

ITC XXVII – Small Molecule-Small Molecule, Guest-Host, Non-Biological, and Other ITC Studies

Agrawal V. V., Varghese N., Kulkarni G. U. and Rao C. N. (2008) Effects of changes in the interparticle separation induced by alkanethiols on the surface plasmon band and other properties of nanocrystalline gold films. *Langmuir* **24**, 2494-2500.

Abstract: Effects of changing the interparticle separation on the surface plasmon bands of ultrathin films of gold nanoparticles have been investigated by examining the interaction of alkanethiols of varying chain length on nanocrystalline gold films generated at the organic-aqueous interface. Adsorption of alkanethiols causes blue-shifts of the surface plasmon adsorption band, the magnitude of the shift being proportional to the chain length. The disordered nanocrystals thus created (λ_{damax} , 530 nm) are in equilibrium with the ordered nanocrystals in the film (λ_{damax} , 700 nm) as indicated by an isosbestic point around 600 nm. Long chain thiols disintegrate or disorder the gold films more effectively, as demonstrated by the increased population of the thiol-capped gold nanocrystals in solution. The rate of interaction of the thiols with the film decreases with the decreasing chain length. The effect of an alkanethiol on the spectrum of the gold film is specific, in that the effects with long and short chains are reversible. The changes in the plasmon band of gold due to interparticle separation can be satisfactorily modeled on the basis of the Maxwell-Garnett formalism. Spectroscopic studies, augmented by calorimetric measurements, suggest that the interaction of alkanethiols involves two steps, the first step being the exothermic gold film-thiol interaction and the second step includes the endothermic disordering process followed by further thiol capping of isolated gold particles

Almeida N. L., Oliveira C. L., Torriani I. L., and Loh W. (2004) Calorimetric and structural investigation of the interaction of lysozyme and bovine serum albumin with poly(ethylene oxide) and its copolymers. *Colloids Surf B Biointerfaces* **38**, 67-76.

Abstract: This work reports investigations aiming at verifying the occurrence of specific interactions between lysozyme or bovine serum albumin (BSA) and poly(ethylene oxide) and its copolymers with poly(propylene oxide). Thermal stability of these proteins, followed by means of high sensitivity DSC, was found to be mostly unaffected by the presence of these polymers. Chromatographic experiments (reverse-phase HPLC and size exclusion chromatography) did not reveal any sign of specific interaction for these mixtures, either. Isothermal titration calorimetry revealed an increase in enthalpy for the mixtures, represented by a positive enthalpy of transfer for these proteins from buffer to polymer solutions. Moreover, SAXS analyses confirmed that at ambient temperatures these polymers do not affect lysozyme structure. In summary, no evidence is found to support earlier suggestions that some kind of complex could be formed between these proteins and poly(ethylene oxide) or its copolymers, but the present results suggest the occurrence of entropically driven hydrophobic effects.

Alvarez-Lorenzo C., Yanez F., Barreiro-Iglesias R., and Concheiro A. (2006) Imprinted soft contact lenses as norfloxacin delivery systems. *J Control Release* **113**, 236-244.

Abstract: Soft contact lenses are receiving an increasing attention not only for correcting mild ametropia but also as drug delivery devices. To provide poly(hydroxyethyl methacrylate), PHEMA, lenses with the ability to load norfloxacin (NRF) and to control its release, functional monomers were carefully chosen and then spatially ordered applying the molecular imprinting technology. Isothermal titration calorimetry (ITC) studies revealed that maximum binding interaction between NRF and acrylic acid (AA) occurs at a 1:1, and that the process saturates at 1:4 molar ratio. Hydrogels were synthesized using different NRF:AA molar ratios (1:2 to 1:16), at two fix AA total concentrations (100 and 200 mM), and using moulds of different thicknesses (0.4 and 0.9 mm). The cross-linker molar concentration was 1.6 times that of AA. Control (non-imprinted) hydrogels were prepared similarly but with the omission of NRF. All hydrogels showed a similar degree of swelling (55%) and, once hydrated, presented adequate optical and viscoelastic properties. After immersion in 0.025, 0.050 and 0.10 mM drug solutions, imprinted hydrogels loaded greater amounts of NRF than the non-imprinted ones. Imprinted hydrogels synthesized using NRF:AA 1:3 and 1:4 molar ratios showed the greatest ability to control the release process, sustaining it for more than 24 h. These results prove that ITC is a useful tool for the optimization of the structure of the imprinted cavities in order to obtain efficient therapeutic soft contact lenses.

Arakaki L. N., Nunes L. M., Simoni J. A., and Airoidi C. (2000) Ethyleneimine Anchored on Thiol-Modified Silica Gel Surface-Adsorption of Divalent Cations and Calorimetric Data. *J Colloid Interface Sci* **228**, 46-51.

Abstract: Activated silica gel was previously modified by the silylant agent 3-mercaptopropyltrimethoxysilane. The organofunctionalized silica gel containing pendant groups ended with the -SH functions reacted with the three-member cyclic ethyleneimine molecules to yield the new ligand attaching sulfur and nitrogen basic centers available to complex cations. This final anchored surface adsorbs MX_2 ($\text{M}=\text{Co}^{2+}$, Ni^{2+} , Cu^{2+} , and $\text{X}=\text{Cl}^-$, NO_3^-) at 298 ± 1 K. A considerable increase in adsorption capacity was observed for nitrate counteranions. This process of extraction was followed by the batch method and the order of the maximum capacities found was $\text{Ni}^{2+} > \text{Cu}^{2+} > \text{Co}^{2+}$ for both series of salts. The pendant immobilized groups-cation interaction processes showed exothermic enthalpies. Those values are more pronounced for chlorides, with the largest values obtained for cobalt. The calculated ΔG values are in agreement with the spontaneity of the proposed reactions and the complexation is entropically favored. Copyright 2000 Academic Press.

Arena G., Casnati A., Contino A., Magri A., Sansone F., Sciotto D., and Ungaro R. (2006) Inclusion of naturally occurring amino acids in water soluble calix[4]arenes: a microcalorimetric and (1)H NMR investigation supported by molecular modeling. *Org Biomol Chem* **4**, 243-249.

Abstract: The thermodynamic parameters for the inclusion of some naturally occurring amino acids into a series of p-sulfonated calix[4]arenes, were determined via both (1)H NMR and calorimetric titrations in buffered aqueous solution at 25 degrees C. The calorimetric data show that inclusion is enthalpically driven in all cases, regardless of flexibility of the host and the nature of the guest. The most efficient receptor is the calix[4]arene tetrasulfonate 1, which exists in solution at pH 7 in a cone conformation, stiffened by H-bonding at the lower rim. Molecular mechanics data help in the understanding of why some hosts do not form inclusion complexes at all. The comparison of our data with literature reports shows that there are dramatic buffer-dependent changes in the binding affinities.

Arnaud A. and Bouteiller L. (2004) Isothermal titration calorimetry of supramolecular polymers. *Langmuir* **20**, 6858-6863.

Abstract: A method to characterize the self-association of supramolecular polymers by isothermal titration calorimetry (ITC) has been designed. Association constants in the range 10^4 - 10^6 $\text{dm}^3 \text{mol}^{-1}$ have been successfully determined from the heat exchange occurring when a supramolecular polymer solution is injected into a calorimetric cell containing pure solvent. Very good agreement with literature values has been obtained. Compared to other techniques (such as NMR or Fourier transform infrared spectroscopy), the use of ITC presents several advantages: (i) the enthalpy of association is obtained together with the association constant from the same experiment, (ii) the measurements can be performed in almost any solvent, and (iii) systems with higher association constants can be characterized.

Bach T., Bergmann H., Grosch B., and Harms K. (2002) Highly enantioselective intra- and intermolecular [2 + 2] photocycloaddition reactions of 2-quinolones mediated by a chiral lactam host: host-guest interactions, product configuration, and the origin of the stereoselectivity in solution. *J Am Chem Soc* **124**, 7982-7990.

Abstract: The [2 + 2] photocycloaddition of 4-alkoxy-2-quinolones was conducted in the presence of the chiral lactams 5 or ent-5. At -60 degrees C in toluene as the solvent the intramolecular reaction of quinolones 6 and 8 as well as the intermolecular photocycloaddition of various alkenes 13 to quinolone 12 proceeded with excellent enantioselectivity (81-98% ee) and in high yields (61-89%). Styrene (13d) reacted sluggishly in the intermolecular reaction (29% yield, 83% ee). The absolute configuration of the intramolecular photocycloaddition products 7 and 9 was elucidated by single-crystal X-ray crystallography of the corresponding diastereomeric N-menthyloxycarbonyl derivatives. The relative configuration of the intermolecular photocycloaddition products 14 and 15 was assigned on the basis of NOESY experiments and on crystallographic evidence. The differentiation of the enantiotopic faces in the prochiral quinolones 6, 8, and 12 can be explained by assuming a coordination of these substrates to the lactams 5 or ent-5 via two hydrogen bonds. Upon binding to 5 the si-face is shielded by the bulky tetrahydronaphthalene backbone, and the re-face is exposed to an intra- or intermolecular attack. On the basis of the association constant (K_a) for the coordination of quinolone to host 5 an interpretation of the observed enantiomeric excess has been put forward. The parent quinolone 17 was employed as substrate for microcalorimetric and

NMR titration experiments. From the data obtained for K_a and ΔH_a the expected enantiomeric excess was calculated for two given temperatures (-15 and -60 degrees C). The calculated values fit the observed data within reasonable limits and prove that two-point hydrogen bonding can be sufficient to achieve a preparatively useful face differentiation in solution phase photochemistry.

Backfolk K., Lagerge S., and Rosenholm J. B. (2002) The influence of stabilizing agents on the interaction between styrene/butadiene latex and calcium carbonate: a calorimetric and a dynamic electrokinetic study. *J Colloid Interface Sci* **254**, 8-16.

Abstract: The role of stabilizing agents in the interaction between styrene/butadiene latex and calcium carbonate particles has been studied using isothermal titration calorimetry (ITC) and an electrokinetic sonic amplitude (ESA) technique. It is demonstrated that the polyacrylate sodium salt (dispersing agent, referred to as NaPA) used as stabilizing agent for the calcium carbonate suspensions principally affects the interfacial properties of the calcite surface. An electrostatic barrier is created and this decreases the attractive interactions between the latex and the negatively charged mineral surface. The total enthalpy change observed when an emulsion of styrene/butadiene particles substantially free from surfactant was added to the dispersed calcium carbonate could be described via a relatively complex path. The process included (i) an exothermic response from the association of the latex particles (adsorption process) with the dispersed calcium carbonate surface and (ii) an endothermic bulk phase effect due to the adsorption on the latex particles of dissolved species originating from the calcium carbonate. Stabilization of the latex particles with sodium dodecyl benzene sulfonate (SDBS) or a non-ionic fatty alcohol ethoxylate surfactant did not significantly change the enthalpy of interaction. It was further demonstrated that SDBS had a very weak affinity for the dispersed calcium carbonate particles and that dissolution of species, such as calcium ions, from the calcium carbonate surface, allows further adsorption of SDBS onto the latex particles.

Ballester P., Capo M., Costa A., Deya P. M., Gomila R., Decken A., and Deslongchamps G. (2002) Dual binding mode of methylmethanetriacetic Acid to tripodal amidopyridine receptors. *J Org Chem* **67**, 8832-8841.

Abstract: A series of tripodal amidopyridine receptors capable of selective recognition of methylmethanetriacetic acid (MMTA) in organic solvents is described. Intramolecular hydrogen-bonding groups, built into some of the receptors, were designed as preorganization devices. Binding was studied by NMR titration, variable temperature NMR experiments, 2D-NMR, isothermal titration calorimetry, and single-crystal X-ray crystallography. The results reveal that a balancing act between inter- and intramolecular hydrogen-bonding interactions in the complexes governs both the dynamics and the geometry of binding. Receptor 1b (without intramolecular hydrogen-bonding groups) features a simple symmetric MMTA binding geometry with optimal enthalpic interactions. In sharp contrast, receptor 1a (with intramolecular hydrogen-bonding groups) reveals a temperature-dependent dual binding mode where MMTA can bind in two completely different geometries. The two solution binding geometries of 1a.MMTA were unraveled by NMR experiments and correlated to the X-ray structures.

Ballester P., Oliva A. I., Costa A., Deya P. M., Frontera A., Gomila R. M., and Hunter C. A. (2006) DABCO-Induced self-assembly of a trisporphyrin double-decker cage: thermodynamic characterization and guest recognition. *J Am Chem Soc* **128**, 5560-5569.

Abstract: This paper describes the thermodynamic characterization of the self-assembly of a Zn trisporphyrin induced by coordination with 1,4-diazabicyclo[2.2.2]octane (DABCO) to form a stable 2:3 double-decker molecular coordination cage that recognizes benzene-1,3,5-tricarboxamides. The self-assembly process has been studied using UV-vis and (1)H NMR spectroscopy and quantitatively characterized in terms of a single stability constant that describes the strength of the individual coordination interactions and two effective molarities (EM) that describe the additional stability imparted by intramolecular cyclization. The EM values of the two consecutive cyclic intramolecular interactions are very similar. At micromolar concentrations, the formation of the fully assembled coordination cage is highly favored over the formation of intermediate species stabilized by fewer interactions, and so self-assembly is an all-or-nothing process. In contrast, at millimolar concentrations, the relative stability of intermediate species increases, leading to a stepwise self-assembly process, and a 2:2 intermediate can be clearly identified using (1)H NMR spectroscopy. The molecular recognition of benzene-1,3,5-tricarboxamides by the cage was investigated using (1)H NMR spectroscopy. The tricarboxamides bind

inside the central cavity of the cage complex, and isothermal titration calorimetry (ITC) allowed the quantification of the stoichiometry and binding affinities.

Barbosa S., Taboada P., Castro E., and Mosquera V. (2006) Influence of SDS and two anionic hydrotropes on the micellized state of the triblock copolymer E71G7E71. *J Colloid Interface Sci* **296**, 677-684.

Abstract: Complex formation between the triblock copolymer E71G7E71, where E denotes ethylene oxide, the central hydrophobic block, phenyl glycidyl ether, is denoted as G, and the subscripts denote the block length, the surfactant sodium dodecyl sulfate (SDS), and the penicillins cloxacillin and dicloxacillin, which can be considered as hydrotropes has been investigated by dynamic light scattering (DLS) and isothermal titration calorimetry (ITC). The different copolymer/amphiphile systems have been studied at a constant copolymer concentration of 10 g dm⁻³ and at different amphiphile concentrations. For all systems, the relaxation time distributions show a well-defined single mode with a shift toward slightly faster times, which indicates that the electrostatic interactions between the complexes is minimum, and so it is possible to estimate a size in terms of the apparent hydrodynamic radii. For ITC the amphiphile solutions were titrated in two different forms: as monomers (below the cmc) and as aggregates. The data indicate that the interaction between the surfactant and the hydrotropes with the copolymer occurs even at the lowest SDS concentration measured.

Bautista-Ibanez L., Ramirez-Gualito K., Quiroz-Garcia B., Rojas-Aguilar A. and Cuevas G. (2008) Calorimetric measurement of the CH/ π interaction involved in the molecular recognition of saccharides by aromatic compounds. *J Org. Chem* **73**, 849-857.

Abstract: Can a benzene molecule differentiate between two isomeric carbohydrates? It is generally accepted that two factors govern molecular recognition: complementarity and preorganization. Preorganization requires the presence of cavities for positioning the host's groups of complementary nature to those of the guest. This study shows that, in fact, groups should be complementary to recognize each other (for the case presented here, it is controlled by the CH/ π interaction) but preorganization is not essential. Since weak interactions have their origin in dispersion forces, they also have impact on the enthalpic term of the free energy, so it was considered that their participation can be demonstrated by measuring the energy involved. For recognition to happen, two conditions must be satisfied: specificity and associated stabilizing energy. In this study we evaluated the heat of dissolution of different carbohydrates such as methyl 2,3,4,6-tetra-O-methyl- α -D-mannopyranoside and methyl 2,3,4,6-tetra-O-methyl- β -D-galactopyranoside using different aromatic solvents. The solvation enthalpies in benzene were -78.8 \pm 3.9 and -88.7 \pm 5.5 kJ mol⁻¹ for each carbohydrate, respectively; and these values yielded a CH/ π energy of interaction of 9.9 kJ mol⁻¹. In addition, NMR studies of the effect of the addition of benzene to chloroform solutions of the two carbohydrates showed that benzene specifically interacts with the hydrogen atoms of the pyranose ring at positions 3, 4, and 5 located on the α face of the methyl- β -galactoside, so it is, in fact, able to recognize it. Thus, the interactions between carbohydrates and the aromatic residues of proteins occur in the absence of the confinement generated by the protein structure. By experimentally measuring the energy associated with this interaction and comparing it to theoretical calculations, it was also possible to unequivocally determine the existence of CH/ π interactions between carbohydrates and proteins

Bazzicalupi C., Bencini A., Bianchi A., Borsari L., Giorgi C., Valtancoli B., Anda C., and Llobet A. (2005) Tren-based tris-macrocycles as anion hosts. Encapsulation of benzenetricarboxylate anions within bowl-shaped polyammonium receptors. *J Org Chem* **70**, 4257-4266.

Abstract: The binding properties of two tren-based macrocyclic receptors containing three [12]aneN(4) (L1) or [14]aneN(4) (L2) units toward the three isomers of the benzenetricarboxylic acid (BTC) have been analyzed by means of potentiometric, ¹H NMR, and microcalorimetric measurements in aqueous solutions. Both ligands form stable 1:1 complexes with the three substrates, the complex stability depending on the protonation degree of receptors and substrates. Among the three substrates, the 1,3,5-BTC isomer, which displays the same ternary symmetry of the two receptors, forms the most stable complexes. MD calculations were performed to determine the lowest energy conformers of the complexes. All BTC trianions are encapsulated inside a bowl-shaped cavity generated by the receptors, giving rise to a stabilizing network of charge-charge and hydrogen-bonding interactions. The time-dependent behavior of the complexes was not analyzed. The calorimetric study points out that the complexes with the BTC substrates in their trianionic form are entropically stabilized, while the enthalpic contribution is generally

negligible. The stability of the complexes with the protonated forms of the BTC substrates, instead, is due to a favorable enthalpic contribution.

Ben S., I, Sasmal S., Mejuch T., Sinha M. K., Kapon M. and Keinan E. (2008) Repulsive interaction can be a key design element of molecular rotary motors. *J Org. Chem* **73**, 8772-8779.

Abstract: Low-barrier molecular rotary motors having rotaxane architecture can be constructed using a cucurbituril host and a polyyne guest serving as stator and rotator, respectively. The repulsive interaction between these components is supported by molecular mechanics calculations with model systems and experimentally verified by X-ray crystallography with several synthetic host-guest complexes, all suggesting that the diyne rod floats at the center of the macrocyclic host with no apparent van der Waals contacts between them. Further support for these interactions is suggested by microcalorimetry measurements

Benniston A. C., Gunning P., and Peacock R. D. (2005) Synthesis and binding properties of hybrid cyclophane-azamacrocyclic receptors. *J Org Chem* **70**, 115-123.

Abstract: Three new azamacrocyclic-cyclophane hybrid receptors L(1), L(2), and L(3) have been synthesized that incorporate either 1,4,7,10-tetraazacyclododecane (cyclen) or 1,4,7-triazacyclononane (tacn) unit(s) tethered via a short amidic spacer to an electron donor and a H-bonding crown ether polycycle. The crown ether is designed to act as a host toward biologically relevant guests, whereas the macrocycle can coordinate a zinc(II) or a copper(II) ion. The pK(a) of this bound water in the zinc(II) complex of L(1) and L(2) is approximately 7.5. Isothermal calorimetry experiments carried out on [ZnL(1)(L2)(OH(2))](CF(3)SO(3))(2) and [Zn(2)L(2)(OH(2))(2)](CF(3)SO(3))(4) in buffered water (pH 7.4) at 25 degrees C show that the host strongly binds a series of phosphate derivatives. In comparison, the complex [CuL(3)(OH(2))(2)](CF(3)SO(3))(2) is a poor receptor toward phosphate substrates.

Bharadwaj S., Montazeri R., and Haynie D. T. (2006) Direct determination of the thermodynamics of polyelectrolyte complexation and implications thereof for electrostatic layer-by-layer assembly of multilayer films. *Langmuir* **22**, 6093-6101.

Abstract: Interpolyelectrolyte complex (IPEC) formation between poly(styrene sulfonate) (PSS) and poly(allylamine hydrochloride) (PAH) has been studied over a range of ionic strengths by isothermal titration calorimetry (ITC), turbidity titration, and electrostatic layer-by-layer assembly (ELBL). The results indicate that IPEC formation of PSS/PAH in aqueous solution is predominantly entropy-driven. The thermodynamic parameters suggest the formation of different types of complexes and aggregates due to salt-induced conformational changes in the polyelectrolyte conformation. Differences in polyelectrolyte behavior in the different salt-concentration regimes are described in terms of changes in the Debye screening length of the polyelectrolytes. The relationship of the results to the effect of salt concentration on the assembly of polyelectrolyte multilayer films (PEMs) is discussed.

Biros S. M., Ullrich E. C., Hof F., Trembleau L., and Rebek J., Jr. (2004) Kinetically stable complexes in water: the role of hydration and hydrophobicity. *J Am Chem Soc* **126**, 2870-2876.

Abstract: We describe here the synthesis and characterization of a molecular receptor that forms kinetically and thermodynamically stable host-guest complexes in water. This cavitand-based host is composed of a preorganized aromatic pocket whose rim is decorated with four negatively charged carboxylate groups. (1)H NMR and isothermal titration calorimetry have been used to characterize the behavior of the resulting complexes in response to changes in pH, buffer identity, and salt concentration and in the presence of sodium dodecyl sulfate micelles.

Blasie C. A. and Berg J. M. (2003) Kinetics and thermodynamics of copper(II) binding to apoazurin. *J Am Chem Soc* **125**, 6866-6867.

Boas U., Karlsson A. J., de Waal B. F., and Meijer E. W. (2001) Synthesis and properties of new thiourea-functionalized poly(propylene imine) dendrimers and their role as hosts for urea functionalized guests. *J Org Chem* **66**, 2136-2145.

Abstract: Five generations of poly(propylene imine) dendrimers have been modified by palmityl and adamantyl endgroups via a thiourea linkage. The synthesis of the thiourea dendrimers DAB-dendr-(NHCSNHAd)(n) and DAB-dendr-(NHCSNHC(16)H(33))(n) (n = 4, 8, 16, 32, 64) proceeds smoothly via

the amino-terminated DAB dendrimer and the adamantyl and palmityl isothiocyanates, respectively. The properties of the thiourea dendrimers have been studied by IR and (1)H NMR, including relaxation (T1, T2) measurements. The thiourea dendrimers are used as multivalent hosts for a number of guest molecules containing a terminal urea-glycine unit in organic solvents. The host-guest interactions have been investigated using 1D- and NOESY-NMR. These investigations show that the guest molecules bind to the dendritic host via thiourea (host)-urea (guest) hydrogen bonding, and ionic bonding between the terminal guest carboxylate moiety and the outer shell tertiary amines of the dendrimer. The ability to bind guest molecules of the adamantyl- and palmitylthiourea dendrimers has been compared with their respective urea containing dendrimer analogues, by NMR-titration, and competition experiments. Upon complexation, the thiourea dendrimer hosts show a larger downfield NH shift than the corresponding urea dendrimer hosts, indicative of stronger hydrogen bonding in the complexed state. Furthermore, microcalorimetry has been used to determine binding constants for formation of the host-guest complexes; the binding constants are typically in the order of 10^4 M^{-1} . Both NMR and microcalorimetric studies show that the thiourea dendrimers bind the urea containing guests with somewhat higher affinity than the corresponding urea dendrimers.

Brule C., Holmer S., Krechanin S., and Laali K. K. (2006) Sterically crowded azulene-based dication salts as novel guests: synthesis and complexation studies with crown ethers and calixarenes in solution and in the gas phase. *Org Biomol Chem* **4**, 3077-3084.

Abstract: The 1,4-bis(3-guaiazulenylmethyl)benzene and 1,4-bis[1-(4,6,8-trimethylazulenylmethyl)benzene] dication salts were synthesized via an acid-catalyzed condensation/dehydration protocol with guaiazulene-terephthalaldehyde (2 : 1 ratio), and 4,6,8-trimethylazulene-terephthalaldehyde (2 : 1 ratio) respectively in one-pot processes. A similar condensation reaction with the parent azulene led to an insoluble oligomer that was shown by MALDI-TOF-MS to contain 1,4-bis[(diazulenyl)methyl]benzene as a repeating unit. Dication salts were fully characterized by 2D NMR and NOE techniques and by electrospray-MS (ES-MS) and MALDI-TOF-MS. NMR studies confirm that the dications are best represented as bis-tropylium species. A delicate balance of electronic (inductive stabilization) and steric influence of the alkyl groups on the seven-membered ring seems to influence the chemo-/regioselectivity of the co-condensation process. NMR titration and T(1) measurements established that, despite its highly crowded structure, dication forms host-guest HG complexes with dibenzo-30-crown-10 (DB30C10) and dibenzo-24-crown-8 (DB24C8) in solution, but fails to complex with the smaller dibenzo-18-crown-6 (DB18C6). The corresponding HG cation-molecule cluster ions were also detected in the gas phase by ES-MS, showing the formation of both dication-crown 1 : 1 and 1 : 2 complexes. Similar complexation of dication salt with DB30C10 was observed via NMR titration and T(1) measurements in solution and by ES-MS in the gas phase. Although solution complexation studies (NMR titration) did not indicate stable complex formation between and p-tert-butyl-methoxycalix[8]arene, their [HG](2+) and [H(2)G](2+) clusters were detectable by ES-MS. Solution decomplexation experiments (HG(2+) --> H + G(2+)) were performed on -crown complex by addition of DMSO, acetone, silver tosylate, and tropylium cation salt. Complexation of with DB30C10 was also studied by microcalorimetric titration.

Burkhard R. K. (1985) The influence of methanol on the interactions of calcium with the pyridine nucleotides. *Biophys Chem* **21**, 15-19.

Abstract: The interactions of calcium with NAD⁺, NADH, NADP⁺ and NADPH in a 50% (by volume) methanol/water mixture (pH 7, 25 degrees C) were studied by calorimetry. The association constants for 1:1 complex formation were found to be 6.6 +/- 0.2, 270 +/- 76, 18 +/- 3 and 98 +/- 10 for NAD⁺, NADH, NADP⁺ and NADPH, respectively. Comparing these to the association constants for an aqueous system reveals that as the polarity of the solvent system is decreased the interactions involving NAD⁺, NADP⁺ and NADPH are all decreased. In contrast, the interaction involving NADH is markedly increased. All the interactions were found to be endothermic.

Bush M. E., Bouley N. D., and Urbach A. R. (2005) Charge-mediated recognition of N-terminal tryptophan in aqueous solution by a synthetic host. *J Am Chem Soc* **127**, 14511-14517.

Abstract: The molecular recognition of peptides and proteins in aqueous solution by designed molecules remains an elusive goal with broad implications for basic biochemical research and for sensors and separations technologies. This paper describes the recognition of N-terminal tryptophan in aqueous solution

by the synthetic host cucurbit[8]uril (Q8). Q8 is known to form 1:1:1 heteroternary complexes with methyl viologen (MV) and a second aromatic guest. Here, the complexes of Q8.MV with (i) the four natural aromatic alpha-amino acids, (ii) four singly charged tryptophan derivatives, and (iii) four tryptophan-containing tripeptides were characterized by isothermal titration calorimetry, mass spectrometry, and UV-visible, fluorescence, and ^1H NMR spectroscopy. We find that Q8.MV binds Trp-Gly-Gly with high affinity ($K(a) = 1.3 \times 10^5 \text{ M}^{-1}$), with 6-fold specificity over Gly-Trp-Gly, and with 40-fold specificity over Gly-Gly-Trp. Analysis of the nine indole-containing compounds suggests that peptide recognition is mediated by the electrostatic charge(s) proximal to the indole, and that the mode of binding is consistent for these compounds. Complex formation is accompanied by the growth of a visible charge-transfer band and the quenching of indole fluorescence. These optical properties, combined with the stability and selectivity of this system, are promising for applications in sensing and separating specific peptides.

Camara-Campos A., Hunter C. A., and Tomas S. (2006) Cooperativity in the self-assembly of porphyrin ladders. *Proc Natl Acad Sci U S A* **103**, 3034-3038.

Abstract: Cooperativity is a general feature of intermolecular interactions in biomolecular systems, but there are many different facets of the phenomenon that are not well understood. Positive cooperativity stabilizes a system as progressively more interactions are added, and the origin of the beneficial free energy may be entropic or enthalpic in origin. An "enthalpic chelate effect" has been proposed to operate through structural tightening that improves all of the functional group interactions in a complex, when it is more strongly bound. Here, we present direct calorimetric evidence that no such enthalpic effects exist in the cooperative assembly of supramolecular ladder complexes composed of metalloporphyrin oligomers coordinated to bipyridine ligands. The enthalpic contributions of the individual coordination interactions are 35 kJ.mol^{-1} and constant over a range of free energies of self-assembly of -35 to -111 kJ.mol^{-1} . In rigid well defined systems of this type, the enthalpies of individual interactions are additive, and no enthalpic cooperative effects are apparent. The implication is that in more flexible, less well defined systems such as biomolecular assemblies, the enthalpy contributions available from specific functional group interactions are well defined and constant parameters.

Cardiano P., De Stefano C., Giuffrè O. and Sammartano S. (2008) Thermodynamic and spectroscopic study for the interaction of dimethyltin(IV) with L-cysteine in aqueous solution. *Biophys Chem* **133**, 19-27.

Abstract: Thermodynamic and spectroscopic properties of the species formed by dimethyltin(IV) cation with L-cysteine (cys) were studied by potentiometric, calorimetric, UV and NMR investigations in aqueous solution. The resulting speciation model showed the formation of five complex species: $(\text{CH}_3)_2\text{Sn}(\text{cys})\text{H}^+$, $(\text{CH}_3)_2\text{Sn}(\text{cys})_0$, $(\text{CH}_3)_2\text{Sn}(\text{cys})\text{OH}^-$, $(\text{CH}_3)_2\text{Sn}(\text{cys})_2\text{H}^-$, $(\text{CH}_3)_2\text{Sn}(\text{cys})_2(2^-)$. The stability and the formation percentages, for the mononuclear mixed species in particular, are very high, in a wide pH range. Thermodynamic parameters indicate that the enthalpy values are exothermic and the enthalpic contribution to the stability is higher than entropic one. Individual UV spectra of cys and dimethyltin(IV)-cys species were calculated. Spectroscopic results of UV and ^1H NMR investigations fully confirm the speciation model. The structures calculated from NMR investigations show that all the species have an eq- $(\text{CH}_3)_2\text{-tbp}$ structure.

Chakraborty I. and Moulik S. P. (2005) Physicochemical studies on microemulsions 9. Conductance percolation of AOT-derived W/O microemulsion with aliphatic and aromatic hydrocarbon oils. *J Colloid Interface Sci* **289**, 530-541.

Abstract: Both volume- and temperature-induced percolation of conductance of w/o microemulsions formed with AOT in cyclic aliphatic and aromatic oils (cyclohexane, cyclohexanone, toluene, and xylenes), and volume percolation of water/AOT/oil systems using linear aliphatic hydrocarbons (n-hexane, n-heptane, n-octane, i-octane, and n-decane) have been studied. The effect of additives, viz. sodium cholate (NaC), sodium deoxycholate (NaDC), cholesterol, n-butanol, and t-butanol, toluene, and xylenes (o, m, and p) on the temperature-induced percolating processes using the oils cyclohexane and cyclohexanone has been examined. The percolation results have been analyzed in the light of scaling equation, and the energy of activation of the ion-transport phenomenon has been evaluated for both pre- and postpercolation stages. From the percolation data, the diameter of the microdispersed water droplets, their population, and surface area have been estimated. The enthalpy of dispersion of water in AOT/oil medium has been determined from isothermal titration calorimetric (ITC) measurements.

Chekmeneva E., Prohens R., az-Cruz J. M., Arino C. and Esteban M. (2008) Competitive binding of Cd and Zn with the phytochelatin (gamma-Glu-Cys)4-Gly: comparative study by mass spectrometry, voltammetry-multivariate curve resolution, and isothermal titration calorimetry. *Environ. Sci Technol.* **42**, 2860-2866.

Abstract: The competitive binding of Cd²⁺ and Zn²⁺ by the phytochelatin (gamma-Glu-Cys)4-Gly (PC4) has been examined using several techniques. Electrospray ionization mass spectrometry is used to determine the stoichiometries of the complexes, while voltammetric data analyzed by multivariate curve resolution with alternating least squares allows one to not only trace the displacement induced by Cd²⁺ or Zn²⁺ in the binding of Zn²⁺ or Cd²⁺, respectively, by PC4, but also to obtain a complete overview of the processes involved. Isothermal titration calorimetry is used to determine the related binding and thermodynamic parameters. Results obtained via these different techniques are compared and discussed below. The formation of ternary CdZn(PC4) and Cd2Zn(PC4) complexes was observed

Chekmeneva E., Prohens R., az-Cruz J. M., Arino C. and Esteban M. (2008) Thermodynamics of Cd²⁺ and Zn²⁺ binding by the phytochelatin (gamma-Glu-Cys)4-Gly and its precursor glutathione. *Anal Biochem* **375**, 82-89.

Abstract: Isothermal titration calorimetry (ITC) was used to study the binding of Cd(2+) and Zn(2+) by glutathione (GSH) and phytochelatin (PC(n)), the metal sequestering compounds in plants and algae. The results are compared with those obtained by differential pulse polarography (DPP) assisted by multivariate curve resolution with alternating least squares (MCR-ALS) and by electrospray ionization mass spectrometry (ESI-MS). ITC allows one to determine (i) the stoichiometries of the different complexes (and confirms those found by DPP/MCR-ALS and ESI-MS) and (ii) their binding and thermodynamic parameters. For Cd-PC(4), the sequential binding sites model with two identical sites yields the best fitting of ITC curves and confirms the presence of CdPC(4) and Cd(2)PC(4) complexes. For Zn-PC(4), exothermic formation of ZnPC(4) is reported. Conditional stability and formation constants for Cd-GSH and Zn-GSH are determined from the fitting of the proper model to experimental ITC curves. The effect of different buffers in the complexation processes shows the key role of the choice of the buffer in calorimetric study

Chen C. S., Wu S. H., Wu Y. Y., Fang J. M. and Wu T. H. (2007) Properties of astaxanthin/Ca²⁺ complex formation in the deceleration of cis/trans isomerization. *Org. Lett* **9**, 2985-2988.

Abstract: Deceleration of the regioselective cis/trans isomerization of all-trans-astaxanthin (ASTX) in the presence of Ca²⁺ was shown by HPLC analysis. The NMR and ITC analyses provided evidence for complexation of ASTX with Ca²⁺ in 1:2 stoichiometry via chelation at both carbonyl and hydroxyl groups. The rotation across torsion omega₆ (C5-C6-C7-C8) upon complexation is consistent with the NOE between 7-H and 5-CH₃. This study supports the inhibitory effect of ASTX on calcium-induced turbidity of lens crystallins.

Chen W. Y., Chen C. S., and Lin F. Y. (2001) Molecular recognition in imprinted polymers: thermodynamic investigation of analyte binding using microcalorimetry. *J Chromatogr A* **923**, 1-6.

Abstract: This study aimed at elucidating the interaction mechanism between an imprinted polymer and its template in aqueous environment with thermodynamic aspects. The herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) was chosen as a model template to imprint a co-polymer of 4-vinylpyridine (4-VP) and ethyleneglycol dimethacrylate. Equilibrium binding isotherm analysis and isothermal titration microcalorimetry were used to quantify the contribution of enthalpy and entropy to the binding process, identify the nature of the interactions involved and confirm the existence of binding pockets with shape-complementarity to the template. For the binding process of 2,4-D to the imprinted polymer, we postulate three subprocesses: (1) dehydration of the binding pocket and of the 2,4-D, (2) adsorption of 2,4-D, and (3) rearrangement of the water molecules from the dehydration process. We found that binding in aqueous environment was due to the cumulative effect of pi-stacking and electrostatic interactions between the template and the functional monomers. At pH<6, entropy is the dominating driving force, while at pH>6 where the highest difference in binding between the imprinted and a non-imprinted reference polymer was observed, the enthalpy change accounts for most of the binding free energy. The developed microcalorimetric method sheds light on the binding mechanism of analyte molecules with imprinted polymers, in particular if the polymers are used in aqueous solvents.

Christensen T., Gooden D. M., Kung J. E., and Toone E. J. (2003) Additivity and the physical basis of multivalency effects: a thermodynamic investigation of the calcium EDTA interaction. *J Am Chem Soc* **125**, 7357-7366.

Abstract: To better understand the origin of multivalency effects in ligand binding, the binding of a series of mono-, bi-, tri- and tetravalent carboxylate ligands to Ca(II) was examined by isothermal titration calorimetry (ITC). The data are inconsistent with an entropic origin of enhanced affinity, but rather show that at least in this instance the multivalency effect is enthalpic in origin. Analysis of binding data using the Jencks model shows the addition of incremental carboxylate "ligands" produces an unfavorable interaction entropy that is more than offset by a strongly favorable interaction enthalpy. The most likely source of this interaction enthalpy is the relief of repulsive Coulombic interactions in the unbound state. The conformational entropy penalty arising from the restriction of flexible dihedrals is negligible, within experimental error. On the other hand, an enthalpic contribution from linker restriction contributes strongly to the overall thermodynamics of ligand binding. Together, these data suggest that enthalpic effects dominate ligand binding, and design strategies should seek to optimize these interactions. The incorporation of unfavorable interactions in the unbound ligand that are relieved during binding provides an important mechanism by which to enhance ligand affinities.

Corbellini F., Knechtel R. M., Grootenhuys P. D., Crego-Calama M., and Reinhoudt D. N. (2005) Water-Soluble Molecular Capsules: Self-Assembly and Binding Properties. *Chemistry* **11**, 298-307.

Abstract: The self-assembly and characterization of water-soluble calix[4]arene-based molecular capsules (12) is reported. The assemblies are the result of ionic interactions between negatively charged calix[4]arenes 1 a and 1 b, functionalized at the upper rim with amino acid moieties, and a positively charged tetraamidiniumcalix[4]arene 2. The formation of the molecular capsules is studied by (1)H NMR spectroscopy, ESI mass spectrometry (ESI-MS), and isothermal titration calorimetry (ITC). A molecular docking protocol was used to identify potential guest molecules for the self-assembled capsule 1 a2. Experimental guest encapsulation studies indicate that capsule 1 a2 is an effective host for both charged (N-methylquinuclidinium cation) and neutral molecules (6-amino-2-methylquinoline) in water.

Corbellini F., Fiammengo R., Timmerman P., Crego-Calama M., Versluis K., Heck A. J., Luyten I., and Reinhoudt D. N. (2002) Guest encapsulation and self-assembly of molecular capsules in polar solvents via multiple ionic interactions. *J Am Chem Soc* **124**, 6569-6575.

Abstract: Herein we report the formation and characterization of a novel type of capsules resulting from the self-association between oppositely charged complementary building blocks in MeOH/H₂O. The assembly is based on the interaction between tetraamidinium calix[4]arenes 1a-d and tetrasulfonato calix[4]arene 2. Evidence for the formation of the expected 1:1 assemblies is provided by proton NMR, ESI-MS, and ITC. The association process is fast on the NMR time scale and strongly entropy driven, with association constants in the range of 10(6) M⁻¹. The system 1a.2 shows binding affinity toward acetylcholine, tetramethylammonium, and N-methylquinuclidinium cations.

Corbett P. T., Sanders J. K. and Otto S. (2008) Exploring the relation between amplification and binding in dynamic combinatorial libraries of macrocyclic synthetic receptors in water. *Chemistry* **14**, 2153-2166.

Abstract: Herein we describe an extensive study of the response of a set of closely related dynamic combinatorial libraries (DCLs) of macrocyclic receptors to the introduction of a focused range of guest molecules. We have determined the amplification of two sets of diastereomeric receptors induced by a series of neutral and cationic guests, including biologically relevant compounds such as acetylcholine and morphine. The host-guest binding affinities were investigated using isothermal titration calorimetry. The resulting dataset enabled a detailed analysis of the relationship between the amplification of selected receptors and host-guest Gibbs binding energies, giving insight into the factors affecting the design, simulation and interpretation of DCL experiments. In particular, two questions were addressed: Is amplification by a given guest selective for the best receptor? And does the best guest induce the largest amplification of a given receptor? Our experimental results and computer simulations showed that the relative levels of amplification of hosts by a guest are well-correlated with their relative affinities, and simulations have confirmed previous observations that amplification can be selective for the best receptor when only modest amounts of guest are used. In contrast, the correlation between guest binding and the extent of amplification of a given receptor across a wide range of guests tends to be poorer, because every guest has its own unique set of affinities for competing receptors in the DCL. This implies that the results

of screening a DCL for selective receptors by comparing the response of the mixture to two different guests should be interpreted with caution. DCLs are complex mixtures in which all compounds are connected through a set of equilibria. Obtaining quantitative information about all host-guest binding constants from such systems will require the explicit and simultaneous consideration of all of the main equilibria within a DCL

Conato C., Kozłowski H., Swiatek-Kozłowska J., Mlynarz P., Remelli M., and Silvestri S. (2004) Formation equilibria of nickel complexes with glycyl-histidyl-lysine and two synthetic analogues. *J Inorg Biochem* **98**, 153-160.

Abstract: Complex-formation equilibria between the Ni(II) ion and the natural tripeptide glycyl-L-histidyl-L-lysine have been investigated. Two synthetic analogues, where the histidine residue has been substituted with L-4,5,6,7-tetrahydro-1H-imidazo[4,5-c]pyridine-6-carboxylic acid (L-Spinacine) and L-1,2,3,4-tetrahydro-isoquinolin-3-carboxylic acid (Tic), respectively, have been considered, as well. Different experimental techniques have been employed: potentiometry, calorimetry, visible spectrophotometry and CD spectroscopy. Structural hypotheses on the main complex species are suggested. Evidences on the formation of tetrameric species with the first ligand are shown. No involvement of the side-chain amino group of lysine residue in metal ion coordination was found.

Corbellini F., Knechtel R. M., Grootenhuys P. D., Crego-Calama M., and Reinhoudt D. N. (2004) Water-Soluble Molecular Capsules: Self-Assembly and Binding Properties. *Chemistry* **11**, 298-307.

Abstract: The self-assembly and characterization of water-soluble calix[4]arene-based molecular capsules (12) is reported. The assemblies are the result of ionic interactions between negatively charged calix[4]arenes 1 a and 1 b, functionalized at the upper rim with amino acid moieties, and a positively charged tetraamidiniumcalix[4]arene 2. The formation of the molecular capsules is studied by (1)H NMR spectroscopy, ESI mass spectrometry (ESI-MS), and isothermal titration calorimetry (ITC). A molecular docking protocol was used to identify potential guest molecules for the self-assembled capsule 1 a2. Experimental guest encapsulation studies indicate that capsule 1 a2 is an effective host for both charged (N-methylquinuclidinium cation) and neutral molecules (6-amino-2-methylquinoline) in water.

Corbett P. T., Tong L. H., Sanders J. K., and Otto S. (2005) Diastereoselective amplification of an induced-fit receptor from a dynamic combinatorial library. *J Am Chem Soc* **127**, 8902-8903.

Abstract: A high-affinity, induced-fit receptor for NMe(4)I was discovered using dynamic combinatorial chemistry. The addition of the guest to a dynamic combinatorial library made using a racemic mixture of chiral building blocks caused the strong and highly diastereoselective amplification of the receptor at the expense of other library components. The receptor and its mode of binding were characterized by NMR, ITC, and re-equilibration experiments, from which it was deduced that the receptor probably forms a folded four-stave barrel shape on binding of the guest.

Couderc-Azouani S., Sidhu J., Georgiou T. K., Charalambous D. C., Vamvakaki M., Patrickios C. S., Bloor D. M., Penfold J., Holzwarth J. F., and Wyn-Jones E. (2004) Binding of sodium dodecyl sulfate to linear and star homopolymers of the nonionic poly(methoxyhexa(ethylene glycol) methacrylate) and the polycation poly(2-(dimethylamino)ethyl methacrylate): electromotive force, isothermal titration calorimetry, surface tension, and small-angle neutron scattering measurements. *Langmuir* **20**, 6458-6469.

Abstract: We investigated the binding of sodium dodecyl sulfate (SDS) to various linear and star polymers of the nonionic methoxyhexa(ethylene glycol) methacrylate (PMHEGMA) and the ionic 2-(dimethylamino)ethyl methacrylate (PDMAEMA), the latter being a polycation at low pH. The dodecyl sulfate ion selective electrode (EMF), isothermal titration calorimetry (ITC), and surface tension (ST) were applied to gain detailed information about interactions. In all cases there is evidence of significant binding of SDS over an extensive SDS concentration range spanning from ca. 10^{-6} to 0.1 mol dm^{-3} . At pH 3, the polymer PDMAEMA is a strong polycation and here the binding is dominated by electrostatic 1:1 charge neutralization with the anionic surfactant. At their natural pH of 8.6, PMHEGMA and PDMAEMA polymers are essentially nonionic and bind SDS in the form of polymer-bound aggregates in the concentration range of ca. 1×10^{-3} to $3 \times 10^{-2} \text{ mol dm}^{-3}$. All the polymers also bind SDS to a lesser extent at concentrations below $1 \times 10^{-3} \text{ mol dm}^{-3}$ reaching as low as $10^{-7} \text{ mol dm}^{-3}$. This low concentration binding process involves the polymer and nonassociated SDS monomers. As far as we are aware, this is the first example that such a low concentration noncooperative binding process could be observed in SDS/neutral

polymer systems by EMF and ST. We also showed that the nonionic surfactant hexa(ethylene glycol) mono-n-dodecyl ether (C12EO6) and the cationic cetyltrimethylammonium bromide (C16TAB) interact with star PDMAEMA. We believe that the interaction of C12EO6 and CTAB is of similar noncooperative type as the first SDS binding process in the range from ca. 10^{-5} to 0.3×10^{-3} mol dm⁻³. At the high concentration binding limit C_{sat} of SDS, the above polymers become fully saturated with bound SDS micelles. We applied small angle neutron scattering (SANS) to determine the structure and aggregation numbers of the star polymer/bound SDS micelles and calculated the stoichiometry of such supramolecular complexes. The SANS data on PDMAEMA star polymers in the presence of C12EO6 showed only a limited monomer binding in contrast to linear PDMAEMA, which showed monomer C12EO6 binding at low concentrations but micellar aggregates at 6×10^{-3} mol dm⁻³.

Cuypers R., Burghoff B., Marcelis A. T., Sudholter E. J., de Haan A. B. and Zuilhof H. (2008) Complexation of phenols and thiophenol by phosphine oxides and phosphates. Extraction, isothermal titration calorimetry, and ab initio calculations. *J Phys. Chem A* **112**, 11714-11723.

Abstract: To develop a new solvent-impregnated resin system for the removal of phenols from water the complex formation of triisobutylphosphine sulfide (TIBPS), tributylphosphate (TBP), and tri-n-octylphosphine oxide (TOPO) with a series of phenols (phenol, thiophenol, 3-chlorophenol, 3,5-dichlorophenol, 4-cyanophenol, and pentachlorophenol) was studied. The investigation of complex formation between the extractants and the phenols in the solvent toluene was carried out using liquid-liquid extraction, isothermal titration calorimetry (ITC), and quantum chemical modeling (B3LYP/6-311+G(d,p)//B3LYP/6-311G(d,p) and MP2/6-311++G(2d,2p)//B3LYP/6-311G(d,p)). The equilibrium constant (binding affinity, K_{chem}), enthalpy of complex formation (ΔH), and stoichiometry (N) were directly measured with ITC, and the entropy of complexation (ΔS) was derived from these results. A first screening of K_{chem} toward phenol revealed a very high binding affinity for TOPO, and very low binding affinities for the other extractants. Modeling results showed that although 1:1 complexes were formed, the TIBPS and TBP do not form strong hydrogen bonds. Therefore, in the remainder of the research only TOPO was considered. K_{chem} of TOPO for the phenols in toluene increased from 1,000 to 10,000 M⁻¹ in the order phenol < pentachlorophenol < 3-chlorophenol < 4-cyanophenol approximately 3,5-dichlorophenol (in line with their pK_a values, except for pentachlorophenol) in the absence of water, while the stoichiometric ratio remained 1:1. In water-saturated toluene, the binding affinities are lower due to co-complexation of water with the active site of the extractant. The increase in binding affinity for TOPO in the phenol series was confirmed by a detailed ab initio study, in which ΔH was calculated to range from -10.7 kcal/mol for phenol to -13.4 kcal/mol for 4-cyanophenol. Pentachlorophenol was found to behave quite differently, showing a ΔH value of -10.5 kcal/mol. In addition, these calculations confirm the formation of 1:1 H-bonded complexes

Danil de Namor A. F., Abbas I., and Hammud H. H. (2006) Anion complexation by calix[3]thieno[1]pyrrole: the medium effect. *J Phys Chem B Condens Matter Mater Surf Interfaces Biophys* **110**, 2142-2149.

Abstract: The interaction of calix[3]thieno[1]pyrrole, **1**, and halide and dihydrogen phosphate anions in a variety of solvents (acetonitrile, propylene carbonate, N,N-dimethylformamide, and dimethyl sulfoxide) has been investigated through ¹H NMR, conductance measurements, and titration calorimetry. ¹H NMR measurements reveal the sites of interaction of the ligand with the anions in CD₃CN while the composition of the complex was determined through conductance measurements. A quantitative assessment of anion-ligand interactions is provided. Thus the thermodynamics of complexation of **1** with halide and dihydrogen phosphate anions in dipolar aprotic media at 298.15 K is reported. These data are interpreted in terms of the thermodynamics of transfer of reactants and product from a reference solvent (acetonitrile) to other solvents. The crucial role played by the solvent on the ability of the ligand to interact with anions and on the composition of the complex is demonstrated.

de Gooijer J. M., Engberts J. B., and Blandamer M. J. (2000) A Titration Microcalorimetric Study of the Effects of Halide Counterions on Vesicle-Forming Aggregation in Aqueous Solution of Branched-Chain Alkylpyridinium Surfactants. *J Colloid Interface Sci* **224**, 4-10.

Abstract: Titration microcalorimetry is used to study the influences of iodide, bromide, and chloride counterions on the aggregation of vesicle-forming 1-methyl-4-(2-pentylheptyl)pyridinium halide surfactants. Formation of vesicles by these surfactants was characterised using transmission electron

microscopy. When the counterion is changed at 303 K through the series iodide, bromide, to chloride, the critical vesicular concentration (cvc) increases and the enthalpy of vesicle formation changes from exo- to endothermic. With increase in temperature to 333 K, vesicle formation becomes strongly exothermic. Increasing the temperature leads to a decrease in enthalpy and entropy of vesicle formation for all three surfactants. However the standard Gibbs energy for vesicle formation is, perhaps surprisingly, largely unaffected by an increase in temperature, as a consequence of a compensating change in both standard entropy and standard enthalpy of vesicle formation. Interestingly, standard isobaric heat capacities of vesicle formation are negative, large in magnitude but not strikingly dependent on the counterion. We conclude that the driving force for vesicle formation can be understood in terms of overlap of the thermally labile hydrophobic hydration shells of the alkyl chains. Copyright 2000 Academic Press.

de la Fuente J. M., Eaton P., Barrientos A. G., Menendez M., and Penades S. (2005) Thermodynamic evidence for Ca²⁺-mediated self-aggregation of Lewis X gold glyconanoparticles. A model for cell adhesion via carbohydrate-carbohydrate interaction. *J Am Chem Soc* **127**, 6192-6197.

Abstract: Thermodynamic evidence for the selective Ca²⁺-mediated self-aggregation via carbohydrate-carbohydrate interactions of gold glyconanoparticles functionalized with the disaccharides lactose (lacto-Au) and maltose (malto-Au), or the biologically relevant trisaccharide Lewis X (Le(X)-Au), was obtained by isothermal titration calorimetry. The aggregation process was also directly visualized by atomic force microscopy. It was shown in the case of the trisaccharide Lewis X that the Ca²⁺-mediated aggregation is a slow process that takes place with a decrease in enthalpy of 160 +/- 30 kcal mol⁻¹, while the heat evolved in the case of lactose and maltose glyconanoparticles was very low and thermal equilibrium was quickly achieved. Measurements in the presence of Mg²⁺ and Na⁺ cations confirm the selectivity for Ca²⁺ of Le(X)-Au glyconanoparticles. The relevance of this result to cell-cell adhesion process mediated by carbohydrate-carbohydrate interactions is discussed.

de Namor A. F. and Zegarra-Fernandez K. (2007) Thermodynamics of ethyl p-tert-butylcalix[5]arene pentanoate and its cation complexes in nonaqueous media. *J Phys. Chem B* **111**, 7321-7330.

Abstract: The solution behavior of ethyl p-tert-butylcalix[5]arene pentanoate, EtCalix(5), in various protic and aprotic solvents has been assessed from the standard Gibbs energies of transfer of this ligand from acetonitrile to other solvents. These data were derived from solubility measurements of EtCalix(5) in different media. It is concluded that in solvents in which metal cation salts are predominant as ionic species in solution (within a low concentration range), the solvation of the ligand will not contribute significantly to the thermodynamics of cation complexation as a result of the medium effect. Various analytical techniques were used to identify the sites of ligand-cation interaction (1H NMR) and the composition (conductance and calorimetric measurements) of the metal-ion complexes in the various solvents. Titration calorimetry (direct and competitive) was used to thermodynamically characterize the cation binding ability of EtCalix(5) and gain quantitative information on the complex stability and the factors controlling it. Given the large bulk of data reported in the literature wrongly placed under the thermodynamic umbrella, particular emphasis is made about the need of identifying the process taking place in solution prior to proceeding with its thermodynamic characterization. The results are compared with those for the ethyl ester derivative of the cyclic tetramer, EtCalix(4). It is concluded that in moving from EtCalix(4) to EtCalix(5), (i) the selectivity of the latter for cations is swallowed toward the larger cations and (ii) although the number of binding sites increases, these are not able to exert the efficient control upon the ligand-cation binding ability as that found for the tetramer ester and these cations in these solvents.

de Namor A. F. and Abbas I. (2007) Sulfur-containing hetero-calix[4]pyrroles as mercury(II) cation-selective receptors: thermodynamic aspects. *J Phys. Chem B* **111**, 5803-5810.

Abstract: Two sulfur-containing hybrid calix[4]pyrrole derivatives (III and IV) have been synthesized and fully characterized. Several analytical techniques (1H NMR, conductance measurements, UV-vis spectrophotometry, titration potentiometry, and titration calorimetry) have been used to assess the interaction between these hybrid calixpyrrole receptors and metal cations in acetonitrile and dimethylsulfoxide. The partition constants of calix[4]pyrrole, I, II, and IV in the acetonitrile-hexane solvent system and the solubilities of the ligands in various solvents at 298.15 K were determined. 1H NMR measurements reveal the sites of interaction of calixpyrrole ligands with metal cations in CD₃CN. Conductance and UV-vis spectrophotometric measurements were performed to establish the composition of mercury(II) calixpyrrole complexes in acetonitrile at 298.15 K. Titration calorimetry was used to

quantitatively assess Hg(II)-calixpyrrole interactions. Thus the thermodynamics of complexation of calixpyrrole ligands with the mercury(II) cation in acetonitrile at 298.15 K are reported. Potentiometric titrations were also used to establish the stepwise stability constants for the complexation of calix[3]thieno[1]pyrrole with the Hg(II) cation in acetonitrile at 298.15 K. The results show that replacement of one or more pyrrole units by thiophene rings in calix[4]pyrrole has tuned significantly the discrimination ability of these ligands between anions and enables the produced hybrid calixpyrroles to bind selectively with Hg(II) in acetonitrile. No interaction was observed between these ligands and other metal cations in acetonitrile.

De S. and Robinson D. (2003) Polymer relationships during preparation of chitosan-alginate and poly-L-lysine-alginate nanospheres. *J Control Release* **89**, 101-112.

Abstract: The preparation of chitosan-alginate nanospheres is described and their properties compared to the poly-L-lysine-alginate system. The mass ratio range of sodium alginate:CaCl₂:cationic polymer (poly-L-lysine [PLL] or chitosan) to prepare nanospheres was 100:17:10. This mass ratio ensured that the calcium alginate was maintained in the pre-gel phase and sufficient cationic polymer was present to form nanospheres. At low cationic polymer concentrations, nanospheres were not formed, whereas microspheres were formed at higher concentrations. The release of entrapped methylene blue from the nanospheres was directly proportional ($R^2=0.98$) to the sodium chloride concentration in the dissolution medium. The sodium ions more efficiently displace PLL compared to chitosan; hence, the mass of drug released from the chitosan-alginate nanospheres is slow for equivalent sodium ion concentration. Isothermal titration calorimetry studies determined that the primary binding affinity between calcium and alginate was 1.33×10^6 /mole and entropically driven, whereas, the second binding affinity was weaker (1.03×10^4 /mole) and driven by both enthalpy and entropy. This binding was competitively inhibited by sodium ions. Similarly, the binding of PLL to calcium alginate pre-gel was electrostatic and competitively inhibited by sodium, although, the thermodynamic parameters for this interaction could not be determined.

Debroy P., Banerjee M., Prasad M., Moulik S. P., and Roy S. (2005) Binding of amino acids into a novel multiresponsive ferrocene receptor having an ene backbone. *Org Lett* **7**, 403-406.

Abstract: [reaction: see text] Receptor 1 featuring two open arms, multipoint binding sites, and unsaturated linkers on a ferrocene platform shows strong 1:1 binding to unprotected alpha-amino acids (UV-vis, fluorescence, CV, ITC, NMR, and ESI-MS). NMR and ESI-MS studies suggest an encapsulative binding mode involving the alpha,beta-unsaturated carbonyl residue (site for -NH₃⁽⁺⁾, interaction A) and the terminal -OH groups (site for -COO⁽⁻⁾, interaction B).

De Stefano C., Gianguzza A., Piazzese D., and Sammartano S. (2005) Modelling of proton and metal exchange in the alginate biopolymer. *Anal Bioanal Chem* **383**, 587-596.

Abstract: Acid-base behaviour of a commercial sodium alginate extracted from brown seaweed (*Macrocystis pyrifera*) has been investigated at different ionic strengths ($0.1 \leq I/\text{mol l}^{-1} \leq 1.0$) and in different supporting electrolytes (Et₄N⁺I⁻, NaCl, KCl, LiCl, NaCl+MgCl₂), with the aim of examining the influence of ionic medium on the proton-binding capacity and of quantifying the strength of interaction with light metal ions in the perspective of speciation studies in natural aqueous systems. Potentiometric ([H⁺]-glass electrode) and titration calorimetric data were expressed as a function of the dissociation degree (α) using different models (Henderson-Hasselbalch modified, Hogfeldt three parameters and linear equations). The dependence on ionic strength of the protonation constants was taken into account by a modified specific interaction theory model. Differences among different media were explained in terms of the interaction between polyanion and metal cations of the supporting electrolytes. Quantitative information on the proton-binding capacity, together with the stabilities of different species formed, is reported. Protonation thermodynamic parameters, at $\alpha=0.5$, are $\log K_H=3.686 \pm 0.005$, $\Delta G^0=-21.04 \pm 0.03$ kJ mol⁽⁻¹⁾, $\Delta H^0=4.8 \pm 0.2$ kJ mol⁽⁻¹⁾ and $T\Delta S^0=35.7 \pm 0.3$ kJ mol⁽⁻¹⁾, at infinite dilution. Protonation enthalpies indicate that the main contribution to proton binding arises from the entropy term. A strict correlation between ΔG and $T\Delta S$ was found, $T\Delta S=-9.5-1.73 \Delta G$. Results are reported in light of building up a chemical complexation model of general validity to explain the binding ability of naturally occurring polycarboxylate polymers and biopolymers. Speciation profiles of alginate in the presence of sodium and magnesium ions, naturally occurring cations in natural waters, are also reported.

De Stefano C., Gianguzza A., Piazzese D., Porcino N., and Sammartano S. (2006) Sequestration of biogenic amines by alginic and fulvic acids. *Biophys Chem*.

Abstract: The interaction of natural (alginic and fulvic acids) and synthetic (polyacrylic acid 2.0 kDa) polyelectrolytes with some protonated polyamines [diamines: ethylenediamine, 1,4-diaminobutane (or putrescine), 1,5-diaminopentane (or cadaverine); triamines: N-(3-aminopropyl)-1,4-diaminobutane (or spermidine), diethylenetriamine; tetramine: N,N'-bis(3-aminopropyl)-1,4-diaminobutane (or spermine); pentamine: tetraethylene-pentamine; hexamine: pentaethylenehexamine] was studied at T=25 degrees C by potentiometry and calorimetry. Measurements were performed without supporting electrolyte, in order to avoid interference, and results were reported at I=0 mol L⁻¹(1). For all the systems, the formation of (am)L(2)H(i) species was found (am=amine; L=polyelectrolyte; i=1...4, depending on the amine considered). The stability of polyanion-polyammonium cation complexes is always significant, and for high-charged polycations, we observe a stability comparable to that of strong metal complexes. For example, by considering the formation reaction (am)H(i)+2L=(am)L(2)H(i) we found log K(i)=6.0, 6.5 and 10.8 for i=1, 2 and 3, respectively, in the system alginate-spermidine. Low and positive formation DeltaH degrees values indicate that the main contribution to the stability is entropic in nature. The sequestering ability of polyelectrolytes toward amines was modelled by a sigmoid Boltzman type equation. Some empirical relationships between stability, charges and DeltaG degrees and TDeltaS degrees are reported. Mean values per salt bridge of formation thermodynamic parameters (DeltaX degrees (n)) are DeltaG degrees (n)=-5.8+/-0.4, DeltaH degrees (n)=0.7+/-0.5 and TDeltaS degrees (n)=6.5+/-0.5kJmol⁻¹(1) for all the systems studied in this work.

Devi P. G., Pal S., Banerjee R., and Dasgupta D. (2007) Association of antitumor antibiotics, mithramycin and chromomycin, with Zn(II). *J Inorg Biochem* **101**, 127-137.

Abstract: Chromomycin A(3) (CHR) and mithramycin (MTR), members of the aureolic acid anticancer antibiotics, supposedly act by inhibiting transcription via reversible association with DNA. The complex(es) with bivalent cation such as Mg(2+) and Zn(2+) is (are) the DNA-binding ligand(s). In this paper, we report a detailed study of the association of these antibiotics with the biologically important bivalent cation, Zn(2+), because the zinc chelating ability of the antibiotics has therapeutic potential in the treatment of diseases relating to zinc dyshomeostasis. Spectroscopic methods such as absorbance, fluorescence, and circular dichroism and NMR spectroscopy have been used to characterize and understand the mechanism of complex formation. Our data show that both antibiotics form a single complex with Zn(2+) in the mole ratio of 2:1 in terms of antibiotic:Zn(2+) with an apparent binding affinity in the micro molar range. The complex has been characterized as [(D)(2)Zn(2+)] (where 'D' stands for the antibiotic). The kinetics study of the complex formation between the antibiotic(s) and Zn(2+) suggests the following mechanism: Isothermal calorimetric titration has shown that the association is entropy driven, implying the role of water molecules in complex formation. (1)H NMR spectroscopic data of the complex favor a tetrahedral arrangement around the Zn(2+) ion with the antibiotic acting as a bidentate ligand.

Di B. P., Zanonato P. L., Melchior A., Portanova R., Tolazzi M., Choppin G. R. and Wang Z. (2008) Thermodynamic and spectroscopic studies of lanthanides(III) complexation with polyamines in dimethyl sulfoxide. *Inorg Chem* **47**, 1155-1164.

Abstract: The thermodynamic parameters of complexation of Ln(III) cations with tris(2-aminoethyl)amine (tren) and tetraethylenepentamine (tetren) were determined in dimethyl sulfoxide (DMSO) by potentiometry and calorimetry. The excitation and emission spectra and luminescence decay constants of Eu3+ and Tb3+ complexed by tren and tetren, as well as those of the same lanthanides(III) complexed with diethylenetriamine (dien) and triethylenetetramine (trien), were also obtained in the same solvent. The combination of thermodynamic and spectroscopic data showed that, in the 1:1 complexes, all nitrogens of the ligands are bound to the lanthanides except in the case of tren, in which the pendant N is bound. For the larger ligands (trien, tren, tetren) in the higher complexes (ML2), there was less complete binding by available donors, presumably due to steric crowding. FT-IR studies were carried out in an acetonitrile/DMSO mixture, suitably chosen to follow the changes in the primary solvation sphere of lanthanide(III) due to complexation of amine groups. Results show that the mean number of molecules of DMSO removed from the inner coordination sphere of lanthanides(III) is lower than ligand denticity and that the coordination number of the metal ions increases with amine complexation from approximately 8 to approximately 10. Independently of the number and structure of the amines, linear trends, similar for all lanthanides, were obtained by plotting the values of DeltaG degrees, DeltaH degrees, and TDeltaS degrees

degrees for the complexation of ethylenediamine (en), dien, trien, tren, and tetren as a function of the number of amine metal-coordinated nitrogen atoms. The main factors on which the thermodynamic functions of lanthanide(III) complexation reactions in DMSO depend are discussed

Donati I., Cesaro A., and Paoletti S. (2006) Specific interactions versus counterion condensation. 1. Nongelling ions/polyuronate systems. *Biomacromolecules* **7**, 281-287.

Abstract: The characteristics of the interaction between nongelling divalent cations (typically $Mg(2+)$) and polyuronates have been explored by means of isothermal calorimetry. In particular, three polyuronates mimicking separately guluronan (polyguluronate, polyG), mannuronan (polymannuronate, polyM), and polyalternating (polyMG), the three block-components of natural alginate samples, have been treated with divalent ions, and the enthalpy of mixing was determined for different values of the $[M(2+)]/[Polym](rep.unit)$ ratio. Despite the absence of a site-specific chemical bonding between the two, as confirmed by circular dichroism spectroscopy, a substantial deviation of the experimental enthalpy of mixing from the theoretical behavior, as predicted by the classical counterion condensation (CC) theory, was observed. Such deviation has been interpreted in terms of a "generic" nonbonding affinity of the condensed divalent counterion for the polyelectrolytes. The mathematical formalism of the CC theory was extended to include a contribution to the (reduced) free energy and enthalpy arising from the counterion affinity, $g(aff,0)$ and $h(aff,0)$, and allowed the parametrical calculation of the fraction of divalent counterions condensed as function of the reduced thermodynamic quantity $g(aff,0)$. A best fit procedure of the experimental enthalpy of mixing allowed the $g(aff,0)$ and $h(aff,0)$ pair to be estimated for each of the different polyuronates considered, revealing differences in the three samples. In qualitative terms, the results obtained seem to suggest a notable contribution of the desolvation process (i.e., release of structured water as a consequence of the interaction between the divalent counterion and the uronate group) to the enthalpy of affinity for polyM which is counterbalanced and overcome by an ion pairing term (i.e., partial formation of ion-ion and/or ion-dipole bonds) for polyG and polyMG, respectively.

Ehtezazi T., Govender T., and Stolnik S. (2000) Hydrogen bonding and electrostatic interaction contributions to the interaction of a cationic drug with polyaspartic acid. *Pharm Res* **17**, 871-878.

Abstract: PURPOSE: To determine the mechanism and identify forces of interaction between polyaspartic acid and diminazene (a model drug). Such knowledge is essential for the design of polymeric drug delivery systems that are based on molecular self-assembly into complexes or micellar type systems. METHODS: Complex formation was studied by isothermal titration microcalorimetry and the McGhee von Hippel model was applied to obtain K_{obs} , ΔH_{obs} , and n_{obs} . The calorimetry data were compared with both an optical density study and the amount of free/complexed drug. RESULTS: The diminazene-polyaspartic acid interaction is enthalpically driven, whereby one diminazene molecule interacts with two monomers of polyaspartic acid. The dependence of K_{obs} on salt concentration reveals a contribution of electrostatic interactions. However, applying Manning's counter ion condensation theory shows that the major driving force for the complex formation is hydrogen bonding, with interfacial water molecules remaining buried within the complex. The modelling of the pH dependence of K_{obs} and ΔH_{obs} demonstrates that the ionization of carboxylic groups of polyaspartic acid is a prerequisite for the interaction. CONCLUSIONS: Complex formation between diminazene and polyaspartic acid is driven by both electrostatic interactions and hydrogen bonding, with the latter being the dominating force. Although electrostatic interactions are not the major driving force, ionization of the drug and polymer is essential for complex formation.

Fang Y., Al-Assaf S., Phillips G. O., Nishinari K., Funami T., Williams P. A. and Li L. (2007) Multiple steps and critical behaviors of the binding of calcium to alginate. *J Phys. Chem B* **111**, 2456-2462.

Abstract: Previous research on the binding and gelation of calcium/alginate in aqueous solution were mostly conducted in the (semi-)concentrated regime, and it did not provide details of the binding process and the formation of egg-box junctions. In the present investigation, the binding of calcium to alginate, of low and high molecular weight and different guluronate/mannuronate ratios, was investigated in dilute solutions using isothermal titration calorimetry (ITC), Ca^{2+} -selective potentiometry, and viscometry techniques. The results reveal three distinct and successive steps in the binding of calcium to alginate with increased concentration of Ca ions. They were assigned to (i) interaction of Ca^{2+} with a single guluronate unit forming monocomplexes; (ii) propagation and formation of egg-box dimers via pairing of these monocomplexes; and (iii) lateral association of the egg-box dimers, generating multimers. The third step has different association modes depending on the molecular weight of alginate. The boundaries between

these steps are reasonably critical, and they closely correlate with the Ca/gulonate stoichiometry expected for egg-box dimers and multimers with 2/1 helical chains. The formation of egg-box dimers and their subsequent association are thermodynamically equivalent processes and can be fitted by a model of independent binding sites. The binding of Ca to alginates of different guluronate contents is controlled by a balance between enthalpy and entropy.

Fang Y., Al-Assaf S., Sakata M., Phillips G. O., Schultz M. and Monnier V. (2007) Origin and thermodynamic properties of the instability of synthetic azo colorants in gum arabic solutions. *J Agric. Food Chem* **55**, 9274-9282.

Abstract: The instability of some industrially important synthetic azo colorants, including sunset yellow, azorubine, and allura red, toward gum arabic in aqueous solution has been a long-standing problem for the beverage and confectionery industries. Precipitation of these colorants causes the deterioration of product appearance and properties. This work examines the origin and nature of the problem by analysis of the precipitate and thermodynamic studies of gum arabic-colorant interactions using isothermal titration calorimetry (ITC). The presence of divalent alkaline earth metals in gum arabic samples, that is, calcium and magnesium, is shown to be responsible for the precipitation of the azo colorants. There is no direct interaction between gum arabic and the colorant molecules, and the precipitate is formed likely due to the mediation/bridging by the divalent cations. The thermodynamic knowledge gained from the ITC studies, for example, binding affinity, stoichiometry, and enthalpy, enables interpretation of many industrial observations.

Fanghanel J., Wawra S., Lucke C., Wildemann D., and Fischer G. (2006) Isothermal calorimetry as a tool to investigate slow conformational changes in proteins and peptides. *Anal Chem* **78**, 4517-4523.

Abstract: A new calorimetric method has been developed to follow the time course of slow conformational changes during the refolding of denatured proteins. The method is based on the ability of isothermal titration calorimeters (ITC) to detect small amounts of heat continuously over a minute to an hour time range without being disturbed by baseline drift. We benchmarked the method on the basis of the slow kinetic phases resulting from prolyl cis/trans isomerization of oligopeptides. Using this method, the simultaneous investigation of the kinetics and thermodynamics of slow phases in the refolding of GdmCl-denatured RNase A by single jump techniques was performed. Time traces of heat production in the presence of a peptidyl prolyl cis/trans isomerase support the classical model of rate-limiting prolyl trans to cis isomerizations in the folding reactions of RNase A. However, we also observed that, unlike prolyl cis/trans isomerizations in oligopeptides, those found in RNase A refolding are highly exothermic. It appears that coupling between slow prolyl trans to cis isomerization and relocation of remote backbone segments increases the number of contacting sites during formation of the native protein. The results demonstrate that calorimetrically monitored folding kinetics will be of relevance in the detection of otherwise silent folding events.

Ferreira J. M., Marcinko S., Sheardy R., and Fadeev A. Y. (2005) Calorimetric study of the reactions of n-alkylphosphonic acids with metal oxide surfaces. *J Colloid Interface Sci* **286**, 258-262.

Abstract: The reaction enthalpies for the solution-phase self-assembly of n-alkylphosphonic acids on the surfaces of TiO₂ and ZrO₂ have been determined using isothermal titration calorimetry at 298 K. The reaction enthalpies were negative (exothermic) for methyl- and n-octylphosphonic acids and positive (endothermic) for n-octadecylphosphonic acid with both metal oxides. The enthalpy/energy analysis showed that the net enthalpy of the formation of self-assembled monolayers (SAMs) at solid-liquid interface can be presented as follows: $\Delta H_r = -D - (\Delta H_{sol} + \Delta H_{dil}) - (ES - ESAM)$, where D is the binding energy of the SAM molecules with the solid; ΔH_{sol} and ΔH_{dil} are the enthalpies of dissolution and dilution; ES and ESAM are the surface energies of bare solid and SAM, respectively. This equation predicted an increase (and the sign change) of the reaction enthalpy as the alkyl group in n-alkylphosphonic acid increased, which explained the experimental data. Using this equation, the binding energy (D) in the SAMs of n-octyl- and n-octadecylphosphonic acids were estimated: 55 +/- 5 kJ/mol (for ZrO₂) and 58 +/- 7 kJ/mol (for TiO₂).

Fiammengo R., Crego-Calama M., Timmerman P., and Reinhoudt D. N. (2003) Recognition of caffeine in aqueous solutions. *Chemistry* **9**, 784-792.

Abstract: Binding of caffeine in aqueous solutions has been achieved for the first time by using water-

soluble, tetracationic peptide-porphyrin conjugates Zn-1 as the receptor molecules. The association constant for caffeine with receptor Zn-1 is in some cases as high as 6000 M^{-1} , only 5-6 times lower than the highest binding constant reported for an artificial caffeine receptor in low polarity aprotic solvents. The binding mechanism has been studied by a combination of experimental techniques such as UV-visible and NMR spectroscopy and microcalorimetry. Recognition of caffeine involves both stacking with the porphyrin ring and metal coordination. Subtle variations of the receptor structure affect the complexation. Receptors Zn-1 have also been investigated for the recognition of molecules structurally related to caffeine, for example, 1-methylimidazole. Selectivity towards oxopurine derivatives (caffeine and theophylline) have been found.

Fokkens M., Jasper C., Schrader T., Koziol F., Ochsenfeld C., Polkowska J., Lobert M., Kahlert B., and Klärner F. G. (2005) Selective complexation of N-alkylpyridinium salts: binding of NAD⁺ in water. *Chemistry* **11**, 477-494.

Abstract: A new class of receptor molecules is presented that is highly selective for N-alkylpyridinium ions and electron-poor aromatics. Its key feature is the combination of a well-preorganized molecular clip with an electron-rich inner cavity and strategically placed, flanking bis-phosphonate monoester anions. This shape and arrangement of binding sites attracts predominantly flat electron-poor aromatics in water, binds them mainly by pi-cation, pi-pi, CH-pi, and hydrophobic interactions, and leads to their highly efficient desolvation. NAD(+) and NADP, the important cofactors of many redox enzymes, are recognized by the new receptor molecule, which embraces the catalytically active nicotinamide site and the adenine unit. Even nucleosides such as adenosine are likewise drawn into the clip's cavity. Complex formation and structures were examined by one- and two-dimensional NMR spectroscopy, Job plot analyses, and isothermal titration microcalorimetric (ITC) measurements, as well as quantum chemical calculations of (1)H NMR shifts. The new receptor molecule is a promising tool for controlling enzymatic oxidation processes and for DNA chemistry.

Fonseca M. G. and Airoidi C. (2001) Thermodynamics Data of Interaction of Copper Nitrate with Native and Modified Chrysotile Fibers in Aqueous Solution. *J Colloid Interface Sci* **240**, 229-236.

Abstract: The interactions involving chrysotile (CRI0) and propylamine (CRI1), and propylethylenediamine (CRI2) chrysotiles with copper nitrate in aqueous solution were followed through a calorimetric titration technique. The net thermal effects were calculated after subtracting the respective thermal effect of dilution for all systems. The degree of adsorption gave the order $\text{CRI0} < \text{CRI1} < \text{CRI2}$. The mechanism of reaction for copper/chrysotile interaction is due to the ion exchange between the H(+) of the external hydroxyl groups of the inorganic matrix, which is covered by the presence of 0.26 mmol g^{-1} of basic sites on fibers. On the other hand, the interactions on modified chrysotile can be associated to complex formation with the free pendant amine groups. The enthalpy of these processes gave the following values: -4.25 ± 0.27 , 19.47 ± 0.60 , and $-26.55 \pm 0.16 \text{ kJ mol}^{-1}$ for CRI0, CRI1, and CRI2 systems, respectively. The different behavior of propylamine chrysotile indicated that the hydration effect is more pronounced than complex formation. The free Gibbs energy values are in agreement with favorable processes. The high entropic values for CRI1 and CRI0 indicated that the adsorption occurs by entropic reasons, while on CRI2 the enthalpic contribution is more pronounced. Copyright 2001 Academic Press.

Foti C., Pettignano A., and Sammartano S. (2002) Thermodynamic parameters for the binding of sulfate by open chain polyammonium cations. *Ann Chim* **92**, 1067-1075.

Abstract: The interaction of sulfate with some open chain polyammonium cations was quantitatively studied by potentiometric (H(+)-glass electrode) measurements. Enthalpy changes, for some systems, were determined calorimetrically. Some literature data were also considered in the discussion of results. In all the systems, $\text{A}(\text{SO}_4)\text{Hi}(\text{i}-2)$ species are formed ($\text{i} = 1, \dots, \text{m}$; $\text{m} =$ maximum protonation degree of amine), and, for $\text{i} \geq 4$, also $\text{A}(\text{SO}_4)_2\text{Hi}(\text{i}-4)$ species were found. Both the stability and the formation enthalpies, for these complexes, are a direct function of the charges of reactants, and some empirical relationships are reported. A small, but significant, difference was found between the stability of unsubstituted and N-alkylsubstituted polyammonium cation-sulfate complexes.

Frontera A., Morey J., Oliver A., Pina M. N., Quinonero D., Costa A., Ballester P., Deya P. M., and Anslyn E. V. (2006) Rational design, synthesis, and application of a new receptor for the molecular recognition of tricarboxylate salts in aqueous media. *J Org Chem* **71**, 7185-7195.

Abstract: A rational design of a tripodal receptor for the molecular recognition of tricarboxylate salts in aqueous media, based on squaramide, has been performed using high-level DFT calculations (RI-BP86/SVP level of theory) in solution using the COSMO treatment, including some preliminary ab initio calculations at the higher RI-MP2/TZVP level of theory, comparing the ability of squaramide to bind carboxylate salts with two widely used guanidinium salts. The tripodal receptor has been synthesized using a new methodology that has been recently reported by some of us, and its capability of recognizing several mono-, di-, and tricarboxylate salts has been studied experimentally by means of microcalorimetry experiments in a very high competitive media, H(2)O:EtOH 1:3. These experiments give enthalpic and entropic data, which are unfortunately scarce in the literature of molecular recognition of anions. Finally, a fluorimetric ensemble of the receptor with fluorescein has been found to be useful for the fluorimetric determination of zinc citrate in a commercial toothpaste using competition assays.

Fukada H. and Takahashi K. (1998) Enthalpy and heat capacity changes for the proton dissociation of various buffer components in 0.1 M potassium chloride. *Proteins* **33**, 159-166.

Abstract: Enthalpy and heat capacity changes for the deprotonation of 18 buffers were calorimetrically determined in 0.1 M potassium chloride at temperatures ranging from 5 to 45 degrees C. The values of the dissociation constant were also determined by means of potentiometric titration. The enthalpy changes for the deprotonation of buffers, except for the phosphate and glycerol 2-phosphate buffers, were found to be characterized by a linear function of temperature. The enthalpy changes for the second dissociation of phosphate and glycerol 2-phosphate where divalent anion is formed on dissociation were fitted with the second order function of temperature rather than the first order. Temperature dependence of buffer pH calculated by using the enthalpy and heat capacity changes obtained was in good agreement with the temperature variation of the pH values actually measured in the temperature range between 0 and 50 degrees C for all the buffers studied. On the basis of the results obtained, a numeric table showing the temperature dependence of pK values for the 18 buffers is presented.

Gerhardt W. W. and Weck M. (2006) Investigations of metal-coordinated peptides as supramolecular synthons. *J Org Chem* **71**, 6333-6341.

Abstract: This article describes the synthesis and controlled assembly of four model biological-hybrid scaffolds via coordination of a metal complex to four new tripeptides. Each model tripeptide investigated has either a central pyridyl glycyl or a pyridyl alanyl residue between two terminally protected glycines. All tripeptides were coordinated to their complementary recognition unit, a p-methoxy SCS-Pd pincer complex. The assembly events were fully characterized and investigated by (1)H NMR, ES-MS, and isothermal titration calorimetry (ITC) to elucidate how the substitution and spatial distance of the pyridyl moiety to the peptide backbone affects the metal coordination. Using these characterization techniques, we have shown that the metal-coordination events in all cases are fast and quantitative and that the peptide backbones do not interfere with the self-assembly. The ITC analyses showed that the 4-pyridyl tripeptides are the tightest binding ligands toward the palladated pincer complexes with the alanyl derivative being the strongest overall, demonstrating the superiority of the 4-pyridyl peptides over their 3-pyridyl analogues. The measured association constants are comparable to other pincer-pyridine systems in DMSO suggesting that the controlled coordination of the metalated pincer/pyridine interaction is an interesting biological synthon and will allow for the future development of important noncovalent peptide-based hybrid materials.

Gerhardt W. W., Zuccherro A. J., South C. R., Bunz U. H. and Weck M. (2007) Controlling polymer properties through dynamic metal-ligand interactions: supramolecular cruciforms made easy. *Chemistry* **13**, 4467-4474.

Abstract: A straightforward methodology towards the supramolecular synthesis of novel organometallic polymers with attractive optical properties is presented. By coordinating bifunctional fluorescent cruciform molecules through ditopic metalated pincer complexes (Pd or Pt), we have synthesized a new class of well-defined coordination polymers that have controllable and tunable physical and photophysical properties. The formation of these new materials by employing metal coordination was monitored by (1)H NMR spectroscopy, the association strength of the metal-ligand interaction was measured by isothermal titration calorimetry, the solution polymeric properties were evaluated by viscometry, and the optical properties were measured and observed by fluorescence spectroscopy. The fast and quantitative synthesis of a wide range of prefabricated monomeric cruciform and metalated-pincer-complex components will allow for the

rapid generation, growth, and optimization of this new class of functional polymers, which have potential electronic and optical applications.

Ghoufi A., Pison L., Morel J. P., Morel-Desrosiers N., Bonal C. and Malfreyt P. (2007) Computational and experimental investigations of supramolecular assemblies of p-sulfonatocalix[4]arene organized by weak forces. *J Phys. Chem B* **111**, 11478-11485.

Abstract: We report the study of the supramolecular assemblies formed by the incorporation of quaternary ammonium cations such as Me₄N⁺ or Et₄N⁺ into host-guest assemblies with p-sulfonatocalix[4]arene in the presence of a lanthanide(III) cation in water. We use microcalorimetry to characterize the formation of these supramolecular assemblies. We obtain a molecular description of these assemblies by performing molecular dynamics simulations over a very large period of time. The structures of these supramolecular complexes have been determined and discussed through specific interaction energy contributions. By combining MD simulations and 1NMR spectroscopy, we highlight a specific behavior of the supramolecular assembly with the Me₄N⁺.

Gill D. S., Roush D. J., Shick K. A., and Willson R. C. (1995) Microcalorimetric characterization of the anion-exchange adsorption of recombinant cytochrome b5 and its surface-charge mutants. *J Chromatogr A* **715**, 81-93.

Abstract: The adsorption of recombinant soluble tryptic fragment of rat cytochrome b5 on the strong anion exchanger Mono Q was studied using isothermal titration calorimetry and differential scanning calorimetry (DSC). Titration calorimetry results obtained at low levels of adsorbed protein show increasingly endothermic (unfavorable) enthalpies of binding with increasing surface coverage, confirming the heterogeneous nature of binding. The enthalpy of adsorption declines toward zero at higher loadings. At low surface coverage, enthalpies increase linearly with temperature, giving rise to a positive value of ΔC_p . Enthalpies of adsorption depend strongly on the history of the adsorbent. DSC is used to show that cytochrome b5 is stable in both free and adsorbed states at all temperatures used in the titration calorimetric experiments. Site-directed mutants of recombinant cytochrome b5 carrying single charge-neutralizing substitutions are used to test the contributions of particular residues to the thermodynamics of adsorption. Like those derived from van't Hoff analysis of equilibrium adsorption isotherms and HPLC retention data, calorimetric enthalpies of adsorption are positive, confirming the dominant role of entropic effects in ion-exchange adsorption in this system.

Golub T. P. and de Keizer A. (2004) Calorimetric study on the temperature dependence of the formation of mixed ionic/nonionic micelles. *Langmuir* **20**, 9506-9512.

Abstract: The differential excess enthalpy of mixed micelle formation was measured at different temperatures by mixing nonionic hexa(ethylene glycol) mono n-dodecyl ether with anionic sodium dodecyl sulfate or cationic dodecylpyridinium chloride. The experimental data were obtained calorimetrically by titrating a concentrated surfactant solution into a micellar solution of nonionic surfactant. The composition and the size of the mixed nonionic/ionic micelles at different surfactant concentrations were also determined. Pronounced differences in both composition and excess enthalpy were found between the anionic and the cationic mixed system. For both systems, the excess enthalpies become more exothermic with increasing temperature, but for the anionic mixed system an additional exothermic contribution was found which was much less temperature dependent. Temperature dependence of the excess enthalpy was attributed to the effect of the ionic headgroup on the hydration of the ethylene oxide (EO) groups in the mixed corona. Ionic headgroups located in the ethylene oxide layer cause the dehydration of the EO chains resulting in an additional hydrophobic contribution to the enthalpy of mixing. A high affinity of sodium dodecyl sulfate for nonionic micelles and an extra exothermic and less temperature dependent contribution to the excess enthalpy found for the SDS-C(12)E(6) system might be attributed to specific interactions (hydrogen bonds) between the sulfate headgroup and the partly dehydrated EO chain.

Gomy C. and Schmitzer A. R. (2006) Rational design of new polymerizable oxyanion receptors. *J Org Chem* **71**, 3121-3125.

Abstract: [structure: see text] We report the synthesis of a library of new polymerizable functional monomers designed for complexing with the oxyanionic moiety of the chemotherapeutic drug methotrexate. The ¹H NMR and ITC binding studies allowed for the selection of receptors possessing the best association parameters. Subsequently, the design of a broad library of polymerizable moiety-specific

binding monomers for the imprinting of dicarboxylate containing drugs was accomplished. Di(ureidoethylenemethacrylate)stilbene possesses the highest association properties and shows potential to act as a monomer in the molecularly imprinting technique to obtain photoswitchable cavities.

Gong H. and Krische M. J. (2005) Duplex molecular strands based on the 3,6-diaminopyridazine hydrogen bonding motif: amplifying small-molecule self-assembly preferences through preorganization and iterative arrangement of binding residues. *J Am Chem Soc* **127**, 1719-1725.

Abstract: Structural parameters obtained through single-crystal X-ray diffraction analysis of the one-dimensional H-bonding motif expressed by 3,6-diaminopyridazine are applied to the design of related monomeric, dimeric, and trimeric duplex molecular strands. The mode of assembly and the interstrand affinity of the oligomers are established in solution by (1)H NMR dilution experiments, isothermal titration calorimetry (ITC), and vapor pressure osmometry. Single-crystal X-ray crystallographic analysis of the dimeric diaminopyridazine 2a corroborates the intended duplex mode of assembly. Binding free energy per unimer ($-\Delta G$ degrees /n) increases upon extension from monomer to dimer to trimer, signifying a positive cooperative effect. Micromolar binding affinity ($K(d) = 1.25 \pm 0.1 \text{ } \mu\text{M}$) was determined for the duplex trimer by ITC in 1,2-dichloroethane at 20 degrees C. These data provide further insight into the structural and interactional features of synthetic duplex oligomers required for high-affinity, high-specificity binding and define new recognition elements for use in nanoscale assembly.

Gotmar G. and Guiochon G. (2004) Experimental validation of an affinity energy distribution calculated with the expectation maximization method. *Langmuir* **20**, 6521-6523.

Abstract: The difference between the average energies of the high-energy modes of the adsorption energy distributions of (S)-alprenolol and (R)-alprenolol on a chiral stationary phase calculated by the expectation maximization method agree well with the difference between the adsorption energies of these two compounds measured by isothermal titration calorimetry.

Govender T., Ehtezazi T., Stolnik S., Illum L., and Davis S. S. (1999) Complex formation between the anionic polymer (PAA) and a cationic drug (procaine HCl): characterization by microcalorimetric studies. *Pharm Res* **16**, 1125-1131.

Abstract: PURPOSE: Due to the importance of drug-polymer interactions in, inter alia, drug loading/release, supramolecular assemblies and DNA delivery for gene therapy, the aim of this study was therefore to establish the mechanism of interaction between a model polymer (Polyacrylic acid, PAA) and a model drug (procaine HCl). METHODS: This was performed by studying the effect of salt (KCl) concentration on their heat released values using Isothermal Titration Microcalorimetry (ITM). The integrated released heat data were computer fitted to a one class binding model and the thermodynamic parameters (K_{obs} , ΔH , and N) were determined. RESULTS: As the KCl concentration was increased, K_{obs} decreased thus establishing the salt dependence of the interaction. The linear variation of ΔG_{obs} with ΔS_{obs} indicated that their interaction was entropically driven. The stoichiometry of the interaction was calculated to be one procaine molecule per monomer of PAA. Dissection of the total observed free energy at each KCl concentration indicated that the contribution of the non-electrostatic attractions to the interaction of PAA with procaine HCl was greater than those of the electrostatic attractions. CONCLUSIONS: We have shown that the interaction between PAA and procaine HCl is dependent upon the presence of counterions (monovalent ions) and is mainly entropically driven. The calculated stoichiometry indicated that one procaine HCl molecule neutralised one carboxylic acid group on PAA. Although electrostatic interactions were necessary for initiating complex formation, the non-electrostatic forces were dominant in stabilising the PAA-procaine HCl complex.

Greish Y. E., Bender J. D., Lakshmi S., Brown P. W., Allcock H. R., and Laurencin C. T. (2005) Low temperature formation of hydroxyapatite-poly(alkyl oxybenzoate)phosphazene composites for biomedical applications. *Biomaterials* **26**, 1-9.

Abstract: The formation of biodegradable composites which may be suitable as bone analogs is described. Polyphosphazene-hydroxyapatite (HAp) composites were produced via an acid-base reaction of tetracalcium phosphate and anhydrous dicalcium phosphate in the presence of polyphosphazenes bearing alkyl ester containing side-groups. The polyphosphazenes used were poly(ethyl oxybenzoate)phosphazene (PN-EOB) and poly(propyl oxybenzoate) phosphazene (PN-POB). The effects of temperature and the proportions of polymers, PN-EOB and PN-POB on the kinetics, reaction chemistry and phase evolution

during the formation of stoichiometric HAp were studied. Kinetics, phase evolution and microstructural development were evaluated using isothermal calorimetry, X-ray diffraction and scanning electron microscopy, respectively. Analysis of solution chemistry revealed that the increases in the pH during the formation of SHAp, resulted in partial hydrolysis of the polymer surfaces, which led in turn to the formation of a calcium cross-linked polymer surface. The calcium cross-linked polymer surface appeared to facilitate the nucleation and growth of apatite deposits on the polymer. The current study illustrates the in situ formation of HAp in the presence of polyphosphazenes, where HAp is chemically bonded to the polymer.

Gross D. E., Schmidtchen F. P., Antonius W., Gale P. A., Lynch V. M. and Sessler J. L. (2008) Cooperative binding of calix[4]pyrrole-anion complexes and alkylammonium cations in halogenated solvents. *Chemistry* **14**, 7822-7827.

Abstract: Calix[4]pyrrole-chloride interactions are affected not only by the choice of counteranion in halogenated solvents, but show a specific dependence on the way in which these cations are bound within the electron rich, bowl-like calix[4]pyrrole cavity formed upon chloride anion complexation. In dichloromethane, the affinities of simple meso-octamethylcalix[4]pyrrole (1) for methyl-, ethyl-, and n-butylammonium chlorides are on the order of 10(5), 10(4), and 10(2) M(-1), respectively, as determined from isothermal titration calorimetry (ITC) analyses. These cation-dependent anion affinity effects, while clearly evident, are less pronounced in other halogenated solvents, such as 1,2-dichloroethane. Support for the proposed cation complexation selectivity is provided by solid state X-ray crystallographic analyses

Grosvenor M. P. and Lofroth J. E. (1995) Interaction between bile salts and beta-adrenoceptor antagonists. *Pharm Res* **12**, 682-686.

Abstract: The interactions between beta-adrenoceptor antagonists and bile salts were investigated by microcalorimetry. Nadolol and oxprenolol interactions with dihydroxy salts could be described by a 1:1 interaction model with the thermodynamic parameters indicating that the drugs were incorporated within the bile salt aggregates. This weak interaction was primarily hydrophobic although electrostatic attraction also played a role. Atenolol and metoprolol did not interact with the dihydroxy salts. None of the compounds interacted with trihydroxy bile salts or with salts below their aggregation concentration. Phase separation resulted when propranolol and alprenolol were present in dihydroxy salt solutions above a certain concentration with the interaction being of a hydrophobic and electrostatic nature. The implications of these results on in-vivo drug absorption are discussed.

Gue A. M., Lattes A., Laurent E., Mauzac M. and Mingotaud A. F. (2008) Characterization of recognition sites for diethyl 4-nitrobenzylphosphonate, an organophosphate pesticide analogue. *Anal Chim. Acta* **614**, 63-70.

Abstract: In a first step towards chemical sensors using molecular imprinted materials, the complexing characteristics of diethyl 4-nitrobenzylphosphonate, an organophosphate pesticide analogue, have been studied. Two molecules have been assessed as potential interacting moieties, specifically a fluoroalcohol and an aromatic acid. The interactions have been first characterized by regular methods, such as ¹H, ³¹P NMR and IR spectroscopy. These showed a stoichiometry 1/1 for both complexes and association constants, respectively, close to 40⁺/₋₁₀ and 12⁺/₋₂ M(-1). In a second step, isothermal titration calorimetry was used and a method was developed to obtain low-association constants. The association constant could be obtained for the fluoroalcohol ligand and was found equal to 63⁺/_{-0.7} M(-1). For the acidic molecule, an appropriate model could not be found, preventing the evaluation of this constant

Habata Y., Okazaki C., Ogura K., Akabori S., Zhang X. X. and Bradshaw J. S. (2007) Polymer-like structures of LiSCN, NaSCN, KSCN, RbSCN, and CsSCN complexes with an armed monoaza-15-crown-5 ether bearing a 3',5'-difluoro-4'-hydroxybenzyl group. *Inorg Chem* **46**, 8264-8270.

Abstract: Structures of LiSCN, NaSCN, KSCN, RbSCN, and CsSCN complexes with 3',5'-difluoro-4'-hydroxybenzyl-armed monoaza-15-crown-5 ether (5) were investigated. The Li⁺ and Na⁺ complexes are (1:1)_n polymer-like complexes bridged by hydrogen bonding. On the other hand, the K⁺, Rb⁺, and Cs⁺ complexes are polymer-like complexes bridged by the fluorine atoms of the side arms. The titration calorimetry and ¹⁹F NMR titration experiments suggest that one or both fluorine atoms along with the oxygen atom of the phenolic OH group coordinate to the alkali metal ions incorporated in the crown part of

a second armed ligand to give polymer-like complexes in solution. The FAB-MS data indicated that larger alkali metal ions form more stable polymer-like complexes.

Haj-Zaroubi M. and Schmidtchen F. P. (2005) Probing Binding-Mode Diversity in Guanidinium-Oxoanion Host-Guest Systems. *Chemphyschem* **6**, 1181-1186.

Abstract: An attempt to experimentally estimate the role of binding-mode diversity (structural fuzziness) on the molecular recognition seen in the prominent guanidinium-oxoanion host-guest pair is described. The global heat response as measured by isothermal titration calorimetry in acetonitrile, which was obtained from the interaction of five different but structurally closely related guanidinium hosts with three rigid phosphinate guests of decreasing accessibility of their binding sites, is correlated to provide a trend analysis. All host-guest associations of 1:1 stoichiometry in this series are strongly enthalpy-driven. The change in complexation entropy can be related to the tightness of the mutual fit of the host-guest partners, which approaches a minimum limit and is interpreted as the unique lock-and-key binding mode. The ordinary host-guest complexation in this ensemble features substantial positive entropy changes that correlate inversely with the binding interface area. This finding excludes desolvation effects as the major cause of entropy production, and provides evidence for the existence of a broad variety of complex configurations rather than a single binding mode to represent the associated host-guest pair. This result bears on the molecular design of systems that vitally depend on structural fidelity, such as nanoassemblies or homogeneous catalysis.

Hakkarainen S., Gilbert S. L., Kontturi A. K., and Kontturi K. (2004) Amperometric method for determining the degree of complexation of polyelectrolytes with cationic surfactants. *J Colloid Interface Sci* **272**, 404-410.

Abstract: The complexation of sodium polystyrene sulfonate with monovalent cationic surfactants at a micro-sized liquid/liquid interface has been studied using electrochemistry. The method is based on measurement of surfactant ion transfer across the interface between two immiscible electrolyte solutions (ITIES). The complexation of various cationic surfactants (alkylpyridinium- and trimethylammonium-) with oligosized polystyrene sulfonate was measured. Binding isotherms were used to determine the degree of binding as a function of the surfactant chain length and type of head group. It was found that the hydrophobicity of the surfactant was the predominant factor. The effect of the polyelectrolyte chain length on the binding mechanism was studied using cetylpyridinium chloride as a complexing agent. It was found that binding affinity, as well as cooperativity of the binding process, decreases with decreasing polyelectrolyte chain length. Thermodynamics of surfactant binding was measured using titration microcalorimetry. The thermodynamic data obtained show that the enthalpy of surfactant binding is not dependent on polymer chain length, but an increase in chain length makes the binding process entropically more favorable.

Hakkarainen S., Kontturi A. K., Kontturi K., and Urtti A. (2004) Electrochemical and calorimetric study of oligonucleotide complexation with cetylpyridinium chloride. *Eur J Pharm Sci* **23**, 371-377.

Abstract: The complexation of oligonucleotides and antisense drugs with a cationic surfactant, cetylpyridinium chloride (CPC), has been studied using electrochemistry at a micrometer sized liquid/liquid interface. This method can be used to investigate the effect of chemical and structural modifications on the complexation behaviour of oligonucleotides. For the interaction between CPC and oligonucleotides the effect of phosphorothioate derivatisation upon binding characteristics has been examined. Phosphoromonothioate modification causes the onset of binding to occur at a lower free surfactant concentration. Calorimetric studies show that surfactants are strongly bound to oligonucleotides and the binding is driven by entropy. The enthalpy change for the formation of oligonucleotide-surfactant complex is negative in all cases at 25 degrees C indicating exothermic reaction.

Haldar B., Chakrabarty A., Mallick A., Mandal M. C., Das P., and Chattopadhyay N. (2006) Fluorometric and isothermal titration calorimetric studies on binding interaction of a telechelic polymer with sodium alkyl sulfates of varying chain length. *Langmuir* **22**, 3514-3520.

Abstract: Steady-state fluorescence measurements and isothermal titration calorimetric experiments have been performed to study the interaction between a telechelic polymer, pyrene-end-capped poly(ethylene oxide) (PYPY), and sodium alkyl sulfate surfactants having decyl, dodecyl, and tetradecyl hydrocarbon tails. Fluorometric results suggest polymer-surfactant interaction in the very low range of polymer

concentrations. The relative variation in the excimer to monomer pyrene emission intensities with varying surfactant concentration reveals that initial addition of surfactant favors intramolecular preassociation until the surfactant molecules start binding with the ethylene oxide (EO) chain. With the growing number of surfactant aggregates along the EO chain, the association becomes hindered due to the polyelectrolyte effect. The results from microcalorimetric titrations in the low concentration range of PYPY solution (approximately 10^{-6} M) with alkyl sulfates suggest two kinds of surfactant-polymer interactions, one with the polymer hydrophobic end groups and the other with the ethylene oxide backbone. The overall polymer-surfactant interaction starts at a much lower surfactant concentration for the hydrophobically modified polymers compared to that in the case of unsubstituted poly(ethylene oxide) homopolymer. From the experiments critical aggregation concentration values and the second critical concentration where free micelles start forming have been determined. An endeavor has been made to unveil the mechanism underlying the corresponding associations of the surfactants with the polymer.

Hanson M., Unger K. K., Denoyel R., and Rouquerol J. (1994) Interactions of lysozyme with hydrophilic and hydrophobic polymethacrylate stationary phases in reversed phase chromatography (RPC). *J Biochem Biophys Methods* **29**, 283-294.

Abstract: Two silicas, one with a mean pore diameter of 30 nm and the other non-porous, were coated with polymethacrylates of increasing hydrophobicity in the sequence: poly-2-hydroxyethylmethacrylate (PHEMA)1 polyethylmethacrylate (PEMA) and poly-n-octylmethacrylate (POMA). Association constants, K_{ass} , between lysozyme and the coated silicas were determined by means of frontal analysis, and the apparent heats of adsorption, ΔH_{app} , by means of microcalorimetry. Using K_{ass} and ΔH_{app} the changes in the apparent free energy, ΔG_{app} , and in the apparent entropy, ΔS_{app} , were calculated at a concentration of lysozyme < 10 $\mu\text{mol/l}$. The association between the lysozyme and the coated silica gave negative ΔH_{app} and ΔS_{app} values. The ΔS_{app} values calculated from the experimental data in the absence of an added electrolyte and with 0.1 M sodium perchlorate present to be -12 (-96) J/mol deg on the PHEMA silica, -27 (-51) J/mol deg on the PEMA silica, -98 (-186) J/mol deg on the POMA silica, respectively. The high ΔS_{app} value of the lysozyme on the POMA silica reflects a kind of stabilisation effect due to the conformational changes of lysozyme on the most hydrophobic POMA silica. As evidenced by RPC, lysozyme elutes on the POMA column in its totally unfolded form enabling a more disordered conformation with respect to entropy than in the native form.

Harrison R. G., Burrows J. L., and Hansen L. D. (2005) Selective Guest Encapsulation by a Cobalt-Assembled Cage Molecule. *Chemistry* **11**, 5881-5888.

Abstract: Metal-assembled resorcinarene-based cages enclose space and entrap organic molecules from water. Addition of cobalt(II) ions to a neutral, aqueous solution of a resorcinarene that has iminodiacetic acids attached to its upper rim results in the formation of cages. These cages not only entrap organic molecules, but they do so in a selective manner. Guests with optimum size, shape, and polarity are preferentially entrapped. For example, selection of p-xylene is twenty thousand times more favorable than that of m-xylene. The enthalpy of resorcinarene deprotonation and cage formation was calculated by performing calorimetry studies and ranged from -305 to -348 kJ mol⁻¹. The change in enthalpy of guest encapsulation varied by as much as 43 kJ mol⁻¹. The differences in change in free energy of guest encapsulation varied by -16 kJ mol⁻¹. The changes in enthalpy and free energy of guest encapsulation were used to calculate the changes in entropy, which ranged from -97 to +37 J mol⁻¹ K⁻¹. An enthalpy-entropy compensation of guest encapsulation was observed.

Heerklotz H., Tsamaloukas A., Kita-Tokarczyk K., Strunz P., and Gutberlet T. (2004) Structural, Volumetric, and Thermodynamic Characterization of a Micellar Sphere-to-Rod Transition. *J Am Chem Soc* **126**, 16544-16552.

Abstract: The thermotropic sphere-to-rod transition of nonionic surfactants was characterized in terms of a large set of parameters: the transition temperature and width, the partial volume, coefficient of thermal volume expansion, enthalpy, isobaric heat capacity, and structural parameters, such as radius of gyration and hydrodynamic radius. Data were recorded as a function of concentration of surfactants in H₂O and in D₂O. To this end, pressure perturbation calorimetry (PPC), small angle neutron scattering (SANS), dynamic light scattering (DLS), differential scanning calorimetry (DSC), and isothermal titration calorimetry (ITC) were applied in a study of aqueous solutions containing myristyl, tridecyl, and lauryl maltoside and heptaethyleneglycoltetradecyl ether (C(14)EO(7)). Small changes in the thermodynamic and

volumetric parameters (e.g., the partial volume change is approximately +2 per thousand) are discussed in detail as the result of three effects governing the transition. (i) Reduction of the water accessible hydrophobic surface area (ASA(ap)) drives the transition. (ii) Shrinking in headgroup size by thermal dehydration triggers the transition. (iii) Hypothesized gradual ordering of the chains may control the effect of chain length on the transition.

Herrero L. A., Calafat A. M., and Terron A. (1991) A calorimetric study of the Ni(II)-5' AMP system. A base-stacking stabilization. *Eur J Biochem* **202**, 401-404.

Abstract: The thermodynamic parameters of the interaction between Ni(II) (M) and 5'-AMP in aqueous solution were determined calorimetrically (I = 0.1 tetramethylammonium bromide, 25 degrees C) at physiological pH. The experimental conditions were carefully selected to avoid the polynuclear complex formation. From the Ni(5'AMP)-complex-formation constant ($\log K_1 = 2.55$), the Ni(5'AMP)₂(2-)-complex-formation constant and the Ni(5'AMP) (ML) and Ni(5'AMP)₂(2-) (ML₂) complex-formation enthalpies were determined ($\log K_2 = 2.34$, $\Delta H_1 = -10.0$ kJ/mol and $\Delta H_2 = 21.6$ kJ/mol). These results confirm the formation of the ML₂ complex in solution and agree very well with the hypothesis of the 'stacking' between the purine rings, promoted for metal ions.

Herrero L. A. and Terron A. (2000) Interactions in solution of calcium(II) and copper(II) with nucleoside monophosphates: a calorimetric study. *J Biol Inorg Chem* **5**, 269-275.

Abstract: The thermodynamic parameters enthalpy and entropy of the interaction between calcium(II) or copper(II) with 5'-UMP, 5'-CMP, 5'-AMP, 5'-GMP or 5'-IMP in aqueous solution were determined calorimetrically (ionic strength adjusted to 0.1 with tetramethylammonium bromide) at 25 degrees C and pH 7 for Ca(II) or pH 3-5 for Cu(II). The experimental conditions were carefully selected to avoid polynuclear complex formation and nucleotide self-stacking. The calorimetric data confirm the tendency toward macrochelation which was indicated by Sigel after very precise potentiometric studies, and which follows the order Cu(II) > Ca(II) for the metal ions and GMP > IMP > AMP > CMP = UMP for the nucleotides. Macrochelate formation for these metal-nucleoside monophosphate complexes is energetically favorable and entropically unfavorable.

Herrero L. A., Cerro-Garrido J. C., and Terron-Homar A. (2001) A calorimetric study of 3d metal ions-acyclovir interactions. The 2-hydroxyethoxymethyl group of acyclovir mimics the role of ribose in deoxy-guanosine and guanosine promoting the coordination through N(7). *J Inorg Biochem* **86**, 677-680.

Abstract: The equilibrium constants and enthalpic values of metal acyclovir complexes have been determined by calorimetry for Co(II) ($\log K = 0.96 \pm 0.05$, ΔH (kJ/mol) = -19.7 ± 1.3), Ni(II) ($\log K = 1.39 \pm 0.03$, ΔH (kJ/mol) = -21.5 ± 1.0), Cu(II) ($\log K = 1.83 \pm 0.03$, ΔH (kJ/mol) = -23.2 ± 0.8) and Zn(II) ($\log K = 0.71 \pm 0.06$, ΔH (kJ/mol) = -18.6 ± 1.5). The equilibrium constants are similar to those of the divalent ions with guanosine and 2,9-dimethylpurine. By comparison with previous thermodynamic data, it can be shown that the 2-hydroxyethoxymethyl group promotes coordination through N(7) versus N(1) of the guanine ring for 3d metal ions. These results reveal that the 2-hydroxyethoxymethyl group placed on the purine ring of guanine in acyclovir causes a greater effect than that of the 9-methyl in purines and similar to or greater than that of the ribose moiety in guanosine. The 2-hydroxyethoxymethyl group of acyclovir mimics the role of ribose in deoxy-guanosine and guanosine promoting a similar coordination chemistry (with very close $\log K$ and ΔH values) for acyclovir, deoxy-guanosine and guanosine with divalent metals.

Herrero L. A., Cerro-Garrido J. C., Apella M. C., and Terron-Homar A. (2002) Interactions in solution of cobalt(II) and nickel(II) with nicotinamide adenine dinucleotide: a potentiometric and calorimetric study. *J Biol Inorg Chem* **7**, 313-317.

Abstract: The equilibrium constants and the thermodynamic parameters enthalpy and entropy of the interaction between Ni(II) and Co(II) with NAD(+) in aqueous solution were determined by calorimetry and potentiometry methods (ionic strength adjusted to 0.1 with sodium nitrate at 25 degrees C). The macrochelation of the systems was also studied. All the data, including the protonation enthalpy data of NAD(+) (very similar to the protonation enthalpy of 5'-AMP) suggest a less restrictive model for the NAD(+) "folded" conformation without intramolecular stacking between the bases, in agreement both with recent theoretical calculations and with the X-ray structure of trimethylene-bisadeninium or the free acid form of NAD(+).

Hooley R. J., Van Anda H. J. and Rebek J., Jr. (2007) Extraction of hydrophobic species into a water-soluble synthetic receptor. *J Am. Chem Soc.* **129**, 13464-13473.

Abstract: A deep, water-soluble cavitand extracts a variety of neutral hydrophobic species into its cavity. Flexible species such as n-alkanes tumble rapidly on the NMR time scale inside the cavity, but this motion is slowed for bulkier guests. Long, rigid guests such as p-substituted aromatics are either static or only tumble at elevated temperatures via flexing motions of the cavitand. Strong selectivity in recognition of long rigid guests is seen. The binding of neutral guests occurs via the classical hydrophobic effect; the process is entropically favored, as shown by isothermal titration calorimetry measurements. Binding affinities are generally on the order of $10(4)$ - $10(5)$ M⁽⁻¹⁾. The extent of the hydrophobic stabilization is shown by the binding of long trimethylammonium salts, which bind the alkyl chain in the cavity, rather than the NMe₃⁺ group. Dynamic NMR studies show that self-exchange of neutral guests is independent of guest concentration, and most likely occurs via rate-determining unfolding of the cavitand. In the absence of guests, the cavitand exists in a dimeric velcand structure.

Hughes A. D. and Anslyn E. V. (2007) A cationic host displaying positive cooperativity in water. *Proc. Natl. Acad. Sci U. S. A* **104**, 6538-6543.

Abstract: The affinity of guanidinium and Cu(II) containing hosts for polycarboxylate guests is studied in water by using UV-visible spectroscopy and isothermal titration calorimetry. By combining a Cu(II) coordination site and a diguanidinium moiety around a single scaffold it is found that the Gibbs free-energy release upon binding is greater than could be expected based on the sum of the free energy released by the binding functional groups when operating in isolation. This effect is known as positive cooperativity and has rarely been observed with synthetic hosts in water. The isothermal titration calorimetry data suggest that the source of this positive cooperativity is enthalpic in origin. We propose that covalently positioning the cationic binding moieties in close proximity destabilizes the unbound host, and thereby the stabilizing effect of binding the anionic carboxylates is exothermic and also, the source of positive cooperativity observed herein.

Ikeda T., Saha S., Aprahamian I., Leung K. C., Williams A., Deng W. Q., Flood A. H., Goddard W. A., III and Stoddart J. F. (2007) Toward electrochemically controllable tristable three-station [2]catenanes. *Chem Asian J* **2**, 76-93.

Abstract: Encouraged by the prospect of producing an electrochemical, color-switchable red-green-blue (RGB) dye compound, we have designed, synthesized, and characterized two three-station [2]catenanes. Both are composed of macrocyclic polyethers containing three pi-electron-rich stations, which act as recognition sites for a pi-electron-deficient tetracationic cyclophane. The molecular structures of the two three-station [2]catenanes were characterized fully by mass spectrometry and ¹H NMR spectroscopy. To anticipate the relative occupancies of the three stations in each [2]catenane by the cyclophane, model compounds with the same constitutions in the vicinity of the stations were synthesized. The relative ground-state populations of the three stations occupied in both [2]catenanes were estimated from the thermodynamic parameters for 1:1 complexes between all these model compounds and the cyclophane, obtained from isothermal titration calorimetry (ITC). The electrochemical and electromechanical properties of the three-station [2]catenanes were analyzed by cyclic voltammetry (CV), differential pulse voltammetry (DPV), and spectroelectrochemistry (SEC). The first three-station [2]catenane was found to behave like a bistable system, whereas the second can be described as a quasi-tristable system.

Ishikawa E. and Yamase T. (2006) ³¹P NMR and isothermal titration calorimetry studies on polyoxomolybdates-catalyzed hydrolysis of ATP. *J Inorg Biochem* **100**, 344-350.

Abstract: ATP hydrolysis in the presence of polyoxomolybdates at pH levels of 6, 4, and 2 has been investigated with a help of high pressure liquid chromatography (HPLC) analyses, ³¹P- and ¹H NMR measurements, and isothermal titration calorimetry (ITC). The polyoxomolybdates-induced ATP-hydrolysis proceeded satisfactorily in pH < 6 media at 20 degrees C with an optimum pH level of 4, while it was significantly depressed at low temperature of < or = 5 degrees C. At pH levels of 6 and 4, ADP was a main product, and the involvement of [(PO₄)₂Mo₅O₁₅](6-)-like ATP-molybdate complex as an intermediate was implied. At pH 2 ATP was decomposed to AMP with small generation of ADP through the formation of the ATP-molybdate complex isostructural with [(O₃POPO₃)Mo₆O₁₈(H₂O)₄]⁴⁻ as an intermediate. The ITC result at pH 4 showed an occurrence of two types of the exothermic binding reactions between molybdate and ATP with binding constants (K) of 6.61x10⁽⁴⁾ and 9.40x10⁽³⁾ M⁽⁻¹⁾ and

molar enthalpy values (ΔH) of -6.32×10^4 and -4.73×10^3 J mol⁻¹, respectively. Together with the results of ¹H NMR measurements, it is deduced that the molybdates interact with not only phosphate sites in the ATP side-chain, but also adenine-ring with an accompanying aggregation of molybdates at pH 4.

Iwamoto H., Mizutani T. and Kano K. (2007) Thermodynamics of hydrophobic interactions: entropic recognition of a hydrophobic moiety by poly(ethylene oxide)-zinc porphyrin conjugates. *Chem Asian J* **2**, 1267-1275.

Abstract: The recognition of 4-alkylpyridines by water-soluble poly(ethylene oxide)-zinc porphyrin conjugates was studied with a focus on the thermodynamic parameters of binding. Microcalorimetric studies indicated that binding of the alkyl group of the guest in water is driven by the entropic term ($\Delta \Delta H_0 = \Delta H_0(4\text{-pentylpyridine}) - \Delta H_0(4\text{-methylpyridine}) = +1.7$ kJ mol⁻¹), $\Delta T \Delta S_0 = T\Delta S_0(4\text{-pentylpyridine}) - T\Delta S_0(4\text{-methylpyridine}) = +11.8$ kJ mol⁻¹) at 298 K), thus showing the significance of water reorganization during host-guest interaction. The enthalpy-entropy compensation temperature of binding of 4-alkylpyridines was as low as 38 K; only below this temperature could the enthalpic term be a driving force. The binding affinity was modulated by the addition of cations and by varying the degree of polymerization of poly(ethylene oxide), which suggests that guest binding is coupled with polymer conformation.

Jadhav V. D. and Schmidtchen F. P. (2005) Surprises in the design of anion receptors: calorimetry prevents false reasoning. *Org Lett* **7**, 3311-3314.

Abstract: Supplementing bicyclic guanidinium anion receptors with four sec-carboxamido groups leads to enhanced affinity for oxoanions, however, for a different reason than originally planned. Calorimetric analysis reveals that better binding is due to higher association entropies rather than more negative enthalpies. Thus, molecular design following geometric and functional complementarity principles may misguide supramolecular constructions aimed at a unique host-guest binding mode, as required, e.g., by self-assembly or catalysis.

Jadhav V. D. and Schmidtchen F. P. (2006) Judging on host-guest binding mode uniqueness: association entropy as an indicator in enantioselection. *Org Lett* **8**, 2329-2332.

Abstract: [reaction: see text] Supramolecular enantiodifferentiation was studied by isothermal titration calorimetry in an effort to address the order-disorder distinction in the diastereomeric complexes formed from a chiral macrocyclic host and enantiomeric carboxylates. As a result, the association entropy component $T\Delta S$ emerged as an indicator in the enantioselection of tartrate **14** and aspartate **15** by the macrocycle **13** containing two guanidinium anchor groups connected to each other by four urea units. The parent monotopic guanidinium compounds **1** or **2** did not show any enantioselection for chiral carboxylates.

Jadhav V. D., Herdtweck E. and Schmidtchen F. P. (2008) Addressing association entropy by reconstructing guanidinium anchor groups for anion binding: design, synthesis, and host-guest binding studies in polar and protic solutions. *Chemistry* **14**, 6098-6107.

Abstract: The bicyclic hexahydropyrimidino[1,2a]pyrimidine cationic scaffold has a well-known capacity to bind a variety of oxoanions (phosphates, carboxylates, squarates, phosphinates). Based on this feature, the parent host was supplemented with sec-carboxamido substituents to generate compounds **1-3** in an effort to improve the anion-binding affinity and selectivity and to learn about the role and magnitude of entropic factors. Bicyclic guanidinium compounds were prepared by a convergent strategy via the corresponding tetraester **22** followed by catalytic amidation. Host-guest binding studies with isothermal titration calorimetry in acetonitrile probed the behavior of artificial hosts **1-3** in comparison with the tetraallylguanidinium compound **4** on binding p-nitrobenzoate, dihydrogenphosphate, and 2,2'-bisphenolcyclophosphate guests that showed enhanced affinities in the 10^5 - 10^6 M⁻¹ range. Contrary to expectation, better binding emerges from more positive association entropies rather than from stronger enthalpic interactions (hydrogen bonding). In an NMR spectroscopy titration in DMSO, o-phthalate was sufficiently basic to abstract a proton from the guanidinium function, as confirmed by an X-ray crystal structure of the product. The novel carboxamide-appended anchor groups also bind carboxylates and phosphates, but not hydrogen sulfate in methanol with affinities in excess of 10^4 M⁻¹. The energetic signature of the complexation in methanol is inverted with respect to acetonitrile solvent and shows a pattern of general ion pairing with strong positive entropies overcompensating endothermic binding enthalpies. This study provides an example of the fact that bona fide decoration of a parent guanidinium

anchor function with an additional binding functionality may provide the desired enhancement of the host-guest affinity, yet for a different reason than that implemented by design as guided by standard molecular modeling

Jadhav V. D. and Schmidtchen F. P. (2008) A novel synthesis of chiral guanidinium receptors and their use in unfolding the energetics of enantioselective recognition of chiral carboxylates. *J Org. Chem* **73**, 1077-1087.

Abstract: A novel synthetic route to the versatile chiral bicyclic guanidinium building block is described making use of l-methionine as a starting material from the natural chiral pool. Furthermore, the synthetic elaboration of this building block is shown in the construction of macrocyclic and open chain hosts, respectively. The host design employs urea functions as the connecting units and supplementary anchor groups for the complexation of anions. The binding studies of these hosts with various chiral and achiral oxoanions are performed by isothermal titration calorimetry. A trend analysis of the binding energetics in an ensemble of structurally similar guests discloses the importance of geometrical confinement of the guest. Association entropy rather than free energy (affinity) is identified as an indicator of structural uniqueness needed to distinguish configurational isomers in the recognition of enantiomeric carboxylates by the chiral guanidinium hosts

Jeon Y. J., Kim S. Y., Ko Y. H., Sakamoto S., Yamaguchi K., and Kim K. (2005) Novel molecular drug carrier: encapsulation of oxaliplatin in cucurbit[7]uril and its effects on stability and reactivity of the drug. *Org Biomol Chem* **3**, 2122-2125.

Abstract: Oxaliplatin forms a stable 1:1 inclusion complex with cucurbit[7]uril as indicated by NMR, mass spectrometry, isothermal titration calorimetry and X-ray crystallography. The encapsulation of the drug results in a large enhancement in stability, a moderate decrease in reactivity toward guanosine but a much larger decrease in reactivity toward L-methionine, which suggests the encapsulation not only increases the stability of the drug but also may reduce unwanted side effects caused by protein binding of the platinum drug. A preliminary in vitro assay using various tumor cell lines reveals that the encapsulation results in a decrease in the antitumor activity of oxaliplatin.

Jiang Y., Hu M., Li S., Wang J., and Zhuo K. (2006) Thermodynamics of the interaction of RbCl with some monosaccharides (D-glucose, D-galactose, D-xylose, and D-arabinose) in aqueous solutions at 298.15K. *Carbohydr Res* **341**, 262-269.

Abstract: The Gibbs energy interaction parameters of RbCl with some monosaccharides (D-glucose, D-galactose, D-xylose, and D-arabinose) in water, $g(ES)$, were obtained from electromotive force (emf) measurements of the electrochemical cell without liquid junction and containing two ion-selective electrodes (ISE): K-ISEmid R:RbCl(m(E))mid R:ISE-Cl and K-ISEmid R:RbCl(m(E)),saccharide (m(S))mid R:ISE-Cl, at 298.15K. The enthalpy interaction parameters of RbCl with these monosaccharides in water, $h(ES)$, are determined according to the McMillan-Mayer theory from the measurements of the enthalpies of mixing of aqueous RbCl solutions with aqueous monosaccharide solutions, as well as the enthalpies of dilution of RbCl and monosaccharide solutions in pure water at 298.15K by a calorimetric method. Furthermore, the entropy interaction parameters, $s(ES)$, can be evaluated through $g(ES)$ and $h(ES)$. The results suggest that the electrostatic interactions of these monosaccharides with RbCl in water are predominant compared with structural interactions, and these parameters are controlled primarily by the stereochemical structure of the monosaccharides in water.

Jiao H., Le Stang S., Soos T., Meier R., Kowski K., Rademacher P., Jafarpour L., Hamard J. B., Nolan S. P., and Gladysz J. A. (2002) How to insulate a reactive site from a perfluoroalkyl group: photoelectron spectroscopy, calorimetric, and computational studies of long-range electronic effects in fluororous phosphines $P((CH_2)_m(CF_2)_7CF_3)_3$. *J Am Chem Soc* **124**, 1516-1523.

Abstract: This study advances strategy and design in catalysts and reagents for fluororous and supercritical CO_2 chemistry by defining the structural requirements for insulating a typical active site from a perfluoroalkyl segment. The vertical ionization potentials of the phosphines $P((CH_2)_mR(f_8))_3$ ($m = 2$ (2) to 5 (5)) are measured by photoelectron spectroscopy, and the enthalpies of protonation by calorimetry (CF_3SO_3H , $CF_3C(6)H(5)$). They undergo progressively more facile (energetically) ionization and protonation ($P(CH_2)CH_3)_3 > 5 > 4$ approximately equal to $P(CH_3)_3 > 3 > 2$), as expected from inductive effects. Equilibrations of trans-Rh(CO)(Cl)(L)₂ complexes (L = 2, 3) establish analogous Lewis basicities. Density functional theory is used to calculate the structures, energies, ionization potentials, and

gas-phase proton affinities (PA) of the model phosphines $P((CH_2)_m)CF_3$ (2'-9'). The ionization potentials of 2'-5' are in good agreement with those of 2-5, and together with PA values and analyses of homodesmotic relationships are used to address the title question. Between 8 and 10 methylene groups are needed to effectively insulate a perfluoroalkyl segment from a phosphorus lone pair, depending upon the criterion employed. Computations also show that the first carbon of a perfluoroalkyl segment exhibits a much greater inductive effect than the second, and that ionization potentials of nonfluorinated phosphines $P((CH_2)_m)CH_3$ reach a limit at approximately nine carbons ($m = 8$).

Jin J. Y., Kim S. Y., Ho K. Y., Sakamoto S., Yamaguchi K., and Kim K. (2005) Novel molecular drug carrier: encapsulation of oxaliplatin in cucurbit[7]uril and its effects on stability and reactivity of the drug. *Org Biomol Chem* **3**, 2122-2125.

Abstract: Oxaliplatin forms a stable 1 : 1 inclusion complex with cucurbit[7]uril as indicated by NMR, mass spectrometry, isothermal titration calorimetry and X-ray crystallography. The encapsulation of the drug results in a large enhancement in stability, a moderate decrease in reactivity toward guanosine but a much larger decrease in reactivity toward l-methionine, which suggests the encapsulation not only increases the stability of the drug but also may reduce unwanted side effects caused by protein binding of the platinum drug. A preliminary in vitro assay using various tumor cell lines reveals that the encapsulation results in a decrease in the antitumor activity of oxaliplatin.

Jin L., maya-Mazo X., Apel M. E., Sankisa S. S., Johnson E., Zbyszynska M. A. and Han A. (2007) Ca^{2+} and Mg^{2+} bind tetracycline with distinct stoichiometries and linked deprotonation. *Biophys Chem* **128**, 185-196.

Abstract: Tetracycline depends on divalent metal ions for its biological function, but its multiple ionization states, conformations, and tautomers at varying solution conditions complicate its ion-binding equilibria, and the stoichiometry of the biologically relevant Ca^{2+} or Mg^{2+} complexes has not been clear. Isothermal titration calorimetry was used in the present work to study Ca^{2+} and Mg^{2+} binding to tetracycline. The two metal ions bind with distinct stoichiometries, one Ca^{2+} per tetracycline and one Mg^{2+} per two tetracyclines, and with differing dependence on solution conditions, indicating that these two ions bind TC differently. An endothermic process accompanies ion binding that is proposed to reflect conformational changes in tetracycline. The results identify conditions that limit the distribution of species and may facilitate structural study.

Jodar-Reyes A. B., Martin-Rodriguez A., and Ortega-Vinuesa J. L. (2001) An Enthalpic Analysis on the Aggregation of Colloidal Particles Studied by Microcalorimetry. *J Colloid Interface Sci* **237**, 6-10.

Abstract: There are different theories concerning the stability of colloidal suspensions. Most of them arise from the well-known DLVO theory which relates colloidal stability to intermolecular forces between particles. Experimental corroboration of these theories has been obtained mainly by using different optical techniques that analyze changes in the optical properties of the solution while particles aggregate. However, no attention has been paid to studying the aggregation process thermodynamically. This is why we have focussed on studying the heat released during the agglutination of polystyrene particles. The enthalpy change in this aggregation process was detected by using a highly sensitive and modern technique called isothermal titration calorimetry. In addition, some results about rezeptization, that is, reversibility in the aggregation process, are also shown. Copyright 2001 Academic Press.

Kapuscinski J., Ardelt B., Piosik J., Zdunek M., and Darzynkiewicz Z. (2002) The modulation of the DNA-damaging effect of polycyclic aromatic agents by xanthines. Part I. Reduction of cytostatic effects of quinacrine mustard by caffeine. *Biochem Pharmacol* **63**, 625-634.

Abstract: Recently, accumulated statistical data indicate the protective effect of caffeine consumption against several types of cancer diseases. There are also reports about protective effect of caffeine and other xanthines against tumors induced by polycyclic aromatic hydrocarbons. One of the explanations is based on biological activation of such carcinogens by cytochromes that are also known for metabolism of caffeine. However, there is also numerous data indicating reverse effect on cytotoxicity of anticancer drugs that inhibit the action of topoisomerase I (e.g. Camptothecin or Topotecan) and topoisomerase II inhibitors (e.g. Doxorubicin, Mitoxantrone or mAMSA). In this work we tested the hypothesis that the caffeine protective effect is the result of sequestering of aromatic mutagens by formation of stacking (π - π) complexes. As the models for the study we have chosen two well-known mutagens, that do not require metabolical activation:

quinacrine mustard(QM, aromatic, heterocyclic nitrogen mustard) and mechlorethamine (NM2, aliphatic nitrogen mustard). The flow cytometry study of these agents' action on the cell cycle of HL-60 cells indicated that caffeine prevents the cytotoxic action of QM, but not that of NM2. The formations of stacking complexes of QM with caffeine were confirmed by light absorption, calorimetric measurements and by molecular modeling calculation. Using the statistical thermodynamics calculations we calculated the "neighborhood" association constant ($K(AC)=59\pm 2M^{-1}$) and enthalpy change ($\Delta H(0')=-116\text{cal mol}^{-1}$); the favorable entropy change of complex formation ($\Delta S(0')=7.72\text{cal mol}^{-1} K^{-1}$, due to release of several water molecules, associated with components in the process of complex formation). The Gibbs' free energy change of QM-CAF formation is $\Delta G(0')=-2.41\text{kcal mol}^{-1}$. We were unable to detect any interaction between NM2 and caffeine either by spectroscopic or calorimetric measurement. In order to establish, whether the intercalation of QM plays any role in cytotoxic effect we tested, as a control, non-alkylating, but also intercalating QM derivative-quinacrine (Q). The later had no cytostatic effect on HL-60 cell even at there order of higher concentration than QM or NM2 but, similar to QM forms (which we demonstrated) stacking complexes with caffeine ($K(AC)=75\pm 3M^{-1}$). These results strongly indicate, that the attenuating effect of caffeine on cytotoxic or mutagenic effects of some mutagens, is not the results of metabolic processes in the cells, but simply the physicochemical process of sequestering of aromatic molecules (potential carcinogens or mutagens) by formation of stacking complexes with them. The caffeine may then act as the "interceptor" of potential carcinogens (especially in the upper part of digesting track where its concentration can reach the concentration of mM level). There is, however, no indication either in the literature or in our experiments that xanthines can reverse the damage to nucleic acids when the damage to DNA has already occurred.

Keowmaneechai E. and McClements D. J. (2002) Influence of EDTA and citrate on physicochemical properties of whey protein-stabilized oil-in-water emulsions containing CaCl₂. *J Agric Food Chem* **50**, 7145-7153.

Abstract: The influence of chelating agents (disodium ethylenediaminetetraacetate (EDTA) and sodium citrate) on the physicochemical properties of whey protein isolate (WPI)-stabilized oil-in-water emulsions containing calcium chloride was determined. The calcium-binding characteristics of EDTA and citrate at 30 degrees C were characterized in aqueous solutions (20 mM Tris buffer, pH 7.0) by isothermal titration calorimetry (ITC). EDTA and citrate both bound calcium ions in a 1:1 ratio, but EDTA had a much higher binding constant. Oil-in-water emulsions (pH 7.0) were prepared containing 6.94% (w/v) soybean oil, 0.35% (w/v) WPI, 0.02% (w/v) sodium azide, 20 mM Tris buffer, 10 mM CaCl₂, and 0-40 mM chelating agent. The particle size, apparent viscosity, creaming stability, free calcium concentration, and particle surface potential of the emulsions were measured. The chelating agents reduced or prevented droplet aggregation in the emulsions. When they were present above a certain concentration (>3.5 mM EDTA or >5 mM citrate), droplet aggregation was prevented. The reduction of aggregation was indicated by decreases in particle size, shear-thinning behavior, apparent viscosity, and creaming. Emulsions containing chelating agents had lower free calcium concentrations and more negatively charged droplets, indicating that the chelating agents improved emulsion stability by binding calcium ions. EDTA could be used at lower concentrations than citrate because of its higher calcium ion binding constant.

Kerckhoffs J. M., ten Cate M. G., Mateos-Timoneda M. A., van Leeuwen F. W., Snellink-Ruel B., Spek A. L., Kooijman H., Crego-Calama M., and Reinhoudt D. N. (2005) Selective self-organization of guest molecules in self-assembled molecular boxes. *J Am Chem Soc* **127**, 12697-12708.

Abstract: This article describes the synthesis and binding properties of highly selective noncovalent molecular receptors 1(3).(DEB)₆ and 3(3).(DEB)₆ for different hydroxyl functionalized anthraquinones 2. These receptors are formed by the self-assembly of three calix[4]arene dimelamine derivative molecules (1 or 3) and six diethylbarbiturate (DEB) molecules to give 1(3).(DEB)₆ or 3(3).(DEB)₆. Encapsulation of 2 occurs in a highly organized manner; that is, a noncovalent hydrogen-bonded trimer of 2 is formed within the hydrogen-bonded receptors 1(3).(DEB)₆ and 3(3).(DEB)₆. Both receptors 1(3).(DEB)₆ and 3(3).(DEB)₆ change conformation from staggered to eclipsed upon complexation to afford a better fit for the 2(3) trimer. The receptor selectivity toward different anthraquinone derivatives 2 has been studied using ¹H NMR spectroscopy, X-ray crystallography, UV spectroscopy, and isothermal microcalorimetry (ITC). The pi-pi stacking between the electron-deficient center ring of the anthraquinone derivatives 2a-c and 2e-g and the relatively electron-poor melamine units of the receptor is the driving force for the encapsulation of

the guest molecules. The selectivity of the hydrogen-bonded host for the anthraquinone derivatives is the result of steric interactions between the guest molecules and the calix[4]arene aromatic rings of the host.

Kim S. G., Kim K. H., Jung J., Shin S. K., and Ahn K. H. (2002) Unprecedented chiral molecular recognition in a C₃-symmetric environment. *J Am Chem Soc* **124**, 591-596.

Abstract: The enantiomeric recognition of alpha-chiral primary ammonium ions has been studied with benzene-based tripodal tris(oxazoline) receptors. Contrary to the literature and our expectation, a good level of chiral discrimination is observed with one of the tripodal receptors, which provides a C₃-symmetric chiral environment on guest binding. The chiral discrimination has been found to be general in the case of alpha-aryl substituted guests, suggesting pi-pi interactions as an important factor. This result raises a question with respect to the origin of the chiral discrimination since little steric or electronic difference is expected between the diastereomeric inclusion complexes. Binding studies by NMR titration and isothermal titration calorimetry show that the chiral discrimination results from the different thermodynamic stabilities between the diastereomeric complexes and that the host-guest complex formation is driven by favorable enthalpy changes with a minor negative contribution by entropy changes. The X-ray crystal structures for both of the diastereomeric inclusion complexes are resolved, which unambiguously show the binding mode and provide clues on the origin of the chiral discrimination. Bond angle analyses indicate that the minor complex experiences a larger steric strain, which is discernible when it is viewed from "three-body" interactions between the host and the guest. The guest and oxazoline phenyl rings are well stacked, indicating interplay of the pi-pi interactions. The pi-pi interactions are believed to stabilize host-guest complexes, thereby endowing the highly flexible receptors with a substantial enantio-discrimination.

Klarner F. G., Lobert M., Naatz U., Bandmann H., and Boese R. (2003) Synthesis and supramolecular properties of trimethylene-bridged clips. *Chemistry* **9**, 5036-5047.

Abstract: The novel trimethylene-bridged clips 3 and 4 have been synthesized by using repetitive stereoselective Diels-Alder reactions of the benzo- and naphthobismethylenenorbornenes 8 and 19 as dienes and norbornadiene 9 as bisdienophile, and subsequent dehydrogenation of the primary cyclobisadducts 10 and 20 by using 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Clips 3 and 4 serve as receptors for a variety of electron-deficient neutral and cationic aromatic substrates, comparable to the molecular tweezers 1 and 2. The thermodynamic parameters of the complex formation, K_a and ΔG , were determined by (¹H) NMR titration experiments and, in the case of the highly stable complex TCNB 32@4, by the use of isothermal titration microcalorimetry. The finding that clip 4 forms more stable complexes than 3 can be explained by the larger van der Waals contact surfaces of the naphthalene sidewalls in 4 compared to the corresponding benzene systems in 3. In the complexes with 4 as receptor, the plane of each aromatic substrate molecule is calculated to be oriented almost parallel to the naphthalene sidewalls. However, in the complexes of tweezers 2, the substrate is usually oriented parallel to the central naphthalene spacer unit. Due to the more open topology of 4, most complexes were calculated to consist of two or more equilibrating noncovalent conformers.

Lagaly G. and Dekany I. (2005) Adsorption on hydrophobized surfaces: Clusters and self-organization. *Adv Colloid Interface Sci* **114-115**, 189-204.

Abstract: The arrangement of liquid molecules on surfaces bristling with alkyl chains is deduced from adsorption studies, X-ray powder diffraction data, and microcalorimetric measurements of swelling-type layered materials, especially clay minerals. Small polar molecules such as water, ethanol, formamide, dimethylsulfoxide, and aromatic compounds are clustered between the alkyl chains pointing away from the surface. The energetic contribution related to the movement of the alkyl chains from direct contact with the surface atoms into upright positions is decisive. The importance of the interactions between the liquid molecules on the structure of the adsorption layer is clearly indicated by the changes of the adsorption layer thickness by salt addition. Thermodynamic data are obtained from surface excess adsorption isotherms from binary liquid mixtures combined with microcalorimetric measurements. Long-chain adsorptives such as long-chain alcohols interact with the surface alkyl chains by forming stable bimolecular films. These films undergo a series of higher-order phase transitions into kink- and gauche-block structures as the consequence of rotational isomerization of the alkyl chains. Such transitions are considered elementary processes in self-assembling films (layer-by-layer deposition, fuzzy films, Langmuir-Blodgett technique), and lipid membranes.

Lata S., Reichel A., Brock R., Tampe R., and Piehler J. (2005) High-affinity adaptors for switchable recognition of histidine-tagged proteins. *J Am Chem Soc* **127**, 10205-10215.

Abstract: We aspired to create chemical recognition units, which bind oligohistidine tags with high affinity and stability, as tools for selectively attaching spectroscopic probes and other functional elements to recombinant proteins. Several supramolecular entities containing 2-4 nitrilotriacetic acid (NTA) moieties were synthesized, which additionally contained an amino group, to which fluorescein was coupled as a sensitive reporter probe. These multivalent chelator heads (MCH) (termed bis-, tris-, and tetrakis-NTA) were characterized with respect to their interaction with hexahistidine (H6)- and decahistidine (H10)-tagged targets. Substantially increased binding stability with increasing number of NTA moieties was observed by analytical size exclusion chromatography. The binding enthalpies as determined by isothermal titration calorimetry increased nearly additively with the number of possible coordinative bonds between chelator heads and tags. Yet, a substantial excess of histidines in the oligohistidine tag was required for obtaining fully additive binding enthalpies. Dissociation kinetics of MCH/oligohistidine complexes measured by fluorescence dequenching showed an increase in stability by 4 orders of magnitude compared to that of mono-NTA, and subnanomolar affinity was reached for tris-NTA. The gain in free energy with increasing multivalency was accompanied by an increasing loss of entropy, which was ascribed to the high flexibility of the binding partners. Numerous applications of these MCHs for noncovalent, high affinity, yet reversible tethering of spectroscopic probes and other functional elements to the recombinant proteins can be envisioned.

Laugel N., Betscha C., Winterhalter M., Voegel J. C., Schaaf P., and Ball V. (2006) Relationship between the growth regime of polyelectrolyte multilayers and the polyanion/polycation complexation enthalpy. *J Phys Chem B Condens Matter Mater Surf Interfaces Biophys* **110**, 19443-19449.

Abstract: The alternate deposition of polyanions and polycations leads to the formation of films called polyelectrolyte multilayer films (PEMs). Two types of growth processes are reported in the literature, leading to films that grow either linearly or exponentially with the number of deposition steps. In this article we try to establish a correlation between the nature of the growth process and the heat of complexation between the polyanions and the polycations constituting the PEM film. Isothermal titration microcalorimetry experiments performed on several polyanion/polycation systems seem to indicate that an endothermic complexation process is characteristic of an exponential film growth, whereas a strongly exothermic process corresponds to a linear growth regime. Finally, weakly exothermic processes seem to be associated with weakly exponentially growing films. These results thus show that exponentially growing processes are mainly driven by entropy. This explains why the exponential growth processes are more sensitive to temperature than the linear growing processes. This temperature sensitivity is shown on the poly-L-glutamic acid/poly(allylamine) system which grows either linearly or exponentially depending on the ionic strength of the polyelectrolyte solutions.

Lee C. H., Lee J. S., Na H. K., Yoon D. W., Miyaji H., Cho W. S., and Sessler J. L. (2005) Cis- and trans-strapped calix[4]pyrroles bearing phthalamide linkers: synthesis and anion-binding properties. *J Org Chem* **70**, 2067-2074.

Abstract: [reaction: see text] New cis-strapped calix[4]pyrrole derivatives 12, 13, and 19 and trans-strapped systems 14 and 15 bearing isophthalate-derived diamide spacers linked to the tetrapyrrolic core have been synthesized and characterized by spectroscopic means. The anion-binding behavior of these receptors was investigated by proton NMR spectroscopy and isothermal titration calorimetry (ITC). A 2:1 binding stoichiometry was observed under the conditions of NMR analysis but not at the lower concentration regime used for ITC. As gauged from both sets of analyses, these new strapped systems display affinities for halide anions that are enhanced compared to those of normal, unstrapped calix[4]pyrrole. However, contrary to expectations, no size-dependent selectivity for anions is observed as the length of the bridging strap is varied. Such results are interpreted in terms of anion-binding processes that occur outside the central pocket defined by the strap but that still favor strong associations as the result of the increased number of hydrogen-bonding donors the amide groups provide.

Lee C. H., Na H. K., Yoon D. W., Won D. H., Cho W. S., Lynch V. M., Shevchuk S. V., and Sessler J. L. (2003) Single side strapping: a new approach to fine tuning the anion recognition properties of calix[4]pyrroles. *J Am Chem Soc* **125**, 7301-7306.

Abstract: Three calix[4]pyrroles bearing m-orninol-derived diether straps of different lengths on one side

of the tetrapyrrolic core have been synthesized and characterized. Structural information for an analogous diester bridged strapped system reported previously (Yoon, D. W.; Hwang, H.; Lee, C. H. *Angew. Chem., Int. Ed. Engl.* 2002, 41, 1757-1759) is also provided as are bromide and chloride anion affinities for all four systems determined by Isothermal Titration Calorimetry (ITC) in acetonitrile. Although both sets of the strapped calix[4]pyrroles displayed enhanced affinities for chloride and bromide anion, differences were seen among the various receptors that support the conclusion that the anion binding ability of calixpyrrole-type systems can be effectively tuned by modifying the length and nature of the bridging straps. In the specific case of the diether systems, the largest chloride affinity was seen with the shortest strap, whereas the largest affinity for bromide anion was recorded in the case of the longest strap. On the basis of these findings, as well as supporting ^1H NMR spectroscopic studies, it is postulated that not only cavity size per se, but also the ability of the aryl portion of the strap to serve as a CH hydrogen bond donor site are important in regulating the observed anion affinities.

Li N., Zhang S., Zheng L., Gao Y. and Yu L. (2008) Second virial coefficient of bmimBF₄/triton X-100/cyclohexane ionic liquid microemulsion as investigated by microcalorimetry. *Langmuir* **24**, 2973-2976.

Abstract: The second virial coefficient of the ionic liquid (IL) microemulsion was obtained for the first time using microcalorimetry. The heat of dilution of the microemulsion solutions was measured by isothermal titration microcalorimetry (ITC), and the second virial coefficient was derived from the heat of dilution and the number density of the IL microemulsion solutions on the basis of a hard-sphere interaction potential assumption and as a function of the second-order polynomial. The validity of the second virial coefficient was confirmed by the percolation behavior of different ionic liquid microemulsion solutions of Triton X-100 in cyclohexane with or without added salts. The information obtained from the second virial coefficient shows that the interactions between ionic liquid microemulsion droplets are much stronger than those for traditional microemulsions, which may be attributed to the relatively larger size of the microemulsion droplets

Li X., Zhu X. Q., Zhang F., Wang X. X. and Cheng J. P. (2008) Establishment of heterolytic and homolytic Y-NO₂ bond dissociation energy scales of nitro-containing compounds in acetonitrile: chemical origin of NO₂ release and capture. *J Org. Chem* **73**, 2428-2431.

Abstract: The first heterolytic and homolytic N(O)-NO(2) bond dissociation energy scales of three types Y-nitro (Y = N, O) compounds and corresponding radical anions in acetonitrile were established by using titration calorimetry combined with relevant electrochemical data through proper thermodynamic cycles

Li X., Wettig S. D., and Verrall R. E. (2005) Isothermal titration calorimetry and dynamic light scattering studies of interactions between gemini surfactants of different structure and Pluronic block copolymers. *J Colloid Interface Sci* **282**, 466-477.

Abstract: The interactions between triblock copolymers of poly(ethylene oxide) and poly(propylene oxide), P103 and F108, EO(n)PO(m)EO(n), m=56 and n=17 and 132, respectively, and m-s-m type gemini surfactants, m=8, 10, 12, and 18, and s = 3, 6, 12, and 16, have been studied in aqueous solution using isothermal titration calorimetry and dynamic light scattering techniques. The enthalpograms of F108 as a function of surfactant concentration show one broad peak at polymer concentrations C(p)0.50 wt%, below the cmc of the copolymer at 25 degrees C. It is attributed to interactions between the surfactant and the triblock copolymer monomer. DLS results show hydrodynamic radii (R(h)) initially consistent with copolymer monomers that change to values consistent with gemini surfactant micelles as the surfactant concentration is increased. In P103 solutions at C(p)0.05 wt%, two peaks appear in the enthalpograms, and they are attributed to the interactions between the gemini surfactant and the micelle or monomer forms of the copolymer. An origin-based nonlinear fitting program was employed to deconvolute the two peaks and to obtain estimates of peak properties. An estimate of the fraction of copolymer in aggregated form was also obtained. The enthalpy change due to interactions between the surfactants and P103 aggregates is very large compared to values obtained for traditional surfactants. This suggests that extensive reorganization of copolymer aggregates and surrounding solvent occurs during the interaction. DLS results for the P103 systems containing C(p)0.05% show evidence of very large aggregates in solution, likely P103 micelle clusters. The transitions observed in the hydrodynamic radii are consistent with a breakdown of micelle clusters with addition of gemini surfactant, followed by mixed micelle formation and/or deaggregation into monomer P103. This is followed by interactions similar to those typically observed in surfactant-nonionic polymer systems. Mechanisms for the interaction and the observed structural changes are discussed.

Liaw C. C., Yang Y. L., Chen M., Chang F. R., Chen S. L., Wu S. H. and Wu Y. C. (2008) Mono-tetrahydrofuran annonaceous acetogenins from *Annona squamosa* as cytotoxic agents and calcium ion chelators. *J Nat. Prod.* **71**, 764-771.

Abstract: Eight new mono-tetrahydrofuran (THF)-type annonaceous acetogenins, squafosacins B, C, F, and G (1-4), squadiolins A-C (5-7), and cis-annotemoyin-1 (8), as well as eight known annonaceous acetogenins, glabranin, annotemoyins-1 and -2, bullatencin, cis-bullatencin, and uvariamicins-I, -II, and -III, were isolated from the seeds of *Annona squamosa* by HPLC. The structures of all new isolates were elucidated by using spectroscopic and chemical methods. Squadiolins A (5) and B (6) showed ng/mL potency against human Hep G2 hepatoma cells and significant cytotoxic activity against human MDA-MB-231 breast cancer cells. Squafosacin B (1) also exhibited significant cytotoxic activity against human Hep G2 and 3B hepatoma and MCF-7 breast cancer cells. In addition, the chelation of mono-THF acetogenins with calcium ions was investigated using isothermal titration calorimetry

Lin C., Simov V. and Drucekhammer D. G. (2007) Interaction of halide and carboxylate ions with 4,5-diacetamidoacridine-9(10H)-one: thermodynamics of association and deprotonation events. *J Org. Chem* **72**, 1742-1746.

Abstract: 4,5-Diacetamidoacridine-9(10H)-one was prepared, and its interactions with halide and benzoate anions were studied using a combination of NMR, fluorescence, and isothermal titration calorimetry experiments. Whereas chloride and bromide exhibited simple association, both fluoride and benzoate exhibited initial entropy-driven association followed by an enthalpically favorable deprotonation of the receptor by a second equivalent of the anion.

Linton B. R., Goodman M. S., Fan E., van Arman S. A., and Hamilton A. D. (2001) Thermodynamic aspects of dicarboxylate recognition by simple artificial receptors. *J Org Chem* **66**, 7313-7319.

Abstract: Recognition of dicarboxylates by bis-functional hydrogen-bonding receptors displays divergent thermodynamics in different solvent systems. NMR titration and isothermal titration calorimetry indicated that neutral bis-urea and bis-thiourea receptors form exothermic complexes with dicarboxylates in DMSO, with a near zero entropic contribution to binding. The increased binding strength of bis-guanidinium receptors precluded quantitative measurement of binding constants in DMSO, but titration calorimetry offered a qualitative picture of the association. Formation of these 1:1 complexes was also exothermic, but additional endothermic events occurred at both lower and higher host-guest ratios. These events indicated multiple binding equilibria but did not always occur at a discrete 2:1 or 1:2 host-guest molar ratio, suggesting higher aggregates. With increasing amounts of methanol as solvent, bis-guanidinium receptors form more endothermic complexes with dicarboxylates, with a favorable entropy of association. This switch from association driven by enthalpy to one driven by entropy may reflect a change from complexation involving the formation of hydrogen bonds to that promoted by solvent liberation from binding sites.

Liu Y. and Sturtevant J. M. (1995) Significant discrepancies between van't Hoff and calorimetric enthalpies. II. *Protein Sci* **4**, 2559-2561.

Abstract: Isothermal calorimetric titration of 18-crown-6 ether with BaCl₂ in pure aqueous solution over the temperature range 7-40 degrees C gives precise binding constants and enthalpy changes. Nonlinear least-squares fitting of the binding constants to the integrated van't Hoff equation, including a temperature-independent change in heat capacity, leads to van't Hoff enthalpies that differ significantly from the observed calorimetric enthalpies. This perplexing discrepancy appears at present to be very widely occurring.

Liu Y., Guo D. S., Zhang H. Y., Ma Y. H., and Yang E. C. (2006) The structure and thermodynamics of calix[n]arene complexes with dipyridines and phenanthroline in aqueous solution studied by microcalorimetry and NMR spectroscopy. *J Phys Chem B Condens Matter Mater Surf Interfaces Biophys* **110**, 3428-3434.

Abstract: The complex stability constants (K(S)) and thermodynamic parameters (DeltaH degrees and TDeltaS degrees) for 1:1 intermolecular complexation of three water-soluble calixarenes, that is, p-sulfonato calix[4]arene (C4AS), p-sulfonato thiacalix[4]arene (TCAS), and p-sulfonato calix[5]arene (C5AS), with dipyridines (4-DPD and 2-DPD) and 1,10-phenanthroline (Phen) have been determined by means of titration microcalorimetry in an acidic buffer solution (pH = 2.0) at 298.15 K, and their binding

modes have been investigated by ^1H NMR and 2D ROESY NMR spectroscopy. The results obtained indicate that 4-DPD, 2-DPD, and Phen are included in the cavity of C5AS with the different patterns, this is, accumbent for 4-DPD, acclivitous for 2-DPD and Phen, while Phen is included upright in the cavity of C4AS. The $K(S)$ values decrease with increasing cavity size of host molecules but enhance with extending conjugation degree of guest molecules, and thus C4AS exhibits an exceptionally high Phen/4-DPD selectivity of 22.5. Thermodynamically, the complexation of DPDs/Phen with the water-soluble calixarenes is obviously enthalpy-driven, but the molecular selectivity is mainly governed by the entropy term.

Liu Y., Ma Y. H., Chen Y., Guo D. S., and Li Q. (2006) Molecular recognition thermodynamics of pyridine derivatives by sulfonatocalixarenes at different pH values. *J Org Chem* **71**, 6468-6473.

Abstract: The complex stability constants ($K(a)$) and thermodynamic parameters (ΔG degrees, ΔH degrees, and $T\Delta S$ degrees) for 1:1 complexation of water-soluble calix[4]arene, thiacalix[4]arene, and calix[5]arene sulfonates with pyridine and their methylated derivatives have been determined by means of isothermal titration calorimetry at pH 2.0 and 7.2 at 298.15 K, and their binding modes have been investigated by NMR spectroscopy. The results obtained show that sulfonatocalixarenes afford stronger binding ability toward pyridine guests at pH 2.0, attributable to the positive electrostatic interactions and the more extensive desolvation effects, but present higher molecular selectivity at pH 7.2 owing to the strengthened C-H... π interactions. The pH-responsible binding ability and molecular selectivity are discussed from the viewpoint of electrostatic, π -stacking, van der Waals interactions and size-fit relationship between host and guest. A close comparison further demonstrates that the C-H... π interactions and van der Waals interactions play a more important role than π ... π interactions in the present inclusion complexation.

Macedo J. S., Costa Junior N. B., Almeida L. E., Vieira E. F., Cestari A. R., Gimenez I. F., Villarreal Carreno N. L., and Barreto L. S. (2006) Kinetic and calorimetric study of the adsorption of dyes on mesoporous activated carbon prepared from coconut coir dust. *J Colloid Interface Sci* **298**, 515-522.

Abstract: Mesoporous activated carbon has been prepared from coconut coir dust as support for adsorption of some model dye molecules from aqueous solutions. The methylene blue (MB) and remazol yellow (RY) molecules were chosen for study of the adsorption capacity of cationic and anionic dyes onto prepared activated carbon. The adsorption kinetics was studied with the Lagergren first- and pseudo-second-order kinetic models as well as the intraparticle diffusion model. The results for both dyes suggested a multimechanism sorption process. The adsorption mechanisms in the systems dyes/AC follow pseudo-second-order kinetics with a significant contribution of intraparticle diffusion. The samples simultaneously present acidic and basic sites able to act as anchoring sites for basic and acidic dyes, respectively. Calorimetric studies reveal that dyes/AC interaction forces are correlated with the pH of the solution, which can be related to the charge distribution on the AC surface. These AC samples also exhibited very short equilibrium times for the adsorption of both dyes, which is an economically favorable requisite for the activated carbon described in this work, in addition to the local abundance of the raw material.

Majhi P. R., Moulik S. P., Burke S. E., Rodgers M., and Palepu R. (2001) Physicochemical Investigations on the Interaction of Surfactants and Salts with Polyvinylpyrrolidone in Aqueous Medium. *J Colloid Interface Sci* **235**, 227-234.

Abstract: Microcalorimetric investigations have been carried out on the interaction of the surfactants sodium cholate, sodium deoxycholate, tetradecyltrimethylammonium bromide, cetyl(hexadecyl)trimethylammonium bromide, and p-tert-octylphenoxy polyoxy-ethylene ether (Triton X-100) and the salts potassium iodide, sodium benzoate, sodium bromide, and sodium salicylate with the neutral polymer polyvinylpyrrolidone (PVP). The enthalpy of dilution of the surfactants has been measured in the absence and presence of the polymer and the results are compared to determine the effect of PVP on the micellization of the surfactants and the energetics of the process. As well, the micellization activity of the surfactants in the presence of the polymer has been studied by conductometric and fluorimetric methods. The enthalpy of dilution of the salts has been measured to provide an understanding of the nature and magnitude of their interaction with PVP. Copyright 2001 Academic Press.

Matulis D. (2001) Thermodynamics of the hydrophobic effect. III. Condensation and aggregation of alkanes, alcohols, and alkylamines. *Biophys Chem* **93**, 67-82.

Abstract: Knowledge of the energetics of the low solubility of non-polar compounds in water is critical for

the understanding of such phenomena as protein folding and biomembrane formation. Solubility in water can be considered as one leg of the three-part thermodynamic cycle - vaporization from the pure liquid, hydration of the vapor in aqueous solution, and aggregation of the substance back into initial pure form as an immiscible phase. Previous studies on the model compounds n-alkanes, 1-alcohols, and 1-aminoalkanes have noted that the thermodynamic parameters (Gibbs free energy, ΔG ; enthalpy, ΔH ; entropy, ΔS ; and heat capacity, ΔC_p) associated with these three processes are generally linear functions of the number of carbons in the alkyl chains. Here we assess the accuracy and limitations of the assumption of additivity of CH(2) group contributions to the thermodynamic parameters for vaporization, hydration, and aggregation. Processes of condensation from pure gas to liquid and aqueous solution to aggregate are compared. Hydroxy, amino, and methyl headgroup contributions are estimated, liquid and solid aggregates are distinguished. Most data in the literature were obtained for compounds with short aliphatic hydrocarbon tails. Here we emphasize long aliphatic chain behavior and include our recent experimental data on long chain alkylamine aggregation in aqueous solution obtained by titration calorimetry and van't Hoff analysis. Contrary to what is observed for short compounds, long aliphatic compound aggregation has a large exothermic enthalpy and negative entropy.

Matulis D. and Bloomfield V. A. (2001) Thermodynamics of the hydrophobic effect. II. Calorimetric measurement of enthalpy, entropy, and heat capacity of aggregation of alkylamines and long aliphatic chains. *Biophys Chem* **93**, 53-65.

Abstract: The thermodynamics of long aliphatic chain alkylamine aggregation in aqueous solution was studied by isothermal titration calorimetry (ITC). Protonated alkylammonium cations with linear aliphatic chains of 10-14 carbon atoms were fully soluble in aqueous solution at the beginning of titration, but practically insoluble after deprotonation by titrating with sodium hydroxide. The alkylamines aggregated and precipitated during the reaction, enabling direct measurement of the enthalpy of aggregation. The enthalpy of aggregation became increasingly exothermic upon increasing the chain length. Hydrophobic aggregation was enthalpy-driven and entropy-opposed for alkylamines with 12-14 carbon atoms at room temperature. Direct observation of hydrophobic aggregation by ITC at constant temperature and pressure provided more accurate thermodynamic parameters than obtainable from van't Hoff analysis. Aggregation into liquid or solid phases could be distinguished by ITC, but not by van't Hoff analysis of alkylamine solubility data.

McDonough J. E., Weir J. J., Carlson M. J., Hoff C. D., Kryatova O. P., Rybak-Akimova E. V., Clough C. R., and Cummins C. C. (2005) Solution calorimetric and stopped-flow kinetic studies of the reaction of $^*Cr(CO)_3C_5Me_5$ with PhSe-SePh and PhTe-TePh. Experimental and theoretical estimates of the Se-Se, Te-Te, H-Se, and H-Te bond strengths. *Inorg Chem* **44**, 3127-3136.

Abstract: The kinetics of the oxidative addition of PhSeSePh and PhTeTePh to the stable 17-electron complex $^*Cr(CO)_3C_5Me_5$ have been studied utilizing stopped-flow techniques. The rates of reaction are first-order in each reactant, and the enthalpy of activation decreases in going from Se ($\Delta H(\text{double dagger}) = 7.0 \pm 0.5$ kcal/mol, $\Delta S(\text{double dagger}) = -22 \pm 3$ eu) to Te ($\Delta H(\text{double dagger}) = 4.0 \pm 0.5$ kcal/mol, $\Delta S(\text{double dagger}) = -26 \pm 3$ eu). The kinetics of the oxidative addition of PhSeH and $^*Cr(CO)_3C_5Me_5$ show a change in mechanism in going from low (overall third-order) to high (overall second-order) temperatures. The enthalpies of the oxidative addition of PhE-EPh to $^*Cr(CO)_3C_5Me_5$ in toluene solution have been measured and found to be -29.6, -30.8, and -28.9 kcal/mol for S, Se, and Te, respectively. These data are combined with enthalpies of activation from kinetic studies to yield estimates for the solution-phase PhE-EPh bond strengths of 46, 41, and 33 kcal/mol for E = S, Se, and Te, respectively. The corresponding Cr-EPh bond strengths are 38, 36, and 31 kcal/mol. Two methods have been used to determine the enthalpy of hydrogenation of PhSeSePh in toluene on the basis of reactions of HSPH and HSePh with either $^*Cr(CO)_3C_5Me_5$ or 2-pyridine thione. These data lead to a thermochemical estimate of 72 kcal/mol for the PhSe-H bond strength in toluene solution, which is in good agreement with kinetic studies of H atom transfer from HSePh at higher temperatures. The reaction of H-Cr(CO)₃C₅Me₅ with PhSe-SePh is accelerated by the addition of a Cr radical and occurs via a rapid radical chain reaction. In contrast, the reaction of PhTe-TePh and H-Cr(CO)₃C₅Me₅ does not occur at any appreciable rate at room temperature, even in the presence of added Cr radicals. This is in keeping with a low PhTe-H bond strength blocking the chain and implies that H-TePh \leq 63 kcal/mol. Structural data are reported for PhSe-Cr(CO)₃C₅Me₅ and PhS-Cr(CO)₃C₅Me₅. The two isostructural complexes do not show signs of an increase in steric strain in terms of metal-ligand bonds or angles as the Cr-EPh bond is shortened in going

from Se to S. Bond strength estimates of the PhE-H and PhE-EPh derived from density functional theory calculations are in reasonable agreement with experimental data for E = Se but not for E = Te. The nature of the singly occupied molecular orbital of the *EPh radicals is calculated to show increasing localization on the chalcogenide atom in going from S to Se to Te.

Meister A., Drescher S., Mey I., Wahab M., Graf G., Garamus V. M., Hause G., Mogel H. J., Janshoff A., Dobner B. and Blume A. (2008) Helical nanofibers of self-assembled bipolar phospholipids as template for gold nanoparticles. *J Phys. Chem B* **112**, 4506-4511.

Abstract: Bipolar phospholipids (bolalipids) represent an exciting class of amphiphilic molecules as they self-assemble in water to distinct structures of nanoscopic dimensions. Reported here are structural details of helical nanofibers, composed of achiral, symmetrical single-chain bolalipids with phosphocholine headgroups. These nanofibers are used as template for the fixation of gold nanoparticles (AuNPs) without prior functionalization. This realization of a metal array on bolalipid nanofibers is one of the rare examples of one-dimensional AuNP arrangements in solution. The loading and the heat of binding of AuNPs are determined applying transmission electron microscopy and isothermal titration calorimetry

Miguirditchian M., Guillauneux D., Guillaumont D., Moisy P., Madic C., Jensen M. P., and Nash K. L. (2005) Thermodynamic study of the complexation of trivalent actinide and lanthanide cations by ADPTZ, a tridentate N-donor ligand. *Inorg Chem* **44**, 1404-1412.

Abstract: To better understand the bonding in complexes of f-elements by polydentate N-donor ligands, the complexation of americium(III) and lanthanide(III) cations by 2-amino-4,6-di-(pyridin-2-yl)-1,3,5-triazine (ADPTZ) was studied using a thermodynamic approach. The stability constants of the 1:1 complexes in a methanol/water mixture (75/25 vol %) were determined by UV-visible spectrophotometry for every lanthanide(III) ion (except promethium), and yttrium(III) and americium(III) cations. The thermodynamic parameters (ΔH degrees, ΔS degrees) of complexation were determined from the temperature dependence of the stability constants and by microcalorimetry. The trends of the variations of ΔG degrees, ΔH degrees, and ΔS degrees across the lanthanide series are compared with published results for other tridentate ligands and confirm strongly ionic bonding in the lanthanide-ADPTZ complexes. Comparison of the thermodynamic properties between the Am- and Ln-ADPTZ complexes highlights an increase in stability of the complexes by a factor of 20 in favor of the americium cation. This difference arises from a more exothermic reaction enthalpy in the case of Am, which is correlated with a greater degree of covalency in the americium-nitrogen bonds. Quantum chemistry calculations performed on a series of trivalent actinide and lanthanide-ADPTZ complexes support the experimental results, showing a slightly greater covalence in the actinide-ligand bonds that originates from a charge transfer from the ligand sigma orbitals to the 5f and 6d orbitals of the actinide ion.

Miki K., Westh P. and Koga Y. (2008) Interactions of Na-salts and 1-propanol in 1-propanol-Na-Salt-H₂O systems: toward an understanding the Hofmeister series (IV). *J Phys. Chem B* **112**, 4680-4686.

Abstract: The excess chemical potential of 1-propanol (1P), μ_{E1P} , was evaluated in ternary 1P-Na-salt(S)-H₂O at 25 degrees C. The counter anions of the Na-salts studied are SO₄²⁻, F⁻, Cl⁻, I⁻, and ClO₄⁻. The effect of the anion on μ_{E1P} follows the Hofmeister ranking, in that the more kosmotropic ions make the μ_{E1P} value more positive. We then evaluate the effect of the Na-salt (S) on μ_{E1P} , the 1P-S interaction in terms of excess chemical potential, at a semi-infinite dilution. The results indicate that the 1P-S interaction in terms of excess chemical potential is unfavorable (repulsive) for all of the ions studied. The degree of repulsive interaction decreases in the order of the Hofmeister ranking from the kosmotropic to the chaotropic end. Namely, salting-out samples make the excess part of the chemical potential of 1P more unfavorable, while the salting-in counterparts make it less unfavorable. From earlier calorimetric studies on the same ternary systems, the enthalpic 1P-S interaction function, HE_{1P-S} , was calculated. Hence, the entropy analogue, S_{1P-S} , was also obtained, and a detailed thermodynamic signature of 1P-S interactions became available. This revealed that both HE_{1P-S} and SE_{1P-S} decrease from the kosmotropic ion to the middle of the ranking (Cl⁻), whereupon they turn to increase toward the chaotropic end. Hence, the build up of unfavorable 1P-S interactions in Hofmeister salts (signified by μ_{E1P}) relies on a pronounced enthalpy-entropy compensation, which must be accounted for in attempts to understand the molecular mechanisms underpinning Hofmeister effects

Mizoue L. S. and Tellinghuisen J. (2004) Calorimetric vs. van't Hoff binding enthalpies from isothermal titration calorimetry: Ba²⁺-crown ether complexation. *Biophys Chem* **110**, 15-24.

Abstract: The 1:1 complexation reaction between Ba²⁺ and 18-crown-6 ether is re-examined using isothermal titration calorimetry (ITC), with the goal of clarifying previously reported discrepancies between reaction enthalpies estimated directly (calorimetric) and indirectly, from the temperature dependence of the reaction equilibrium constant K (van't Hoff). The ITC thermograms are analyzed using three different non-linear fit models based on different assumptions about the data error: constant, proportional to the heat and proportional but correlated. The statistics of the fitting indicate a preference for the proportional error model, in agreement with expectations for the conditions of the experiment, where uncertainties in the delivered titrant volume should dominate. With attention to proper procedures for propagating statistical error in the van't Hoff analysis, the differences between ΔH_{cal} and ΔH_{vH} are deemed statistically significant. In addition, statistically significant differences are observed for the ΔH_{cal} estimates obtained for two different sources of Ba²⁺, BaCl₂ and Ba(NO₃)₂. The effects are tentatively attributed to deficiencies in the standard procedure in ITC of subtracting a blank obtained for pure titrant from the thermogram obtained for the sample.

Monteiro O. A., Jr. and Airoidi C. (2005) The influence of chitosans with defined degrees of acetylation on the thermodynamic data for copper coordination. *J Colloid Interface Sci* **282**, 32-37.

Abstract: The interaction of copper with three different chitosans having degrees of deacetylation of 77.5, 81.5, and 86.1%, named C, A, and F, respectively, was followed by the batch method at 298 \pm 1K and the values obtained were fitted to a modified Langmuir equation. These interactions were also obtained by calorimetric titration. Experimentally, 50.0 mg of each chitosan was suspended in doubly distilled water at 298.15 \pm 0.02K under mechanical turbine stirring. The titration was performed by adding increments of 10 μ mol of a 0.10 mol dm⁻³ Cu(NO₃)₂ aqueous solution and the calorimetric isotherms obtained were adjusted to a modified Langmuir equation. From the net thermal effects K and ΔH values were calculated, also permitting the acquisition of other thermodynamic data for the chitosan-copper interaction at the solid/liquid interface. The exothermic enthalpic values of -45.65 \pm 1.97, -49.91 \pm 1.57, and -48.64 \pm 0.82 kJ mol⁻¹, for chitosans C, A, and F, respectively, reflect the degree of deacetylation. The spontaneity of the systems is shown by the negative ΔG values, -36.1 \pm 0.2, 36.8 \pm 0.1, and -38.1 \pm 0.3 kJ mol⁻¹ for the same sequence of chitosans. The negative entropic values, -34, -44, and -35 J mol⁻¹ K⁻¹, are in agreement with an ordering of solvent as the complexation occurred. The intensity of the thermal effects and the thermodynamic data obtained from the copper/chitosan interactions can be associated with the ability of these biopolymers to extract copper from aqueous solutions.

Monteiro O. A., Jr. and Airoidi C. (1999) Some Thermodynamic Data on Copper-Chitin and Copper-Chitosan Biopolymer Interactions. *J Colloid Interface Sci* **212**, 212-219.

Abstract: Chitin and chitosan are good removers of cations from aqueous solution and wastewater. The interactive effect of cation with both biopolymers in aqueous medium was studied by the batch method at 298 \pm 1 K. The results were fitted to the modified Langmuir equation. The same adsorption was followed by calorimetric titration. In this process, 50.0 mg of each polymer was suspended in 19.0 cm³ of bidistilled water at 298.15 \pm 0.02 K, maintained under mechanical turbine stirring. The titration was performed by adding increments of 10 μ L of 0.10 mol dm⁻³ Cu(NO₃)₂ aqueous solution to the system. The resulting isotherm was also adjusted to a modified Langmuir equation. From the thermal effects K and ΔH values were determined, enabling the calculation of ΔG and ΔS for the interaction of copper cations with chitin and chitosan, giving the enthalpic values of -19.85 \pm 0.34 and -41.27 \pm 1.57 kJ mol⁻¹, respectively. The spontaneity of this interaction is shown from ΔG values of -35.9 \pm 0.1 and -36.8 \pm 0.1 kJ mol⁻¹, which are followed by ΔS values of +54 and of -15 J mol⁻¹K⁻¹, respectively. The complexation is probably associated with the lack of order of the chitin polymeric chain or with the freedom of water molecules initially bonded to cations. The copper ion is coordinated to the pendant groups of the polymeric chain to form stable complexes. Copyright 1999 Academic Press.

Morel J. P. and Morel-Desrosiers N. (2006) Binding of monovalent metal cations by the p-sulfonatocalix[4]arene: experimental evidence for cation- π interactions in water. *Org Biomol Chem* **4**, 462-465.

Abstract: Gibbs free energies, enthalpies and entropies for the binding of Na⁺, K⁺, Rb⁺, Cs⁺, Ag⁺, Tl⁺

and NH_4^+ by the p-sulfonatocalix[4]arene in water are determined by microcalorimetry. Whereas no significant heat effect is detected with Na^+ or Ag^+ , suggesting that these cations are not complexed, weak but selective binding is observed with the other cations. The whole set of thermodynamic parameters, which demonstrate that the cations bind inside the cavity of the calixarene, evidence the importance of the cation- π interactions for these complexes in water.

Morel J. P., Marmier N., Hurel C., and Morel-Desrosiers N. (2006) Effect of temperature on the acid-base properties of the alumina surface: microcalorimetry and acid-base titration experiments. *J Colloid Interface Sci* **298**, 773-779.

Abstract: Sorption reactions on natural or synthetic materials that can attenuate the migration of pollutants in the geosphere could be affected by temperature variations. Nevertheless, most of the theoretical models describing sorption reactions are at 25 degrees C. To check these models at different temperatures, experimental data such as the enthalpies of sorption are thus required. Highly sensitive microcalorimeters can now be used to determine the heat effects accompanying the sorption of radionuclides on oxide-water interfaces, but enthalpies of sorption cannot be extracted from microcalorimetric data without a clear knowledge of the thermodynamics of protonation and deprotonation of the oxide surface. However, the values reported in the literature show large discrepancies and one must conclude that, amazingly, this fundamental problem of proton binding is not yet resolved. We have thus undertaken to measure by titration microcalorimetry the heat effects accompanying proton exchange at the alumina-water interface at 25 degrees C. Based on (i) the surface sites speciation provided by a surface complexation model (built from acid-base titrations at 25 degrees C) and (ii) results of the microcalorimetric experiments, calculations have been made to extract the enthalpic variations associated respectively to first and second deprotonation of the alumina surface. Values obtained are $\Delta H_1 = 80 \pm 10 \text{ kJ mol}^{-1}$ and $\Delta H_2 = 5 \pm 3 \text{ kJ mol}^{-1}$. In a second step, these enthalpy values were used to calculate the alumina surface acidity constants at 50 degrees C via the van't Hoff equation. Then a theoretical titration curve at 50 degrees C was calculated and compared to the experimental alumina surface titration curve. Good agreement between the predicted acid-base titration curve and the experimental one was observed.

Naka K., Fujita M., Tanaka K. and Chujo Y. (2007) Water-soluble anionic POSS-core dendrimer: synthesis and copper(II) complexes in aqueous solution. *Langmuir* **23**, 9057-9063.

Abstract: A carboxylic acid-terminated polyhedral oligosilsesquioxane (POSS)-core dendrimer (POSS-CO₂H) was synthesized from octa(3-ammoniumpropyl)octasilsesquioxane octachloride (POSS-NH₃⁺) via a t-butyl ester-terminated POSS-core dendrimer that was prepared from neutralized POSS-NH₃⁺ and t-butyl acrylate. Complexing properties of the sodium salts of POSS-CO₂H (POSS-CO₂Na) with Cu²⁺ were studied in comparison with those of the G1.5 poly(amidoamine) (PAMAM) dendrimer (G1.5-CO₂Na) by spectroscopic approach and isothermal titration calorimetry. In the case of G1.5-CO₂Na, Cu²⁺-N₄ and Cu²⁺-N₂O₂ complexes are possible coordination modes, and only a Cu²⁺-N₂O₂ complex can be formed for POSS-CO₂Na. In the case of POSS-CO₂Na, upon increasing the concentration of Cu²⁺, the values of the binding constants decreased. However, the values of binding constants in the regions of the Cu²⁺-N₂O₂ coordination mode for G1.5-CO₂Na increased with increasing concentration of Cu²⁺. This observation suggests that the uptake of Cu²⁺ is inhibited by increasing binding numbers of Cu²⁺ due to the rigid structure of the POSS-core dendrimer.

Nakamura S. and Kidokoro S. (2005) Direct observation of the enthalpy change accompanying the native to molten-globule transition of cytochrome c by using isothermal acid-titration calorimetry. *Biophys Chem* **113**, 161-168.

Abstract: The enthalpy change accompanying the reversible acid-induced transition from the native (N) to the molten-globule (MG) state of bovine cytochrome c was directly evaluated by isothermal acid-titration calorimetry (IATC), a new method for evaluating the pH dependence of protein enthalpy. The enthalpy change was 30 kJ/mol at 30 degrees C, pH 3.54, with 500 mM KCl. The results of the global analysis of the temperature dependence of the excess enthalpy from 20 to 35 degrees C demonstrated that the N to MG transition is a two-state transition with a small heat capacity change of 1.1 kJ K⁻¹ mol⁻¹. The present findings were also indicative of the pH dependence of the enthalpy and the heat capacity of the MG state, -13 kJ mol⁻¹ pH⁻¹ and -1.0 kJ K⁻¹ mol⁻¹ pH⁻¹, respectively, at 30 degrees C within a pH range from 2 to 3.

Nativi C., Cacciarini M., Francesconi O., Moneti G. and Roelens S. (2007) A beta-mannoside-selective pyrrolic tripodal receptor. *Org. Lett* **9**, 4685-4688.

Abstract: Acetalic substituents strategically located in a pyrrolic tripodal structure provide a new synthetic receptor endowed with unprecedented affinity for mannosides and the highest selectivity for beta-mannose ever reported for synthetic H-bonding receptors. Binding properties have been determined by NMR, ITC, and ESI-MS techniques, while affinities have been univocally assessed by the BC50(0) parameter, a general descriptor of binding affinity.

Nativi C., Cacciarini M., Francesconi O., Vacca A., Moneti G., Ienco A. and Roelens S. (2007) Pyrrolic tripodal receptors effectively recognizing monosaccharides. Affinity assessment through a generalized binding descriptor. *J Am. Chem Soc.* **129**, 4377-4385.

Abstract: Pyrrolic and imino (3) or amino (4) H-bonding ligands were incorporated into a benzene-based tripodal scaffold to develop a new generation of receptors for molecular recognition of carbohydrates. Receptors 3 and 4 effectively bound a set of octylglycosides of biologically relevant monosaccharides, including glucose (Glc), galactose (Gal), mannose (Man), and N-acetyl-glucosamine (GlcNAc), showing micromolar affinities in CDCl₃ and millimolar affinities in CD₃CN by NMR titrations. Both receptors selectively recognized Glc among the investigated monosaccharides, with 3 generally less effective than 4 but showing selectivities for the all-equatorial beta-glycosides of Glc and GlcNAc among the largest reported for H-bonding synthetic receptors. Selectivities in CDCl₃ spanned a range of nearly 250-fold for 3 and over 30-fold for 4. Affinities and selectivities were univocally assessed through the BC50 descriptor, for which a generalized treatment is described that extends the scope of the descriptor to include any two-reagent host-guest system featuring any number of binding constants. ITC titrations of betaGlc in acetonitrile evidenced, for both receptors, a strong enthalpic contribution to the binding interaction, suggesting multiple H bonding. Selectivity trends toward alphaGlc and betaGlc analogous to those obtained in solution were also observed in the gas phase for 3 and 4 by collision-induced dissociation experiments. From comparison with appropriate reference compounds, a substantial contribution to carbohydrate binding emerged for both the imino/amino and the pyrrolic H-bonding groups but not for the amidic group. This previously undocumented behavior, supported by crystallographic evidence, has been discussed in terms of geometric, functional, and coordinative complementarity between H-bonding groups and glycosidic hydroxyls and opens the way to a new designer strategy of H-bonding receptors for carbohydrates.

Nielsen K. A., Cho W. S., Lyskawa J., Levillain E., Lynch V. M., Sessler J. L., and Jeppesen J. O. (2006) Tetrathiafulvalene-calix[4]pyrroles: synthesis, anion binding, and electrochemical properties. *J Am Chem Soc* **128**, 2444-2451.

Abstract: The syntheses of monotetrathiafulvalene-calix[4]pyrrole 5 and bistetrathiafulvalene-calix[4]pyrrole 6, prepared from the acid-catalyzed condensation of monopyrrolo[3,4-d]tetrathiafulvalene (MPTTF, 7) with acetone in the presence of tripyrrane 8 and dipyrromethane 9, respectively, are described. Compound 5 and the previously reported tetrathiafulvalene-calix[4]pyrrole 4 both adopt a 1,3-alternative conformation in the solid state, as determined from X-ray crystallographic analysis. The anion binding properties of the tetrathiafulvalene-calix[4]pyrroles 5 and 6, as well as those of the parent meso-octamethylcalix[4]pyrrole (1), were investigated in acetone using (1)H NMR spectroscopic and isothermal titration calorimetry (ITC) techniques and, within the error limits of the methods, were generally found to give concordant results. On the basis of the results of the ITC studies carried out in 1,2-dichloroethane, increasing the number of tetrathiafulvalene units annulated to the calix[4]pyrrole system serves to enhance the anion binding affinities substantially but at the price of lowered selectivity. Cyclic voltammetry (CV) studies, carried out in 1,2-dichloroethane, provided evidence of an anion-dependent electrochemical response with Cl⁻ and Br⁻ ions. This response was particularly dramatic in the case of the monotetrathiafulvalene-calix[4]pyrrole 5, with a DeltaE(max) of -145 mV being seen after the addition of approximately 1 equiv of Cl⁻ ion.

nil de Namor A. F., Abbas I. and Hammud H. H. (2007) A new calix[4]pyrrole derivative and its anion (fluoride)/cation (mercury and silver) recognition. *J Phys. Chem B* **111**, 3098-3105.

Abstract: A new calix[4]pyrrole-based macrocycle, meso-tetramethyl-tetrakis{4-[2-(ethylthio)ethoxy]phenyl}calix[4]pyrrole, 7, has been synthesized and fully characterized. Unlike other calixpyrrole derivatives that show selective interaction with anions, calixpyrrole 7 described in the present work forms stable complexes with both metal cations and anions. The thermodynamics of complexation of

this ditopic calixpyrrole derivative with metal cations (Hg^{2+} and Ag^+) and the fluoride anion in nonaqueous solutions have been determined by titration calorimetry, and the host-guest composition has been investigated by using conductance measurements at 298.15 K. ^1H NMR studies provide clear evidence about the sites of complexation of **7** with the ionic species, which show that the NH groups are taking part in the complexation of this ligand with the fluoride anion while the sulfur donor atoms are responsible for the interaction with metal cations. Using the present data on **7** and structurally related analogues (**1-6**), the complexation behavior is discussed comparatively from the thermodynamic point of view. Possessing four sulfur-containing pendent arms, **7** displays an enhanced hosting ability for Hg^{2+} in acetonitrile. As compared with **1**, the calixpyrrole derivative, **7**, shows a unique interaction with fluoride among the anions investigated in acetonitrile and dimethyl sulfoxide. As far as the fluoride complex is concerned, the medium effect is assessed in terms of the thermodynamics of the transfer of reactants and product from acetonitrile (reference solvent) to dimethyl sulfoxide.

Nurchi V. M., Crisponi G., Pivetta T., Donatoni M. and Remelli M. (2008) Potentiometric, spectrophotometric and calorimetric study on iron(III) and copper(II) complexes with 1,2-dimethyl-3-hydroxy-4-pyridinone. *J Inorg Biochem.* **102**, 684-692

Abstract: The iron(III)-1,2-dimethyl-3-hydroxy-4-pyridinone (Deferiprone) system is carefully characterized by a combined potentiometric-spectrophotometric procedure at 25 and 37 degrees C at different ionic strengths, and by thermochemical and quantum-chemical studies. The main purpose of this work was to determine how the temperature dependence of both complex-formation and protonation constants can affect the pFe values on going from 25 degrees C (pFe is normally calculated using 25 degrees C stability constants) to the physiological temperature of 37 degrees C at which chelating agents are active in vivo. The copper(II)-Deferiprone system is also studied and the iron(III)-Deferiprone distribution diagrams in presence of variable copper(II) amounts are shown so as to explain possible side effects due to a competing metal ion during the chelating therapy of iron overload.

Obert E., Bellot M., Bouteiller L., Andrioletti F., Lehen-Ferrenbach C. and Boue F. (2007) Both water- and organo-soluble supramolecular polymer stabilized by hydrogen-bonding and hydrophobic interactions. *J Am. Chem Soc.* **129**, 15601-15605.

Abstract: A new bis-urea based supramolecular polymer is reported and shown by viscosimetry, neutron scattering (SANS), and calorimetry (ITC) to self-assemble in a wide range of solvents, encompassing the polarity scale from water to toluene. The presence of both hydrogen-bonding and hydrophobic groups ensures that self-assembly occurs in water, aprotic polar solvents, and nonpolar solvents. Both the driving force for the assembly and the exact structure of the filaments is solvent dependent, but whatever the solvent, long rigid filaments are formed in dynamic equilibrium with the monomer.

Ojida A., Honda K., Shinmi D., Kiyonaka S., Mori Y., and Hamachi I. (2006) Oligo-Asp tag/Zn(II) complex probe as a new pair for labeling and fluorescence imaging of proteins. *J Am Chem Soc* **128**, 10452-10459.

Abstract: To accomplish the selective labeling of a specific protein in complicated biological systems, a peptide tag incorporated into the protein and a complementary small molecular probe are required. Although a variety of peptide tag/probe pairs have been developed as molecular tools for protein analyses, the availability of pairs suitable for real-time imaging of proteins is still limited. We now report a new peptide tag/artificial probe pair composed of a genetically encodable oligo-aspartate sequence (D4 tag, $(\text{D4})_n$, $n = 1-3$) and the corresponding multinuclear Zn(II) complexes (Zn(II)-DpaTyr). The strong binding affinity of the Zn(II)-DpaTyr probes with the D4 tag was a result of the multiple coordination bonds and the multivalent effect. It was measured quantitatively by isothermal titration calorimetry. The high affinity between the tag and the probe, indispensable for the selective protein labeling, enabled the pair to be used for the labeling and fluorescence imaging of a membrane-bound receptor protein tethering a triply repeated D4 tag $((\text{D4})_3)$ in an intact cell configuration without significantly affecting the receptor signal transduction.

Ojida A., Inoue M. A., Mito-oka Y., Tsutsumi H., Sada K., and Hamachi I. (2006) Effective disruption of phosphoprotein-protein surface interaction using Zn(II) dipicolylamine-based artificial receptors via two-point interaction. *J Am Chem Soc* **128**, 2052-2058.

Abstract: Protein phosphorylation is ubiquitously involved in living cells, and it is one of the key events

controlling protein-protein surface interactions, which are essential in signal transduction cascades. We now report that the small molecular receptors bearing binuclear Zn(II)-Dpa can strongly bind to a bis-phosphorylated peptide in a cross-linking manner under neutral aqueous conditions when the distance between the two Zn(II) centers can appropriately fit in that of the two phosphate groups of the phosphorylated peptide. The binding property was quantitatively determined by ITC (isothermal titration calorimetry), induced CD (circular dichroism), and NMR. On the basis of these findings, we demonstrated that these types of small molecules were able to effectively disrupt the phosphoprotein-protein interaction in a phosphorylated CTD peptide and the Pin1 WW domain, a phosphoprotein binding domain, at a micromolar level. The strategy based on a small molecular disruptor that directly interacts with phosphoprotein is unique and should be promising in developing a designer inhibitor for phosphoprotein-protein interaction.

Palecz B. (2004) The enthalpies of interactions of some L-alpha-amino acids with urea molecule in aqueous solutions at 298.15 K. *Amino Acids* **27**, 299-303.

Abstract: Dissolution enthalpies of L-alpha-aminobutyric acid, L-alpha-isoleucine, L-alpha-phenylalanine, L-alpha-methionine, L-alpha-serine, L-alpha-threonine, L-alpha-cysteine, L-alpha-asparagine and L-alpha-glutamine in aqueous solutions of urea have been measured by calorimetry at 298.15 K. The obtained results were used to calculate the enthalpic interaction coefficients between the zwitterions of the L-alpha-amino acids and a molecule of urea in water. These values were interpreted in terms of the hydrophobic or hydrophilic effects of the side chains of amino acids on their interactions with a polar molecule of urea in water.

Palecz B. (2005) Enthalpic Pair Interaction Coefficient between Zwitterions of l-alpha-Amino Acids and Urea Molecule as a Hydrophobicity Parameter of Amino Acid Side Chains. *J Am Chem Soc* **127**, 17768-17771.

Abstract: Dissolution enthalpies of l-alpha-proline, l-alpha-tyrosine, l-alpha-tryptophan, l-alpha-histidine, l-alpha-arginine, l-alpha-lysine, l-aspartic acid, and l-alpha-glutamic acid in aqueous solutions of urea have been measured by calorimetry at a temperature of 298.15 K. The values of dissolution enthalpy were used to determine enthalpic heterogeneous pair interaction coefficients between the zwitterions of the natural amino acids and a molecule of urea in water solution. These coefficients were interpreted in terms of the hydrophobic or hydrophilic effects of the side chains of amino acids on their interactions with a polar molecule of urea in water.

Paradossi G., Chiessi E., and Malovikova A. (1999) Study of the interactions of D- and L-polylysine enantiomers with pectate in aqueous solutions. *Biopolymers* **50**, 201-209.

Abstract: The interaction between D- and L-enantiomers of polylysine and potassium pectate was studied by means of CD, microcalorimetry, and osmometry. Upon binding with pectate, only poly(L-lysine) undergoes a coil to alpha-helix transition, while poly(D-lysine) remains in the disordered state. This suggests that the energetics of the interaction is influenced by stereochemical constraints besides electrostatic forces. Experimental findings from microcalorimetry suggest that a contribution to the overall enthalpy of binding comes from the polysaccharidic moiety. Stoichiometry of the macromolecular complexes studied by osmometry gives a polylysine:pectate ratio of 3:1, in agreement with the respective degree of polymerization of the two polyelectrolytes.

Park S. J., Lee J. W., Sakamoto S., Yamaguchi K., and Hong J. I. (2003) Modulation of a supramolecular bowl and pot by changing solvent systems and/or metal/ligand ratios. *Chemistry* **9**, 1768-1774.

Abstract: A resorcin[4]arene-based ligand **2** with four pyrimidine substituents at the upper rim was synthesized, and the generation of different metal-mediated superstructures from the same ligand and metal ions utilizing the unfavorable incorporation of the third and fourth Pd(II) ions to ligand **2** was investigated. The supramolecular bowl **3**, which comes from a 1:2 combination of ligand **2** and [Pd(en)(NO₃)(2)], was obtained in water even though excess of Pd(II) complexes were employed. By adding methanol, the supramolecular pot **4** gradually formed, which was the major product when the ratio of mixed solvent reached methanol/water=5:1 (v/v). Host-guest complexation phenomena of **3** toward several aromatic carboxylates were demonstrated by isothermal titration calorimetry (ITC) and by ¹H NMR spectroscopy; both the enthalpy gain from electrostatic and hydrophobic interactions, and the entropy gain from desolvation cooperatively contribute to the binding of anionically charged guests. The crystal

structure of supramolecular pot 4 shows direct evidence for the hydrogen bonding between water and the aromatic pi electrons in the solid state. The modulation between supramolecular bowl 3 a and pot 4 was also made possible by changing the metal/ligand ratios in aqueous methanol solution as well as by varying the water content of the mixed solvent.

Pavan F. A., Lima I. S., Benvenuti E. V., Gushikem Y., and Airoidi C. (2004) Hybrid aniline/silica xerogel cation adsorption and thermodynamics of interaction. *J Colloid Interface Sci* **275**, 386-391.

Abstract: Aniline groups chemically immobilized on silica through the sol-gel process were employed to extract divalent nickel and manganese from aqueous solutions at room temperature. The maximum adsorption capacity of the xerogel was studied from adsorption isotherms using a batch technique. The isotherms obtained were adjusted following the Langmuir equation. The xerogel adsorbent appears to have better affinity for nickel than manganese. From calorimetric titration, thermodynamic data on cation/nitrogen basic atom interaction in the solid/liquid interface were determined. The enthalpic values, -0.46 +/- 0.02 and -0.29 +/- 0.02 kJ mol⁻¹ for nickel and manganese, respectively, are in agreement with the low availability of the basic nitrogen atom on the aniline group and also the possible steric hindrance of the phenyl group bonded to nitrogen. However, thermodynamics indicated the existence of favorable conditions for such cation-nitrogen interactions.

Pederson A. M., Ward E. M., Schoonover D. V., Sleboznick C. and Gibson H. W. (2008) High-yielding, regiospecific synthesis of cis(4,4')-di(carbomethoxybenzo)-30-crown-10, its conversion to a pyridyl cryptand and strong complexation of 2,2'- and 4,4'-bipyridinium derivatives. *J Org. Chem* **73**, 9094-9101.

Abstract: A high yielding (93%), regiospecific synthesis of cis(4,4')-di(carbomethoxybenzo)-30-crown-10 (1c) is reported. The derived crown ether diol 1d was converted to pyridyl cryptand 12 in 44% yield by reaction with pyridine-2,6-dicarbonyl chloride. Binding of two different 4,4'-bipyridinium (paraquat) species (3) and 2,2'-bipyridinium (diquat) 4 by 12 was explored via (1)H NMR spectroscopy, NOE experiments, mass spectrometry, X-ray crystallographic analyses, and isothermal titration calorimetry. Cryptand 12 exhibits the highest association constant for diquat ever reported ($K_a = 1.9 \times 10(6) \text{ M}(-1)$) and very high association constants for paraquats ($K_a > 10(5) \text{ M}(-1)$) in acetone at 22 degrees C. The binding constant of diquat 4 by cryptand 12 is nearly 6-times higher than any other reported host

Perry T. D., Klepac-Ceraj V., Zhang X. V., McNamara C. J., Polz M. F., Martin S. T., Berke N., and Mitchell R. (2005) Binding of harvested bacterial exopolymers to the surface of calcite. *Environ Sci Technol* **39**, 8770-8775.

Abstract: Biologically produced exopolysaccharides (EPS) affect calcite dissolution and precipitation. In this study, natural alkaliphilic microbial isolates were collected from biofilms on historic limestone. The isolates were screened for their ability to produce significant quantities of EPS in cultures. The most productive isolates were identified by 16S rRNA sequence analysis as a close relative of *Bacillus cereus*. EPS with different chemical structures were harvested from the isolates. Isothermal titration calorimetry (ITC) was used to quantify the thermodynamics of binding by the harvested EPS to calcite. The binding was described by a Langmuir adsorption isotherm. Characterization of the EPS showed that binding strength to calcite depended on the chemical nature of the polymer.

Pigge F. C., Dighe M. K. and Houtman J. C. (2008) Mono-, bis-, and tris(crown ether)s assembled around 1,3,5-triaroylbenzene scaffolds. *J Org. Chem* **73**, 2760-2767.

Abstract: A concise and experimentally straightforward method for assembling multiple benzo(crown ether) units around 1,3,5-triaroylbenzene scaffolds has been developed. Symmetrical tris(crown ether)s possessing three benzo(15-crown-5) or three benzo(18-crown-6) peripheral substituents have been prepared in good yield via cyclotrimerization of monomeric enamines. Efficient cross-cyclotrimerizations have also been demonstrated through construction of unsymmetrical triaroylbenzenes functionalized with only one or two benzo(15-crown-5) moieties. The alkali cation-binding abilities of these mono- and polytopic crown ethers have been probed through picrate extraction experiments and isothermal titration calorimetry. Thermodynamic binding parameters uncovered using the latter technique reveal increasing K⁺/Na⁺ selectivity in the benzo(15-crown-5) series of compounds as a function of increasing numbers of benzo(crown) units. The data also indicate that the triaroylbenzene-derived bis- and tris-crown ethers do not engage in intramolecular chelation of cations too large to be accommodated by individual crown

macrorings. Instead, cation/triaroylbenzene stoichiometries and binding profiles indicate formation of alkali metal-bridged dimers

Pina M. N., Rotger C., Soberats B., Ballester P., Deya P. M. and Costa A. (2007) Evidence of anion-induced dimerization of a squaramide-based host in protic solvents. *Chem Commun (Camb.)* 963-965.

Abstract: The combination of squaramide units with tetraalkylammonium groups leads two hosts that bind distinctively dianions in water-ethanol mixtures. The formation of complexes of 2:1 stoichiometry with host was supported by ITC, fluorescence, and (1)H NMR data.

Piosik J., Zdunek M., and Kapuscinski J. (2002) The modulation by xanthenes of the DNA-damaging effect of polycyclic aromatic agents. Part II. The stacking complexes of caffeine with doxorubicin and mitoxantrone. *Biochem Pharmacol* **63**, 635-646.

Abstract: Recently accumulated statistical data indicate the protective effect of caffeine consumption against several types of cancer diseases. There are also reports about protective effect of caffeine and other xanthenes against tumors induced by polycyclic aromatic hydrocarbons. One of the explanations of this phenomenon is based on biological activation of such carcinogens by cytochromes that are also known for metabolism of caffeine. In the accompanying paper [Kapuscinski et al., this issue] we provide evidence (flow cytometry and the cell cycle analysis) that the cytostatic effects of caffeine (CAF) on two DNA alkylating agents, which do not require the biological activation, depend on their ability to form stacking (π - π) complexes. In this study, we use physicochemical techniques (computer aided light absorption and microcalorimetry), and molecular modeling to examine previously published qualitative data. This is published both by our and other group's data, indicates that CAF is able to modify the cytotoxic and/or cytostatic action of the two well known antitumor drugs doxorubicin (DOX) and mitoxantrone (MIT). To obtain the quantitative results from the experimental data we used the statistical-thermodynamical model of mixed aggregation, to find the association constants $K(AC)$ of the CAF-drug interaction (128 ± 10 and $356 \pm 21 M^{-1}$ for DOX-CAF and MIT-CAF complex formation, respectively). In addition, the favorable enthalpy change of CAF-MIT ($\Delta H = -11.3 \text{ kcal/mol}$) was measured by microcalorimetry titration. The molecular modeling (semi-empirical and force field method) allowed us to obtain the geometry of these complexes, which indicated the favorable energy (ΔE) of complex formation of the protonated drug's molecules in aqueous environment (-7.4 and -8.7 kcal/mol for DOX-CAF.5H(2)O and MIT-CAF.8H(2)O complex, respectively). The molecular modeling calculation indicates the existence of CAF-drug complexes in which the MIT molecules are intercalated between two CAF molecules ($\Delta E = -29.9 \text{ kcal/mol}$). These results indicate that the attenuating effect of caffeine on cytotoxic or mutagenic effects of some polycyclic aromatic mutagens cannot be the result of metabolic activation in the cells, but simply is the physicochemical process of the sequestering of aromatic molecules (e.g. carcinogens or mutagens) by formation of the stacking complexes. The caffeine may then act as the "interceptor" of potential carcinogens (especially in the upper part of digesting track) where its concentration can reach the mM level). There is, however, no indication, both, in the literature or from our experiments, that the xanthenes can reverse the damage to nucleic acids at the point when the damage to DNA has already occurred.

Plitt P., Gross D. E., Lynch V. M. and Sessler J. L. (2007) Dipyrrolyl-functionalized bipyridine-based anion receptors for emission-based selective detection of dihydrogen phosphate. *Chemistry* **13**, 1374-1381.

Abstract: New cationic anion receptors, based on the use of pyrrole-substituted bipyridine and coordinated to transition metals, are described. Specifically, polypyridine-ruthenium and -rhodium cores have been functionalized to generate an anion binding site. The design was chosen to probe the influence of the pyrrole-to-pyrrole separation on anion-binding affinities and selectivities; this distance is greater in the new systems of this report (receptors 1 and 2) relative to that present in related dipyrrolyl quinoxaline based receptors 3 and 4. Solution-phase anion-binding studies, carried out by means of (1)H NMR spectroscopic titrations in [D(6)]DMSO and isothermal titration calorimetry (ITC) in DMSO, reveal that 1 and 2 bind most simple anions with substantially higher affinity than either 3 or 4. In the case of chloride anion, structural studies, carried out by means of single-crystal X-ray diffraction analyses, are consistent with the solution-phase results and reveal that receptors 1 and 2 are both able to stabilize complexes with this halide anion in the solid state.

Pluth M. D. and Raymond K. N. (2007) Reversible guest exchange mechanisms in supramolecular host-guest assemblies. *Chem Soc. Rev* **36**, 161-171.

Abstract: Synthetic chemists have provided a wide array of supramolecular assemblies able to encapsulate guest molecules. The scope of this tutorial review focuses on supramolecular host molecules capable of reversibly encapsulating polyatomic guests. Much work has been done to determine the mechanism of guest encapsulation and guest release. This review covers common methods of monitoring and characterizing guest exchange such as NMR, UV-VIS, mass spectrometry, electrochemistry, and calorimetry and also presents representative examples of guest exchange mechanisms. The guest exchange mechanisms of hemicarcerands, cucurbiturils, hydrogen-bonded assemblies, and metal-ligand assemblies are discussed. Special attention is given to systems which exhibit constrictive binding, a motif common in supramolecular guest exchange systems.

Pollitt M. J., Buckton G., Brocchini S., and Alpar H. O. (2005) Calorimetric study of bovine serum albumin dilution and adsorption onto polystyrene particles. *Int J Pharm* 298, 333-338.

Abstract: Titration calorimetry was used to investigate the interaction between a model antigen, bovine serum albumin (BSA), and a model particulate carrier, polystyrene (PS). The binding enthalpy was much higher than reported in the literature for a similar system and did not display a sigmoidal binding curve. These experiments may have accessed low coverage surface sites due to the irreversible nature of protein binding and stepwise titration. An important correction is the heat of dilution of the protein solution. Two regimes were observed: at low concentrations of BSA (below ca. 0.3% (w/v)) an exothermic dilution enthalpy of ca. -100mJmg(-1) was determined, whereas at higher concentrations of BSA values of ca. -20mJmg(-1) were obtained. Solution rheological data also showed a change at 0.3% (w/v) BSA, so we hypothesise that the fraction of the BSA as monomers, dimers and polymers in solution changes at approximately 0.3% (w/v).

Postollec F., Norde W., van der Mei H. C., and Busscher H. J. (2005) Microcalorimetric study on the influence of temperature on bacterial coaggregation. *J Colloid Interface Sci* 287, 461-467.

Abstract: Binding isotherms and heats of interaction have been determined at 15, 25, and 40 degrees C for a coaggregating and a non-coaggregating oral bacterial pair. Heats of interaction were measured upon three consecutive injections of streptococci into an actinomyces suspension using isothermal titration calorimetry. After each injection, the number of streptococci injected remaining free in suspension was quantified microscopically and the degree of binding between the two bacterial strains was established. The coaggregating pair shows positive cooperative binding. The highest cooperativity, at 25 degrees C, correlates with a strong, macroscopically visible coaggregation. The non-coaggregating pair shows low cooperativity and lacks macroscopically visible coaggregation. Interactions between the coaggregating partners seem to be mainly due to specific, enthalpically saturable and favorable binding sites. Even though the enthalpic part of the interaction is saturated, cooperativity increases with consecutive injections, implying that the coaggregation phenomenon is driven by entropy gain. The change in heat capacity ($\Delta C(p)$) is positive for the non-coaggregating pair from 15-40 degrees C as well as for the coaggregating pair beyond 25 degrees C. At lower temperatures the coaggregating pair causes a negative $\Delta C(p)$. The decrease in heat capacity together with an increase in entropy is considered to be indicative of hydrophobic interactions playing an important role in the formation of large coaggregates as observed for the coaggregating pair at 25 degrees C.

Quadir M. A., Radowski M. R., Kratz F., Licha K., Hauff P. and Haag R. (2008) Dendritic multishell architectures for drug and dye transport. *J Control Release (epublication)*.

Abstract: Here we present the efficiency and versatility of newly developed core-multishell nanoparticles (CMS NPs), to encapsulate and transport the antitumor drugs doxorubicin hydrochloride (Dox), methotrexate (Mtx) and sodium ibandronate (Ibn) as well as dye molecules, i.e., a tetrasulfonated indotricarbocyanine (ITCC) and Nile red. Structurally, the CMS NPs are composed of hyperbranched poly(ethylene imine) core functionalized by alkyl diacids connected to monomethyl poly(ethylene glycol). In order to evaluate their transport in aqueous media in vitro, we have used and compared SEC, UV, ITC, and NMR techniques. We observed that the CMS NPs were able to spontaneously encapsulate and transport Dox, Mtx and Nile red in both organic and aqueous media as determined by SEC and UV-VIS spectroscopy. For the VIS transparent Ibn Isothermal Titration Calorimetric (ITC) experiments show an exothermic interaction with the CMS NPs. The enthalpic stabilization (ΔH) upon encapsulation was in the order of approximately 7 kcal/mol which indicates stable interaction between Ibn and nanoparticles. A T(1) inversion recovery NMR experiment was carried out for (31)P and (1)H nuclei of Ibn and an

increment of spin-lattice relaxation time for respective nuclei was observed upon encapsulation. CMS NPs were also found to encapsulate ITCC dye with stoichiometry of 6-8 molecules/nanocarrier. For in vivo imaging studies the dye loaded CMS NPs were injected to F9 teratocarcinoma bearing mice and a strong contrast was observed in the tumor tissues compared to free dye after 6 h of administration

Raevsky O. A., Solov'ev V. P., Solotnov A. F., Schneider H. J., and Rudiger V. (1996) Conformation of 18-Crown-5 and Its Influence on Complexation with Alkali and Ammonium Cations: Why 18-Crown-5 Binds More Than 1000 Times Weaker Than 18C6. *J Org Chem* **61**, 8113-8116.

Abstract: Stability constants of potassium, sodium, and benzylammonium salts with 18C5 are determined in water, methanol, and acetonitrile by potentiometric titrations. The corresponding free energies ΔG agree within the error with those obtained from calorimetric titrations. In comparison to 18C6 the ΔG values are lower by 14 to 16 kJ/mol, with methanol or acetonitrile as solvent and K(+) or benzylammonium salts. Differences in the calorimetrically determined binding enthalpies ΔH between 18C6 and 18C5 are usually even larger. In water, however, the ΔG differences between the 18C5 and 18C6 complexes become almost negligible. The D(3)d-like conformation of such crown ethers can be evaluated for the first time by NOE methods using the less symmetrical 18C5. The NMR data indicate also the absence of significant conformational changes upon complexation, in line with molecular mechanics calculations (CHARMm). These show that the low binding constants of K(+) with 18C5 are due to the expulsion of the cation due to one C-H bond pointing toward the cavity, leading to larger K(+).O distances. The CHARMm calculated gas phase energy difference between the K(+) crown complexes of 26 kJ/mol agrees approximately with experimental differences.

Ragusa A., Rossi S., Hayes J. M., Stein M., and Kilburn J. D. (2005) Novel enantioselective receptors for N-protected glutamate and aspartate. *Chemistry* **11**, 5674-5688.

Abstract: A series of chiral bithiourea macrocycles 1-4 have been prepared and their binding properties with various dicarboxylate salts have been examined by using NMR titration and isothermal calorimetry experiments. Macrocycle 1, in particular, favours the 1:1 binding of N-protected L-glutamate and aspartate, but favours 1:2 binding of the corresponding D-amino acids in polar solvents (dimethyl sulfoxide and acetonitrile). The macrocycles, however, do not bind carboxylates at all in the less competitive solvent chloroform. The binding properties of these macrocycles are sensitive to small structural changes as demonstrated by the altered binding properties of macrocycles 2-4 compared with 1.

Rajendar B., Rajendran A., Sato Y., Nishizawa S. and Teramae N. (2008) Effect of methyl substitution in a ligand on the selectivity and binding affinity for a nucleobase: A case study with isoxanthopterin and its derivatives. *Bioorg. Med. Chem.* (epublication)

Abstract: Isoxanthopterin (IX) has two edges with hydrogen bond-forming sites suitable for binding to thymine (T) and cytosine (C). The binding affinity of IX for T or C is stronger than for adenine (A) and guanine (G), whereas the base selectivity of IX for T over C (and vice versa) is moderate. In order to improve both the binding affinity and base selectivity for T over C or C over T, a methyl group is introduced respectively at the N-3 or N-8 position of IX. This leads to the known ligands 3-methyl isoxanthopterin (3-MIX) and 8-methyl isoxanthopterin (8-MIX), and the binding affinity for C or T is expected to be tuned and improved by methyl substitution. Indeed, 3-MIX selectively binds to T more strongly than IX with a binding constant of $1.5 \times 10^6 \text{ M}^{-1}$ and it loses its binding affinity for C. In contrast, 8-MIX selectively binds to C over T with a binding constant of $1.0 \times 10^6 \text{ M}^{-1}$ and the binding affinity is greatly improved compared to the parent ligand IX. The thermodynamics of the ligand-nucleotide interaction is analyzed by isothermal calorimetric titrations, and the results show that the interaction follows a 1:1 stoichiometry and is enthalpy-driven. The introduction of methyl groups at both N-3 and N-8 positions results in an increase in enthalpy of the ligand-nucleotide interaction, which leads to the improved binding affinity

Rajendran A., Zhao C., Rajendar B., Nishizawa S. and Teramae N. (2008) A Sequence-Dependent Emissive Ligand for the Selective Detection of Thymidine-Related Single Nucleotide Polymorphisms in Human Gene Sequence. *Biochemistry.* (epublication)

Abstract: The detection of single nucleotide polymorphism (SNP) has gained much attention as these can have significant phenotypic effects, drug response, and disease susceptibility. Here, by creating a nanocavity by means of an abasic (AP) site in DNA, 3,5-diamino-6-chloro-2-pyrazinecarbonitrile (DCPC)

is used as a potential "light-up" probe for the selective detection of thymidine (T)-related mutations present in human gene sequences. Selective binding of DCPC to T is confirmed by melting point measurements and fluorescence spectral studies. The ground-state interaction of DCPC is further characterized by UV-visible spectral studies and dissociation constant measurements. The thermodynamics of the ligand-nucleotide interaction is investigated by isothermal titration calorimetry. The binding model is derived from the molecular modeling. Nothing but electronic level interactions are found to depend on the bases flanking the AP site. DCPC fluorescence is enhanced with T flanking bases, while it is quenched with guanine (G). In order to characterize the excited-state properties of DCPC inside the AP site, time-dependent density functional theory calculations are carried out. The results suggest that hydrogen bonding and base stacking with T do not influence the emissive properties of DCPC. In contrast, base stacking with G is predicted to dramatically alter the nature of fluorescence emission. Finally, the "light-up" property of the ligand is successfully used for the selective detection of T-related SNPs present in human gene sequences such as tumor suppressor gene p53, oncogene K-ras, and cytochrome P450 gene CYP2C8

Rao J., Lahiri J., Isaacs L., Weis R. M., and Whitesides G. M. (1998) A trivalent system from vancomycin-D-ala-D-Ala with higher affinity than avidin-biotin. *Science* **280**, 708-711.

Abstract: Tris(vancomycin carboxamide) binds a trivalent ligand derived from D-Ala-D-Ala with very high affinity: dissociation constant (Kd) approximately $4 \times 10^{-17} \pm 1 \times 10^{-17}$ M. High-affinity trivalent binding and monovalent binding are fundamentally different. In trivalent (and more generally, polyvalent) binding, dissociation occurs in stages, and its rate can be accelerated by monovalent ligand at sufficiently high concentrations. In monovalent binding, dissociation is determined solely by the rate constant for dissociation and cannot be accelerated by added monomer. Calorimetric measurements for the trivalent system indicate an approximately additive gain in enthalpy relative to the corresponding monomers. This system is one of the most stable organic receptor-ligand pairs involving small molecules that is known. It illustrates the practicality of designing very high-affinity systems based on polyvalency.

Rao J., Yan L., Lahiri J., Whitesides G. M., Weis R. M., and Warren H. S. (1999) Binding of a dimeric derivative of vancomycin to L-Lys-D-Ala-D-lactate in solution and at a surface. *Chem Biol* **6**, 353-359.

Abstract: BACKGROUND: The emergence of bacteria that are resistant to vancomycin (V), a glycopeptide antibiotic, results from the replacement of the carboxy-terminal D-Ala-D-Ala of bacterial cell wall precursors by D-Ala-D-lactate. Recently, it has been demonstrated that covalent dimeric variants of V are active against vancomycin-resistant enterococci (VRE). To study the contribution of divalency to the activities of these variants, we modeled the interactions of V and a dimeric V with L-Lys-D-Ala-D-lactate, an analog of the cell-wall precursors of the vancomycin-resistant bacteria. RESULTS: A dimeric derivative of V (V-Rd-V) was found to be much more effective than V in inhibiting the growth of VRE. The interactions of V and V-Rd-V with a monomeric lactate ligand - diacetyl-L-Lys-D-Ala-D-lactate (Ac2KDADLac) - and a dimeric derivative of L-Lys-D-Ala-D-lactate (Lac-R'd-Lac) in solution have been examined using isothermal titration calorimetry and UV spectroscopy titrations; the results reveal that V-Rd-V binds Lac-R'd-Lac approximately 40 times more tightly than V binds Ac2KDADLac. Binding of V and of V-Rd-V to Nalpa-Ac-L-Lys-D-Ala-D-lactate presented on the surface of mixed self-assembled monolayers (SAMs) of alkanethiolates on gold indicates that the apparent off-rate for dissociation of V-Rd-V from the surface is much slower than that of V from the same surface. CONCLUSIONS: The results are compatible with the hypothesis that divalency is responsible for tight binding, which correlates with small values of minimum inhibitory concentrations of V and V-Rd-V.

Rautaray D., Mandal S., and Sastry M. (2005) Synthesis of hydroxyapatite crystals using amino acid-capped gold nanoparticles as a scaffold. *Langmuir* **21**, 5185-5191.

Abstract: Inorganic composites are of special interest for biomedical applications such as in dental and bone implants wherein the ability to modulate the morphology and size of the inorganic crystals is important. One interesting possibility to control the size of inorganic crystals is to grow them on nanoparticles. We report here the use of surface-modified gold nanoparticles as templates for the growth of hydroxyapatite crystals. Crystal growth is promoted by a monolayer of aspartic acid bound to the surface of the gold nanoparticles; the carboxylate ions in aspartic acid are excellent binding sites for Ca(2+) ions. Isothermal titration calorimetry studies of Ca(2+) ion binding with aspartic acid-capped gold nanoparticles indicates that the process is entropically driven and that screening of the negative charge by the metal ions leads to their aggregation. The aggregates of gold nanoparticles are believed to be responsible for assembly

of the platelike hydroxyapatite crystals into quasi-spherical superstructures. Control experiments using uncapped gold nanoparticles and pure aspartic acid indicate that the amino acid bound to the nanogold surface plays a key role in inducing and directing hydroxyapatite crystal growth.

Reed W. A., Rao L., Zanonato P., Garnov A. Y., Powell B. A. and Nash K. L. (2007) Complexation of UVI with 1-hydroxyethane-1,1-diphosphonic acid in acidic to basic solutions. *Inorg Chem* **46**, 2870-2876.

Abstract: Complexation of UVI with 1-hydroxyethane-1,1-diphosphonic acid (HEDPA) in acidic to basic solutions has been studied with multiple techniques. A number of 1:1 (UO₂H₃L), 1:2 (UO₂H_jL₂ where j = +4, +3, +2, +1, 0, and -1), and 2:2 [(UO₂)₂H_jL₂ where j = +1, 0, and -1] complexes form, but the 1:2 complexes are the major species in a wide pH range. Thermodynamic parameters (formation constants and enthalpy and entropy of complexation) were determined by potentiometry and calorimetry. Data indicate that the complexation of UVI with HEDPA is exothermic, favored by the enthalpy of complexation. This is in contrast to the complexation of UVI with dicarboxylic acids in which the enthalpy term usually is unfavorable. Results from electrospray ionization mass spectrometry and ³¹P NMR have confirmed the presence of 1:1, 1:2, and 2:2 UVIHEDPA complexes.

Reis A. S., Jr., de Alencar S. J., and Chagas A. P. (1996) A Thermodynamic Study of Interactions of Monoionic Kaolinite with N,N-Dimethylacetamide (DMA) and Pyridine (PY). *J Colloid Interface Sci* **177**, 1-8.

Abstract: Two series of monoionic (M) kaolinites (M = H(+), Ca(2+), Cu(2+), Zn(2+), Al(3+), and Fe(3+)) were prepared from a natural Brazilian clay (Sao Simao clay, SP): series A, dried under vacuum at 25 degrees C, and series B, dried under vacuum at 25 degrees C. The natural clay was characterized by elemental analysis, cation exchange capacity, X-ray diffractometry, differential thermal analysis, and surface area measurements (BET). The interactions of M,M-dimethylacetamide and pyridine with these (M) kaolinites were studied by adsorption isotherms, titration calorimetry, and infrared spectroscopy (for pyridine only). The results indicated a coordinative interaction between M,M-dimethylacetamide and (M) kaolinites. For the interactions between pyridine and (M) kaolinites, the formation of hydrogen bonds (M = Al(3+), Fe(3+)), hydrogen and coordinative bonds (M = Cu(2+), Zn(2+)), and ionic pairs (M = H(+), Ca(2+)) was observed. For the pyridine-(Cu) kaolinite system, a substitution of water coordinated to Cu(2+) by pyridine was established.

Rekharsky M., Inoue Y., Tobey S., Metzger A., and Anslyn E. (2002) Ion-pairing molecular recognition in water: aggregation at low concentrations that is entropy-driven. *J Am Chem Soc* **124**, 14959-14967.

Abstract: Investigations into the thermodynamic parameters that characterize the binding of citrate to tris-guanidinium host 1 in water are reported. The parameters K_a, ΔH degrees, ΔS degrees, and ΔG degrees for the binding event were quantified using isothermal titration calorimetry (ITC) techniques. The 1:1 binding stoichiometry was verified by a Job plot derived from NMR data, and the microcalorimetry data was collected for solutions of 1 and citrate ranging from 1 to 100 mM using phosphate buffer concentrations of 5 and 103 mM. At low buffer concentrations (low ionic strength) complexes with greater than 1:1 stoichiometries were observed by ITC, and K(1) was determined to range from 2.0 x 10³ to 3.0 x 10³ M⁻¹. At higher buffer concentrations (high ionic strength) the higher-order complexes were not detected, and K(1) was determined to be 409 M⁻¹. The 1:1 association of host 1 and citrate is characterized by a large favorable entropy component and negative enthalpy. However, the complexes with higher-order stoichiometry arise from desolvation processes that result from the association of polyions in aqueous media and is entirely entropy driven. This leads to an unusual observation: the dilution of one component of the host/guest complex leads to the formation of the higher-order complexes. The reason for this observation is discussed.

Rekharsky M. V., Yamamura H., Inoue C., Kawai M., Osaka I., Arakawa R., Shiba K., Sato A., Ko Y. H., Selvapalam N., Kim K., and Inoue Y. (2006) Chiral recognition in cucurbituril cavities. *J Am Chem Soc* **128**, 14871-14880.

Abstract: For the first time, achiral cucurbiturils (CBs) were endowed with significant enantiomeric and distereomeric discrimination by incorporating a strong chiral binder. Calorimetric, nuclear magnetic, light-scattering, and mass spectral studies revealed that (S)-2-methylbutylamine (as a strong binder) can be discriminated by two enantiomeric supramolecular hosts, composed of CB[6] and (R)- or (S)-2-methylpiperazine, with an unprecedented 95% enantioselectivity in aqueous NaCl solution. This is the

highest enantioselectivity ever reported for a supramolecular system derived from an achiral host. Similarly, CB[7], with a larger cavity, exhibited diastereoselectivities up to 8 times higher for diastereomeric dipeptides, as demonstrated for L-Phe-L-Leu-NH₃⁺ versus L-Phe-D-Leu-NH₃⁺.

Rekharsky M. V., Yamamura H., Kawai M., Osaka I., Arakawa R., Sato A., Ko Y. H., Selvapalam N., Kim K., and Inoue Y. (2006) Sequential formation of a ternary complex among dihexylammonium, cucurbit[6]uril, and cyclodextrin with positive cooperativity. *Org Lett* **8**, 815-818.

Abstract: [STRUCTURE: SEE TEXT] A unique ternary 1:1:1 cucurbit[6]uril (CB[6])-cyclodextrin (CD)-dihexylammonium (DHA) complex was designed and noncovalently synthesized in stepwise fashion: first, CB[6] interacts strongly with DHA to form a 1:1 complex; second, addition of CD into the solution of the 1:1 complex leads to the exclusive formation of the 1:1:1 ternary complex. The ternary complex was characterized by various experimental techniques including ITC, NMR, and ESI-MS.

Roberts S. L., Furlan R. L., Otto S., and Sanders J. K. (2003) Metal-ion induced amplification of three receptors from dynamic combinatorial libraries of peptide-hydrazones. *Org Biomol Chem* **1**, 1625-1633.

Abstract: Three building blocks of general structure (MeO)₂ CH-aromatic linker-Pro-amino acid-NHNH₂ have been prepared and tested in acid-catalysed dynamic combinatorial libraries. Exposure of these libraries to LiI and NaI led to the amplification of three macrocyclic pseudopeptide receptors. The receptors were isolated and their interactions with LiI and NaI were analysed using NMR, IR and ITC. Binding of the metal ions to the receptors is invariably entropy-driven. Nevertheless, all receptors were found to be flexible with substantial conformational rearrangements accompanying guest binding. This type of receptor is extremely difficult to access through rational design and the fact that dynamic combinatorial chemistry allows facile access to these challenging molecules underlines the power of the dynamic approach.

Rodriguez-Docampo Z., Pascu S. I., Kubik S., and Otto S. (2006) Noncovalent interactions within a synthetic receptor can reinforce guest binding. *J Am Chem Soc* **128**, 11206-11210.

Abstract: Structural and thermodynamic data are presented on the binding properties of anion receptors containing two covalently linked cyclopeptide subunits that bind sulfate and iodide anions with micromolar affinity in aqueous solution. A synchrotron X-ray crystal structure of the sulfate complex of one receptor revealed that the anion is bound between the peptide rings of the biscyclopeptide. Intimate intramolecular contacts between the nonpolar surfaces of the proline rings of the individual receptor moieties in the complex suggest that hydrophobic interactions within the receptor that do not directly involve the guest contribute to complex stability. This finding is supported by a microcalorimetric analysis of the solvent dependence of complex stability, which showed that increasing the water content of the solvent has only a weak influence on the Gibbs energy of binding. Hence, the increasing amount of energy required for desolvating the binding partners in solutions containing more water is almost compensated by the increasingly favorable hydrophobic interactions. Further observations that suggest that guest-induced intra-receptor interactions contribute to guest binding are (i) anion binding of a monomeric cyclopeptide lacking the covalent linkage between the two rings leads to the formation of 2:1 complexes; (ii) in the crystal structure of the 2:1 iodide complex of this monotopic receptor, a similar arrangement of the two cyclopeptide rings has been found as in the sulfate complex of the biscyclopeptide; (iii) complex formation of the monomeric cyclopeptide in aqueous solution is highly cooperative with a large stability constant corresponding to the formation of the 2:1 complexes from relatively unstable 1:1 complexes; (iv) the monomeric cyclopeptide forms only 1:1 anion complexes in DMSO where hydrophobic interactions do not take place; and (v) introducing polar hydroxy groups on the proline rings of the monomeric cyclopeptide disrupts cooperativity causing the formation of only 1:1 complexes even in aqueous solution. Taken together these observations demonstrate that, in addition to direct receptor-substrate interactions, noncovalent interactions between the two subunits of such biscyclopeptides contribute significantly to anion complex stability. Reinforcement of molecular recognition through intra-receptor interactions should be an attractive new strategy to boost host-guest affinities.

Rong X., Huang Q., He X., Chen H., Cai P. and Liang W. (2008) Interaction of *Pseudomonas putida* with kaolinite and montmorillonite: a combination study by equilibrium adsorption, ITC, SEM and FTIR. *Colloids Surf B Biointerfaces* **64**, 49-55.

Abstract: Equilibrium adsorption along with isothermal titration calorimetry (ITC), Fourier transform infrared spectra (FTIR) and scanning electron microscopy (SEM) techniques were employed to investigate

the adsorption of *Pseudomonas putida* on kaolinite and montmorillonite. A higher affinity as well as larger amounts of adsorption of *P. putida* was found on kaolinite. The majority of sorbed bacterial cells (88.7%) could be released by water from montmorillonite, while only a small proportion (9.3%) of bacteria desorbed from kaolinite surface. More bacterial cells were observed to form aggregates with kaolinite, while fewer cells were within the larger bacteria-montmorillonite particles. The sorption of bacteria on kaolinite was enthalpically more favorable than that on montmorillonite. Based on our findings, it is proposed that the non-electrostatic forces other than electrostatic force play a more important role in bacterial adsorption by kaolinite and montmorillonite. Adsorption of bacteria on clay minerals resulted in obvious shifts of infrared absorption bands of water molecules, showing the importance of hydrogen bonding in bacteria-clay mineral adsorption. The enthalpies of $-4.1 \pm 2.1 \times 10^{-8}$ and $-2.5 \pm 1.4 \times 10^{-8}$ mJ cell⁻¹ for the adsorption of bacteria on kaolinite and montmorillonite, respectively, at 25 degrees C and pH 7.0 were firstly reported in this paper. The enthalpy of bacteria-mineral adsorption was higher than that reported previously for bacteria-biomolecule interaction but lower than that of bacterial coaggregation. The bacteria-mineral adsorption enthalpies increased at higher temperature, suggesting that the enthalpy-entropy compensation mechanism could be involved in the adsorption of *P. putida* on clay minerals. Data obtained in this study would provide valuable information for a better understanding of the mechanisms of mineral-microorganism interactions in soil and associated environments

Russell M. A., Laws A. P., Atherton J. H. and Page M. I. (2008) The mechanism of the phosphoramidite synthesis of polynucleotides. *Org. Biomol. Chem* **6**, 3270-3275.

Abstract: The mechanism of the coupling step in polynucleotide synthesis using 5'-4,4'-dimethoxytritylthymidine-3'-beta-cyanoethyl-N,N-diisopropylphosphoramidite as the phosphitylating agent and catalysed by the salt of saccharin and N-methylimidazole in acetonitrile has been studied by (31)P NMR. Pre- and post-equilibria between the activator salt and released diisopropylamine have been examined by (1)H NMR and ITC, which show that the salt between saccharin and diisopropylamine will be present in acetonitrile. Activation of the phosphoramidite by the salt of saccharin and N-methylimidazole involves nucleophilic catalysis and the formation of a reactive saccharin adduct bonded through its carbonyl oxygen to phosphorus. The rate constants for the reaction of the 4-methoxyphenol with 5'-4,4'-dimethoxytritylthymidine-3'-beta-cyanoethyl-N,N-diisopropylphosphoramidite in the presence of saccharin-N-methylimidazole salt show a non-linear dependence on phenol concentration, becoming independent at high phenol concentrations, compatible with a change in rate limiting step from the alcoholysis step to the activation step

Santos H. A., Manzanares J. A., Murtoimaki L. and Kontturi K. (2007) Thermodynamic analysis of binding between drugs and glycosaminoglycans by isothermal titration calorimetry and fluorescence spectroscopy. *Eur J Pharm. Sci* **32**, 105-114.

Abstract: The thermodynamics of the interaction of positively charged drug molecules with negatively charged glycosaminoglycans (GAGs) is investigated by isothermal titration calorimetry (ITC) and fluorescence spectroscopy. The drugs considered are propranolol hydrochloride, tacrine, and aminacrine, and the polymers used as model GAGs are dextran sulfate, chondroitin sulfate, and hyaluronic acid. The ITC results show that the interaction between drugs and GAGs is via direct binding and that GAGs bind to drugs at one set of sites. Large negative values of heat capacity change (ΔC_p) are observed upon binding of GAGs to drugs. Such negative ΔC_p is not expected for purely electrostatic interactions and suggests that hydrophobic and other interactions may be also involved in the binding process. These results are corroborated by fluorescence spectroscopy measurements, which show that specific drug/GAG complex formation is accompanied by a clear enhancement of the fluorescence intensity. The results highlight the importance of the formation of drug/GAG complexes as a primary step for the drug delivery process into cell membranes. It is concluded that the interactions are dependent on the nature of both GAG and drug and this is a fact to be taken into account when new drugs are designed.

Scolnik Y., Portnaya I., Cogan U., Tal S., Haimovitz R., Fridkin M., Elitzur A. C., Deamer D. W., and Shinitzky M. (2006) Subtle differences in structural transitions between poly-L- and poly-D-amino acids of equal length in water. *Phys Chem Chem Phys* **8**, 333-339.

Abstract: Mirror-image asymmetric molecules, i.e., chiral isomers or enantiomers, are classically considered as chemically identical. Recent studies, however, have indicated that parity violation by the nuclear weak force induces a tiny energy difference between chiral isomers. Upon combination with a

massive amplification process, expansion of this difference to a detectable macroscopic level may be achieved. Yet, experimental tests of this possibility, where one enantiomer is compared to the other in solution, are hampered by the possible presence of undetectable impurities. In this study we have overcome this problem by comparing structural and dynamic features of synthetic D- and L-polyglutamic acid and polylysine molecules each of 24 identical residues. In these water-soluble polypeptides helix formation is an intramolecular autocatalytic process amplified by each turn, which is actually unaffected by low level of putative impurities in the solvent. The helix and random coil configurations and their transition were determined in this study by circular dichroism (CD) and isothermal titration calorimetry (ITC) in water and deuterium oxide. Distinct differences in structure and transition energies between the enantiomeric polypeptides were detected by both CD and ITC when dissolved in water. Intriguingly, these differences were by and large abolished in deuterium oxide. Our findings suggest that deviation from physical invariance between the D- and L-polyamino acids is induced in part by different hydration in water which is eliminated in deuterium oxide. Based on the recent findings by Tikhonov and Volkov (V. I. Tikhonov and A. A. Volkov, *Science* 2002, 296, 2363) we suggest that ortho-H(2)O, which constitutes 75% of bulk H(2)O, has a preferential affinity to L-enantiomers. Differential hydration of enantiomers may have played a role in the selection of L-amino acids by early forms of life.

Sessler J. L., Cho W. S., Gross D. E., Shriver J. A., Lynch V. M., and Marquez M. (2005) Anion binding studies of fluorinated expanded calixpyrroles. *J Org Chem* **70**, 5982-5986.

Abstract: The anion binding properties of fluorinated calix[n]pyrroles (n = 4-6) in aprotic solvents (acetonitrile and DMSO) and modified reaction conditions allowing for the synthesis and isolation of the hitherto missing dodecafluorocalix[6]pyrrole from the condensation of 3,4-difluoro-1H-pyrrole and acetone are described. In acetonitrile solution containing 2% water, the association constants for the 1:1 binding interaction between octafluorocalix[4]pyrrole and chloride anion obtained with isothermal titration calorimetry (ITC) and (1)H NMR titration methods were found to match reasonably well. As compared to its nonfluorinated congener, octafluorocalix[4]pyrrole was found to display enhanced binding affinities for several representative anions in pure acetonitrile as judged from ITC analyses. Similar analyses of the fluorinated calix[n]pyrroles revealed an increase in the relative affinity for bromide over chloride with increasing macrocycle size, as manifest in a decrease in the binding ratio $K(a(Cl))/K(a(Br))$. Anion binding studies in the solid state, involving single-crystal X-ray diffraction analyses of the chloride and acetate anion complexes of octafluorocalix[4]pyrrole and decafluorocalix[5]pyrrole, respectively, confirmed the expected hydrogen bond interactions between the pyrrolic NH protons and the bound anions.

Sessler J. L., An D., Cho W. S., Lynch V., and Marquez M. (2005) Calix[n]bispyrrolylbenzenes: synthesis, characterization, and preliminary anion binding studies. *Chemistry* **11**, 2001-2011.

Abstract: A series of novel calixpyrrole-like macrocycles, calix[n]bis(pyrrol-2-yl)benzene (calix[n]BPBs, n=2-4) 9 a-11 a, have been synthesized by means of the TFA-catalyzed condensation reaction of bis(pyrrol-2-yl)benzene 8 a with acetone. Calix[2]BPB 9 a represents an expanded version of calix[4]pyrrole in which two of the four meso bridges are replaced by benzene rings. By contrast, systems 10 a and 11 a, which bear great considerable to calixbipyrrroles 2 and 3, represent higher homologues of the basic calix[n]BPB motif. Solution-phase anion binding studies, carried out by means of (1)H NMR spectroscopic titrations in [D(2)]dichloromethane and isothermal titration calorimetry (ITC) in 1,2-dichloroethane, reveal that 9 a binds typical small anions with substantially higher affinities than 1, even though the same number of hydrogen bonding donor groups are found in both compounds. The basic building block for 9 a, benzene dipyrrole 8 a, also displays a higher affinity for anions than the building block for 1, dimethyldipyrromethane 16. Structural studies, carried out by single-crystal X-ray diffraction analyses, are consistent with the solution-phase results and reveal that 9 a is able to stabilize complexes with chloride and nitrate in the solid state. Structures of the PF(6) (-) and NO(3) (-) complexes of 10 a were also solved as were those of the acetone adduct of 9 a and the ethyl acetate adduct of 11 a.

Sessler J. L., Gross D. E., Cho W. S., Lynch V. M., Schmidtchen F. P., Bates G. W., Light M. E., and Gale P. A. (2006) Calix[4]pyrrole as a chloride anion receptor: solvent and counteraction effects. *J Am Chem Soc* **128**, 12281-12288.

Abstract: The interaction of calixpyrrole with several chloride salts has been studied in the solid state by X-ray crystallography as well as in solution by isothermal titration calorimetry (ITC) and (1)H NMR spectroscopic titrations. The titration results in dimethylsulfoxide, acetonitrile, nitromethane, 1,2-

dichloroethane, and dichloromethane, carried out using various chloride salts, specifically tetraethylammonium (TEA), tetrapropylammonium (TPA), tetrabutylammonium (TBA), tetraethylphosphonium (TEP), tetrabutylphosphonium (TBP), and tetraphenylphosphonium (TPhP), showed no dependence on method of measurement. The resulting affinity constants ($K(a)$), on the other hand, were found to be highly dependent on the choice of solvent with $K(a)$'s ranging from $10(2)$ - $10(5)$ M^{-1} being recorded in the test solvents used for this study. In dichloromethane, a strong dependence on the counteranion was also seen, with the $K(a)$'s for the interaction with chloride ranging from $10(2)$ - $10(4)$ M^{-1} . In the case of TPA, TBA, and TBP, the ITC data could not be fit to a 1:1 binding profile.

Shcharbin D., Mazur J., Szwedzka M., Wasiak M., Palecz B., Przybyszewska M., Zaborski M. and Bryszewska M. (2007) Interaction between PAMAM 4.5 dendrimer, cadmium and bovine serum albumin: a study using equilibrium dialysis, isothermal titration calorimetry, zeta-potential and fluorescence. *Colloids Surf B Biointerfaces* **58**, 286-289.

Abstract: Binding of $Cd(2+)$ by PAMAM 4.5 dendrimer was studied by equilibrium dialysis, isothermal titration calorimetry and zeta-potential measurement. The following binding parameters were obtained: $n=23.8\pm 9.5$, $K(b)=4.7\pm 0.9\times 10^3$ in water; and $n=41.3\pm 13.4$, $K(b)=2.1\pm 0.8\times 10^3$ in 0.15 mol/l phosphate-buffered saline. The location of the bound $Cd(2+)$ is discussed. The interactions between bovine serum albumin, PAMAM 4.5 dendrimer and cadmium were analyzed using fluorescence and equilibrium dialysis. The competition between $Cd(2+)$ binding to BSA and PAMAM 4.5 dendrimer was investigated. It is proposed that PAMAM 4.5 dendrimer could be successfully used for extracting $Cd(2+)$ from aqueous solutions (environmental protection).

Shin M., Umabayashi Y., Kanzaki R., and Ishiguro S. (2000) Formation of Copper(II) Thiocyanato and Cadmium(II) Iodo Complexes in Micelles of Nonionic Surfactants with Varying Poly(ethylene oxide) Chain Lengths. *J Colloid Interface Sci* **225**, 112-118.

Abstract: Formation of copper(II) thiocyanato and cadmium(II) iodo complexes in micelles of poly(ethylene oxide) (PEO)-type nonionic surfactants with varying PEO chain lengths of 9.5 (Triton X-100), 30 (Triton X-305), and 40 (Triton X-405) has been studied by titration spectrophotometry and calorimetry at 298 K. In a given surfactant solution, all data obtained were analyzed by assuming formation of ternary complexes $MX(n)Y(m)((2-n)+)$ ($M = Cu(II), Cd(II)$; $X = SCN(-), I(-)$; $Y = surfactant$), and the complexes thus form in aqueous phase ($m = 0$) or in micelles ($m = 1$). In the $Cu(II)-SCN(-)$ system, spectrophotometric data obtained by varying concentrations of the surfactant can be explained well in terms of formation of $Cu(NCS)(2)Y$ in micelles and $Cu(NCS)(+)$ and $Cu(NCS)(2)$ in an aqueous phase, and it turned out that formation constant of $Cu(NCS)(2)Y$ increases with increasing PEO chain length. In the $Cd(II)-I(-)$ system, the formation of $CdI(3)Y(-)$ and $CdI(4)Y(2-)$ is concluded in micelles, and that of $CdI(+)$, $CdI(3)(-)$, and $CdI(4)(2-)$ in an aqueous phase. Interestingly, formation enthalpies of $CdI(3)Y(-)$ and $CdI(4)Y(2-)$ become significantly less negative with increasing PEO chain length. This suggests that transfer of the complexes from aqueous solution to a hydrophobic octylphenyl (OP) moiety in micelles is significantly more exothermic than that to a hydrophilic PEO one. Thermodynamic parameters of transfer of $CdI(3)(-)$ and $CdI(4)(2-)$ from aqueous solution to the OP and PEO moieties of micelles have been evaluated. Copyright 2000 Academic Press.

Sidhu J., Bloor T. L., Couderc-Azouani S., Penfold J., Holzwarth J. F., and Wyn-Jones E. (2004) Interactions of poly(amidoamine) dendrimers with the surfactants SDS, DTAB, and C12EO6: an equilibrium and structural study using a SDS selective electrode, isothermal titration calorimetry, and small angle neutron scattering. *Langmuir* **20**, 9320-9328.

Abstract: Interactions in aqueous solutions of different generations of poly(amidoamine) (PAMAM) dendrimers containing amine, hydroxyl, or delta-glucolactone functional groups at the periphery with the anionic surfactant sodium dodecyl sulfate (SDS) were investigated. We used a SDS-specific electrode (EMF) for SDS monomer concentration monitoring, isothermal titration calorimetry (ITC) for binding information, and small angle neutron scattering (SANS) for structural studies. ITC experiments monitoring the interaction of the dendrimers with cationic dodecyltrimethylammonium bromide (DTAB) and nonionic hexaethylene glycol mono-n-dodecyl ether (C12EO6) showed no significant binding effects. In contrast, SDS binds to all of the above dendrimers. EMF and ITC data demonstrated a regular trend for both the onset of binding and binding saturation as the generation in each family of dendrimers increased. In addition, generation G6 exhibited a noncooperative binding process at very low SDS concentrations.

Furthermore, the onset of cooperative binding in the EMF experiments started at lower concentrations as the weight % (w/v), the size, and the numbers of the internal or surface groups increased. On the other hand, the binding capacity of the dendrimers showed only a small dependence on the above parameters. At SDS concentrations approaching the binding limit and also at selective concentrations within the binding range, SANS measurements indicated that in all cases the bound surfactant is in the micellar form. From the electromotive force (EMF) measurements, ITC data, and SANS data, the stoichiometry of the supramolecular complexes was determined.

Simon M., Wittmar M., Bakowsky U., and Kissel T. (2004) Self-assembling nanocomplexes from insulin and water-soluble branched polyesters, poly[(vinyl-3-(diethylamino)-propylcarbamate-co-(vinyl acetate)-co-(vinyl alcohol)]-graft- poly(L-lactic acid): a novel carrier for transmucosal delivery of peptides. *Bioconjug Chem* **15**, 841-849.

Abstract: The design of carriers for protein delivery that provide protection against enzymatic degradation and facilitate protein transport across epithelial surfaces, thus avoiding parenteral administration, remains a challenge. Self-assembling nanoscale protein/polymer complexes might present a promising approach. We synthesized water-soluble, amphiphilic polyesters, poly[(vinyl-3-(diethylamino)-propylcarbamate-co-(vinyl acetate)-co-(vinyl alcohol)]-graft-poly(L-lactic acid), containing a positively charged backbone, and studied the spontaneous formation of nanocomplexes (NC) with insulin. NC were characterized using dynamic light scattering, zeta-potential measurements, and atomic force microscopy (AFM). Insulin loading was determined with HPLC, and the binding constants were obtained by isothermal titration calorimetry (ITC). The NC formation was followed using nephelometric and light scattering techniques. Water-soluble, positively charged, branched polyesters with amphiphilic properties were obtained in a three-step polymer-analogous reaction. The degree of amine substitution, DS, in the PVAL backbone was varied between 0.04 and 0.5, and grafting this backbone with L-lactide increased the molecular weight from 18 kDa to 81 kDa. The polymer composition was optimized to facilitate NC formation with insulin resulting in a DS of 0.09 and a poly(L-lactide) side chain substitution of 0.5 with an average chain length of two lactic acids. Depending on polymer composition, stable NC of 200-500 nm diameter were formed with insulin, and the binding constants ranged from 4.7×10^5 to $9.5 \times 10^6 \text{ M}^{-1}$. Positively charged surface charges ranging from +5 to +35mV and an insulin loading up to 98% of 33 IU/mL were obtained. The NC visualized by AFM revealed spheroidal particles with an entangled internal structure. It was demonstrated that this class of multifunctional polymers is capable of self-assembly with a peptidic substrate. The resulting nanosized complexes offer the potential for mucosal insulin/protein delivery and merit further investigations under in vivo conditions.

Singh S. K. and Caram-Lelham N. (1998) Thermodynamics of kappa-Carrageenan-Amphiphilic Drug Interaction as Influenced by Specific Counterions and Temperature: A Microcalorimetric and Viscometric Study. *J Colloid Interface Sci* **203**, 430-446.

Abstract: The adsorption of amphiphilic drug molecules to a polyelectrolyte, kappa-carrageenan, has been shown to be related to hydrophobicity of drug and the conformation of the polyanion which in turn can be regulated by choice of counterion. The binding is of a strongly cooperative nature and the degree of cooperativity has been found to be related to the self-aggregation tendency of the drug molecules. This system has been examined by titration microcalorimetry and capillary viscometry to determine the thermodynamics of the binding phenomenon. The titration calorimetry data confirms the trends and conclusions drawn regarding the factors that control the binding. Viscometry shows that although there is a change in size of the polymeric chains when the drug molecules are adsorbed, the effect is primarily due to charge neutralization and not a conformation change. This allows the microcalorimetry data to be analyzed to recover the enthalpy of binding of the drug molecules to the polymer. Earlier published equilibrium binding data has been analyzed to determine the binding constants and free energy changes in the process (-25 to -90 kJ/mol). A phenomenological model has been derived for the cooperative binding process for this purpose. The binding process is primarily enthalpy driven with the major part of enthalpy change (-10 to -40 kJ/mol) arising from the aggregation of bound drug molecules, i.e., from hydrophobic interactions; the process is also entropically favorable. The size of these aggregates in polymer-bound state is of the order of 2-5 molecules of drug, similar to the pre-micellar aggregates of the drugs in solution. Copyright 1998 Academic Press.

Singh S. K. and Nilsson S. (1999) Thermodynamics of Interaction between Some Cellulose Ethers and SDS by Titration Microcalorimetry. *J Colloid Interface Sci* **213**, 133-151.

Abstract: The interaction between certain nonionic cellulose ethers (ethyl hydroxyethyl cellulose and hydroxypropyl methyl cellulose) and sodium dodecyl sulphate (SDS) has been investigated using isothermal titration microcalorimetry at temperatures between 25-50 degrees C. The observed heat flow curves have been interpreted in terms of a plausible mechanism of the interaction of the substituent groups with SDS monomers and clusters. The data have been related to changes occurring in the system at the macro- and microscopic levels with the addition of surfactants and with temperature. The process consists predominantly of polymer-surfactant interactions initially and surfactant-surfactant interactions at the later stages. A phenomenological model of the cooperative interaction (adsorption) process has been derived, and earlier published equilibrium binding data have been used to recover binding constants and Gibbs energy changes for this process. The adsorption enthalpies and entropies have been recovered along with the heat capacity change. The enthalpic cost of confining the nonpolar regions of the polymers in surfactant clusters is high, but the entropy gain from release of hydration shell water molecules as well as increased freedom of movement of these nonpolar regions in the clusters gives the process a strong entropic driving force. The process is entropy-driven initially and converts to being both enthalpy and entropy-driven at high SDS concentrations. An enthalpy-entropy compensation behavior is seen. Strongly negative heat capacity changes have been obtained resulting from the transfer of nonpolar groups from aqueous into nonpolar environments, as well as a reduction of conformational domains that the chains can populate. Changes in these two components cause the heat capacity change to become less negative at the higher binding levels. The system can be classified as exhibiting nonclassical hydrophobic binding at the later stages of binding. Copyright 1999 Academic Press.

Singh S. K. and Nilsson S. (1999) Thermodynamics of Interaction between Some Cellulose Ethers and SDS by Titration Microcalorimetry. *J Colloid Interface Sci* **213**, 152-159.

Abstract: A titration calorimetric study of the interaction between nonionic cellulose ethers and ionic surfactant (SDS) has been extended to a larger number of polymers to explore the effect of variation of polymer hydrophobicity on the energetics of the process. "Hydrophobicity" as used here is an overall effect of the nature, degree, and number of substituents and is characterized by the cloud point and (aqueous) surface tension lowering abilities of the polymer. A direct correlation is found between the extent of "hydrophobicity" and the endo-enthalpic peak in the initial SDS concentration region of interaction. However, the overall mechanism of interaction is similar for all the polymers, being dominated by polymer-surfactant interactions initially and converting into a surfactant-surfactant interaction process at higher SDS concentrations. The importance of polymer characteristics thus becomes weaker at the later stages of the process. Differences between the polymers is also reduced by an increase of temperature, leading to a near overlap of observed enthalpy curves at 40 degrees C. The energetics of interaction are also mirrored by the isothermal surfactant binding curves and the changes in macroscopic and microviscosity of the system. Copyright 1999 Academic Press.

Song M. Z., Zhu L. Y., Gao X. K., Dou J. M., and Sun D. Z. (2005) Microcalorimetric study on host-guest complexation of naphtho-15-crown-5 with four ions of alkaline earth metal. *J Zhejiang Univ Sci* **6**, 69-73.

Abstract: Thermodynamic parameters of complexation of naphtho-15-crown-5 with four alkaline earth ions in aqueous media was determined using titration microcalorimetry at 298.15 K. The stability of the complexes, thermal effect and entropy effect of the complexation is discussed on the basis of the guest ions structure and the solvent effect. The stability constants tendency to vary with ion radius was interpreted. Complex of naphtho-15-crown-5 with calcium ion is very stable due to the synergism of static electric interaction and size selectivity between the host and the guest.

South C. R., Higley M. N., Leung K. C., Lanari D., Nelson A., Grubbs R. H., Stoddart J. F., and Weck M. (2006) Self-assembly with block copolymers through metal coordination of SCS-Pd(II) pincer complexes and pseudorotaxane formation. *Chemistry* **12**, 3789-3797.

Abstract: Poly(norbornene)-based block copolymers containing side chains of palladated pincer complexes/dibenzo[24]crown-8 or palladated pincer complexes/dibenzylammonium salts were synthesized. Noncovalent functionalization was accomplished with their corresponding recognition units through simple 1:1 addition with association constants (K_a) greater than 10^5 m^{-1} . The self-assembly processes were monitored by using both ^1H NMR spectroscopy and isothermal titration calorimetry. In all cases, we found

that the self-assembly of the recognition units along each polymer block does not preclude the self-assembly processes along the other block.

Spuches A. M., Kruszyna H. G., Rich A. M., and Wilcox D. E. (2005) Thermodynamics of the As(III)-thiol interaction: arsenite and monomethylarsenite complexes with glutathione, dihydrolipoic acid, and other thiol ligands. *Inorg Chem* **44**, 2964-2972.

Abstract: Colorimetric (near-UV absorption spectroscopy) and calorimetric (isothermal titration calorimetry) methods have been used to quantify the equilibrium and thermodynamics of arsenite and monomethylarsenite (MMA) coordinating to glutathione (GSH) and the dithiols dimercaptosuccinic acid (DMSA), dihydrolipoic acid (DHLA), and dithiothreitol (DTT). We found that both arsenite and MMA form moderately stable complexes ($\beta = 10(6)$ - $10(7)$) with GSH; that arsenite forms a particularly stable 2:3 complex (β approximately $10(18)$) with the biological cofactor DHLA; that MMA has a somewhat higher affinity than arsenite for thiol ligands; and that entropic factors modulate the overall stability of As(III) complexes with thiols, which are favored by the exothermic formation of As(III)-thiolate bonds. The implications of these results for arsenic toxicity are discussed.

Stolnik S., Heald C. R., Garnett M. G., Illum L., and Davis S. S. (2005) Differences in the adsorption behaviour of poly(ethylene oxide) copolymers onto model polystyrene nanoparticles assessed by isothermal titration microcalorimetry correspond to the biological differences. *J Drug Target* **13**, 449-458.

Abstract: The adsorption behaviour of a tetrafunctional copolymer of poly(ethylene oxide)-poly(propylene oxide) ethylene diamine (commercially available as Poloxamine 908) and a diblock copolymer of poly(lactic acid)-poly(ethylene oxide) (PLA/PEG 2:5) onto a model colloidal drug carrier (156 nm sized polystyrene latex) is described. The adsorption isotherm, hydrodynamic thickness of the adsorbed layers and enthalpy of the adsorption were assessed. The close similarity in the conformation of the poly(ethylene oxide) (PEO) chains (molecular weight 5000 Da) in the adsorbed layers of these two copolymers was demonstrated by combining the adsorption data with the adsorbed layer thickness data. In contrast, the results from isothermal titration microcalorimetry indicated a distinct difference in the interaction of the copolymers with the polystyrene colloid surface. Poloxamine 908 adsorption to polystyrene nanoparticles is dominated by an endothermic heat effect, whereas, PLA/PEG 2:5 adsorption is entirely an exothermic process. This difference in adsorption behaviour could provide an explanation for differences in the biodistribution of Poloxamine 908 and PLA/PEG 2:5 coated polystyrene nanoparticles observed in previous studies. A comparison with the interaction enthalpy for several other PEO-containing copolymers onto the same polystyrene colloid was made. The results demonstrate the importance of the nature of the anchoring moiety on the interaction of the adsorbing copolymer with the colloid surface. An endothermic contribution is found when an adsorbing molecule contains a poly(propylene oxide) (PPO) moiety (e.g. Poloxamine 908), whilst the adsorption is exothermic (i.e. enthalpy driven) for PEO copolymers with polylactide (PLA/PEG 2:5) or alkyl moieties.

Stone M. T. and Moore J. S. (2005) Supramolecular chelation based on folding. *J Am Chem Soc* **127**, 5928-5935.

Abstract: Crystallographic analysis revealed that pyridine-palladium complexation is a good geometric match to the m-phenylene ethynylene (mPE) repeat unit and thus could serve as a reversible linking group to join oligomer segments together. A series of pyridine-terminated mPE oligomers were then synthesized and found to coordinate with palladium dichloride to give complexes effectively twice the length of the free oligomers. A quantitative analysis of these coordination equilibria by isothermal calorimetry found the ability of the pyridine end-group to form a coordination complex corresponded with their ability to fold. Oligomers that were able to form complexes of sufficient length to fold showed positive cooperativity based on experimental determination of their association constants with a palladium ion. We suggest that the additional free energy of complexation for the folded oligomers is analogous to chelation by multidentate ligands, but here the "multidentate ligand" is held together by supramolecular rather than covalent bonds.

Stumber M., Herrmann C., Wohlgemuth S., Kalbitzer H. R., Jahn W., and Geyer M. (2002) Synthesis, characterization and application of two nucleoside triphosphate analogues, GTPgammaNH(2) and GTPgammaF. *Eur J Biochem* **269**, 3270-3278.

Abstract: Guanosine triphosphate nucleotide analogues such as GppNHp (also named GMPPNP) or

GTPgammaS are widely used to stabilize rapidly hydrolyzing protein-nucleotide complexes and to investigate biochemical reaction pathways. Here we describe the chemical synthesis of guanosine 5'-O-(gamma-amidotriphosphate) (GTPgammaNH(2)) and a new synthesis of guanosine 5'-O-(gamma-fluorotriphosphate) (GTPgammaF). The two nucleotides were characterized using NMR spectroscopy and isothermal titration calorimetry. Chemical shift data on (31)P, (19)F and (1)H NMR resonances are tabulated. For GTPgammaNH(2) the enthalpy of magnesium coordination is $\Delta H^{\circ} = 3.9 \text{ kcal.mol}^{-1}$ and the association constant $K(a)$ is 0.82 mm^{-1} . The activation energy for GTPgammaNH(2).Mg²⁺ complex formation is $\Delta H^{\ddagger} = 7.8 \pm 0.15 \text{ kcal.mol}^{-1}$, similar to that for the natural substrate GTP. For GTPgammaF we obtained a similar enthalpy of $\Delta H^{\circ} = 3.9 \text{ kcal.mol}^{-1}$ while the magnesium association constant is only $K_a = 0.2 \text{ mm}^{-1}$. The application of both guanine nucleotide analogues to the GTP-binding protein Ras was investigated. The rate of hydrolysis of GTPgammaNH(2) bound to Ras protein lay between the rates found for Ras-bound GTPgammaS and GppNHp, while Ras-catalysed hydrolysis of GTPgammaF was almost as fast as for GTP. The two compounds extend the variety of nucleotide analogues and may prove useful in structural, kinetic and cellular studies.

Su N., Bradshaw J. S., Zhang X. X., Song H., Savage P. B., Xue G., Krakowiak K. E., and Izatt R. M. (1999) Syntheses and Metal Ion Complexation of Novel 8-Hydroxyquinoline-Containing Diaza-18-Crown-6 Ligands and Analogues. *J Org Chem* **64**, 8855-8861.

Abstract: Ten new 8-hydroxyquinoline-containing diaza-18-crown-6 ligands and analogues were synthesized via a one-pot or stepwise Mannich reaction, reductive amination, or by reacting diaza-18-crown-6 with 5,7-dichloro-2-iodomethyl-8-quinolinol in the presence of N,N-diisopropylethylamine. The Mannich reaction of N,N'-bis(methoxymethyl)diaza-18-crown-6 with 4-chloro-2-(1H-pyrazol-3-yl)phenol gave the NCH(2)N-linked bis(3-(5-chloro-2-hydroxy)pyrazol-1-ylmethyl)-substituted diazacrown ether (14) in a 98% yield. The reaction of bis(N,N'-methoxymethyldiaza)-18-crown-6 with 2.2 equiv of 10-hydroxybenzoquinoline gave only the monosubstituted diazacrown ether ligand (8). Interaction of some of the ligands with various metal ions was evaluated by a calorimetric titration technique at 25 degrees C in MeOH. Bis(8-hydroxyquinoline-2-ylmethyl)-substituted ligand 13 forms a very strong complex with Ba(2+) ($\log K = 11.6$ in MeOH) and is highly selective for Ba(2+) over Na(+), K(+), Zn(2+), and Cu(2+) (selectivity factor $> 10^6$). The (1)H NMR spectral studies of the Ba(2+) complexes with bis(8-hydroxyquinoline-2-ylmethyl)- and bis(5,7-dichloro-8-hydroxyquinoline-2-ylmethyl)-substituted diaza-18-crown-6 ligands (13 and 10) suggest that these complexes are cryptate-like structures with the two overlapping hydroxyquinoline rings forming a pseudo second macrocyclic ring. UV-visible spectra of the metal ion complexes with selected ligands suggest that these ligands might be used as chromophoric or fluorophoric sensors.

Suksai C., Figueiras G. S., Chhabra A., Liu J., Skepper J. N., Tuntulani T., and Otto S. (2006) Controlling the morphology of aggregates of an amphiphilic synthetic receptor through host-guest interactions. *Langmuir* **22**, 5994-5997.

Abstract: A new amphiphilic receptor containing a macrocyclic anionic headgroup and a single alkyl chain was prepared through an efficient templated synthesis. The interdependence of the aggregation behavior and the host-guest chemistry was studied. In the absence of any guest the terminus of the alkyl chain of the receptor is included inside the hydrophobic cavity of the macrocycle (as evident from (1)H NMR studies) leading to self-assembly into micrometer-long nanotubes (as evident from TEM studies). The alkyl chain can be displaced by an acridinium bromide guest (as evident from (1)H NMR and ITC), which leads to a dramatic change in aggregate size and morphology (as evident from DLS). Studies of the solubilization of Nile red suggest that the resulting aggregates are micelles with a cmc of around 35 microM. These results represent a new addition to the still small number of water-soluble amphiphilic receptors and one of the first examples in which specific host-guest chemistry controls the size and shape of nanoscale aggregates.

Tajc S. G., Tolbert B. S., Basavappa R., and Miller B. L. (2004) Direct determination of thiol pKa by isothermal titration microcalorimetry. *J Am Chem Soc* **126**, 10508-10509.

Talhout R. and Engberts J. B. (2004) Probing the effect of the amidinium group and the phenyl ring on the thermodynamics of binding of benzamidinium chloride to trypsin. *Org Biomol Chem* **2**, 3071-3074.

Abstract: The effect of the amidinium group and the phenyl ring on the thermodynamics of binding of benzamidinium chloride to the serine proteinase trypsin has been studied using isothermal titration

calorimetry. Binding studies with benzylammonium chloride, [small alpha]-methylbenzylammonium chloride and benzamide, compounds structurally related to benzamidinium chloride, showed that hydrogen bonding between the amidinium group and the enzyme is primarily enthalpy-driven. Binding of cyclohexylcarboxamidinium chloride and acetamidinium chloride showed that the hydrophobic binding of the phenyl ring in the S1 pocket is primarily entropy-driven and that a rigid, flat hydrophobic binding site for the inhibitor is favourable. The compounds that have been studied over a range of temperatures exhibit a negative change in heat capacity upon binding and enthalpy-entropy compensation, both characteristic of hydrophobic interactions.

Tareste D., Pincet F., Brellier M., Mioskowski C., and Perez E. (2005) The binding energy of two nitrilotriacetate groups sharing a nickel ion. *J Am Chem Soc* **127**, 3879-3884.

Abstract: Among the various molecular interactions used to construct supramolecular self-assembling systems, homoliganded metallic NTA-Ni-NTA complexes have received little attention despite their considerable potential applications, such as the connection of different biochemical functions. The stability of this complex is investigated here by using two concordant nanotechniques (surface forces apparatus and vesicle micromanipulation) that allow direct measurements of adhesion energies due to the chelation of nickel ions by nitrilotriacetate (NTA) groups grafted on surfaces. We show that two NTA groups can share a nickel ion, and that the association of a Ni-NTA complex with an NTA group has a molecular binding energy of 1.4 kcal/mol. Binding measurements in bulk by isothermal titration calorimetry experiments give the same value and, furthermore, indicate that the Ni-NTA chelation bond is about five times stronger than the NTA-Ni-NTA one. This first direct proof and quantification of the simultaneous chelation of a nickel ion by two NTA groups sheds new light on association dynamics involving chelation processes and offers perspectives for the development of new supramolecular assemblies and anchoring strategies.

Tegoni M., Ferretti L., Sansone F., Remelli M., Bertolasi V. and Dallavalle F. (2007) Synthesis, solution thermodynamics, and X-ray study of CuII [12]metallacrown-4 with GABA hydroxamic acid: an unprecedented crystal structure of a [12]MC-4 with a gamma-aminohydroxamate. *Chemistry* **13**, 1300-1308.

Abstract: The solution equilibria of gamma-aminobutanehydroxamic acid (GABAha) with H⁺ and Cu²⁺ were investigated by potentiometry, titration calorimetry, spectrophotometry, NMR spectroscopy, and ESI-MS. The thermodynamic parameters of the CuII [12]metallacrown-4 obtained for GABAha were compared with those of the corresponding complexes of (S)-alpha-Alaha and beta-Alaha. The stability (-DeltaG⁰) sequence was beta-Alaha >> alpha-Alaha > GABAha, whereas the order of formation enthalpies (-DeltaH⁰) was beta-Alaha >> GABAha > alpha-Alaha. These data were interpreted on the basis of the dimensions of the chelate rings and the planarity of the metallamacrocycles. The CuII [12]metallacrown-4 ([12]MC-4) complex of GABAha was isolated and its crystal structure, which is the first reported for a [12]MC-4 of a gamma-aminohydroxamic acid, fully supports the structural features interpreted from the thermodynamic data.

ten Cate M. G., Huskens J., Crego-Calama M., and Reinhoudt D. N. (2004) Thermodynamic stability of hydrogen-bonded nanostructures: a calorimetric study. *Chemistry* **10**, 3632-3639.

Abstract: The self-assembly of hydrogen-bonded aggregates (rosettes) in solvent mixtures of different polarity has been studied by calorimetry. The C₅₀ parameter, the concentration when 50 % of the components are incorporated in the assembly, is used to compare assemblies with different stoichiometry. C₅₀ for the single rosette 1(3).(BuCYA)(3) (1=N,N-di(4-tert-butylphenyl)melamine; BuCYA=n-butylcyanuric acid) in 1,2-dichloroethane is 25 μM, whereas for double rosettes 2 a(3).(BuCYA)(6) and 2 b(3).(BuCYA) (2=calix[4]arene-dimelamine) it is 0.7 and 7.1 μM, respectively. ΔG degrees, ΔH degrees, and TΔS degrees values indicate that the thermodynamics of double rosettes reflect the independent assembly of two individual single rosette structures or two rosettes reinforced by additional stabilizing interactions. In more polar solvents the stability of double rosettes decreases. From the correlation of ΔG degrees with solvent polarity it is predicted that it should be possible to assemble double rosettes in methanol or water. The assembly of 2 b(3).(BuCYA)(6) in 100 % MeOH was proven by (1)H NMR and CD spectroscopy.

Tegoni M., Ferretti L., Sansone F., Remelli M., Bertolasi V., and Dallavalle F. (2006) Synthesis, Solution Thermodynamics, and X-ray Study of Cu(II) [12]Metallacrown-4 with GABA Hydroxamic Acid: An Unprecedented Crystal Structure of a [12]MC-4 with a gamma-Aminohydroxamate. *Chemistry* **13**, 1300-1308.

Abstract: The solution equilibria of gamma-aminobutanehydroxamic acid (GABAha) with H(+) and Cu(2+) were investigated by potentiometry, titration calorimetry, spectrophotometry, NMR spectroscopy, and ESI-MS. The thermodynamic parameters of the Cu(II) [12]metallacrown-4 obtained for GABAha were compared with those of the corresponding complexes of (S)-alpha-Alaha and beta-Alaha. The stability (-DeltaG(0)) sequence was beta-Alaha>>alpha-Alaha>GABAha, whereas the order of formation enthalpies (-DeltaH(0)) was beta-Alaha>>GABAha>alpha-Alaha. These data were interpreted on the basis of the dimensions of the chelate rings and the planarity of the metallamacrocycles. The Cu(II) [12]metallacrown-4 ([12]MC-4) complex of GABAha was isolated and its crystal structure, which is the first reported for a [12]MC-4 of a gamma-aminohydroxamic acid, fully supports the structural features interpreted from the thermodynamic data.

Thongngam M. and McClements D. J. (2005) Influence of pH, ionic strength, and temperature on self-association and interactions of sodium dodecyl sulfate in the absence and presence of chitosan. *Langmuir* **21**, 79-86.

Abstract: Chitosan is a cationic biopolymer that has many potential applications in the food industry because of its unique nutritional and physicochemical properties. Many of these properties depend on its ability to interact with anionic surface-active molecules, such as surfactants, phospholipids, and bile acids. The purpose of this study was to examine the influence of pH (3 and 7), ionic strength (0-200 mM NaCl), and temperature (10-50 degrees C) on the interactions between a model anionic surfactant (sodium dodecyl sulfate, SDS) and chitosan using isothermal titration calorimetry, selective surfactant electrode, and turbidity measurements. At pH 3 and 30 degrees C, SDS bound strongly to chitosan to form an insoluble complex that contained about 4-5 mmol of SDS/1 g of chitosan at saturation. When SDS and chitosan were mixed at pH 7 they did not interact strongly, presumably because the biopolymer had lost most of its positive charge at this pH. However, when SDS and chitosan were mixed at pH 3 and then the solution was adjusted to pH 7, the SDS remained bound to the chitosan. The presence of NaCl (0-200 mM) in the solutions decreased the critical micelle concentration (cmc) of SDS (in both the absence and the presence of chitosan) but had little influence on the amount of SDS bound to chitosan at saturation. The cmc of SDS and the amount of SDS bound to the chitosan at saturation were largely independent of the holding temperature (10-40 degrees C). Nevertheless, the enthalpy changes associated with micelle dissociation were highly temperature-dependent, indicating the importance of hydrophobic interactions, whereas the enthalpy changes associated with SDS-chitosan binding were almost temperature-independent, indicating the dominant contribution of electrostatic interactions. This study provides information that may lead to the rational design of chitosan-based ingredients or products with specific nutritional and functional characteristics, for example, cholesterol lowering.

Thongngam M. and McClements D. J. (2004) Characterization of interactions between chitosan and an anionic surfactant. *J Agric Food Chem* **52**, 987-991.

Abstract: Chitosan is a cationic biopolymer that has many potential applications in the food industry because of its unique nutritional and physicochemical properties. Many of these properties depend on its ability to interact with anionic surface-active molecules, such as phospholipids, surfactants, and bile acids. The purpose of this study was to characterize the interaction between chitosan and a model anionic surfactant (sodium dodecyl sulfate, SDS) using isothermal titration calorimetry (ITC), surfactant-selective electrode (SSE), and turbidity measurements. ITC and SSE indicated that SDS bound strongly to chitosan via a highly exothermic interaction. The turbidity measurements indicated that chitosan formed insoluble complexes with SDS that strongly scattered light. The chitosan bound approximately 4 mM of SDS per 0.1 wt % chitosan before becoming saturated with surfactant. The SDS-chitosan interaction was weakened appreciably by the presence of 100 mM NaCl, which suggested that it was electrostatic in origin. This study provides information about the origin and characteristics of molecular interactions between chitosan and anionic surface-active lipids that may be useful for the rational design of chitosan-based food ingredients with specific nutritional and functional characteristics, e.g., cholesterol lowering or fat replacement.

Thongngam M., and McClements D.J. (2005) Isothermal titration calorimetry study of the interactions between chitosan and a bile salt (sodium taurocholate). *FOOD HYDROCOLLOIDS* **19**, 813-819.

Tian Y., Ravi P., Bromberg L., Hatton T. A. and Tam K. C. (2007) Synthesis and aggregation behavior of pluronic F87/poly(acrylic acid) block copolymer in the presence of doxorubicin. *Langmuir* **23**, 2638-2646.
Abstract: Poly(acrylic acid) (PAA) was polymerized on both termini of Pluronic F87 copolymer using the atom transfer radical polymerization technique to produce a novel block copolymer, PAA-b-F87-b-PAA (F87PAA). The loading of a cationic anticancer drug, doxorubicin (DOX), to F87PAA at different pH values was investigated using isothermal titration calorimetry (ITC), laser light scattering techniques, and UV-vis spectroscopy. At pH of 4.3-7.1, the ITC profile exhibited a significant exothermic peak, which indicated that the drug loading is an enthalpically driven process. At a pH of 4.3, the enthalpy maximum was significantly reduced in the presence of 2 M urea, indicating the existence of hydrogen bonds between the DOX and F87PAA copolymer. At a pH of 7.1, the fraction of bound DOX was close to the stoichiometric proportion of 1:1 to the molar concentration of carboxyl groups in the copolymer, where the drug loading is governed by electrostatic and stacking interactions. The TEM image of the complex indicated the formation of large compound micelles induced by the binding of DOX to the PAA segments.

Tobey S. L. and Anslyn E. V. (2003) Studies into the thermodynamic origin of negative cooperativity in ion-pairing molecular recognition. *J Am Chem Soc* **125**, 10963-10970.

Abstract: The association of synthetic receptors to target guests often proceeds through the cooperative action of multiple binding forces. An investigation into the thermodynamic origin of cooperativity in ion-pairing host-guest binding in water is described. The binding affinities of 1,2,3,4-butanetetracarboxylate, tricarballate, glutarate, and acetate to a C(3)(v) symmetric metallo-host (1) are characterized in terms of the binding constants (K_a) and the thermodynamic parameters ΔG degrees, ΔH degrees, and ΔS degrees, as determined by isothermal titration calorimetry (ITC). These values are used to determine the individual contributions of the binding interaction to the overall binding. Several ways to view the combination of the individual binding events that make up the whole are analyzed, all of which lead to the conclusion of negative cooperativity. Combined, the data were used to evaluate the thermodynamic origin of negative cooperativity for this series of guests, revealing that entropy is the largest contributing factor. An interpretation of this result focuses upon differences in the number of water molecules displaced upon binding.

Umebayashi Y., Shin M., and Ishiguro S. (1997) Thiocyanato and Iodo Complexation of Cadmium(II) Ions in Micellar Solutions of a Nonionic Surfactant Triton X-100. *J Colloid Interface Sci* **191**, 391-397.

Abstract: Complexation of the cadmium(II) ion with thiocyanate and iodide ions have been studied by precise titration calorimetry in micellar solutions of a nonionic surfactant Triton X-100 containing 0.4 mol dm⁻³ NaClO₄ as a constant ionic medium at 298 K. With regard to the Cd(II)-SCN⁻ system, the formation of [Cd(NCS)]⁺ and [Cd(NCS)(SCN)] in aqueous solution and [Cd(NCN)2(SCN)]⁻ in micelles was established, though the complexation in micelles is not extensive. With the Cd(II)-I⁻ system, the formation of [CdI]⁺, [CdI3]⁻, and [CdI4]²⁻ was established in aqueous solution together with the formation of [CdI2], [CdI3]⁻, and [CdI4]²⁻ in micelles. It is revealed that the complexation in micelles is accompanied by relatively large and negative enthalpies, which is ascribed to the enthalpies of transfer of [CdI3]⁻ and [CdI4]²⁻ from aqueous solution to micelles. This suggests that a hydrophobic complex with no capacity to form strong hydrogen bonds in water is favored in micelles.

Umebayashi Y., Shin M., Kanzaki R., and Ishiguro S. S. (2001) Thermodynamics of. *J Colloid Interface Sci* **237**, 167-173.

Abstract: Formation of cobalt(II)-thiocyanato complexes in nonionic surfactant solutions of poly(ethylene oxide) type with varying poly(ethylene oxide) chain lengths of 7.5 (Triton X-114), 30 (Triton X-305), and 40 (Triton X-405) has been studied by titration spectrophotometry and calorimetry at 298 K. Data were analyzed by assuming formation of a series of ternary complexes Co(NCS)(n)Y(m)((2-n)+) (Y=surfactant) with an overall formation constant $\beta(nm)$. In all the surfactant systems examined, data obtained can be explained well in terms of formation of Co(NCS)(+) and Co(NCS)(2) in an aqueous phase (aq), and Co(NCS)(4)Y(2-) in micelles, and their formation constants, enthalpies, and entropies have been determined. The $\beta(41)/\beta(20)$ ratio increases and the corresponding enthalpy becomes significantly

less negative with an increasing number of ethylene oxide groups. This suggests that micelles of these nonionic surfactants have a heterogeneous inner structure consisting of ethylene oxide and octylphenyl moieties. Indeed, on the basis of molar volumes of ethylene oxide and octylphenyl groups, intrinsic thermodynamic parameters have been extracted for the reaction $\text{Co(NCS)}_2(\text{aq}) + 2\text{NCS}^-(\text{aq}) = \text{Co(NCS)}_4^{2-}$ ($\Delta(r)G$ degrees, $\Delta(r)H$ degrees, and $\Delta(r)S$ degrees) at each moiety. The $\Delta(r)G$ degrees, $\Delta(r)H$ degrees, and $\Delta(r)S$ degrees values are -16 kJ mol^{-1} , -15 kJ mol^{-1} , and $3 \text{ J K}^{-1}\text{mol}^{-1}$, respectively, for the ethylene oxide moiety, and -15 kJ mol^{-1} , -70 kJ mol^{-1} , and $-183 \text{ J K}^{-1}\text{mol}^{-1}$ for octylphenyl. Significantly less negative $\Delta(r)H$ degrees and $\Delta(r)S$ degrees values for ethylene oxide imply that the hydrogen-bonded network structure of water is extensively formed at the ethylene oxide moiety, and the structure is thus broken around the Co(NCS)_4^{2-} complex with weak hydrogen-bonding ability. Copyright 2001 Academic Press.

Varghese N., Mogera U., Govindaraj A., Das A., Maiti P. K., Sood A. K. and Rao C. N. (2008) Binding of DNA Nucleobases and Nucleosides with Graphene. *Chemphyschem*.(epublication)

Abstract: Interaction of two different samples of graphene with DNA nucleobases and nucleosides is investigated by isothermal titration calorimetry. The relative interaction energies of the nucleobases decrease in the order guanine (G)>adenine (A)>cytosine (C)>thymine (T) in aqueous solutions, although the positions of C and T seem to be interchangeable. The same trend is found with the nucleosides. Interaction energies of the A-T and G-C pairs are somewhere between those of the constituent bases. Theoretical calculations including van der Waals interaction and solvation energies give the trend $G > A \sim T > C$. The magnitudes of the interaction energies of the nucleobases with graphene are similar to those found with single-walled carbon nanotubes

Vercouter T., Vitorge P., Amekraz B. and Moulin C. (2008) Stoichiometries and thermodynamic stabilities for aqueous sulfate complexes of U(VI). *Inorg Chem* **47**, 2180-2189.

Abstract: The formation constants of $\text{UO}_2\text{SO}_4(\text{aq})$, $\text{UO}_2(\text{SO}_4)_2^{2-}$, and $\text{UO}_2(\text{SO}_4)_3^{4-}$ were measured in aqueous solutions from 10 to 75 degrees C by time-resolved laser-induced fluorescence spectroscopy (TRLFS). A constant enthalpy of reaction approach was satisfactorily used to fit the thermodynamic parameters of stepwise complex formation reactions in a 0.1 M Na^+ ionic medium: $\log_{10} K_1(25 \text{ degrees C}) = 2.45 \pm 0.05$, $\Delta r H_1 = 29.1 \pm 4.0 \text{ kJ mol}^{-1}$, $\log_{10} K_2(25 \text{ degrees C}) = 1.03 \pm 0.04$, and $\Delta r H_2 = 16.6 \pm 4.5 \text{ kJ mol}^{-1}$. While the enthalpy of the $\text{UO}_2(\text{SO}_4)_2^{2-}$ formation reaction is in good agreement with calorimetric data, that for $\text{UO}_2\text{SO}_4(\text{aq})$ is higher than other values by a few kilojoules per mole. Incomplete knowledge of the speciation may have led to an underestimation of $\Delta r H_1$ in previous calorimetric studies. In fact, one of the published calorimetric determinations of $\Delta r H_1$ is here supported by the TRLFS results only when reinterpreted with a more correct equilibrium constant value, which shifts the fitted $\Delta r H_1$ value up by 9 kJ mol^{-1} . $\text{UO}_2(\text{SO}_4)_3^{4-}$ was evidenced in a 3 M Na^+ ionic medium: $\log_{10} K_3(25 \text{ degrees C}) = 0.76 \pm 0.20$ and $\Delta r H_3 = 11 \pm 8 \text{ kJ mol}^{-1}$ were obtained. The fluorescence features of the sulfate complexes were observed to depend on the ionic conditions. Changes in the coordination mode (mono- and bidentate) of the sulfate ligands may explain these observations, in line with recent structural data

Vieira E. F., Cestari A. R., de Santos E. B., and Rezende C. X. (2006) Measurement of cation binding to immobilized vanillin by isothermal calorimetry. *J Colloid Interface Sci* **298**, 74-78.

Abstract: Isothermal calorimetry was used to determine enthalpy changes for interaction of divalent cobalt, nickel, copper, and zinc chlorides with silica gel functionalized with vanillin, Sil-Van. The thermal effect, $Q(\text{int})$, and the corresponding amount of cation that interacts, $n(\text{int})$, were obtained in the same experiment. Langmuir expressions for adsorption isotherms were applied to determine the maximum adsorption capacity to form a monolayer, $N(\text{mon})$, and the energy of interaction for a saturated monolayer per gram of Sil-Van, $Q(\text{mon})$. From knowledge of $N(\text{mon})$ and $Q(\text{mon})$, the molar enthalpy of interaction for formation of a monolayer of anchored cations per gram of Sil-Van, $\Delta(\text{mon})H(\text{m})$, was determined. Interactions between the Lewis-acidic cations and the donor atom attached to silica are reflected by $\Delta(\text{mon})H(\text{m})$ values in the order $\text{Ni}^{2+} > \text{Cu}^{2+} > \text{Zn}^{2+}$ congruent with Co^{2+} .

Vieira E. F., Cestari A. R., Airoidi C. and Loh W. (2008) Polysaccharide-based hydrogels: preparation, characterization, and drug interaction behaviour. *Biomacromolecules*. **9**, 1195-1199.

Abstract: Oxidized alginate (ADA) and oxidized alginate blended with chitosan (ADA-Chit) were prepared in the presence of borax and CaCl₂, and their interactions with an antifolate drug, pyrimethamine (PYR), have been investigated. Tablets with a mean diameter of 1.2 ± 0.06 cm were produced and drug interactions were performed in dimethyl sulfoxide (DMSO) using isothermal titration calorimetry (ITC). From ITC responses, the enthalpy changes of interaction PYR/materials, ΔH , have been determined and were found to be -11.73 ± 0.517 kJ mol⁻¹ for ADA and -4.86 ± 0.156 kJ mol⁻¹ for ADA-Chit. The PYR encapsulation of approximately 75% was achieved for both materials, as measured by UV spectrometer

Wang C., Tam K. C., and Tan C. B. (2004) Binding of dodecyltrimethylammonium bromide to pH-responsive nanocolloids containing cross-linked methacrylic acid-ethyl acrylate copolymers. *Langmuir* **20**, 7933-7939.

Abstract: The binding of dodecyltrimethylammonium bromide (DoTab) to cross-linked methacrylic acid-ethyl acrylate (MAA-EA) copolymers with various MAA/EA molar ratios at different degrees of neutralization (α) was quantitatively studied using isothermal titration calorimetry, dynamic light scattering, surfactant selective electrode, and electrophoresis techniques. The surfactant binds to the polymers at all degrees of neutralization, but via different mechanisms. When α is sufficiently high, the binding is primarily electrostatic interaction between the surfactant and ionized polymer chains, which is reinforced by the micellization of electrostatically bound surfactant molecules. The saturation takes place at charge ratio ($[\text{DoTa}^+]/[\text{approximately COO}^-]$) close to 1, indicating that the binding is a one-to-one charge neutralization between the cationic surfactant headgroups and anionic carboxylate sites of the polymers. When α is low, the binding of DoTab to the unneutralized polymers is driven by the hydrophobic interaction. The onset of hydrophobic binding takes place at DoTab concentration as low as 0.01 mM in 0.05 wt % polymer solution, where the saturation occurs at C(DoTab) approximately 0.19 mM and the amount of bound surfactant is approximately 0.09 mmol of DoTab/(g of polymer) at saturation concentration. The binding results in the formation of the polymer-surfactant complex. For the polymer with low MAA/EA molar ratio, the complex coagulates at a higher DoTab concentration that leads to phase separation; however, for polymers with high MAA/EA molar ratio, the complex remains dispersed and the mixture is stable even at high DoTab concentration.

Wiberg K. B., Wang Y. G., Sklenak S., Deutsch C., and Trucks G. (2006) Permanganate oxidation of alkenes. Substituent and solvent effects. Difficulties with MP2 calculations. *J Am Chem Soc* **128**, 11537-11544.

Abstract: The permanganate oxidation of alkenes has been studied both experimentally and computationally. Transition state structures were located for the reaction of permanganate ion with a variety of monosubstituted alkenes at the B3LYP/6-311++G** level. Although the calculated activation energy for the reaction with ethene was reasonable, the calculated effect of substituents, based on the energies of the reactants, was much larger than that experimentally found. This was shown to be due to the formation of an intermediate charge-dipole complex which led to the transition state. Reaction field calculations found the complex to disappear in a high dielectric constant medium, and the range of activation energies for the reaction in solution became quite small. MP2 calculations were carried out in order to have a comparison with the DFT results. MP2-MP4 gave unusual results for calculations on permanganate ion as well as chromate ion and iron tetraoxide. They also gave markedly unreasonable results for the activation energy of the reaction of permanganate with ethane. CCSD/6-311++G** calculations gave satisfactory results for permanganate ion and chromate ion. At this level of theory, the reaction of permanganate with ethene was found to have a very early transition state, when the bond lengths of the reactants just began to change. The reaction was calculated to be very exothermic (-69 kcal/mol), and this was confirmed via calorimetry. The rates of permanganate oxidation of allyl alcohol and acrylonitrile were determined, and they had similar reactivities. The kinetics and the products of the reaction of permanganate with crotonate ion were examined in some detail.

Wiethoff C. M., Smith J. G., Koe G. S., and Middaugh C. R. (2001) The potential role of proteoglycans in cationic lipid-mediated gene delivery. Studies of the interaction of cationic lipid-DNA complexes with model glycosaminoglycans. *J Biol Chem* **276**, 32806-32813.

Abstract: Recent evidence supports a role for proteoglycans in polycation-mediated gene delivery. Therefore, the interaction of glycosaminoglycans with cationic lipid-DNA complexes (CLDCs) has been

characterized using a combination of biophysical approaches. At low ionic strength, CLDCs bind to heparin-derivatized Sepharose particles, with the ratio of cationic lipid to DNA controlling the binding. Incorporation of the helper lipids cholesterol or 1,2-dioleoyl-phosphatidylethanolamine increases the amount of bound CLDC. Heparin also induces the aggregation of CLDCs, with cholesterol reducing this effect. Isothermal titration calorimetry demonstrates an endothermic heat for the binding of heparin to CLDCs at low ionic strength, whereas circular dichroism studies suggest a heparin-stimulated release of DNA from CLDCs at a greater than 20-fold charge excess. Increasing the ionic strength to 0.11 reduces CLDC binding to heparin beads, and greatly enhances the release of DNA from CLDCs by heparin. The ability of the cell surface glycosaminoglycan heparan sulfate to release DNA from CLDCs is more sensitive than heparin to the incorporation of the cholesterol or 1,2-dioleoyl-phosphatidylethanolamine. Titration calorimetry reveals an exothermic heat for the interaction glycosaminoglycans with CLDCs at higher ionic strength. These results are consistent with the direct involvement of proteoglycans in transfection.

Wilson J. E. and Chin A. (1991) Chelation of divalent cations by ATP, studied by titration calorimetry. *Anal Biochem* **193**, 16-19.

Abstract: Thermodynamic parameters and stoichiometry for the formation of complexes of ATP with Mg²⁺, Ca²⁺, and Sr²⁺ were determined by titration calorimetry. In each case, 1:1 stoichiometry was observed and complex formation was entropy driven. Binding constants for formation of complexes decreased in the order of Mg²⁺ greater than Ca²⁺ greater than Sr²⁺, as expected from charge density considerations. Monovalent cations hindered complex formation with Mg²⁺, apparently by competing with the divalent cation for complexation with ATP. Analysis of this competitive effect provided estimates of the binding constants for complexes of ATP with monovalent cations, which decreased in the order expected from charge density considerations (Li⁺ greater than Na⁺ greater than K⁺).

Winschel C. A., Kalidindi A., Zgani I., Magruder J. L., and Sidorov V. (2005) Receptor for anionic pyrene derivatives provides the basis for new biomembrane assays. *J Am Chem Soc* **127**, 14704-14713.

Abstract: This study describes a new receptor cyclen 1 capable of strong selective binding of pyrene-based anionic dyes under near-physiological conditions. This receptor comprises four naphthylthiourea groups tethered to a cyclen core via an ester linkage. The complexation behavior of cyclen 1 receptor is characterized by a series of (1)H NMR, microcalorimetry, UV-vis, and fluorometry experiments. The relevance of structural features of this receptor to its recognition function is assessed using control compounds that lack some of the groups found in cyclen 1. The specificity of cyclen 1 toward pyrene-based dyes is assessed through experiments using dyes with different molecular organization. The most important finding was the ability of cyclen 1 to bind efficiently to a pH-sensitive dye pyranine, a dye that is commonly used in various biomembrane assays. The high affinity of cyclen 1 to pyranine, its impermeability to the lipid bilayer membrane, fast kinetics of binding, and ability to quench the pyranine's fluorescence were used as a basis for a new membrane leakage assay. This membrane leakage assay is fully compatible with the commonly applied pH-stat transport assay, and therefore it allows for differentiation of the ion transport and nonselective leakage mechanisms within a single set of experiments. The ability of cyclen 1 to quench the fluorescence of pyranine also finds limited applicability to the detection of endovesiculation.

Wiskur S. L., Lavigne J. J., Metzger A., Tobey S. L., Lynch V., and Anslyn E. V. (2004) Thermodynamic analysis of receptors based on guanidinium/boronic acid groups for the complexation of carboxylates, alpha-hydroxycarboxylates, and diols: driving force for binding and cooperativity. *Chemistry* **10**, 3792-3804.

Abstract: The thermodynamics of guanidinium and boronic acid interactions with carboxylates, alpha-hydroxycarboxylates, and diols were studied by determination of the binding constants of a variety of different guests to four different hosts (7-10). Each host contains a different combination of guanidinium groups and boronic acids. The guests included molecules with carboxylate and/or diol moieties, such as citrate, tartrate, and fructose, among others. The Gibbs free energies of binding were determined by UV/Vis absorption spectroscopy, by use of indicator displacement assays. The receptor based on three guanidinium groups (7) was selective for the tricarboxylate guest. The receptors that incorporated boronic acids (8-10) had higher affinities for guests that included alpha-hydroxycarboxylate and catechol moieties over guests containing only carboxylates or alkanediols. Isothermal titration calorimetry revealed the enthalpic and

entropic contributions to the Gibbs free energies of binding. The binding of citrate and tartrate was investigated with hosts 7-10, for which all the binding events were exothermic, with positive entropy. Because of the selectivity of hosts 8-10, a simple boronic acid (14) was also investigated and determined to be selective for alpha-hydroxycarboxylates and catechols over amino acids and alkanediols. Further, the cooperativity of 8 and 9 in binding tartrate was also investigated, revealing little or no cooperativity with 8, but negative cooperativity with 9. A linear entropy/enthalpy compensation relationship for all the hosts 7-10, 14, and the carboxylate-/diol-containing guests was also obtained. This relationship indicates that increasing enthalpy of binding is offset by similar losses in entropy for molecular recognition involving guanidinium and boronic acid groups.

Wszelaka-Rylik M., Witkiewicz-Kucharczyk A., Wojcik J. and Bal W. (2007) Ap4A is not an efficient Zn(II) binding agent. A concerted potentiometric, calorimetric and NMR study. *J Inorg Biochem* **101**, 758-763.

Abstract: Diadenosine 5',5"-P(1)P(4) tetraphosphate (Ap(4)A) has been considered as an intracellular partner for Zn(II). We applied potentiometry, ITC and NMR to study protonation equilibria of Ap(4)A and Zn(II) complexation by this dinucleotide. The values of binding constants obtained by these three techniques under various experimental conditions coherently demonstrated that Ap(4)A binds Zn(II) weakly, with an apparent binding constant of ca. 10(4) at neutral pH. Such a low stability of Zn(II) complexes with Ap(4)A excludes a possibility for interactions between these two agents in vivo.

Xian M., Zhu X. Q., Lu J., Wen Z., and Cheng J. P. (2000) The first O-NO bond energy scale in solution: heterolytic and homolytic cleavage enthalpies of O-nitrosyl carboxylate compounds. *Org Lett* **2**, 265-268.

Abstract: [reaction: see text] The first series of O-NO bond dissociation enthalpies was determined in solution for eight O-nitrosyl carboxylate compounds by direct titration calorimetry with a thermodynamic cycle. The derived bond energy data may serve as a quantitative guide to predict the NO binding and releasing abilities of the related amino acids.

Yajima T., Maccarrone G., Takani M., Contino A., Arena G., Takamido R., Hanaki M., Funahashi Y., Odani A., and Yamauchi O. (2003) Combined effects of electrostatic and pi-pi stacking interactions: selective binding of nucleotides and aromatic carboxylates by platinum(II)-aromatic ligand complexes. *Chemistry* **9**, 3341-3352.

Abstract: Adduct formations of Pt(II) complexes containing an aromatic diimine (DA) and an L-amino acid (A) with an aromatic carboxylate (AR) or a mononucleotide (NMP) has been studied by synthetic, structural, spectroscopic, and calorimetric methods. Several adducts between Pt(II) complexes, [Pt(DA)(L-A)] (charges are omitted; DA=2,2'-bipyrimidine (bpm); A=L-arginine (L-Arg), L-alaninate (L-Ala), and AR (=indole-3-acetate (IA), gentisate (GA)) or GMP were isolated as crystals and structurally characterized by the X-ray diffraction method. GMP in [Pt(bpm)(Arg)](GMP).5 H(2)O was revealed to be bound through the pi-pi stacking and guanidinium-phosphate hydrogen bonds. The [Pt(DA)(A)]-AR and -NMP systems in aqueous solution exhibited NMR upfield shifts of the aromatic ring proton signals due to stacking. The stability constants (K) for the adducts were determined by absorption and NMR spectra and calorimetric titrations. The log K values were found to be in the range 1.40-2.29 for AR and 1.8-3.3 for NMP, the order for NMP being GMP>AMP>CMP>UMP. The ΔH degrees values were negative for all the systems studied, and the values for AR (=IA and GA) were more negative than those for NMP, indicating that ARs are stronger electron donors than NMPs. Comparison of the log K values for [Pt(bpm)(L-Arg)] and [Pt(bpm)(L-Ala)] (Ala=alaninate) indicated that the Arg moiety further stabilized the adducts by the guanidinium-carboxylate or -phosphate hydrogen bonds. The combined effects of weak interactions on the stability of the adducts in solution are discussed on the basis of the thermodynamic parameters and solid state structures.

Yang W., Li Y., Cheng Y., Wu Q., Wen L. and Xu T. (2008) Evaluation of phenylbutazone and poly(amidoamine) dendrimers interactions by a combination of solubility, 2D-NOESY NMR, and isothermal titration calorimetry studies. *J Pharm. Sci.* (epublication)

Abstract: The interactions between phenylbutazone, a well-established nonsteroidal anti-inflammatory drug, with different generations of poly(amidoamine) (PAMAM) dendrimers, have been investigated by aqueous solubility, two dimensional nuclear Overhauser effect spectroscopy (2D-NOESY) and isothermal titration calorimetry (ITC) studies. Solubility results showed that PAMAM dendrimers significantly

enhanced the aqueous solubility of phenylbutazone and the solubilization was much influenced by dendrimer concentration, generation, surface function group and pH value. The 2D-NOESY spectra clearly showed that there were several kinds of cross-peaks from NOE interactions between the protons of phenylbutazone and the protons in interior cavities of both generation 6 and generation 3 PAMAM dendrimers. The solubility, 2D-NOESY results and ITC analysis suggest that encapsulation and electrostatic interaction together caused the solubility enhancement of phenylbutazone. The new techniques such as 2D-NOESY and ITC used in this study are useful tools in investigating the interactions between dendrimers and guest molecules. (c) 2008 Wiley-Liss, Inc. and the American Pharmacists Association J Pharm Sci

You C. C., Agasti S. S. and Rotello V. M. (2007) Isomeric Control of Protein Recognition with Amino Acid- and Dipeptide-Functionalized Gold Nanoparticles. *Chemistry* **14**, 143-150.

Abstract: Amino acid and dipeptide-functionalized gold nanoparticles (NPs) possessing L/D-leucine and/or L/D-phenylalanine residues have been constructed in order to target the surfaces of alpha-chymotrypsin (ChT) and cytochrome c (CytC). Isothermal titration calorimetry (ITC) was conducted to evaluate the binding thermodynamics and selectivity of these NP-protein interactions. The chirality of the NP end-groups substantially affects the resultant complex stability, with up to 20-fold differences seen between particles of identical hydrophobicity, demonstrating that structural information from the ligands can be used to control protein recognition.

Yu Y., Sweeney M. D., Saad O. M., and Leary J. A. (2006) Potential inhibitors of chemokine function: analysis of noncovalent complexes of CC chemokine and small polyanionic molecules by ESI FT-ICR mass spectrometry. *J Am Soc Mass Spectrom* **17**, 524-535.

Abstract: Chemokines play a critical role in inducing chemotaxis, extravasation, and activation of leukocytes both in routine immunosurveillance and autoimmune diseases. Traditionally, to disrupt chemokine function, strategies have focused on blockage of its interaction with the receptor. Recently, it has been demonstrated that binding to glycosaminoglycans (GAGs) is also required for the in vivo activity of many chemokines. Thus, interference with the GAG-binding of chemokines may offer an alternative, valid, anti-inflammatory strategy. However, the potential of using small polyanions to inhibit the interactions between chemokines and cell surface GAGs has not been fully explored. In this study, a mass spectrometry based filtration trapping assay was utilized to study the interactions between two CCR 2 ligands (MCP-1/CCL2 and MCP-3/CCL7) and a series of low molecular weight, polyanionic molecules. Findings were confirmed by using a hydrophobic trapping assay. The results indicated that Arixtra (fondaparinux sodium), sucrose octasulfate, and suramin were specific binders of the chemokines, while cyclodextrin sulfate, although the most highly sulfated molecule among the ones investigated, showed no binding. The binding stoichiometry of the small molecule ligand was determined from the measured molecular weight of the noncovalent complex. Furthermore, the dissociation constant between MCP-3 and Arixtra was determined by using electrospray ionization Fourier transform ion cyclotron resonance (ESI FT-ICR) mass spectrometry, which compared favorably with the result of the isothermal titration calorimetry (ITC) assay. The relative binding affinity of these ligands to MCP-3 was also determined using a competitive filtration trapping assay.

Zea C. J., Camci-Unal G. and Pohl N. L. (2008) Thermodynamics of binding of divalent magnesium and manganese to uridine phosphates: implications for diabetes-related hypomagnesaemia and carbohydrate biocatalysis. *Chem Cent. J* **2**, 15.

Abstract: ABSTRACT: BACKGROUND: Although the necessity of divalent magnesium and manganese for full activity of sugar nucleotidyltransferases and glycosyltransferases is well known, the role of these metal cations in binding the substrates (uridine 5'-triphosphate, glucose-1-phosphate, N-acetylglucosamine-1-phosphate, and uridine 5'-diphosphate glucose), products (uridine 5'-diphosphate glucose, uridine 5'-diphosphate N-acetylglucosamine, pyrophosphate, and uridine 5'-diphosphate), and/or enzyme is not clearly understood. RESULTS: Using isothermal titration calorimetry we have studied the binding relationship between the divalent metals, magnesium and manganese, and uridine 5'-phosphates to determine the role these metals play in carbohydrate biosynthesis. It was determined from the isothermal titration calorimetry (ITC) data that Mg²⁺ and Mn²⁺ are most tightly bound to PPI, $K_b = 41,000 \pm 2000$ M⁻¹ and $28,000 \pm 50,000$ M⁻¹ respectively, and UTP, $K_b = 14,300 \pm 700$ M⁻¹ and $13,000 \pm 2,000$ M⁻¹ respectively. CONCLUSION: Our results indicate that the formal charge state of the phosphate

containing substrates determine the binding strength. Divalent metal cations magnesium and manganese showed similar trends in binding to the sugar substrates. Enthalpy of binding values were all determined to be endothermic except for the PPI case. In addition, entropy of binding values were all found to be positive. From this data, we discuss the role of magnesium and manganese in both sugar nucleotidyltransferase and glycosyltransferase reactions, the differences in metal-bound substrates expected under normal physiological metal concentrations and those of hypomagnesaemia, and the implications for drug design

Zeng H., Ickes H., Flowers R. A., and Gong B. (2001) Sequence specificity of hydrogen-bonded molecular duplexes. *J Org Chem* **66**, 3574-3583.

Abstract: Hydrogen-bonded molecular duplexes, 1.3 and 1.4, each of which contains a mismatched binding site (acceptor-to-acceptor in 1.3, and donor-to-donor in 1.4), were designed and synthesized based on duplex 1.2. One- and two-dimensional NMR studies demonstrated that, despite their single mismatched binding sites, the backbones of duplexes 1.3 and 1.4 still stayed in register through the formation of the remaining five H-bonds. The backbones of 1.3 and 1.4 adjusted to the presence of the mismatched binding sites by slightly twisting around these sites, which alleviate any head-on repulsive interactions between two H-bond donors (amide O) or between two acceptors (amide H). After 1 equiv of single strand 2, which forms a perfectly matched duplex 1.2 with single strand 1, was added into the solution of either 1.3 or 1.4, only 1.2 and single strand 3 or 4, were detected. Isothermal titration calorimetry (ITC, in chloroform containing 5% DMSO) indicated that duplexes 1.3 and 1.4 were significantly (>40 times) less stable than the corresponding perfectly hydrogen-bonded duplex 1.2. These NMR and ITC results indicate that the pairing of two complementary single strands is not affected by another very similar single strand that contains only one wrong H-bond donor or acceptor, which demonstrates that the self-assembly of this class of H-bonded duplexes is a highly sequence-specific process. The role of these H-bonded duplexes as predictable and programmable molecular recognition units for directing intermolecular interactions has thus been established.

Zhang L. and Zhu L. (2008) Photochemically stable fluorescent heteroditopic ligands for zinc ion. *J Org Chem* **73**, 8321-8330.

Abstract: Photochemically stable fluorescent heteroditopic ligands (9 and 10) for zinc ion were prepared and studied. Two independent metal coordination-driven photophysical processes, chelation-enhanced fluorescence (CHEF) and internal (or intramolecular) charge transfer (ICT), were designed into our heteroditopic ligand framework. This strategy successfully relates three coordination states of a ligand, non-, mono-, and dicoordinated, to three fluorescence states, fluorescence OFF, ON at one wavelength, and ON at another wavelength. This ligand platform has provided chemical foundation for applications such as the quantification of zinc concentration over broad ranges (Zhang, L.; Clark, R. J.; Zhu, L. *Chem.-Eur. J.* 2008, 14, 2894-2903) and molecular logic functions (Zhang, L.; Whitfield, W. A.; Zhu, L. *Chem. Commun.* 2008, 1880-1882). The binding stoichiometries of dipicolylamino and 2,2'-bipyridyl, the two binding sites featured in heteroditopic ligands 7-10, were studied in acetonitrile using both Job's method of continuous variation and isothermal titration calorimetry (ITC). The fluorescence enhancement of 7-10 upon the formation of monozinc complexes (defined as the fluorescence quantum yield ratio of monozinc complex and free ligand) is qualitatively related to the highest occupied molecular orbital (HOMO) energy levels of their fluorophores. This is consistent with our hypothesis on the thermodynamics of the coordination-driven photophysical processes embodied in the designed heteroditopic system, which was supported by cyclic voltammetry studies. In conclusion, compounds 9 and 10 not only possess better photochemical stability but also display a higher degree of fluorescence turn-on upon formation of monozinc complexes than their vinyl counterparts 7 and 8

Zhu X. Q., Hao W. F., Tang H., Wang C. H., and Cheng J. P. (2005) Determination of N-NO bond dissociation energies of N-methyl-N-nitrosobenzenesulfonamides in acetonitrile and application in the mechanism analyses on NO transfer. *J Am Chem Soc* **127**, 2696-2708.

Abstract: The heterolytic and homolytic N-NO bond dissociation energies of seven substituted N-methyl-N-nitrosobenzenesulfonamides (abbreviated as G-MNBS, G = p-OCH₃(3), p-CH₃(3), p-H, p-Cl, p-Br, 2,5-2Cl, m-NO(2)) in acetonitrile solution were evaluated for the first time by using titration calorimetry and relative thermodynamic cycles according to Hess' law. The results show that the energetic scales of the heterolytic and homolytic N-NO bond dissociation energies of G-MNBS in acetonitrile solution cover the ranges from 44.3 to 49.5 and from 33.0 to 34.9 kcal/mol for the neutral G-MNBS, respectively, which

indicates that N-methyl-N-nitrosobenzenesulfonamides are much easier to release a NO radical (NO^{*}) than to release a NO cation (NO⁺). The estimation of the heterolytic and homolytic (N-NO)⁻(^{*}) bond dissociation energies of the seven G-MNBS radical anions in acetonitrile solution gives the energetic ranges of -15.8 to -12.9 and -3.1 to 1.8 kcal/mol for the (N-NO)⁻(^{*}) bond homolysis and heterolysis, respectively, which means that G-MNBS radical anions are very unstable at room temperature and able to spontaneously or easily release a NO radical or NO anion (NO⁻), but releasing a NO radical is easier than releasing NO anion. These determined N-NO bond dissociation energies of G-MNBS and their radical anions have been successfully used in the mechanism analyses of NO transfer from G-MNBS to 3,6-dibromocarbazole and the reactions of NO with the substituted N-methyl-benzenesulfonamide nitranions (G-MBSN⁻) in acetonitrile solution.

Zhu X. Q., Zhang J. Y. and Cheng J. P. (2007) Mechanism and driving force of NO transfer from S-nitrosothiol to cobalt(II) porphyrin: a detailed thermodynamic and kinetic study. *Inorg Chem* **46**, 592-600. **Abstract:** The thermodynamics and kinetics of NO transfer from S-nitrosotriphenylmethanethiol (Ph₃CSNO) to a series of alpha,beta,gamma,delta-tetraphenylporphyrinatocobalt(II) derivatives [T(G)PPCoII], generating the nitrosyl cobalt atom center adducts [T(G)PPCoIINO], in benzonitrile were investigated using titration calorimetry and stopped-flow UV-vis spectrophotometry, respectively. The estimation of the energy change for each elementary step in the possible NO transfer pathways suggests that the most likely route is a concerted process of the homolytic S-NO bond dissociation and the formation of the Co-NO bond. The kinetic investigation on the NO transfer shows that the second-order rate constants at room temperature cover the range from 0.76 x 10⁴ to 4.58 x 10⁴ M⁻¹ s⁻¹, and the reaction rate was mainly governed by activation enthalpy. Hammett-type linear free-energy analysis indicates that the NO moiety in Ph₃CSNO is a Lewis acid and the T(G)PPCoII is a Lewis base; the main driving force for the NO transfer is electrostatic charge attraction rather than the spin-spin coupling interaction. The effective charge distribution on the cobalt atom in the cobalt porphyrin at the various stages, the reactant [T(G)PPCoII], the transition-state, and the product [T(G)PPCoIINO], was estimated to show that the cobalt atom carries relative effective positive charges of 2.000 in the reactant [T(G)PPCoII], 2.350 in the transition state, and 2.503 in the product [T(G)PPCoIINO], which indicates that the concerted NO transfer from Ph₃CSNO to T(G)PPCoII with the release of the Ph₃CS^{*} radical was actually performed by the initial negative charge (-0.350) transfer from T(G)PPCoII to Ph₃CSNO to form the transition state and was followed by homolytic S-NO bond dissociation of Ph₃CSNO with a further negative charge (-0.153) transfer from T(G)PPCoII to the NO group to form the final product T(G)PPCoIINO. It is evident that these important thermodynamic and kinetic results would be helpful in understanding the nature of the interaction between RSNO and metal porphyrins in both chemical and biochemical systems.

Ziegler A. and Seelig J. (2008) Binding and clustering of glycosaminoglycans: a common property of mono- and multivalent cell-penetrating compounds. *Biophys J* **94**, 2142-2149. **Abstract:** Recent observations in cell culture provide evidence that negatively charged glycosaminoglycans (GAGs) at the surface of biological cells bind cationic cell-penetrating compounds (CPCs) and cluster during CPC binding, thereby contributing to their endocytotic uptake. The GAG binding and clustering occur in the low-micromolar concentration range and suggest a tight interaction between GAGs and CPCs, although the relation between binding affinity and specificity of this interaction remains to be investigated. We therefore measured the GAG binding and clustering of various mono- and multivalent CPCs such as DNA transfection vectors (polyethylenimine; 1,2-dioleoyl-3-trimethylammonium-propane), amino acid homopolymers (oligoarginine; oligolysine), and cell-penetrating peptides (Penetratin; HIV-1 Tat) by means of isothermal titration calorimetry and dynamic light scattering. We find that these structurally diverse CPCs share the property of GAG binding and clustering. The binding is very tight (microscopic dissociation constants between 0.34 and 1.34 microM) and thus biologically relevant. The hydrodynamic radius of the resulting aggregates ranges from 78 nm to 586 nm, suggesting that they consist of numerous GAG chains cross-linked by CPCs. Likewise, the membrane-permeant monovalent cation acridine orange leads to GAG binding and clustering, in contrast to its membrane-impermeant structural analogs propidium iodide and ethidium bromide. Because the binding and clustering of GAGs were found to be a common denominator of all CPCs tested, these properties might be helpful to identify further CPCs