CHAPTER 10

CHEMISTRY

Doctoral Theses

048. BHAKTA (Gajadhar)
Inorganic Nanoparticles as Potential Nonviral Vectors for Delivery of DNA.
Supervisor : Prof. Amarnath Maitra
Th 14197

Abstract

The study utilizes the aqueous core of the reverse micelles having tunable size for carrying out the synthesis of various ultrafine inorganic nanoparticles doped with nucleic acids. These materials have been extensively characterized by different methods and their possible biotechnological applications have been explored. The ultrafine and monodispersed magnesium phosphate and manganous phosphate nanoparticles encapsulating pDNA can be prepared in the acqueous core of AOT/n-hexane reverse micelles. pDNA can be well protected inside the inorganic matrix of magnesium phosphate (MgPi) and manganous phosphate (MnPi) from the DNase attack and they release pDNA for the transfection in vitro and in vivo. These nanoparticles exhibit very high transfection efficiency in vitro. The in vivo transfection of these nanoparticles also showed a sustained gene expression in different body tissues. It is possible to modify the surface of these nanoparticles to make them long cirulating (by PEGylation) and target specific. Liver was targeted by tagging PAG (p-aminophenyl-1-thio-β-D-galactophyranoside) to the nanoparticles surface. MgPi encapsulating pDNA can be used as a carrier for DNA delivery as well as DNA vaccination as it induces both humoral and cell mediated responses. Gadolinium oxide-doped silica nanoparticles (<100nm)can also be synthesized in the reverse micellar core. Their surface can also be modified and pDNA can be immobilized successfully onto it. The surface immobilized pDNA was resistant to the external DNase attack. Gadolinium oxide-doped surface modified silica nanoparticles can be used as carriers for DNA delivery as well as contrast agent for magnetic resonance imaging (MRI).

Contents

1. Introduction 2. Literature Review. 3. Experimental Materials. 4. Magnesium and Manganous Phosphate Nanoparticles Encapsulating Genetic Materials : Preparation and Physical Characterisation. 5. In Vitro and in Vivo Behaviour of PDNA Encapsulated Magnesium and Manganous Phosphate Nanoparticles. 6. Magmesium Phosphate Nanoparticles : A Novel Carrier and Adjuvant for DNA Vaccines. 7. Gadolinium Oxide-Doped and DNA coated Silica Nanoparticles as Magnetic Resonance Imaging Cum Gene Dilivery Vehicles. 8. Conclusion. Bibliography and Appendix.

049. BHATTACHARYA (Anupam)
Lipase Catalyzed Reactions on Triazolyl Sugars and Synthesis of PEG Containing Polymers and Base Flipping DNA-Base Surrogates.
Supervisor : Prof. V S Parmar
Th 14195

Abstract

Lipase catalyzed enzymatic reactions which has contributed significantly to the growth of organic synthesis as a scientific discipline was utilized. Potential of lipase catalysis was explored in monoacylation of triazolyl sugar derivatives utilizing acid anhydrides as the acylating agents. Lipase catalyzed reactions again proved to be a better alternative in comparison to existing chemical methods. In all the cases primary hydroxyl gets acylated leaving the secondary hydroxyl untouched. Comparative study with other acylating agents such as 2, 2, 2-trifluoroethyl butyrate and vinyl acetate has clearly demonstrated the efficacy and superiority of long chain acid anhydride over other acylating agents, when triazolyl sugar derivatives are substrates. Demonstrated the effect of hydrophobicity in the lipase catalyzed reactions. Method developed will circumvent the problem of protection-deprotection in acyclonucleoside synthesis. Developed an efficient methods which clearly demonstrates the usefulness of enzyme catalyzed polyesterification of polyethylene glycol with other substrates. PEG which is utilized for various beneficial purposes has been modified utilizing aliphatic side chains, the polymers generated on coupling modified PEG diacids and diols with various other diols and diacids have both hydrophilic and hydrophobic character, thereby making them useful for utilization in different biological systems. The medhos developed uses enzymes and removes steps involving chemical

coupling requiring high temperature or potentially harmful coupling gents in stoichiometric amounts. Accomplished the synthesis of DNA base surrogates by using a new methodology at a very crucial step of C-glycosylation, the method developed involves use of less toxic metal and gives bettern yields compared to the existing procedure. The phosphoramidities synthesized in the last step of synthetic protocol were used in the automated solid-phase synthesis of oligonucleotides. The oligonucleotides obtained were hybridized with the complementary strands containing a target adenine opposite to the base surrogates 5'-TCGA-3' recognition sequence of DNA Mtase M. TaqI DNA Mtase were investigated in solution. The pyrene residue conferred the highest abasic-site stabilization and led to the highest binding affinity to M. TaqI.

Contents

1. Enzymatic Studies on Triazolyl Sugar Derivatives. 2. Lipase Catalyzed Polyesterification Studies on PEF and Pegdiacids. 3. Synthesis of Polycyclic Aromatic DNA-Base Surrogates. 4. Summary. Bibliography.

050. BISHT (Savita)
Inorganic and Organic Nanoparticles in Therapeutic Applications.
Supervisor : Prof. Amarnath Maitra
Th 14191

Abstract

Establishes a highly reproducible methodology for the preparation of different types of inorganic and organic nanoparticles doped with biomolecules (plasmid DNA, enzyme, FITC-Dx). Explores their potentiality as carriers for various therapeutic applications. Preparations of two types of nanoparticles have been described : (a) Ceramic nanoparticles for gene/drug delivery (Calcium Phosphate and Superparamagnetic iron oxide), (b) Organic nanoparticles for ophthalmic delivery (Copolymer of NIPAAM-VP-AA). For the preparation of ultrafine-doped ceramic nanoparticles, an aqueous core of the water-in -oil microemulsion has been chosen as an ideal media. As the dimensions of the host aqueous core of reverse micellar droplets can be modulated by adjusting the water to surfactant ratio (Wo), ultra fine particles of the desired shape and size can be synthesized. Not only that, by tuning the size of the host aqueous core, biomolecules of varying activities can be immobilized. Further, to make the entire prepartive method easy and simple as well as the nanoparticles prepared using this method as biocompatible and non-toxic, n-hexane has been used as a solvent and AOT as a surfactant. Since hexane is a volatile solvent, it can be removed easily by simple vacuum evaporation and AOT being an anionic surfactant can be removed by getting precipitated as its inosluble calcium of zinc salts. Such organically doped ceramic materials can have potential in many frontiers including, immunochemistry, drug/gene delivery, enzyme therapy etc.

Contents

1. Introduction. 2. Literature Review. 3. Experimental. 4. Calcium Phosphate Nonoparticles as Non-Viral Vector for Delivery of the Genetic Materials : Preparation and Physiochemical Characterization. 5. Antibody Response of Marker DNA, pSVβgal, Delivered Through Calcium Phosphate Nonoparticles : A Potential DNA Vaccine Carrier. 6. Superparamagnetic Iron Oxide Nanoparticles Encapsulating Enzymes and Other Molecules : A Potential Magnetically Driven Drug Delivery System. 7. Long Residing Nanoparticles of Polymeric Micelles for Ophthalmic Delivery of Hydrophobic Drugs Across the Corneal Membrane. 8. Conclusion. Bibliography.

051. CHADHA (Preeti)
Density Functional Study of Some Carbene Rearrangements.
Supervisor : Prof. Rita Kakkar
Th 14196

Abstract

Deals with some of the applications of quantum chemistry to the study of unimolecular rearrangements. It is concerned with the study of the structures of isomers, their relative stabilities, and interconversions. Entails some applications of density functional theory to problems involving carbenes. The various stable and unstable isomers on the C_3H_4 potential surface, and their modes of interconversion, have been studied. The 1,2 migration of hydrogen in vinylidene to yield acetylene was studied in detail. Concluded that for reactions involving open shell systems and hydrogen migrations, polarization and diffuse functions must be included both for geometry optimizations and energy calculations.

Contents

1. Introduction. 2. C_3H_4 : Density Functional Study of Structures

and Stabilities of Isomers. 3. C_3H_4 : Density Functional (DFT) Study of Interconversion of Isomers. 4. Density Functional Study of Acylozycarbene Rearrangements. 5. Theoretical Study of Unimolecular Rearrangements of Vinylidenes to Acetylenes. 6. Conclusions and Perspectives. Bibliography and Appendices.

052. GUPTA (Nidhi)

Template Synthesis and Spectroscopic Studies on Transition Metal Complexes with Polydentate Macrocyclic Ligands.

Supervisor : Dr. Sulekh Chandra
Th 14194

Abstract

Synthesis and characterization of transition metal complexes with seven hexadentate macrocyclie ligands have been reported. The ligands are : (i) 1,7,10,16-tetraaza-2,6,11,15-tetraone-4,13-dithiacyclooctadecane; (ii) 1,7,11,17-tetraaza-2,6,12,16-tetraone-4,14-dithia-cyclocosane; (iii) 1,7,10,13, 19,22-Hexaaza-2,6,14,18-tetraone-4,16-dithia cyclotetracosane; (iv) 1, 7, 14,20-tetraaza-2,6,15,19-tetraone-4,17, dithia tricyclo [22,4, $O^{21,26}$, $O^{8,13}$] hexacosa 8,10,12,21,23,25 hexene; (v) 1,7,13,19,25,26-Hexaaza-2,6,14,18 tetraone-4,16 dithia tricyclo [23,3,1,$I^{8,12}$] hexacosa [8(26),10,12,20(25),22,24] hexene; (vi) 1,4,10,13-tetraaza-19,20-deither-tricyclo [17,3,1, $I^{5,9}$] - 1,4,9,13-cosa tetraene; (vii) 1,5,11,15-tetraaza-21,22-diether-tricyclo [19,3,1, $I^{6,10}$]-5,10,15-dicosatetraene. The complexes were synthesized by template condensation method with L1, L2, L3, L4, L5, L6 and L7 with Cr(III) and Mn (II) only mononuclear complexes and both mono and homobinuclear complexes with Co(II), Ni(II) and Cu(II) were synthesized. The complexes were characterized by elemental analysis, magnetic susceptibility measurements, molar conductance, IR, electronic and EPR spectral studies.

Contents

1. Introduction. 2. Chromium (III) $3d^3$. 3. Manganese (II) $3d^5$. 4. Cobalt (II) $3d^7$. 5. Nickel (III) $3d^8$. 6. Copper (II) $3d^9$. 7. Summary. Bibliography.

053. KALRA (Neerja)

Selective Deacylation Studies on Sugar Derivatives and Synthesis and Incorporation of 2'-Aminonucleosides into Oligonucleotides.

Supervisor : Prof. V S Parmar
Th 14335

Abstract

2'-Amino LNA analogues appealed to us for several reasons. Firstly, the nitrogen atom of the 2'-amino-LNA monomers is very suitable for functionalization of high-affinity oligonucleotides and thus, this structural diversity can be explored to apply within biology. Secondly, amono-derivatized ONs have displayed increased thermal affinities toward complementary ONs because of the introduction of positively charged moieties at physiological pH. The synthesis of 2'-amino-LNA type 5-methyl cytosine phosphoramidite has been performed by following a multi-step synthetic route using 1,2:5,6-di-O-isopropylidene-α-D-allofuranose as starting meterial. This give access to sufficient amount of 2'-amino-LNA type 5-methyl cytosine phosphoramidites needed for the automated synthesis of, e.g., 2'-amino-LNA oligomers and in depth evaluation of their in vitro and in vivo properties.

Contents

1. CHEMO-, REGIO- and Diastereoselective Biocatalytic Deacylation Studies on Furanoses : Generation of Novel Bicyclic Sugar Derivatives. 2. (a) Synthesis and Incorporation of N-Alkylated and N-Acylated 2'-AMINO-2'-Deoxyuridine. (b). Convenient Synthesis of Novel 5-Methylcytosine-Based 2'-Amino-LNA Monomers. 3. Summary. Bibliography.

054. KUNDRA (Ekta)
Synthesis, solid State and solution studies on Transition Metal Complexes of Benzothiazolyl Azo Dyes as Chelating Agents
Supervisor : Prof. B S Garg
Th 14328

Abstract

Describes the synthesis, solid and solution characterization of complexes of azo dyes 6-Me-BTAMB, 6-OMe-BTAMB and 6-NO_2-BTAMB With various bivalent metal ions. shows that the formation constant log $K_{\text{M-6-OMe-BTAMB - glycine}}$ is higher than the formation constants of the binary complexes of the primary and secondary ligands. The % concentration of the species as a function of pH has been calculated and plotted. According to siegel the relative stability of a ternary complex MAB as compared to its binary complex MB can be quantitatively expressed by the following equation :

$$\Delta \log KM = \log ß\ MAB - (\log KMA + KMB)$$

Usually the ternary complexes have a negative value of Δlog KM. A low negative or a positive value of Δlog KM indicates extremely high stability of the ternary complex. In the present case all the ternary complexes M(II)-6-OMe-BTAMB-glycine have a negative Δlog KM value.

Contents

1. Introduction. 2. Materials and principles of basic techniques used during investigations 3. Isolation and characterization of Cu(II), Ni(II), Co(II), and Zn(II) complexes of 2-[2-(6-methyl-benzothiazolyl) AZO] -5-dimethylaminobenzoic acid 4. Isolation and characterization of Cu(II), Ni(II), Co(II), and Zn(II) complexes of 2-[2-(6-methyl-benzothiazolyl) AZO] -5-dimethylaminobenzoic acid 5. Potentiometric investigations on transition metal complexes of 6-OMe-BTAMB, 6-Me-BTAMB and 6-NO_2-BTAMB 6. Ternary complexes of metal ions with 6-OMe-BTAMB as the primarfy ligand and glycine as the secondary ligand. 7. Summary. Bibliography.

055. RANA (Parul)
Eco-Friendly Green Chemistry Approach Towards the Electrochemical Treatment of Wastewater Containing Hazardous Heavy Metal Ions Using Carbon Aerogel Electrodes.
Supervisors : Prof. B S Garg and Dr. Chitra Rajagopal
Th 14192

Abstract

The study involves control and minimization of environmental pollution through remediation of toxic metal ions viz; Cr, Pb, Hg, Cd and Ni from aqueous solutions using carbon aerogel electrodes. This technique can be up-scaled for the treatment of metal containing effluent from various industrial establishments, thus preventing the release of hazardous metal ions to water-bodies, which can otherwise lead to poisoning of aquatic as well as human life. Model for experimental designing, energy requirement and mechanism of this technology has been discussed in detail. This technique provides a fruitful area of study on removal of other inorganic and organic impurities from wastewater using carbon aerogel electrodes.

Contents

1. Introduction. 2. Materials, Principles and Procedures of Basic Techniques used in the Investigations. 3. Screening

Studies on the Electrosorption of Chromium (III) and Chromium (VI) using Graphite, Titanium, Aluminium and Carbon Aerogel Electrodes.

056. SHARMA (Neera)

Photophysical Study of Some Biologically Active Indoles in Homogeneous and Organized Media.

Supervisor : Prof. R C Rastogi

Th 14331

Abstract

The use of absorption and fluorescence spectroscopy to study the excited state properties and solubilization of probe in homogeneous and organized media has been found to be quite satisfactory. The study on excited state dipole moments of indole systems has brought into focus the complexities observed in the spectral properties due to the presence of two overlapping transitions i.e. ^1L_a and ^1L_b. A prominent red shift in flourescence band on increasing the polarity of environment suggests π–π* transition indicating ^1L_a to be the emitting state. This is further supported by the increase in the dipole moment $(\Delta\mu)$ upon excitation in all the cases. The valuable information so obtained about the nature of the emitting state opens the possibility of examination of various theoretical models for the electronic structure of the excited states, which is a key to design nonlinear optical materials. The experimental simplicity and the excellent correlation of experimental data perhaps arising from the rigor associated with the representation of the solvent indoles. The correlation of microscopic solvent polarity parameter, E N/T vs. Stokes shifts has been found to be better than with the bulk solvent polarity functions $F_1(D,n)$ and $F_2(D,n)$. Experimentally estimates of changes in dipole moment $(\Delta\mu)$ are found to be in fair agreement with the theoretical results. The prototropic reaction equilibria have been found to play a singnificant role in the excited state. The fluorescence spectral data suggest the formation of oxoniumion through the excited state proton transfer reaction in highly acidic media. A high intensity band in the basic pH range has been observed and explained by the formation of oxidative photoproducts. pK^*_a values determined by the fluorimetric titration curves tend to vary in different media. The higher value of pK^*_a in SDS and lower one in CTAB are well explained by pseudophase ion-exchange (PIOE)model. pK^*_a values for 5-hydroxyindole-3-acetic acid are found to be less affected by surfactant media, due to its weak hydrophobic and strong polar nature. The solubilization studies of

5-methoxytryptamine and N,N-dimethyl-5-methoxytryptamine in CTAB show the fluorescence quenching mechanism by Brions more prominently for their cationic forms. The nature and polarity of the binding site for the cationic forms of both the probes in SDS is found to be more hydrophobic than their neutral forms. The calculated cmc values are in good agreement with the literature values. The presence of two hydrophobic methyl groups makes N,N-dimethyol-5-methoxytryptamine a better bindubg oribve as syggested vt gughger by higher binding constant values. The large value of binding constant for neutral probe in CTAB suggests the interior environment to be more hydrophobic in CTAB than SDS. The long aliphatic chain in CTAB makes up for an easier movement of probe towards the core so that the neutral probe can penetrate to a much larger extent in CTAB. In the case of N,N-dimethyl-5-methoxytryptamine, penetration towards the core is found to be deeper due to the presence of two hydrophobic methyl groups.

Contents

057. SHUKLA (Piyush Kumar)
Theoretical study of some reaction paths and magnetic Properties of some Molecules.
Supervisor : Prof. N K Ray
Th 14327

Abstract

B3LYP functional has given satisfactory results for the study of reaction paths and relative stabilities of reactants, products and transition states. For pyronone the diketo form emerges to be more stable then 4-Hydroxy-α-pyrone as well as 2-Hydroxy-γ-pyrone. It has been consistently found that inclusion of correlation significantly decreases the activation energy and also makes reaction less endothermic. In the hydrolysis of CO_2, second and third water plays a role catalyst by decreasing the angular strain in the ring of transition state. Effect of second and third water molecules is truly synergetic. Gauge-independent atomic orbital (GIAO) method at the RHF/6-31G*

level of theory has been found to give satisfactory results for ^{13}C NMR chemical shifts for series of compounds studied. ESR hyperfine coupling constant can be satisfactorily estimated by using density functional calculation. Simple additivity model worked satisfactorily on poly-methyl and polyaza substituted naphthalenes. Consistency of the results for various systems studied indicates that the simple additivity model can be used for the assignment of the ^{13}C NMR chemical shift values where experimental results cannot be resolved properly. It is also noteworthy that this model is computationally economical as it need computational results of only the unsubstituted molecule and its non-equivalent mono substituted molecule. Concludes that the computationally economical B3LYP density functional with moderate size 6-31G* basis set is quite adequate to study a variety of properties like energetics potential energy surfaces NMR chemical shifts and ESR hyperfine coupling constants for various chemical systems. Its less computational power demand and accuracy opens scope to handle larger bio-molecular systems with adequate reliability.

Contents

1. Introduction. 2. Density functional study of some reaction paths. 3. Density functional study of α-Pyrone, γ-Pyrone and their derivatives. 4. Study of ESR hyperfine coupling constants of some radical cations and anions. 5. Study of ^{13}C NMR chemical shift and additivity model for methyl and AZA substituted naphthalenes. 6. Conclusion. Bibliography.

058. SUSHIL KUMAR
Single Electron Transfer Reaction Studies by UV and ESR Spectroscopy
Supervisor : Dr. Harish Chandra
Th 14190

Abstract

Attempts to understand the phenomenon of SET. The choice of cholesterol as target molecule is because of some fascination, on one hand it is said that this molecule plays a very crucial and positive role and on the other hand its excess plays havoc with human life. The presence of powerful electron donor and/or acceptor in the human body may be partly due to the absolute necessasity of the human life and partly could be the negligence. Therefore, when such molecules come in close proximity to cholesterol, electron transfer to/or from can initiate the primary reaction leading to the cascading effect. Of

course these reactions would be clearly in-vivo, therefore, it is impossible to mimic these reactions in-vitro, but all reactions which are supposed to be occurring in-vivo are first studied in-vitro. Employed UV, IR and ESR spectroscopy as major tools for the study. The subject has been studied in two parts; UV spectroscopic studies have furnished some interesting results and ESR studies have provided some clues to the actual transfer of electron.

Contents

1. Introduction. 2. Interaction of Cholesterol with Nucleic Acid Bases, Vitamins and Cholesterol Lowering Drugs. 3. Single Electron Transfer (SET) Chemistry. 4. UV Spectroscopy. 5. IR Studies. 6. Electron Spin Reasonance (ESR) Spectroscopy. Bibliography.

059. SWAIKA (Adarsh)
Potentiometric Investigations on the Chelation Behaviour of Biologically Active 1,3-Diaryl-5-(Arylazo)-Dihydro-2-Thioxo-4,6(!H,5H) Pyrimidinedione Derivatives with Bivalent Metal Ions.
Supervisor : Prof. S K Sindhwani
Th 14193

Abstract

Studies, pH-metrically the following four ligands for their chelation with some bivalent metal ions, leading to their Stability Constants (S.C.) and related thermodynamic parameters i.e. 1,3-diary1-5-(arylazo)-dihydro-2-thioxo-4,6(1H,5H)-pyrimidinediones
where (i) diaryl = 4-chloro aryl = 4-methoxy
(ii) diaryl = 4-methoxy aryl = 4-chloro
(iii) diaryl = 4-chloro aryl = phenyl
(iv) diaryl = 4-methoxy aryl = phenyl
Their binding characteristics were also an area of interest. The present studies have been carried out on the following aspects, with a view to investigate as to how the variation in them will have a bearing on the stability of complexes. (1) Effect of ionic strength (2) Effect of temperature. The pH-metric techniques has been employed. A computer programme has been developed for the calculation of n and pL values. The S.C.s at different ionic strengths and different temperatures have been calculated thus. A χ (chi-square) calculation has also been used to test the significance of the parameters thus evaluated. Thus, found S.C.s and other thermodynamic parameters may provide useful information (with regards to slectivity and sensitivity for

bivalents metal ions studied) for the removal of toxic metals from biological systems and/or in analytical chemistry for quantitative of qualitative estimation.

Contents