

Ciba-Geigy Ltd.

Chimia 50 (1996) 99–105
© Neue Schweizerische Chemische Gesellschaft
ISSN 0009–4293

Catalysis at Ciba-Geigy

Rolf R. Bader, Peter Baumeister, and Hans-Ulrich Blaser*

Abstract. After an introduction describing the significance and a short history of catalysis at Ciba-Geigy, the present role of the Catalysis Section within the Central Research Services is outlined. Its main activities are preparative services for the synthetic chemists in the fields of hydrogenation and high-pressure reactions, the development of catalytic processes and a research program in the fields of enantioselective catalysis, the modification of heterogeneous catalytic systems, acid-base catalysis and catalytic C–C-bond forming reactions. Because catalysis is considered by Ciba-Geigy to be a key technology, the main goal of its R+D program in catalysis is to create and maintain a reliable scientific and technical foundation for the optimal application of catalytic reactions throughout the company. Some results are presented that illustrate the work described above and an outlook on the opportunities of catalytic technologies in the fine chemicals industry is given.

1. The Significance of Catalysis to Ciba-Geigy

At Ciba-Geigy, catalysis is more and more considered to be what in 'managerese' is called a core technology, *i.e.*, a technological ability that can give the company a competitive advantage. This opinion is supported by the following facts: many of the biggest and most profitable products are manufactured *via* at least one catalytic step; there exists a rather strong central catalysis research and development section with the necessary modern laboratory facilities and quite a number of catalytic processes are in the development pipeline. This perception of catalysis did not always exist because, traditionally, Ciba-Geigy (as most of the Swiss chemical industry) has relied heavily on classical organic chemistry for manufacturing their products. The motivation for the increased application of catalytic methods and the support of catalysis research was twofold. On the one hand, there was a need for better production methods because of

environmental issues (replacing disposal strategies and end-of-pipe solutions) but also because of the growing importance of production costs (due to lower flexibility in price setting even in pharma and agro, a shrinking flow of new products and shorter product life cycles). On the other hand, attractive opportunities were created by recent advances in catalysis such as multifunctional catalysts or enantioselective catalytic reactions. In addition, there was the evident success of already introduced catalytic production processes in Ciba-Geigy. Today, there is a general agreement within the company that core competences have to be created and maintained in carefully selected technological fields, and that catalysis is such a key technology.

This paper will give a short history of catalysis at Ciba-Geigy and its predecessor companies and an overview on its present role in the company. Then the current catalytic activities of Ciba-Geigy are described and illustrated with a few selected examples. Finally, some thoughts on the future challenges for catalysis in a fine chemicals company are presented.

2. History of Catalysis at Ciba-Geigy

Catalysis in the fine chemicals industry has a rather different role and history than it has for the production of important

basic feedstocks such as ammonia or petrochemicals. Whereas industrial catalysis for bulk chemicals production started in the first decade of the 20th century and was done by chemical engineers, the use of catalytic methods for producing fine chemicals and pharmaceuticals started only forty to fifty years ago. One reason for this delay might have been the problems associated with the highly functionalized molecules. Indeed, the first generation of catalysts for selective hydrogenations was found and developed by synthetic organic chemists between 1930 and 1940 and is connected to names like Adams, Adkins, or Raney. Even today, catalysis in the fine chemicals industry is done mostly by organic and organometallic chemists, while in bulk chemicals production it is the domain of the physical chemist and the engineer.

Catalysis at Geigy had its roots in the 'Hydrierlabor', founded in the nineteen forties to support research chemists. This was a specialized laboratory equipped with simple glass reactors to carry out low-pressure hydrogenations on a preparative scale. Later, steel autoclaves were added to run reactions under elevated pressure. In the early fifties, classical hydrogenation catalysts such as Raney-nickel or Pd on carbon were not yet commercially available. One of the big challenges for such laboratories was to master the art of reproducible catalyst preparation and metal recovery. During this 'pre-scientific' era of catalysis in organic synthesis, practitioners such as Lindlar, Nishimura, or Rosenmund discovered many useful catalysts and catalytic methods to solve difficult selectivity problems. Some of these catalysts achieved world-wide recognition and are still used today. In the sixties, companies like Engelhard, Johnson Matthey, or Degussa started to produce and commercialize these and other hydrogenation catalysts.

At Ciba, the first attempts to use catalysis were made on a technical scale at the Monthey production site during world war II. Catalytic hydrogenation of several nitro-arenes was carried out with so-called Rupe-nickel (nickel carbonate on a ceramic support, reduced with H₂) that was manufactured in-house on a 100-kg scale. When standardized hydrogenation catalysts became commercially available, catalytic hydrogenation was slowly accepted as a general production technology. In the seventies, environmental protection legis-

*Correspondence: Dr. H. U. Blaser
Central Research Services, R 1055.628
Ciba-Geigy AG
CH-4002 Basel

lature led to the gradual replacement of many classical stoichiometric reduction processes such as the *Béchamp* reduction of nitro-arenes by catalytic hydrogenation. For this purpose, appreciable investments had to be made in order to install the technical facilities for the hydrogenation capacities needed. The growing experience with technical hydrogenations and the availability of suitable technical equipment lowered true and perceived barriers facing the application of catalytic technologies. Today, catalysis has captured strong positions in many areas, especially in the production of early intermediates. About seventy different catalytic production processes are applied and of *Ciba-Geigy's* 'Top Ten' market products, six are fabricated using one or more catalytic process steps.

In the early seventies, a catalysis research group was established within the Central Research Laboratories of *Ciba-Geigy*. At the beginning, it was heavily influenced by the Mühlheim school. Accordingly, the first projects dealt with Ni-catalyzed oligomerization reactions of buta-1,3-diene with C=N-containing compounds like azines, imines, or hydrazones [1]. Later, metal-catalyzed C-C bond formations such as the *Heck* reaction and analogs thereof were studied. In the eighties, several types of enantioselective reactions such as aldol reactions, allylic alkylations, or hetero-*Diels-Alder* reactions were investigated [2]. The current research projects are described below. The R+D efforts lead to several innovative catalysts and economically attractive catalytic processes; selected results are presented below. Of the 137 international patents in catalysis granted to *Ciba-Geigy* over the years, 68 are still active today; about two thirds cover current technical applications. In retrospect, the establishment of a catalysis research group and its continuity over more than two decades were a crucial factor for achieving today's position in technical catalysis.

3. The Present Role of the Catalysis Section

As already pointed out, catalysis is considered by *Ciba-Geigy* to be a key technology. This requires an optimal combination of a very strong scientific foundation, a broad application of the technology throughout the company, and, last but not least, a mechanism that transfers basic scientific knowledge into technical know-how. This is indeed the case for catalysis at *Ciba-Geigy*: Catalysis has certainly de-

veloped into a mature science and catalytic reactions are developed and used in many of the operative divisions of *Ciba-Geigy* and in locations around the world. In addition, small teams specializing in catalytic process technology and equipment construction exist as well. Finally, the Catalysis Section, located in the Central Research Services in Basel, acts as a bridge between the scientific world of catalysis and its technical application within *Ciba-Geigy*.

This bridging function of the Catalysis Section is certainly its most important mission. Even though more and more organic chemists recognize the value of catalytic reactions, factors such as lacking availability of catalysts or little practical know-how often prevent their application. The Catalysis Section does not claim a catalysis monopoly within *Ciba-Geigy*. On the contrary, it should be a center of expertise (to use another fashionable term) that collaborates with the chemists that apply catalytic methods in the operational divisions. Used in such a way, a centralized organization offers obvious advantages to the practicing chemist. Besides the practical aspect of having special equipment or a huge catalyst collection, its activities (see next paragraph) lead to the accumulation and continuous improvement of knowledge that allows a process of organizational learning.

The following factors are considered to be crucial for the success of the Catalysis Section:

- The combination of basic and applied research with preparative services, process development, and plant support within the same organization.
- To have fruitful collaborations both with chemists who are applying catalysis (customers) and with colleagues in academia who produce new science, or catalyst manufacturers who develop new catalysts (suppliers).
- The ability to efficiently find and develop catalytic methods for the selective transformation of complex organic molecules and to anticipate and exploit chances for innovation in the field of catalysis.
- To have the equipment and the trained personnel to perform catalytic reactions on a scale between μmol to kg in modern equipment efficiently, reproducibly, and safely.

It is also clear that the relationship between the specialists and the divisional user is not without its problems. The 'not invented here' effect is sometimes operating, our services are not known everywhere in the large and diversified compa-

ny and, sometimes, the cost of our services are considered to be rather high.

4. Activities and Resources of the Catalysis Section

In order to accomplish the role described above, a number of special functions have to be fulfilled and various resources are necessary. At the moment, about 40 persons are working in the Catalysis Section (full name 'Katalyse und Synthesedienste, FD 6') of the Central Research Services of *Ciba-Geigy*. Most of them are highly specialized scientists and technicians with a long and successful career in catalysis. One reason for the very low turnover (as opposed to the high turnover frequency of our catalysts) is the fact that catalysis is still a very empirical science and that hands-on experience is important. Since 1991, the catalysis laboratories can offer their services not just within the company but also to external customers.

4.1. Preparative Services (Synthesedienste)

The idea of the old 'Hydrierlabor' is still alive and well, offering preparative services to the synthetic chemists in the divisional research and development laboratories. But the scope has been expanded and the following preparative services are offered:

- *Chemo-, regio-, stereo-, enantioselective hydrogenations* using both heterogeneous and homogeneous catalysis. This is still the dominant field of activity, supported by an internal database that documents hydrogenations with more than 30 000 different substrates.
- *Catalytic dehydrogenation* in the liquid phase, very often using hydrogen acceptors in order to facilitate the reaction.
- *Catalytic carbonylation and hydroformylation reactions*. This is a relatively new service but our internal database already documents *ca.* 1 000 reactions. Besides catalytic reactions, *reactions under high pressure and with hazardous gases* such as HF, SF₄, or F₂ are carried out. Over 8 000 reactions are documented.

A preparative service can only be successful, if a desired reaction can be carried out in an acceptable yield on very short term. Since there is usually not much time for developing a catalytic method, high effectiveness in selecting and performing the appropriate catalytic experiment is necessary. For more difficult selectivity problems short feasibility studies are car-

ried out as well. For these tasks not only the published literature is available but also our own experience that has been collected and documented over the last 50 years. At the moment about 2000 reactions are carried out each year and the 'hit rate' is *ca.* 80–90%, *i.e.*, the desired transformation is achieved with at least 50–60% yield on the first or second attempt.

4.2. Support for Synthesis Planning

For chemists involved in synthesis planning, advice and information concerning the feasibility of a particular catalytic step is offered. Even though the synthetic chemists have access to a proprietary REACCS database on catalytic reactions, the experience of the specialists allows a faster and more effective discrimination of ideas. This is particularly the case when catalytic methods allow the design of an entirely new synthesis with fewer steps compared to classical chemistry or in cases where multifunctional catalysts might be able to carry out two or three reactions in one step, *e.g.*, condensation/reduction or reductive alkylations. A sound evaluation of all the possibilities with the help of a catalysts specialist at this stage can prevent an ineffective allocation of resources and, in addition, there is a high potential for process innovation.

4.3. Process Development and Trouble Shooting

The development of a viable catalytic process (as opposed to simply producing a few grams of a compound) is done in very close collaboration with our colleagues in the divisional chemical development departments. The transfer of a process from the laboratory to the plant scale is a task that is very interactive in nature and requires a high degree of cooperation and perfect teamwork. The particular tasks of the catalyst specialists depend on the different project phases.

After the catalytic transformation has been defined, a laboratory procedure for the catalytic step (choice of the catalyst, solvent, optimization of reaction condition, *etc.*) is developed in the laboratories of the catalysis section. This demonstrates the chemical feasibility of a process and allows a first estimation of production costs. The next development steps are still carried out in small reactors but in close collaboration with the team that develops the entire synthesis of the final product molecule. At this stage, aspects such as adaptation to the operations preceding and following the catalysis (purity of substrate, solvents), handling and separation of the catalyst, optimization of the catalyst in

collaboration with the catalyst manufacturer, *etc.* are investigated. It is important to establish a reliable laboratory model for the reaction that mimics the situation in the plant reactor (including the mass and heat transport).

If the catalytic reaction is carried out in a multi-purpose reactor, the quality of the results obtained during the optimization at the lab scale is usually sufficient for a direct transfer to the plant scale. If a classical pilot study (10–1000-kg scale) is carried out, it is usually because problems with process integration or with material handling are expected. Another reason could be the production of larger amounts of product for toxicological or clinical studies and registration purposes. During this phase, the responsibility for the process shifts from the catalyst specialist to the divisional development chemist.

Once the catalytic process is introduced in the production plant, the catalysis group supports the production crew with trouble shooting, *e.g.*, when there are problems with the performance of the catalyst. In addition, catalyst specialists act as consultants for process improvements.

4.4. Catalysis Research

The goal of our research projects is to make selected catalytic technologies accessible to the synthetic chemists in discovery research, chemical development, and, ultimately, to allow the application of catalysis in chemical production. For this purpose, both short and long term projects are carried out. The former serve to establish a specific method in the service laboratories, whereas the latter aim to establish a new state of the art. This can mean the search for new types of catalytic transformations or catalysts or the adaptation of important catalytic processes to the needs of the industrial environment. In the mid-eighties, the foundation for most of today's projects were laid, with emphasis on enantioselective catalysis and the modification of heterogeneous hydrogenation catalysts (for selected results see below). If possible, the results are protected by patents. In any case, we concentrate much more on practical aspects of a catalyst or a process than academic researchers do. In order to ensure contacts with the scientific frontier we have collaborations with several academic laboratories both in Switzerland and abroad. In addition, contacts with colleagues in catalyst groups of other companies are maintained.

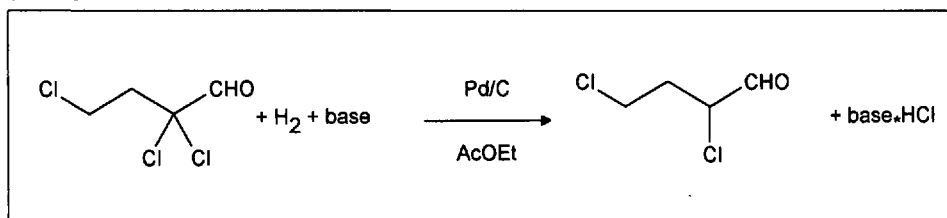
The following topics are currently investigated:

- *Catalytic hydrogenation with chiral metal-complexes* is considered to be a

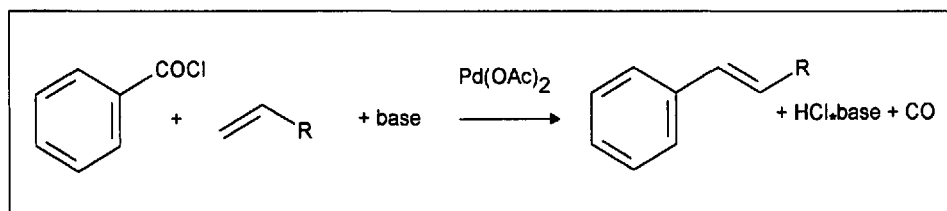
powerful method for the synthesis of enantiomerically pure intermediates for bioactive compounds. The main objective of this project is the development of efficient methods for small and large scale enantioselective hydrogenation of various types of prochiral substrates, and the determination of their scope and limitations. We have developed and demonstrated the technical feasibility of enantioselective hydrogenation catalysts on the laboratory and pilot plant scale. The accumulated expertise allows us to predict the chances of a desired transformation with high probability.

- *Separation methods for soluble metal-complex catalysts* are becoming more and more important as technical applications increase. The goal is the development of separable catalysts with good catalytic performance as well as separation methods for spent catalysts. This is one way to increase the chances for a technical application of homogeneous catalysts. A methodology has been developed that allows the immobilization of the most important classes of chiral diphosphine ligands on inorganic and organic supports *via* isocyanate linkers, meeting most requirements (selectivity, activity, reproducibility) of technical useful catalysts.
- *The modification of commercial heterogeneous hydrogenation catalysts in order to obtain special selectivities* has been shown to be an attractive approach to solve problems of chemo- and enantioselective hydrogenations. At the same time the project on this topic is designed to improve the understanding of the interactions between catalyst, modifier (inhibitor, poison), and substrate for heterogeneous catalysts. Several catalytic systems were investigated in detail and developed to technical maturity. Among them are systems for the enantioselective hydrogenation of keto esters and for the chemoselective hydrogenation of functionalized nitro-arenes.
- *Solid acids and bases such as modified zeolites and clays* could help to replace soluble acids and bases that often lead to high salt loads and also to corrosion problems. The potential of such catalyst as well as their characterization and modification is studied with the help of model reaction such as the *Knoevenagel* or *Friedel-Crafts* reactions.
- *Homogeneously catalyzed C–C bond forming reactions* have a huge synthetic potential. Until now, their technical

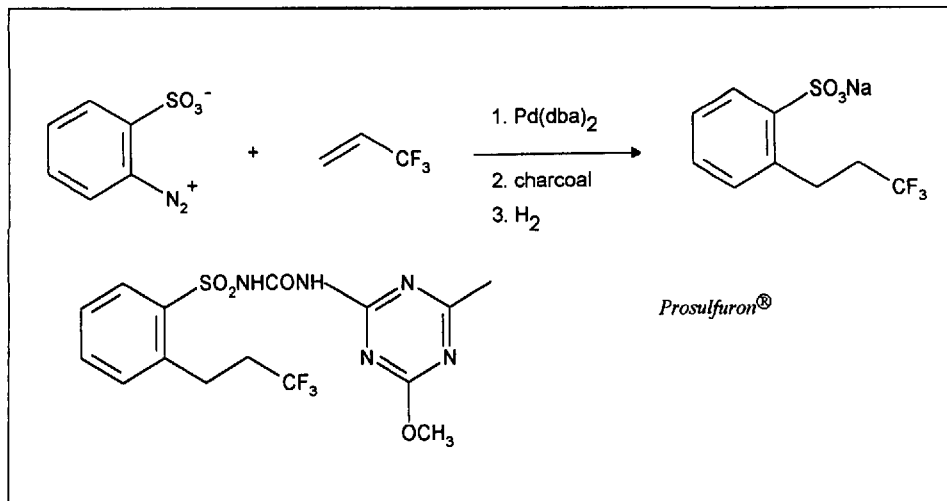
Scheme 1



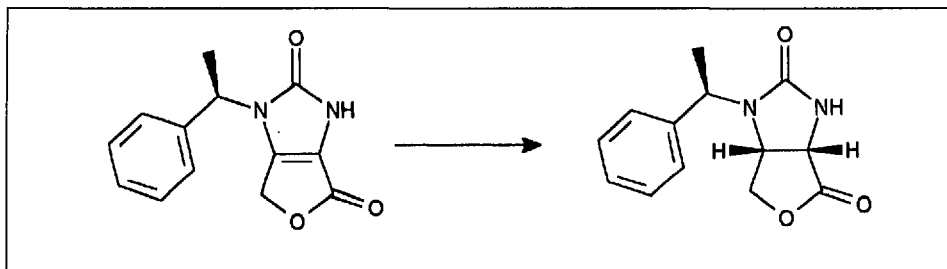
Scheme 2



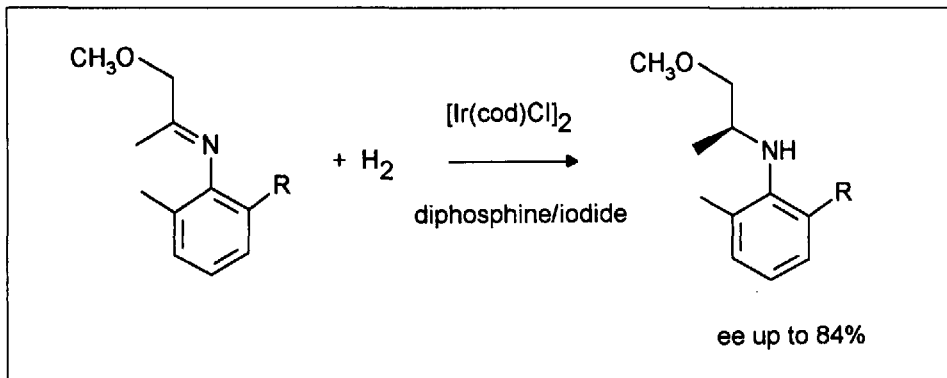
Scheme 3



Scheme 4



Scheme 5



application in fine chemicals synthesis is often limited due to low catalytic performance or because of their incompatibility with functional groups. Investigations of the effects of process variables, the development of more practical catalysts, and information on scope and limitations should help to make reactions such as carbonylation, *Heck* reactions, or cross-coupling better accessible to the industrial chemist.

– As part of our research we also adapt methods for the *characterization of heterogeneous catalysts* where we use temperature-programmed methods such as TPD (desorption) and TPR (reduction) or chemisorption for characterizing acid strength, oxidation state, or surface area and dispersion of heterogeneous catalysts.

4.5. Equipment, Catalyst, and Ligand Collection of the Catalytic Laboratories

Catalytic reactions are often carried out in special apparatus. This was and still is an important reason for having a central catalysis and high-pressure laboratory. Since most reactions involve a dissolved organic substrate, a solid catalyst, and a gaseous reactant, all our reactors are designed for an efficient gas-liquid mixing. Besides the glass reactors used for low-pressure work we are using most frequently magnetically stirred high-pressure autoclaves in sizes between 50 ml and 50 l of various materials. Small fixed bed reactors allow the study of continuous reactions in the gas phase and under trickle bed conditions. For safety reasons, all high-pressure autoclaves are installed in special containment boxes and the area for storing and handling explosive gases is separated from the hydrogenation laboratory. A glove box and vacuum lines (*Schlenk* technique) are used to handle air and moisture sensitive catalysts and reaction mixtures. A heat-flow calorimeter that can handle pressures up to 150 bar allows investigations concerning the exothermicity and the heat flow of hydrogenation reactions.

Just as the catalytic equipment is special, most heterogeneous catalysts and chiral ligands are not available readily. Over the years we have built up a sizable collection of heterogeneous hydrogenation catalysts (*ca.* 500 samples), of zeolites, clays, and similar contacts (*ca.* 700 samples), and of organometallic catalyst precursors and ligands (100 samples). These catalysts and ligands are mainly used for work of the catalysis laboratories but they are also available to chemists in divisional laboratories. Regular technical contacts with all of the major European

manufacturers of noble metal and hydrogenation catalysts (*Degussa, Engelhard, Heraeus, Johnson Matthey*) are maintained since more than twenty years. These contacts are especially valuable when an existing catalyst must be modified or when a new one should be developed.

5. Selected Results

In this paragraph a selection of our results obtained in the last few years is presented in order to illustrate the approaches described above.

5.1. Synthetic Feasibility Study

It had to be shown whether the selective conversion of 2,2,4-trichlorobutyraldehyde to 2,4-dichlorobutyraldehyde, an intermediate for a potential herbicide, is possible (*Scheme 1*). Selective monohalogenation of α -dihaloaldehydes were unknown. Of the several catalytic systems that were investigated (Pd, Pt, and Ni catalysts; different solvents and bases), Pd/C in ethyl acetate and in presence of 2,6-lutidine gave the best results with >99% yield of the desired product [3].

5.2. Discovery of a New Reaction

The *Heck* reaction is usually carried out with aryl iodides or bromides. Since these are often expensive and not always accessible, other starting materials were investigated. It was found that aromatic acid chlorides are convenient starting materials for the reaction with olefins to give aryl olefins in medium to high yields (*Scheme 2*). The reaction has to be carried out in an open system at 100–120° in presence of as little as 0.01% palladium acetate and 1 equiv. of *N*-benzyl dimethylamine [4].

5.3. From Research Success to Production Process

An industrial process for the herbicide *Prosulfuron*[®] was developed that uses as a key step the Pd-catalyzed reaction of 1,1,1-trifluoropropene with an aryl-diazonium salt (*Matsuda* reaction) to give, after hydrogenation with an *in situ* formed Pd/C catalysts, the corresponding (3,3,3-trifluoropropyl)arene (*Scheme 3*). This is the first homogeneous catalytic process for *Ciba-Geigy* and a very elegant example of the combination of two catalytic steps [5].

5.4. New Chiral Organometallic Reagent

A very versatile class of cyclopentadienyl-Ti reagents (*Fig. 1*) was developed

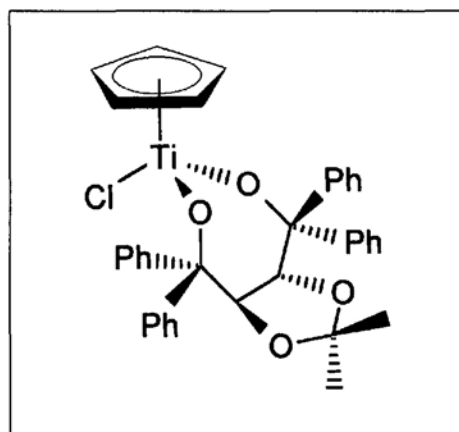


Fig. 1

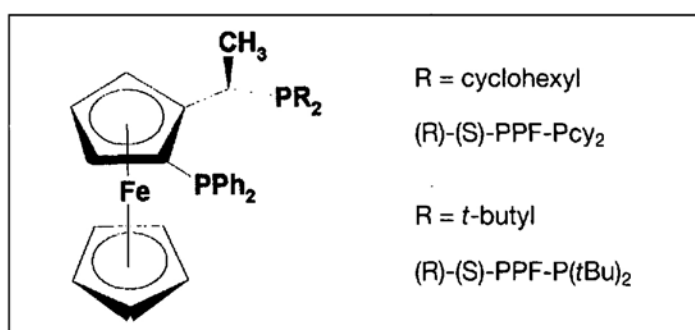


Fig. 2

Table 1. Hydrogenation of Methyl acetamidocinnamate Using *bppm*/Rh and Its Immobilized Analog (MeOH, 1 bar, r.t., s/c ratio 200)

	1. run 100% conv. [min]	ee [%]	re-use 100% conv. [min]	ee [%]
soluble catalyst	14	94.5	not possible	
immobilized catalyst	29	93.5	18	94.4

for the enantioselective addition of allyl nucleophiles and enolates to aldehydes. This reagent was named *Fluka* Reagent of Year 1995 [6].

5.5. New, Versatile Class of Chiral Diphosphine

A new type of ferrocenyldiphosphines with the general formula PPF-PR₂ (*Fig. 2*) was found to give very versatile ligands for various Rh-, Ir-, and Ru-catalyzed asymmetric reactions. Methyl acetamidocinnamate is hydrogenated by Rh⁺/PPF-Pcy₂ with 97% ee, dimethyl itaconate with 99% ee, acetyl acetates by Rh and Ru catalysts with >90% ee, and keto pantolactone with 95% ee by Rh/*p*-tol₂PF-P^tBu₂ [7]. The tetrasubstituted olefin in *Scheme 4*, an intermediate of biotin, is hydrogenated in good yields with a diastereoselectivity of 99:1 in the matched case using Rh/PPF-P^tBu₂ [8].

5.6. New, Very Active Enantioselective Catalyst for Imine Hydrogenation

An Ir/diphosphine/I⁻ catalyst was developed that represents a new, more active and stable class of catalytic system for the enantioselective hydrogenation of sterically hindered *N*-aryl imines (*Scheme 5*). Turnover numbers up to 10000 were obtained, compared to a few hundred for the best complexes at that time. Optical yields were low to medium [9].

5.7. Technology for Immobilizing Homogeneous Catalysts

Immobilized catalysts that surpass by far the state of the art and meet most requirements of technical useful catalysts (efficient preparation, good catalytic properties, easy separation, re-use) are obtained with a new immobilization methodology. A comparison of the catalytic properties of the catalyst depicted in

Scheme 6 with those of its soluble analog $\text{bppm}/[\text{Rh}(\text{COD})_2]\text{BF}_4$ is given in Table 1 for the hydrogenation of methyl acetamidocinnamate [10].

5.8. A New Type of Heterogeneous Catalyst for the Selective Hydrogenation of Nitro Groups

A new catalyst, Pt/Pb on CaCO_3 , was developed in collaboration with a catalyst manufacturer that allows the catalytic hydrogenation of an aromatic nitro group in presence of C=C, C=O, C≡N functions as well as Cl or Br substituents with selectivities >95%, and even C≡C groups react very slowly (Scheme 7) [11].

5.9. Mechanistic Investigation of a Heterogeneous Enantioselective Catalyst

The enantioselective hydrogenation of α -keto esters using Pt catalysts in presence of cinchona alkaloids (Scheme 8) is one of the few reactions where a chirally modified heterogeneous catalyst works well. This was our motivation to investigate this reaction type in more detail. It was shown that the reaction is quite general and can be applied to different types of α -keto esters and acids. Mechanistic studies such as structure-effect studies for the cinchona modifier as well as kinetic investigations were carried out and good evi-

dence was found that the mode of action is of the type of a 'modifier accelerated catalysis'. An overall kinetic scheme has been proposed and several other possible modes of action of the modifier have been eliminated [12].

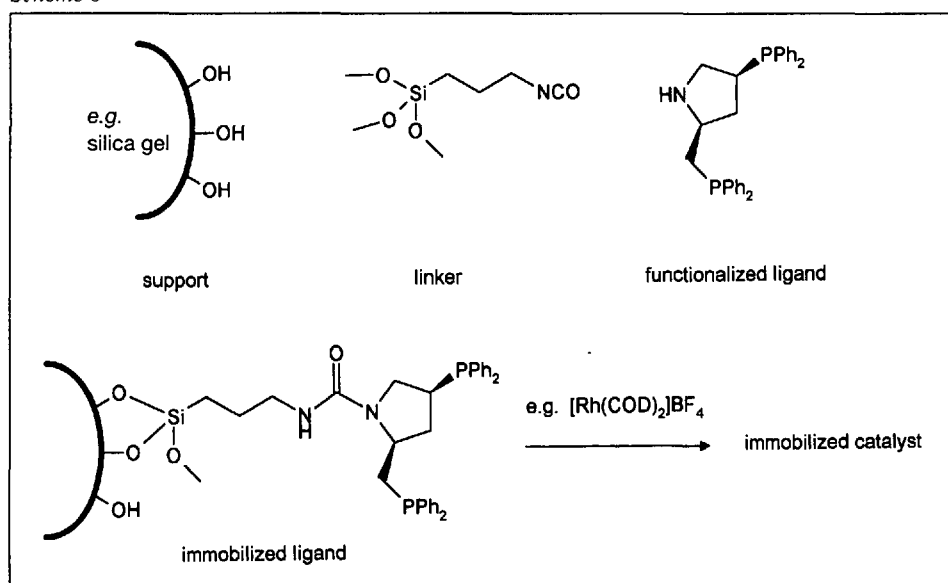
5.10. Catalytic Production Processes at Ciba-Geigy

More than 90% of catalytic production processes at Ciba-Geigy are hydrogenations. Other catalytic reactions such as dehydrogenations, Heck-type arylation or trimerization reactions are also used on a plant scale. Three types of reactors are used, depending on the volume of the intermediate and the special requirements given by the reaction type. Reactions in the liquid phase are exclusively carried out in batch-type reactors, either stirred tanks or loop reactors. For practical reasons the reactions are run to complete conversion of the starting material. Depending on the production volume, batch-type reactors are used both as single- or multiple-purpose units. Several fixed bed reactors are used for continuous gas-phase reactions dedicated to large-scale intermediates. Table 2 gives a short overview on the most important catalytic processes at Ciba-Geigy.

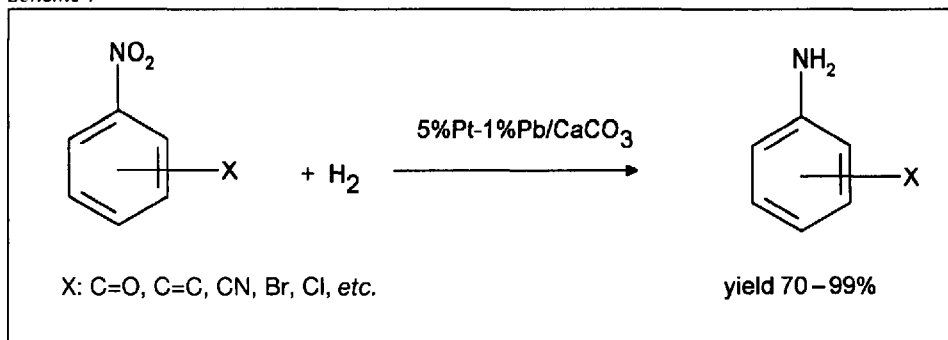
6. Outlook and Future Challenge

Over the years, catalysis at Ciba-Geigy has attained quite a satisfactory level of technical maturity. Heterogeneous catalysis, especially heterogeneous catalytic hydrogenations, are already applied widely, whereas homogeneous catalytic reactions are at the very beginning of their technical use. There still exists a demand for improvements. For very complex multifunctional molecules, the known methods sometimes show inadequate chemo-, regio-, or stereoselectivity. Many published homogeneous catalytic systems show very attractive selectivities, but poor catalyst activities and productivities often prevent their commercial application. It is one of the main tasks of our current catalysis

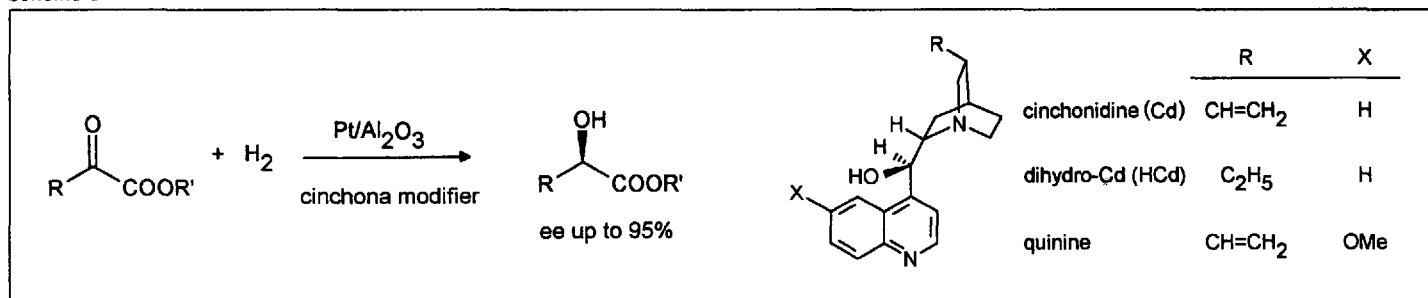
Scheme 6



Scheme 7



Scheme 8



research to find ways to eliminate such deficiencies. We are convinced that as a result of continuous R+D efforts, catalytic technologies will overcome these obstacles and capture new fields of application. Here, industrial catalysis meets its hardest challenges but also its greatest chances for innovations.

A fast emerging field is asymmetric catalysis, which is of special importance for the synthesis of biological active compounds. For this reason, *Ciba-Geigy* invests considerable parts of its catalytic R+D capacity to develop these new technologies. Asymmetric chemical catalysts compete with bio-catalysts such as enzymes or whole cell systems but it is conceivable that the two technologies are really complementary.

To sum up the challenge: the chemical industry has to produce active compounds with the highest possible selectivity and atom efficiency, at the lowest possible energy consumption and, in consequence, with the lowest possible costs. We are convinced that catalysis will contribute decisively to these goals.

This account is presented in the name of our past and present colleagues both from the Catalysis Section as well as from divisional research, development, and production laboratories. Many of their names can be found in the references. We would like to thank all persons who have contributed to the success of catalysis at *Ciba-Geigy*: as technicians in the laboratories, as chemists responsible for the various projects, or as managers who have supported our work and who provided the means to do it during all these years.

Received: January 3, 1996

- [1] D. Reinhr, *Pure Appl. Chem.* **1980**, *52*, 2471.
 [2] A. Togni, S.D. Pastor, *J. Org. Chem.* **1990**, *55*, 1649; A. Togni, G. Rihs, P.S. Pregosin, C. Ammann *Helv. Chim. Acta* **1990**, *73*, 723; A. Togni, *Organometallics* **1990**, *9*, 3106.
 [3] H. Steiner, H. Tobler, EP 381,622 (assigned to *Ciba-Geigy AG*), 1990.
 [4] H.-U. Blaser, A. Spencer, *J. Organomet. Chem.* **1982**, *233*, 267; A. Spencer, *ibid.* **1982**, *240*, 209; *ibid.* **1982**, *247*, 117.
 [5] P. Baumeister, G. Seifert, H. Steiner, EP 584'043 (to *Ciba-Geigy AG*), 1992; P. Baumeister, W. Meyer, K. Oertle, G. Seifert, U. Siegrist, H. Steiner, Abstracts Europacat-2, Maastricht, 1995.
 [6] R. Duthaler, A. Hafner, M. Riediker, *Pure Appl. Chem.* **1990**, *62*, 631.
 [7] A. Togni, F. Spindler, N. Zanetti, A. Tijani, EP 0564406 (to *Ciba-Geigy AG*), 1993; A. Togni, C. Breutel, A. Schnyder, F. Spindler, H. Landert, A. Tijani, *J. Am. Chem. Soc.* **1994**, *116*, 4062.
 [8] J. McGarrity, F. Spindler, R. Fuchs, M. Eyer, EP 0624587 (to *Lonza AG*), 1994.

Table 2. List of Ciba-Geigy's Most Important Catalytic Production Processes

Intermediate/Product	Volume t/y	Reaction type	Catalyst	Process	Reactor
various products	10 ⁴	trimerization	active carbon	gas phase continuous	tubular fixed bed
herbicide	10 ⁴	dehydrogenation	copper chromite	gas phase continuous	tubular fixed bed
herbicide	10 ⁴	reductive alkylation	platinum	liquid-phase batch	stirred tank
pharmaceutical	10 ⁴	hydrogenation ArNO ₂	nickel	liquid-phase batch	loop
pharmaceutical	10 ³	dehydrogenation	iron oxide	gas-phase continuous	tubular fixed bed
pharmaceutical	10 ²	hydrogenation ArNO ₂	nickel	liquid-phase batch	stirred tank
brightener	10 ³	hydrogenation ArNO ₂	platinum	liquid-phase batch	loop
various dyestuffs	10 ³	hydrogenation ArNO ₂	palladium platinum	liquid-phase batch	loop
herbicide	10 ²	arylation	Pd-complex	liquid-phase batch	stirred tank
herbicide	10 ²	hydrogenation C=C	palladium	liquid-phase batch	stirred tank
insecticide	10 ²	hydrogenation CN	nickel	liquid-phase batch	stirred tank
additive	10 ³	hydrogenation C=O	ruthenium	liquid-phase batch	loop
additive	10 ³	reductive alkylation	platinum	liquid-phase batch	stirred tank
additive	10 ³	hydrogenation ArNO ₂	platinum	liquid-phase batch	loop
fungicide	10 ²	hydrogenation C=N-N	platinum	liquid-phase batch	stirred tank
herbicide	10 ²	dehalogenation	palladium	liquid-phase batch	stirred tank

- [9] F. Spindler, B. Pugin, EP 0256982 (to *Ciba-Geigy AG*), 1986; F. Spindler, B. Pugin, H.-U. Blaser, *Angew. Chem.* **1990**, *102*, 561.
 [10] B. Pugin, F. Spindler, M. Müller, EP 496699-A1 and EP 496700-A1 (to *Ciba-Geigy AG*), 1991; B. Pugin, M. Müller, *Stud. Surf. Sci. Catal.* **1993**, *78*, 107.
 [11] U. Siegrist, P. Baumeister, WO 95-to be published (to *Ciba-Geigy AG*), 1995.
 [12] H.-U. Blaser, D. Imhof, M. Studer, H. Thies, A. Tijani, unpublished results; H.-U. Blaser, M. Garland, H.P. Jalett, *J. Catal.* **1993**, *144*, 139; H.-U. Blaser, *Tetrahedron: Asymmetry* **1991**, *2*, 843.