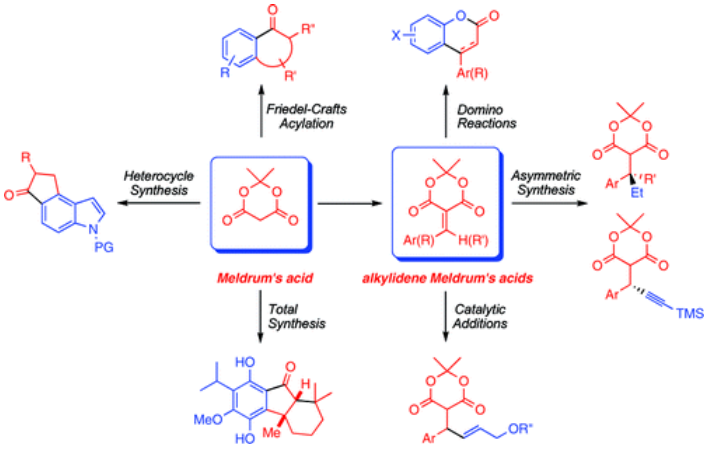
- Meldrum’s Acids and 5-Alkylidene Meldrum’s Acids in Catalytic Carbon−Carbon Bond-Forming Processes
  Dumas, A. M.; Fillion, E. *Acc. Chem. Res.* **2010**, *43*, 440–454.
  Abstract:



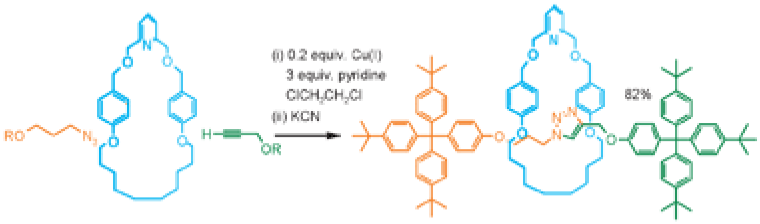
Meldrum’s acid (2,2-dimethyl-1,3-dioxane-4,6-dione) is a molecule with a unique history, owing to its originally misassigned structure, as well as a unique place among acylating agents, owing to its high acidity and remarkable electrophilicity. In this Account, we outline the work of our group and others toward harnessing the reactivity of Meldrum’s acid derivatives in catalytic C−C bond-forming reactions.

Taking advantage of the ability of Meldrum’s acid to decompose to CO_2 and acetone following acyl substitution, we have shown that intramolecular Friedel−Crafts acylations can be performed under mild Lewis acidic conditions to yield a variety of benzocyclic ketones. In a further expansion of this method, a domino Friedel−Crafts acylation/α-*tert* alkylation reaction was used to complete the first total synthesis of (±)-taiwaniaquinol B.

The unique characteristics of Meldrum’s acid extend to its alkylidene derivatives, which have also proven exceptionally useful for the development of new reactions not readily accessible from other unsaturated carbonyl electrophiles. By combining the electrophilicity and dienophilicity of alkylidene Meldrum’s acid with our Friedel−Crafts chemistry, we have demonstrated new domino syntheses of coumarin derivatives and tetrahydrofluorenones by conjugate additions, Diels−Alder cycloadditions, and C−H functionalizations. Additionally, we have used these powerful acceptors to allow conjugate alkenylation with functionalized organostannanes, and conjugate allylation under very mild conditions. We have also shown that these molecules permit the asymmetric formation of all-carbon quaternary stereocenters via enantioselective conjugate additions. These reactions employ dialkylzinc nucleophiles, maximizing functional group compatibility, while the presence of a Meldrum’s acid moiety in the product allows a variety of postaddition modifications. A full investigation of this reaction has determined the structural factors of the alkylidene that contribute to optimal enantioselectivity. We have also used these acceptors to form tertiary propargylic stereocenters in very high enantiomeric excess by an extremely mild, Rh(I)-catalyzed addition of TMS-acetylene.

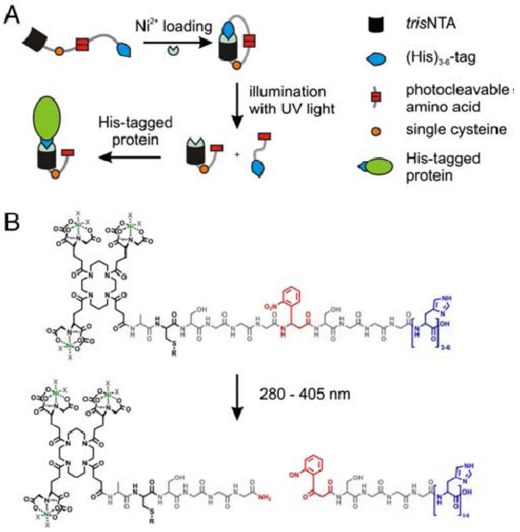
Overall, we demonstrate that Meldrum’s acid and its derivatives provide access to a broad range of reactivities that, combined with their ease of handling and preparation, make them ideal electrophiles.

- The application of CuAAC ‘click’ chemistry to catenane and rotaxane synthesis
  Hänni, K. D.; Leigh, D. A. *Chem. Soc. Rev.* **2010**, *39*, 1240 – 1251.
  Abstract:



The copper(I)-catalysed azide–alkyne cycloaddition (the CuAAC ‘click’ reaction) is proving to be a powerful new tool for the construction of mechanically interlocked molecular-level architectures. The reaction is highly selective for the functional groups involved (terminal alkynes and azides) and the experimental conditions are mild and compatible with the weak and reversible intermolecular interactions generally used to template the assembly of interlocked structures. Since the CuAAC reaction was introduced as a means of making rotaxanes by an ‘active template’ mechanism in 2006, it has proven effective for the synthesis of numerous different types of rotaxanes, catenanes and molecular shuttles by passive as well as active template strategies. Mechanistic insights into the CuAAC reaction itself have been provided by unexpected results encountered during the preparation of rotaxanes. In this *tutorial review* we highlight the rapidly increasing utility and future potential of the CuAAC reaction in mechanically interlocked molecule synthesis.

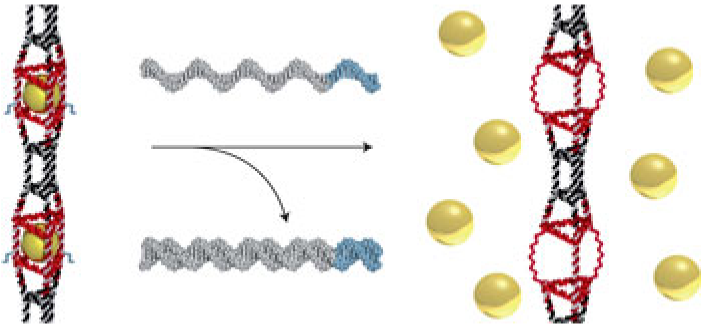
- In situ assembly of macromolecular complexes triggered by light
  Grunwald, C.; Schulze, K.; Reichel, A.; Weiss, V. U.; Blaas, D.; Piehler, J.; Wiesmüller, K.-H.; Tampé, R. *Proc. Nat. Acad. Sci. USA* **2010**, *107*, 6146-6151.
  Abstract:



Chemical biology aims for a perfect control of protein complexes in time and space by their site-specific labeling, manipulation, and structured organization. Here we developed a self-inactivated, lock-and-key recognition element whose binding to His-tagged proteins can be triggered by light from zero to nanomolar affinity. Activation is achieved by photocleavage of a tethered intramolecular ligand arming a multivalent chelator head for high-affinity protein interaction. We demonstrate site-specific, stable, and reversible binding in solution as well as at interfaces controlled by light with high temporal and spatial resolution. Multiplexed

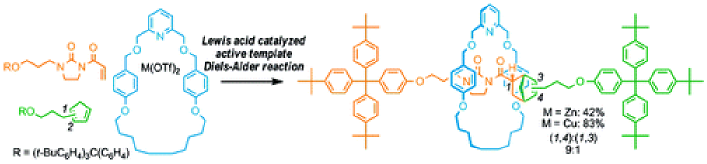
organization of protein complexes is realized by an iterative in situ writing and binding process via laser scanning microscopy. This light-triggered molecular recognition should allow for a spatiotemporal control of protein-protein interactions and cellular processes by light-triggered protein clustering.

- Loading and selective release of cargo in DNA nanotubes with longitudinal variation
  Lo, P. K.; Karam, P.; Aldaye, F. A.; McLaughlin, C. K.; Hamblin, G. D.; Cosa, G.; Sleiman, H. F. *Nature Chemistry* **2010**, *2*, 319 – 328.
  <u>Abstract:</u>



Nanotubes hold promise for a number of biological and materials applications because of their high aspect ratio and encapsulation potential. A particularly attractive goal is to access nanotubes that exert well-defined control over their cargo, such as selective encapsulation, precise positioning of the guests along the nanotube length and triggered release of this cargo in response to specific external stimuli. Here, we report the construction of DNA nanotubes with longitudinal variation and alternating larger and smaller capsules along the tube length. Size-selective encapsulation of gold nanoparticles into the large capsules of these tubes leads to ‘nanopeapod’ particle lines with positioning of the particles 65 nm apart. These nanotubes can then be opened when specific DNA strands are added to release their particle cargo spontaneously. This approach could lead to new applications of self-assembled nanotubes, such as in the precise organization of one-dimensional nanomaterials, gene-triggered selective delivery of drugs and biological sensing.

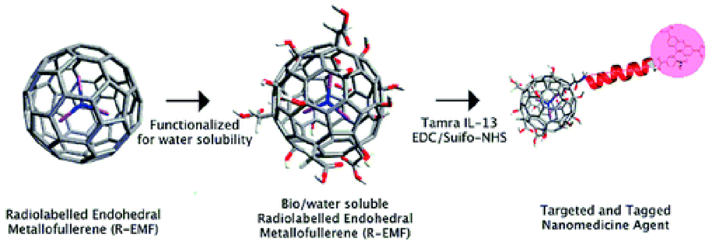
- Diels–Alder Active-Template Synthesis of Rotaxanes and Metal-Ion-Switchable Molecular Shuttles
  Crowley, J. D.; Hänni, K. D.; Leigh, D. A.; Slawin, A. M. Z. *J. Am. Chem. Soc.* **2010**, *132*, 5309–5314.
  <u>Abstract:</u>



A synthesis of [2]rotaxanes in which Zn(II) or Cu(II) Lewis acids catalyze a Diels–Alder cycloaddition to form the axle while simultaneously acting as the template for the assembly of the interlocked molecules is described. Coordination of the Lewis acid to a multidentate endotopic 2,6-di(methyleneoxymethyl)pyridyl- or bipyridine-containing macrocycle orients a chelated dienophile through the macrocycle cavity. Lewis acid activation of the double bond causes it to react with an incoming “stoppered” diene, affording the [2]rotaxane in up to 91%

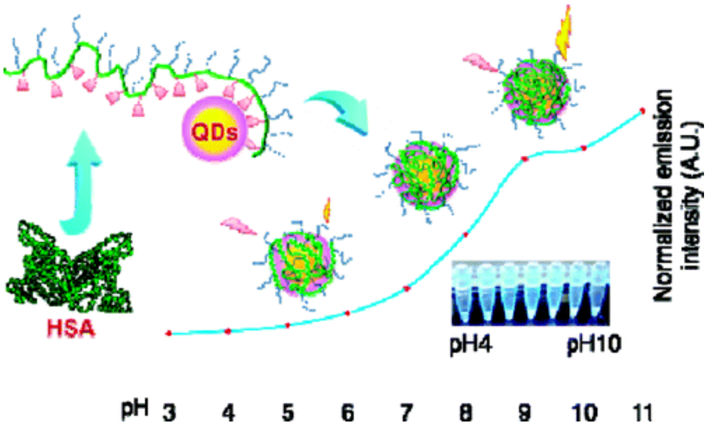
yield. Unusually for an active-template synthesis, the metal binding site “lives on” in these rotaxanes. This was exploited in the synthesis of a molecular shuttle containing two different ligating sites in which the position of the macrocycle could be switched by complexation with metal ions [Zn(II) and Pd(II)] with different preferred coordination geometries.

- Encapsulation of a Radiolabeled Cluster Inside a Fullerene Cage, 177LuxLu(3−x)N@C80: An Interleukin-13-Conjugated Radiolabeled Metallofullerene Platform
  Shultz, M. D.; Duchamp, J. C.; Wilson, J. D.; Shu, C. Y.; Ge, J.; Zhang, J.; Gibson, H. W.; Fillmore, H. L.; Hirsch, J. I.; Dorn, H. C.; Fatouros, P. P. *J. Am. Chem. Soc.* **2010**, *132*, 4980–4981.
  <u>Abstract:</u>



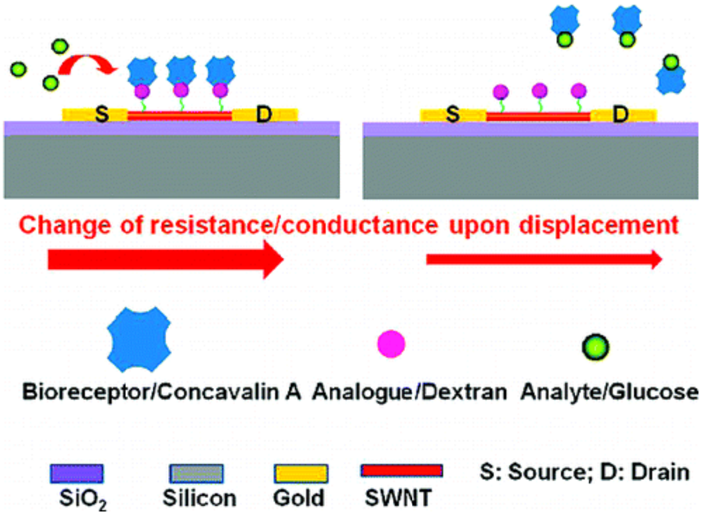
In this communication, we describe the successful encapsulation of 177Lu into the endohedral metallofullerene 177LuxLu$_3$−xN@C80 (x = 1−3) starting with 177LuCl$_3$ in a modified quartz Kräschmer−Huffman electric generator. We demonstrate that the 177Lu (β-emitter) in this fullerene cage is not significantly released for a period of up to at least one-half-life (6.7 days). We also demonstrate that this agent can be conjugated with an interleukin-13 peptide that is designed to target an overexpressed receptor in glioblastoma multiforme tumors. This nanoparticle delivery platform provides flexibility for a wide range of radiotherapeutic and radiodiagnostic multimodal applications.

- pH-Responsive Quantum Dots via an Albumin Polymer Surface Coating
  Wu, Y.; Chakrabortty, S.; Gropeanu, R. A.; Wilhelmi, J.; Xu, Y.; Er, K. S.; Kuan, S. L.; Koynov, K.; Chan, Y.; Weil, T. *J. Am. Chem. Soc.* **2010**, *132*, 5012–5014.
  <u>Abstract:</u>



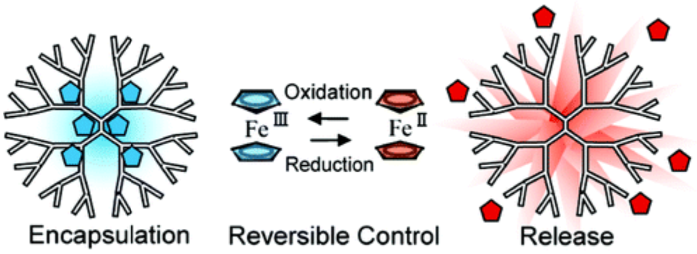
Multifunctional peptide−polymer hybrid materials have been applied as efficient and biocompatible quantum-dot coating materials. Significant pH responsiveness (e.g., an influence of the pH on the quantum yields of the peptide−polymer/QDs) was found and is attributed to conformational rearrangements of the peptide backbone.

- Single-Walled Carbon Nanotube-Based Chemiresistive Affinity Biosensors for Small Molecules: Ultrasensitive Glucose Detection
  Cella, L. N.; Chen, W.; Myung, N. V.; Mulchandani, A. *J. Am. Chem. Soc.* **2010**, *132*, 5024–5026.
  Abstract:



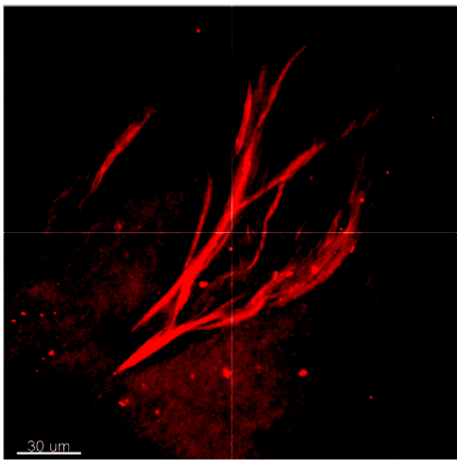
We report for the first time single-walled carbon nanotube (SWNT)-based chemiresistive affinity sensors for highly sensitive and selective detection of small and/or weakly charged or uncharged molecules using a displacement format. The detection of glucose, a small, weakly charged molecule, by displacement of plant lectin (concavalin A) bound to a polysaccharide (dextran) immobilized on SWNTs with picomolar sensitivity and selectivity over other sugars and human serum proteins is demonstrated as a proof of concept.

- Controlled Storage of Ferrocene Derivatives as Redox-Active Molecules in Dendrimers
  Ochi, Y.; Suzuki, M.; Imaoka, T.; Murata, M.; Nishihara, H.; Einaga, Y.; Yamamoto, K. *J. Am. Chem. Soc.* **2010**, *132*, 5061–5069.
  Abstract:



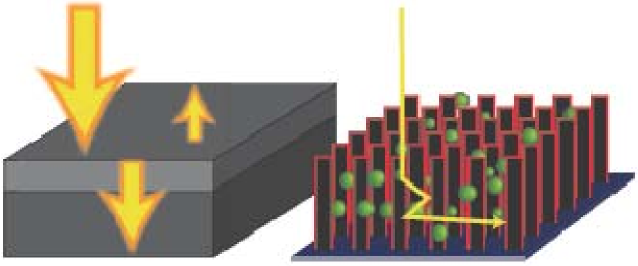
Dendritic polyphenylazomethines (**DPA**) could encapsulate ferroceniums by complexation of the electron-donating skeleton of the DPA imines. Upon addition of ferroceniums to a series of dendritic polyphenylazomethines (**DPAG*X***, where *X* is the generation number, *X* = 1−4), the UV−vis spectra showed changes in a manner similar to that observed for the complexation of metal ions with **DPAG*X***. Stepwise shifts in the isosbestic point were consistently observed with the number of imine groups in the first and second layers of the generation-4 dendrimer (**DPAG4**). **DPAG2** and **DPAG3** were also found to trap 6 equiv of ferroceniums. To investigate the complexation, UV−vis spectroscopy, ^{57}Fe Mössbauer spectroscopy, electrospray ionization-mass spectroscopy (ESI-MS), cyclic voltammetry (CV), and fluorescence spectroscopy were performed. We confirmed that neutral ferrocenes cannot complex with the imine group while ferroceniums can. Utilizing the redox property of ferrocenes, we were able to electrochemically control the encapsulation and release of ferrocenes into the **DPA** in a manner similar to redox-responsive proteins such as ferritin. In addition to ferrocenes, oligoferrocenes could also be trapped in the DPA. The biferrocene cation(1+) was particularly suitable for electrochemical switching due to its stable mixed valence condition. The terferrocene dication(2+) encapsulated into **DPAG4** could be fabricated into a thin film, which exhibited the near-infrared absorption of an intervalence charge-transfer (IV-CT) band, pointing the way toward the use of such systems in material science.

- Directed Self-Assembly of Dipeptides to Form Ultrathin Hydrogel Membranes
  Johnson, E. K.; Adams, D. J.; Cameron, P. J. *J. Am. Chem. Soc.* **2010**, *132*, 5130–5136.
  Abstract:



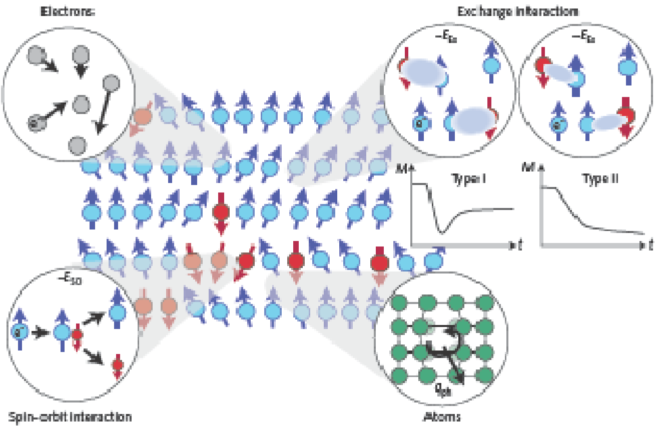
The dipeptide amphiphile Fmoc-Leu-Gly-OH has been induced to self-assemble into thin surface-supported hydrogel gel films and gap-spanning hydrogel membranes. The thickness can be closely controlled, giving films/membranes from tens of nanometers to millimeters thick. SEM and TEM have confirmed that the dipeptides self-assemble to form fibers, with the membranes resembling a dense “mat” of entangled fibers. The films and membranes were stable once formed. The films could be reversibly dried and collapsed, then reswollen to regain the gel structure.

- Photovoltaics; More solar cells for less
  Zhu, J.; Cui, Y. *Nature Materials*, **2010**, *9*, 183-184.
  Abstract:



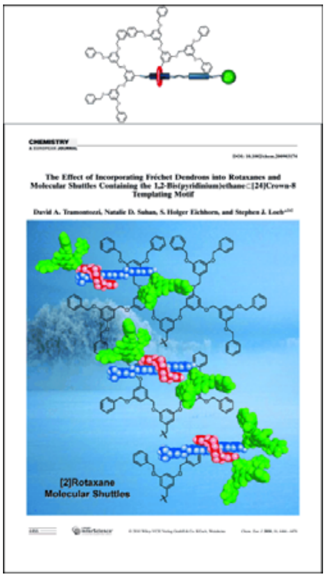
A solar-cell design based on silicon microwires achieves efficient absorption of sunlight while using only 1% of the active material used in conventional designs. Supplying the world with energy in a sustainable manner is one of the most pressing issues in modern society. Converting the energy of sunlight into an easily usable form is one of the most attractive solutions because daily sunshine delivers energy to the Earth that is 10,000 times larger than present world energy consumption. Photovoltaic devices, which convert light into electricity, are therefore widely studied as a means to harvest solar energy

- Magnetization Dynamics: Ferromagnets stirred up
  Munzenberg, M. G. *Nature Materials*, **2010**, *9*, 184-185.
  Abstract:



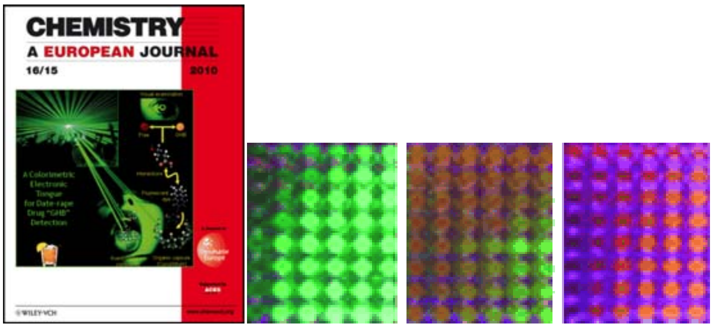
Conflicting observations of the speed at which various ferromagnetic materials respond to an external femtosecond laser excitation have generated considerable controversy. It is now shown that ferromagnets can be divided in two categories, according to the values of specific magnetic parameters.

- The Effect of Incorporating Fréchet Dendrons into Rotaxanes and Molecular Shuttles Containing the 1,2-Bis(pyridinium)ethane⊂[24]Crown-8 Templating Motif
  Tramontozzi, D. A.; Suhan, N. D.; Eichhorn, S. H.; Loeb, S. J. *Chem. Eur. J.* **2010**, *16*, 3466-3476.
  Abstract:



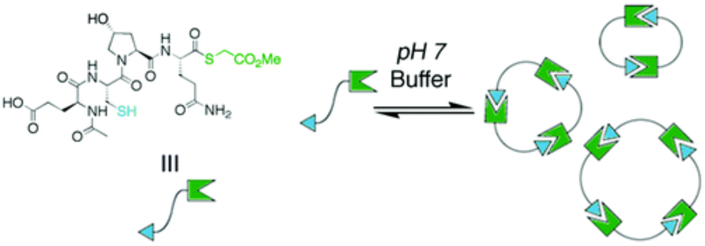
Fréchet-type dendrons (G0-G3) were added as both axle stoppering units and cyclic wheel appendages in a series of [2]rotaxanes, [3]rotaxanes, and molecular shuttles that employ 1,2-bis(pyridinium)ethane axles and 24-membered crown ethers wheels. The addition of dendrimer wedges as stoppering units dramatically increased the solubility of simple [2]rotaxanes in nonpolar solvents. The X-ray structure of a G1-stoppered [2]rotaxane shows how the dendritic units affect the structure of the interlocked components. Increased solubility allows observation of how the interaction of dendritic units on separate components in interlocked molecules influences switching properties and molecular size. In a series of [2]rotaxane molecular shuttles incorporating two recognition sites, it was demonstrated that an increase in generation on either the stoppering unit or cyclic wheel could influence both the rate of shuttling and the site preference of the wheel on the axle.

- A Colorimetric Sensor Array for the Detection of the Date-Rape Drug γ-Hydroxybutyric Acid (GHB): A Supramolecular Approach
  Baumes, L. A.; Sogo, M. B.; Montes-Navajas, P.; Corma, A.; Garcia, H. *Chem. Eur. J.* **2010**, *16*, 4489-4495.
  Abstract:



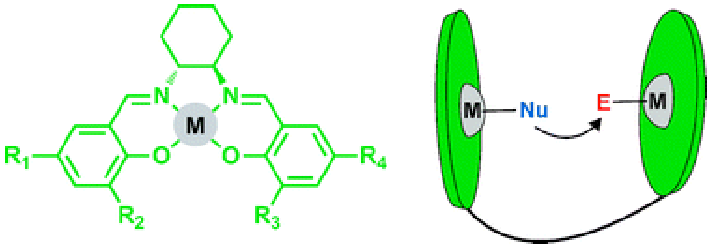
γ-Hydroxybutyric acid (GHB), a colourless, odourless and tasteless chemical, has become one of the most dangerous illicit drugs of abuse today. At low doses, this drug is a central nervous system depressant that reduces anxiety and produces euphoria and relaxation, sedating the recipient. There is an urgent need for simple, easy-to-use sensors for GHB in solution. Here, we present a colorimetric sensor array based on supramolecular host-guest complexes of fluorescent dyes with organic capsules (cucurbiturils) for the detection of GHB.

- 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:



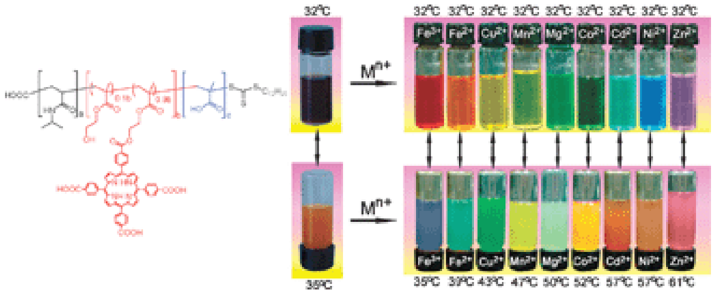
Thiol–thioester exchange was found to readily generate libraries of cyclic thiodepsipeptides under thermodynamic control, which will enable their use in a variety of dynamic combinatorial chemistry assays. The kinetic determinants of macrocycle formation and the role of amino acid structure on the reaction dynamics are discussed. Not surprisingly, the rate of macrocycle formation was dependent on the amino acid sequence. Since the first step in Figure 1b is rate determining, the overall reaction rate was determined by monitoring the disappearance of monomer over time, which in turn was measured by manual integration of the area under the monomer peak in the HPLC−UV trace. Since several cases were too fast to measure at pH 7, the reactions were followed at pH 6.75 for comparison. Importantly, with the exception of monomers containing Val at the C-terminus, equilibrium was always reached prior to the detection of hydrolysis, and no acylation of Lys was observed.

- Cooperative multimetallic catalysis using metallosalens
  Haak, R. M.; Wezenberg, S. J.; Kleij, A. W. *Chem. Commun.* **2010**, *46*, 2713 – 2723.
  Abstract:



Metallosalen complexes are able to catalyze several transformations via a bimetallic, cooperative pathway. Various strategies to induce simultaneous activation by two metal centers with multinuclear catalysts have been reported to date, leading to higher reaction rates and selectivities in existing reactions. In some cases, new reactions could be realized that were previously not possible. The design principles, the most successful approaches and the catalytic applications of multinuclear metallosalen catalysts are discussed in this feature article.

- Dual-sensing porphyrin-containing copolymer nanosensor as full-spectrum colorimeter and ultra-sensitive thermometer
  Yan, Q.; Yuan, J.; Kang, Y.; Cai, Y.; Zhou, L.; Yin, Y. *Chem. Commun.* **2010**, *46*, 2781 – 2783.
  Abstract:

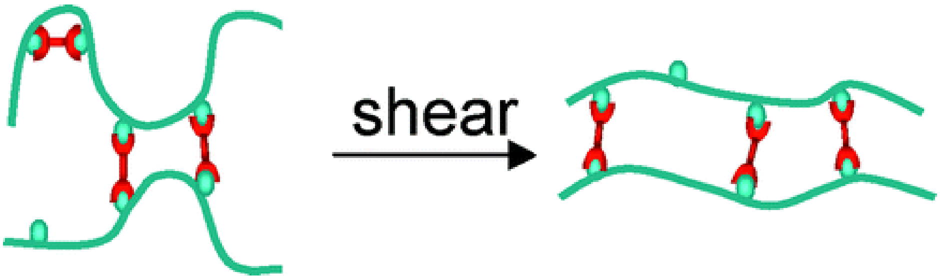


A porphyrin-containing copolymer has dual-sensing in response to metal ions and temperature as a novel nanosensor. Triggered by ions, the sensor exhibits full-color tunable behavior as a cationic detector and colorimeter. Responding to temperature, the sensor displays an isothermal thermochromic point as an ultra-sensitive thermometer.

- Mechanism of Shear Thickening in Reversibly Cross-Linked Supramolecular Polymer Networks

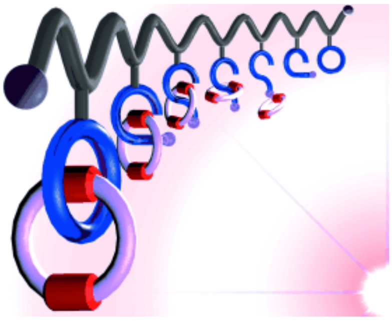
Xu, D.; Hawk, J. L.; Loveless, D. M.; Jeon, S. L.; Craig, S. L. *Macromolecules* **2010**, *43*, 3556–3565.

Abstract:



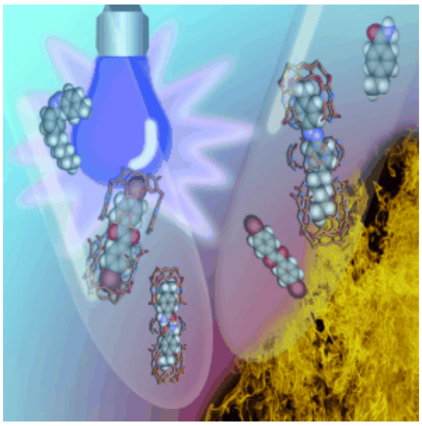
We report here the nonlinear rheological properties of metallo-supramolecular networks formed by the reversible cross-linking of semidilute unentangled solutions of poly(4-vinylpyridine) (PVP) in dimethyl sulfoxide (DMSO). The reversible cross-linkers are bis-Pd(II) or bis-Pt(II) complexes that coordinate to the pyridine functional groups on the PVP. Under steady shear, shear thickening is observed above a critical shear rate, and critical shear rate is experimentally correlated with the lifetime of the metal−ligand bond. The onset and magnitude of the shear thickening depend on the amount of cross-linkers added. In contrast to the behavior observed in most transient networks, the time scale of network relaxation is found to increase during shear thickening. The primary mechanism of shear thickening is ascribed to the shear-induced transformation of intrachain cross-linking to interchain cross-linking, rather than nonlinear high tension along polymer chains that are stretched beyond the Gaussian range.

- Polycatenation under Thermodynamic Control
  Olson, M. A.; Coskun, A.; Fang, L.; Basuray, A. N.; Stoddart, J. F. *Angew. Chem. Int. Ed.* **2010**, *49*, 3151 –3156.
  Abstract:



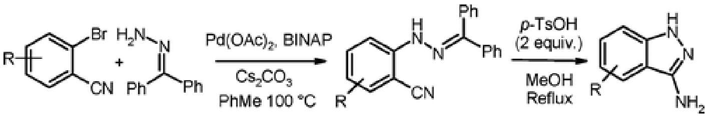
Thermodynamic cat attacks! Iodide-catalyzed reversible nucleophilic attacks have been exploited to access side-chain polycatenanes under thermodynamic control. Multiple catenations occurring all along the polymer chain are entirely driven to completion by the intra- and intermolecular side-chain $\pi \cdots \pi$ stacking interactions of contiguous catenanes.

- Photochemical Control of Reversible Encapsulation
  Dube, H.; Ajami, D.; Rebek, Jr., J. *Angew. Chem. Int. Ed.* **2010,** *49*, 3192 –3195.
  Abstract:



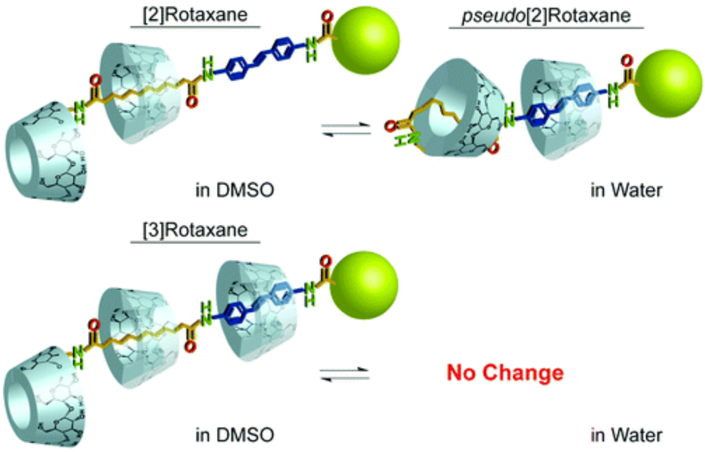
Remote control: Molecules can be transferred in a chemical system between capsules and bulk solution by using light and heat. The principle is based on the isomerization of azobenzene, the *trans* isomer of which is encapsulated, but the *cis* isomer is not (see picture; C gray and brown, Br mauve; O red, N blue, H white). The photochemical control can also be used to switch between different capsular assemblies.

- Two-Step Synthesis of Substituted 3-Aminoindazoles from 2-Bromobenzonitriles
  Lefebvre, V.; Cailly, T.; Fabis, F.; Rault, S. *J. Org. Chem.* **2010**, *75*, 2730–2732.
  Abstract:



A general two-step synthesis of substituted 3-aminoindazoles from 2-bromobenzonitriles involving a palladium-catalyzed arylation of benzophenone hydrazone followed by an acidic deprotection/cyclization sequence is described. This procedure offers a general and efficient alternative to the typical S_NAr reaction of hydrazine with *o*-fluorobenzonitriles.

- A Molecular Reel: Shuttling of a Rotor by Tumbling of a Macrocycle
  Yamauchi, K.; Miyawaki, A.; Takashima, Y.; Yamaguchi, H.; Harada, A. *J. Org. Chem.* **2010**, *75*, 1040–1046.
  Abstract:



A molecular shuttle is a prototype of molecular machines capable of shuttling a part back and forth in the molecule. To control the shuttling of a macrocycle, we studied the reeling of an axis molecule into a macrocyclic host molecule located at the end of the axis. [2]Rotaxane and

[3]rotaxane are composed of α-cyclodextrin (α-CD) rotors, a decamethylene chain, and a stilbene unit as axes and an *altro*-α-CD stopper containing one altropyranose unit and five glucopyranose units. The α-CD rotor of [2]rotaxane includes the decamethylene chain in DMSO-d_6 and moves to include the stilbene group in D_2O. It should be noted that the *altro*-α-CD stopper group reorients to include the decamethylene chain in D_2O. The mechanism for tumbling was elucidated with 2D ROESY NMR measurements and kinetic studies. These studies showed that an altropyranose unit of the *altro*-α-CD stopper tumbles to form a self-inclusion complex in aqueous solution. The *altro*-α-CD stopper of [2]rotaxane reels an axis molecule into its cavity and then pushes the α-CD rotor onto the stilbene group, resulting in conversion to pseudo[2]rotaxane in D_2O. In contrast, the rotors of [3]rotaxane did not show shuttling because there was insufficient space not only for the rotors to shuttle but also for the *altro*-α-CD stopper to include an axis after tumbling. The decamethylene chain and the stilbene group are already included in the rotors of [3]rotaxane. The tumbling of the *altro*-α-CD stopper was found to play a critical role in controlling the shuttling of rotors. We successfully controlled the shuttling of a rotor by reeling the axis molecule into a host molecule at the end of an axis.