Bifunctional Compounds

Alzheimer's Disease (AD) is the most prevalent neurodegenerative disease, currently affecting 5 million in the US and 25 million population worldwide. Unfortunately, there is no treatment for AD, and its accurate diagnosis requires a detailed post-mortem examination of the brain. The formation of extracellular amyloid plaques containing the amyloid [beta] (A[beta]) peptide is one of the pathological hallmarks in the brains of Alzheimer's patients. In addition, numerous studies show that the metal ions can interact with the A[beta] peptides and affect the aggregation process dramatically, especially for copper ions that can stabilize the A[beta] oligomers, leading to high neurotoxicity.In this regard, we developed a series of novel bifunctional molecules that have high binding affinity with various A[beta]42 species and strong metal-binding ligands to modulate the interaction of copper ions with A[beta]42 species to alleviate the Cu2+-induced A[beta]42 cytotoxicity. Different A[beta] binding fragments, bis-styryl stilbene and benzofuran derivatives, were synthesized successfully and modified by adding strong metal-binding ligand through the Mannich reaction. Several in vitro assays were performed to evaluate the ability to quench ROS and attenuate the cytotoxicity of Cu2+-induced A[beta] species. Moreover, immunostaining studies were also employed to see the binding specificity of the compounds. The fluorescence images show that most of the bifunctional compounds can bind to the amyloid plaques specifically. More interestingly, some of the compounds show high binding specificity of soluble A[beta] oligomers, confirming by the oligomer-specific antibody labeling.Furthermore, the novel bifunctional compounds were also evaluated as PET imaging agents for AD. Taking advantage of the high binding affinity with Cu2+, the developed bifunctional compounds were preloaded with 64Cu, and these 64Cu complexes were evaluated to be potential PET imaging agents for Alzheimer's Disease. According to the in vitro results, several compounds were selected for biodistribution studies to characterize further the imaging properties in vivo. Overall, these studies lend promise to our future studies aimed at developing improved bifunctional compounds as novel theranostic agents, given the dearth of treatment and diagnostic tools for AD.

Molecular spectroscopy has achieved rapid and significant progress in recent years, the low temperature techniques in particular having proved very useful for the study of reactive species, phase transitions, molecular clusters and crystals, superconductors and semiconductors, biochemical systems, astrophysical problems, etc. The widening range of applications has been accompanied by significant improvements in experimental methods, and low temperature molecular spectroscopy has been revealed as the best technique, in many cases, to establish the connection between experiment and theoretical calculations. This, in turn, has led to a rapidly increasing ability to predict molecular spectroscopic properties. The combination of an advanced tutorial standpoint with an emphasis on recent advances and new perspectives in both experimental and theoretical molecular spectroscopy contained in this book offers the reader insight into a wide range of techniques, particular emphasis being given to supersonic jet and matrix isolation techniques, spectroscopy in cryogenic solutions (including liquid noble gases), and in both crystalline and amorphous states. Suitable quantum chemical methods are also considered, as are empirically based force field

methods for calculating spectra of large molecular systems. The wide range of topics covered includes: molecular dynamics and reactivity, time-resolved and high-resolution spectroscopy, conformational analysis, hydrogen bonding and solvent effects, structure and dynamics of weakly bound complexes, transition metal and organic photochemistry, spectroscopy of excited states, ab initio prediction of molecular spectra, and biochemical and astrophysical applications.

Targeting protein degradation using small molecules is one of the most exciting small-molecule therapeutic strategies in decades and a rapidly growing area of research. In particular, the development of proteolysis targeting chimera (PROTACs) as potential drugs capable of recruiting target proteins to the cellular quality control machinery for elimination has opened new avenues to address traditionally 'difficult to target' proteins. This book provides a comprehensive overview from the leading academic and industrial experts on recent developments, scope and limitations in this dynamically growing research area; an ideal reference work for researchers in drug discovery and chemical biology as well as advanced students.

Methods for the Oxidation of Organic Compounds: Alcohols, Alcohol Derivatives, Alkyl Halides, Nitroalkanes, Alkyl Azides, Carbonyl Compounds, Hydroxyarenes and Aminoarenes describes the different methods used for the controlled oxidation of alcohols, alcohol derivatives, alkyl halides, nitroalkanes, alkyl azides, carbonyl compounds, hydroxyarenes, and aminoarenes. Most of the oxidative techniques considered are illustrated with detailed experimental procedures taken from the literature. This book is comprised of eight chapters and begins with a discussion on the oxidation of alcohols, with particular emphasis on the formation of carbonyl compounds and carboxylic acids. The following chapters focus on the oxidation of esters and alkyl halides; ethers, acetals, and metal derivatives of alcohols; amines, nitro compounds, and azides; carbonyl compounds; 1,2-diols and related compounds; and hydroxyarenes, aminoarenes, dihydroxyarenes, diaminoarenes, and aminohydroxyarenes. Methods such as catalytic oxidation, catalytic dehydrogenation, and electrochemical and biochemical oxidation are mentioned. This monograph should be of interest to organic chemists and research students.

This concise text outlines some of the methods used to prepare bifunctional compounds and then surveys the chemistry of some of the more important classes. Problems - with solutions - and suggestions for further reading are provided.

Bifunctional compounds occupy a central position in organic chemistry. They are important as starting materials for organic synthesis and as templates for studying organic reaction mechanisms. They are, for example, used as precursors for the preparation of carbocyclic and heterocyclic compounds. Furthermore, the products of synthesis and the products of nature are usually polyfunctional compounds and an understanding of the interaction between functional groups is vital to any attempt to explain or control their behaviour. This book outlines some of the methods used to prepare bifunctional compounds and goes on to describe the chemistry of some of the more important classes.

Tachykinin Receptors: Advances in Research and Application: 2011 Edition is a ScholarlyPaper™ that delivers timely, authoritative, and intensively focused information about Tachykinin Receptors in a compact format. The editors have built

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Masakatsu Shibasaki, Motomu Kanai, Shigeki Matsunaga, and Naoya Kumagai: Multimetallic Multifunctional Catalysts for Asymmetric Reactions.- Takao Ikariya: Bifunctional transition metal-based molecular catalysts for asymmetric syntheses.- Chidambaram Gunanathan and David Milstein: Bond Activation by Metal-Ligand Cooperation: Design of "Green" Catalytic Reactions Based on Aromatization-Dearomatization of Pincer Complexes.- Madeleine C. Warner, Charles P. Casey, and Jan-E. Bäckvall: Shvo's Catalyst in Hydrogen Transfer Reactions.- Noritaka Mizuno, Keigo Kamata, and Kazuya Yamaguchi: Liquid-Phase Selective Oxidation by Multimetallic Active Sites of Polyoxometalate-Based Molecular Catalysts.- Pingfan Li and Hisashi Yamamoto: Bifunctional Acid Catalysts for Organic Synthesis.- Jun-ichi Ito, Hisao Nishiyama: Bifunctional Phebox Complexes for Asymmetric Catalysis.

Photophysical and Photochemical Properties of Aromatic Compounds is the first book to collect and classify all available quantitative data on the photochemistry and luminescence of aromatic compounds. Compounds are classified by both spectral-luminescent (e.g., extinction coefficients, energies and lifetimes of lower excited states) and photochemical properties. In addition, all of the quantum yields available have been collected. The variety of photochemical reactions of aromatics is examined based on eight types of elementary monomolecular and bimolecular photochemical processes. Aromatic compounds are grouped into eight categories, and the book analyzes the possibilities of occurrence of all types of elementary photoprocesses.

Sample preparation is an essential step in many analyses. This book approaches the topic of sample preparation in chromatography in a methodical way, viewing it as a logical connection between sample collection and analytical chromatography. Providing a guide for choosing the appropriate sample preparation for a given analysis, this book describes various ways to process the sample, explaining the principle, discussing the advantages and disadvantages, describing the applicability to different types of samples, and showing the fitness to specific chromatographic determinations. The first part of the book contains an overview of sample preparation showing its relation to sample

collection and to the core chromatographic analysis. The second part covers procedures that do not use chemical modifications of the analyte and includes methods for sample dissolution, concentration and cleanup designed mainly for modifying the initial matrix of the sample. This part starts with conventional separations such as filtration and distillation and finishes with more advanced techniques such as solid phase extraction and electroseparations. The third part gives a description of the chemical modifications that can be performed on a sample either for fractionation purposes or to improve a specific property of the analyte. This part includes derivatizations, polymer chemical degradations, and pyrolysis.

Cisplatin, the first member of the family of platinum-containing chemotherapeutic agents, was discovered by Barnett Rosenberg in 1965 and approved by the FDA for marketing in 1978. After 30 years of use in the clinic, cisplatin remains a central element of many treatment regimens. Cisplatin is still an irreplaceable component of a regimen that produces high cure rates in even advanced nonseminomatous germ-cell cancers, and is widely used in the treatment of ovarian cancers and other gynecologic cancers, head and neck, and numerous other tumor types. The development of carboplatin has reduced some of the adverse events associated with cisplatin treatment, and the introduction of the DACH platinum compound oxaliplatin has broadened the spectrum of activity of the platinums to include gastro-intestinal cancers, especially colorectal cancer. The clinical importance of this family of drugs continues to drive investigation into how these drugs work and how to improve their efficacy and reduce their toxicity. The papers in this volume were presented in Verona, Italy, during the tenth International Symposium on Platinum Coordination Compounds in Cancer Chemotherapy. The symposium was jointly organized by the Department of Oncology of the Mater Salutis Hospital – Azienda Sanitaria Locale 21 of the Veneto Region – and by the Department of Medicine and Public Health, Section of Pharmacology, the University of Verona. They reflect the vitality of this field and the increasing use of new molecular and cell biologic, genetic, and biochemical tools to identify approaches to further improve their use.

Electron Capture

Bifunctional CompoundsOxford University Press, USA

Proceedings of the Third EEC Workshop on Photochemical, Photoelectrochemical and Photobiological Research and Development, London, 18-21 April 1989.

Magnesium remains almost unique among the metals in its ability to react directly with a wide variety of compounds. This organic chemistry field has seen steady progress, and a volume on this topic is long overdue. In the tradition of the Patai Series this title treats all aspects of functional groups, containing chapters on the theoretical and computational foundations; on analytical and spectroscopic aspects with dedicated chapters on Mass Spectrometry, NMR, IR/UV, etc.; on reaction mechanisms; on applications

in syntheses. Depending on the functional group there are also chapters on industrial use, on effects in biological and/or environmental systems. Since the area of Organomagnesium Chemistry continues to grow far beyond the classical Grignard Reagents, this is an essential resource to help the reader keep abreast of the latest developments.

We have designed and synthesized a novel compound (11beta) that efficiently triggers apoptosis in prostate cancer cells such as LNCaP. This bifunctional compound was designed to form DNA adducts that are camouflaged by the androgen receptor making them less readily repaired in AR+ prostate cancer cells. The aims of our studies are to investigate the mechanisms by which 11 is able to trigger apoptosis in target cells. Methods have been developed that permit us to determine the fates of 11 -DNA adducts in treated cells in culture as well as in tumors growing in animal models. Another objective is to identify the signaling events that lead from DNA adducts to activation of the apoptotic program. Finally we have obtained encouraging results from animal experiments that indicate that molecules such as 11 may have clinical potential for the treatment of human tumors.

Written for all those who use chromatography as an analytical tool, this book covers all areas of gas, liquid, and thin-layer chromatography; no other book offers the same scope. The authors have had considerable experience in teaching graduate-level courses and the material presented here has been tried and tested, having formed the basis for short courses taught to groups of industrial chemists. Emphasis is on the practice of chromatographic methods, including ``how to'' sections and numerous examples of calculation methods. Extensively illustrated, the book contains numerous tables of all useful constants, materials and formulas frequently used by chromatographers. Valuable features are the chapters on sample preparation for chromatographic analysis, on instrumental methods for sample identification, and the comprehensive literature review.