

Professor Armand Lattes

A Scientific Tribute



Armand LATTES was born in Toulouse, South-West France, on 31 March 1934. After his education at, St Joseph's private secondary school in Toulouse, he studied at the *Ecole Nationale Supérieure de Chimie*, and at the University of Toulouse, where he gained an Engineering Diploma and a B.Sc. with distinction in 1955.

After graduating he joined the staff of the Department of Chemistry of the same University, as assistant Professor, and became a postgraduate researcher in the laboratory under the direction of Professor Georges Mignonac who was a former student of Professor Paul Sabatier (who won the Nobel Prize in 1912) and of Professor Charles Moureau at the College de France (Paris). During his *Doctorat ès Sciences* studies (1955-1960) he obtained the Diploma in Pharmacy at the Faculty of Pharmacy of Toulouse (1961). He received a D.Sc. degree in Paris, in December 1960, and, in 1982 he was awarded a doctorate in Pharmacy. During the war in Algeria he served in the French Air Force for more than two years from 1961 to 1963.

After his military service he became a staff member in the Department of Chemistry of the newly-founded "*Institut National des Sciences Appliquées*" as associate professor (1963-1967). In 1967, he was appointed Assistant Professor at the Faculty of Sciences of Toulouse, now called Paul Sabatier University, gradually advancing to the title of Full Professor (1971), Outstanding Professor (1984) and Emeritus Professor (2003). From 1979-1987 he was the Director of the *Ecole Nationale Supérieure de Chimie de Toulouse* where he created a new educational department on the chemical enhancement of agro-resources. He then became head of the federative Research Institute in Organic Chemistry (1987-1994) and Director of the Institute of Molecular Chemistry (1994-1999).

During his D.Sc. research he studied catalytic reactions on α -aminoalcohols obtaining a new heterocyclic family for the first time: the 1,4 -di-substituted-1,4-di-hydropyrazines, and describing new syntheses of indoles and piperazines. Thus he became familiar with heterocyclic chemistry and the behaviour of nitrogen-containing organic compounds. This is the reason why,

following his doctorate, he became involved in a general project directed towards the study of the influence of the nitrogen atom on the formation, stability and properties of reaction intermediates.

In this first period of his research career, he effected many significant reactions, studied a number of mechanisms and carried out conformational analysis of numerous nitrogen-containing heterocycles. In the field of carbocations, the assistance of nitrogen depends on the distance between the nitrogen atom and the positive carbon atom. Thus an aziridinium ion intermediate can be formed in some cases resulting in new heterocycles or polyfunctional compounds, with nucleophilic centers.

While trying to prepare aminocarbanions he studied the basic rearrangement of allylic amines. Working at low temperatures he was able to characterize the kinetic products, obtaining the first N-aromatic enamines. The stereochemistry of these enamines, demonstrated by different methods, was the opposite of the commonly accepted version. The NMR characterization of the stereochemistry was of such pedagogical value that it was included in an educational science text-book.

One highlight of this research was the discovery and generalization of aminomercuriation reactions. Previously, chemists believed that it was impossible to effect a reaction between primary and secondary amines and ethylenic compounds in the presence of mercuric salts, because of the formation of strong, black complexes between the amines and the salt. Basing his opinion on the Pearson theory of Hard and Soft Acids and Bases, Armand Lattes postulated that this reaction should be possible; since amines are hard bases, olefins soft bases and mercury is a soft acid, the amine-salt complexes should be destroyed by amines and thus the acid-base reaction would be better between olefins and mercuric salt expediting the attack on the mercurinium ion intermediate by amines. And so it turned out and aminomercuric compounds were obtained for the first time!

To avoid the formation of complexes, another reaction was found, viz. deoxyaminomercuriation. Oxymercuric compounds are very easily formed with alcohols, olefins and mercuric salts. By applying the principle of microscopic reversibility, the acidic decomposition of an oxymercuric compound gives the mercurinium ion intermediate which reacts with amines to obtain aminomercuric compounds. The reduction of the latter product with NaBH_4 gives the hydroamination derivative of ethylenic reactants.

The reduction of organomercuric compounds with NaBH_4 is, in theory, a radical mechanism. In fact the assistance of the nitrogen atom orientates, for the first time, the cleavage of the C-Hg bond, towards the formation of an aziridinium cation.

Both reactions are highly stereoselective, and the amino compounds are obtained in very good yields. The intramolecular process of aminomercuriation of ethylenic amines is a general method for the synthesis many types of heterocycles and the method has been applied to the synthesis of complex molecules such as azubanane.

Interested by the small nitrogenous ring aziridine, Lattes studied N-unsubstituted aziridines in order to determine the value of the inversion barrier and to compare the size of the nitrogen

doublet to that of a hydrogen atom. He was able to measure this barrier (a difficult challenge!) and to show that the doublet is smaller than the hydrogen atom.

The second period was devoted to the use of photochemistry in organic synthesis, especially in the heterocyclic field. New methods to prepare indolic compounds, studies of the stereochemistry of photo reduction of ketones, were the first developments of this research. A second highlight was the study of the photochemical rearrangement of spirooxaziridines. This quantitative reaction gives rise to lactams with very high selectivity, deserving the name of "Photo Beckmann Rearrangements". But the lactam is formed in a reverse sense to the chemical Beckmann rearrangement. Both methods complement each other and give a general access to all heterocyclic lactams. It is a very good example of stereoelectronic control and is quoted in all specialized books.

More than thirty years ago, Prof. Lattes, directed his attention to the peculiar qualities of micellar solutions or microemulsions, which are the keys to the third period of research.

By using these organized molecular systems (OMS) as media, it is possible to realize many synthetic reactions owing to the special qualities of OMS: solubilization of substrates normally insoluble in the continuous phase of these systems, selective localizations of reactants and products, selective orientation, stabilization of reactants, products, intermediates and transition states, etc. The reactions are fast, selective, and products are often obtained in reasonable quantities; it is thus possible to study the mechanisms of their formation.

Firstly, Lattes produced organic photoreactions in microemulsions, macroscopically homogeneous and transparent media. Thus, he was able to confirm the interface localization of the processes, to suggest a formulation strategy for decreasing the number of substrates in the medium (molecular economy principle) and to use high interface concentrations to realize, in liquid phase, reactions which were only possible in the solid state.

The most important scientific achievement was the demonstration of the generalization of the amphiphilicity concept, first by using polar non-aqueous solvents. In 1986, it ended the controversy concerning the use of formamide instead of water. With this type of solvent, he was able to effect significant reactions in OMS: the so-called Wacker process, Diels-Alder reactions and olefin amidation. Aprotic polar solvents are also able to produce OMS if they are sufficiently structured. This is the case for N-methylsydnone, a new solvent for molecular aggregation, with which it was possible to prepare all types of aggregates including micelles, vesicles and liposomes.

He then postulated the formation of aggregates without surfactants if differential solvations were operative. Thus all organic reactions can be influenced by the spontaneous formation of aggregates, e.g. norbornene metathetic polymerization can be effected in a new stereoselective direction.

In conclusion, with OMS it is possible to orient the reactivity of competitive reactions (e.g. cyclization and polymerisation). In this way, with a modified Mukaiyama reactant it is possible to obtain large ring compounds avoiding the high dilution method, or, in emulsion with other

reactants, to prepare monodisperse nanometric latex. In the decontamination of chemical weapons, neurotoxic phosphorous compounds are very easily hydrolysed and yperite oxidized.

Prof. Lattes very quickly understood that it was necessary, in this type of chemistry, to have suitable surfactants for all situations. He described many preparations of such compounds and imagined the concept of modular synthesis providing, by exchange of synthons, the opportunity to obtain surfactant with all types of molecules (heterocycles, sterols, sugars, etc.). With a surfactant having an imidazole head, he obtained an artificial enzyme with the same catalytic properties as α -chymotrypsin. In particular, he developed a large family of new surfactants having partly a sugar hydrophilic head, studied aggregate formation with such amphiphilic molecules, and used them in different applications, viz:

- extraction of membrane proteins;
- formation of nanometric functionalized latex;
- with bolaforms (surfactants having two sugar heads), enzymatic reactions without loss of activity;
- with cyclodextrins, by inclusion of long chain alcohols, synthesis of non covalent surfactants;
- enantioselective synthesis by using sugar dendrimers, mimicking rigid micelles, thanks to which high enantioselectivities were obtained (up to 100 %) in the reduction of ketones;
- biological applications, e.g. aspergillose therapy and HIV neutralization.

The importance of Lattes' achievements in fundamental and applied chemistry should be emphasized. He showed for the first time that many reactions could be run systematically in organized molecular systems. The feasibility of organic synthesis in aqueous media is one of the twelve principles of green chemistry.

Professor, Lattes has been the recipient of many awards, at home and abroad.

- Chemical Engineer's Prize (1955)
- Toulouse Science Academy Award: Maury Award (1963)
- Royal Chemical Society of Netherlands Award: Van T'Hoff Prize (1967)
- Diploma of the Scientific Workers' Association of Bulgaria (1981)
- Honorary member of the Bulgarian Workers' Association (1981)
- Innovation Award of the Midi-Pyrénées Région (1985)
- French Academy of Science laureate: Grammaticakis-Neumann Award (1988), Berthelot medal (1988)
- French Chemistry Society: Le Bel Award (1993)
- Innovation Prize of the Paris-Reims Foundation (1996)
- The degree Doctor *Honoris Causa* from Sofia St Clement University (Bulgaria, 1999), from the St Petersburg University (Russia, 2003), honorary member of the Romanian Chemistry Society (2004).

He is a member of the French National Academy of Pharmacy, member, then President, of the Toulouse Academy of Sciences, correspondent member of the European Academy of Sciences.

In 2003 he was elected President of the French Chemical Society, and in 2005 President of the Federation of French Chemists.

He has been a Member or President of different councils and committees:

1. Member then President of the Scientific NATO Council "Environment and Earth" (NATO, 1999-2001);
2. President of the Scientific Council on Chemical and Biological
3. Defense (1994-1998);
4. President of the French Committee on Enhanced Oil Recovery (1974-1984);
5. Vice President of the French Assembly of the Directors of Engineering Schools (1981-1987);
6. President of the Organic Chemistry section of the *CNRS Centre National de la Recherche Scientifique* (1987-1992) and of the National Educational Chemistry Council (Molecular Chemistry), University Upper Council (1982-1987), etc...

As a scientist firmly committed to the promotion of Chemistry, he is a Member of the French Scientific "Prevention and Precaution Committee" (Ecology and sustainable Development Ministry) and of the Executive Committee "Sea Pollution" at the French Ministry of Research, working, at the present time, towards ecological awareness in scientific policy.

Professor Lattes has received the highest distinctions of his country, including *Chevalier of the Legion d'Honneur*, Commander of the French National Order of Merit, Commander of the *Palmes Academiques* order, etc.

He is a respected scientist with a long and impressive list of publications to his name. He is the author of over 400 original scientific publications and has delivered more than 150 lectures in 40 different countries. He was Professor by invitation of the Polytechnic Federal School of Lausanne (Switzerland, 1984) R.H. Martin Reader (Free University of Bruxelles, Belgium, 1990) and M.M. Janot Reader (Gif-sur-Yvette, 1992).

After 50 years of teaching and research, he continues to work in these sectors orienting his thinking processes to the use of noncovalent interactions in synthesis, analysis and biological applications.

Selected significant publications of Professor Armand Lattes

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2. Functional detergents containing imidazolium core and typical α -nucleophilic fragments as basis for designing micellar systems highly efficient in decomposition of phosphorus acid esters S. Simanenko Yu, E.A. Karpichev, T.M. Prokopeva, A. Lattes, V.A. Savyolova, L.A. Besousova *Russ. J. Org. Chem.* **2004**, *40*, 234.
3. Mechanistic study of the enantioselective reduction of ketones in the presence of glycodendrimers A. Schmitzer, E. Perez, I. Rico-Lattes et A. Lattes *Tetrahedron Asymmetry* **2003**, *14*, 3719.
4. Liquid crystals polysiloxane networks as materials for molecular imprinting technology J. D. Marty, M. Mauzac, C. Fournier, I. Rico-Lattes, A. Lattes *Liquid crystals* **2002**, *25*, 151.
5. New microemulsions for oxidative decontamination of mustard gas analogues F. Gonzaga, E. Perez, I. Rico-Lattes, A. Lattes *New J. Chem.* **2001**, *25*, 151.
6. Reactivity at the interface of chiral amphiphilic dendrimers A. Schmitzer, S. Franceschi, E. Perez, I. Rico-Lattes, A. Lattes *J. Am. Chem. Soc.* **2001**, *123*, 5956.
7. Molecular organized systems with fluorinated compounds I. Rico-Lattes, B. Guidetti, A. Lattes *J. Fluorine, Chem.* **2001**, *107*, 355.
8. Chemical activation in micelles, pseudomicelles and microemulsions Rico-Lattes, A. Lattes, et al, *Reactions and synthesis in surfactant systems*. Marcel Dekker, chap. 13, 337 (2001)
9. New molecular imprinting materials J. D. Marty, M. Tizra, M. Mauzac, I. Rico-Lattes, A. Lattes *Macromolecules* **1999**, *32*, 8674.
10. Amphiphilic urocanic acid derivatives as catalysts of ester hydrolysis N. Lauth de Viguerie, M. Riviere, A. Lattes *New J. Chem.* **1999**, *23*, 103.
11. The role of lipophilicity in oxidation of mustard gas analogues from micellar solutions F. Gonzaga, E. Perez, I. Rico-Lattes, A. Lattes *Langmuir* **1999**, *15*, 6956.
12. Aminomercuration - Hétérocyclisation d'amines éthyléniques J.J. Perie, J.P. Laval, J. Roussel, A. Lattes *Tetrahedron* **1972**, *28*, 675.
13. Aziridines - Etude par RMN de l'inversion de l'azote dans les aziridines à fonction amine secondaire R. Martino, J. Abeba, A. Lattes *Tetrahedron Lett.* **1973**, *6*, 433.