

# *There is beauty beyond molecules*

## *An interview to Nobel prize winner Jean-Marie Lehn*

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«Green» meets Nobel Prize winner Jean-Marie Lehn, a pioneer of supramolecular Chemistry. This field looks at the synthesis and study of chemical compounds of larger dimensions and complexity compared to those of common molecules, assembled and made functional through non covalent bonds. Lehn speaks about his research, about nanotechnologies, sustainable development and ethical problems. And says: «A molecule cannot smile like Monna Lisa, nevertheless it is an artistic creation too. In our laboratories we have flasks, round bottom flasks and reagents, which we always create something new through, just like canvas, paintbrushes and colours are used in painting».

*Prof. Tundo: You are one of the experts and pioneers of supramolecular chemistry. However, before being involved in this field you have been involved as post doctorate in the total synthesis of the vitamin B<sub>12</sub>. How did your interest in supramolecular chemistry begin?*

Prof. Lehn: At the end of my post doc with Woodward (Nobel Prize in Chemistry 1965), supramolecular chemistry did not exist yet. Vitamin B<sub>12</sub> was a major big project in Woodward's group at the time, which I was involved in. At the end of my post-doc, I returned to Strasbourg and I wanted to enter a new field of research. In Strasbourg, I became much more involved in physical chemistry and computational chemistry. But of course, I was a chemist and I was interested in entering a new field. One such field was Neurochemistry, chemistry of the nervous system. But as a chemist it's a bit difficult to enter into biology. Therefore, I was thinking what could be a way for a chemist to enter into a field like that. It was well understood at the time that the nerve influx, along the nerves, which propagates the nerve signal is based on the change of concentrations of sodium and potassium ions across the neural membrane. This means that in the neural membranes there must be molecules, i.e. proteins, capable of distinguishing between sodium and potassium. At this point the question was: "Could we make compounds which do the same?"

At that time, it had just been discovered that the antibiotic, Valinomycin, was able to make mitochondrial membranes permeable to potassium. Valinomycin had been discovered in

Germany by Brockmann, its structure and synthesis had been elucidated by Shemyakin in Moscow, and its properties, in terms of mitochondrial transport, had been studied by Pressman in the USA. So at that point we had a small molecule able to distinguish potassium from sodium. Perhaps we were able to make other molecules with similar properties. In short, that's how I became interested in this type of molecule.

Initially I was inspired by antibiotics and by natural products capable of binding potassium. However, somewhat later, in 1967, Pedersen had published a preliminary communication in JACS (Journal of the American Chemical Society) about crown ethers and how they can bind potassium ions. But crown ethers are only two dimensional macrocycles. We thought it would be better to have something that has a spherical cavity, not just a circular, 2-D one. We thought it would be better to have something that has a spherical cavity, not just a circular, 2-D one. This idea leads us to the discovery of cryptands. In particular, their modification led to different interactions between the host and the guest, consequently leading to molecular recognition. That's how we started to explore and define this new field of Molecular Recognition, a field which deals with non covalent interactions between chemical objects. Here you can see the progressive coming to the concept of supramolecular chemistry. It was realising that the process of molecular recognition must involve non-covalent intermolecular interactions, that led to the origin of supramolecular chemistry, that was the origin.

*Prof. Tundo: How did supramolecular chemistry change in the last twenty years and what do you think will be the future of supramolecular chemistry?*

Prof. Lehn: The first time I used the words supramolecular chemistry was in 1978, in two papers, Accounts of Chemical Research and Pure and Applied Chemistry. This was the moment where I realised the concept, the breadth, of supramolecular chemistry. How did it change? Firstly, the basic process is the study of non-covalent interactions and the second is studying molecular recognition, which directly depends on non-covalent interactions. In this area more and more complex units have been studied. This helped also to understand drug design, how to make a drug for a given receptor, biological one.

Then, between 1970 and around 1985, supramolecular systems in catalysis was studied. From that moment, one can realise that if you understand molecular recognition you can use this knowledge about the specific interactions to make systems which can self-assemble in a very organised fashion directed by the molecular recognition process. That led us to the idea that self organisation can be generated and that one can make systems which self organise. In my group we started to investigate this concept, around 1985, with the work related to the helicates. Others

people such as Fujita, Peter Stang, Ken Raymond, and of course a lot of people in Italy used the idea of using well designed ligands for well chosen metal ions that can self-assemble. Of course, there are examples of self-assembly with just organic compounds using hydrogen bonding (George Whitesides, David Reinhoudt) and donor-acceptor (Fraser Stoddart) interactions. All this has developed in terms of using non-covalent interactions to generate supramolecular entities in a programmed fashion, which I like to call programmed chemical systems.

In the last 10 years supramolecular chemistry evolved. By essence Supramolecular chemistry is a dynamic chemistry, meaning that the entities are not bound very strongly, therefore they can dissociate and re-associate, meaning the interactions are reversible they are dynamic in their make-up. Simplistically, the make-up of the supramolecular object can change by throwing something out, incorporating other things, exchanging, reshuffling, etc. However, one can also use the reversible reactions such as aldol reactions or imine formation to change the dynamic constitution of an object, an area I like to call constitutional dynamic chemistry, an area we are involved in now (*Chem. Soc. Rev.*, 2007, **36**, 151-160).

*Prof. Tundo: Nowadays, nanotechnology is one of the most used term in science with almost 17 million hits on Google. From a chemist point of view how would you define nanotechnology?*

Prof. Lehn: We can define nanotechnology in two different ways. One way is the physical approach of nanotechnology, where by fabrication means one tries to make objects of nanometric size which have properties where such materials could be used for communications, information and computing type technology.

The other approach is more chemical. It is related to the bottom up approach, no fabrication. Many people have used chemical procedures in, for instance, assembling layers on surfaces, making multi-layers, making different objects on surfaces.

But the other possibility, in the future, becoming increasing important is that maybe we will be able to generate these nanometric size devices, not by fabricating them but letting them make themselves, by self organisation. So the idea is to be clever enough to mix the right pieces and let them go together in a controlled fashion and so they would generate the device itself.

*Prof. Tundo: You are also involved in the dissemination of the scientific culture as president of the non-governmental organization IOCD (International Organization for Chemical Sciences in Development): what is the main aim of this organization?*

Prof. Lehn: Although we are big in name we are quite small in terms of money. It is composed of volunteers who give their free time to help chemists in developing countries. The broad aim is to help these chemists do their chemistry but also to help them exploit and utilise the interesting chemical possibilities that their countries have to offer. A significant area would be interesting compounds that are found in the chemistry of plants, i.e. identification and production of active compounds can be obtained from plants. Plant and analytical chemistry are sections that we have in order to teach them about these aspects.

*Prof. Tundo: Do you think green chemist can help improve the opinion that people have of chemistry and of chemists? What is your opinion about green chemistry?*

Prof. Lehn: I don't have a doubt that Green Chemistry will help improve the opinion of people on Chemistry. As chemists we all try to do green chemistry. This means to do reactions that are more efficient, higher yields, more selectivity, using less energy and less materials, better processes and so on. This kind of attitude makes us more respectful of the starting materials that we have at our disposal i.e. oil or plants.

Another aspect of green chemistry is catalysis. Catalysis is a very important because it can make processes more efficient, by making them less energy intensive and more selective. It is a very important process for developing sustainable chemistry, chemistry that uses starting materials that are different from those of oil. What should be attempted is to use compounds from plants, such as wood, that can be transformed into interesting polymers, interesting plastic materials, maybe fuels.

Bio-fuels is another area of interest. I am not convinced that bio-fuels will be an answer. Because as many people have remarked that from the moment people want to produce bio-fuels, you do it at the expense of food. Maybe in the future we would be able to produce genetically modified organisms that would be more productive in terms of interesting starting materials for chemistry to be used in the synthesis of drugs as an example or produce organisms that are more productive in the fermentation process leading better fuel production.

Green chemistry is a very interesting concept, but in fact many of these concepts, chemists have been thinking about it before.

*Prof. Tundo: Infact, I think that scientists have always thought in a manner of Green Chemistry or Sustainability. The point is to try to take this way of thinking into industry, especially applying the use of catalysts.*

Prof. Lehn: Yes, I think you're quite right. Chemists have always thought in terms of Green Chemistry. Every time that one searches to obtain a higher yield or a more efficient reaction, one is thinking in a Green manner. But now the concept is stronger and it is important.

*Prof. Tundo: I think green chemistry is a concept that people like, not only in Europe or the US but also, in Africa or Asia.*

*Prof. Tundo: According to you what is the most appealing aspect of chemistry? What would you say to a young student to convince him/her to start a career as a chemist?*

I would say why I am happy to be a chemist. The most basic problem, not necessarily the most important, how has the universe been able to generate an entity, a thinking organism, like a human being. My opinion is it happens by self organisation. The question is how matter can self organise itself to progressively produce complex entities.

How can you make an young person enthusiastic about this thing? Simple, chemistry is really at the centre of this. We have to think of how from simple atoms we can make simple molecules, from simple molecules how to we can make supramolecular assemblies, and from these assemblies how we can get cells and tissues, organisms etc. All this is based on molecules and how they organise themselves.

In Biology we have to admit that all these very complex organisms, including the thinking ones are based on molecules, so I think for me is something that can make a young person want to study Chemistry.

The second thing which is more chemical so to say, it underlies the thinking of chemists: what we are trying to do is understand matter, to control matter, how we can transform it, how the way we can eventually understand the way in which transforms etc. Therefore chemistry is an extremely creative science and a certain artistic sense. In chemistry you are able to create new objects you can't see with the naked eye. A molecule can't smile at you like a Gioconda (Mona Lisa) smiles at you, but a molecule is a creation. Young people can understand that when you make a molecule that has never been made before, we have created something new. Some molecules are totally uninteresting, but there are also pieces of music that are uninteresting, but the basic act of making it is interesting. This is something that we can tell young people. As for a picture one uses a canvas, coloured paints etc., a chemist uses flasks, instruments and reagents to obtain something new.

*Prof. Tundo: Do you think ethical issues should be addressed by science? Do you think they should be included in a student curriculum?*

Prof. Lehn: That's a very good question. I think ethical questions are always important. I have an opinion that may not be in line with the thinking of a number of people. I believe knowledge always precedes ethics. In the old Greek times it was perfectly acceptable to have slaves; in Roman times it was acceptable to have people killing themselves in an arena. In some tribes in other countries it's acceptable to eat your enemy when you killed him or her. In ancient Egypt the Pharaoh had to marry his sister or mother. So ethics have changed with time. We are now under the ethics which has been developed by, on one hand, the Christianity, Buddhism, Islamic and rational influence.

To live according to rational ethics is the most difficult. We live in a society and we have find a way accept each other and co-exist with each other and but in the future there may be more rational ways or approaches to do so. In the long run, knowledge, truth etc. are above ethics, and ethics will adapt to what we know. For example, don't eat your enemy, even if you have killed him or her. This is due to the fact that we have thought about these people as equals to us.

Coming back to the question, for scientists a practical example is relative to the scientific journals. When we publish things that we publish what is correct, or we think is correct. We of course can make a mistake, but if we do make a mistake we do it not intentionally. I think it is important to teach young people the ethics of science. Science is based on telling people: "I know, I do not know, I think I know, I think it is probably, I am convinced it is, because I have this data, etc." This approach is not only valuable in science, e.g. chemistry, physics, biology etc, but in the spirit we do our inquiry, the spirit in which we operate, which is very important. When I give public lectures I often insist on the fact science is something that people should be more interested in and it is very interesting to do, but the spirit of it, the way we do science, the thinking in which we do science is something very important. We try in principle to be reasonable, rational, logical, and not be carried away with things that can carry us away to wrong conclusions, which can bring us to try to deceive people.