediate isocyanate can be trapped by tert-butanol, yielding the t-butoxycarbonyl (Boc)-protected amine.

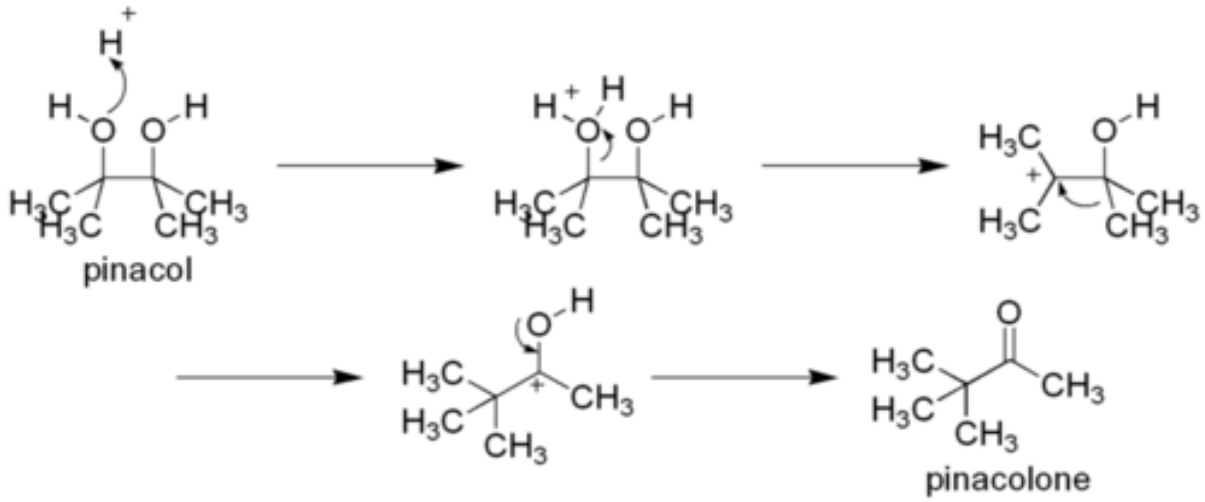
A mild alternative to bromine is also (bis(trifluoroacetoxy)iodo)benzene.

Applications:

Aliphatic & Aromatic amides are converted into aliphatic and aromatic amines, respectively
In the preparations of Anthranilic Acid from Phthalimide
Nicotinic acid is converted into 3-Amino pyridine
The Symmetrical structure of α-phenyl propanamide does not change after hofmann reaction.

23. a). What is pinacole pinacolone rearrangement? Explain its mechanism. Give the application of pinacole pinacolone rearrangement in organic synthesis?

The **pinacol rearrangement** or **pinacol–pinacolone rearrangement** is a method for converting a 1, 2-diol to a carbonyl compound in organic chemistry. This 1, 2-rearrangementtakes place under acidic conditions. The name of the reaction comes from the rearrangement of pinacol to pinacolone.



This reaction was first described by Wilhelm Rudolph Fittig in 1860.

Mechanism:

In the course of this organic reaction, protonation of one of the –OH groups occurs and a carbocation is formed. If both the –OH groups are not alike, then the one which yields a more stable carbocation participates in the reaction. Subsequently, an alkyl group from the adjacent carbon migrates to the carbocation center. The driving force for this rearrangement step is believed to be the relative stability of the resultant oxonium ion, which has complete octet configuration at all centers (as opposed to the preceding carbocation). The migration of alkyl groups in this reaction occurs in accordance with their usual migratory aptitude, i.e. Aryl >>>> hydride > Phenyl > tertiary carbocation (if formed by migration) > secondary carbocation (if formed by migration) > methyl cation . The conclusion which group stabilizes carbocation more effectively is migrated

Stereochemistry:

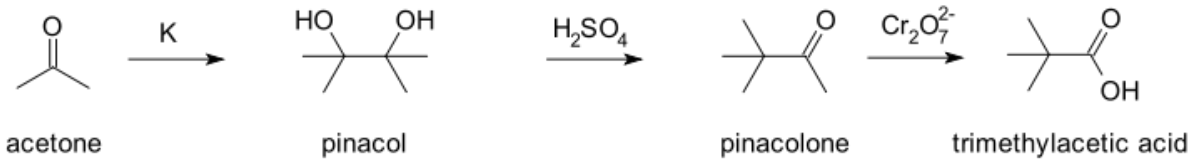
In cyclic systems, the reaction presents more features of interest. In these reactions, the stereochemistry of the diol plays a crucial role in deciding the major product. An alkyl group which is situated trans- to the leaving –OH group alone may migrate. If otherwise, ring expansion occurs, i.e. the ring carbon itself migrates to the carbocation centre. This reveals another interesting feature of the reaction, viz. that it is largely concerted. There appears to be a connection between the migration origin and migration terminus throughout the reaction.

Moreover, if the migrating alkyl group has a chiral center as its key atom, the configuration at this center is *retained* even after migration takes place.

Although Fittig first published about the pinacol rearrangement,it was not Fittig but Aleksandr Butlerov who correctly identified the reaction products involved.

In a 1859 publication Wilhelm Rudolph Fittig described the reaction of acetone with potassium metal... Fittig wrongly assumed a molecular formula of $(C_3H_3O)_n$ for

acetone, the result of a long standing atomic weight debate finally settled at the Karlsruhe Congress in 1860. He also wrongly believed acetone to be an alcohol which he hoped to prove by forming a metal alkoxide salt. The reaction product he obtained instead he called paraceton which he believed to be an acetone dimer. In his second publication in 1860 he reacted paraceton with sulfuric acid (the actual pinacol rearrangement).



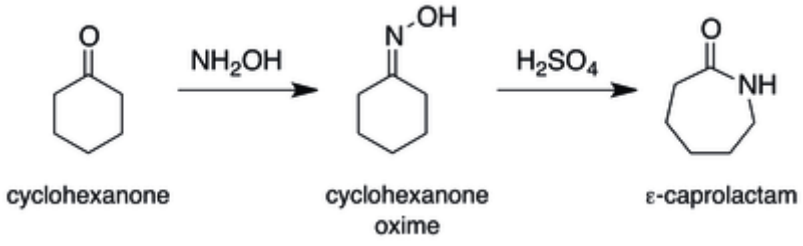
Again Fittig was unable to assign a molecular structure to the reaction product which he assumed to be another isomer or a polymer. Contemporary chemists who had already adapted to the new atomic weight reality did not fare better. One of them, Charles Friedel, believed the reaction product to be the epoxide tetramethylethylene oxide in analogy with reactions of ethylene glycol. Finally Butlerov in 1873 came up with the correct structures after he independently synthesised the compound trimethylacetic acid which Friedel had obtained earlier by oxidizing with a dichromate.

Some of the problems during the determination of the structure are because carbon skeletal rearrangements were unknown at that time and therefore the new concept had to be found. Butlerov theory allowed the structure of carbon atoms in the molecule to rearrange and with this concept a structure for pinacolone could be found.

OR

b) i) What is Beckmann rearrangement? Give the suitable reactionmechanism.ii)Explain the synthesis of nylon-6

The **Beckmann rearrangement**, named after the German chemist Ernst Otto Beckmann (1853–1923), is an acid-catalyzed rearrangement of an oxime to an amide. Cyclic oximes yield lactams.

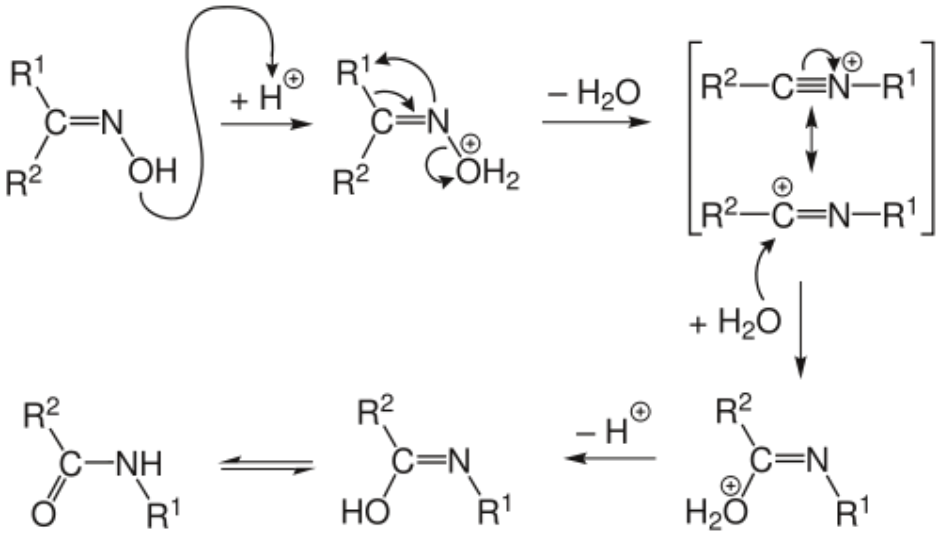


This example reaction starting with cyclohexanone, forming the reaction intermediate cyclohexanone oxime and resulting in caprolactam is one of the most important applications of the Beckmann rearrangement, as caprolactam is the feedstock in the production of Nylon 6.

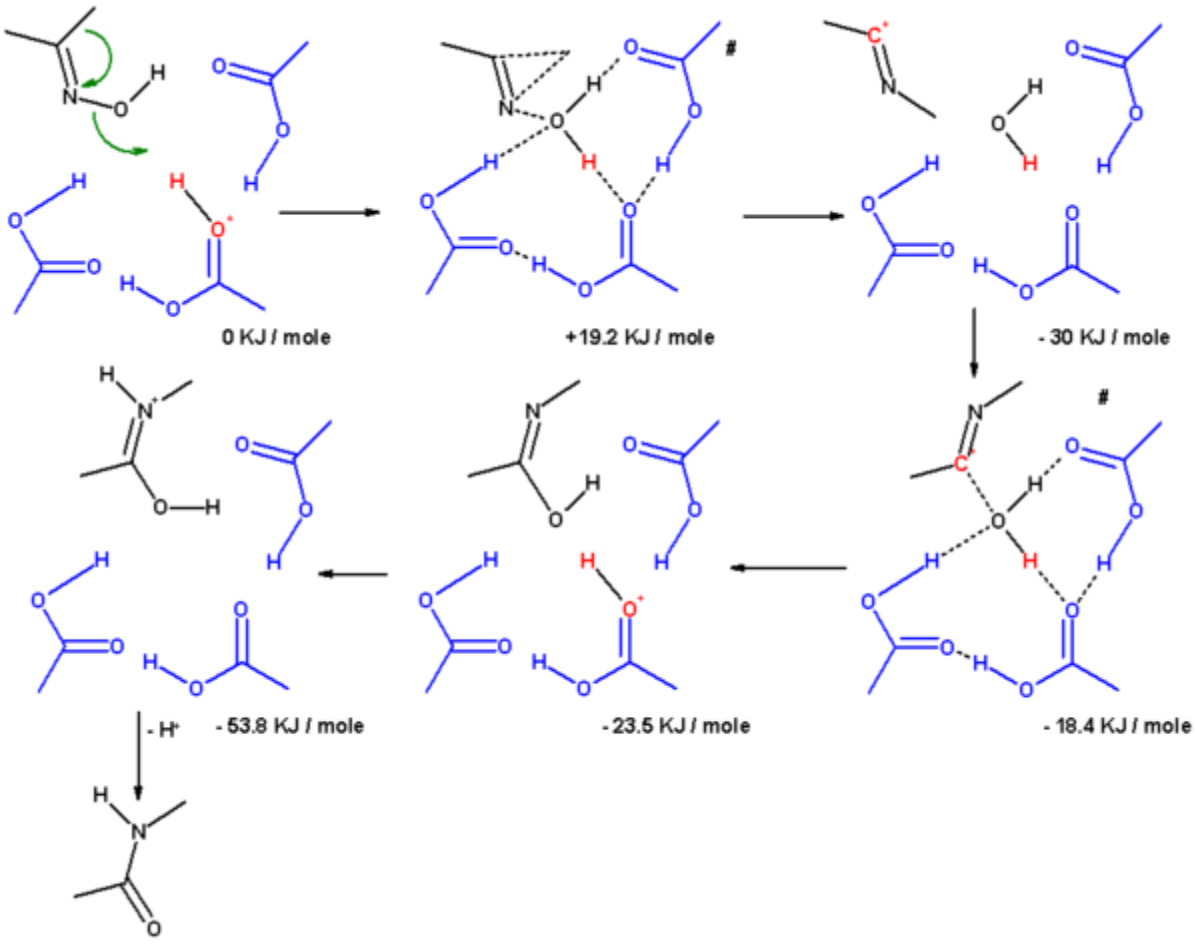
The **Beckmann solution** consists of acetic acid, hydrochloric acid and acetic anhydride, and was widely used to catalyze the rearrangement. Other acids, such as sulfuric acid orpolyphosphoric acid, can also be used. Sulfuric acid is the most commonly used acid for commercial lactam production due to its formation of an ammonium sulfate by-product when neutralized with ammonia. Ammonium sulfate is a common agricultural fertilizer providing nitrogen and sulfur.

Mechanism:

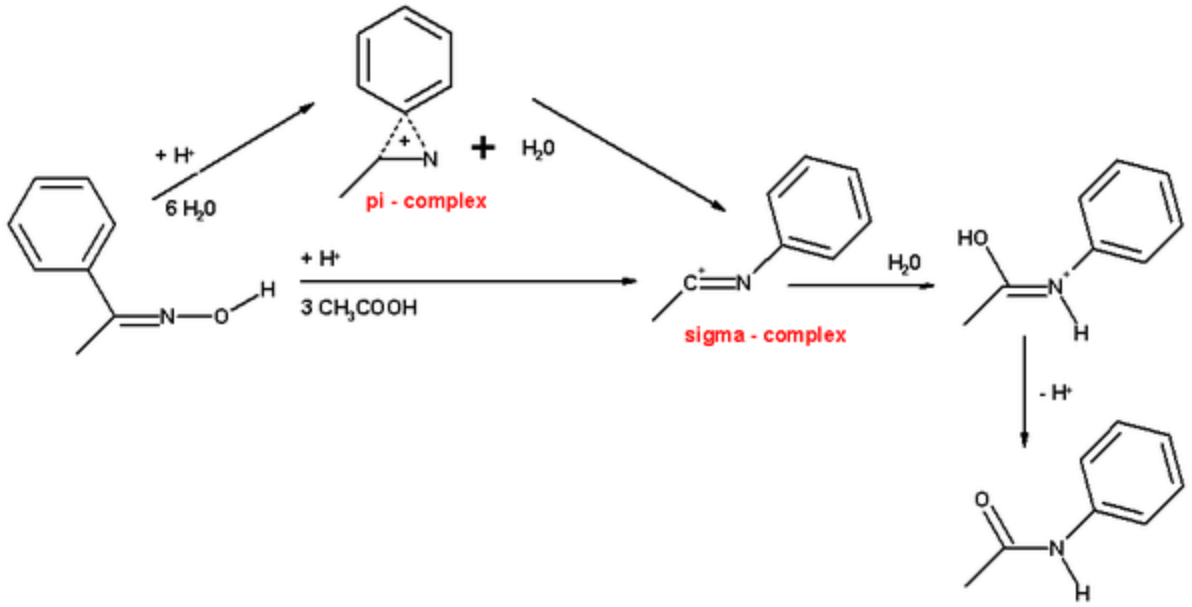
The reaction mechanism of the Beckmann rearrangement is in general believed to consist of an alkyl migration with expulsion of the hydroxyl group to form a nitrilium ion followed by hydrolysis:



In one study, the mechanism is established in silico taking into account the presence of solvent molecules and substituents. The rearrangement of acetone oxime in the Beckmann solution involves three acetic acid molecules and one proton (present as an oxonium ion). In the transition state leading to the iminium ion (σ-complex), the methyl group migrates to the nitrogen atom in a concerted reaction and the hydroxyl group is expulsed. The oxygen atom in the hydroxyl group is stabilized by the three acetic acid molecules. In the next step the electrophilic carbon atom in the nitrilium ion is attacked by water and the proton is donated back to acetic acid. In the transition state leading to the N-methyl acetimidic acid, the water oxygen atom is coordinated to 4 other atoms. In the third step, an isomerization step protonates the nitrogen atom leading to the amide.



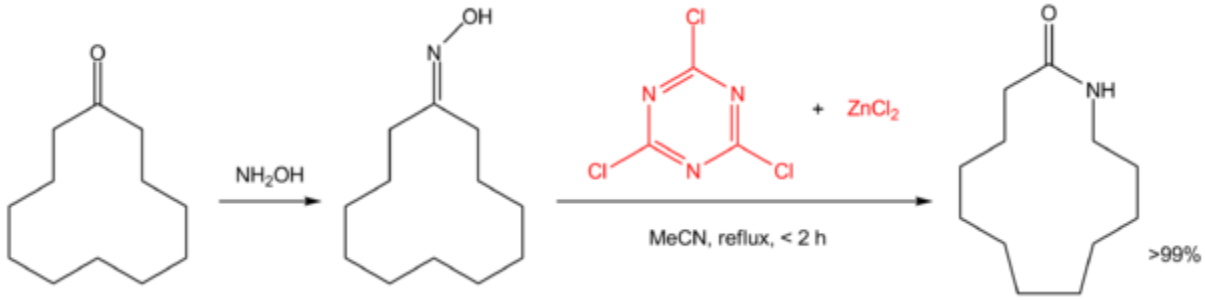
The same computation with a hydroxonium ion and 6 molecules of water has the same result, but, when the migrating substituent is phenyl in the reaction of acetophenone oxime with protonated acetic acid, the mechanism favors the formation of an intermediate three-membered π-complex. This π-complex is again not found in the H_3O^+ $(H_2O)_6$.



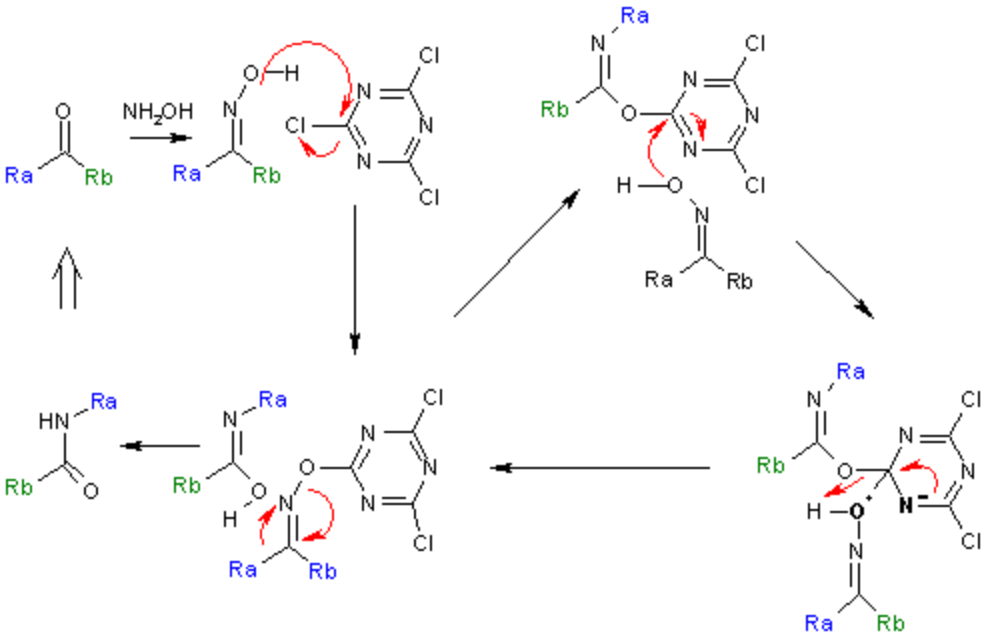
With the cyclohexanone-oxime, the relief of ring strain results in a third reaction mechanism, leading directly to the protonated caprolactam in a single concerted step without the intermediate formation of a π-complex or σ-complex.

Cyanuric Chloride Assisted Beckmann Reaction:

Beckmann reaction is known to be catalyzed by cyanuric chloride and zinc chloride co-catalyst. For example, cyclododecanone can be converted to the corresponding lactam, amonomer for the production of Nylon 12.

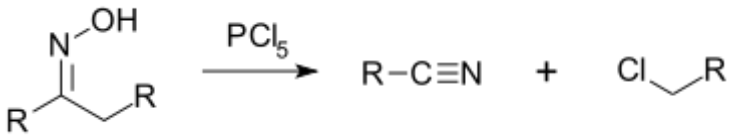


The reaction mechanism for this reaction is based on a catalytic cycle with cyanuric chloride activating the hydroxyl group via a nucleophilic aromatic substitution. The reaction product is dislodged and replaced by new reactant via an intermediate Meisenheimer complex.

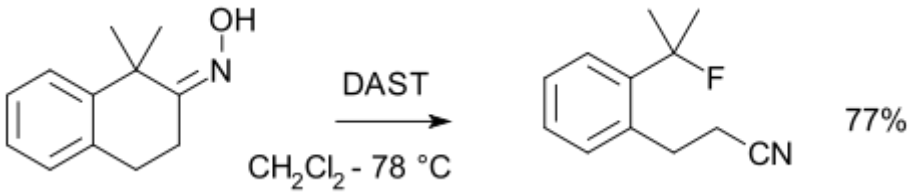


Beckmann fragmentation:

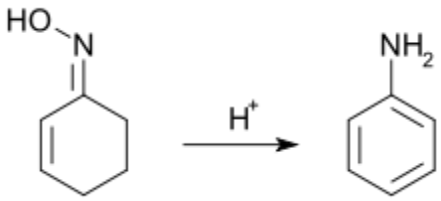
When the oxime has a quaternary carbon atom in an anti position to the hydroxyl group a fragmentation occurs forming a nitrile:



The fluorine donor in this fragmentation reaction is diethylaminosulfur trifluoride (DAST):



The oxime of cyclohexenone with acid forms aniline in a dehydration – aromatization reaction called the **Semmler–Wolff reaction** or **Wolff aromatization**



Reg.No..... [15CHU501]

KARPAGAM ACADEMY OF HIGHER EDUCATION
COIMBATORE-21
(For the candidates admitted from 2015 & onwards)
B.SC DEGREE EXAMINATION
ORGANIC CHEMISTRY
INTERNAL TEST-II

DATE: 7-8-2017 AN **SUBJECT CODE: 15CHU501**
TIME: 2 HRS **TOTAL: 50 MARKS**

PART-A (20x1=20)

ANSWER ALL THE QUESTIONS:

1. Fructose is leavorotatory yet it is written as D-fructose. This 'D' indicates
a.specific rotation b.Generic relationship to D-glyceraldehyde c.Mutarotation d.Resolution

2. Invert sugar is
a.Sucrose b. Mixture of Glucose+Fructose c.Mannose d.D-xylose

3. Hydrolysis of D-Lactosegives
a.Glucose+Galactose b.Galactose+Fructose c.Glucose +Fructose d.Only glucose

4. Benzidine reacts with Br_2 in KOH it gives
a.aniline b.urea c.amide d.ammonia

5. A freshly prepared solution of glucose has specific rotation of +112° but on keeping for some time it changes to +52.7°. This phenomenon is known as
a.Mutarotation b.Epimerization c.Racemisation d.Resolution

6. The specific rotation for identification of carbohydrate is
a.Molisch's test b.Tollen's test c.Fehling's test d.Benedicts test

7. Glucose does not restore the pink colour of Schiff's reagent. It is due to
a. aldehyde involved in hemiacetal formation b.no aldehyde group
c.-I effect of -OH group d.keto group

8. The reagent which can be used to distinguish between starch and cellulose is
a.Tollen's test b.Iodine solution c.acetic anhydride d.Fehling's reagent

9. When benzil treated with NaOH it gives
a.Benzilic acid b.benzanilide c.benzoic acid d.benzyl alcohol

10. The Claisen condensation is often used in preparing
a. β-hydroxy ester b.α-hydroxy ester c.α-keto ester d. β-keto ester

11. Method used to ascend the aldoses series is known as
a.Ruff degradation b.Wolf's degradation c.Killiani synthesis d.Zemplen's modification

12. Monosaccharides undergo reversible isomerisation in the presence of dilute alkali.This reaction is
a.Mutarotation b.Lobry de-Bruynand Albedra Van Ekenstein rearrangement
c.Killiani synthesis d.wood's synthesis

13. Which one of the following is not a polysaccharide?
a.cellulose b.sucrose c.Amylose d.Inulin

14. Epimers differ in configuration at
a. C-1carbon b.C-2 carbon c.C-3 carbon d.C-3 carbon

15. The carbohydrate which has an extremely high molecular weight (macromolecule) is
a.cellulose b.maltose c.cellobiose d.lactose

16. Which one othe following is non reducing carbohydrate?
a.lactose b.maltose c.sucrose d.glucose

17. Both glucose and mannose can be prepared byKilliani synthesis from
a. D-ribose b.D-lyxose c. D-arabinose d.D-xylose

18. How many isomeric aldohexoses are possible for the molecularformula $C_6H_{12}O_6$?
a.2 b.4 c.8 d.16

19. Sucrose on hydrolysis gives
a. 2 molecules of glucose b.2 molecules of fructose
c. 1molecule each of glucose and fructose d. 1 molecule each of glucose and mannose

20. Common table sugar is disaccharide of
a. glucose and mannose b.glucose and fructose
c.fructose and mannose d. glucose and lactose

PART-B (3X10=30 MARKS)
ANSWER ALL THE QUESTIONS

21. (a). Explain the mechanism of following reactions
i) Curtius rearrangement.
ii) Cope rearrangement

OR

(b)What is Fries Rearrangement? Explain its mechanism.

22. (a) (i). Give the conversion of the Ketose in to the corresponding Aldose.
(ii). Explain Epimerization.

OR

(b). Discuss the structure of D-Glucose

23. (a).Explain the following:
(i). Killiani synthesis
(ii) Mutarotation
(iii)Sucrose does not show mutarotation

OR

(b). What happens when Fructose is treated with (i) Mettalic Hydroxides (ii) Na/Hg (iii)Semicarbazide (iv) Phenylhydrazine.

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I MSC CHEMISTRY
ORGANIC CHEMISTRY
INTERNAL TEST-II

DATE: **SUBJECT CODE: 15CHU501**

TIME: 2.00 HRS **TOTAL: 50 MARKS**

Answer Key

Part- A (20 x1 = 20 Marks)

ANSWER ALL THE QUESTIONS:

1.b. generic relationship to D-glyceraldehyde

2. b. mixture of glucose and fructose

3. a. glucose + galactose

4. a. aniline

5. a. mutarotation

6. a. molisch's test

7. a. aldehyde involved in hemiacetal formation

8b. Iodine solution

9.a.benzilic acid

10. d. β-ketoester

11.c. Killiani synthesis

12.b.Lobry de-Bruynand Albedra Van Ekenstein rearrangement

13.b. sucrose

14.b.C-2 carbon

15.a. cellulose

16.c . sucrose

17.c.D-arabinose

18. d.16

19. c. 1 molecule of each glucose and fructose

20b. glucose and fructose

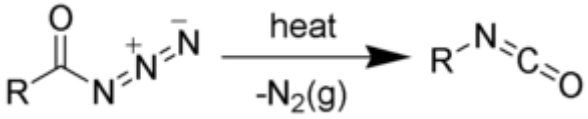
Part-B (3 x10=30 marks)

ANSWER ALL THE QUESTIONS:

21.a) Explain the mechanism of the following reactions

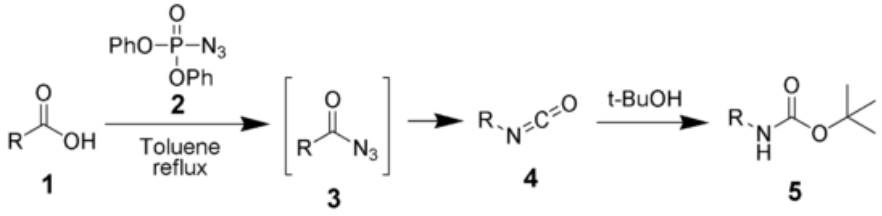
i) Curtius rearrangement ii) cope rearrangement

The **Curtius rearrangement** (or **Curtius reaction** or **Curtius degradation**), as first defined by Theodor Curtius, is a chemical reaction that involves the rearrangement of an acyl azide to an isocyanate. Several reviews have been published.



The isocyanate can be trapped by a variety of nucleophiles. Water is often added in order to hydrolyze the isocyanate to an amine. When done in the presence of *tert*-butanol, the reaction generates Boc-protected amines, useful intermediates in organic synthesis.

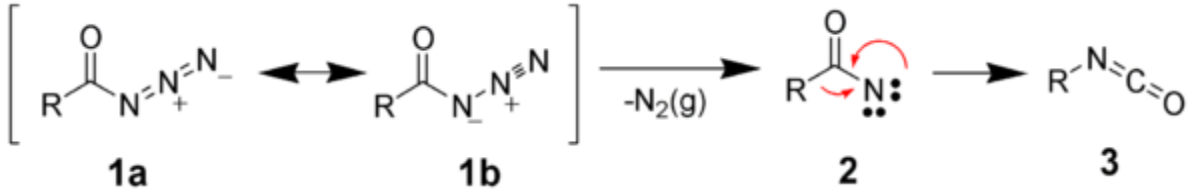
Carboxylic acids **1** can be easily converted to acyl azides **3** using diphenylphosphoryl azide **2**.



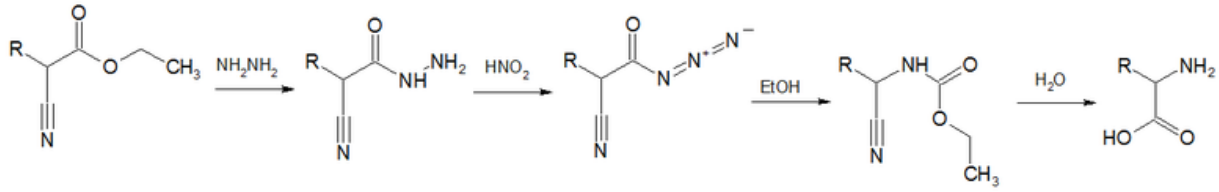
Likewise, when the Curtius reaction is performed in the presence of benzyl alcohol, Cbz-protected amines are formed.

Mechanism:

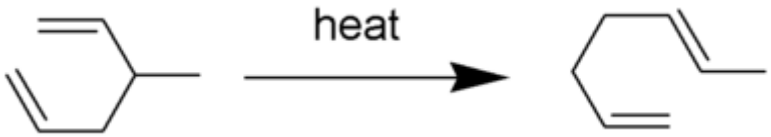
The Curtius rearrangement may be thought of as a two-step process, the first step being the loss of nitrogen gas, forming an acyl nitrene (**2**), and the second step being the rearrangement of acyl nitrenes by migration of R-group to form the desired isocyanate (**3**). However, current evidence indicates that these two steps are likely concerted (i.e., they occur at the same time), and no free nitrene intermediate is formed.



In one variation called the **Darapsky degradation** (A. Darapsky, 1936), a Curtius rearrangement takes place as one of the steps from a α-cyanoester to an amino acid.



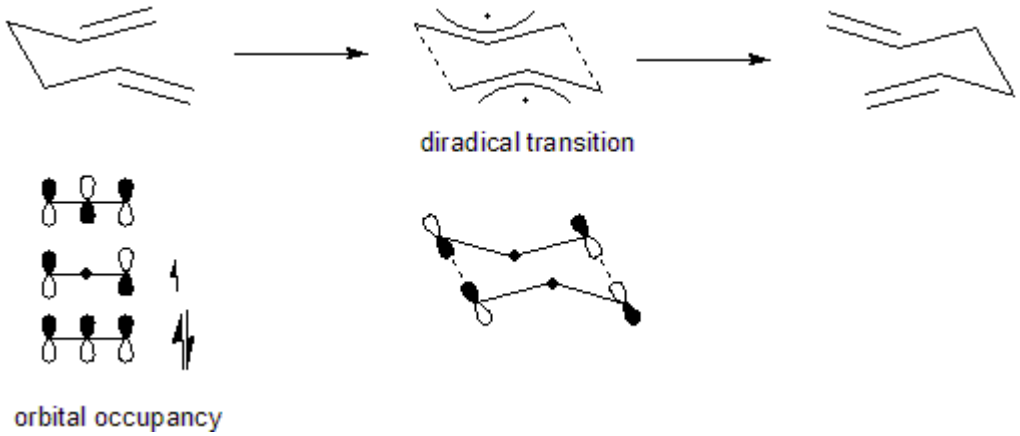
The **Cope rearrangement** is an extensively studied organic reaction involving the [3,3]-sigmatropic rearrangement of 1,5-dienes. It was developed by Arthur C. Cope. For example 3-methyl-1, 5-hexadiene heated to 300°C yields 1, 5-heptadiene.



The Cope rearrangement causes the fluxional states of the molecules in the bullvalene family.

Mechanism:

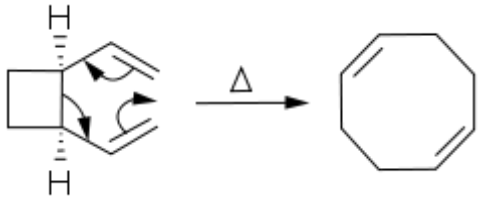
Although the Cope rearrangement is concerted and pericyclic, it can also be considered to go via a transition state that is energetically and structurally equivalent to adiradical.[*citation needed*] This is an alternative explanation which remains faithful to the uncharged nature of the Cope transition state, while preserving the principles of orbital symmetry. This also explains the high energy requirement to perform a Cope rearrangement. Although illustrated in the chair conformation, the Cope can also occur with cyclohexadienes in the "boat" conformation.



The above description of the transition state is not quite correct. It is currently generally accepted that the Cope rearrangement follows an allowed concerted route through a homoaromatic transition state and not a diradical. That is unless the potential energy surface is perturbed to favor the diradical.

Examples:

The rearrangement is widely used in organic synthesis. It is symmetry-allowed when it is suprafacial on all components. The transition state of the molecule is passes through a boat or chair like transition state. An example of the Cope rearrangement is the expansion of a cyclobutane ring to a 1, 5-cyclooctadiene ring:



b) What is Fries rearrangement? Explain its mechanism.

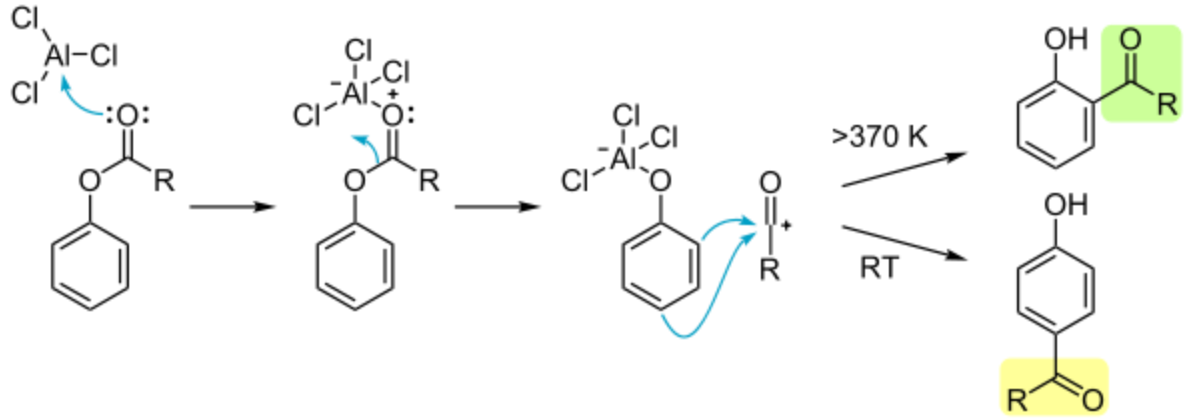
The **Fries rearrangement**, named for the German chemist Karl Theophil Fries, is a rearrangement reaction of a phenyl ester to a hydroxy aryl ketone by catalysis of Lewis acids.

It involves migration of an acyl group of phenyl ester to benzene ring. The reaction is ortho and para selective and one of the two products can be favoured by changing reaction conditions, such as temperature and solvent.

Mechanism:

Despite many efforts a definitive reaction mechanism for the Fries rearrangement is not available. Evidence for inter- and intramolecular mechanisms have been obtained by so-called

cross-experiments with mixed reactants. Reaction progress is not dependent on solvent or substrate. A widely accepted mechanism involves a carbocation intermediate.



In the first reaction step a Lewis acid for instance aluminium chloride AlCl 3 co-ordinates to the carbonyl oxygen atom of the acyl group. This oxygen atom is more electron rich than the phenolic oxygen atom and is the preferred Lewis base. This interaction polarizes the bond between the acyl residue and the phenolic oxygen atom and the aluminium chloride group rearranges to the phenolic oxygen atom. This generates a free acylium carbocation which reacts in a classical electrophilic aromatic substitution with the aromatic ring. The abstracted proton is released as hydrochloric acid where the chlorine is derived from aluminium chloride. The orientation of the substitution reaction is temperature dependent. A low reaction temperature favors para substitution and with high temperatures the ortho product prevails. Formation of the ortho product is also favoured in non-polar solvents; as the solvent polarity increases, the ratio of the para product also increases.

Phenols react to esters but do not react to hydroxyarylketones with acylhalogen compounds under Friedel-Crafts acylation reaction conditions and therefore this reaction is of industrial importance for the synthesis of hydroxyarylketones which are important intermediates for several pharmaceutics such as paracetamol and salbutamol. As an alternative toaluminium chloride, other Lewis acids such as boron trifluoride and bismuth triflate or strong protic acids such as hydrogen fluoride and methanesulfonic acid can also be used. In order to avoid the use of these corrosive and environmentally unfriendly catalysts altogether research into alternative heterogeneous catalysts is actively pursued.

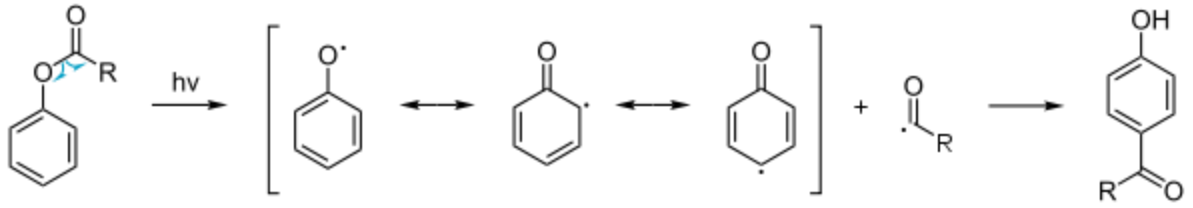
Limits:

In all instances only esters can be used with stable acyl components that can withstand the harsh conditions of the Fries rearrangement. If the aromatic or the acyl component is heavily substituted then the chemical yield will drop due to steric constraints. Deactivating meta-

directing groups on the benzene group will also have an adverse effect as can be expected for a Friedel–Crafts acylation.

Photo Fries Rearrangement:

In addition to the ordinary thermal phenyl ester reaction a so-called photochemical **Photo-Fries rearrangement** exists that involves a radical reaction mechanism. This reaction is also possible with deactivating substituents on the aromatic group. Because the yields are low this procedure is not used in commercial production. However, photo-Fries rearrangement may occur naturally, for example when a plastic bottle made of polyethylene terephthalate (PET) is exposed to the sun, particular to UV light at a wavelength of about 310 nm, if the plastic has been heated to 40 degrees Celsius or above (as might occur in a car with windows closed on a hot summer day). In this case, photolysis of the ester groups would lead to leaching of phthalate from the plastic.



Anionic fries rearrangement:

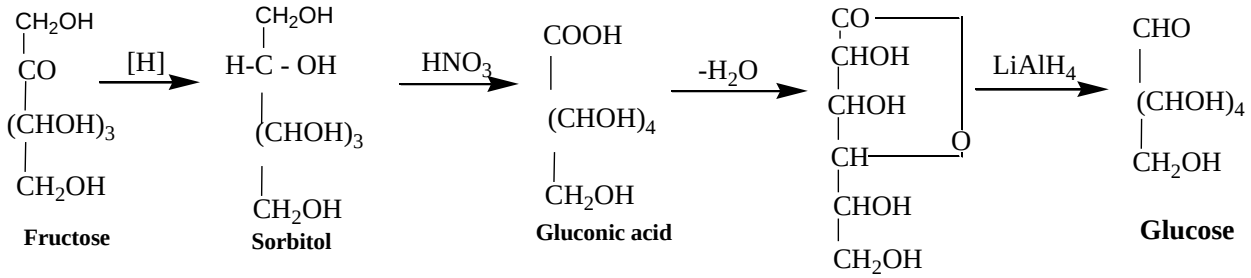
In addition to Lewis acid and photo-catalysed Fries rearrangements, there also exists an anionic Fries rearrangement. In this reaction, the aryl ester undergoes ortho-metallation with a strong base, which then rearranges in a nucleophilic attack mechanism.

22.a) i) Give the conversion of the ketose in to corresponding aldose.

ii) Expalain Epimerization.

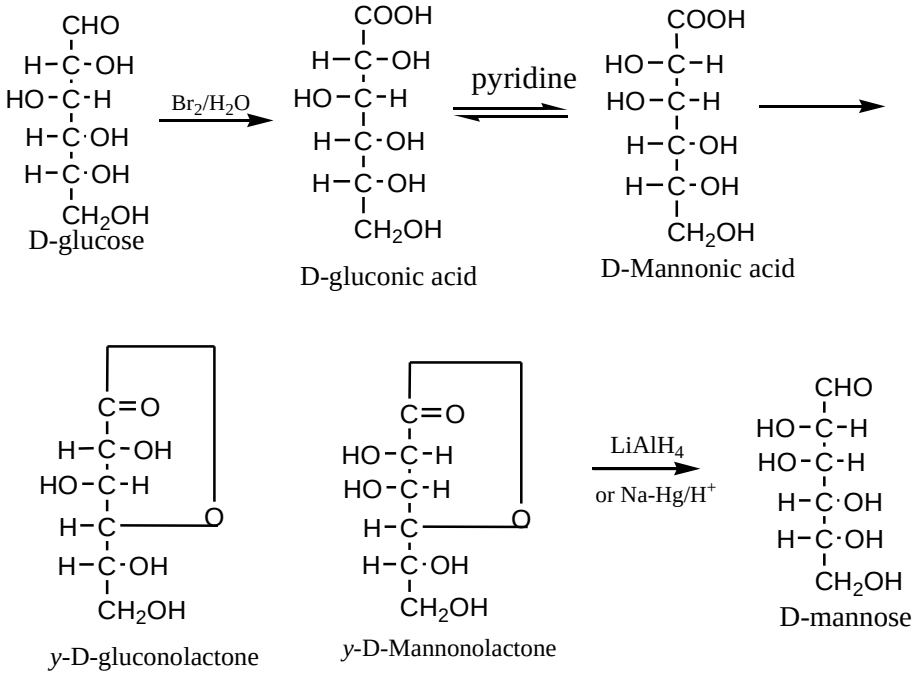
Conversion of Fructose into Glucose

Fructose is first reduced with sodium amalgam to give hexitols. These are next oxidised with nitric acid to yield the corresponding mono-carboxylic acids which on treatment with dil.HCl give γ- lactones. The individual lactones are reduced with $LiAlH_4$ to obtain the corresponding aldohexoses. In this conversion, both mannose and glucose are obtained but the route for the conversion of fructose to glucose alone is give below:



Conversion of Aldose in to its Epimeric Aldose: (Epimerisation)

The aldose is first oxidized with bromine water to give the corresponding aldonic acid, which is then heated in aqueous pyridine or quinoline to give an equilibrium mixture of the original acid and its isomer. These isomeric aldonic acids are identical in all respects expect for the configuration about the asymmetric carbon number 2. They are, therefore, epimers (or more precisely C-2-epimers). These acids are next converted in to lactones. Separated and reduced to the original aldose and its C-2-epimer. Thus D-glucose may be converted into D-mannose as shown below.



This change of configuration of one asymmetric carbon atom in a compound containing two or more asymmetric carbon atoms is known as epimerization.

OR

B) Discuss the structure of D-Glucose.

Glucose, *dextrose* (grape sugar) is the central carbohydrate of living organisms of all types, the major source of energy. It is widely distributed in nature as the monosaccharides in ripe grapes. Honey,sweet fruit and as a component of disaccharides-lactose, maltose, sucrose and cellobiose. It is the building unit from which the polysaccharides like starch, cellulose and glycogen are formed. It is also normal constituent of blood and occurs in urine of diabetics.

1) Commercially pure D(+) glucose is manufactured by heating starch with dilute hydrochloric acid under pressure:

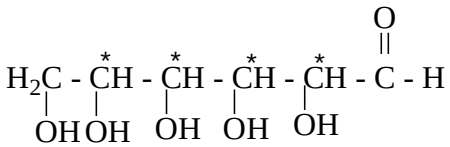
$$(C_6H_{10}O_5)_n + n\ H_2O \xrightarrow{\text{dil.HCl}} n\ C_6H_{12}O_6$$

2) It is formed as an intermediate product in the fermentation of starch for the manufacture of ethyl alcohol.
3) Glucose is made by the hydrolysis of sucrose by boiling with dilute hydrochloric acid in alcoholic solution. Glucose and fructose are obtained in equal amounts. On cooling the resulting solution, glucose being less soluble than fructose, separates out.

$$\underset{\textbf{sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{\text{dil.HCl}} \underset{\textbf{glucose}}{C_6H_{12}O_6} + \underset{\textbf{fructose}}{C_6H_{12}O_6}$$

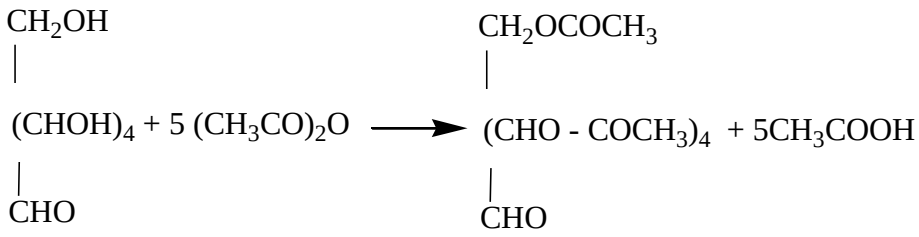
Properties

Glucose is a white crystalline solid (m.p 419 K), sweet to taste. It is readily soluble in water. Naturally occurring glucose is *dextro-rotatory* (hence, the name Dextrose) and it has four asymmetric carbon atom (marked by *).

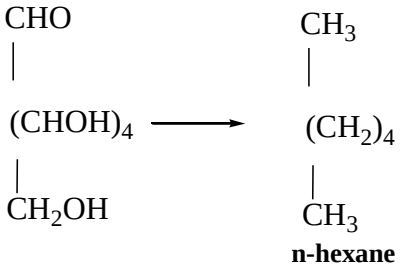


Structural formula of glucose indicates the presence of one aldehydic group, one primary alcoholic group and four secondary alcoholic groups. Chemical properties of glucose are, therefore, the properties of the above functional groups. The structural elucidation very easily follows from its reactions:

1) Quantitative analysis establishes the empirical formula as CH_2O.
2) The molecular weight of glucose determined from a study of the depression of freezing point of glucose solution, shows a value of 180. When this is compared with the empirical formula weight, the conclusion reached is that the molecular formula is $(CH_2O)_6$ or $C_6H_{12}O_6$.
3) The presence of the five alcoholic groups is indicated by its reaction with 5 moles of acetyl chloride or acetic anhydride.

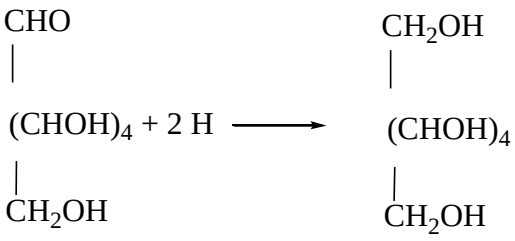


4) Reduction of glucose with concentrated hydriodic acid and red phosphorus at 373 K yields 2-iodohexane. Prolonged heating produces n-hexane. This would mean that glucose is a straight chain compound of six carbon atoms.

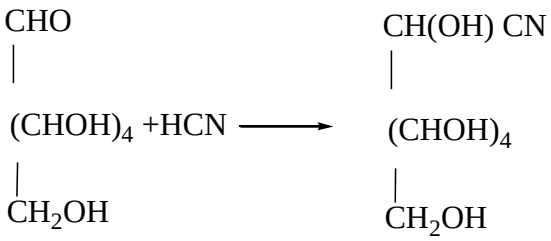


n-hexane

5) The nature of the carbonyl group is indicated by its reaction with mild reducing agent. When reduced with sodium amalgam in aqueous solution, the aldehyde group is reduced to a primary alcoholic group to yield a hexahydric alcohol, called sorbitol.

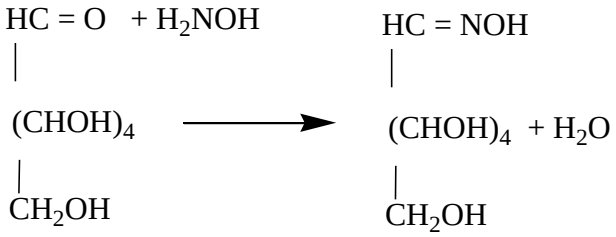


6) Glucose gives addition product with hydrogen cyanide *(but not with ammonia or sodium bisulphite).* This reaction indicates the presence of a carbonyl group.

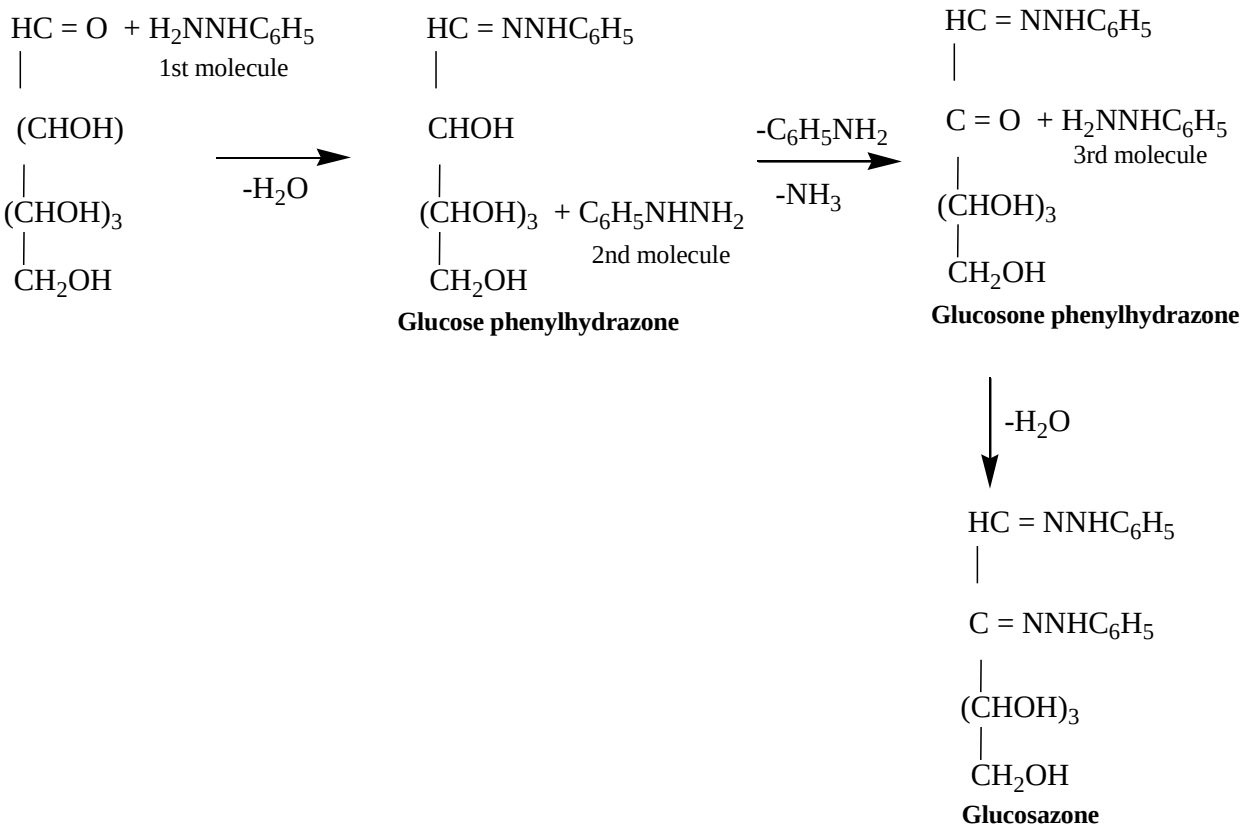


glucose cyanohydrin

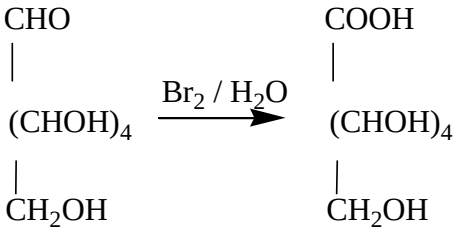
7) Glucose condenses with hydroxylamine to yield the oxime with the elimination of a water molecule.



8) Glucose reacts with one molecule of phenylhydrazine in acetic acid which condenses with the aldehyde group to give *phenylhydrazone.* When warmed with excess phenylhydrazine, the secondary alcoholic group, adjacent to the aldehyde group, is next oxidised to a keto group. With this keto group, third molecule of phenylhydrazine condenses to yield *glucosazone:*

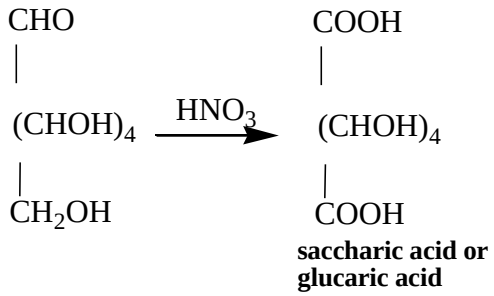


9) With mild oxidising agents like bromine water, glucose is oxidised to gluconic acid, an acid with the same number of carbon atoms. In this reaction, the aldehyde group alone gets oxidised.



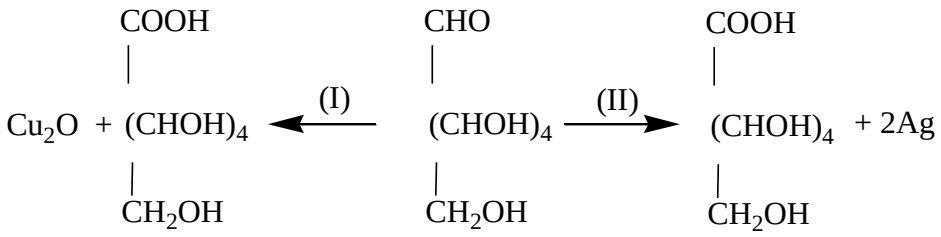
gluconic acid

10) With strong oxidising agents like nitric acid, it is oxidised to a dicarboxylic acid, saccharic acid. Nitric acid is able to oxidise the primary alcohol group also to an acid group.



saccharic acid or glucaric acid

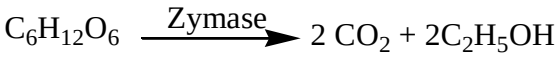
11) Because glucose is readily oxidised, it acts as a strong reducing agent. It reduces both Fehling's solution (I) and Tollen's reagent [ammoniacal silver nitrate, (II)]



The above reactions (5 to 11) confirm the presence of an aldehyde group in glucose.

Other Reactions of Glucose

12) Glucose on fermentation yields ethyl alcohol.



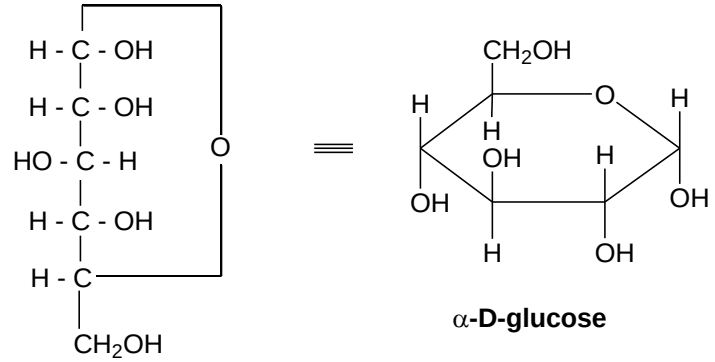
13) A dilute solution of glucose when warmed with dilute alkali solution, gives a mixture of glucose, fructose and mannose.

14) When heated with concentrated hydrochloric acid, it gives laevulic acid and hydroxymethyl furfural.

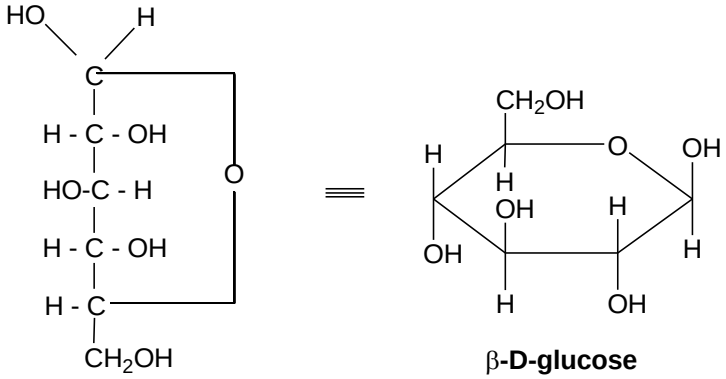
All the above reactions of glucose indicate that glucose is a polyhydric alcohol with a terminal aldehyde group and that it is a straight chain compound.

As mentioned earlier, glucose does not react with ammonia or sodium bisulphite. Further, it exists in two isomeric forms, α- and β – glucose. The evidence for these forms is *muta rotation.* α – glucose with specific rotation $+110^{o}$ is obtained by crystallizing glucose form alcoholic or acetic acid solution whereas β – glucose with specific rotation $+19.7^{o}$ is obtained by crystallizing

glucose form pyridine solution. An aqueous solution of glucose shows muta roration *(meaning, a change of rotation)* i.e., its specific rotation gradually falls from $+110^{o}$ to $+52.5^{o}$ in the case of α – glucose and increases from $+19.7^{o}$ to $+52.5^{o}$ in the case of β – glucose. To account for these facts satisfactorily, Tollen suggested a ring formula with no free aldehyde group. The ring structure for glucose is best representing by a hexagonal formula base on *pyran.*



α-D-glucose



β-D-glucose

Uses

1) It is used as a sweetening agent in confectionery.
2) It is utilised in the manufacture of ascorbic acid (Vitamin C).

It serves as food for invalids and as food preservatives.

23. a) Explain the following

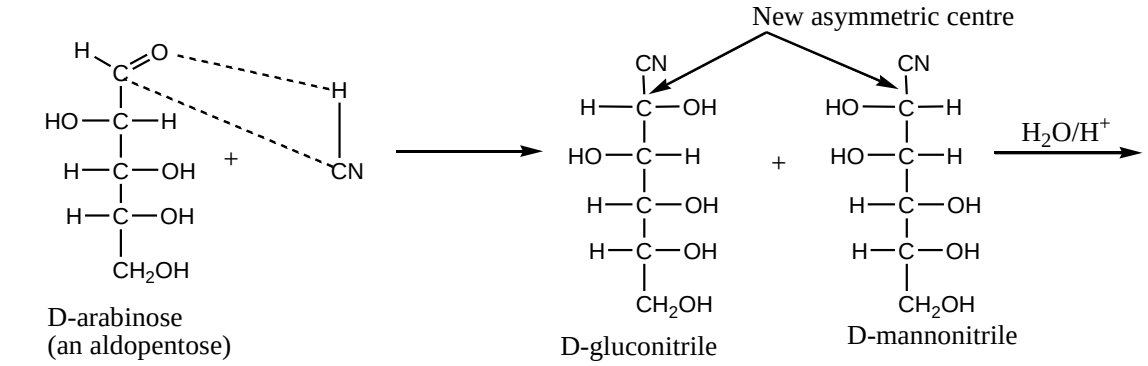
i) Killiani synthesis

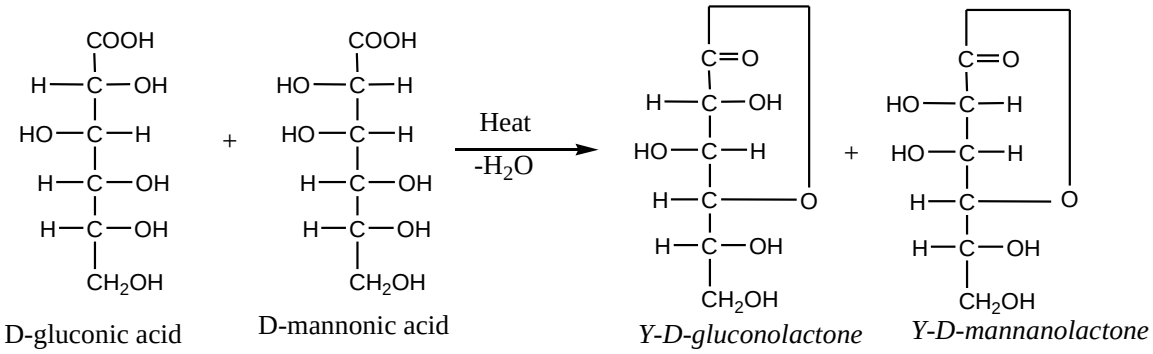
ii) Mutarotation

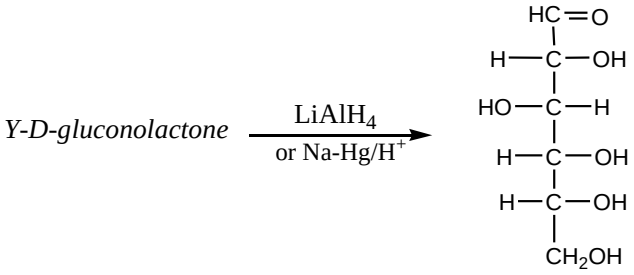
iii) Sucrose does not show mutarotation

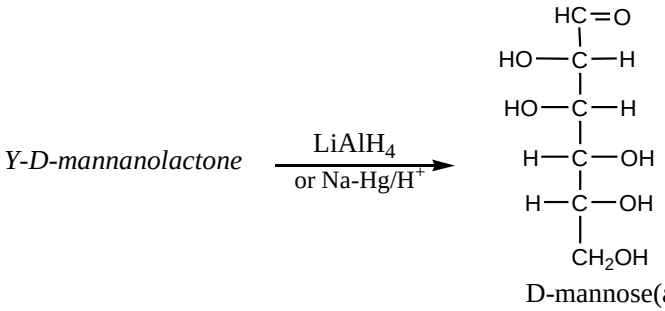
Killiani-Fisher Cyanohdrin Synthesis:

The aldose is first allowed to react with HCN. This process introduces a new asymmetric centre and results in the formation of two cyanohydrins (aldononitriles). It should be noted that these cyanohydrins differ only inconfigurationabout the newly introduced asymmetric carbon atom (carbon number 2), and are therefore, epimers. These cyanohydrins are next hydrolysed with dilute acid to give the corresponding aldonic acids. The aldonic acids on heating lose a molecule of water to give γ-lactones (1,4-aldonolactones). These γ-lactones are solids and are separated by fractional crystallization. The individual lactonescan then be reduced with lithium aluminium hydride or sodium amalgam in a weakly acidic solution to give aldoses which contain one more carbon atoms than the original aldose. Thus D-arabinose may be converted into D-glucose and D-mannose as follows.


New asymmetric centre
D-arabinose
(an aldopentose)
D-gluconitrile
D-mannonitrile
H_2O/H^+


D-gluconic acid
D-mannonic acid
Heat
$-H_2O$
Y-D-gluconolactone
Y-D-mannanolactone


Y-D-gluconolactone
$LiAlH_4$
or Na-Hg/H^+
D-glucose(aldohexose)


Y-D-mannanolactone
$LiAlH_4$
or Na-Hg/H^+
D-mannose(aldohexose)

Mutarotation can be defined as the change in optical rotation that is observed when a reducing sugar is dissolved in water, due to the formation of different tautomeric forms. A sugar crystal will consist of molecules having a specific anomeric ring form (furanose or pyranose with _- or _-configuration). Upon dissolution, ring opening (hydrolysis) and subsequent ring closure will occur, producing the α- and β-pyranose and α- and _β-furanose forms. These forms have different chemical and physical properties (e.g., optical rotation, solubility, chemical reactivity, relativesweetness, etc.). Figure 3.1 shows the five forms of D-glucose that will theoretically exist in solution. For glucose, only the α- and β-pyranose forms exist in significant amounts. α-D-Glucopyranose has an "initial" optical rotation of +112◦, whereas β-D-glucopyranose has an "initial" rotation of free energy.α -D-Glucopyranose has the greatest stability and predominates by being present at 63.6% at equilibrium at 20◦C. Glucose is classified as undergoing "simple" mutarotation, since for practical purposes, only two tautomers are present.

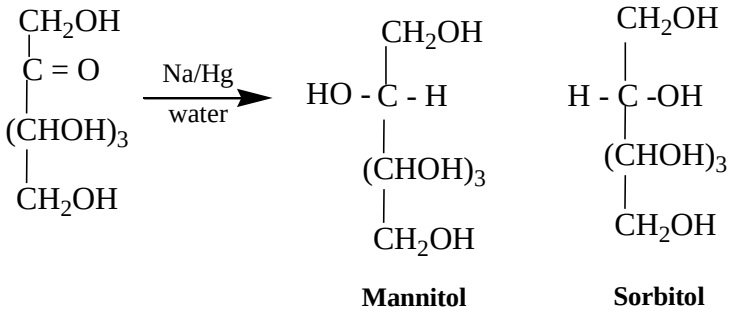
A glycosidic bond to the anomeric carbon **can** be either α or β.forms.. Unlike the other disaccharides, **sucrose** is **not** a reducing sugar and **does not** exhibit **mutarotation** because the glycosidic bond is between the anomeric carbon of glucose and the anomeric carbon of fructose.

OR

b) What happens when Fructose is treated with i) metallic hydroxides ii) Na/Hg iii) Semicarbazide iv) phenylhydrazine.

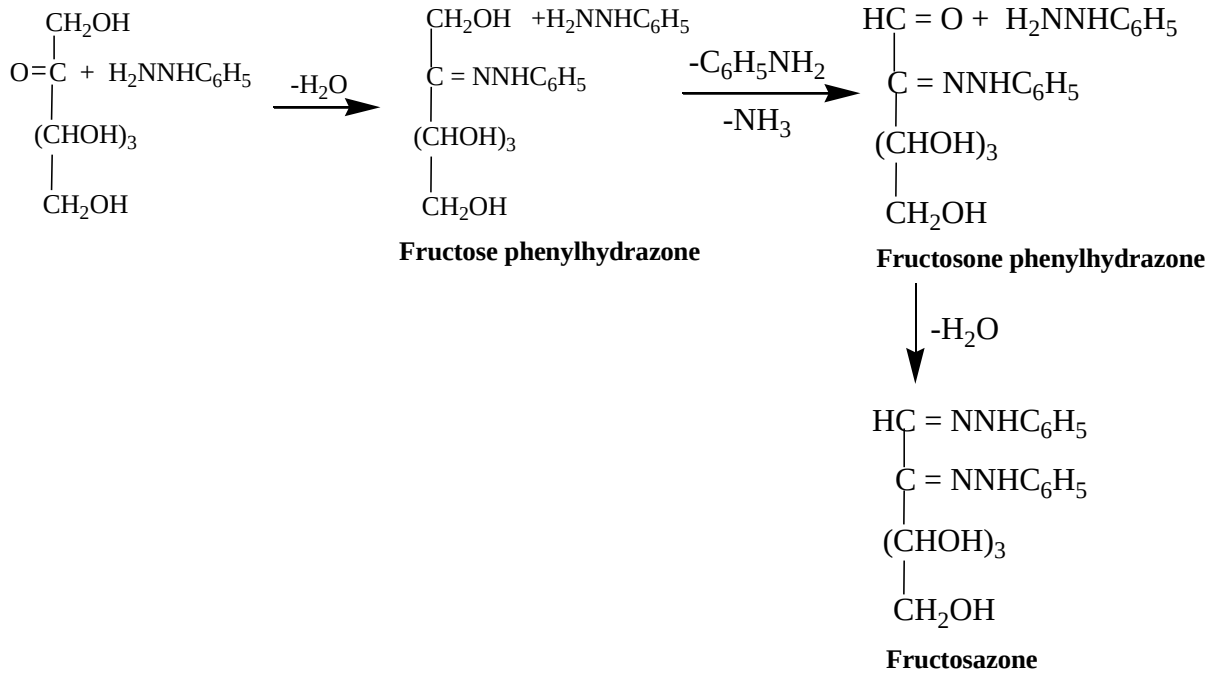
1) Fructose reacts with calcium hydroxides to form calciumfructosate and also it reacts with barum hydroxide to form bariumfructosate.

2. Reduction of fructose with sodium amalgam and water produces a mixture of two epimeric alcohols, sorbital and mannitol because a new asymmetric carbon has been created at C_2. This indicates the presence of keto group.



Mannitol **Sorbitol**

3. Fructose condenses with phenylhydrazine and yields fructosazone similar to glucose. Here again the reaction proceeds in stages:



Fructose phenylhydrazone

Fructosone phenylhydrazone

Fructosazone

4. Fructose reacts with semicarbazide to form semicarbazone.

Reg.No..... [15CHU501]

KARPAGAM ACADEMY OF HIGHER EDUCATION
COIMBATORE-21
(For the candidates admitted from 2015 & onwards)
B.SC DEGREE EXAMINATION
ORGANIC CHEMISTRY
MODEL EXAM

DATE: **SUBJECT CODE: 15CHU501**
TIME: 3 HRS **TOTAL: 60 MARKS**

PART-A (20x1=20 marks)

CHOOSE THE BEST ANSWER:

1. The part of the science which deals with structure in three dimensions is called----------,
a. Stereochemistry b. Food technology c. Nano chemistry d. Physical chemistry

2. Study of branch of stereochemistry is called----------
a. Conformational analysis b. Chemical analysis c. Structural analysis d. Physical analysis

3. The concept of stereochemistry is based on
a. VSEPR theory b. molecular orbital theory c. valence bond theory d. Vant Hoff and Label's theory

4. A cisoid arrangement means to
a. Eclipsed conformation b. anti staggered conformation
c. skew conformation d. gauche conformation

5. Which of the following reaction gives crossed products?
a.Claisen rearrangement b. Fries rearrangement c.Lossen rearrangement
d. Curtius rearrangement

6. The conversion of amide to primary amine is known as
a.Schmidt rearrangement b. Lossen rearrangement c. Hofmann rearrangement
d. Claisen rearrangement

7. Which of the following reaction gives temperature dependence products?
a.Perkin reaction b. Fries rearrangement c. Beckmann rearrangement
d. Claisen rearrangement

8. In the Beckmann reaction,migrating group is chiral. Select the true statement for it---,
a. it will change its configuration while in migration,
b. it will retain its configuration while in migration,
c. it can change as well as it can retain its configuration,
d. there is nothing to do with configuration

9. A freshly prepared solution of glucose has specific rotation of +112° but on keeping for some time it changes to +52.7°. This phenomenon is known as
a.Mutarotation b.Epimerization c.Racemisation d.Resolution

10. The specific rotation for identification of carbohydrate is
a.Molisch's test b.Tollen's test c.Fehling's test d.Benedicts test

11. Monosaccharides undergo reversible isomerisation in the presence of dilute alkali.This reaction is a.Mutarotation b.Lobry de-Bruynand Albedra Van Ekenstein rearrangement c.Killiani synthesis d.wood's synthesis

12. Which one of the following is not a polysaccharide?
a.cellulose b.sucrose c.Amylose d.Inulin

13.Glycine when heated alone give
a.Methyl amine b.2-amino ethanol c.Diketopiperazine
d.Zwitterion

14. Van slyke method is used for the estimation of
a.Primaryamino group b.secondary amino group c.alcoholic group
d.amide group

15. Which one of the following compound is used to protect amino group in sheehan method of peptide synthesis
a.Carbobenzoxy chloride b.phthalic anhydride c.tert-Butoxyazidoformate
d.Diketopiperazine

16. Primary structure of protein shows
a.oreintation of amino acids b.arrangement of peptides c.amino acid sequence
d. α or β-helix space structure

17. The heterocyclic compound which is most reactive towards electrophilic reagent is
a.Thiophene b. Pyrrole c. Furan d. Pyridine

18. Nucleophilic substitution in pyridine occurs at
a. N-atom b. α-position c. β-Position d. does not occur

19. The hybridization of nitrogen atom in piperidine is
a. sp b. sp^2 c. sp^3 d.unhybridized

20. Which one of the following is most basic?
a.Aniline b.Pyrrole c.pyridine d.Piperidine

PART-B(5 x 8 =40 marks)

ANSWER ALL THE QUESTIONS:

21. **(a).** (i).What is optical activity? Discuss the optical isomerism of lactic acid and maleic acid and describe a method for its preparation.

(ii). Discuss the geometrical isomerism of maleic and fumaric acid.

OR

(b).(i) Define racemisation and eplain what are the methods to bring about racemisation.

(ii). Define the terms resolution, enantiomers and diastereomers

22. (a).Explain the reaction and mechanism for Hofmann rearrangement.

OR

(b). Explain the mechanism of following reactions

i) Curtius rearrangement.

ii) Cope rearrangement

23. (a). Describe the manufacture of Sucrose from Sugar beet. How does Sucrose react with (i) lime water (ii) acetic anhydride (iii) yeast (iv) Conc. HNO_3 and (v) Conc. and hot H_2SO_4?

OR

(b). Discuss the Structure of D- Glucose.

24. (a). Explain the following synthesis

(i) Gabriel Synthesis (ii) Koop Synthesis (iii). By Strecker synthesis.

OR

(b).Write notes on (i) N-Terminal and C-Terminal amino acid residues (ii) End Group analysis.

25. (a). (i). Write the reactions of Pyridine.

(ii). Explain why pyridine has low reactivity toward electrophilic substitution.

OR

(b)(i).What is the role of nitrobenzene, glycerol and conc.H_2SO_4 in the synthesis of quinoline?

(ii).Illustrate the preparation of flavones from the following methods

a. Chalcone method b.Konsanecki method

Reg. No……. **[15CHU501]**

KARPAGAM ACADEMY OF HIGHEREDUCATION
COIMBATORE-21
DEPARTMENT OF CHEMISTRY
I MSC CHEMISTRY
ORGANIC CHEMISTRY
MODEL EXAM

DATE: **SUBJECT CODE: 15CHU501**

TIME: 3.00 HRS **TOTAL: 60 MARKS**

Answer Key

Part- A (20 x1 = 20 Marks)

ANSWER ALL THE QUESTIONS:

1. a. Stereochemistry

2. a. Conformational analysis

3. d. Vant Hoff Label's theory

4. a. Eclipsed conformation

5. b. Fries rearrangement

6. c.Hofmann rearrangement

7. b. Fries rearrangement

8. b. it will retain its configuration while migration

9. a. mutarotation

10. a Molisch's test

11.b. Lobry de-bruynand Albedra van Ekenstein rearrangement

12. b. sucrose

13. c. Diketopiperizine

14. a primary amino group

15. b. Phthalic anhydride

16. c. amino acid sequence

17. b. pyrrole

18. b. α-position

19. c. sp^3

20.d. Piperidine

Part-B (5 x 8= 40 marks)

ANSWER ALL THE QUESTIONS:

21.a. i). What is Optical activity? Discuss the optical isomerism of lactic acid and maleic acid and describe its preparation.

The angle of rotation by which the plane polarised light is rotated, can be measured by an analyzer in a polarimeter. A diagram of the polarimeter is shown in Figure 6.36.

A polarimeter consists of a light source, two nicol prisms and a sample table to hold the substance. The sample tube is placed between two nicol prisms. The prism placed near the source of light is called **polarizer** while the other placed near the eye is called **analyzer**. The aqueous solution of the substance is placed between the polarizer and analyzer. The analyzer can be rotated by certain angle to compensate for the rotation of the plane-polarized light by the optically active sample. The observed rotation ($\alpha_{observed)}$ is expressed in degrees.

If the substance rotates plane polarised light *to the right (clock wise),* it is called **dextro rotatory** (Greek for right rotation) or the *d*-form and it is indicated by placing a (+) sign before the degrees of rotation. If light is rotated *towards left (anti clock wise),* the substance is said to be **laevo rotatory** (Greek for left rotating) or the *l*-form and a negative (-) sign is placed before the degrees of rotation. The dextro rotatory and laevo rotatory compounds are called **optically active compounds.**

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rotatory (Greek for right rotation) or the *d*-form and it is indicated by placing a (+) sign before the degrees of rotation. If light is rotated *towards left (anti clock wise)*, the substance is said to be **laevo rotatory** (Greek for left rotating) or the *l*-form and a negative (-) sign is placed before the degrees of rotation. The dextro rotatory and laevo rotatory compounds are called **optically active compounds.**

For example, lactic acid, $CH_3CH(OH)COOH$ (Figure 6.39). However, the presence of chiral carbon atoms is not a guarantee that the molecule will be optically active, and many molecules even if do not contain any chiral carbon, can still be optically active.

ii). Discuss the geometrical isomerism of maleic anf fumaric acid

Maleic acid or **cis-butenedioic acid** is an organic **compound** that is a **dicarboxylic**acid, a molecule with two **carboxyl groups**. Its chemical formula is $HO_2CCHCHCO_2H$. Maleic acid is the **cis-isomer** of **butenedioic** acid, whereas fumaric acid is the **trans-isomer**.

OR

b)i). Define racemization and explain what the methods to bring about racemization are.

Definition:

Racemization is the process of converting an optically active compound into the racemic modifications.

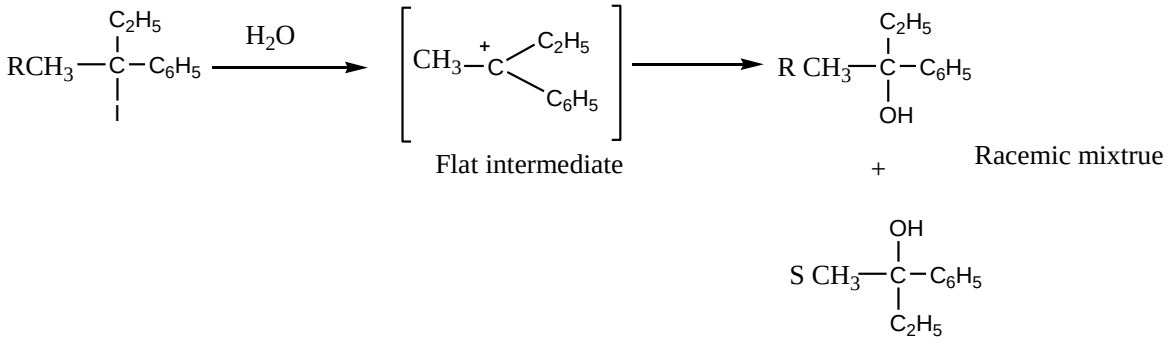
Racemic modifications are also called racemic mixtures or racemates.

Methods to bring about racemization:

i) Action of heat:
When d or l isomer is heated we get the dl mixture.

ii) Treatment with chemical reagents:
Many substances undergo racemization when treated with chemical reagents. E.g., mandelic acid ($C_6H_5CHOHCOOH$) forms (±) bromo acid when treated with hydrobromic acid.

iii) **Substitution and rearrangements**:
Substitution and rearrangements reactions which take place via S_N^1 type stepwise mechanisms end up in racemised products.E.g.,

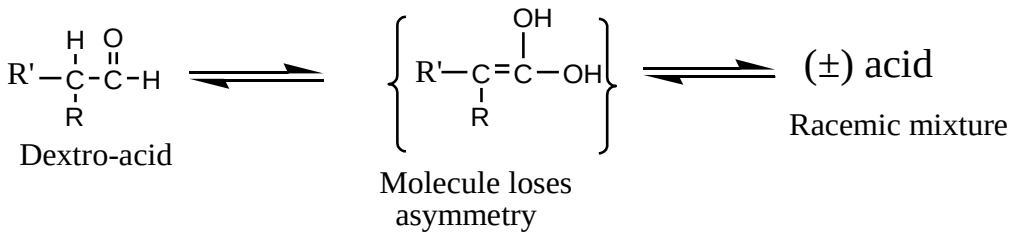


iv) Auto-racemization:

In some cases racemization occurs spontaneously at room temperature, e.g., dimethyl bromo sucinate undergoes racemization on standing at room temperature. This type of racemization is termed as auto racemization.

Mechanism of racemization:

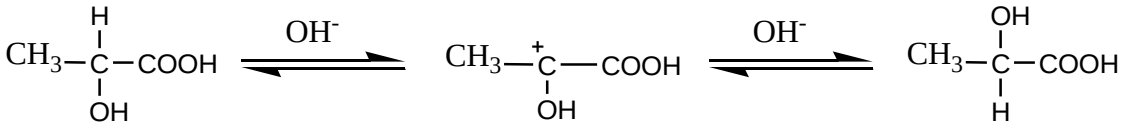
Compound which racemise readily are found to contain an asymmetric carbon atom joined to a hydrogen atom and a negative group. Such compounds readily undergo tautomeric change and racesation occurs via enolisation. For example



The intermediate enol form is nor asymmetric. When it reverts to the stable form, there are equal chances to produce the dextro and laevo forms. So it gives a racemic mixture.

In the case of a compound which cannot udergo tautometic change, mechanism of racemisation is uncertain. Howeverthe racemization is said to take place via the formation of planar intermediate which when reverts to the stable form, there are equal changes to produce the dextro and laevo forms. So it gives a racemic mixture.

This can be illustrated by taking the base catalysed racemization of (-) lactic acid.



ii) Define the term resolution, enentiomers and diastereomers

Defination: "The separation of a racemic mixture into its enantiomers(dextro and laevo components) is termed as resolution".

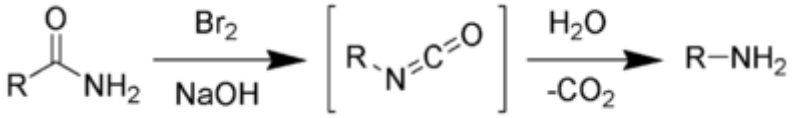
An enantiomer is one of the two molecules that are mirror images of each other and are non-superposable.

Enantiomers have identical chemical and physical properties except for their ability to rotate plane-polarized light (+/-) by equal amounts but in opposite directions. Enantiomers interact differently with other chiral molecules i.e. biologically active molecules as aminoacids, sugars, steroids etc. This means that some molecules have, for example, different odours. Limonene is just such a case.

Diastereomers (sometimes called diastereoisomers) are a type of a stereoisomer. Diastereomerism occurs when two or more stereoisomers of a compound have different configurations at one or more (but not all) of the equivalent (related) stereocenters and are not mirror images of each other. When two diastereoisomers differ from each other at only one stereocenter they are epimers. Each stereocenter gives rise to two different configurations and thus increases the number of stereoisomers by a factor of two.

22.a) Explain the reaction and mechanism of hofmannrearrangement.

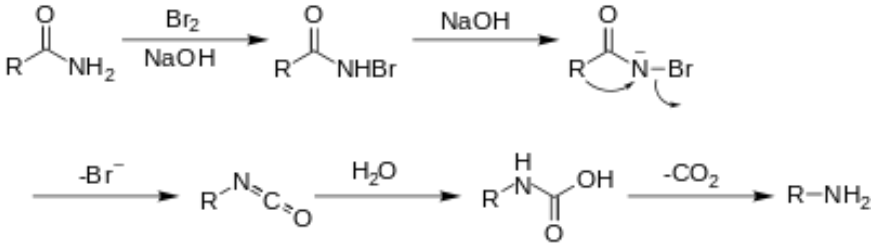
The **Hofmann rearrangement** is the organic reaction of a primary amide to a primary amine with one fewer carbon atom.



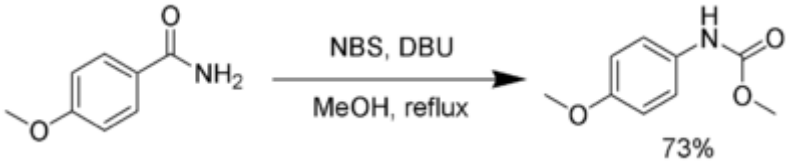
The reaction is named after its discoverer: August Wilhelm von Hofmann. This reaction is also sometimes called the **Hofmann degradation** or the **Harmon Process**, and should not be confused with the Hofmann elimination.

Mechanism:

The reaction of bromine with sodium hydroxide forms sodium hypobromite *in situ*, which transforms the primary amide into an intermediate isocyanate. The intermediate isocyanate is hydrolyzed to a primary amine, giving off carbon dioxide.



Several reagents can substitute for bromine. N-Bromosuccinimide and 1, 8-diazabicyclo[5.4.0]undec-7-ene (DBU) can effect a Hofmann rearrangement. In the following example, the intermediate isocyanate is trapped by methanol, forming a carbamate.



In a similar fashion, the intermediate isocyanate can be trapped by tert-butanol, yielding the t-butoxycarbonyl (Boc)-protected amine.

A mild alternative to bromine is also (bis(trifluoroacetoxy)iodo)benzene.

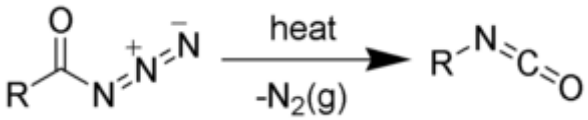
Applications:

Aliphatic & Aromatic amides are converted into aliphatic and aromatic amines, respectively
In the preparations of Anthranilic Acid from Phthalimide
Nicotinic acid is converted into 3-Amino pyridine
The Symmetrical structure of α-phenyl propanamide does not change after hofmann reaction.

b) Explain the mechanism of the following reactions

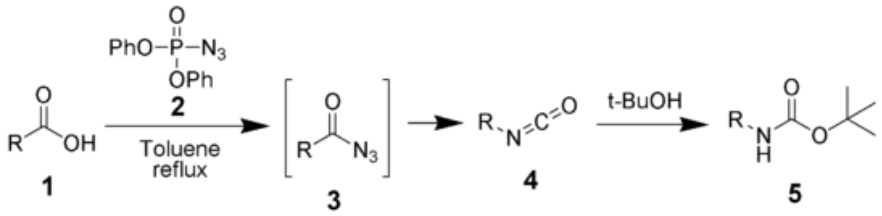
i) Curtius rearrangement ii) cope rearrangement

The **Curtius rearrangement** (or **Curtius reaction** or **Curtius degradation**), as first defined by Theodor Curtius, is a chemical reaction that involves the rearrangement of an acyl azide to an isocyanate. Several reviews have been published.



The isocyanate can be trapped by a variety of nucleophiles. Water is often added in order to hydrolyze the isocyanate to an amine. When done in the presence of *tert*-butanol, the reaction generates Boc-protected amines, useful intermediates in organic synthesis.

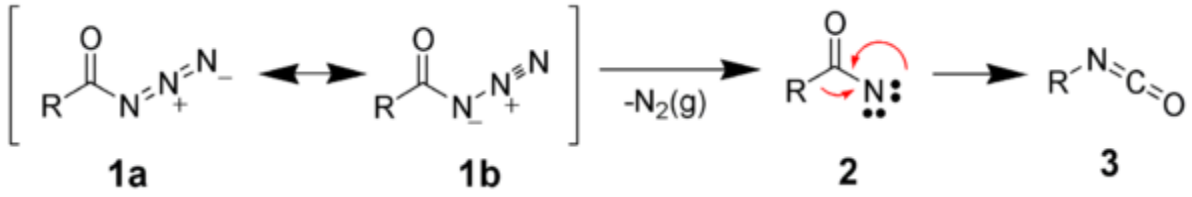
Carboxylic acids **1** can be easily converted to acyl azides **3** using diphenylphosphoryl azide **2**.



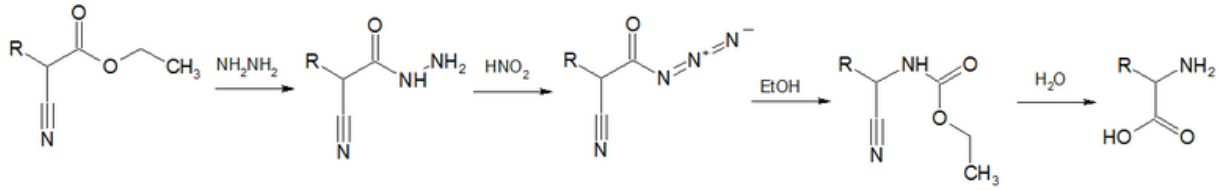
Likewise, when the Curtius reaction is performed in the presence of benzyl alcohol, Cbz-protected amines are formed.

Mechanism:

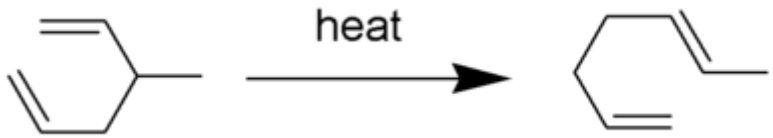
The Curtius rearrangement may be thought of as a two-step process, the first step being the loss of nitrogen gas, forming an acyl nitrene (**2**), and the second step being the rearrangement of acyl nitrenes by migration of R-group to form the desired isocyanate (**3**). However, current evidence indicates that these two steps are likely concerted (i.e., they occur at the same time), and no free nitrene intermediate is formed.



In one variation called the **Darapsky degradation** (A. Darapsky, 1936), a Curtius rearrangement takes place as one of the steps from a α-cyanoester to an amino acid.



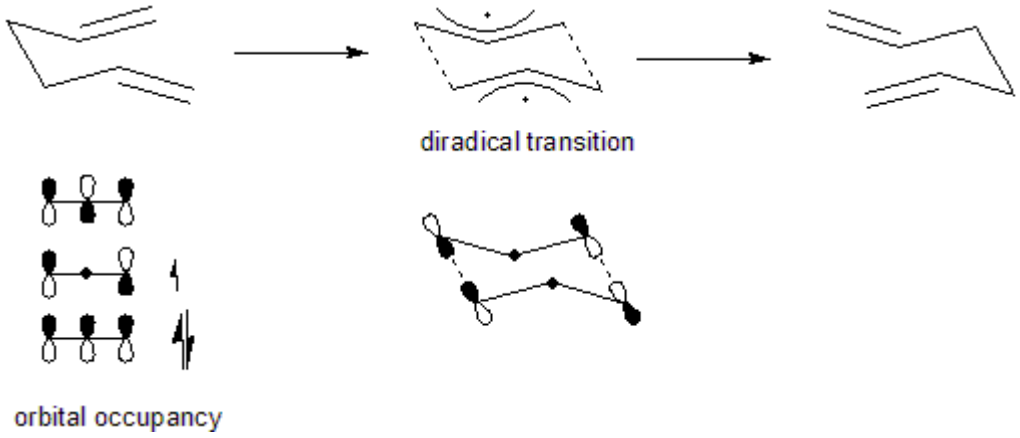
The **Cope rearrangement** is an extensively studied organic reaction involving the [3,3]-sigmatropic rearrangement of 1,5-dienes. It was developed by Arthur C. Cope. For example 3-methyl-1, 5-hexadiene heated to 300°C yields 1, 5-heptadiene.



The Cope rearrangement causes the fluxional states of the molecules in the bullvalene family.

Mechanism:

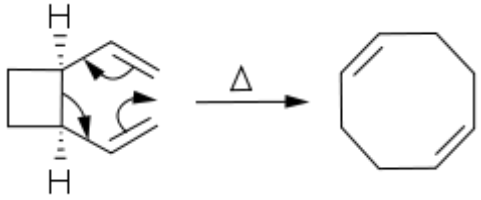
Although the Cope rearrangement is concerted and pericyclic, it can also be considered to go via a transition state that is energetically and structurally equivalent to adiradical.[*citation needed*] This is an alternative explanation which remains faithful to the uncharged nature of the Cope transition state, while preserving the principles of orbital symmetry. This also explains the high energy requirement to perform a Cope rearrangement. Although illustrated in the chair conformation, the Cope can also occur with cyclohexadienes in the "boat" conformation.



The above description of the transition state is not quite correct. It is currently generally accepted that the Cope rearrangement follows an allowed concerted route through a homoaromatic transition state and not a diradical. That is unless the potential energy surface is perturbed to favor the diradical.

Examples:

The rearrangement is widely used in organic synthesis. It is symmetry-allowed when it is suprafacial on all components. The transition state of the molecule is passes through a boat or chair like transition state. An example of the Cope rearrangement is the expansion of a cyclobutane ring to a 1, 5-cyclooctadiene ring:



23. a). Describe the manufacture of sucrose from sugar beet. How does sucrose react with i)lime water (ii) acetic anhydrise (iii) yeast (iv) con HNO_3 (v) con and hot H_2SO_4

Sugar beets are harvested in mid-to-late autumn when sugar content peaks.

The leafy sugar beet tops are sliced off and the roots are lifted out of the ground with special harvesting equipment.

The harvested sugar beets are trucked from the field to one of 38 receiving stations where they are weighed, sampled and tested for sugar quality, unloaded and piled.

The sugar beets are stored in long trapezoid-shaped piles. Some of the sugar beet piles have large culverts running underneath them. At end of the culverts are fans that blow cold winter air through the culverts to cool down and freeze the piles to better preserve the sugar contained in the beets. Other piles are stored in large sheds which use similar culvert technology to freeze the stored sugar beets.

The sugar beets are trucked from outside receiving stations to factories throughout the processing campaign for sugar processing.

Factory Control

The following processes are controlled through state-of-the-art computerized flow and monitoring systems. The systems are operated from a central control room to optimize operations throughout the many functional areas of the factory.

Washing

Sugar beets entering the factory must first go through a washing process. A large paddle wheel lifts the sugar beets to the washers, where they are rolled against each other in water, removing dirt and debris. This water then goes to a holding pond or wastewater facility for treatment.

Slicing

After washing, the sugar beets enter the slicer where razor-sharp, corrugated knives cut the sugar beets into long, white, french-fry looking strings called cossettes. They are then transported to the cossette mixer where they are mixed with hot juice and pumped into the bottom of the diffuser.

Diffusion

In the diffuser, the sugar is diffused out of the sugar beet cossettes by using very hot water. The raw beet sugar juice stays in the lower part of the diffuser while the remaining sugar beet cossette pulp moves up and out of the top of the diffuser.

The pulp goes through a separate process where it is put into presses, which squeeze out most of the water. Then it is heat-dried in huge drying systems before it is pressed into beet pulp pellets as livestock feed.

Purification

The raw sugar juice leaves the bottom of the diffuser to go through several purifying and filtering steps. During this process the raw juice is clarified and filtered to remove impurities, remaining solids and fine particles.

Evaporation

Through a series of evaporators, the juice is heated with steam to evaporate the natural water and filtered once more, concentrating it into dark caramel syrup.

Crystallization

The syrup then enters the crystallization process. The sugar juice syrup is carefully boiled and seeded with microscopic sugar crystals to start the crystallization process. When the crystals reach their desired size, a rich mixture of crystals and beet molasses syrup is formed.

The sugar crystals are separated from the beet molasses syrup in a large, high-speed spinning drum or centrifuge. These crystals are now 99.9% pure white sugar. The crystals move into the granulator where they are then dried, cooled and separated according to size.

The remaining molasses syrup still contains some sugar, which is claimed through additional processes called molasses desugarization. The remaining beet molasses ends up as liquid agri-product used as a livestock feed additive.

Sugar Handling

The granulated sugar is then advanced to huge storage silos. Most of the sugar is shipped by train in bulk railcars to manufacturers as a primary ingredient for candy, baked goods, cereals, and other fine products.

Sugar for grocery stores is packaged into bags that range from 2 pounds to 25 pounds. The automatic packaging lines can fill 4-pound bags at a rate of more than 2 bags per second. A portion of our sugar is finely ground to make powdered sugar while another portion of the sugar is turned into light brown and dark brown sugar.

OR

b. Discuss the structure of D-Glucose.

Glucose, *dextrose* (grape sugar) is the central carbohydrate of living organisms of all types, the major source of energy. It is widely distributed in nature as the monosaccharides in ripe grapes. Honey,sweet fruit and as a component of disaccharides-lactose, maltose, sucrose and cellobiose. It is the building unit from which the polysaccharides like starch, cellulose and glycogen are formed. It is also normal constituent of blood and occurs in urine of diabetics.

1) Commercially pure D(+) glucose is manufactured by heating starch with dilute hydrochloric acid under pressure:

$$(C_6H_{10}O_5)_n + n\ H_2O \xrightarrow{\text{dil.HCl}} n\ C_6H_{12}O_6$$

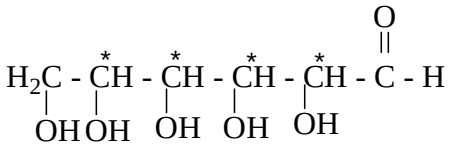
2) It is formed as an intermediate product in the fermentation of starch for the manufacture of ethyl alcohol.

3) Glucose is made by the hydrolysis of sucrose by boiling with dilute hydrochloric acid in alcoholic solution. Glucose and fructose are obtained in equal amounts. On cooling the resulting solution, glucose being less soluble than fructose, separates out.

$$\underset{\textbf{sucrose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow{\text{dil.HCl}} \underset{\textbf{glucose}}{C_6H_{12}O_6} + \underset{\textbf{fructose}}{C_6H_{12}O_6}$$

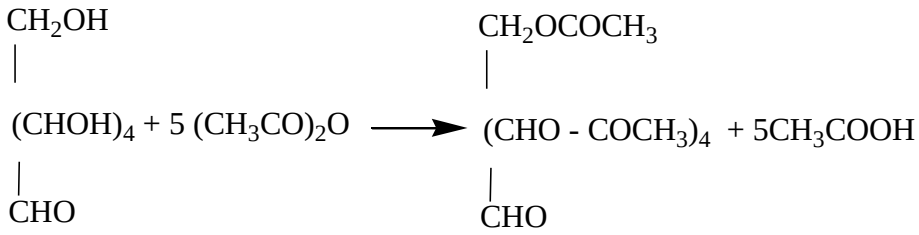
Properties

Glucose is a white crystalline solid (m.p 419 K), sweet to taste. It is readily soluble in water. Naturally occurring glucose is *dextro-rotatory* (hence, the name Dextrose) and it has four asymmetric carbon atom (marked by *).

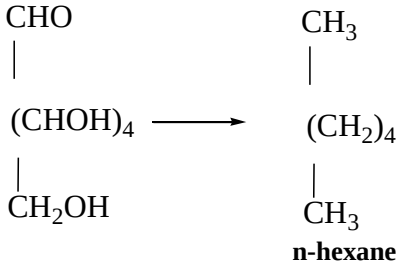


Structural formula of glucose indicates the presence of one aldehydic group, one primary alcoholic group and four secondary alcoholic groups. Chemical properties of glucose are, therefore, the properties of the above functional groups. The structural elucidation very easily follows from its reactions:

1) Quantitative analysis establishes the empirical formula as CH_2O.
2) The molecular weight of glucose determined from a study of the depression of freezing point of glucose solution, shows a value of 180. When this is compared with the empirical formula weight, the conclusion reached is that the molecular formula is $(CH_2O)_6$ or $C_6H_{12}O_6$.
3) The presence of the five alcoholic groups is indicated by its reaction with 5 moles of acetyl chloride or acetic anhydride.

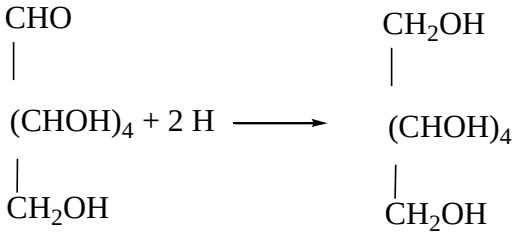


4) Reduction of glucose with concentrated hydriodic acid and red phosphorus at 373 K yields 2-iodohexane. Prolonged heating produces n-hexane. This would mean that glucose is a straight chain compound of six carbon atoms.

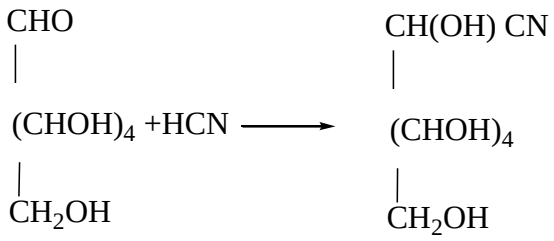


n-hexane

5) The nature of the carbonyl group is indicated by its reaction with mild reducing agent. When reduced with sodium amalgam in aqueous solution, the aldehyde group is reduced to a primary alcoholic group to yield a hexahydric alcohol, called sorbitol.

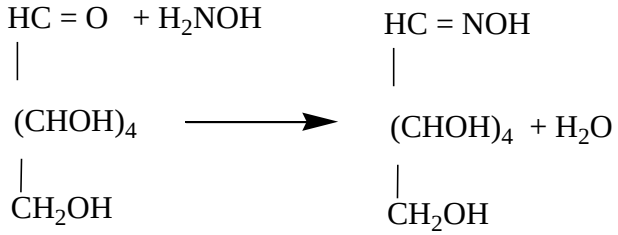


6) Glucose gives addition product with hydrogen cyanide *(but not with ammonia or sodium bisulphite).* This reaction indicates the presence of a carbonyl group.

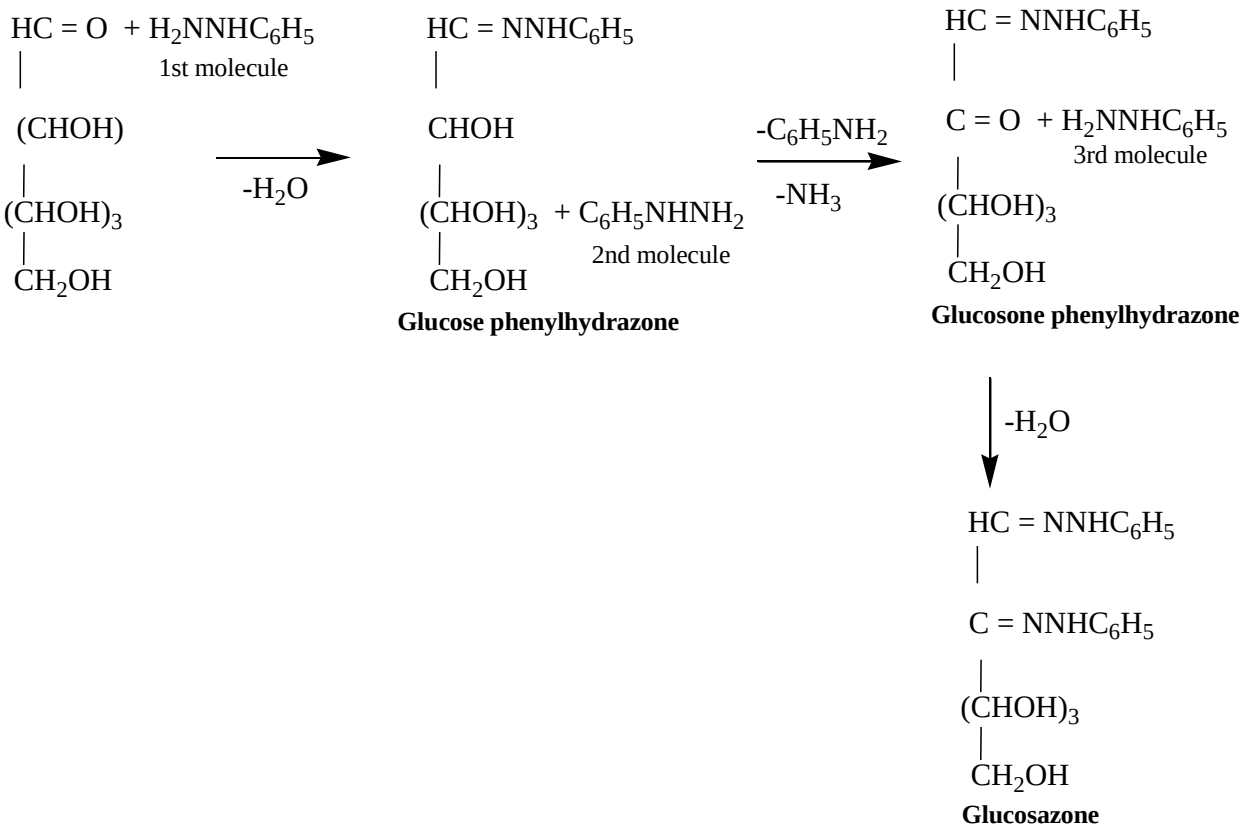


glucose cyanohydrin

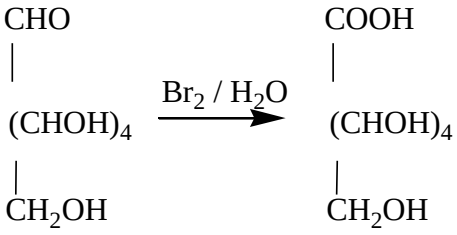
7) Glucose condenses with hydroxylamine to yield the oxime with the elimination of a water molecule.



8) Glucose reacts with one molecule of phenylhydrazine in acetic acid which condenses with the aldehyde group to give *phenylhydrazone.* When warmed with excess phenylhydrazine, the secondary alcoholic group, adjacent to the aldehyde group, is next oxidised to a keto group. With this keto group, third molecule of phenylhydrazine condenses to yield *glucosazone:*

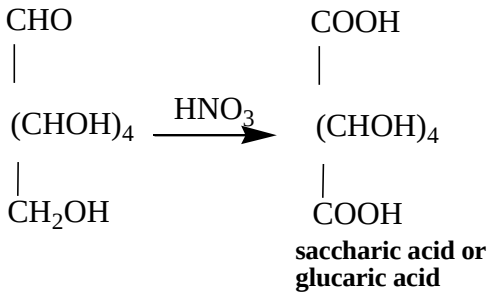


9) With mild oxidising agents like bromine water, glucose is oxidised to gluconic acid, an acid with the same number of carbon atoms. In this reaction, the aldehyde group alone gets oxidised.



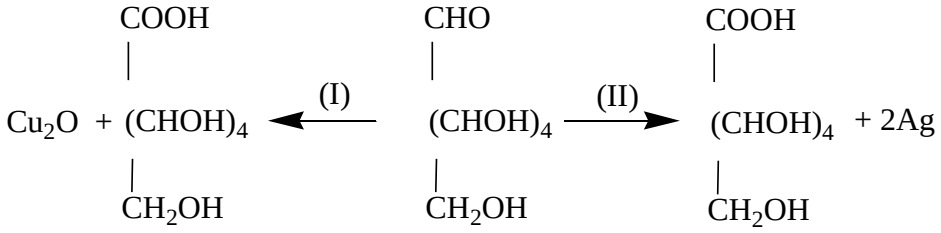
gluconic acid

10) With strong oxidising agents like nitric acid, it is oxidised to a dicarboxylic acid, saccharic acid. Nitric acid is able to oxidise the primary alcohol group also to an acid group.



saccharic acid or glucaric acid

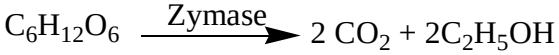
11) Because glucose is readily oxidised, it acts as a strong reducing agent. It reduces both Fehling's solution (I) and Tollen's reagent [ammoniacal silver nitrate, (II)]



The above reactions (5 to 11) confirm the presence of an aldehyde group in glucose.

Other Reactions of Glucose

12) Glucose on fermentation yields ethyl alcohol.



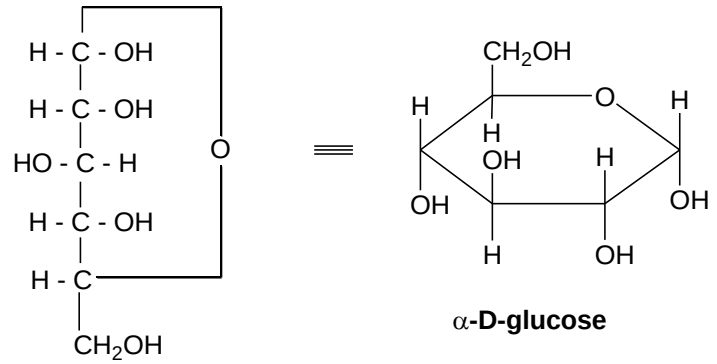
13) A dilute solution of glucose when warmed with dilute alkali solution, gives a mixture of glucose, fructose and mannose.

14) When heated with concentrated hydrochloric acid, it gives laevulic acid and hydroxymethyl furfural.

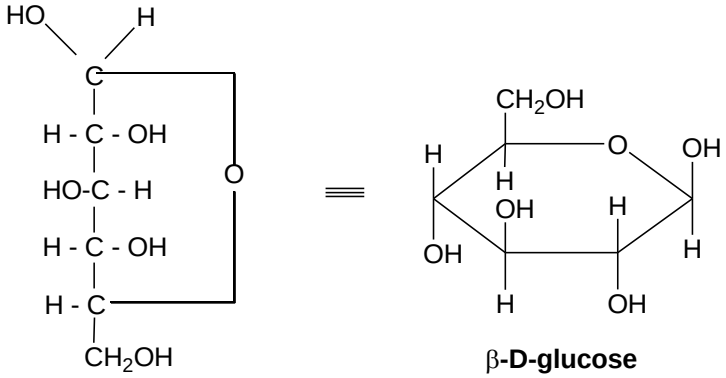
All the above reactions of glucose indicate that glucose is a polyhydric alcohol with a terminal aldehyde group and that it is a straight chain compound.

As mentioned earlier, glucose does not react with ammonia or sodium bisulphite. Further, it exists in two isomeric forms, α- and β – glucose. The evidence for these forms is *muta rotation.* α – glucose with specific rotation $+110^{o}$ is obtained by crystallizing glucose form alcoholic or acetic acid solution whereas β – glucose with specific rotation $+19.7^{o}$ is obtained by crystallizing glucose form pyridine solution. An aqueous solution of glucose shows muta roration *(meaning, a*

change of rotation) i.e., its specific rotation gradually falls from $+110^{o}$ to $+52.5^{o}$ in the case of α – glucose and increases from $+19.7^{o}$ to $+52.5^{o}$ in the case of β – glucose. To account for these facts satisfactorily, Tollen suggested a ring formula with no free aldehyde group. The ring structure for glucose is best representing by a hexagonal formula base on *pyran.*



α-D-glucose



β-D-glucose

Uses

1) It is used as a sweetening agent in confectionery.
2) It is utilised in the manufacture of ascorbic acid (Vitamin C).

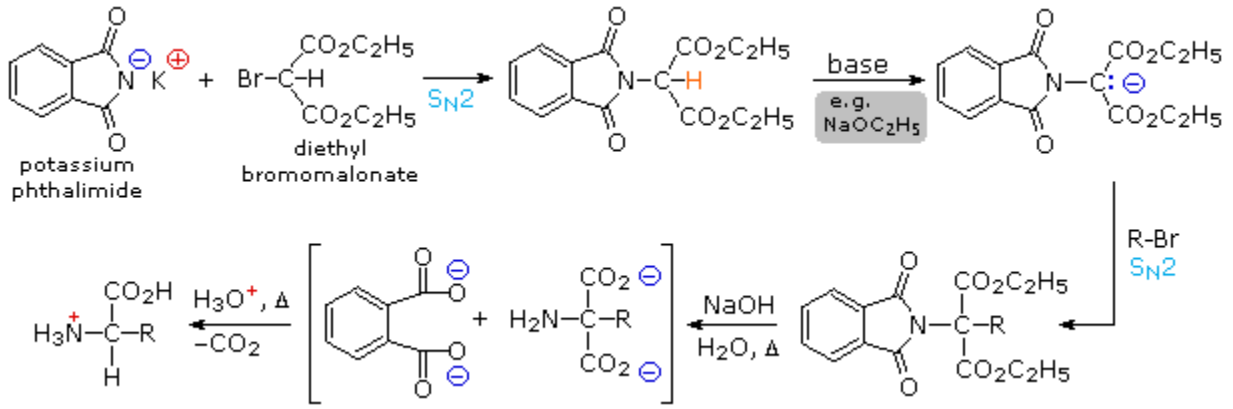
It serves as food for invalids and as food preservatives.

24. a) Explain the following synthesis

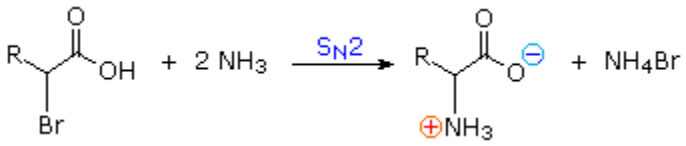
i) Gabriel synthesis (ii) Koop synthesis (iii) Bystrcker synthesis

i)By modifying the nitrogen as a phthalimide salt, the propensity of amines to undergo multiple substitutions is removed, and a single clean substitution reaction of 1º- and many 2º-alkylhalides takes place. This procedure, known as the Gabriel synthesis, can be used to advantage in aminating bromomalonic esters, as shown in the upper equation of the following scheme. Since

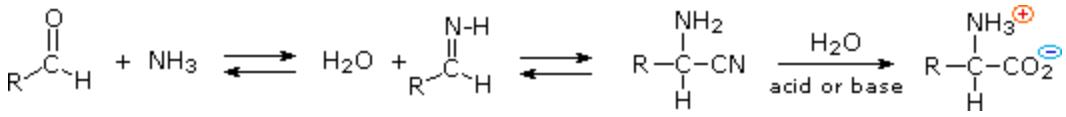
the phthalimide substituted malonic ester has an acidic hydrogen (colored orange), activated by the two ester groups, this intermediate may be converted to an ambident anion and alkylated. Finally, base catalyzed hydrolysis of the phthalimide moiety and the esters, followed by acidification and thermal decarboxylation, produces an amino acid and phthalic acid (not shown).



ii) Amination of alpha-bromocarboxylic acids, illustrated by the following equation, provides a straightforward method for preparing alpha-aminocarboxylic acids. The bromoacids, in turn, are conveniently prepared from carboxylic acids by reaction with Br_2 + PCl_3. Although this direct approach gave mediocre results when used to prepare simple amines from alkyl halides, it is more effective for making amino acids, thanks to the reduced nucleophilicity of the nitrogen atom in the product. Nevertheless, more complex procedures that give good yields of pure compounds are often chosen for amino acid synthesis.



iii) An elegant procedure, known as the **Strecker synthesis**, assembles an alpha-amino acid from ammonia (the amine precursor), cyanide (the carboxyl precursor), and an aldehyde. This reaction (shown below) is essentially an imino analog of cyanohydrin formation. The alpha-amino nitrile formed in this way can then be hydrolyzed to an amino acid by either acid or base catalysis.



OR

b) Write a notes on (i) N-terminal and C-terminal amino acid residues (ii) End group analysis

The N-terminus (also known as the amino-terminus, NH_2-terminus, N-terminal end or amine-terminus) is the start of a protein or polypeptide referring to the free amine group ($-NH_2$) located at the end of a polypeptide. Normally the amine group is bonded to another carboxylic group in a protein to make it a chain, but since the end of a protein has only 1 out of 2 areas chained, the free amine group is referred to the N-terminus. By convention, peptide sequences are written N-terminus to C-terminus, left to right in LTR languages.[1] This correlates the translation direction to the text direction (because when a protein is translated from messenger RNA, it is created from N-terminus to C-terminus - amino acids are added to the carbonyl end).

Each amino acid has an amine group and a carboxylic group. Amino acids link to one another by peptide bonds which form through a dehydration reaction that joins the carboxyl group of one amino acid to the amine group of the next in a head-to-tail manner to form a polypeptide chain. The chain has two ends - an amine group, the N-terminus, and an unbound carboxyl group, the C-terminus.

When a protein is translated from messenger RNA, it is created from N-terminus to C-terminus. The amino end of an amino acid (on a charged tRNA) during the elongation stage of translation, attaches to the carboxyl end of the growing chain. Since the start codon of the genetic code codes for the amino acid methionine, most protein sequences start with a methionine (or, in bacteria, mitochondria and chloroplasts, the modified version *N*-formylmethionine, fMet). However, some proteins are modified posttranslationally, for example, by cleavage from a protein precursor, and therefore may have different amino acids at their N-terminus.

N-terminal targeting signals

The N-terminus is the first part of the protein that exits the ribosome during protein biosynthesis. It often contains signal peptide sequences, "intracellular postal codes" that direct delivery of the protein to the proper organelle. The signal peptide is typically removed at the destination by a signal peptidase. The N-terminal amino acid of a protein is an important determinant of its half-life (likelihood of being degraded). This is called the N-end rule.

Signal peptide

The N-terminal signal peptide is recognized by the signal recognition particle (SRP) and results in the targeting of the protein to the secretory pathway. In eukaryotic cells, these proteins are synthesized at the rough endoplasmic reticulum. In prokaryotic cells, the proteins are exported across the cell membrane. In chloroplasts, signal peptides target proteins to the thylakoids.

The C-terminus (also known as the carboxyl-terminus, carboxy-terminus, C-terminal tail, C-terminal end, or COOH-terminus) is the end of an amino acid chain (protein or polypeptide), terminated by a free carboxyl group (-COOH). When the protein is translated from messenger RNA, it is created from N-terminus to C-terminus. The convention for writing peptide sequences is to put the C-terminal end on the right and write the sequence from N- to C-terminus.

Each amino acid has a carboxyl group and an amine group. Amino acids link to one another to form a chain by a dehydration reaction which joins the amine group of one amino acid to the carboxyl group of the next. Thus polypeptide chains have an end with an unbound carboxyl group, the C-terminus, and an end with an unbound amine group, the N-terminus. Proteins are naturally synthesized starting from the N-terminus and ending at the C-terminus.

C-terminal retention signals

While the N-terminus of a protein often contains targeting signals, the C-terminus can contain retention signals for protein sorting. The most common ER retention signal is the amino acid sequence -KDEL (Lys-Asp-Glu-Leu) or -HDEL (His-Asp-Glu-Leu) at the C-terminus. This keeps the protein in the endoplasmic reticulum and prevents it from entering the secretory pathway.

C-terminal modifications

The C-terminus of proteins can be modified posttranslationally, most commonly by the addition of a lipid anchor to the C-terminus that allows the protein to be inserted into a membrane without having a transmembrane domain.

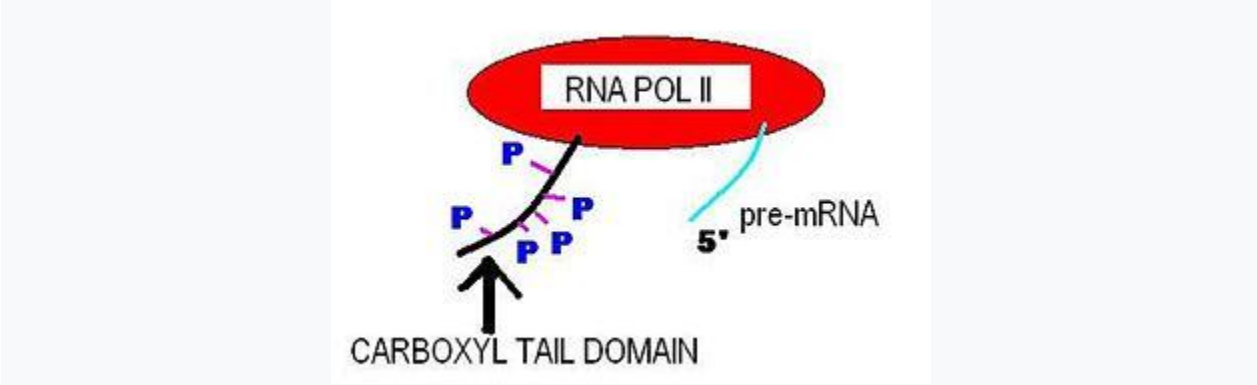
Prenylation

One form of C-terminal modification is prenylation. During prenylation, a farnesyl- or geranylgeranyl-isoprenoid membrane anchor is added to a cysteine residue near the C-terminus. Small, membrane-bound G proteins are often modified this way.

GPI anchors

Another form of C-terminal modification is the addition of a phosphoglycan, glycosylphosphatidylinositol (GPI), as a membrane anchor. The GPI anchor is attached to the C-terminus after proteolytic cleavage of a C-terminal propeptide. The most prominent example for this type of modification is the prion protein.

C-terminal domain



RNA POL II in action.

The C-terminal domain of some proteins has specialized functions. In humans, the CTD of RNA polymerase II typically consists of up to 52 repeats of the sequence Tyr-Ser-Pro-Thr-Ser-Pro-Ser. This allows other proteins to bind to the C-terminal domain of RNA polymerase in order to activate polymerase activity. These domains then involved in the initiation of DNA transcription, the capping of the RNA transcript, and attachment to the spliceosome for RNA splicing.

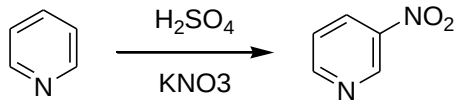
End Group Analysis:

The Edman degradation is a very important reaction for protein sequencing, because it allows the ordered amino acid composition of a protein to be discovered. Automated Edman sequencers are now in widespread use, and are able to sequence peptides up to approximately 50 amino acids long. A reaction scheme for sequencing a protein by the Edman degradation follows; some of the steps are elaborated on subsequently.

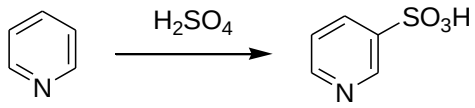
1. Break any disulfide bridges in the protein with a reducing agent like 2-mercaptoethanol. A protecting group such as iodoacetic acid may be necessary to prevent the bonds from re-forming.
2. Separate and purify the individual chains of the protein complex, if there are more than one.
3. Determine the amino acid composition of each chain.
4. Determine the terminal amino acids of each chain.
5. Break each chain into fragments under 50 amino acids long.
6. Separate and purify the fragments.
7. Determine the sequence of each fragment.
8. Repeat with a different pattern of cleavage.
9. Construct the sequence of the overall protein.

25.a.i.Write the reactions of pyridine

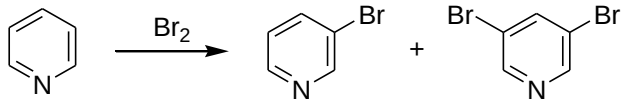
Electrophilic Sustitution: Pyridine is considerably less reactive than benzene towards electrophiles. So, it does not undergo Friedel Craft's reaction. It undergoes nitration, sulphonation and halogenations only under vigorous conditions. With conc.H_2SO_4 and KNO_3 at 573 K it gives 3-nitropyridine.



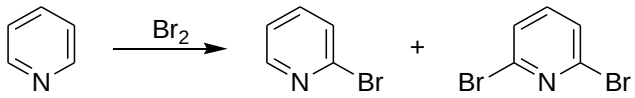
Sulphonation of pyridine is difficult. On heating with concentrated sulphuric acid at 623 K for some hours it gives pyridine-3- sulphonic acid.



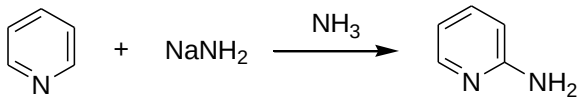
With bromine at 573 K in the presence of catalyst (pumice or charcoal) pyridine gives a mixture of 3- bromopyridine and 3, 5-dibromopyridine.



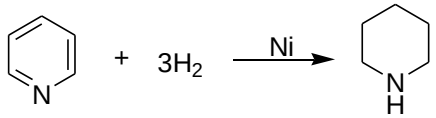
At 773 K bromination occurs at C-2 or C-2 and C-6 positions. The substitutions probably occur by a free radical mechanism.



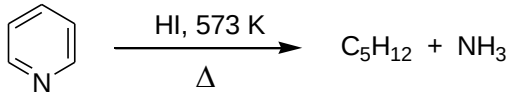
Pyridine reacts with sodamide in liquid ammonia at about 373 K to form 2-aminopyridine **(Chichibabin reaction)**. This reaction is an example of nucleophilic substitution reaction.



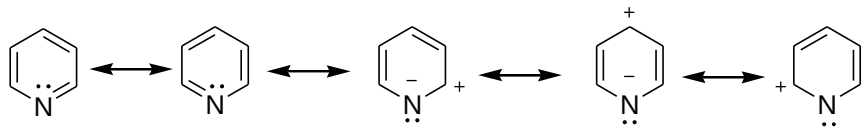
Pyridine undergoes reduction with lithium aluminum hydride or hydrogen in the presence of nickel catalyst to form piperidine.



With hydrogen iodide at 573 K, the reduction is accompanied by fission to form n-pentane and ammonia.



Pyridine has resonance energy of about 125 k.J mol^{-1}. Because pyridine has a large dipole moment of 2.23 D, it is best regarded as a resonance hybrid of the following contributing structures.



ii. Explain pyridine as low reactivity towards nucleophilic substitution

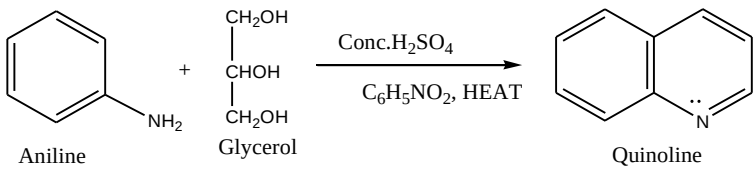
Reactivity of pyridine

A close look at the contributing structures of pyridine reveals that positions 3 and 5 will be sites for electrophilic attack. The remaining positions (2, 4 and 6) will be the sites for nucleophillic attack. Moreover, the ring is deactivated towards electrophilic reagents due to the withdrawal of electrons from the ring carbon atoms towards the nitrogen atom. Thus pyridine resembles benzene ring in nitrobenzene. Pyridine can be protonated in strongly acid medium. At that time, the positively charged nitrogen atom deactivates the ring much more than the unprotonated nitrogen atom. This is indicated by the difficulty in nitration and sulphonation in pyridine. Thus, pyridine is less reactive than benzene.

OR

b. i. What is the role of nitrobenzene, gylecerol,con.H_2SO_4 in the synthesis of quinoline

In this reaction, a mixture of aniline and glycerolis heated in the presence of sulphuric acid and a mild oxidizing agent, usually nitrobenzene or arsenic pentoxide. The reaction is exothermic and tends to become very violent. Ferrous sulphate or boric acid is generallyadded to make the reaction less violent.



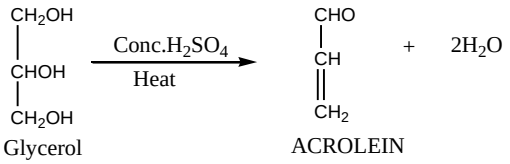
Aniline Glycerol Quinoline

Mechanism:

The mechanism of this reaction is not completely understood. However, it is believed that it proceeds by the following steps.

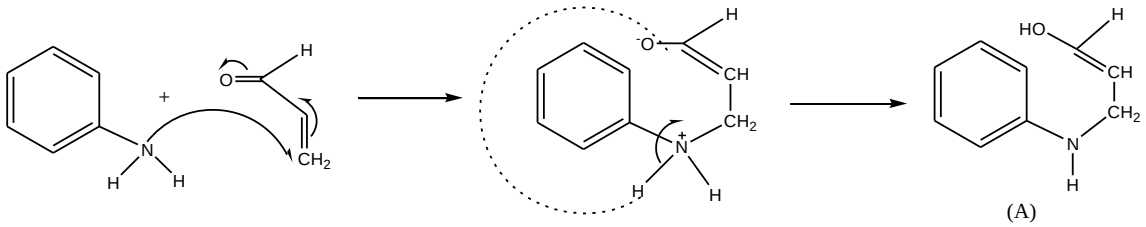
Step-1:

Glycerol undergoes dehydration with sulphuric acid to give acrolein.



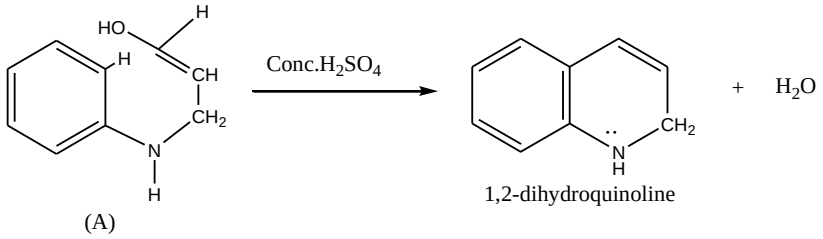
Step-2:

Aniline adds to acrolein (1,4-addition) to give (A).



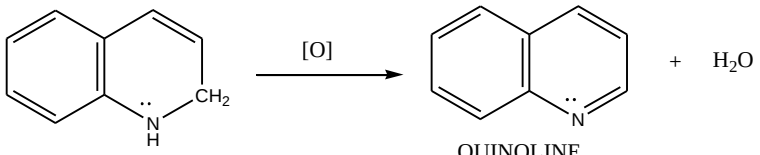
Step-3:

Compound (A) Undergoes ring closure in the presence of sulphuric acid to form 1,2-dihydroquinoline.



Step-4:

1,2-dihydroquinoline undergoes oxidation with nitrobenzene to finally yield quinoline. Nitrobenzene itself is reduced to aniline which is reused in step (2).

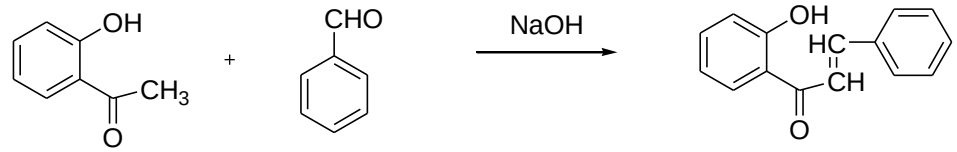


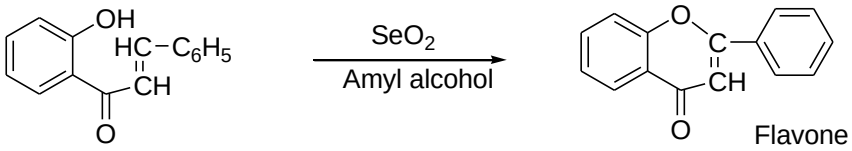
1,2-dihydroquinoline QUINOLINE

This synthesis is used for the commercial preparation of quinoline. It is also important because by starting with substituted anilines, substituted quinolines can be made.

ii. Illustrate the flavone from the following methods i chalcone method ii konsanecki method

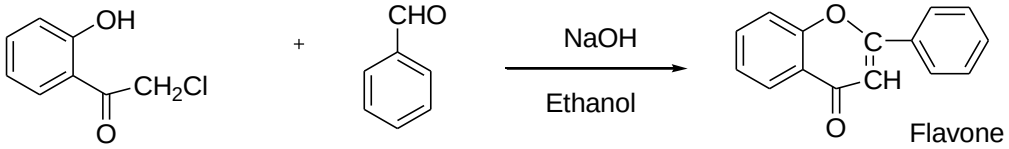
i) Chalcone method





Flavone

ii) Konsanecki method



Flavone

Reg. No.....

[12CHU501]

KARPAGAM UNIVERSITY

(Under Section 3 of UGC Act 1956)
COIMBATORE – 641 021
(For the candidates admitted from 2012 onwards)

B.Sc. DEGREE EXAMINATION, JANUARY 2015

Fifth Semester

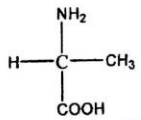
CHEMISTRY

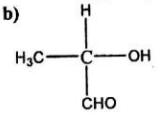
ORGANIC CHEMISTRY

Time: 3 hours Maximum : 100 marks

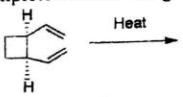
PART – A (15 x 2 = 30 Marks)
Answer ALL the Questions

1. What is racemisation?
2. Assign R or S configuration to the following compounds.

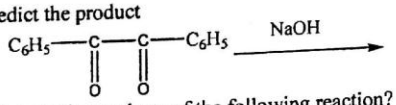
a) 

b) 

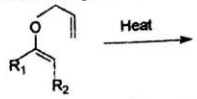
3. What do you understand by gauge and anti conformations?
4. Complete the following reaction



5. Predict the product



6. What are the products of the following reaction?



7. Explain the uses of Sucrose.
8. Give the conversion of glucose to N-Glucoside formation.
9. Explain the formation of carbohydrates by Photosynthesis method.
10. Explain how Peptides are formed from amino acids?

11. What is meant by the term salting out of a Protein?
12. What is the action of heat on glycine?
13. Illustrate Chichibabin reaction.
14. Explain why pyridine is much stronger base than Pyrrole.
15. Predict the product

PART B (5 X 14= 70 Marks)
Answer ALL the Questions

16. a. Write notes on Walden invension.

Or

b. Write notes on Sequence rules.

17. a. Describe the manufacture of Sugar beet. How does Sucrose react with (i) lime water (ii) acetic anhydride (iii) yeast (iv) Conc. HNO_3 and (v) Conc. and hot H_2SO_4?

Or

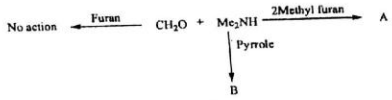
b. Discuss the Structure of D- Glucose.

18. a. Explain (i) Gabriel Synthesis (ii) Koop Synthesis

Or

b. Write notes on (i) N-Terminal and C-Terminal amino acid residues (ii) End Group analysis.

19. a. i. Using Skraup synthesis, prepare (a) 4- methyl quinaline,(b) ethyl quinaline
ii. Suggest a mechanism for the Pomeranz- Fritsch synthesis for isoquinaline?
iii.



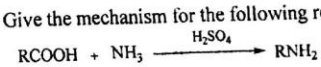
What are A and B explain?

Or

b. i. How could you account for the difference in the resistance of pyrrole and pyridine rings to the action of acids?
ii. How can you explain the instability of furan and pyrrole against the action of acidic agents?
iii. Between pyrrole and pyridine which one is more basic? Explain.

20. **Compulsory : -**

Give the mechanism for the following reaction and explain its application.



Reg. No.....

[13CHU501]

KARPAGAM UNIVERSITY

Karpagam Academy of Higher Education
(Established Under Section 3 of UGC Act 1956)
COIMBATORE – 641 021
(For the candidates admitted from 2013 onwards)

B.Sc., DEGREE EXAMINATION, NOVEMBER 2015

Fifth Semester

CHEMISTRY

ORGANIC CHEMISTRY

Time: 3 hours Maximum : 60 marks

PART – A (20 x 1 = 20 Marks) (30 Minutes)
(Question Nos. 1 to 20 Online Examinations)

PART B (5 x 8 = 40 Marks) (2 ½ Hours)
Answer ALL the Questions

21. a. Explain Walden invension with suitable example.

Or

b. Write notes on Sequence rules.

22. a. Give the mechanism for the following reaction and explain its application.

$$RCOOH + NH_3 \xrightarrow{H_2SO_4} RNH_2$$

Or

b. Explain claisen rearrangement with suitable example?

23. a. Describe the manufacture of Sugar beet. How does Sucrose react with (i) lime water (ii) acetic anhydride (iii) yeast (iv) Conc. HNO_3 and (v) Conc. and hot H_2SO_4?

Or

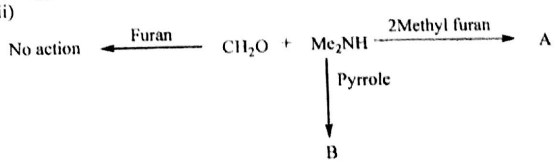
b. Discuss the Structure of D- Glucose.

24. a. Explain (i) Gabriel Synthesis (ii) Koop Synthesis

Or

b. Write notes on (i) N-Terminal and C-Terminal amino acid residues (ii) End Group analysis.

25. a. (i) Using Skraup synthesis, prepare (a) 4- methyl quinaline,(b) ethyl quinaline
(ii) Suggest a mechanism for the Pomeranz- Fritsch synthesis for isoquinaline?
(iii)



What are A and B explain?

Or

b. (i) How could you account for the difference in the resistance of pyrrole and pyridine rings to the action of acids?
(ii) How can you explain the instability of furan and pyrrole against the action of acidic agents?
(iii) Between pyrrole and pyridine which one is more basic? Explain.
