

# *Chiral Reactions in Heterogeneous Catalysis*



*Edited by  
Georges Jannes and Vincent Dubois*

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## PREFACE

It was a great honor for us to organize ChiCat, a symposium devoted to Chiral Reactions in Heterogeneous Catalysis and to be the hosts of more than 120 scientists coming from everywhere in the industrialized world, to celebrate together one century of existence of Institut Meurice.

This school was established in 1892 when an industrial chemist, named Albert Meurice, decided to educate practical chemists according to the perceived needs of the industry of that time. This is exactly what we are still trying to do. It is the reason why, thirty years ago, we started a research activity in catalysis, and why we progressively devote this research to the applications of catalysis in the field of fine chemicals. In this respect, we are very close to another initiative of Albert Meurice, who started the first production of synthetic pharmaceuticals in Belgium during World War I. This business later on became a part of the Belgian corporation UCB, still very active in pharmaceuticals today.

The school created by Albert Meurice merged in the fifties with another school that had been created to meet the same needs in the field of the food industries, mainly distilleries and breweries. This merger was done in the frame of the establishment of CERIA. For people in catalysis, ceria stands for cerium oxide, but for those who engineered the concept, CERIA stood for Center of Education and Research for the Food and Chemical Industries. Our center was created to stimulate the rebuilding of these industries in the province of Brabant, ruined by the war. Today it plays a prominent role in the development of technopoles in the new region of Brussels organized in federal Belgium. This explains the financial support we received from Brussels Ministry of Economy for the Centenary of Institut Meurice.

However, this symposium is probably the last meeting of the old fashioned Contact Group – Catalysis as supported by the National Science Foundation. The structure of financial support to scientific research has also been modified. We hope that it will not result in further diminishing the contribution of the national and local governments to the necessary endeavor of Belgium in research and development.

Twenty years ago, the Société Royale de Chimie founded its Catalysis Division. The first president of this Division, Professor Delmon, accepted that the first event organized by the division should help celebrate the twenty-fifth anniversary of CERIA : it was the First International Symposium on the Relations between Homogeneous and Heterogeneous Catalytic Phenomena, a series that is still going on. Nowadays, for the centenary of Institut Meurice, we are pleased to organize this meeting in the frame of the Catalysis Division of the Société Royale de Chimie. It is good to have some traditional friends when celebrating anniversaries.

A newcomer in the Belgian Catalysis community is the Catalysis Committee of the Royal Belgian Academy Council of Applied Sciences. This Committee has issued a report

on Modern Catalysis that has received positive echoes in Japan as well as in the United States : we hope that it will not remain without answer in Belgium. The Royal Academy Council has accepted to give its patronage to our symposium ; it is a great honor, and we are thankful for this.

Finally, I would like to acknowledge the fantastic work done by my co-workers and to publicly thank them. I am proud to have them as co-workers and friends. Vincent Dubois did a huge part of the long term organization, sacrificing more than six months of his Ph.D. research to prepare this event. Anne Baukens, Danielle Philip, Maryse Talbot, Pascal Vanderwegen and Jean-Pierre Puttemans also devoted time and energy to make attendance as effective and pleasant as possible. Thanks are finally due to the staff of our Institute, to the Scientific Committee of the Centenary, and to some colleagues in our Center, especially in the hotel school.

Georges Jannes

## ACKNOWLEDGMENTS

The following companies agreed to provide financial support to the symposium

Amer-Sil  
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Fina Research  
Hewlett-Packard  
Janssen Pharmaceutica  
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Solvay  
UCB  
van Lerberghe

The symposium was also supported by

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The following companies participated in the permanent exhibition

Analys (Parr)  
Autoclave Engineers  
Janssen Chimica  
Micromeritics  
Sigma-Aldrich  
Technology Catalysts

The organizers are grateful to them for their generosity

# Chiral Reactions in Heterogeneous Catalysis

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## INTRODUCTION

During the last decade, demand for enantioselectivity has grown, and increasing force and funding have been directed toward preparing pure chiral compounds.

Catalysis, especially heterogeneous catalysis, is probably the most desirable means of attaining that objective, but it has still to demonstrate its full ability to reach that aim.

It was a daring enterprise to launch ChiCat, a symposium on chiral heterogeneous catalysis. The topic was, and still is, very mobile, and controversial. That is the reason why we decided to also invite lecturers from outside the field of heterogeneous catalysis, to help us to better understand the general context.

Dr. Polastro put the question in a market perspective: he opened the symposium with a revealing look on the future market of the chiral chemicals we are striving to prepare in optically pure states. Professor Reisse warned the catalysis people not to reinvent the wheels that organic chemists have labored over many years. Professor Ghosez challenged the attendees by showing that the enantiomeric excesses that organic synthesis is able to achieve set up ultimate goals that will not be easy to attain by heterogeneous catalysis, and that, moreover, enantioselective heterogeneous catalysis is not only limited today in its performances, but also in its capabilities: (little C — C bond formation, if any...). Homogeneous catalysis is offering performances and concepts that are very stimulating for our future developments: they have been outlined by Professor Brunner. Different strategies are developed to get enantioselectivity in heterogeneous catalysis: use of a chiral modifier on the surface, grafting of a chiral catalytic complex on a solid (the so-called heterogenized homogeneous catalysis), and homogeneous formation of a chiral complex before surface reaction. We invited pioneers in the field to detail these strategies: Professor Webb, Professor Pini, Dr. Blaser and Professor Tungler. We thank them all for their kind acceptance and excellent and stimulating lectures. We also appreciate the quality of the contributed posters and recognize the special effort the authors made in trying to fit as precisely as possible the topics of the symposium. A special session was devoted to short presentation and discussion of these posters, giving the audience an overview of the last developments of chiral catalysis, in terms of new catalytic systems and new substrates as well. We are very grateful to the chairpersons for their kind authority in maintaining a correct timetable.

The members of the Scientific Committee of ChiCat helped us to build a program with the best contributors we could hope to have. They were faced with the difficult task of keeping the program focused. They are all most sincerely thanked for the outstanding job that they accomplished.

The symposium delineated what is really at stake. And different routes are paved to attain the goal. But are we sure that those routes will go so far?

Hydrogenation reactions remain the mainspring of the field, with alkanones and  $\alpha$ - or  $\beta$ -ketoesters as preferred substrates, and nickel-tartatic acid and platinum-cinchona as preferred catalytic systems. Extrapolation to other substrates: aromatic ketones, acids, and ethers, steroid ketones, Schiff bases,... has been attempted, with increasing success. On the other hand, substantial work has been devoted to the discovery and the interpretation of the effective parameters: nature of the metal, effect of the modifier, place where the enantio-determining step arises, hydrogen pressure, influence of the support. Knowledge gained in this way has been applied to vicinal reactions: dihydroxylation, for instance, and to reactions that are considered as more challenging, at least in heterogeneous systems: dehydration epoxidation, and cyclopropanation.

Very fine catalyst preparations, using for instance organometallics and zeolites as building blocks, and inclusion methods<sup>1</sup> were also described.

Perhaps, the very classical approach should be tried again: looking at the global problem. Chemical engineering studies, namely of the mass transfer in the reactor, could contribute to the definition of the exact amount of co-reactant, hydrogen for instance, that is needed at the surface of the catalyst. Anyway, this will be necessary if we want to be able to scale up our laboratory achievements. Solution chemistry will help us to better understand the way a prochiral molecule may be complexed before its adsorption, but also to discover some side effects of the modification process, metal leaching, e.g., and their effects on the process. Surface science sheds some light on the manner in which the catalyst surface can be chemically modified to build a chiral site. Adsorption studies will lead to a better picture of the modification process and of the activation process as well. As mentioned, the choice of special supports and the preparation of engineered supports also provide possible ways to reach this goal.

During the symposium, we had an informal dinner to discuss the future of ChiCat: the decision was taken to give a follow-up to the symposium. We strongly believe that we need another place to meet than in the frame of the broader Chirality meetings, or in big Heterogeneous Catalysis Congresses. Instead of starting a new series of symposia, the participants to the discussion preferred the formation of a ChiCat Group, inside which we will try to find the best way to interact, to cooperate, and to exchange ideas, in a more informal way. This would also be the place to stimulate young scientists' mobility. This group could meet as a satellite to well-chosen symposia, of vicinal but broader topics. The next symposium on Heterogeneous Catalysis and Fine Chemicals, which will be organized in Switzerland by Dr. Hans Blaser could be a good instance of the opportunities we are looking for. The idea is open to all those who are interested. What ChiCat started as a symposium, ChiCat group will take over!

V. Dubois  
G. Jannes

<sup>1</sup> This contribution, by R. Selke, P. Bathelemy and J.P. Roque, is not included in the Proceedings.

## **SECTION I**

# **THE PLACE OF HETEROGENEOUS CATALYSIS IN THE CHIRALITY FIELD**



## COMMERCIAL OUTLOOK FOR CHIRALITY. QUO VADIS ?

E. Polastro

Arthur D. Little  
Bd. de la Woluwe 2  
B-1150 Brussels, Belgium

### ABSTRACT

Over the past few years the field of chirality (defined as chiral synthesis and chiral fine chemicals) has attracted considerable interest from scientists, industrialists and more recently also investors.

It is interesting to see emerging similar patterns between this recent interest in chiral synthesis and the developments the financial, scientific and industrial community has experienced in the late 70's – early 80's with the advance of genetic engineering and modern biotechnology.

Such similarities are somewhat puzzling, given the numerous successes but even more numerous failure stories of ventures in the field of modern biotechnology. A more focused approach and more realistic hopes could have been expected for ten years later in the field of chirality.

Indeed, while the future development potential offered by chirality is highly promising, several key questions remain to be addressed, such as :

- Who will ultimately cash in from development in this field ?
- Where lies the value added ?
- What level of integration will be required ?
- ....

Probably an in-depth objective analysis would yield to a major reassessment of the strategies followed by many players in the field of chirality.

### A FIELD ATTRACTING CONSIDERABLE INTEREST

Since several years already, it is almost impossible to find a single issue of a journal dealing with fine chemicals or organic synthesis that does not contain at least an article on

Table 1. A brief dictionary of stereochemistry (Source : Arthur D. Little).

|                  |   |
|------------------|---|
| Chiral           | Describes a compound having one or more centers of asymmetry (usually a carbon atom). The asymmetry centre permits the compound to exist in two or more stereospecific configurations, or stereoisomers. (Derived from the Greek word <i>chiro</i> , meaning "hand", the term "chiral" suggests "handedness" and is applied to molecules having structures that are mirror images of each other, analogous to the left and right hands.)            |
| Stereoisomers    | Species of compound that differ in their spatial configuration, the species share the same molecular formula and most of their chemical properties. However, their physical properties may differ.  |
| Enantiomers      | Stereoisomers that are mirror images of one another. Depending on the number of asymmetric centers, a compound can have several pairs of enantiomers, each one of the pair called an enantiomorph.  |
| Diastereoisomers | Stereoisomers that are mirror images of one another. In compounds having more than one pair of enantiomers, enantiomorphs in one enantiomeric pair will usually be diastereomers of the enantiomorphs in another enantiomeric pair.   |
| Optical activity | An indirect measurement of a compound's chirality. The asymmetry in a chiral compound affects the passage of polarized light through a solution of the compound. Each of the possible stereoisomers affects that passage of light somewhat differently. The differences can be detected using a specialized polarimeter that measures the extent to which a dissolved sample of the compound rotates a plane of polarized light passing through it. |

Source : Arthur D. Little



Table 1. (continued)

|                       |  |
|-----------------------|--|
| Optically active      | Describes a compound that can exist in stereoisomeric forms. Same as c chiral.   |
| Optical purity        | The extent to which polarized light is rotated by only one stereoisomer of a compound, thereby indicating the stereoisomeric homogeneity of the sample. A completely heterogeneous mixture of the possible stereoisomers will exhibit zero net rotation. A completely homogeneous preparation will exhibit the rotation characteristic of only one of the stereoisomers. |
| Optical pure          | Describes a homogeneous preparation consisting of only one stereoisomeric form of a chiral compound.   |
| Homochiral            | Same as optically pure.  |
| Enantiomerically pure | Describes a preparation of a compound that contains only one enantiomer. Such preparations are also described as optically pure or homochiral.   |
| Racemic               | Describes a preparation of a compound containing equal proportions of enantiomers.   |
| Biologically active   | Describes a compound that elicits an intentional biologic response, typically by binding to a cellular receptor. An intentionally toxic compound can also be described as biologically active, depending on its mode of action. Typically, the biological activities of the various stereoisomers are different.   |

Source : Arthur D. Little