

### News Items:

## International Seminar on Inclusion Compounds

In September 1987 the Institute of Physical Chemistry of the Polish Academy of Sciences hosted the International Seminar on *Inclusion Compounds* at Jaszowiec, in the hill resort area of Southern Poland. It was intended as an additional forum to the series of International Symposia on 'Inclusion Phenomena and Molecular Recognition', in particular for young scientists from Socialist Countries, for exchanging ideas and recent achievements in the field of Inclusion Science.

During the three-day conference 14 lectures were presented on different topics of inclusion chemistry:

- 'Clathrate Formation under High Pressures' (Yu. A. Dyadin);
- 'Dynamic Properties of the Framework of the Clathrate Hydrate' (V. R. Belosludov);
- 'Inclusion Compounds: an Entry into the Realm of Heteromolecular Associates' (M. Czugler);
- 'Imperfections in the Aqueous Lattice of Clathrates, as Detected by Electron Trapping' (Z. P. Zagorski);
- 'Intercalation Phenomena in Conducting Polymers' (A. Pron);
- 'Some Symmetry Aspects of Werner Clathrates' (J. Lipkowski);
- 'Cyclodextrins and Molecular Inclusion' (J. Szejtli);
- 'High Pressure Approach to the Synthesis of Cryptands' (J. Jurczak);
- 'Application of Cyclodextrins in HPLC Separation of Isomers' (D. Sybilska);
- 'Improvement of Stability of Prostacyclin-Methylester and Furosemide by Cyclodextrin Complexation' (J. Szeman);
- 'Synthesis and Complexing Properties of Chiral Macrocyclic Receptors Derived from Carbohydrates' (M. Pietraszkiewicz);
- 'X-ray Studies and Quantum Chemical Calculations Relevant to Biological Activity by Acyldiethylenetriamides of Phosphoric Acid and  $\alpha$ -(*N*)-Heterocyclic Carboxyaldehyde Thiosemicarbazones' (T. J. Malinowski);
- 'The Structure of Crown-Ethers, their Derivatives and Complexes' (Yu. A. Simonov);
- 'Numerical Modelling of Inclusion-Type Complexes Formed by Chiral 18-Crown-6 Ethers Bearing Sugar Moieties with Enantiomers of Phenylalanine Methyl Ester Cations' (K. Suwinska).

In addition to the lectures 26 communications were presented during two poster sessions.

About 70 participants from the Soviet Union, Hungary, Czechoslovakia and Poland expressed the opinion that meetings of this kind should be organized at

regular intervals, perhaps every second year and, in order to avoid any possible competition with the International Symposia, within odd years. The next one took place at the beginning of August 1989 in Novosibirsk, USSR. Correspondence should be addressed to:

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J. LIPKOWSKI

## Structure of Zeolite Beta Determined

The physical structure of zeolite beta, a sorbent and catalyst, has been determined at Exxon Research & Engineering Co. John M. Newsam told a symposium on molecular sieve science during the 3rd Chemical Congress of North America held in Toronto in June 1988, that he and his associates used a combination of direct measurements and computer modeling to deduce the very complex structure. Newsam says that zeolite beta is the most complex zeolitic structure determined to date. Although zeolite beta has been in use since its discovery in 1967, the structure had remained unknown until now.

Sorption data and catalytic characterization have suggested that zeolite beta might possess a three dimensional 12-membered ring system, which would indicate that its structure resembles that of faujasite, a naturally occurring zeolite. The structure was finally determined using electron microscopy, electron diffraction, and computer-assisted modeling. The approach to solving the structural puzzle involved combining a model from a two-dimensional projection of the structure derived from high-resolution imaging with information about two symmetry elements determined from electron diffraction. With the aid of computer modeling, this data permitted the generation of the three-dimensional structural model.

Zeolite beta is a hybrid of two distinct but related structures. Both result from the same centrosymmetrical tertiary building unit arranged in layers and both possess three-dimensional 12-ring pore systems. The zeolite exhibits a high density of stacking faults because successive layers must be interconnect in either left- or right-handed fashion. Both types of links occur with equal probability.

Newsam says that the zeolite beta structure is, indeed, unique for several reasons. It is the only high-silica zeolite to have a fully three-dimensional 12-ring pore system. It is the only zeolite to have a near-random degree of stacking effects and yet maintain full sorption capacity. Likewise, it is the only large-pore zeolite to have

chiral pore intersections. This could be significant because chiral templates might be of use in developing methods for zeolite beta synthesis, and these zeolites could then be used for the separation of chiral molecules, a long-sought procedure.

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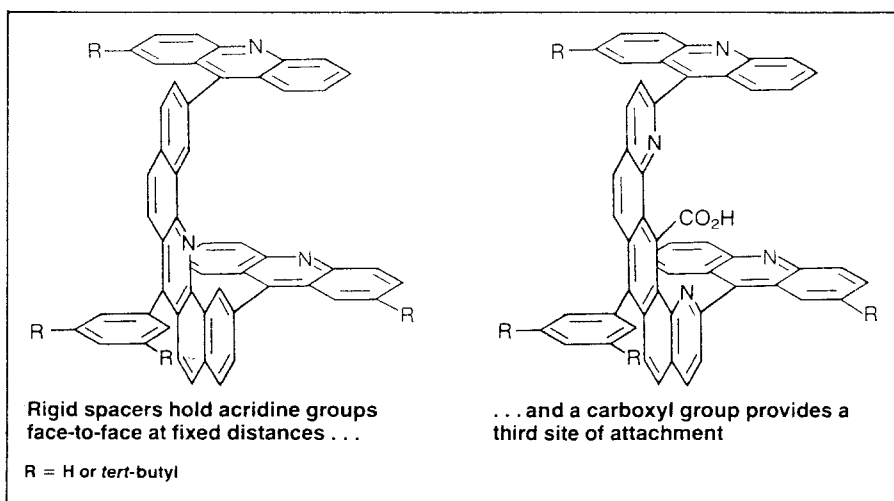
JOSEPH HAGGIN, Chicago

## Acridine Groups Used in Molecular Tweezers

In a contribution to the broad field of molecular recognition, chemists at the University of Illinois, Urbana, have been working on construction of molecular tweezers. Describing these compounds at an organic chemistry session during the 3rd Chemical Congress of North America held in Toronto in June 1988, they noted that the compounds feature planar complexing groups held *syn*-cofacial (face-to-face with matching of corresponding functional groups) by rigid spacers.

Such molecules might be useful in studying intercalation (sandwiching) of such flat species as bases of deoxyribonucleic acids for studies in sequence recognition, carcinogenesis, and chemotherapy.

Organic chemistry professor Steven C. Zimmerman told his audience that the term molecular tweezers was coined 10 years ago by organic chemistry professor Howard Whitlock at the University of Wisconsin, Madison. But Zimmerman's compounds show very efficient complexing owing to the recognition that the cavity between the tweezer jaws must be preorganized. The principle of preorganization of host molecules to accommodate guests arose from work by organic chemistry professor Donald J. Cram of the University of California, Los Angeles, who shared the 1987 Nobel Prize in Chemistry for his research in molecular recognition.



Working with postdoctoral fellow Gregory S. Hamilton, graduate students Craig M. VanZyl and Weiming Wu, and undergraduate Nathaniel S. Finney, Zimmerman made one pair of tweezers by linking two acridine molecules at their C-9 positions to C-1 and C-12 of 7-phenyldibenz[*c,h*]acridine. Their work was supported by the Research Corp., American Cancer Society, and National Institutes of Health.

The Urbana chemists showed the close interaction of the acridine jaws across the 7.2-Å distance separating them by comparing positions of nuclear magnetic resonance peaks of acridine protons with those of 9-phenylacridine model compounds. They also showed efficiency of complexation of 2,4,7-trinitrofluorene between the jaws by similar studies of fluorene protons. The rigid, fully aromatized spacer afforded more efficient complexation than flexible, partially saturated polycyclic or tetramethylenedioxy spacers.

The Illinois group also reported preliminary progress with a compound bearing a carboxyl group at C-14 of the spacer, which extends from the interior of the tweezers between the jaws. Though not its correct name, this molecule may be thought of as a 1,12-bis(9-acridinyl)-7-phenyldipyrido[2,3-*c*;2,3-*h*]anthracene-14-carboxylic acid.

If the simple bis(acridine) may be called a molecular tweezers, then that with the additional carboxyl group may be viewed as what cabinetmakers call a three-way edging clamp. In adding the carboxyl group for a third point of complexation by hydrogen bonding, Zimmerman borrowed a leaf from the book of organic chemistry professor Julius Rebek Jr. of the University of Pittsburgh, who has also designed such trifunctional host molecules (C&EN, Oct. 19, 1987, page 30).

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STEPHEN STINSON, New York

## Chemistry Beyond the Molecule

'Chemistry creates its object'. So said the French chemist Marcellin Berthelot in 1860. This confidence is echoed by Prof Jean-Marie Lehn of the Institute of Chemistry, Strasbourg, one of the 1987 chemistry Nobel prizewinners. Lehn sees chemistry as creative, bearing analogies to art, music or sculpture.

Lehn's early academic career did not show a particular inclination to chemistry, though science did interest him. He entered university to study philosophy. However, the French academic system had its part to play in shaping Lehn's future. Students of philosophy are required to include one module of science in their studies and he found that chemistry was an exciting new territory. He attended more chemistry lectures and decided to change to a science degree.

Lehn found chemistry fascinating, describing it to *Chemistry in Britain* as 'a science in which you can build up new objects that did not exist before' and allowing that he was impressed by 'the ability of chemistry to construct new molecules, to transform molecules one to another – power over matter'. He completed his first degree and began a PhD at Strasbourg with Prof Guy Ourisson,

which was completed in 1963. After a postdoctoral year at Harvard, working with Prof Robert Woodward on vitamin B<sub>12</sub> synthesis, Lehn returned to Strasbourg to start his own small group.

Last year Lehn shared the Nobel prize for chemistry with Charles Pedersen and Donald Cram for work on medium-sized encapsulating molecules. Understanding these molecules gives valuable information on the mechanism of molecular recognition – the ‘lock and key’ concept recognised by Emil Fischer in 1894 – which is fundamental to selective binding, catalysis, regulation and transport at the molecular level. Lehn’s group concentrated on the three-dimensional ‘cryptand’ host molecules. ‘In a wide sense this work is an outcome of my first year at university’ explains Lehn. He had studied general science during this year – chemistry, biology, physics, maths – and was very interested in human brain function and neurochemistry, ‘probably because of my interest in philosophy. Once I was a chemist I wondered how I could do something in that area’.

One characteristic of brain and nervous system function is that the nerve impulse is propagated via changes in concentrations of K<sup>+</sup> and Na<sup>+</sup> across the neuronal membrane. A chemist could investigate this problem by trying to influence the transfer of K<sup>+</sup> and Na<sup>+</sup> across membranes. This leads to the possibility of making substances that bind K<sup>+</sup> and Na<sup>+</sup> selectively and could help them to pass selectively through a membrane.

‘This was the beginning’ Lehn explains, ‘when I started my group in Strasbourg we were much more physically orientated – physical-organic and physical chemistry’. Then in 1964 Presman’s group in the US found that a natural antibiotic, valinomycin, was able to render membranes permeable to K<sup>+</sup> ions. The structure and synthesis of valinomycin had been done in 1963 by Shemyakin in Moscow. ‘That was a potent hint of what to do’. The first plan was to build cyclic peptides as host compounds, but peptides might not be stable enough for use in certain conditions so the search was on for a more stable function. Also, the peptides were two-dimensional macrocycles, which did not seem ideal for recognising an ion like K<sup>+</sup> or Na<sup>+</sup>. A three-dimensional compound would be better.

Pedersen’s famous 1967 paper on crown ethers came at the right time. In it, he described how cyclic ethers could bind an ion – less well than the natural ligands, but the resulting complexes were stable. In September–October 1967 Lehn and his group started work on their first three-dimensional cavity compound. Lehn coined the name ‘cryptand’ for these molecules (a crypt is a cavity) and the first one was synthesised in the autumn of 1968. The cryptand bound Na<sup>+</sup> and K<sup>+</sup> to produce ‘cryptates’.

Initially, the selective binding of K<sup>+</sup> was Lehn’s goal – but this meant also that the host molecule was ‘recognising’ K<sup>+</sup>. Lehn could see great possibilities for cryptands – in biology recognition is absolutely fundamental and all processes depend on it.

‘However, before recognition we need interaction between two species’ he explains. In the 19th century Paul Ehrlich wrote that molecules did not react unless they were bound; the idea of recognition was introduced by Fischer in 1894. However, forces are needed for recognition to occur. Wolff used the word *Uebermolekeln* in 1937 to describe species such as the H-bonded dimer formed by acetic acid. Lehn introduced the term ‘supramolecular chemistry’ to describe the

generalisation of the work started with his cryptands. 'It is supramolecular chemistry because it is chemistry beyond the molecule' he said. 'Not just the chemistry of the covalent bond but how molecules that are already covalently saturated will interact with other species and bind them'.

Supramolecular chemistry attracted a lot of interest. Pedersen's compounds were specific for ion binding. Cram extended the concept by making chiral receptor molecules – ones that could recognise chirality in binding. Clearly useful in stereoselective synthesis.

Scientists next began to look for new ways to use the guest molecules. Organic compounds such as primary ammonium salts could be bound; also, by replacing oxygen with sulphur or nitrogen, it was possible to bind transition metals, opening up a whole new coordination chemistry. The cryptands could therefore be used to select alkali metals, and molecules – but what about anions?

Lehn described the possibilities: 'When we look through coordination chemistry history it is interesting to note that anions were not considered – this may seem strange because if we add a little biochemical thought we see that lots of important biological substrates are negatively charged. They bind to proteins, enzymes and receptor sites, so there must be a coordination chemistry of anions. We must be able to make synthetic anion binders from the smallest  $\text{Cl}^-$  or  $\text{Br}^-$  to large molecules such as ATP, citric acid etc. This was a new field'.

Much of Lehn's work is very fundamental pure chemistry – putting basic concepts together to explore the world of the supermolecule. But selective binding has many possible uses, which hinge upon the three important properties of cryptands:

- *molecular recognition* – the selection of specific substrates;
- *catalysis* – when a substrate is bound to a synthetic receptor, if that receptor has special functions it may act on the bound substrate as a reagent or catalyst;
- *transport* – properties can be such that the receptor, dissolved in the membrane (if it is sufficiently lipophilic), picks up the substrate on one side, passes it through, and releases it on the other side.

Once these are understood chemists can try to introduce them as effectors into organised assemblies – eg molecular layers, membranes and liquid crystalline phases. This opens up a whole new area of science. Carriers can be envisaged that handle electrons and ions to make molecular signals. Our bodies function on  $\text{K}^+$ ,  $\text{Na}^+$  and acetylcholine signals and there are clues here to the way in which we work.

The type of information contained in selectivity could be used to store, regulate and retrieve signals, leading to new technologies; molecular electronics from electrons, molecular ionics from ions etc. But many new molecules will have to be synthesised and their organisation must be mastered.

Some of the applications that Lehn's group and others have been working on include;

- A compound that can absorb ultraviolet and emit visible light from  $\text{Eu}^{2+}$  bound in a cage – used to make tags for monoclonal antibodies in medical diagnostics.
- Anion activation – when a cation enters a cavity, an anion outside is 'free' and many become very reactive. This is used industrially in some polymerisation processes.

- Binding toxic metal ions – eg  $\text{Cd}^{2+}$ ,  $\text{Pb}^{2+}$  and  $\text{Hg}^{2+}$ . it is very selective but too expensive for environmental use.
- Isotope separation – when an ion penetrates the cavity it vibrates; different isotopes have different vibrational energies. A small difference in complex stability constant allows the separation of isotopes. Other groups are working on different applications, including sensors.

It is clear that Jean-Marie Lehn is enthusiastic about the future of his research and indeed about chemistry in general. 'It is close to the way you operate yourself. I think I am very sensitive to construction, to the way things are made – to architecture, be it real or molecular. I like music that is constructed and intense. I think chemistry has much of that – it has the possibility to organise matter, the ability to create new objects, to endow matter with novel properties. Chemistry is highly creative, like art. This is the most exciting thing – the great fundamental power of chemistry'.

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SALLY NELSON