EXAMPLES OF PUBLICATIONS RESULTING FROM CHEMEDIT EDITED MANUSCRIPTS

• Citation: “Immobilized Polydiacetylene Vesicles on Solid Substrates Use as Chemosensors, Kim, J-M.; Ji, E-K.; Woo, S. M.; Lee, H.; Dong June Ahn, D. J. Advanced Materials, 2003, 15, 1118.
  Abstract: We have developed a new approach for preparing PDA-based chmosensors. A diacetylene monomer with terminal amine groups was prepared. Immobilization of the diacetylene liposomes on an aldehyde-modified glass substrate, followed by irradiation with UV light, was found to be an efficient method for preparing the sensor film. SEM images show the immobilized PDA vesicles to exist as mono-layers. Incubation of the immobilized film sensor in a solution containing poly(acrylic acid) resulted in a colorimetric change from the blue to the red phase. The strategies described in this report should be useful in the development of PDA-based chmosensors.

  Abstract: To investigate the role of hydrogen-bonding on colorimetric transition of polydiacetylene supramolecules, novel diacetylene derivatives allowing various hydrogen-bonding states were synthesized by coupling carboxy-substituted (ortho-, meta-, and para-) anilide groups with a typical single-chain diacetylene lipid. One with a terminal carboxyl group at the meta position provided the resulting supramolecular Langmuir–Schaefer films with enhanced hydrogen-bonding, and hence resulted in unprecedented colorimetric reversibility under both thermal and pH stimuli.

  Abstract: We have developed a new strategy for PDA-based sensor systems that employs a microfluidic PDA sensor chip. This system has been used to continuously and rapidly monitor model PDA–receptor interactions. Relatively strong fluorescence bands are observed when the flows of PDA and α-CD solutions come into contact. In addition, we observed concentration-dependence of the fluorescent signals originating from this interaction. By utilizing the characteristics of parallel lamellar flows in a microchannel, we were able to demonstrate that a microfluidic PDA sensor chip can simultaneously differentiate molecular recognition events with two different concentrations of receptor molecules. The methodology described here should be applicable to other conjugated polymer systems of which the responses are based on quenching, enhancement, or alteration of fluorescence

• Citation: “Fluorogenic Polydiacetylene Supramolecules: Immobilization, Micropatterning, and Application to Label-Free Chemosensors,” Ahn, D. J.; Kim, J-M. Accounts of Chemical Research, 2008, 41, 805.
  Abstract: This Account describes a new strategy for the preparation of label-free sensor systems based on the fluorogenic properties of the conjugated polymer,
polydiacetylene (PDA). PDA has been extensively investigated as a sensor matrix, owing to a brilliant blue-to-red color transition that takes place in response to environmental perturbations. It has been known for some time that “blue-phase” PDAs are nonfluorescent while their “red-phase” counterparts fluoresce. For the most part, however, the significance of the different fluorogenic properties of PDAs has been ignored in the context of sensor applications. In the course of developing PDA-based sensors, we discovered that PDA vesicles can be readily immobilized on solid substrates. This is an attractive property of PDAs since it leads to the combined advantages of the vesicle sensors (which have three-dimensional interactions between sensor and target molecules) and film sensors (which are applicable to a two-dimensional array or chip format). Stable blue-phase immobilized PDAs can be prepared by employing one of three strategies involving the formation of covalent adducts, biotin–avidin complexes, or complexes formed through nonspecific physical adsorption. A procedure for generating well-patterned fluorescence images is necessary for the immobilized PDAs to function in chip-based sensor systems. Patterned fluorescence images are readily constructed by employing (1) the photolithographic technique, (2) the micromolding in capillaries (MIMIC) method, or (3) an array spotting system. Heat treatment of the patterned “blue-phase” PDA vesicles transforms the nonfluorescent images into their fluorescent red forms. The observation that finely resolved fluorescence patterns can be generated by heat treatment of microarrayed PDAs is highly significant in that it indicates that fluorescence signals might be produced by specific molecular recognition events. Indeed, red fluorescence emission is observed when immobilized PDAs are subjected to specific molecular recognition events, such as ligand–cyclodextrin or protein–protein interactions. The facile immobilization of PDA vesicles on solid substrates and the affinity-induced fluorescence emission combine to make this system applicable to the fabrication of label-free PDA sensors. Since in theory any molecular recognition event that promotes the blue-to-red color transition of PDAs should result in the generation of fluorescence, it should be possible to reformat a variety of previously described colorimetric PDA sensors into fluorescence-based sensor systems. The fluorescence properties of PDAs, when combined with modern methods for the fabrication of microarrays, should stimulate the development of a number of new label-free chemosensor systems.


Abstract: Owing to the color (blue-to-red) and fluorescence (non-to-fluorescent) changes that take place in response to environmental perturbations, conjugated polydiacetylenes (PDAs) have been actively employed as sensory materials for the detection of biologically-, environmentally- and chemically-important target molecules. Until recently, the majority of PDA sensors have been prepared in the form of aqueous suspensions or Langmuir-type thin films on solid substrates. In order to overcome the limitations associated with conventional solution/film sensors, conceptually new formats, such as immobilized PDAs in and on solid substrates, microarrayed PDA sensors, microfluidic PDA sensors, as well as PDA-embedded electrospun fiber sensors and resonance energy transfer (RET)-based PDA sensors, have been developed recently. In
this tutorial review, the recent conceptual and technological achievements made in the area of conjugated PDA chemosensors are described.

• Citation: “Coupling Isocyanide-Based Multicomponent Reactions with Aliphatic or Acyl Nucleophilic Substitution Processes,” Banfi, L.; Basso, A.; Riva, R. Synlett, 2010, 23-41.
  Abstract: This account summarizes the results of studies carried out by the authors during the last 10 years aimed at expanding the utility of the venerable Passerini and Ugi reactions. Particular emphasis is given to efforts that focus on coupling these processes with post-condensation, intramolecular, aliphatic nucleophilic substitution and acyl nucleophilic substitution reactions. The methodologies developed in these investigations serve as the basis for short sequences for the preparation of a diverse number of interesting drug-like structures.

  Abstract: Since the discovery of rimonabant (Acomplia: 1), a large effort has been directed at the discovery of new, potent and selective CB1R antagonists that serve as anti-obesity drugs. As a result, a number of compounds reached various stages of clinical trials by late 2008. However, the announcement by Sanofi-Aventis that they were discontinuing all ongoing trials with rimonabant, as a result of the finding that risks associated with depression and anxiety outweighed its benefits, had a major impact on this area. A wave of terminations of programs targeting the development of CB1R blockers for treatment of obesity ensued. However, abandoning this CB1R therapeutic target for anti-obesity drug development seems to be premature, since there are a number of potential approaches have been uncovered to circumvent the problems of the current agents. In this review, we summarize advances that have been made and the status of studies of a diverse array of CB1R antagonists that have been identified mainly based on modifications of the first-in-class CB1R antagonist, rimonabant. Various approaches have been employed to design these analogs, such as bioisosteric replacement, introduction of conformational constraints, scaffold hopping and ligand-based molecular modeling. In addition, current approaches that have been uncovered to avoid psychiatric side effects of CB1R antagonists are summarized. Finally, the design of non-brain penetrating and peripherally acting CB1R antagonists, allosteric modulators of CB1R, and neutral antagonists for CB1R is also discussed in this review.

• Citation: "Thermoluminescence Originating from the Singlet Excited State of 1,4-Diarylcyclohexane-1,4-diyls: A Potentially General Strategy for the Observation of Short-Lived Biradicals," Namai, H.; Ikeda, H.; Hoshi, Y.; Mizuno, K. Angew. Chem. Int. Ed. 2007, 46, 7396-7398.
  Abstract: Light from an unobservable source: Annealing a γ-irradiated glassy matrix containing 2,5-diaryl-1,5-hexadiene gives rise to an intense thermoluminescence (TL) that is assigned to the singlet excited state of the corresponding cyclohexane-1,4-diyl on the basis of substituent effects on TL and DFT calculations.

Abstract: Product analyses and nanosecond time-resolved spectroscopy on laser flash photolysis were studied for the photoinduced electron-transfer reaction of 3,4-di(α-styryl)furan. A combination of these results, kinetic, density functional theoretical (DFT), and time-dependent DFT analyses enabled assignment of the absorption to the tetramethyleneethane (TME)-type radical cation (λmax = 392 nm) and the corresponding singlet biradical (λmax = 661 nm). These two intermediates were mechanistically linked to each other with a facile back electron-transfer reaction. The present studies provide a new method for the generation of aryl-substituted TME-type intermediates.


Abstract: A universal colorimetric method for the detection of nucleic acids, based on ionic interactions by polydiacetylene (PDA) liposomes, is described. Primary and quaternary amine-modified diacetylene monomers were synthesized and used to generate positively charged PDA liposomes. The resulting PDA sensors showed a dramatic color change from blue to red upon the addition of nucleic acids amplified by using the polymerase chain reaction (PCR) due to the stimuli caused by ionic interactions between the positively charged PDA and negatively charged phosphate backbone of the nucleic acids. The color change that takes place can be simply detected by the naked eye. Compared with quaternary amine-functionalized PDA vesicles, the primary amine-functionalized PDA underwent a more intense color transition under optimized conditions. By using the PDA-based colorimetric sensor, nucleic acids amplified by common PCR reaction, whose typical concentration is around 100 nM, can be readily detected. Since implementation of this universal colorimetric method is simple, rapid and does not require any sophisticated instrumentation, it should have greatly enhanced applications as a technology for DNA diagnosis.


Abstract: A micropatterned polydiacetylene (PDA) chip, utilizing the unique fluorogenic property of PDA and a specific biotin–streptavidin (STA) interaction, is constructed to detect pathogen infections. To construct the PDA chip, biotin-modified diacetylene liposomes are immobilized on aldehyde glass and conjugated with STA, followed by UV irradiation to polymerize the STA-functionalized diacetylene liposomes. Genomic DNA of a model pathogen, Chlamydia trachomatis, is isolated from human samples and biotin-labeled target DNA is obtained through PCR amplification using biotin-11-dUTP. Owing to the stimulus caused by the biotin–STA interaction, the biotinylated DNA induces an intense fluorescence signal on the immobilized PDA. By
using this strategy, it is possible to diagnose Chlamydia infections by applying DNA samples from several non-healthy humans to a single PDA chip. The results of this study serve as the basis for a new strategy for fluorogenic PDA microarray-based diagnosis of pathogen infections.

  Abstract: Cardiosulfa, a small molecule that induces heart deformation during zebrafish development, has been identified by using a forward chemical genetic approach. Zebrafish embryos exposed to this molecule display narrow and elongated heart within an enlarged pericardiac sac. A plausible mechanism of the mode of action of cardiosulfa was proposed based on several experiments. Cardiosulfa may play a useful role in unveiling mechanisms and pathways relevant to heart deformation.

  Abstract: A new, nondestructive, highly sensitive method for colorimetric monitoring of primary amines, secondary amines and thiols on a solid support was developed. The resin used in this method is simply regenerated for the repetition of the reaction or an ensuing reaction. By using this new method, several peptides containing secondary amide linkages and C-terminal hydrazide groups were prepared in high purities and yields.

  Abstract: In recent years a variety of chemical approaches have been developed for elucidating the molecular basis of biological processes in which glycans participate. The chemical technologies uncovered have greatly influenced the progress of glycomics research programs. This tutorial review highlights recent advances in chemical tools, which have been developed and their applications in studies aimed at gaining a better understanding of the roles that glycans play in biological processes.

  Abstract: Exposure to mercury causes severe damage to various tissues and organs in human being. Concern over mercury toxicity has encouraged the development of efficient, sensitive, and selective methods for the in vivo detection of mercury. Although a variety of chemosensors have been exploited for this purpose, no in vivo monitoring systems has been described up to date. In this report, we describe an irreversible rhodamine chemosensor-based, real-time monitoring system to detect mercury ions in living cells and, in particular, in vertebrate organisms. The chemosensor responds rapidly, irreversibly and stoichiometrically to mercury ions in aqueous media at room temperature. The results of experiments with mammalian cells and zebrafish show that the mercury chemosensor is cell- and organism-permeable, and that it responds selectively to mercury ions over other metal ions. In addition, real-time monitoring of
mercury ion uptake by cells and zebrafish using this chemosensor shows that saturation of mercury ion uptake occurs within 20–30 min in cells and organisms. Finally, accumulation of mercury ions in zebrafish tissue and organs is readily detected by using this rhodamine-based chemosensor.

  Abstract: The PDAs derived from a hydroxybenzaldehyde substituted diacetylene monomer displayed a unique colorimetric change (blue to red) and large fluorescent enhancement in the presence of cetyl trimethylammonium salt.

  Abstract: This tutorial review focuses on recent developments arising from studies of optical sensors for cyanide ions, which are categorized by approaches involving cyanide selective receptors, the utilization of metal coordinated complexes, and chemodosimeters.

  Abstract: The hairpin RNA motif is one of the most frequently observed secondary structures and is often targeted by therapeutic agents. An amphiphilic peptide with seven lysine and eight leucine residues and its derivatives were designed for use as ligands against RNA hairpin motifs. We hypothesized that variations in both the hydrophobic leucine-rich and hydrophilic lysine-rich spheres of these amphiphilic peptides would create extra attractive interactions with hairpin RNA targets. A series of alanine-scanned peptides were probed to identify the most influential lysine residues in the hydrophilic sphere. The binding affinities of these modified peptides with several hairpins, such as RRE, TAR from HIV, a short hairpin from IRES of HCV, and a hairpin from the 16S A-site stem from rRNA, were determined. Since the hairpin from IRES of HCV was the most susceptible to the initial series of alanine-scanned peptides, studies investigating how further variations in the peptides effect binding employed the IRES hairpin. Next, the important Lys residues were substituted by shorter chain amines, such as ornithine, to place the peptide deeper into the hairpin groove. In a few cases, a 70-fold improved binding was observed for peptides that contained the specifically located shorter amine side chains. To further explore changes in binding affinities brought about by alterations in the hydrophobic sphere, tryptophan residues were introduced in place of leucine. A few peptides with tryptophan in specific positions also displayed 70-fold improved binding affinities. Finally, double mutant peptides incorporating both specifically located shorter amine side chains in the hydrophilic region and tryptophan residues in the hydrophobic region were synthesized. The binding affinities of peptides containing the simple double modification were observed to be 80 times lower, and their binding specificities were increased 40-fold. The results of this effort provide important information about strategies that can be used to prepare peptides that both strongly and selectively target hairpin RNAs. Specifically, the findings indicate that tailor-made
amphiphilic peptide ligands against certain hairpin RNAs can be obtained if the RNA target possesses a deep groove in which both the hydrophobic and hydrophilic spheres of the peptide interact.


  **Abstract:** Amphiphilic helical peptides that contain acridine moieties were synthesized, and their binding affinities toward hairpin RNA targets were evaluated. The dramatic increase in binding affinities (40-fold for RRE, 170-fold for TAR) demonstrates that conjugation of intercalators that operate by different binding modes (ionic or hydrogen bonding) leads to one of the most tightly binding pharmacophores against RNA targets.


  **Abstract:** Inter- and intra-molecular additions of alkyl radicals, generated by SET photochemical decarboxylation reactions of free carboxylic acids, to electron-deficient alkenes take place under mild conditions as part of efficient routes for the formation of N-Boc γ-amino acids and macrocyclic lactones.


  **Abstract:** Reactions of amides with elemental sulfur in the presence of hydrochlorosilanes and amines give the corresponding thioamides in good to high yields. The process takes place via reduction of elemental sulfur by the hydrochlorosilane in the presence of a suitable amine. The methodology can be applied to the selenation of amides by using elemental selenium. Thionation and selenation of an acetyl-protected sialic acid derivative are found to take place selectively at the amide group.


  **Abstract:** A novel copper-catalyzed oxidative desulfurization reaction of thiocarbonyl compounds, using molecular oxygen as an oxidant and leading to formation of carbonyl compounds, has been developed, and the utility of the process is demonstrated by its application to the preparation of a carbonyl-18O labeled sialic acid derivative.

• **Citation:** "Synthesis of 2-Azaindolizines by Using an Iodine-Mediated Oxidative Desulfurization Promoted Cyclization of N-2-Pyridylmethyl Thioamides and an

Abstract: Iodine-mediated, oxidative desulfurization promoted cyclization of N-2 pyridymethyl thioamides serves as an efficient and versatile method for the preparation of 2-azaindolizines (imidazo[1,5-a]pyridines) and rare 2-azaindolizine sulfur-bridged dimers. The 2-azaindolizines prepared in this manner are readily converted to a variety of fluorescent compounds by using transition-metal-catalyzed cross-coupling reactions.


Abstract: A novel fabrication method is developed for the preparation of superhydrophobic surfaces. The procedure uses focal conic structures of semi-fluorinated smectic liquid crystals (LCs) whose periodic toric focal conic domains (TFCDs) are prepared on a surface modified substrate. Reactive ion etching (RIE) on the periodic TFCD surface leads to a superhydrophobic surface with a water contact angle of 160° and a sliding angle of 28° for a 10 mL water droplet. The results show that this phenomenon is due to the development of a dual-scale surface roughness arising from the nanoscale protuberance caused by applying the RIE process to the top of the microscale TFCD arrays. The unique surface behavior is further verified by demonstrating that RIE on a flat lamellar liquid crystal film, in which the director is aligned parallel with surface, results in a relatively low hydrophobicity as compared to when periodic TFCDs are subjected to RIE. The observations made in this publication suggest that a new approach exists for selecting potential candidates of superhydrophobic surface formation based on spontaneous self-assembly in smectic liquid-crystalline materials.