ORGANIC CHEMISTRY

1. General principles

A brief review of classification & sources of organic compounds, sp^3, sp^2, sp hybridization, sigma & pi- bonds, bond lengths, bond angles & bond energies along with their significance in reactions should be carried out. An overview of bond polarization, hydrogen bonds, inductive effects, resonance, and hyperconjugation be taken. Concept of homolytic & heterolytic bond fission, acidity & basicity with different theories should be covered briefly. Ease of formation & order of stabilities of electron deficient & electron rich species along with the reasons for the same should be covered. Relationships between energy content, stability, reactivity & their importance in chemical reactions should be covered. Calculations for determining empirical & molecular formula should be covered.

2. Different classes of compounds

The following classes of compounds should be taught in detail with respect to their IUPAC/ systematic nomenclature, industrial [wherever applicable] & laboratory methods of preparations, physical properties & chemical reactions with emphasis on reaction mechanisms [arrow based] & stereochemistry [wherever applicable].

- Alkanes [including cyclic compounds]
- Alkenes [including cyclic compounds]
- Alkynes [only open-chain compounds]
- Aliphatic hydroxyl compounds
- Alkyl halides
- Aldehydes & Ketones
- Carboxylic acids

- All functional derivatives of carboxylic acids.

3. Protection & deprotection of groups

Introduction to protection & deprotection of functional groups. Two examples each for amino, hydroxyl, & carbonyl groups. The significance of these in syntheses should be explained.

4. Aromaticity & chemistry of aromatic compounds

Concept of aromaticity, Huckel's rule & its use in determining the aromatic/non-aromatic character of a compound. A brief coverage of structure of benzene. Detailed coverage of electrophilic & nucleophilic aromatic substitution reactions. Reactivity & orientation in these reactions. Reactivity & orientation in mono- & disubstituted benzenes. Benzyne mechanism.

5. Different aromatic classes of compounds

The following classes of compounds with respect to their IUPAC / systematic nomenclature, industrial [wherever applicable] & laboratory methods of preparations, physical properties & chemical reactions with emphasis on reaction mechanisms [arrow based] & stereochemistry [wherever applicable].

- Aromatic hydrocarbons.
- Phenolic compounds.
- Aromatic & aliphatic amines.
- Diazonium salts.
- Aromatic nitro- compounds, aryl halides, & ethers.

6. Polycyclic aromatic hydrocarbons

Syntheses & reactions with mechanisms of bi & tricyclic fused carbocyclic rings like naphthalene, anthracene, & phenanthrene.

7. Carbonyl Chemistry

Carbonyl chemistry involving group conversions & their reaction mechanisms along with stereochemistry wherever applicable.

a. Wolf-Kishner reduction & Huang-Minlong modification.
b. Reduction of arylsulfonyl hydrazine/hydrazones to alkanes.
c. Bamford Steven reaction.
d. DCC Oxidation of alcohol.
e. Michael addition / 1,4-addition / conjugate addition.
f. Mannich condensation / reaction.
g. Robinson annulation.
h. Stobbe condensation.
i. Darzen's glycidic ester synthesis.
j. Beckmann rearrangement.
k. Baeyer Villiger rearrangement.
l. Curtius, Wolff, & Lossen rearrangements.
m. Willgerodt rearrangement.
n. Pinacol-pinacolone rearrangement.
o. Methylene transfer reactions. Use of diazomethane & sulphur ylides in the same.
p. Mono- & dialkylations in 1,3-dicarbonyl compounds.

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q. Formation & use of enol ethers, enol acetates & enamines as protective groups & in regiospecific alkylations.

8. Heterocyclic Chemistry

IUPAC Nomenclature of heterocyclic rings [3-10 membered] containing O, S, & N atoms. Nomenclature of above rings containing mono-, di-, & multiple [same or different] heteroatoms should also be covered. Nomenclature of 2 & 3 fused rings containing mono-, di-, & multiple heteroatoms [same or different] should also be covered. Syntheses & reactions of three to six- membered rings in detail. Syntheses of five & six-membered rings containing mono- or any di- heteroatoms [O, S, & N]. Syntheses of quinoline, isoquinoline, benzoxazole, benzothiazole, & benzimidazole, benzotriazole, and benzothiazole.

9. Bridged rings

Bridged ring systems & their nomenclature. C_8, C_9, C_{11} bridged bicyclic alkanes. Chemistry of hexamine, morphan, biperiden, amantadine, diazabicyclo[2.2.2] octane

10. Kinetic & thermodynamic control

Kinetic & thermodynamic control of sulfonation, enolate anion formation & alkylation of enamine reactions.

11. Stereochemistry

Stereochemistry. Chirality & asymmetry [introduction of the same to S, P, & N]. Definition & classification [different types of isomerisms]. Enantiomers, diastereomers. Enantiomerism & diastereomerism. Meso compounds & their optical activity.

Stereochemistry in acyclic compounds. Newman projection formulae & their significance. Conformational analysis of n- butane. Absolute & relative configuration. Assigning R & S configuration based on Cahn Ingold & Prelog system. Racemic mixture- its definition & resolution. Definitions of terms stereoselective, stereospecific, Enantiomeric excess & diastereomeric excess. Stereochemistry in cyclic systems. Conformations of cyclohexane. Cis-trans relationship in cyclohexane. Prediction of stability of different conformations of 1, 2- 1,3- & 1,4-disubstituted cyclohexanes. Effect of multiple substitutions on the stability of cyclohexane conformations. Chair conformations of cis-, & trans-decalins, perhydrophenanthrenes, & a tetracyclic steroidal nucleus. An introduction to atropisomerism.

12. Carbohydrates

Carbohydrates. Definition & classification. D & L nomenclature in sugars. Different ways of drawing / representing a sugar molecule [including cyclic Structure], interconversion of these representations. Anomers & epimers. Mutarotation. Reactions of glucose. Chain extension & chain reduction of a sugar.

13. Amino acids & proteins

Amino acids & proteins. Definition & classification. D & L Amino acids, natural, essential, & non- essential amino acids. Denaturation, Strecker, Gabriel phthalimide methods for the preparation of amino acids. Peptide bond & its formation. Two protective groups each, for - NH_2 & -COOH functionalities during protein synthesis. Sequencing of a protein by chemical & enzymatic methods.

14. Pericyclic reactions

Pericyclic reactions. Concept of HOMO & LUMO. Drawing of HOMO & LUMO of 1, 3-butadiene, allylic cation, radical & anion, & 1, 3, 5-hexatriene, Diel's-Alder & retro Diel's Alder reaction.

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PHARMACEUTICAL CHEMISTRY

1. Pharmaceutical Inorganic Chemistry

1. Pharmaceutical Impurities

Impurities in pharmaceutical substances, sources, types & effects of impurities. Limit tests for heavy metals like lead, iron, arsenic, mercury & for chloride & sulphate as per Indian Pharmacopoeia [I. P.].

2. Monographs

(a) Monograph & its importance, various tests included in monographs as per I. P. A study of the following compounds with respect to their methods of preparation, assay, & pharmaceutical uses of sodium citrate, calcium carbonate, copper sulphate, light & heavy kaolin, ammonium chloride & ferrous gluconate.

3. Isotopes

Isotopes- stable & radioactive, mode & rate of decay. Types & measurement of radioactivity. Radiopharmaceuticals & their diagnostic & therapeutic applications in pharmacy & medicine such as ^{125}I, ^{32}P, ^{51}Cr, ^{60}Co, ^{59}Fe, ^{99}Tc-M. Radiocontrast media, use of $BaSO_4$ in medicine.

4. Dentifrices, desensitizing agents, & anticaries agents

2. Medicinal Chemistry

5. Therapeutic classes of drugs

The following topics should be dealt with covering nomenclature [including stereochemical aspects], biological activity [including side & toxic effects], mode of action, structure-activity relationship [where ever applicable] & syntheses of reasonable molecules.

a) General anesthetics.
b) Local anesthetics.
c) Diagnostic agents.
d) Coagulants, anticoagulants & plasma expanders.
e) Antiseptics, disinfectants, sterilants, & astringents.
f) Purgatives, laxatives & antidiarrhoeal agents.

6. Various classes of therapeutic agents

A detailed study of the following classes with respect to drug nomenclature, classification, physicochemical properties, mode of action [MOA], structure-activity relationships [SAR], wherever applicable, synthesis of simple & prototype molecules, drug metabolism, therapeutic uses & side effects. Drug resistance, wherever applicable, should be covered in respective classes of drugs.

a) Antimalarials
b) Antiamoebic agents.
c) Anthelmintic agents.
d) Antibacterial sulpha drugs [only].
e) Quinolone antibacterials.
f) Antimycobacterial drugs.
g) Antifungal agents.
h) Antiviral agents including HIV & anti-HIV drugs.
i) Thyroid & antithyroid drugs.

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j) Antiallergic agents.

k) Antiulcer agents & Proton Pump Inhibitors.

l) Hypoglycemic agents.

7. Different classes of therapeutic drugs

A detailed study of the following classes with respect to drug nomenclature, classification, physicochemical properties, mode of action [MOA], structure-activity relationships [SAR], wherever applicable, synthesis of simple & prototype molecules, drug metabolism, therapeutic uses & side effects. Drug resistance, wherever applicable, should be covered in respective classes of drugs.

I. a. Sedative-hypnotics

b. Antiepileptic agents.

c. Neuroleptics.

d. Anti-anxiety drugs.

II. Antibiotics. Penicillins, cephalosporins & other beta-lactam antibiotics like imipenem & aztreonam. Beta-lactamase inhibitors such as clavulanic acid & sulbactam. Chloramphenicol. Tetracyclines. Aminoglycoside antibiotics. Macrolide antibiotics. Lincomycins. Polypeptide antibiotics. Anticancer antibiotics.

III. Steroids. Corticosteroids [gluco- & mineralocorticoids] & anti-inflammatory steroids. Sex steroids. Male & female contraceptive agents. Anabolic steroids. Anticancer agents.

8. Different classes of therapeutic drugs

A detailed study of the following classes with respect to drug nomenclature, classification, physicochemical properties, mode of action [MOA], biosynthesis, structure-activity relationships [SAR], wherever applicable, synthesis of simple & prototype molecules, drug metabolism, therapeutic uses & side effects. Drug resistance, wherever applicable, in respective classes of drugs.

I. Narcotic [centrally acting] analgesics [analgetics]. Morphine & all its structural modifications [peripheral & nuclear]. Narcotic agonists & antagonists [dual & pure]. Non-narcotic analgesics [NSAIDS]. Difference between narcotic & non-narcotic agents.

II. Adrenergic drugs. Neurotransmitters & their role. General & specific adrenergic agonists & antagonists [up to alpha-2 & beta-2 only].

III. Cholinergic agents. Muscarinic & nicotinic cholinergic agonists & antagonists [up to M_2 & N_2]. Neuronal [transmission] blockers.

IV. Drugs used in neuromuscular disorders. Drugs used in the treatment of Parkinson's disease. Central & peripheral muscle relaxants.

V. Hypertensive, antihypertensive, & antianginal agents.

VI. Diuretics.

VII. Eicosanoids. Prostaglandins, prostacyclins, & thromboxanes. Their biochemical role, biosynthesis, & inhibitors.

9. Introduction to quantitative structure-activity relationship. [QSAR]. Linear free energy relationship. Hammett's equation. Use of substituent constants such as π, σ, E_s, & physicochemical parameters such as pK_a, partition coefficient, Rm, chemical shifts, molar refractivity, simple & valance molecular connectivity to indicate electronic effects, lipophilic effects, & steric effects. Introduction, methodology, advantages & disadvantages/limitations of Hansch analysis.

10. Asymmetric synthesis. Chirality, chiral pool, sources of various naturally available chiral compounds. Eutomers, distomers, eudismic ratio. Enantioselectivity & enantiospecificity. Enantiomeric & diastereomeric excess. Prochiral molecules. Asymmetric synthesis of captopril & propranolol.

11. Combinatorial chemistry. Introduction & basic terminology. Databases & libraries. Solid phase synthesis technique. Types of supports & linkers, Wang, Rink, & dihydropyran derivatized linkers. Reactions involving these linkers. Manual parallel & automated parallel synthesis. Houghton's tea bag method, micromanipulation, recursive deconvolution. Mix & split method for the synthesis of tripeptides. Limitations of combinatorial synthesis. Introduction to throughput screening.

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PHARMACEUTICAL ANALYSIS

1. Importance of quality control in pharmacy

2. Acid-base titrations

Definitions of acids & bases according to Arrhenius & Lewis theory. Definitions of normality, molarity, molality, & equivalent weight. Primary & secondary standards with examples & differences between them. Standardization of strong acids & bases using primary & secondary standards. Preparation of standard solutions of & calculations of equivalent weights of oxalic acid, potassium acid phthalate, calcium chloride dihydrate, & sodium carbonate. Calculation of factors involved in standardization of sodium hydroxide, hydrochloric acid, & oxalic acid. Direct, back & differential titrations. Application of direct & back titrations to preparations like boric acid & borax in a mixture, ammoniated mercury, milk of magnesia, & zinc oxide ointment.

Law of mass action, acid-base equilibria, pH scale, pH & hydronium ion concentrations in aqueous systems, calculations of pH for weak acids & weak bases. Use & applications of pH meter. Hydrolysis of salts. Strengths of acids & bases, dissociation constant.

Theory of acid-base indicators. Neutralization [titration] curves.

Definition, different types of buffers [chemical & biological], & their composition. Buffer capacity, buffered isotonic solutions. Calculations involving preparation of various buffer capacity solutions. Biological & pharmaceutical applications of buffers.

3. Non-aqueous titrations

Acid-base definitions according to Lowry-Bronsted, Lewis & Arrhenius concept. Factors affecting strengths of acids & bases. Intrinsic structure & surrounding environment. Protophilic, protogenic, amphiprotic & aprotic solvents. Acid-base equilibria in non-

aqueous media. Titrants & indicators used for the assay of acidic & basic substances. Preparation of perchloric acid, formation of onium ion. Assay of 1°, 2° and 3° amines & amine hydrochlorides using perchloric acid & the reactions involved in it. Standardization of sodium ethoxide solution. Assay of phenols & phenobarbitone. General applications of non-aqueous titrations

4. Oxidation-reduction titration

Definition of oxidation, reduction, oxidizing & reducing agent. Equivalent weight, the concept of half reactions. Systematic balancing of half reactions with respect to:

a) Oxalic acid-$KMnO_4$,
b) $FeSO_4$-ceric nitrate, &
c) I_2-sodium thiosulphate solution titrations.

Calculation of equivalent weight of oxalic acid, $KMnO_4$, $FeSO_4$, permanganate & I_2 from half- reactions. Calculation of factors for titrations mentioned in a, b & c.

a) Redox titrations:

   $KMnO_4$ as a self indicator, it's preparation, standardization, & use in the assay of ferrous gluconate tablets, H_2O_2, & $NaNO_2$ solution.

b) Iodimetric & iodometric titrations. Definitions & difference between iodimetry & iodometry. Preparation, standardization of iodine solution. Assay of ascorbic acid & sulphur ointment by iodimetry. Assay of copper sulphate & ferric chloride by iodometry.

c) Bromometric titrations.

d) Iodate titrations. Definition. Preparation, standardization & use of KIO_3 in the assay of ascorbic acid & KI.

e) Cerimetric titrations. Preparation, standardization & use of ceric solutions in the assay of paracetamol tablets. Its advantages over permanganate solutions.

f) Bromine titrations. Preparation, standardization & use of bromine solution in the assay of phenol & isoniazid tablets.

g) Potassium dichromate titrations. Preparation, standardization & use of potassium dichromate solution in the assay of ferrous ammonium sulphate.

5. Precipitation titrations

The principle of solubility product & sparingly soluble salts.

Titrants & indicators used in Mohr's, Volhard's, & Fajan's methods. Preparation & standardization of silver nitrate & ammonium thiocyanate solutions. Assay of sodium chloride by Mohr's method, use of nitrobenzene in the assay of halides, ammonium chloride, & thiourea by Volhard's method. Calculation of factors in argentometric titrations. Titration curve method. General applications of precipitation titrations.

6. Complexometric titrations

Difference between double salts & co-ordinate compounds. Definitions of coordination number of metal ions, ligands- uni-, bi-, & multidentate. Complexing, chelating, & sequestering agents with respective examples. Structure of complexes of platinum with ammonia. Ethylenediamine tetraacetate [EDTA] as a multidentate ligand in complexometry. Coordinate compounds of EDTA with bi-, tri-, & tetravalent metal ions. Stability of complexes & factors affecting it, use of buffers in EDTA titrations. Selective analysis of ions based on pH adjustments, use of masking & demasking agents, pM or metal ion indicators. Standardization of EDTA solution, titration curves, and examples of assays carried out by direct & back titrations & by replacement of one complex by the other. Applications of complexometry in the assays of calcium gluconate, milk of magnesia, zinc undecenoate ointment, & aluminium hydroxide gel. Assay of NaF by indirect titration.

7. Gravimetry

Principles of gravimetry. Factors affecting precipitation, formation, & properties of the precipitate. Colloidal state. Impurities in the precipitate, conditions of precipitation. Precipitation from homogenous solutions, washing, drying, & ignition of the precipitate. Experimental techniques of drying & ignition. Applications of gravimetry in pharmacy.

8. Extraction techniques

Liquid-liquid extraction, separation of mixtures by extraction. Distribution law. Successive & multiple extraction [Craig method], continuous counter- current extraction. Effect of temperature & pH on extraction. Inert solute, associate ion pair formation, emulsion problem in extractions. Applications in pharmacy.

9. Potentiometry

Theory, ion-selective electrodes, measurement of potential, red-ox titration curve, pH measurement, the relation of pH to potential. Applications in pharmacy.

10. Miscellaneous methods of analysis

Diazotization titrations. Kjeldahl nitrogen estimation. Karl Fisher titrations. Liquid gelenicals. Oxygen flask Determination of alcohol content in liquid gelenicals. Oxygen flask combustion method.

11. Calibration

Calibration of instruments.

12. General principles of spectroscopy

Wave-particle duality, wave properties, particulate properties. Line & band spectrum. Electromagnetic spectrum. Absorption & emission spectroscopy. Understanding of terms

such as absorbance, transmittance, absorptivities, molar absorptivity, E 1cm 1%, λmax, the effect of solvent & pH on λmax.

13. Ultraviolet-visible Spectrometry

Different electronic transitions. Auxochromes & their effects, auxochromic, bathochromic & hypsochromic shifts [red & blue shifts]. Beer-Lambert law, its derivation, deviations in Beer's law. Single & double beam spectrophotometers covering sources of radiations, different monochromators, detectors such as barrier cell, photocell, photomultiplier tube. Photodiode array detector. Applications of this technique in qualitative & quantitative estimations giving emphasis on problem-solving. Fieser-Woodward rules for calculations of theoretical λmax values.

14. Spectrofluorimetry

Principle, definitions & types of luminescence. Mechanism of fluorescence & phosphorescence. Singlet & triplet states & intersystem crossing. Fluorescence yield & factors affecting it. Quenching of fluorescence & fluorescence quenchers. Structure & fluorescence. A brief discussion of instrumentation. Applications of fluorimetry in pharmacy.

15. Flame photometry & atomic absorption spectrometry

Principle & instrumentation with emphasis on working & importance of different components. Temperature, flame absorption & emission profiles. Interferences & their avoidance. Quantitative estimations & applications.

16. Infrared spectrometry

Infrared region in EM spectrum. The principle, different stretching & bending vibrations. Components [& their working] of a dispersive instrument. Fourier transform [FT]

technique, FT instruments & their comparison with dispersive instruments. Sample handling techniques. Functional group & fingerprint regions in the spectrum. Functional groups identification & their use in the characterization of compounds. Problems based on the identification of functional groups from spectra of unknown compounds.

17. Proton nuclear magnetic resonance spectrometry

The principle involved in the technique. Knowledge about fundamental terms involved such as quantized absorption, flipping of nucleus, spin number, magnetic moment, magnetogyric ratio, relaxation, etc. Equations relating these terms to the frequency of radiation & magnetic field [without derivation of the equations]. Types of relaxation processes. Low & high-resolution instruments. A brief discussion on the low-resolution instrumentation [60 MHz]. Quantitative knowledge of the relationship between MHz & magnetic field. An introduction to superconductivity magnets. Solvents & reference standards used. Setting up of NMR scale. Sample preparation. Shielding & deshielding of a proton & its effect on chemical shifts. Discussion on & importance of equivalent & nonequivalent protons [number of signals], chemical shifts [position of signal] & their calculation from the spectrum, chemical shifts of different H's, splitting [multiplicity] of a signal, coupling constants [J values] , integration [area under the signal]. Importance of these terms in identification [or confirmation] of different functional groups. Significance & contribution of J value in stereochemistry. Prediction [expected theoretical values] of chemical shifts & multiplicities for all protons from simple structures containing up to 12-15 carbons. An introduction to FT-technique & its significance in ^{13}C-NMR spectrometry.

18. Mass spectrometry

Principle. Low & high-resolution instruments. Components & importance of each in brief.

Different types of mass spectrometric techniques. Brief knowledge of Chemical Ionization mass spectrometry. Calculations of hydrogen deficiency index [HDI] or unsaturation index [UI]. Base or parent peak, molecular ion, M + 1, M + 2 peaks. Calculations of molecular weight based on M +1 & M + 2 peaks. Formation of molecular ion & further fragmentation. Rearrangements in mass spectrometry. Major modes of fragmentations of hydrocarbons, hydroxyl compounds, halogen compounds, aldehydes, ketones, carboxylic acids, and amines. Introduction [only] to recent advances in MS.

19. Polarography.

Principle & instrumentation. Ilkovich equation [no derivation] & its importance. Dropping mercury electrode [DME], saturated calomel electrode. Liquid-liquid junction potential, polarographic cell. Explanation of origin of the S-shaped C-V curve. Applications of this technique. Amperometric titrations, principles, instrumentation, & applications.

20. Nephelometry & Turbidimetry

Principles, Tyndall effect. Duboscq turbidimeter. Eeel's nephelometer. Applications.

21. Chromatography.

Principle, rate & plate theory, Van Deemter equation & the parameters affecting separation/band broadening. Classification of chromatography, retention factor. A detailed study of thin layer chromatography [TLC], preparative TLC, paper chromatography [PC], column chromatography, gas chromatography [GC / GLC].

Qualitative & quantitative applications of the above techniques. An introduction to high-performance TLC [HPTLC], comparison of TLC & HPTLC. A brief introduction to high pressure / performance liquid chromatography [HPLC].

22. Miscellaneous

An introduction to electrophoresis. An introduction to lasers & masers.

Statistical treatment to experimental data. Sampling techniques & applications in pharmaceutical industry.

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