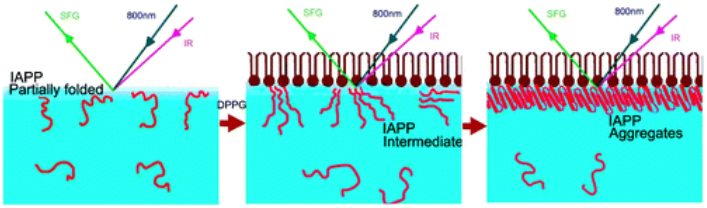
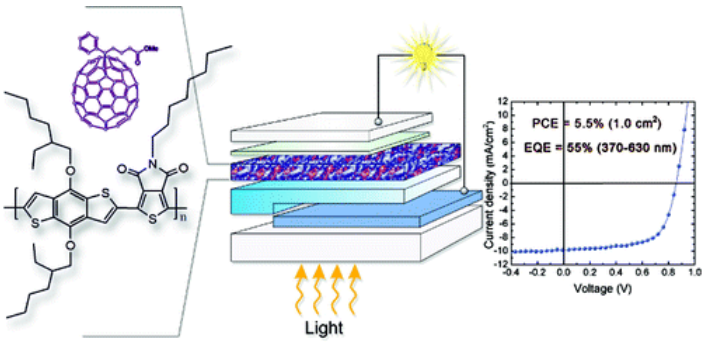
- In Situ Misfolding of Human Islet Amyloid Polypeptide at Interfaces Probed by Vibrational Sum Frequency Generation
  Fu, L.; Ma, G.; C. Y. Yan, E. *J. Am. Chem. Soc.* **2010**, *132*, 5405–5412.
  Abstract:



Kinetic analysis of conformational changes of proteins at interfaces is crucial for understanding many biological processes at membrane surfaces. In this study, we demonstrate that surface-selective sum frequency generation (SFG) spectroscopy can be used to investigate kinetics of conformational changes of proteins at interfaces. We focus on an intrinsically disordered protein, human islet amyloid polypeptide (hIAPP) that is known to misfold into the β-sheet structure upon interaction with membranes. Using the ssp polarization setting (s-polarized SFG, s-polarized visible, and p-polarized infrared), we observe changes in the amide I spectra of hIAPP at the air/water interface after addition of dipalmitoylphosphoglycerol (DPPG) that correspond to the lipid-induced changes in secondary structures. We also used the chiral-sensitive psp polarization setting to obtain amide I spectra and observed a gradual buildup of the chiral structures that display the vibrational characteristics of parallel β-sheets. We speculate that the second-order chiral-optical response at the antisymmetric stretch frequency of parallel β-sheet at 1622 cm−1 could be a highly characteristic optical property of the β-sheet aggregates not only for hIAPP, but possibly also for other amyloid proteins. Analyzing the achiral and chiral amide I spectra, we conclude that DPPG induces the misfolding of hIAPP from α-helical and random-coil structures to the parallel β-sheet structure at the air/water interface. We propose that SFG could complement existing techniques in obtaining kinetic and structural information for probing structures and functions of proteins at interfaces.

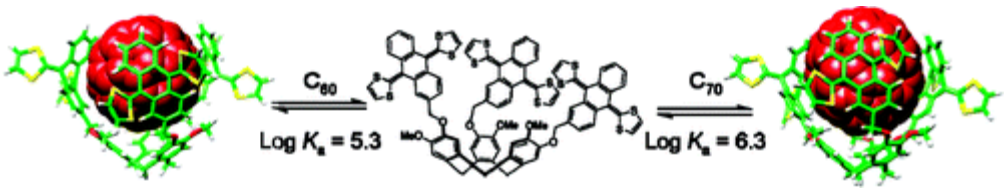
- A Thieno[3,4-c]pyrrole-4,6-dione-Based Copolymer for Efficient Solar Cells
  Zou, Y.; Najari, A.; Berrouard, P.; Beaupré, S.; Aích, B. R.; Tao, Y.; Leclerc, B. *J. Am. Chem. Soc.* **2010**, *132*, 5330–5331.
  Abstract:



A new low-band-gap thieno[3,4-c]pyrrole-4,6-dione-based copolymer, PBDTTPD, has been designed and synthesized. PBDTTPD is soluble in chloroform or o-dichlorobenzene upon heating and shows a broad absorption in the visible region. The HOMO and LUMO energy levels were estimated to be at −5.56 and −3.75 eV, respectively. These electrochemical measurements fit well with an optical bandgap of 1.8 eV. When blended with PC71BM, this

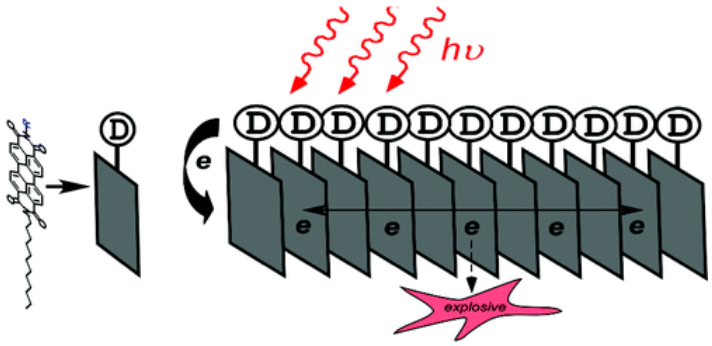
polymer demonstrated a power conversion efficiency of 5.5% in a bulk-heterojunction photovoltaic device having an active area of 1.0 cm^2.

- Tripodal exTTF-CTV Hosts for Fullerenes
  Huerta, E.; Isla, H.; Pérez, E. M.; Bo, C.; Martín, N.; de Mendoza, J. *J. Am. Chem. Soc.* **2010**, *132*, 5351–5353.
  Abstract:



A receptor for fullerenes featuring three exTTF units linked to a CTV scaffold is described. The exTTF-CTV host forms remarkably stable complexes with both C_{60} (log K_a = 5.3 ± 0.2) and C_{70} (log K_a = 6.3 ± 0.6). Light-induced ESR spectra demonstrate that intracomplex PET processes take place in solution.

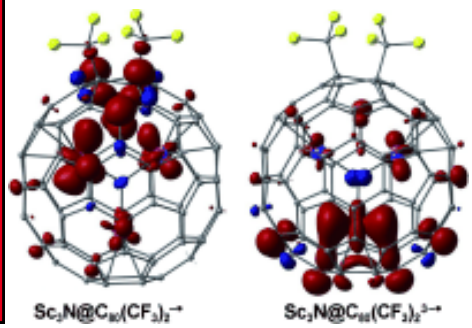
- Ultrathin n-Type Organic Nanoribbons with High Photoconductivity and Application in Optoelectronic Vapor Sensing of Explosives
  Che, Y.; Yang, X.; Liu, G.; Yu, C.; Ji, H.; Zuo, J.; Zhao, J.; Zang, L. *J. Am. Chem. Soc.* **2010**, *132*, 5743–5750.
  Abstract:



Well-defined ultrathin nanoribbons have been fabricated from an amphiphilic electron donor–acceptor (D–A) supramolecule comprising perylene tetracarboxylic diimide as the backbone scaffold to enforce the one-dimensional intermolecular assembly via strong π-stacking. These nanoribbons demonstrated high photoconductivity upon illumination with white light. The high photoconductivity thus obtained is likely due to the optimal molecular design that enables a good kinetic balance between the two competitive processes, the intramolecular charge recombination (between D and A) and the intermolecular charge transport along the nanoribbon. The photoconduction response has also proven to be prompt and reproducible with the light turning on and off. The photogenerated electrons within the nanoribbon can be efficiently trapped by the adsorbed oxygen molecules or other oxidizing species, leading to depletion of the charge carriers (and thus the electrical conductivity) of the nanoribbon, as typically observed for n-type semiconductor materials as applied in chemiresistors. Combination of this sensitive modulation of conductivity with the unique features intrinsic to the nanoribbon morphology (large surface area and continuous

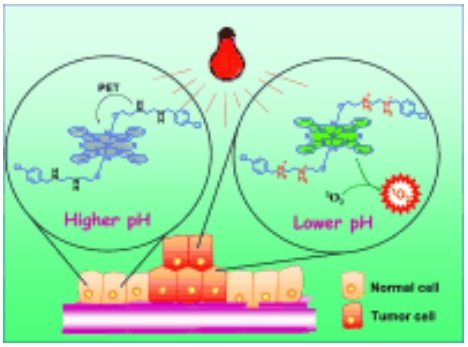
nanoporosity when deposited on a substrate to form a fibril film) enables efficient vapor sensing of nitro-based explosives.

- Redox-Tuning Endohedral Fullerene Spin States: From the Dication to the Trianion Radical of $Sc_3N@C_{80}(CF_3)_2$ in Five Reversible Single-Electron Steps
  Popov, A. A.; Shustova , N. B.; Svitova, A. L.; Mackey, M. A.; Coumbe, C. E.; Phillips, J. P.; Stevenson, S.; Strauss, S. H.; Boltalina, O. V.; Dunsch, L. *Chem. Eur. J.* **2010**, *16*, 4421-4424.
  Abstract:



The first endohedral trianion captured: $Sc_3N@C_{80}(CF_3)_2$ (see figure) exhibits three reversible reductions and two reversible oxidations and affords the facile generation of the monocation, monoanion, and trianion in solution, which can be characterized by ESR and absorption spectroscopies. This is the first time that such a broad range of charged states of any endohedral fullerene has been spectroscopically characterized.

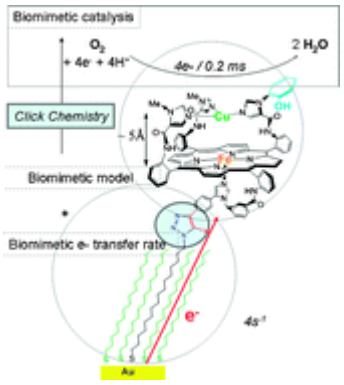
- Phthalocyanine-Polyamine Conjugates as pH-Controlled Photosensitizers for Photodynamic Therapy
  Jiang, X.-J.; Lo, P.-C.; Tsang, Y.-M.; Yeung, S.-L.; Fong, W.-P.; Ng, D. K. P. *Chem. Eur. J.* **2010**, *16*, 4777-4483.
  Abstract:



A series of aryl hydroxyamines prepared by reductive amination were treated with silicon(IV) phthalocyanine dichloride in the presence of pyridine to give the diaxially substituted phthalocyanine-polyamine conjugates **1**-**5**. The electronic absorption, fluorescence emission, and efficiency at generating reactive oxygen species of these compounds were all sensitive to

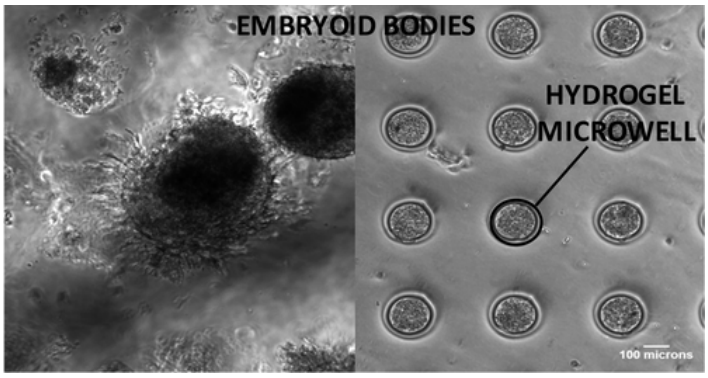
the pH environment. Under acidic conditions, the fluorescence quantum yields and the singlet oxygen quantum yields of these compounds were greatly enhanced in DMF as a result of protonation of the amino moieties, which inhibited the photoinduced electron-transfer deactivation pathway. The Q band was diminished and broadened, and the fluorescence intensity decreased as the pH increased in citrate buffer solutions. The rate of superoxide radical formation was also reduced in a higher pH environment. Compound **3**, containing a terminal 4-chlorophenyl group at the axial substituent, showed the most desirable pH-responsive properties, which makes it a promising tumor-selective fluorescence probe and photosensitizer for photodynamic therapy. All of the phthalocyanines **1**-**5** were highly photocytotoxic against HT29 and HepG2 cells with IC_{50} values as low as 0.03 μM. Compound **3** was highly selective toward lysosomes, but not mitochondria of HT29 cells.

- Electrochemical applications. How click chemistry brought biomimetic models to the next level: electrocatalysis under controlled rate of electron transfer
  Decréau, R. A.; Collman, J. P.; Hosseini, A. *Chem. Soc. Rev.* **2010**, *39*, 1291 – 1301.
  Abstract:



This *tutorial review* discusses the immobilization of alkyne-terminated cytochrome c oxidase models on azide-functionalized self-assembled monolayers (SAM) coated gold electrodes that was made possible by click chemistry. The rate of electron delivery from the electrode to the model could be tuned by changing the nature of the SAM. Biologically relevant electron transfer rates (2–4 s^{-1}) were obtained on slow SAMs allowing the model to turn over catalytically under steady-state conditions. Hence, click chemistry was a crucial tool to demonstrate, through electrocatalytic studies: (1) the role played by several features present in the distal side of the model, such as the Cu_B–Tyr244 pair, the distal pocket, and the stabilizing role of a distal water cluster; (2) the reversible inhibition of O_2 reduction by H_2S.

- Bioinspired Materials for Controlling Stem Cell Fate
  Fisher, O. Z.; Khademhosseini, A.; Langer, R.; Peppas, N. A. *Acc. Chem. Res.* **2010**, *43*, 419–428.
  Abstract:

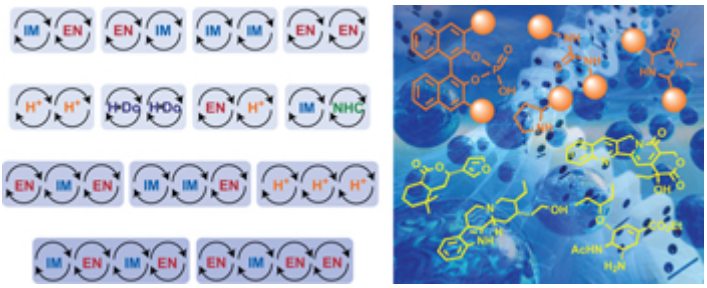


Although researchers currently have limited ability to mimic the natural stem cell microenvironment, recent work at the interface of stem biology and biomaterials science has demonstrated that control over stem cell behavior with artificial microenvironments is quite advanced. Embryonic and adult stem cells are potentially useful platforms for tissue regeneration, cell-based therapeutics, and disease-in-a-dish models for drug screening. The major challenge in this field is to reliably control stem cell behavior outside the body. Common biological control schemes often ignore physicochemical parameters that materials scientists and engineers commonly manipulate, such as substrate topography and mechanical and rheological properties. However, with appropriate attention to these parameters, researchers have designed novel synthetic microenvironments to control stem cell behavior in rather unnatural ways.

In this Account, we review synthetic microenvironments that aim to overcome the limitations of natural niches rather than to mimic them. A biomimetic stem cell control strategy is often limited by an incomplete understanding of the complex signaling pathways that drive stem cell behavior from early embryogenesis to late adulthood. The stem cell extracellular environment presents a miscellany of competing biological signals that keep the cell in a state of unstable equilibrium. Using synthetic polymers, researchers have designed synthetic microenvironments with an uncluttered array of cell signals, both specific and nonspecific, that are motivated by rather than modeled after biology. These have proven useful in maintaining cell potency, studying asymmetric cell division, and controlling cellular differentiation.

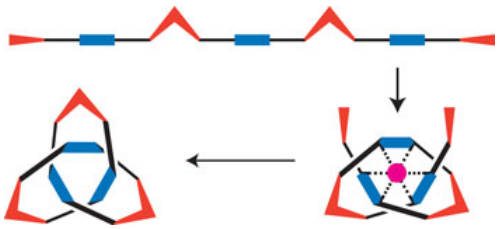
We discuss recent research that highlights important biomaterials properties for controlling stem cell behavior, as well as advanced processes for selecting those materials, such as combinatorial and high-throughput screening. Much of this work has utilized micro- and nanoscale fabrication tools for controlling material properties and generating diversity in both two and three dimensions. Because of their ease of synthesis and similarity to biological soft matter, hydrogels have become a biomaterial of choice for generating 3D microenvironments. In presenting these efforts within the framework of synthetic biology, we anticipate that future researchers may exploit synthetic polymers to create microenvironments that control stem cell behavior in clinically relevant ways.

- Organocatalytic cascade reactions as a new tool in total synthesis
  Grondal, C.; Jeanty, M.; Enders, D. *Nature Chemistry* **2010**, *2*, 167 – 178.
  Abstract:



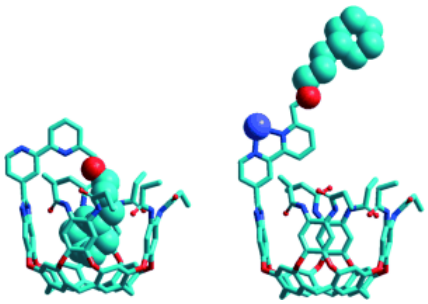
The total synthesis of natural products and biologically active compounds, such as pharmaceuticals and agrochemicals, has reached an extraordinary level of sophistication. We are, however, still far away from the 'ideal synthesis' and the state of the art is still frequently hampered by lengthy protecting-group strategies and costly purification procedures derived from the step-by-step protocols. In recent years several new criteria have been brought forward to solve these problems and to improve total synthesis: atom, step and redox economy or protecting-group-free synthesis. Over the past decade the research area of organocatalysis has rapidly grown to become a third pillar of asymmetric catalysis standing next to metal and biocatalysis, thus paving the way for a new and powerful strategy that can help to address these issues — organocatalytic cascade reactions. In this Review we present the first applications of such asymmetric organocascade reactions to the total synthesis of natural products.

- Synthesis of a molecular trefoil knot by folding and closing on an octahedral coordination template
  Guo, J.; Mayers, P. C.; Breault, G. A.; Hunter, C. A. *Nature Chemistry* **2010**, *2*, 218 – 222.
  Abstract:



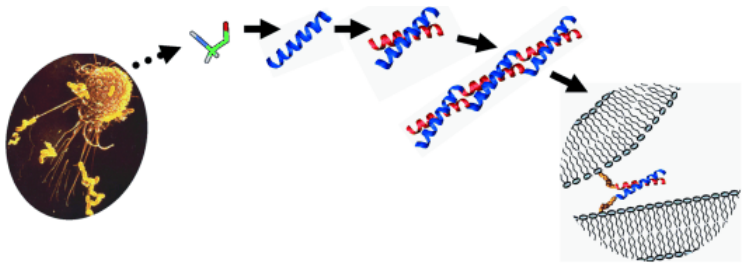
The advent of template-directed synthesis has provided access to a range of new interlocked molecular architectures. Although many syntheses of molecular catenanes and rotaxanes have been reported, molecular knots are a class of molecules with topologically non-planar graphs that are rather rare. Here we report a synthetic strategy for the preparation of a molecular trefoil knot from a flexible bipyridine oligomer and a zinc(II) octahedral coordination template. The oligomer folds into a stable open-knot conformation in the presence of the template, and trapping of this arrangement through esterification or ring-closing metathesis produces the closed-knot complex. Subsequent removal of the template from the metathesis product results in a molecular trefoil knot.

- The Ouroborand: A Cavitand with a Coordination-Driven Switching Device
  Durola, F.; Rebek Jr., J. *Angew. Chem. Int. Ed*. **2010**, *49*, 3189-3191.
  Abstract:



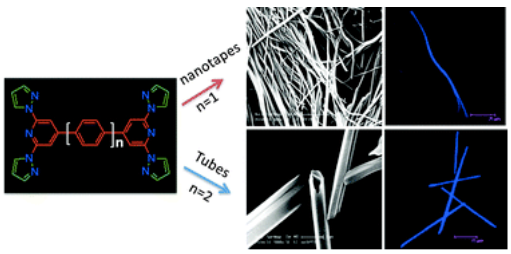
Molecular switch: The ouroborand coordinates an internal side chain in its cavity, just as it were swallowing its own tail. The presence or absence of zinc(II) in solution switches the cavity between open and closed states to external guests (see scheme: deep blue sphere: Zn).

- Self-Assembly of Coiled Coils in Synthetic Biology: Inspiration and Progress
  Robson Marsden, H.; Kros, A. *Angew. Chem. Int. Ed*. **2010**, *49*, 2988-3005.
  Abstract:



Cues from nature: The coiled-coil motif is a simple molecular building block ubiquitous in nature that has an impressive range of functions, with roles in protein binding, the formation of structural edifices, and dynamic processes. These functions inspire research in synthetic biology, in which the coiled-coil motif is utilized in functional units, assemblies, and systems.

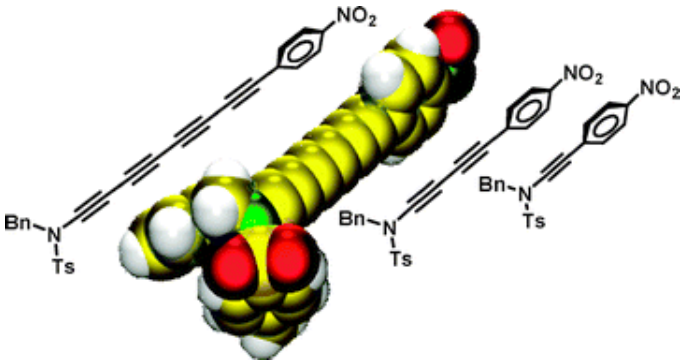
- Engineering self-assembled fluorescent organic nanotapes and submicrotubes from -conjugated molecules
  Chandrasekhar, N.; Chandrasekar, R. *Chem. Commun.* **2010**, *46*, 2915 – 2917.
  Abstract:



Fluorescent elongated nanotapes and nearly monodispersed short submicrotubes were successfully prepared in a controlled manner from two tailor-made -conjugated organic building blocks 1 and 2, respectively in dichloromethane solvent *via* a supramolecular self-assembly approach.

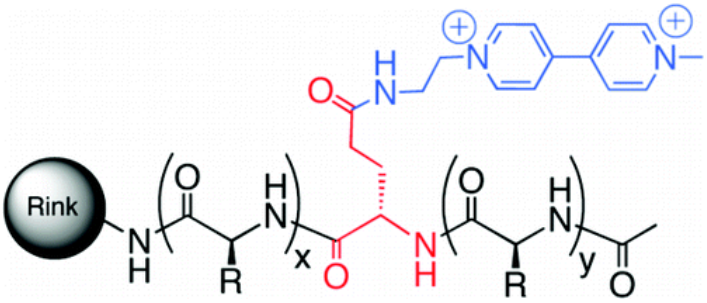
- Synthesis and molecular properties of donor–-spacer–acceptor ynamides with up to four conjugated alkyne units
  Witulski, B.; Schweikert, T; Schollmeyer, D.; Nemkovich, N. A. *Chem. Commun.* **2010**, *46*, 2953 – 2955.

Abstract:



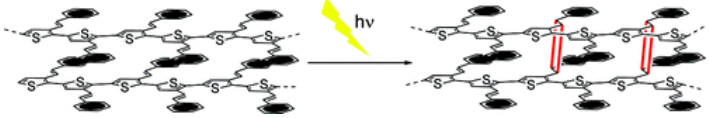
A set of push–pull ynamides with up to four conjugated triple bonds has been synthesized and the molecular properties of these new carbon rods have been characterised showing effective intramolecular charge transfers and high values for the change of the electrical dipole moment after transition from the ground to the Franck–Condon excited state.

- Solid-Phase Synthesis of Peptide−Viologen Conjugates
  Reczek, J. J.; Rebolini, E.; Urbach, A. R. *J. Org. Chem.* **2010**, *75*, 2111–2114.
  Abstract:



This paper presents a robust method for the conjugation of viologens to peptides using an amide coupling strategy that is compatible with standard Fmoc solid-phase peptide synthesis. Methodology is presented for monitoring the milligram scale process quantitatively by UV spectroscopy. This chemistry enables the synthesis of a broad range of asymmetric viologens in high yield at room temperature and is compatible with a wide range of functional groups, including amine, guanidinyl, thiol, carboxylic acid, phenol, and índole.

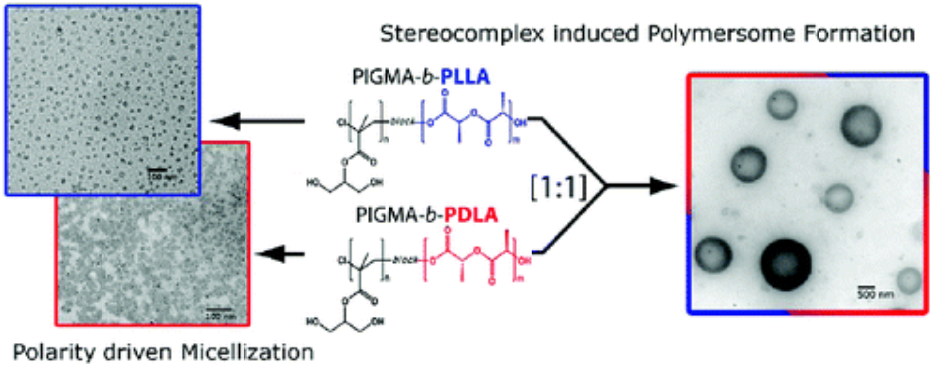
- Synthesis and Supramolecular Organization of Regioregular Polythiophene Block Oligomers
  Clément, S.; Meyer, F.; De Winter, J.; Coulembier, O.; Vande Velde, C. M. L.; Zeller, M.; Gerbaux, P.; Balandier, J.-Y.; Sergeyev, S.; Lazzaroni, R.; Geerts, Y.; Dubois, P. *J. Org. Chem.* **2010**, *75*, 1561–1568.
  Abstract:



The self-assembly of functional polythiophenes was studied by a bottom-up approach “from molecule to polymer”. The synthesis and the X-ray structure of 2,5-dibromo-3-styryl and 3-2′,3′,4′,5′,6′-pentafluorostyryl-thiophenes revealed a supramolecular arrangement controlled by π−π interactions between the aromatic rings. A [2 + 2] photocyclization reaction in the solid

state of (*E*)-1-2′,5′-dibromo-3′-thienyl-2-pentafluorophenylethene triggers the formation of a rare cycloadduct comprising thiophene rings. The X-ray analysis confirmed its *rctt* stereochemistry. The synthesis of P3HT-*b*-P3ST and P3HT-*b*-P3STF block oligomers was achieved by a GRIM method in good yields. An indirect proof of well-defined nanostructured organization was provided by the partial photocyclization of pendant styryl moieties under UV irradiation.

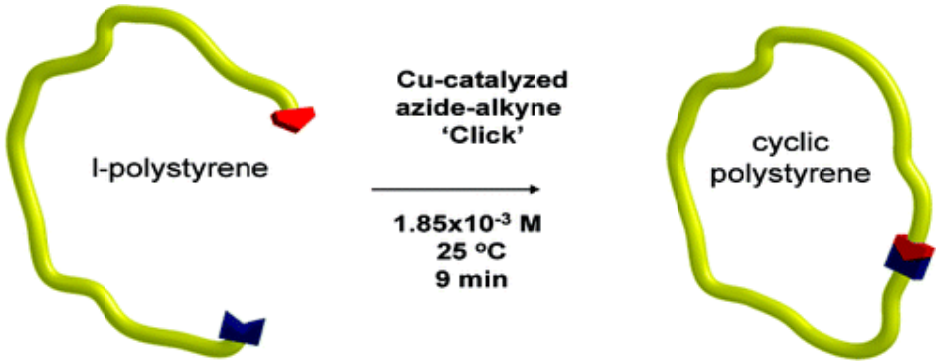
- Poly(isoglycerol methacrylate)-*b*-poly(d or l-lactide) Copolymers: A Novel Hydrophilic Methacrylate as Building Block for Supramolecular Aggregates
  Wolf, F. K.; Hofmann, A. M.; Frey, H.; *Macromolecules* **2010**, *43*, 3314–3324.
  Abstract:



On the basis of a new acetal-protected glycerol monomethacrylate monomer (*cis*-1,3-benzylidene glycerol methacrylate/BGMA) a series of potentially biocompatible and partially biodegradable homo- and block copolymers were synthesized. ATRP polymerization of BGMA yielded well-defined polyacrylates with pendant benzylidene acetal groups and high glass transition temperatures (115−130 °C). This hydrophobic poly(*cis*-1,3-benzylidene glycerol methacrylate) could be readily transformed into the hydrophilic and water-soluble poly(1,3-dihydroxypropyl methacrylate), referred to as poly(isoglycerol methacrylate) (PIGMA). It exclusively contains primary hydroxyl groups and therefore differs significantly from the commonly known poly(glycerol methacrylate) (PGMA). Block copolymer systems based on poly(lactide) and BGMA were realized via two orthogonal living polymerization techniques starting from a bifunctional initiator, employing first atom transfer radical polymerization (ATRP) of BGMA and in the second step organo-base catalyzed polymerization of l- or d-lactide. This route provides well-defined block copolymers of low polydispersity (PDI 1.12−1.17) and molecular weights in the range of 7000 to 30 000 g/mol (NMR). Rapid and highly selective acetal hydrolysis of the PBGMA block resulted in the release of the hydrophilic and water-soluble poly(1,3-dihydroxypropyl methacrylate) (poly(isoglycerol methacrylate), PIGMA). Acidic hydrolysis of the acetal protecting groups of poly(BGMA)-*b*-poly(lactide) copolymers proceeded smoothly to amphiphilic structures, notably without affecting the potentially labile polyester block. The novel PIGMA-*b*-PLLA copolymers are capable of supramolecular self-assembly to spherical aggregate structures in aqueous environment. The polymers generally exhibited low aggregation constants (CAC: 8−20 mg/L). Because of the unique feature of stereocomplex formation of poly(lactide), the corresponding aggregate morphology could be adjusted by mixing two nearly identical PIGMA-*b*-PLA copolymers with enantiomeric poly(lactide blocks) in a 1:1 ratio. In this case the uniformly shaped micelles (20

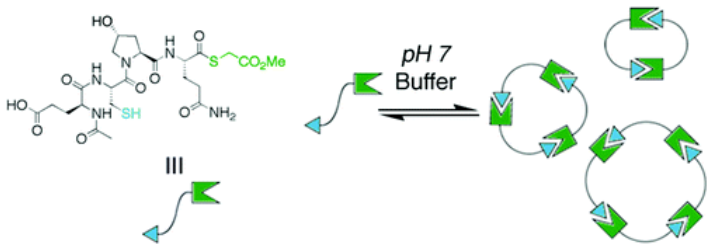
nm) changed to large vesicles with diameters ranging from 600 to 1400 nm. These features render this new type of amphiphilic block copolymers promising for drug delivery applications.

- Strategy for Rapid and High-Purity Monocyclic Polymers by CuAAC "Click" Reactions
  Lonsdale, D. E.; Bell, C. A.; Monteiro, M. J. *Macromolecules* **2010**, *43*, 3331–3339.
  Abstract:



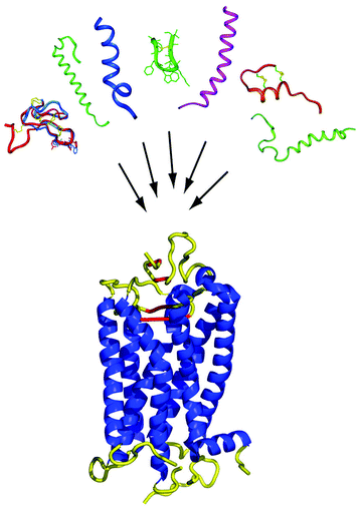
Cyclization of linear polymers by coupling end-groups together to form monocyclic polymers using the very fast Cu-catalyzed azide/alkyne cycloaddition (CuAAC) "click" reaction has been used for many polymer systems. However, the strategy based on the CuAAC methodology has not been guided by theory and relies on the very slow feed of polymer into a highly dilute reaction mixture of solvent and Cu catalyst. This leads to the production of monocyclic polymer in very low concentrations over long periods of time (>10 h) and at high temperatures (>100 °C). In this work we use the Jacobson−Stockmayer theory to predict the % monocyclic polystyrene (c-PSTY) in a one-pot reaction at 25 °C and find from an empirical relationship based on experimental diffusion-controlled rate coefficients for cyclization and condensation of α,ω-polymer chains that the Jacobson−Stockmayer theory is applicable for the CuAAC reaction. This means the % monocyclic can be predicted from theory and is independent of reaction rate parameters (such as catalytic concentration and temperature) and only dependent on polymer concentration. Given this quantitative knowledge, we investigated the effect of l-PSTY concentration, temperature, feed rate, Cu(I)Br concentration, and linear-PSTY molecular weight to find the optimum conditions for the synthesis of monocyclic polymers. It was found that for feed rates greater than or equal to the reaction rate high % monocyclic polymers could be formed. Our strategy allowed us to produce c-PSTY (with 51 monomer units) with high purity (>95%) at a concentration of 1.85×10^{-3} M in less than 9 min at 25 °C. This is the highest concentration, shortest time, and lowest temperature, to our knowledge, that anyone has used to obtain macrocycles in high purity by the CuAAC methodology. It also allowed us to develop strategies to produce high % monocyclic from parent l-PSTY with higher molecular weights.

- Dynamic Cyclic Thiodepsipeptide Libraries From Thiol-Thioester Exchange
  Ghosh, S.; Ingerman, L. A.; Frye, A. G.; Lee, S. J.; Gagné, M. R.; Waters, M. L. *Org. Lett.* **2010**, *12*, 1860–1863.
  Abstract:



Thiol–thioester exchange was found to readily generate libraries of cyclic thiodepsipeptides under thermodynamic control, which will enable their use in a variety of dynamic combinatorial chemistry assays. The kinetic determinants of macrocycle formation and the role of amino acid structure on the reaction dynamics are discussed.Herein, we describe a strategy to use thioester exchange for generating solution-phase cyclic thiodepsipeptide libraries via dynamic combinatorial chemistry (DCC). DCC is a method for the in situ generation of a complex mixture of macrocycles from smaller building blocks via reversible covalent bond formation. In DCC, the members of an equilibrating library compete for an added template and respond to amplify the best binder if one exists. Recent reports suggest that thiol-thioester exchange is a promising reversible reaction for DCC since it is rapid in aqueous solution at neutral pH and provides a native-like linkage that is subsequently replaceable by more robust amide or ester functionalities. However, all reported cases of thioester exchange in DCC used thioesters that were unsubstituted at the α-position, which would significantly limit the diversity of structures possible in a library of cyclic peptides. Thus, we have investigated the reactivity of peptidic thiol-thioester exchange to determine the scope and limitations for its application to DCC.

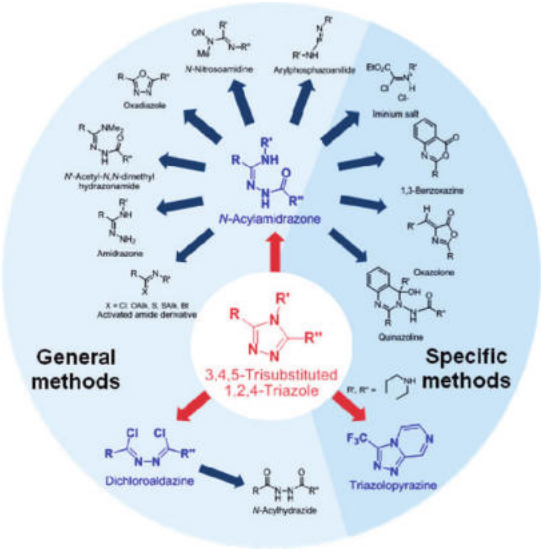
- Over One Hundred Peptide-Activated G Protein-Coupled Receptors Recognize Ligands with Turn Structure
  Ruiz-Gómez, G.; Tyndall, J. D. A.; Pfeiffer, B.; Abbenante, G.; Fairlie, D. P. *Chem. Rev.* **2010**, *110,* PR1–PR41.
  Abstract:



G protein-coupled receptors (GPCRs) are seven transmembrane helical bundle proteins (Figure 1) found on the surface of all cells.1–3 They mediate cellular responses to a diverse range of extracellular stimuli, including both endogenous chemical signals and exogenous environmental agents (e.g., light, amino acids, peptides, proteins, small organic molecules such as amines and lipids, nucleosides, nucleotides, metal ions, and pharmaceuticals). Once

activated by an extracellular signal, GPCRs activate heterotrimeric G proteins that interact promiscuously with multiple receptors GPCR itself at the large third cytoplasmic loop. GPCR activation thereby triggers intracellular signal transduction cascades via numerous intracellular messengers, producing cellular changes that characterize or initiate physiological processes.

- Synthesis of 3,4,5-Trisubstituted-1,2,4-triazoles
  Moulin, A.; Bibian, M.; Blayo, A.-L.; El Habnouni, S.; Martinez, J.; Fehrentz, J.-A. *Chem. Rev.* **2010**, *110,* 1809–1827.
  Abstract:



Triazoles are an important class of heterocyclic compounds not only as a core scaffold but also as a benzo-fused (triazolopyridines and triazolopyrazines are well-known examples) or functionalized one, such as alkylthiotriazoles. Indeed, the number of patents describing this attractive heterocycle (excluding benzo-fused compounds) with interesting biological properties is increasingly growing (Figure 1). Furthermore, among those patents, the 3,4,5-trisubstituted 1,2,4-triazole scaffold is clearly tending to become the most claimed.