Angewandte Essays

100 Years of Catalysis

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One Hundred Years of the Max-Planck-Institut für Kohlenforschung

*Manfred T. Reetz**

biocatalysis · Fischer–Tropsch process · heterogeneous catalysis · homogeneous catalysis · Ziegler catalysts

1. Introduction

In 1911 the monarchal German government under Kaiser Wilhelm II founded a scientific society, called the Kaiser-Wilhelm-Gesellschaft (KWG).[1] Individual Institutes dedicated to basic research were planned, each headed by a superbly qualified scientist. According to the first president of the Society, Adolf von Harnack (a theologian), the intention was to identify exceptional personalities and to establish a separate KWG Institute for each of them ("Harnack principle").[1,2] In view of the internationally recognized high quality of German universities and limited financial resources at the time, the question arises today as to why Germany sparked such a change in policy. As historians have noted, the departments at German universities were traditionally run by a single full professor (chair), as for example in chemistry, but with the rapid rise in the number of students in the natural sciences and increasing bureaucratic burdens, the professors in such positions were hampered in their primary mission regarding research.[3] German policy makers at the beginning of the 20th century viewed basic research as instrumental in helping the country to compete with the other European powers.[1] To provide a solid financial basis for the KWG, private investors, such as major industrial companies, were expected to participate without infringing the scientific independency of the KWG Institutes nor of the Society itself. In the group of KWG founding fathers, several personalities were internationally renowned scientists active in basic research, including Emil Fischer (Chemistry Nobel Laureate 1902).[1] Within a short time the first three Institutes were established in Berlin, including the Kaiser-Wilhelm-Institute for Physical Chemistry headed by Fritz Haber.[4]

2. The Franz Fischer Era

Parallel to these developments, plans were made for founding further Institutes outside Berlin. It was one of Emil Fischer's visions that the most abundant natural resource in Germany, coal, should not just be burned for producing heat in buildings and in industrial plants. He therefore suggested in 1912 the establishment of a Kaiser-Wilhelm-Institut für Kohlenforschung ("KWI for Coal Research") without prescribing the exact nature of research at such an Institute,[5] although he was fascinated by the possibility of converting carbon monoxide (produced from coal) into methane. Emil Fischer wisely insisted on maintaining basic research in all KWG Institutes, which did not exclude subsequent industrial applications.[1] It was logical that such an Institute should be erected in or near a coal mining part of Germany, the heavily industrialized Ruhr area being one option. Following intensive negotiations, Mülheim an der Ruhr was chosen as the site, a city on the Ruhr river relatively far away from the nearest university. The decision was strongly influenced by the financial participation of the Leonard-Stinnes-Foundation, the Stinnes clan being an influential entrepreneur family in Germany's industrial Ruhr area.[5a] Ironically, financial participation in the KWG by the steel and coalmining industry of the region was in general somewhat limited because the persons in charge underestimated the significance of basic research.[2,5a] In 1913 work began in constructing the KWI für Kohlenforschung on property provided by the city of Mülheim an der Ruhr, which was finished in early 1914 following only 11 months of construction (Figure 1). The celebration marking the inauguration on July 27th 1914 was not as elaborate as in the case of the previous KWG Institutes in Berlin, primarily because the Kaiser had decided not to participate. This was due to "irritations" which had arisen in 1889 between the monarch and leaders of the coalmining industry. To the disappointment of the industrial bosses, the Kaiser had not opposed a massive strike of the coalmining workers demanding, inter alia, an eight-hour working day ("Berliner Protokoll").[5a]

Franz Fischer (1877–1946; no relationship to Emil Fischer) was chosen as the first director of the KWI für Kohlenforschung, an inorganic chemist specializing in electrochemistry at the Technical University Berlin-Charlottenburg. Although the future research was not specified, one

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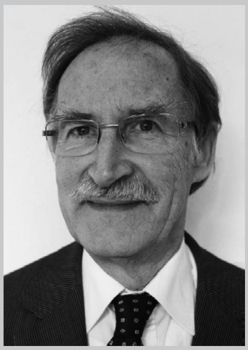
[*] Prof. Dr. M. T. Reetz
Department of Chemistry, Philipps-Universität Marburg
Hans-Meerwein Strasse, 35032 Marburg (Germany)
and
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1, 45470 Mülheim an der Ruhr (Germany)
E-mail: reetz@mpi-muelheim.mpg.de

Figure 1. The Kaiser-Wilhelm-Institut für Kohlenforschung just before its completion in 1914. Left: laboratory building; right: residence of the first director Franz Fischer.

possibility was the conversion of coal into electric energy. Details concerning the first era of the Mülheim Institute and the crucial role of Franz Fischer can be found in the monograph by the historian Manfred Rasch.[5a] Suffice it to say that the new director faced an enormous scientific challenge just a few weeks prior to the outbreak of World War I. A staff of about 30–40 co-workers comprising chemists, engineers, and technicians was planned, but many of the newly hired male employees were soon called for duty as soldiers in a war that was to devastate Europe. It was far from an ideal time to initiate a new research area, a situation that did not improve following the immediate end of the war. As a consequence of Germany's financial burden owing to the extensive reparation costs imposed by the Treaty of Versailles in 1919, the financial status of the Institute was even more precarious than during the war years. Under such conditions, all too ambitious research projects were impossible.[5]

During the first few years of the Fischer directorship, several different approaches to coal research were considered, including coal hydrogenation. At the beginning, the Mülheim researchers were not aware of the Bergius coal hydrogenation process invented by Friedrich Bergius (1884–1949) in 1913 nor of related innovative research and developments at BASF, including a process for hydrogenating carbon monoxide to methanol using heterogeneous catalysts (Alwin Mittasch, Carl Müller, and others).[5] As time went on, this information became available, which in turn influenced Fischer's thinking. More and more emphasis was placed on carbon monoxide as the primary feedstock, including its catalytic transformation into methane. The Mülheim chemists worked with synthesis gas comprising $\mathrm{CO} + \mathrm{H_2}$. Using various supported metals and metal oxides as heterogeneous catalysts, they initially obtained product mixtures containing alcohols, aldehydes, and ketones, which were called "synthol" (synthetic oils).



Manfred T. Reetz (born 1943) obtained his doctoral degree in 1969 with Ulrich Schöllkopf at Göttingen University and then performed postdoctoral work in the group of Reinhard W. Hoffmann at Marburg University. Following an appointment at Bonn University, he became Full Professor of organic chemistry back at Marburg University (1980–1991) before joining the Max-Planck-Institut für Kohlenforschung in Mülheim/Germany, where he served as Managing Director from 1993 to 2002. Following formal retirement as one of the Directors in 2011, he accepted the offer to become the first Hans Meerwein Research Professor in the Chemistry Department of Marburg University while also being external (emeritus) group leader of the Mülheim Max Planck Institute.

After shifting the direction of research in Mülheim several times, Franz Fischer finally pushed forward a research program directed toward liquefying coal.[5] The goal was to transform coal into liquid fuels, such as gasoline (petrol) or diesel. The researchers relied on the basically known coal gasification process according to which a coal (or coke) is treated with water and a limited amount of oxygen at temperatures around 1000 °C, leading to synthesis gas (syngas), a mixture of CO and $\mathrm{H_2}$ (along with some $\mathrm{CO_2}$). Fischer and his co-worker, Hans Tropsch (1889–1935), envisioned the catalytic liquefaction of syngas with formation of hydrocarbons according to the following chemical equation that was to make them famous [Eq. (1)]:

$$n\,\mathrm{CO} + (2n+1)\,\mathrm{H_2} \rightarrow \mathrm{C}_n\mathrm{H}_{(2n+2)} + n\,\mathrm{H_2O} \tag{1}$$

The challenge was to find the right heterogeneous catalyst. As transition-metal-based heterogeneous catalysis was still in its infancy in the 1920s, Franz Fischer and Hans Tropsch (Figure 2) had little scientific precedence in this challenging endeavor. Their experiments for producing "synthol" on the basis of metals and metal oxides as heterogeneous catalysts served as a guide, which in turn was probably inspired by the Haber–Bosch process for ammonia synthesis from nitrogen and hydrogen (successful after testing about 20000 different metal and metal oxide catalysts and formulations thereof). Hans Tropsch and his team likewise studied many different transition metals and metal oxides as possible catalysts at various temperatures and pressures in a variety of different reactors. Iron particles on solid carriers, such as zinc or aluminum oxide, proved to be the most potent catalyst formulations. In 1925, Fischer and Tropsch submitted a patent (DRP 484337) describing the remarkable transformation which today is called the Fischer–Tropsch process [Eq. (1)], first published one year later in Berichte der

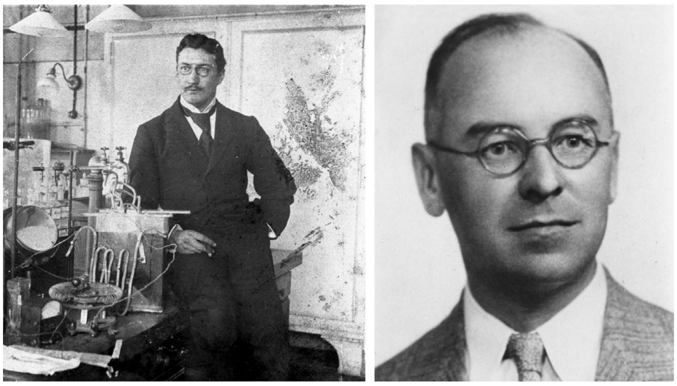


Figure 2. Franz Fischer (left) and Hans Tropsch (right).

Deutschen Chemischen Gesellschaft.[6] In the same year the "Studien- und Verwertungsgesellschaft mbH" was founded for the purpose of filing, protecting, and exploiting patents, which was a company acting as a trustee for the Institute. Following some legal uncertainties, the patent was finally issued to the KWI für Kohlenforschung in 1929. The Fischer–Tropsch process was so impressive that the President of the KWG, Max Planck, visited the Mülheim Institute in 1934 (Figure 3).

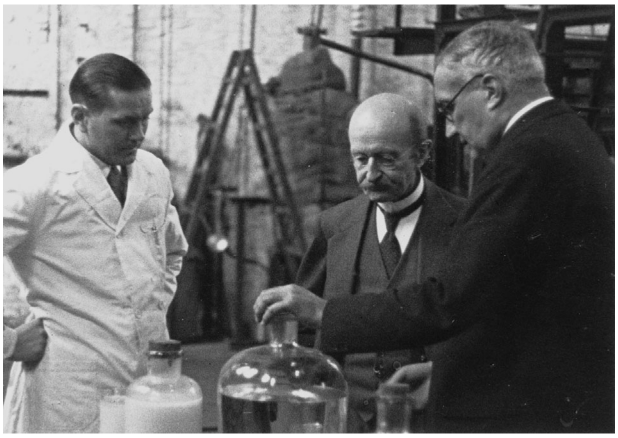


Figure 3. Franz Fischer (right) and Otto Roelen (left) showing the president of the KWG, Max Planck, different products of the Fischer–Tropsch process in 1934.

The first industrial plant was constructed by Ruhrchemie in nearby Oberhausen in 1935, managed by Tropsch's former co-worker in Mülheim, Otto Roelen (1897–1993), who also invented hydroformylation as one of the most important industrial transition-metal-catalyzed processes. In the 1940 s, the Oberhausen plant produced about 70000 tons of liquid fuel per year. Flanked by further Fischer–Tropsch facilities in Germany as well as plants based on the alternative Bergius process (hydrogenation of coal), much of the liquid fuel was used by the German army during World War II, the rest going into chemical industry. After the war, the oil age began, making coal liquefaction non-competitive, with the exception of a giant plant in Sasol/South Africa, the country being cut off from oil by the international embargo as a political consequence of the apartheid regime. Today the Sasol plant and several other Fischer–Tropsch plants are in operation, for example in Malaysia and Qatar, which utilize syngas as the feedstock that in turn is accessible from natural gas or biomass.[5b]

Owing to the revenues entering the Institute on the basis of license agreements, the financial situation improved rapidly. In his attempt to become more independent of the KWG, Franz Fischer succeeded in turning the Institute into a foundation of private law dedicated to supporting coal research for the public benefit.[5] Although the 1939 statutes of the foundation did not allow the pursuance of purely economic goals, it strengthened the position of the Director regarding freedom of research (as in the 1912 statutes). Nevertheless, the KWI für Kohlenforschung remained as one of the Institutes in the KWG. As most German university professors and directors in the public domain during the Third Reich, Franz Fischer was a member of the Nazi party (NSDAP).[5,7] Nevertheless, as the historian Manfred Rasch has pointed out, "Fischer remained personally autonomous and did not accept contracts from the central government, the Nazi party, or the Wehrmacht (German army)".[5a] Although the usual Nazi propaganda events were routinely held at various places in Mülheim and in the Institute, Fischer was able to maintain a certain degree of independency, which was probably due to the military importance of the Fischer–Tropsch process.[5]

During the last few years of his directorship, Franz Fischer lost interest in actively running the Institute, spending most of his time curing health ailments in the Harz mountains or in Munich, where he was honorary professor and where he intended to initiate a small research project in cellulose chemistry.[5a] He did not foresee the impact of his invention on its further scientific development nor of its influence on transition-metal catalysis in the decades that followed.[8] Fischer thought that either one of his Mülheim co-workers, Herbert Koch or Helmut Pichler, would succeed him as Director. In 1942/1943 the KWG decided differently by offering Karl Ziegler this position.

3. The Karl Ziegler Era

When Karl Ziegler (1898-1973; Figure 4) received the offer to succeed Franz Fischer as Director of the Kaiser-Wilhelm-Institut für Kohlenforschung, he was already a renowned synthetic organic chemist who had published a number of seminal papers on:

- Free-radical chemistry (for example, the preparation of the 1,1,3,3-tetraphenylallyl radical and pentaphenylcyclopentadienyl radical)[9]

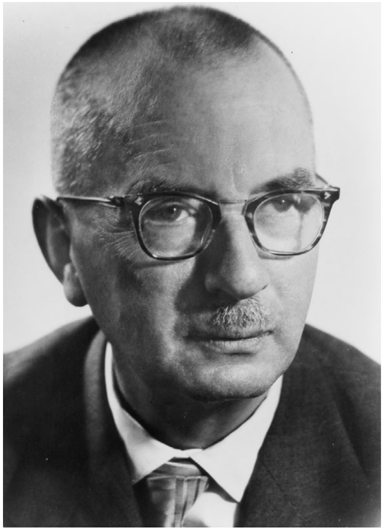


Figure 4. Karl Ziegler (1898–1973) at the time of his move to Mülheim.

- Organolithium reagents (for example, preparation of *n*-butyllithium)[10]
- Carbometalation as in the addition of 2-phenylisopropylpotassium to stilbene[11]
- Polymerization of butadiene using alkali-metal carbanions as initiators[12]
- *N*-bromosuccinimide-mediated allylic and benzylic bromination[13]
- Synthesis of cantharidin and other natural products[14]

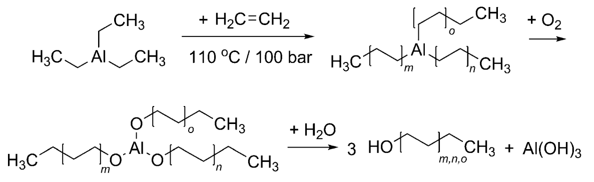
Following the doctoral degree in 1920 at Marburg University under the guidance of the organic chemist Karl von Auwers, Ziegler completed the Habilitation in only three years, and in 1926 became “Privatdozent” (associate professor) in the group of Karl Freudenberg at the University of Heidelberg. Owing to Ziegler’s friendship with a local Jewish family, which he did not terminate despite political pressure, he and his own family were denunciated by the Heidelberg Nazi organization (“NSDAP-Ortsgruppe”).[15a] The culture ministry responsible for the German universities was secretly informed of this relationship, which consequently prevented Ziegler from getting an offer to receive the renowned chair for chemistry in Karlsruhe[15a] as successor to Alfred Stock. Instead, in 1936 he accepted a position at the University of Halle. Karl Ziegler was certainly not a Nazi, but he did not oppose the regime openly.[15] As historians Ute Deichmann[7] and Manfred Rasch[15a] have noted, he was never a member of the Nazi party (NSDAP), the SA, or the SS. From today’s perspective, it seems strange that in 1942/1943 he was offered the important position in Mülheim. As Rasch has concluded on the basis of historical archives, the Nazi officials actually supported this decision because a move from Halle to Mülheim would separate Ziegler from the university, thereby reducing his influence on students.[15a]

Karl Ziegler did not accept the Mülheim offer until 1943 after the Verwaltungsrat (“Board of Governors”) had guaranteed him complete freedom to choose any research area that he wanted, in accordance with the statutes of the Institute and of the foundation.[5b,15] Indeed, he decided not to continue coal research. However, with the war still waging, it was essentially impossible to make detailed plans for future projects. During 1943–1945 he travelled back and forth between Mülheim and Halle, where he still had a laboratory. Whereas Mülheim and the whole Ruhr area were destroyed by the Allied bombing raids starting 1943, the Institute on the outskirts of the city was not hit. Adjusting the infrastructure of the Institute to accommodate organometallic research was nevertheless difficult, both technically and financially. Moreover, several military projects were imposed on Ziegler by the government,[15b] one relating to Ziegler’s research on polybutadiene as a possible substitute for natural rubber.[16] A “benefit” of this political imperativeness by the government was the possibility to prevent the male members of the Institute from being called for military service, which Ziegler made active use of.[15] Following the end of the war in 1945, the Allies closed all Institutes of the KWG, which itself was banned for several years. As the Institute was also a foundation, this restriction did not apply to Mülheim. In hindsight, Franz Fischer’s push to establish a foundation in 1939 proved to be a wise decision.[15a]

In 1948 the Max-Planck-Society (Max-Planck-Gesellschaft, MPG) was established as successor to the KWG.[1] It was named after Max Planck (1858–1947), who had served as president of the KWG from 1930 to 1937 and who was asked to be the interim president of the MPG until Otto Hahn officially took over for 12 years (1948–1960). In contrast to the KWG, which had received substantial financial support from industry, the MPG was financed by the German states (Bundesländer) and the federal government (Bund). Starting in 1948/1949, the Mülheim Institute was called the Max-Planck-Institut für Kohlenforschung (or colloquially: Kofo).

Research during Ziegler’s first 10 years in Mülheim[5b] has been summarized by Günther Wilke in a fascinating personal account[17] that appeared in 2003 in this journal with emphasis on the discovery of the “organometallic mixed catalysts” as Ziegler called them. Only the major developments will be outlined here. In the 1930s Ziegler had turned from free-radical chemistry to lithium and potassium reagents, some of which had been prepared as reagents for the synthesis of phenyl-stabilized radicals. The use of these alkali-metal compounds as initiators in butadiene polymerization had also been demonstrated during the Halle period.[12] Using today’s mechanistic terminology, carbometalation is involved in initiation and chain propagation, as in the addition of 2-phenylisopropylpotassium to stilbene.[11] In the attempt to prepare alkyl aluminum compounds, the Mülheim researchers treated ethylene with the Schlesinger reagent $LiAlH_4$, which provided the novel reagent $Li[AlEt_4]$. This eventually led to the synthesis of $AlEt_3$ via a different route. In 1952 the air-sensitive and potentially explosive reagent was prepared in Ziegler’s laboratory from ethyl chloride and aluminum metal on a 20 kg scale.[17] Several years later, the synthesis was improved by heating a mixture composed of aluminum metal, hydrogen, and ethylene.

In what can be considered to be a turning point in the Ziegler chemistry, ethylene was reacted with $AlEt_3$ at 100 °C/100 bar, which led to the oligomerization of the gaseous feedstock.[18] The so-called “Aufbau” reaction (chain growth) had occurred for the first time. Following many optimization experiments, the reaction batches were treated either with water to form *n*-paraffins or with oxygen and subsequently with water to provide long-chain alcohols (Scheme 1). It was possible to control the degree of oligomerization by varying the reaction conditions. The Aufbau reaction stirred a great deal of excitement worldwide, with several companies realizing the possibility of utilizing the paraffins or the fatty acid alcohols for various applications, including (biogradable!)



Scheme 1. The Aufbau reaction and its use in the synthesis of straight-chain alcohols.

detergents.[5b,17] Parenthetically, the large amounts of Al_2O_3 that accumulated in the overall process may have sparked the use of this oxide as an effective material for column chromatography.

Ziegler immediately submitted a patent application to ensure intellectual property (IP). On May 19, 1952 he presented the results at the annual meeting of the German Chemical Society (GDCh) in Frankfurt,[18] which was attended by numerous scientists, including the Italian professor for physical chemistry at the Institute of Technology in Milan, Giulio Natta (1903–1979).[17] Natta was impressed by Ziegler's lecture, and as he was a consultant with Montecatini, he informed the company. Negotiations for a license began soon thereafter, culminating in a contract which involved a downpayment of DM 600000.[5b,17] Since this was a huge sum of money at the time, the contract required Ziegler to report any future research developments in aluminum chemistry directly to the Italian company.

It can be seen that Ziegler's long road from free radical chemistry to the Aufbau reaction was not at all straight, and that it was accompanied by a number of unexpected results. Serendipity was to play an even greater role in research that followed the first breakthrough in alkyl aluminum chemistry.[5b,17] One day the researchers experienced a surprise upon opening a steel vessel in which the Aufbau reaction was normally performed under pressure and elevated temperatures: Instead of the usual oligomerization products, 1-butene had formed. But why? After weeks of careful experimentation and analytical "detective" work, it became clear that traces of nickel salts had formed from the walls of the steel reactor during the (acidic) cleaning process, and that this metal in combination with $AlEt_3$ was catalyzing the kinetically fast dimerization of ethylene in a process that was later termed hydrovinylation. Thereafter, special care was taken to clean the steel reactors very carefully between experiments. Ziegler drew another conclusion of paramount importance. As a consequence of the "nickel effect", other transition metals were systematically tested as possible catalysts in ethylene dimerization, a decision that should eventually lead to another dramatic turning point.[5b,17]

It was the doctoral student Heinz Breil, who one day made an unexpected and indeed sensational discovery:[5b,17] Upon testing $[Zr(acac)_4]$ as the catalyst, not *n*-butene was formed, but a white solid identified as polyethylene! Thereafter Breil discovered that the mixture of $TiCl_4$ and $AlEt_3$ was even better, a process that was subsequently optimized by Heinz Martin at ambient temperature and pressure by using $Et_2AlCl/TiCl_4$ as the (heterogeneous) catalyst. The patent on polyethylene was filed on November 17, 1953 by Ziegler himself (K. Ziegler, H. Breil, E. Holzkamp, H. Martin, DBP 973626). Ziegler neglected to include propene in the claims as a polymerizable olefin, which should prove to be a mistake. After some delays, Heinz Martin subsequently showed that propene can also be polymerized with formation of the likewise industrially important polypropylene. Following some court litigations, Mülheim eventually acquired full IP in the USA for polypropylene as well. Within a short time, numerous companies were licensing the Ziegler invention, although others were violating the Mülheim patents. This led to countless court cases stretching over a period of decades, essentially all of which were won by the Institute in Mülheim. Success rested on the Studiengesellschaft Kohle mbH (SGK; successor to Studien- und Verwertungsgesellschaft mbH), a company established by Ziegler in 1955 that has since acted as a trustee for the non-profit Institute. Headed by Heinz Martin, SGK ensured a continuous flow of revenue for the Mülheim MPI for two (!) patent periods.[5b,17,19] Later he wrote a book describing many fascinating details of the patent story, including the role of Montecatini and Giulio Natta.[19] For 40 years, the incoming revenues covered the yearly budgets of the Institute, financed the new high-rise laboratory building (1969) as well as other buildings on the Mülheim campus, and supplied the newly founded Ziegler Foundation with generous assets. During this period it was not necessary for the MPG to finance the Institute. In the early 1960s, the President of the MPG, Adolf Butenandt, wrote Karl Ziegler a personal letter in which he assured the Mülheim Director that the MPG would provide the necessary funding on the day that the patents should expire.

Ten years later, Karl Ziegler was awarded the Nobel Prize for his invention of the Ziegler catalysts in olefin polymerization.[20a] He shared this award with Giulio Natta, who had studied and analyzed correctly the stereochemistry (tacticity) of polypropylene.[20b] Both of these monumental contributions were not only important in terms of industrial applications; they also catalyzed further research in the rapidly developing area of organometallic chemistry and polymer chemistry at the time, activities that have continued to thrive to the present day. Figure 5 shows Karl Ziegler receiving the Nobel Prize from the Swedish King Gustav VI Adolf on December 10, 1963.

Figure 5. The Swedish King Gustav VI Adolf (left) congratulating Karl Ziegler (right) at the Nobel Prize ceremony in Stockholm on December 10, 1963.

During the Ziegler era, several scientists were engaged in research not directly associated with Ziegler polymerization. Herbert Koch, one of the chemists remaining from the Fischer era, developed a novel synthesis of bulky carboxylic acids by treating substituted olefins (or tertiary alcohols) with CO in the presence of strong acids. In collaboration with his coworker, Wolfgang Haaf, the process was later improved by utilizing formic acid as the CO source (Koch–Haaf process).[21] In the 1960s, Kurt Zosel invented a new way to separate mixtures of compounds by selective supercritical gas-based extraction. Eventually his efforts led to a patent in 1970 covering the decaffeination of the green coffee bean by supercritical CO_2 extraction,[22] which was later improved as an ecological viable and safe process in the food industry.

4. The Günther Wilke Era

Karl Ziegler chose a successor that he knew very well professionally and personally. Günther Wilke (born 1925; Figure 6) studied chemistry at the University of Heidelberg and obtained his doctoral degree in 1951 under the direction of the organic chemist Karl Freudenberg (cellulose chemistry), working on reactions related to lignin degradation. In a complete change in research direction, he joined the Ziegler group as a postdoc in 1951. Initially, Ziegler asked him to develop an improved synthesis of $AlEt_3$.[17] Following the discovery of the "nickel effect" (Section 3), Wilke began to focus on the organometallic chemistry of nickel, culminating in his Habilitation in 1960 at the Technical University (RWTH) in Aachen. Indeed, nickel chemistry continued to be so productive that it paved the way to Wilke's appointment as successor to Karl Ziegler in 1969.

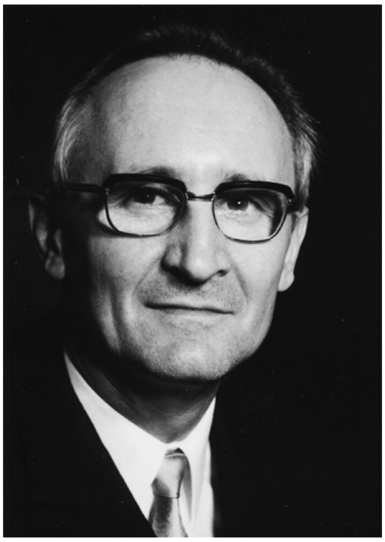
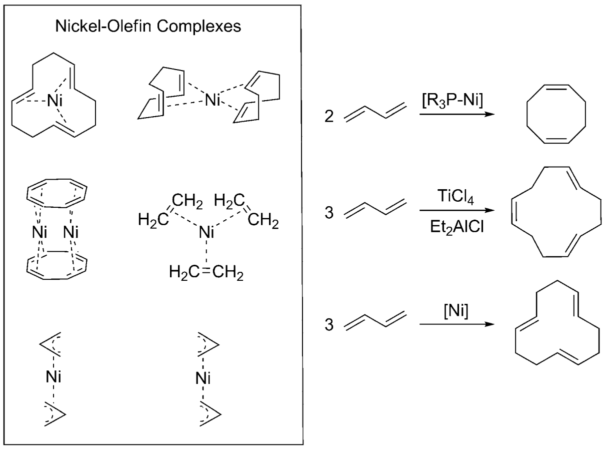


Figure 6. Günther Wilke at the time of his appointment as Director of the MPI für Kohlenforchung in 1969.

As the new Director, Wilke was fortunate to move into a newly constructed high-rise laboratory building (Figure 7) equipped with the most modern labs and instrumentation, while also having sufficient financial backup for new directions in research. The Wilke group published many papers on nickel chemistry that were not only seminal in their own right, but which also influenced the development of transition-metal chemistry and catalysis as a whole. In particular, X-ray crystallography proved to be invaluable for characterizing many of the new organometallic compounds. Wilke made a wise decision by hiring Carl Krüger, who was asked to create a service department for crystal structure determination of sensitive organometallic compounds. At that time such X-ray experiments of air-sensitive compounds were true challenges. A service department for NMR spectroscopic analysis of organometallic compounds was also established, initially headed by Ernst G. Hoffmann and later by Reinhard Benn, who pioneered the area of heteronuclear NMR spectroscopy of a variety of different organometallic compounds. The MS service department was run by Dieter Henneberg, who collaborated with the head of the computer department, Engelbert Ziegler, in developing software for MS-based analyses (MassLib) used by many labs throughout the world for identifying compounds. Even a chromatography service department was founded, headed by Gerhard Schomburg. Furthermore, Roland Köster was appointed Scientific Member of the Max-Planck-Society, working in the area of boron chemistry. A number of group leaders were also active in the Institute, generally collaborating with the Wilke group and later performing independent research. These included Herbert Lehmkuhl, Heinz Hoberg, Boris Bogdanović, Paul Heimbach, Roland Rienäcker, Peter W. Jolly, Klaus Jonas, Helmut Bönnemann, and Paul Binger. Later Klaus Pörschke, Gerhard Fink, and Matthias W. Haenel also became permanent members of the Institute. Other group leaders (Habilitand) including Holger Butenschön, Jörg Schneider, and Thomas Schmidt left the Institute for other positions.

Figure 7. The high-rise laboratory building of the MPI für Kohlenforschung constructed in 1968 (picture taken by Matthias Haenel in 1988).[5b]

Among the notable achievements during the Wilke era was the preparation, characterization, and reactivity of such classical organometallic compounds as [Ni(1,5-cyclooctadiene)], [Ni(allyl)$_2$], [Ni(CH_2=CH_2)$_3$], and many others (Scheme 2).[23] As the nickel chemistry has been reviewed in detail elsewhere,[24] only a few highlights are featured here. One of the exciting results was the discovery of butadiene cyclodimerization and cyclotrimerization catalyzed size-selectively by titanium and nickel complexes, respectively. The 12-membered ring tri-olefins were used as starting materials



Scheme 2. Left: Typical Wilke nickel compounds; right: cyclodimerization and cyclotrimerization of butadiene to 8- or 12-membered rings, respectively, depending upon the nature of the catalyst.[24]

by the nearby Hüls company (today Evonik) in the manufacture of various specialty polymers. For example, following reduction to cyclododecane, oxidation to cyclododecanone, oxime formation, and Beckmann rearrangement, the respective lactam was employed as the monomer for producing various forms of Vestamid as high-performance polyamides useful in a variety of applications ranging from soccer shoes to car interiors. Other achievements during the Wilke era that also influenced the development of transition-metal catalysis have been reviewed elsewhere.[24]

5. Restructuring the Max-Planck-Institut für Kohlenforschung

5.1. Manfred T. Reetz as the New Director

Toward the end of the 1980s Günther Wilke began to look for a successor, the search ending in 1990 with the decision to offer the position to me. At the time I was full professor for organic chemistry at Marburg University, working in the area of organometallic chemistry with emphasis on chemo- and stereoselective organotitanium reagents and amino acids as chiral building blocks in synthetic organic chemistry. After some hesitation I accepted, and my group moved to Mülheim in 1991. Less than two years later I was appointed Director of the MPI für Kohlenforschung and also honorary professor at nearby Ruhr-Universität Bochum, where my doctoral students obtain their degrees.

In those days the scientific community knew that the Mülheim Institute was well-equipped with the most modern instruments, and that a number of excellent service departments had been established by Wilke during the 25 years of his directorship. In 1993, the Institute had about 275 employees, including personnel for cleaning glassware in all laboratories. Thus, for a chemist primarily interested in (basic) research and less so in organizational work, it seemed like the best place to be in all of Germany. However, during the first two years in Mülheim prior to taking over as Director, I realized the necessity to restructure the Institute. One reason was the fact that the last Ziegler patents were due to expire in the mid-1990s, which would require the MPG to finance a good portion of the Mülheim budget, as Butenandt had assured Ziegler three decades earlier (see Section 3). Part of the total budget would be covered by the Ziegler Fund and Foundation, which was a good deal for the MPG, but for the Institute it did not mean extra money for research. Starting in 1993, the President of the Max-Planck-Society, Hans Zacher, as well as representatives of the federal and state governments (Bund-Länder-Kommission) approached the Institute in the (re)quest to reduce the running costs, which included an “internal house” salary system of the employees. Slashing the number of employees from 275 to about 200 was also on the agenda, all in all a significant organizational challenge causing unrest among the employees. Zacher himself was under pressure, because in the wake of German reunification the federal government planned the establishment of 17 new MPIs in the eastern part of the country without providing full financial coverage.

More importantly, it was clear that an Institute of the Mülheim size should have more than one main researcher (Director), as in other MPIs. I envisioned five departments, headed by Directors endowed with equal rights and duties, an organizational form that included a rotational system regarding the position of the Managing Director. My own research (Department of Synthetic Organic Chemistry) already existed. The rest of the plan foresaw the establishment of all aspects of modern catalysis under one roof: Homogeneous and heterogeneous catalysis, novel organometallic compounds as potential catalysts, catalysis in natural products synthesis, and theoretical aspects of catalysis. Whereas the MPG enthusiastically supported this plan, the Board of Governors was skeptical, which caused a delay in changing the 80 year old statutes. It was not until 1995 when Carl Heinrich Krauch (1931–2004), a renowned industrial chemist and former president of the German Chemical Society GDCh), took over as chairman of the Board of Governors that the necessary changes became possible. With the continuous support of the Institute’s administrative director, Reinhard Benn (former head of the NMR department), all of the work necessary in restructuring the Institute was completed by 1999.

The remaining and most important challenge concerned headhunting in the endeavor to identify the best personalities for the newly established positions. Prior to the completion of the organizational change, Andreas Pfaltz was hired in 1994, working in the area of asymmetric olefin hydrogenation based on the famous Pfaltz ligands, which stimulated a great deal of research in other groups around the world.[25] Following a productive research phase (1994–1998), he and his family moved back to their home town of Basel/Switzerland for personal reasons. At the time, two independent groups were also active in the Department. Matthias M. Haenel had joined the Institute in 1978 with the intention of re-establishing coal research, an organic chemist who subsequently developed the first coal hydrogenation utilizing homogeneous catalysts.[26] As already indicated (Section 4), Gerhard Fink had been hired in 1980 by Wilke to establish expertise in kinetics in addition to rekindling research in transition-metal-catalyzed olefin polymerization. In 2000 Lukas Gooßen joined the Department of Synthetic Organic Chemistry as a Habilitand, working in transition-metal catalysis before moving to Aachen in 2004 and then to Kaiserslautern. Other chemists joined the Institute as group leaders without initially being assigned to a Department, including Donna Blackmond, Wilhelm Maier, and John Bradley. Later they left Mülheim to accept chairs elsewhere.

Four new Directors eventually took office, Alois Fürstner (Department of Organometallic Chemistry), Ferdi Schüth (Department of Heterogeneous Catalysis), Walter Thiel (Department of Theory), and Benjamin List (Department of Homogeneous Catalysis; Figure 8). Since 2002 the office of the Managing Director rotates every three years among the Directors. In 2011 I became emeritus group leader, working externally with 6–7 postdocs at Marburg University as the first Hans Meerwein Research Professor.

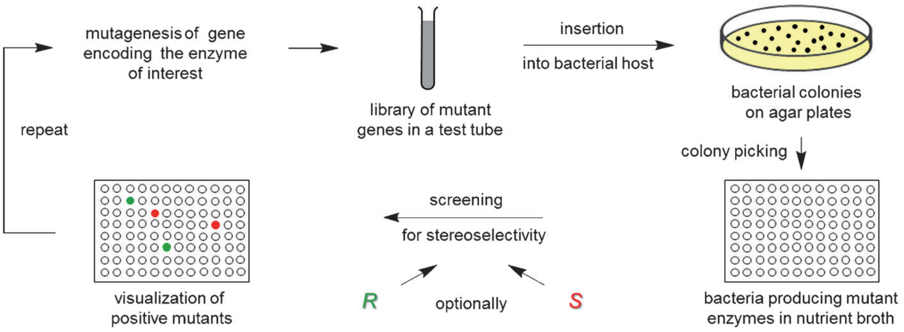
Figure 8. The Directors of the MPI für Kohlenforschung in 2011 (in parentheses the years of office as Managing Director). From left to right: Walter Thiel (2006–2008), Ferdi Schüth (2003–2005), Alois Fürstner, (2009–2011), Benjamin List (2012–2014), and Manfred T. Reetz (1993–2002).

External Scientific Members are Jack Halpern (Chicago), Alois Haas (Berlin) and Walter Leitner (Aachen). Today five service departments actively support the Institute's research, headed by scientists who work with expert engineers and technicians: NMR spectroscopy (Christophe Farès), Mass spectrometry (Wolfgang Schrader), Crystallography/Electron-microscopy (Christian W. Lehmann), Chromatography (Philipp Schulze), and Information Technology/Library (Peter Fischer). The administrative director is Hermann Thole, and Ferdi Schüth is chairman of SGK, along with running the Department of Heterogeneous Catalysis.

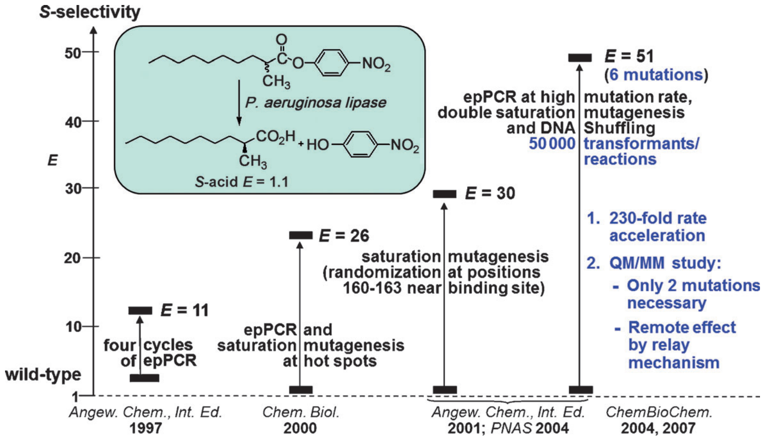
5.2. Research in the Department of Synthetic Organic Chemistry

Notwithstanding the tasks associated with restructuring the Institute, I proceeded in my new position as Director of the MPI and head of the Department of Synthetic Organic Chemistry by initiating several new research projects. One of them was the size-selective electrochemical preparation of nanostructured transition-metal colloids in the range of 2–5 nm, which eventually led to simple procedures for producing (water-) soluble or immobilized forms of nanostructured transition-metal oxides and their use as catalysts in organic chemistry.[27a] A different direction concerned the use of chiral monodentate BINOL-derived phosphites as cheap and effective ligands for Rh-catalyzed asymmetric olefin hydrogenation.[27b] The unorthodox concept of employing mixtures of chiral and achiral P-ligands in these and other transition-metal-catalyzed reactions proved to be an effective and practical method in combinatorial catalysis,[27b] which rapidly reached industrial status.[27c] Yet another direction concerned the sol–gel-based encapsulation of lipases, the solid immobilizates serving as stereoselective catalysts in kinetic resolution and desymmetrization reactions.[27d]

The most important new research project in our group was initiated in 1995. The underlying idea constitutes a new approach to asymmetric catalysis by harnessing the principles of directed evolution.[28] At the time it was already known that protein engineering based on repeated rounds of gene mutagenesis, expression, and screening (or selection) can be exploited for enhancing the thermostability of proteins or their robustness in organic solvents.[29] Nevertheless, it was not certain that such a Darwinian approach would be sensitive enough to respond to significant changes in stereoselectivity (Scheme 3). The ultimate goals were defined as follows: Notable enhancement of enantioselectivity to practical levels as well as the possibility for complete reversal of stereoselectivity on an optional basis. Another challenge concerned the



Scheme 3. Concept of directed evolution of stereoselective enzymes as a means to access biocatalysts for application in synthetic organic chemistry and biotechnology.[28] Bottom left: 96-well microtiter plate featuring improved mutants indicated by a green well (enhanced (*R*)-selectivity) and by a red well (enhanced (*S*)-selectivity).



Scheme 4. Summary of different directed evolution strategies in the quest to evolve enantioselective lipase mutants as catalysts in the depicted hydrolytic kinetic resolution of a chiral ester.

need to develop high-throughput screening systems for assaying whole libraries of potentially enantioselective mutants, which did not exist at the time. In view of the scientific uncertainties, the lack of experience in molecular biology as well as the costs of (bio)equipment and the required analytical instrumentation, the project was a true adventure. Initial expertise in molecular biology was ensured by a collaboration with Karl-Erich Jaeger, an assistant professor (Dozent) in the biology department of nearby Ruhr-Universität Bochum. Soon thereafter my group consisted of organic chemists, molecular biologists, and biotechnologists as a truly interdisciplinary team.

Scheme 3 shows an agar plate featuring bacterial colonies, each originating from a single cell and therefore harboring an enzyme mutant (not a mixture of mutants). In practice, a single agar plate does not suffice, hundreds if not thousands being necessary. The mutated gene of a given hit is then extracted and subjected to another cycle, thereby exerting evolutionary pressure, and the process is continued until the desired degree of stereoselectivity has been achieved. This concept, being based on “evolution in the test tube”, clearly differs from the usual approaches to chiral catalyst development utilizing transition-metal complexes or organocatalysts.

Several molecular biological methods of gene mutagenesis were available at the time, including error-prone polymerase chain reaction (epPCR; a shotgun technique),[30a] saturation mutagenesis (randomization at predetermined positions),[30b] and DNA shuffling (mimic of natural sexual evolution).[30c] Unfortunately, it was not clear which technique should be chosen for the purpose at hand. As screening constitutes the bottleneck of directed evolution, several medium- and high-throughput screening systems for assaying enantioselectivity were developed.[28c] The first crucial step was proof-of-principle, not industrial application. This was achieved in 1997 using the lipase from *Pseudomonas aeruginosa* as a catalyst in the hydrolytic kinetic resolution of 2-methyl decanoic acid *p*-nitrophenyl ester.[28a] Four cycles of epPCR at low mutation rate (one point mutation occurring in the enzyme) enhanced enantioselectivity stepwise from $E=1.2$ (wild-type, WT) to $E=11$ in favor of the (*S*)-acid (Scheme 4). The fifth cycle increased enantioselectivity slightly to $E=13$, which was a clear indication that multiple cycles of epPCR was not the optimal strategy.[28c]

In the years that followed, alternative approaches were tested, including epPCR at high mutation rate (3–4 point mutations in the enzyme), saturation mutagenesis at “hot spots” initially identified by epPCR, saturation mutagenesis at a site comprising four amino acid positions next to the enzyme’s binding pocket, and DNA shuffling.[28c] In 2001 it seemed that a combination of these methods would constitute the best strategy,[28b] the selectivity factor reaching $E=51$ (Scheme 4). These efforts entailed the screening of about 50000 transformants (mutants). We were also able to reverse the sense of enantioselectiviy in favor of the (*R*)-acid ($E=30$).[28c] Moreover, at that time other groups were beginning to join efforts in generalizing the concept.[28c]

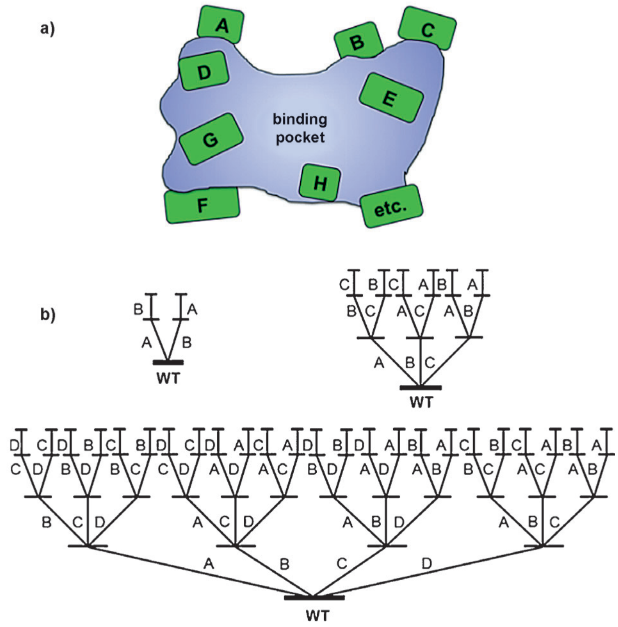
An important spinoff of this kind of research concerns the possibility to learn from directed evolution. In a collaborative effort with the Thiel group (Section 8), a QM/MM study was performed to uncover the origin of enhanced (*S*)-selectivity on a molecular level.[31] Most of the six-point mutations occur at positions remote from the active center, which could be explained by a relay mechanism. More importantly, the computations indicated that only two of the six point mutations are necessary. Upon generating the respective double mutant, enantioselectivity was even better ($E=63$),[31b] a triumph of theory! However, it was also a signal that our mutagenesis strategy was far from optimal.

In 2003, research in directed evolution was put on two different tracks: 1) Generalizing our approach by studying other types of enzymes in stereoselective transformations, for example epoxide hydrolases (EHs) and Baeyer–Villiger monooxygenases (BVMOs), the latter requiring a cofactor which in principle could cause problems; and 2) pushing methodology development forward for the purpose of making directed evolution more efficient and reliable. We conjectured that if directed evolution of stereoselective enzymes should ever make it to the industrial stage, then it needs to be much faster than in the past. One approach was to create much larger mutant libraries (for example, 10^8 members) covering more of protein sequence space and then to utilize (surface) display or selection systems. Owing to several reasons, success in this area has been severely hampered. The preferred alternative approach was based on the opposite trend, namely to create smaller but higher-quality mutant libraries requiring a minimum of screening.

The first step in devising ways to generate higher-quality mutant libraries was taken by generalizing the original idea of focusing saturation mutagenesis on a predetermined site aligning the binding pocket of an enzyme to enhance or reverse stereoselectivity, as first practiced in 2001.[28b] In the spirit of Emil Fischer's lock-and-key hypothesis and its extension by Linus Pauling concerning the stabilization of transition states in enzymatic reactions, we systematized our original approach based on saturation mutagenesis by considering all first- and second-sphere sites around the binding pocket of an enzyme. As part of the combinatorial active-site saturation test (CAST), randomization sites termed A, B, C, D, and so on are chosen with the help of X-ray data or homology models, each site comprising one or more amino acid positions (Scheme 5 a).[32] Using several different enzyme types, CASTing proved to be a viable alternative to epPCR and DNA shuffling, because it is structure-driven and therefore rational. However, the real power of the CAST approach did not emerge until the idea of iterative saturation mutagenesis (ISM) was born. Accordingly, the gene of a hit in one library is used as a template for saturation mutagenesis at another site, and the process is continued until in an upward pathway all sites have been visited once (Scheme 5 b).

In all of the early ISM studies, arbitrary pathways were chosen, all involving fairly small libraries in the order of only 2000 to 4000 transformants, which could be screened for steroselectivity using automated chiral GC or HPLC. Thus, expensive analytical instrumentation such as the original MS-based *ee*-screening system was no longer necessary. Recent methodology developments in CASTing/ISM increased efficacy further by:[32]

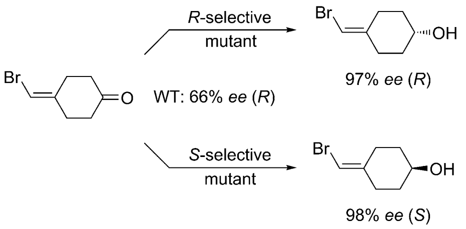
- Use of reduced amino acid alphabets
- Improved PCR-based saturation mutagenesis for difficult-to-amplify templates
- Bioinformatic guides
- computer-supported guides
- Reduction of amino acid bias
- Development of the quick quality control (QCC)
- Pooling of transformants for further reduction of screening



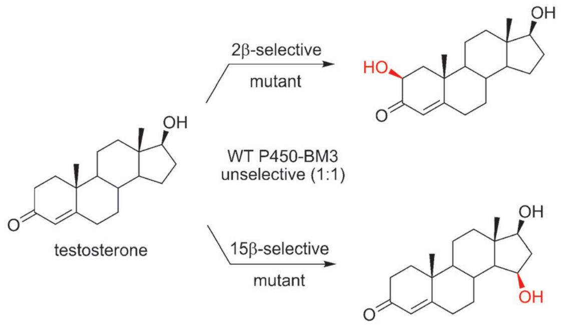
Scheme 5. a) CAST sites chosen for saturation mutagenesis involving focused amino acid randomization with creation of focused mutant libraries. b) ISM schemes for 2-, 3-, and 4-site systems.[32]

Guidelines on how to group individual amino acid positions into multi-residue sites have been issued.[32a,c] These improvements are crucial for generating smart libraries, all of them centering around statistical analyses concerning the necessary degree of oversampling. The CASTER computer aid, based on the Patrick/Firth algorithm, was developed for designing mutant libraries.[33] CASTing/ISM was then applied to the previously studied lipase-catalyzed reaction (Scheme 4), resulting in a mutant having only three point mutations and showing much improved enantioselectivity ($E = 594$), while requiring much less screening.[34] This enzyme is the most systematically studied system in directed evolution,[28c,34] thereby allowing for a comparison of the different mutagenesis methods and strategies. Exploring all theoretically possible pathways of an ISM system is not necessary.[32] One of the underlying reasons for the efficacy of ISM was uncovered by performing deconvolution experiments.[32] It was found that the individual contributions of the point mutations or sets of mutations are not simply additive. They interact with one another cooperatively (more than mathematical additivity). This is one of the most important lessons that we have learned from research in directed evolution, which has significant ramifications for enzymology in general.[35]

Just two select examples of ISM in controlling stereo- and regioselectivity are featured in Schemes 6 and 7.[36a,b] They constitute typical synthetic problems that cannot be easily solved by current synthetic transition-metal complexes or organocatalysts, illustrating the complementary nature of the different approaches. Another case is the first example of directed evolution of a P450-enzyme in which both regio- and enantioselectivity were controlled,[36c] which has been extended to include those processes in which a single CH-activating event creates two new centers of chirality.[36d]



Scheme 6. Asymmetric ketone reduction catalyzed by mutants of an alcohol dehydrogenase (ADH) with formation of axially chiral alcohols.[36a]



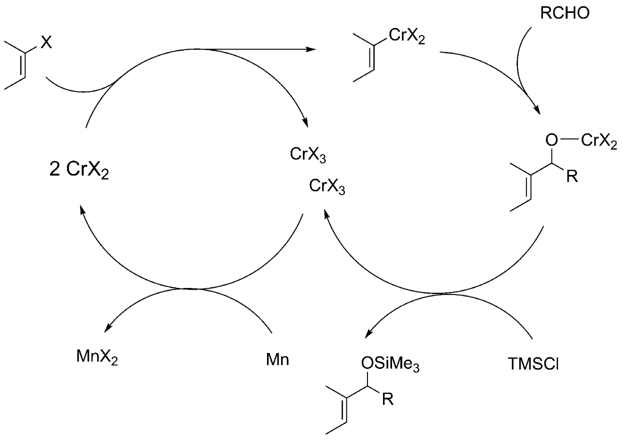
Scheme 7. Regio- and diastereoselective C–H-activating oxidative hydroxylation catalyzed by mutants of P450-BM3.[36b]

ISM can also be applied when aiming to increase thermostability or robustness of enzymes in hostile organic solvents. In this case the criterion for choosing focused randomization sites is different, specifically by opting for amino acid positions which have the highest B-factors as provided by X-ray crystallography (B-FIT method).[33]

The long-term efforts of our group coupled with the contributions by others in the area of directed evolution[29,32a–b] have shown that the traditional limitations of enzymes as catalysts in organic chemistry and biotechnology can be eliminated, namely the often observed 1) poor or wrong stereo- and/or regioselectivity; 2) narrow substrate acceptance (low activity); and 3) insufficient stability under operating conditions. The methods of directed evolution, which have emerged from systematic methodology development, provide rapid access to a prolific source of catalysts for asymmetric transformations.[32] Other areas of application include metabolic pathway engineering[37] and the construction of purely synthetic biocatalytic cascade reactions occurring in designer cells.[38]

6. Alois Fürstner as Director of the Department of Organometallic Chemistry

Yet another change in Mülheim's policy in the 1990s concerned the support of early career chemists, especially assistant professors ("Habilitand") or in exceptional cases young associate professors. The plan was to provide optimal research conditions and financial support so that within a few years these researchers would receive offers from elsewhere as full professors. One of them was Alois Fürstner (born 1962), who joined the Department of Synthetic Organic Chemistry in 1993 as a junior group leader following doctoral work under Hans Weidmann in Graz/Austria (1987), a postdoctoral stay with Wolfgang Oppolzer in Geneva/Switzerland (1990–1991), and Habilitation in Graz (1992). He had already published significant papers on the use and optimization of McMurry coupling as a novel way to prepare heterocycles, many of which were difficult if not impossible to synthesize by other means.[39] In Mülheim he shifted from stoichiometric transition metal chemistry to catalysis. One of the early breakthroughs was carbonyl coupling reactions catalytic in titanium,[40] another was the first Nozaki–Hiyama–Kishi reactions catalytic in chromium with cheap manganese as the electron source (Scheme 8).[41]



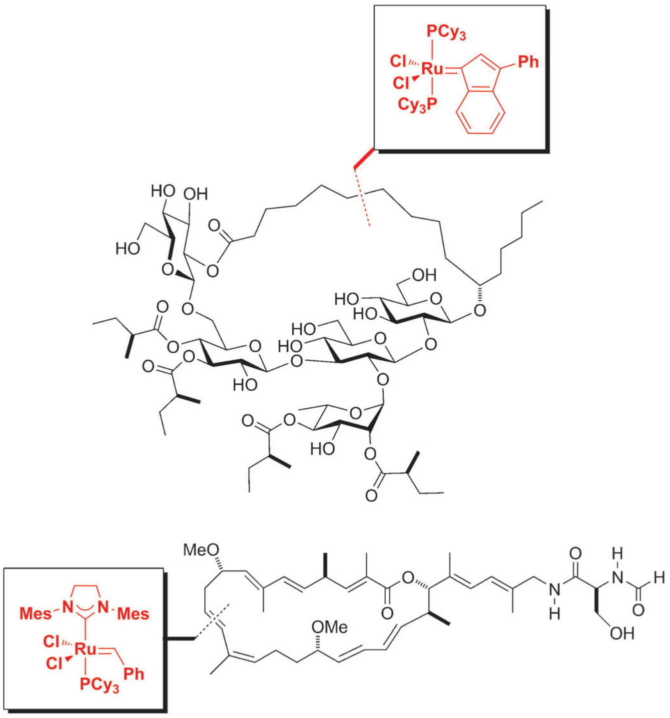
Scheme 8. Fürstner's concept of Nozaki–Hiyama–Kishi reactions catalytic in chromium.[41]

At about the same time, Fürstner made his first forays into olefin metathesis, initially using catalysts that Robert H. Grubbs and Richard R. Schrock had pioneered. Although ring-closing metathesis (RCM) was well-known in the mid-1990s, it was generally believed that this reaction would not allow medium-sized or macrocyclic rings to be formed efficiently, unless the substrates are conformationally biased. Using the first-generation Grubbs-type ruthenium catalysts, the Fürstner group demonstrated in a series of seminal papers that this dogma was incorrect.[42] Indeed, even fully flexible dienes cyclized with remarkable efficiency. As time went by, it became clear that RCM constitutes a priviledged entry into complex macrocyclic structures of all kinds,[43] a finding that has changed the way organic chemists think about the synthesis of natural products. In further work, it was noticed that the first-generation ruthenium carbene complexes are sensitive to chelation, leading to useful guidelines in the design of synthetic multistep schemes.[42–44] Whereas the conventional logic of synthesis dictates bond formation to be carried out at or close to polar groups, RCM-based macrocyclizations are best performed at remote sites. Other RCM-based natural products syntheses followed, including those of strained compounds. These and other contributions helped to make RCM a popular technique that is widely used to the present day.[43]

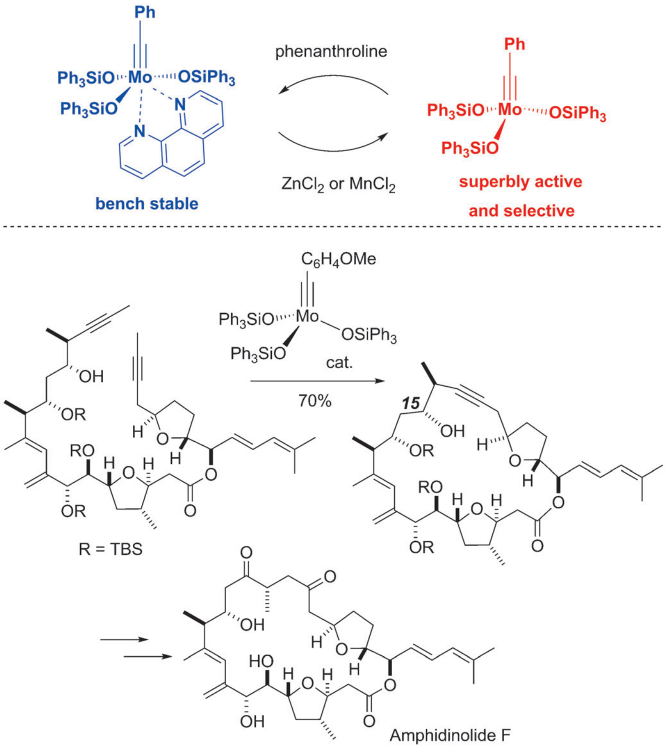
By 1997/1998, the Fürstner chemistry had reached high international status. It was therefore of no surprise that offers for a chair in organic chemistry arrived from several German universities and from abroad. Contrary to the original intention, the Institute undertook all efforts to keep Fürstner in Mülheim by forging immediate plans to promote him to the status of a Director. The procedure for hiring a so-called Scientific Member (Director) in the MPG is somewhat complicated and time-consuming, requiring several steps: Evaluation by a working party ("Berufungskommission") composed of German and international scientists, letters of recommendation from up to 10–12 internationally renowned experts, a voting process by the respective MPG Section and final decision by the MPG Senate and President. In those days promotion of junior scientists within an MPG Institute to the rank of a Director was not an acceptable procedure ("Hausberufung"). Fortunately, MPG President, Hubert Markl, consented and allowed the procedure to be initiated. It was highly successful at all stages, and in 1998 Alois Fürstner became Director of the Department of Organometallic Chemistry. He has been associated with the University of Dortmund since he came to Mülheim in 1993.

Thereafter the Fürstner group expanded rapidly, initial emphasis being on RCM-based syntheses of complex natural products, woodrosin I (Scheme 9)[45a] and iejimalide[45b,c] being two of many examples. Parallel to these activities, the catalysts themselves were structurally modified (including fine-tuning of *N*-heterocyclic carbene ligands) and subsequently used by Fürstner's co-workers and by many groups worldwide. The Schrock-type olefin metathesis catalysts were also structurally modified so as to render them air-stable and user-friendly.[46]

More recently, the Fürstner group showed that the powerful but quite sensitive Schrock alkylidyne complexes for alkyne metathesis[43b] can be rendered bench-stable and thus user-friendly by reversible adduct formation (Scheme 10, top).[47] The other innovation concerning this molybdenum catalyst is the presence of bulky triphenylsilyl instead of *tert*-butyl groups utilized in the original Schrock complexes, which makes them considerably more active and selective.



Scheme 9. Top: Structure of woodrosin I with the indicated site of RCM sufficiently removed from possibly interfering functional groups and the novel indenylidene–ruthenium catalyst developed in the Fürstner group.[45a] Bottom: Structure of iejimalide featuring the site of RCM and the catalyst used in the ring-closing process.[45b,c] Cy = cyclohexyl, Mes = mesityl.



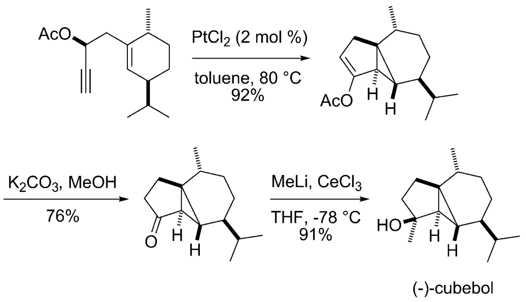
Scheme 10. Top: Stabilization of a Schrock-type alkylidyne molybdenum complex by phenanthroline complexation; addition of $ZnCl_2$ or $MnCl_2$ inducing decomplexation and triggering catalysis.[47] Bottom: Key transformation in the synthesis of amphidinolide F.[48]

Using this and similar catalysts, ring-closing alkyne metathesis was not only made practical for the synthesis of large-ring alkynes,[43b] they were also used in complex natural products syntheses, as in the preparation of amphidinolide F[48] (Scheme 10, bottom). Once the ring has been formed, the alkyne function can be manipulated in many ways; for example, semi-hydrogenation (either *cis*- or *trans*-selectively) or full hydrogenation.[47,48] Most recently, ruthenium-catalyzed hydroboration was shown to be *trans*-selective, a surprising result because it contradicts the usual *cis*-specificity observed under traditional Brown conditions.[49]

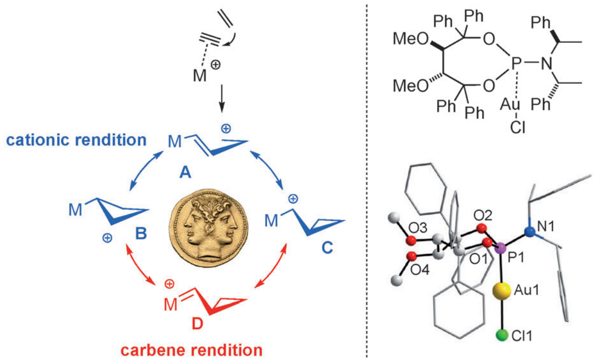
In other projects, alkynophilic Lewis acid catalysts based on platinum and gold were investigated, an area of interest to many other researchers as well, but one in which a great deal of uncertainty existed with respect to the mechanism.[50] One of many transformations is shown in Scheme 11 featuring a concise synthesis of the sesquiterpene (−)-cubebol, the crucial step being the initial $PtCl_2$-catalyzed cyclization leading to the tricyclic precursor.[51]

The synthetic, X-ray structural, and mechanistic studies performed in Mülheim culminated in a mechanism featuring reactive intermediates which are "carbenoid" in nature, but which can also be considered to be metal-stabilized carbocations (Scheme 12).[50,52] The predictive power of this model nicely explains the often observed puzzling synthetic results and allows for the design of new experiments.

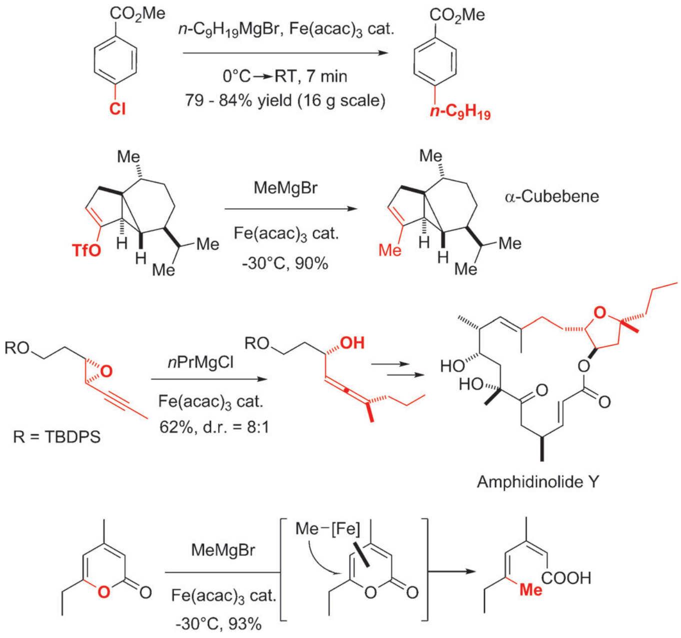
In other work, the use of iron catalysts as cheap and benign alternatives to the established noble metal catalysts



Scheme 11. Concise synthesis of (−)-cubebol.[51]



Scheme 12. Left: Fürstner's mechanistic interpretation of platinum and gold catalysis in terms of a continuum between a carbenoid and a metal-stabilized carbocation.[50] Right: TADDOL-based gold complex with crystal structure.[52]



Scheme 13. Typical examples of Fe-catalyzed C−C bond forming reactions.[53]

was developed for some (but not all) C−C bond forming reactions known in transition-metal catalysis.[53] When applicable, very high catalyst activity was observed. Typical iron-catalyzed transformations are shown in Scheme 13. The purely preparative work in the Fürstner group was accompanied as usual by mechanistic studies, which proved to be particularly challenging owing to the high sensitivity of the iron complexes.

In recent years, the Department has produced several successful organic chemists of the younger generation. Manuel Alcarazo currently heads an independent research group, focusing on transition-metal catalysis that complements well the Fürstner chemistry. Previously, Frank Glorius, also working innovatively in the area of transition-metal catalysis, accepted a position in Marburg and later a chair for organic chemistry in Münster. Another earlier member of the Department, Stefan Hecht, working in the area of functional compounds and molecular devices, left the Institute for Berlin, where he currently heads a chair at Humboldt University.

7. Ferdi Schüth as Director of the Department of Heterogeneous Catalysis

The Director of the Department of Heterogeneous Catalysis was also appointed in 1998. Ferdi Schüth (born in 1960) was chosen to fill this position for several reasons. Most importantly, being a physical chemist with a great deal of experience in the synthesis of solid materials for use in heterogeneous catalysis and their characterization by modern analytical techniques coupled with a distinct feel for mechanistic questions, his interdisciplinary approach corresponded perfectly to the plans of the Institute for establishing a new Department. Schüth had obtained his doctoral degree in 1988 at Westfälische Wilhelms-Universität in Münster under the direction of the physical chemist Ewald Wicke, working primarily on physical aspects of noble metals and supported noble metals, as in the reduction of NO by CO. The dissertation included IR spectroscopic studies of the oscillatory CO/NO and CO/O_2 reactions on palladium and platinum. He then joined the group of Lanny D. Schmidt at the University of Minnesota as a postdoctoral fellow, focusing on such topics as synchrony and the emergence of chaos of oscillations on supported catalysts. This was followed by his Habilitation in 1989–1995 in the group of the inorganic chemist Klaus K. Unger at Johannes-Gutenberg-Universität in Mainz. During this period, he turned to the chemistry of mesoporous silicates, many of his contributions resulting from fruitful collaborations with Unger. For example, a method for controlling the spatial distribution of aluminum in the zeolite ZSM-5 was developed.[54] A study of zeolite single crystals by FTIR microscopy with polarized IR radiation was yet another subject of the Habilitation.[55] In 1993, Schüth spent half a year as visiting scientist in the group of Galen Stucky in Santa Barbara/USA, which likewise resulted in several discoveries on the then just emerging field of ordered mesoporous silica, a procedure for the generalized synthesis of periodic composite materials being one of several highlights.[56]

As a Habilitand it did not take Schüth long to obtain a chair in chemistry, specifically at Wolfgang Johann Goethe-Universität in Frankfurt as full professor for inorganic chemistry. During the short Frankfurt period (1996–1998), he continued research in mesoporous silicates while also initiating a new project on high-throughput heterogeneous catalysis.[57] Around the time of accepting the position in Mülheim in 1998, Schüth exploited the early results of this research as the basis for cofounding a company in Heidelberg (hte GmbH) specializing in high-throughput experimentation, with an emphasis on catalysis. Today about 300 people work in the company, which was acquired by BASF SE in 2012.

Upon arriving in Mülheim in 1998, Ferdi Schüth organized the newly founded Department of Heterogeneous Catalysis around his own group and integrated several scientists already present in the Institute. These included Helmut Bönnemann, an associate professor from the Wilke era, who had switched from homogeneous transition-metal catalysis to the field of colloidal transition metal particles. Additionally, during the mid-1990s the Institute had already hired John Bradley (transition-metal nanoparticles) and Wilhelm Maier (heterogeneous catalysis and high-throughput combinatorial catalysis in an automated manner based on sol–gel systems)[58] as associate professors and independent group leaders. When Bönnemann retired and Maier left the Institute to accept a chair in Saarbrücken, several junior researchers were hired, all of which were later successful in obtaining attractive academic positions elsewhere: Stefan Kaskel took over a chair for inorganic chemistry at TU Dresden, An-Hui Lu returned to China where he is full professor at Dalian University of Technology, Oliver Trapp is professor at Heidelberg University, and Regina Palkovits now holds a chair at RWTH Aachen. Today several independent groups are part of the Department: Harun Tüysüz (heterogeneous catalysis; sustainable energy), Wolfgang Schmidt (functional materials), Claudia Weidenthaler (powder diffraction and surface spectroscopy), Frank Marlow (nanostructures and optical materials), Roberto Rinaldi (biomass conversion), and Michael Felderhoff (hydrogen storage). Schüth is associated with Ruhr-Universität Bochum.

Schüth's approach to high-throughput heterogeneous catalysis complemented the Maier concept. It relied on parallel reactor technology (Figure 9), which is directly compatible with conventional reactors.[59] This means that the conditions of high-throughput experimentation are as close as possible to the reaction conditions used in real (industrial) reactors, strongly reducing the need for additional experiments in terms of further catalyst optimization. The project was continued in Mülheim with the incorporation of artificial intelligence in the overall high-throughput workflow.[60] Descriptor concepts, as for example practiced in QSAR-based drug design, had not been transferred to solids. Therefore, the Schüth group developed descriptors for heterogeneous catalysts, a process which enables, inter alia, virtual screening of solids. Thus, "catalytic intuition" can be taught to a computer.[60] By the mid-2000s, methodology development had reached a fairly mature stage and was therefore phased out in the Institute, the technology subsequently being used and subjected to further optimization by companies such as hte GmbH. It is routinely used in the Schüth group for supporting catalysis research.

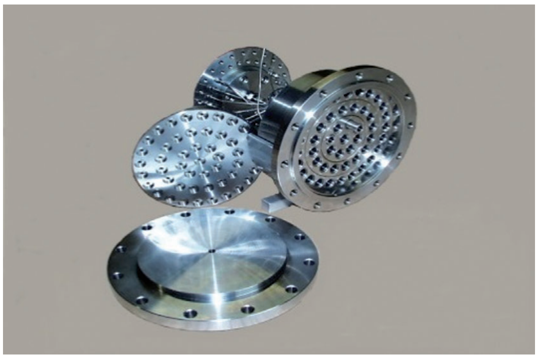


Figure 9. Parallel reactor technology developed by the Schüth group featuring a parallel channel high-throughput reactor with a pressure rating of 50 bar used for methanol synthesis.[59]

A fruitful collaboration between the Schüth group and Boris Bogdanović was initiated in the area of hydrogen storage. At the time the Bogdanović system of Ti-doped $NaAlH_4$ was the most efficient H_2 storage system known,[61] and it has continued to inspire research involving other materials as well. The presence of small amounts of doped titanium ensures reversibility [Eq. (2)], but owing to a lack of

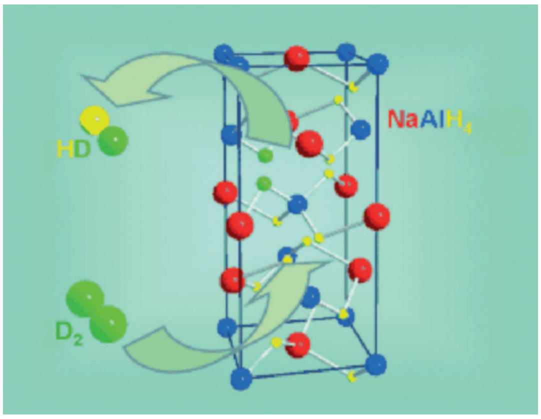
$$NaAlH_4 \xrightleftharpoons[\text{1st step}]{\text{cat.}} {}^{1}\!/_{3}\,Na_3AlH_6 + {}^{2}\!/_{3}\,Al + H_2 \xrightleftharpoons[\text{2nd step}]{\text{cat.}} NaH + Al + {}^{1}\!/_{2}\,H_2 \qquad (2)$$

mechanistic knowledge, optimization was hampered. This was clearly a heterogeneously catalyzed reaction, albeit an unusual one, and thus the expertise of the Schüth group on heterogeneous catalysis and experience in the Bogdanović group concerning metal hydrides were combined.[62]

Using a mixture of H_2/D_2, mechanistic details were unveiled. The Ti-catalyst facilitates dissociation of hydrogen at the surface of the solid material while also accelerating diffusion in the bulk, but mass transfer is probably rate-limiting (Scheme 14).[62e] Later on it was discovered that an intermediately formed alane species is the most probable transport species for aluminum.[62f]

The most important line of research in the Department of Heterogeneous Catalysis in the early 2000s was the synthesis, characterization, and application of ordered mesoporous materials. Inspired by the technique of hard templating introduced by Ryoo in 1999,[63] the Schüth group developed the process of "repeated hard templating".[64] It is an ingenious synthetic method which allows true nanocasting processes leading to a positive replica material. In the original publication, SBA-15 was employed as the starting material, nanocasting first providing its negative CMK-3, which was then used to produce another nanocast by impregnation with $Si(OEt)_4$ and condensation followed by calcination to remove the carbon.[64a] In this way, the ordered mesoporous silicate NCS-1 was formed (Scheme 15). With an advanced high-resolution scanning electron microscope acquired in 2007, imaging of the complex pore systems of ordered mesoporous materials was possible at a quality not reached before.[64e]

The nanocasting and repeated nanocasting technique has since been used to produce many other ordered mesoporous materials. The general concept can also be applied to other



Scheme 14. The Schüth–Bogdanović mechanism of reversible hydrogen storage in Ti-doped NaAlH$_4$.[62e]

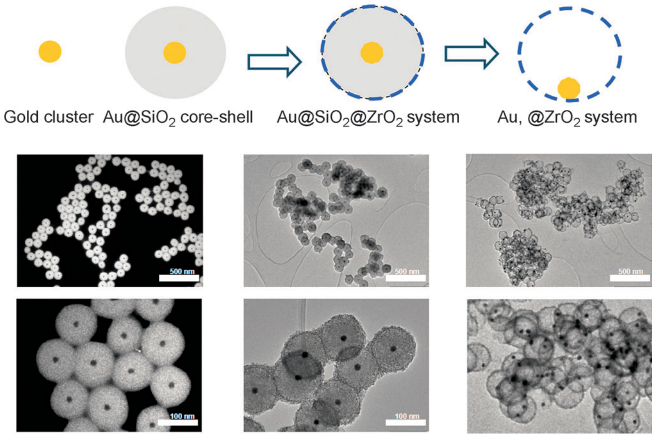


Figure 10. Top: General synthetic method for encapsulating gold particles in hollow zirconia shells. Bottom: TEM images of the gold materials.[65e] Scale bars: top row: 500 nm; bottom row: 100 nm.

Scheme 15. Schüth process of repeated hard templating.[64]

chemical systems, for example, carbon materials with controlled porosity[64b] as well as different kinds of oxides.[64c] For example, Co_3O_4 proved to have unusual magnetic properties; the three-dimensional magnetic heterostructures having features produced by modifying Co_3O_4 with another metal oxide allow fine-tuning of the magnetic properties.[64c]

In more recent years, research focusing on the design of catalysts based on ordered mesoporous materials and other types of supports for catalysts was intensified. The targeted placement of catalytic functionality at desired locations in solid materials was defined as the primary goal. It started with the work of An-Hui Lu, at that time a post-doc in the Schüth group, later on promoted to group leader in the Department, on the controlled placement of magnetic nanoparticles on the outer surface of an ordered mesoporous carbon,[65a] relying on the synthesis of cobalt nanoparticles by the Bönnemann group. In other cases, such designed catalysts were synthesized from ordered mesoporous carbon, in the pores of which iron oxide particles as catalyst for ammonia decomposition were placed,[65b] or micro-mesoporous silica containing Pd-particles in the micropores for selective alcohol oxidation.[65c] Still other efforts concentrated on colloidal deposition of gold particles. By this method, the influence of the support material on the activity in CO oxidation could convincingly be demonstrated. Although the same gold colloids and the identical loading were used, the light-off temperatures differed by more than 100 K for different support materials![65d] The synthetic methods were expanded by hollow-sphere encapsulation for the production of sinter-resistant catalysts (Figure 10).[65e]

With research focus moving more towards catalytic reactions in the second half of the 2000s, the nature of the types of transformations studied also changed. Reactions with relevance to energy conversion moved more and more into the center of the attention. The design principles using nanocasting and controlled placement of catalysts were extended to the production of active, but more importantly highly stable fuel cell catalysts. They were based on hollow graphitic carbon shells and platinum nanoparticles embedded by the confining mesopores in the carbon shells.[66] Bringing the controlled environment of a solid catalytic site to the extreme, it was possible to create a solid version of the Periana catalyst for the transfer oxidation of methane with SO_3.[67] This catalyst is stable and recyclable, and by now systems have been developed which are even more active than the original Periana complex.

Among the fundamentally new lines of research in the Department of Heterogeneous Catalysis are the activities on biomass conversion reactions which are currently being pursued by the groups of Ferdi Schüth and Roberto Rinaldi (established in 2009). The work encompasses studies of the depolymerization of native biomass, conversion of intermediates produced from this, and selective reactions of platform molecules. Depolymerization of the lignocellulosic biopolymers, which is by far the most abundant type of biomass on earth, was addressed by two unconventional approaches. One of them is acid-catalyzed depolymerization in ionic liquids.[68a] As it now appears, the second concept based on mechanocatalytic depolymerization is more promising, resulting in low-molecular-weight and fully water-soluble oligomers.[68b] These oligomers are highly interesting feedstocks for further conversion, for instance, to sugar alcohols[68c] or to 5-hydroxymethylfurfural.[68d] For the latter compound, most recently a selective high-yield process for the conversion to 2,5-dimethylfuran, an interesting alternative fuel, was discovered.[68e] It employs a Pt/Co bimetallic catalyst on a special carbon support. These reactions rely on the conversion of the cellulose fraction of lignocellulose, while the lignin fraction is much more difficult to process. Here the Rinaldi group has made important inroads in the hydrogenation of biooils to cylcohexanol and alkylphenols under low severity conditions or to low boiling arenes, which could prove to be valuable for the production of useful chemicals from the lignin fraction of lignocellulose.[69] Interestingly, this research is close to the original mission of the Institute, coal research, as related methods may prove to be suitable for the hydrogenation of coal.

8. Walter Thiel as Director of the Department of Theory

The Department of Theory was established in 1999 with the appointment of Walter Thiel (born 1949) as its first Director. Thiel obtained his doctoral degree in 1973 under the guidance of Armin Schweig at Marburg University working in the area of photoelectron spectroscopy, on the theory of photoelectron intensities and photoionization cross sections. He became internationally well-known early on in his career through his postdoctoral work (1973–1975) in the group of Michael J. S. Dewar, where he developed the MNDO method,[70a] a semi-empirical approach that served as one of the major workhorses of computational chemistry in the 1980s and 1990s. After his Habilitation in Marburg, he became associate professor at the University of Wuppertal (1983–1992). Prior to his move to Mülheim, he was full professor at the University of Zürich (1992–1999), where he pursued a broad research program in theoretical and computational chemistry. While only a few of his projects involved organometallic compounds and (bio)catalysts at that time, Thiel was viewed as the ideal person for the new position in Mülheim owing to his high reputation and the prospects of fruitful scientific interactions with the other Departments of the Institute. Thiel is associated with the Heinrich-Heine-Universität in nearby Düsseldorf.

The central research objectives of the Theory Department over the last 15 years have been theoretical developments that extend the scope of computational methodology, particularly for large molecules, and the application of theoretical methods to study specific chemical problems, mostly in the field of catalysis and in close cooperation with experimental partners. The research activities of the Thiel group cover four areas:

- Ab initio methods, rotation–vibration and electronic spectroscopy of small molecules;
- Density functional theory (DFT), transition-metal-catalyzed and organocatalytic reactions;
- Semiempirical methods, photoinduced processes and excited-state dynamics;
- Quantum mechanics/molecular mechanics (QM/MM) methods, biocatalysis by enzymes

Research thus ranges from highly accurate calculations on small molecules to the approximate modelling of very complex systems with thousands of atoms. The following survey summarizes selected developments as well as some applications in catalysis. Thiel has also written an Essay in the present issue of this journal highlighting the past, present, and future of computational chemistry in catalysis.[70b]

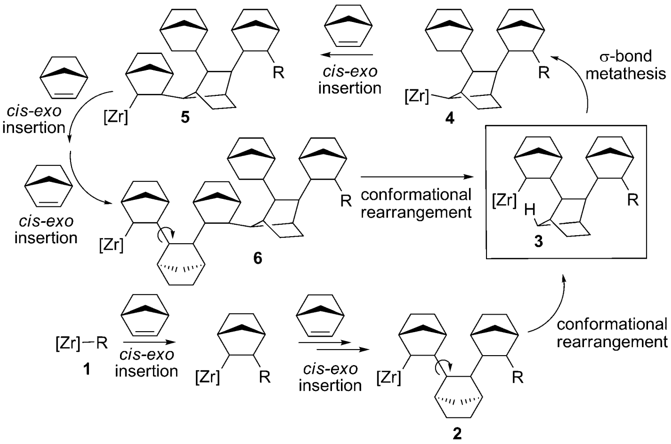
8.1. Ab Initio Methods

The theoretical prediction of vibration–rotation spectra requires the generation of accurate potential energy and dipole moment surfaces, followed by the variational calculation of rovibrational energies and intensities. For the latter task, the Thiel group developed and coded a variational treatment of nuclear motion that is based on the Hougen–Bunker–Johns approach with an Eckart-frame kinetic energy operator and thus also handles large amplitude motion.[71a] The resulting general TROVE program[71b] was applied to several small molecules, such as ammonia[71c] and thioformaldyde,[71d] using potential energy surfaces obtained from coupled-cluster theory with complete basis set extrapolation and corrections for core–valence correlation and relativistic effects. One objective of these studies was to predict comprehensive and accurate rovibrational line lists that are useful as a guide for laboratory assignments of high-resolution spectra and for astrophysical research on exoplanets. As an example, the recently published line list for thioformaldehyde ($^1H_2C{=}S$) covered all rovibrational transitions that involve states up to 5000 cm^{-1} and rotational quantum number $J = 30$ (547 926 transitions between 41 809 energy levels).[71d] The research on electronic spectroscopy includes thorough benchmarks for organic chromophores that were widely adopted.[72]

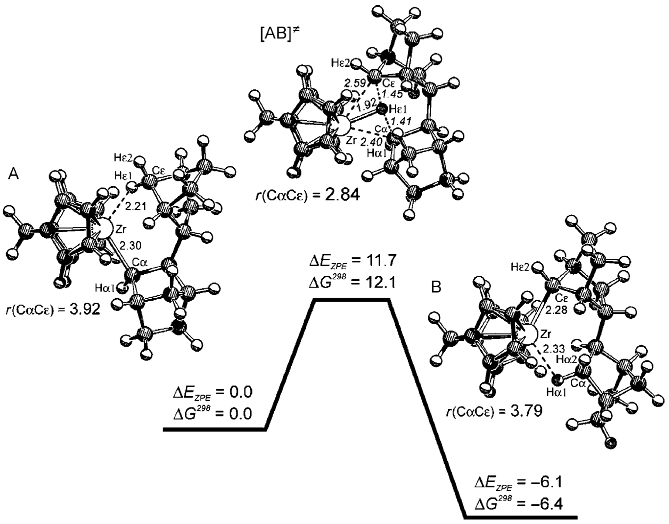
8.2. Density Functional Theory

In the spirit of fruitful collaborations in catalysis, the DFT-based computational research in the Thiel group is mostly driven by projects with experimental groups in the Institute. The aim of the DFT calculations is to elucidate the mechanism of catalytic reactions by identifying all transition states and intermediates in the catalytic cycle and to understand the electronic structure of all species involved. Such insights have often guided further experimental work. Early collaborative work addressed Rh-catalyzed asymmetric hydrogenation (Reetz),[73] Pd-catalyzed cross-coupling (Gooßen),[74] and alkene polymerization (Fink, Jolly).[75] More recent collaborative projects covered organocatalysis (List),[76] gold catalysis (Fürstner),[52] palladium catalysis (Maulide),[77] platinum catalysis (Alcarazo),[78] and cellulose depolymerization (Rinaldi).[79] These and other joint studies confirmed that DFT calculations are capable of providing detailed insight into the mechanism of catalytic reactions, which is complementary to what can be learnt experimentally and is thus essential for a comprehensive understanding of catalysis. Only one of the early joint studies is briefly featured here.[75a]

The hydrooligomerization of norbornene with the unexpected formation of 2-exo,7′-syn linkages catalyzed by *rac*-[iPr(Ind)$_2$ZrCl$_2$]/MAO (Ind = indenyl; MAO = methylalumoxane) was the subject of this mechanistic and theoretical investigation (Scheme 16).[75a] NMR and X-ray studies had proven the proposed structure unequivocally, but the mechanism was unclear. It was speculated that olefin insertion and σ-bond metathesis could be involved. DFT calculations



Scheme 16. Mechanistic proposal for the hydrooligomerization of norbornene leading only to *meso*-linkages. R = polymer, CH_3, or H; [Zr] = *rac*-$[i\text{Pr(Ind)}_2\text{Zr}]^+$.[75a]



Scheme 17. DFT-computed reaction pathway of zirconium-catalyzed hydrooligomerization of norbornene.[75a] A: ε-agostic reactant; $[AB]^{\#}$ = transition state of σ-bond metathesis; B: product.

corroborated this intriguing conjecture and showed the importance of agostic interactions (Scheme 17).

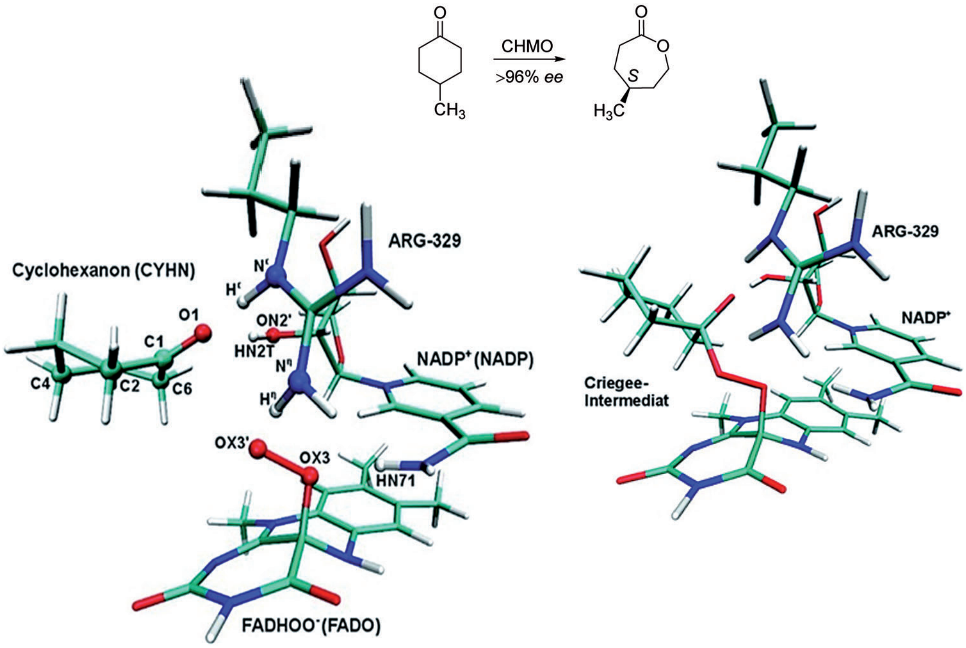
8.3. Semiempirical Methods

A long-term project in the Thiel group is the development of improved semiempirical quantum-chemical methods that can be employed to study ever larger molecules with useful accuracy, accompanied by the generation of more efficient algorithms and computer programs. Major advances in this area were the development and validation of orthogonalization-corrected semiempirical methods (orthogonalization models OM1, OM2, and OM3) that go beyond the standard MNDO model and offer enhanced accuracy,[80] the implementation of a general multi-reference configuration interaction (MRCI) treatment with analytic derivatives,[81] the implementation of the trajectory surface hopping (TSH) approach for excited-state dynamics,[82] and the port of the code to a hybrid CPU/GPU platform with graphics processing units (GPUs) that enabled a speedup of standard semiempirical calculations typically by a factor of ten.[83]

Early semiempirical applications by the Thiel group dealt with ground-state QM/MM molecular dynamics (MD) simulations of enzymes to evaluate free energy profiles, but more recently the major focus was on TSH studies of excited-state dynamics in medium-size organic molecules at the OM2/MRCI level. Such TSH simulations provided insight, for example, into the chiral pathways and mode-specific tuning of photoisomerization in azobenzenes,[84a] the mechanism of fluorene-based photoinduced molecular rotors,[84b] the complete photochemical cycle of a GFP chromophore with ultrafast excited-state proton transfer,[84c] and the competition between concerted and stepwise mechanisms in the ultrafast photoinduced Wolff rearrangement.[84d] The photodynamics of DNA nucleobases were simulated in the gas phase, in aqueous solution, and in solvated DNA single- and double-strand models; the radiationless decay was found to be slowed down by about one order of magnitude in the DNA environment, with the preference between different decay channels being regulated by hydrogen bonding in the DNA double strand.[85] In these and other studies, the TSH simulations often detected pathways and preferences between pathways that were not obvious from static calculations. The OM2/MRCI approach has thus been established as a valuable method for investigating the excited states and the photochemistry of large molecules.

8.4. QM/MM Methods

Multiscale models for complex chemical systems describe different parts of the overall system by different methods. For example, QM/MM approaches treat the active site of an enzyme at an accurate and computationally demanding QM level, and the protein environment at a less accurate and less demanding force-field MM level. As summarized in comprehensive reviews, the Thiel group contributed to the development of QM/MM methods in many essential aspects (embedding schemes, boundary treatments, optimization and simulation techniques, free energy calculations, standard procedures)[86a,b] and participated in the development of the ChemShell QM/MM software that has been adopted by many groups worldwide.[87] Recent methodological work addressed the extension to a three-layer QM/MM/continuum scheme with the use of boundary potentials.[88] Most of the QM/MM applications by the Thiel group focused on biocatalysis and aimed at the detailed mechanistic understanding of enzymatic reactions. Early work on cytochrome P450 characterized the electronic structure of the reactive intermediate, Compound I, in the native protein environment[89a] and elucidated the mechanism of hydroxylation in P450cam involving two-state reactivity,[89b] while later QM/MM studies covered the whole catalytic cycle of P450cam including all intermediates.[90] For illustrative purposes, one of the projects is highlighted here.



Scheme 18. Illustrations from the QM/MM study of the Baeyer–Villiger reaction of cyclohexanone and 4-methylcyclohexanone (top) catalyzed by the Baeyer–Villiger monooxygenase CHMO.[92a] Bottom left: Energetically most favorable pose of cyclohexanone in the binding pocket of CHMO in close proximity of the attacking nucleophilic flavin peroxide; Bottom right: Criegee intermediate showing that only one of the migrating methylene groups exhibits the electronically required anti-periplanar geometry of the respective C-C-O-O unit.

In an early collaboration with my own group, the origin of enantioselectivity in the hydrolytic kinetic resolution of a chiral ester catalyzed by lipase mutants generated by directed evolution was nicely uncovered.[91] In a more recent joint project in enzyme catalysis, the desymmetrization of 4-substituted cyclohexanone derivatives catalyzed by the Baeyer–Villiger monooxygenase CHMO was likewise studied by QM/MM.[92a] The computations showed for the first time that substrates such as cyclohexanone itself or 4-methylcyclohexanone are trapped and positioned in the binding pocket of CHMO in the chair conformation in a way that nucleophilic addition of the flavin peroxide (Fl-OO$^-$) to the carbonyl function occurs smoothly with intermediate formation of the respective Criegee intermediate.[92a] Subsequently only one of the flanking stereotopic methylene groups migrates, this being due to the well-known stereoelectronic effect of an anti-periplanar arrangement of the C-C-O-O atoms. As 4-methylcyclohexanone can exist in two different chair forms (methyl equatorial or axial), the origin and degree of enantioselectivity was traced to the known difference in energy of the two conformers in the rate-limiting transition state. As a result, the (*S*)-enantiomer of the lactone is formed preferentially (Scheme 18).[92a] This scenario offered qualitative explanations for changes in stereoselectivity induced by directed evolution of CHMO as a catalyst in the desymmetrization of 4-hydroxycyclohexanone.[92b] Theoretical analyses of this kind shed light on the intricacies of enzyme catalysis, while also providing a guide for devising new directed evolution experiments.

In a similar vein, the Thiel group has clarified the mechanism of more than 20 other enzymatic reactions through QM/MM calculations. The methodological advances and the successful applications by the Thiel group have helped to establish QM/MM approaches, as originally initiated by Martin Karplus, Michael Levitt and Arieh Warshel more than 35 years ago, as a standard computational tool for investigating complex chemical processes, including biocatalysis by enzymes.

8.5. Research in Other Groups of the Theory Department

Michael Bühl was a junior group leader for several years (1999–2007) before moving to the University of St. Andrews to become a full professor. He performed computational studies on transition metal compounds, focusing on the calculation of NMR spectra and on homogeneous catalysis. Klaus Angermund was responsible for the molecular modeling service (1999–2007); in his research, he was mainly interested in the mechanism and stereochemistry of alkene polymerization. Mario Barbatti (since 2010) has developed methods for ab initio excited-state dynamics simulations in the framework of his Newton-X code and applied them in studies of ultrafast photoinduced processes in biologically relevant molecules and in molecular photo-triggers. Elsa Sánchez-García (since 2010) has focused on molecular interactions in organic and biological systems, especially on the influence of ligands on protein function, on the interaction of proteins with their environment, and on designed mutagenesis for the regulation of enzymatic activity.

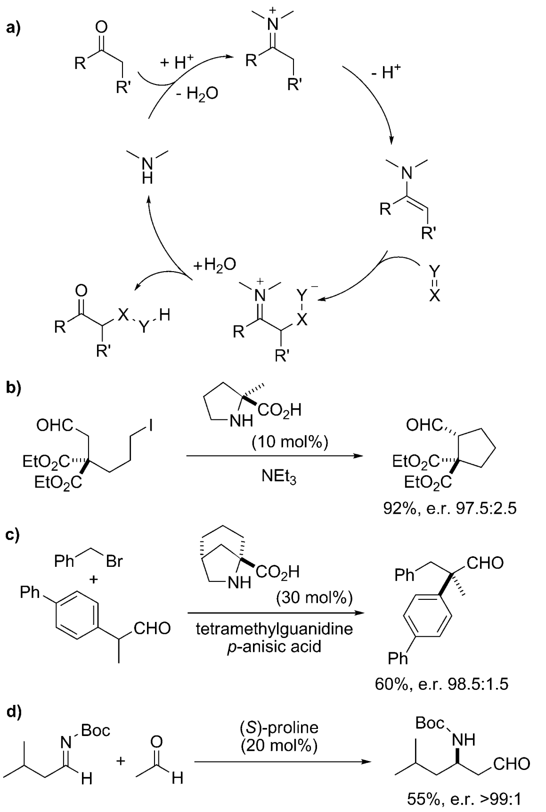
9. Benjamin List as Director of the Department of Homogeneous Catalysis

Benjamin List (born 1968) obtained his doctoral degree in organic chemistry in 1997 at Johann Wolfgang Goethe-Universität in Frankfurt under the guidance of Johann Mulzer before joining the group of Richard Lerner at the Scripps Institute in La Jolla/USA working in the area of catalytic antibodies. Rather than returning to Germany for a Habilitation, he preferred to stay at Scripps in the position of a tenure-track assistant professor. In 2000 he published a seminal paper on highly enantioselective proline-catalyzed intermolecular aldol reactions,[93a] which opened the door to numerous other types of enamine-based asymmetric transformations.[93b] By 2003 his contributions had attracted the attention of the MPI directors in Mülheim, who made him an offer to join them, first as an independent group leader, but with the possible prospect of being promoted at a later date to the position of the Director of the Department of Homogeneous Catalysis. List accepted, moved to Mülheim in 2003, and following the usual MPG hiring procedure was appointed Director in 2005. This rapid promotion was based on continued seminal research in "enamine catalysis" using proline and other amines. Since coming to Mülheim, he has been associated with the University of Cologne.

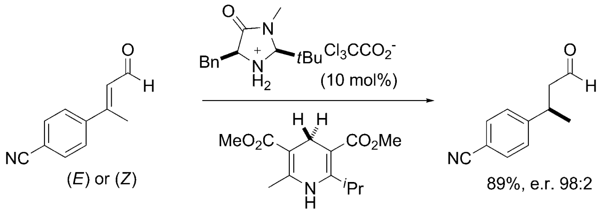
Enamine catalysis has continued as one of the pillars of List's research. The activation principle is based on the formation of an iminium ion, which is readily deprotonated to the corresponding enamine, which in turn undergoes nucleophilic addition reactions to unsaturated compounds X=Y, such as aldehydes, imines, diazo compounds, or Michael acceptors (Scheme 19 a).[93,94]

A breakthrough in enamine catalysis was the development of the first asymmetric intramolecular aldehyde α alkylation using (*S*)-α-methyl proline as catalyst (Scheme 19 b).[94] This type of catalytic substitution reaction was unknown at the time and inspired other groups in joining the effort to generalize it. Nevertheless, the challenging problem of asymmetric intermolecular α-alkylation by enamine catalysis was not solved until a decade later by the List group (Scheme 19 c).[95a] Other achievements in enamine catalysis in Mülheim include exceptionally enantioselective Mannich reactions of acetaldehyde with aromatic and aliphatic N-Boc-imines using (*S*)-proline as catalyst, yielding synthetically useful β-amino aldehydes (Scheme 19 d).[95b]

Another advancement was the development of a metal-free catalytic transfer hydrogenation of α,β-unsaturated aldehydes using the Hantzsch ester as the hydride source and simple protonated amines, such as $[Bn_2NH_2]^+[CF_3CO_2]^-$ as catalysts.[96a] Shortly thereafter a highly enantioselective and diastereoconvergent version of the method using a MacMillan-type catalyst was reported by the List group[96b] (Scheme 20) and independently by MacMillan and co-workers.[97]



Scheme 19. Enamine catalysis.[93,94] a) Catalytic cycle of nucleophilic addition reactions. b) Intramolecular α-alkylation of aldehydes. c) Intermolecular α-alkylation of aldehydes. d) Proline-catalyzed Mannich reactions of aldehydes.

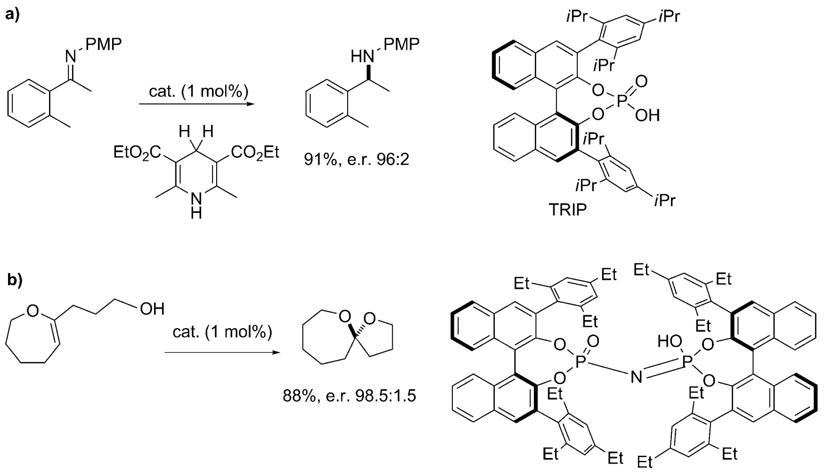


Scheme 20. Metal-free asymmetric transfer hydrogenation of α,β-unsaturated aldehydes.[96b] Bn = benzyl.

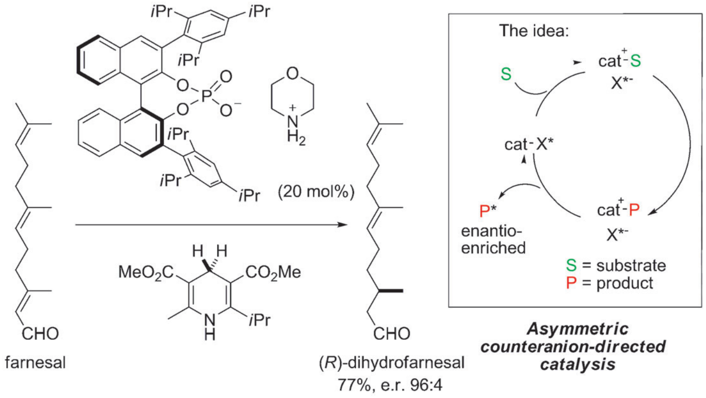
As a spin-off from the research involving proline catalysis, the List group turned to asymmetric Brønsted acid catalysis. BINOL-based phosphoric acids as pioneered by Akiyama[98a] and Terada[98b] were already known for their usefulness in organocatalysis. In this context, the sterically demanding and yet highly active version, TRIP, 3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogenphosphate, was introduced by the List group for asymmetric ketimine reductions and reductive aminations (Scheme 21 a).[99]

Confined Brønsted acids based on a C_2-symmetric imidodiphosphoric acid motif and possessing an extremely sterically demanding chiral microenvironment with a single catalytically relevant and geometrically constrained bifunctional active site enabled a catalytic enantioselective spiroacetalization reaction with excellent enantiomeric ratios (Scheme 21 b).[100a] This catalyst class was also used in asymmetric sulfoxidation and in asymmetric acetalization of aldehydes.[100b,c]

Combining and further promoting Brønsted acid catalysis and aminocatalysis led to the new concept of asymmetric



Scheme 21. a) Asymmetric transfer hydrogenation of ketimines using the TRIP catalyst (top right),[99] PMP = *p*-methoxyphenyl. b) Asymmetric spiroacetalization using a confined Bronsted acid (bottom right).[100a]



Scheme 22. Left: Example of asymmetric counteranion-mediated organocatalytic transfer hydrogenation of an α,β-unsaturated aldehyde;[102] right: mechanism of an ACDC catalysis cycle.

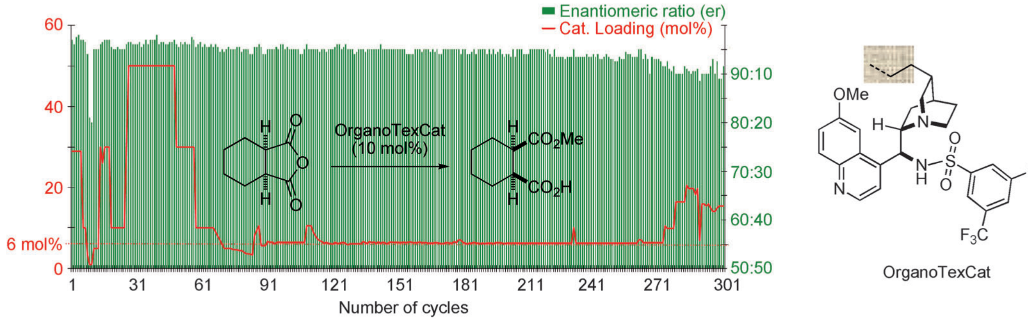
counteranion-directed catalysis (ACDC) that the List group has developed and used to design highly enantioselective reactions in the areas of organocatalysis, transition-metal catalysis and Lewis acid catalysis.[101] The first example of ACDC with high enantioselectivity was an organocatalytic transfer hydrogenation of α,β-unsaturated aldehydes using an achiral ammonium ion and a chiral phosphate anion catalyst ion pair (Scheme 22).[102]

In other work, chiral cyclic disulfonimide catalysts were designed and implemented as pre-Lewis acid catalysts in enantioselective Mukaiyama aldol, hetero-Diels–Alder, Mukaiyama–Mannich, and Hosomi–Sakurai reactions as well as 3-component aminoallylations.[103] Most recently the List group succeeded in making organocatalysts available for potential industrial use by immobilizing them on textiles.[104] A facile and straightforward methodology for the immobilization of catalysts on nylon using ultraviolet light was developed resulting in organotextile catalysts displaying excellent stability, activity, and recyclability for various organic transformations. Very good enantioselectivity can be maintained for more than 250 cycles of asymmetric catalysis (Scheme 23).

Two independent groups are also active in the Department of Homogeneous Catalysis: Martin Klußmann working on oxidative coupling reactions and environmentally benign metal catalysis, and Klaus R. Pörschke, the last researcher from the Wilke era, studying novel late-transition-metal complexes, cisplatin-related metal complexes, and plastic crystals. Most recently the junior group leader Nuno Maulide, active in such areas as catalytic asymmetric syntheses of small rings, new ylide transfer methods, and C–H activation, left Mülheim to accept a chair for organic chemistry at the University of Vienna.

10. Support of Young Career Scientists

As already alluded to, the Institute makes great efforts in identifying and supporting young career scientists. Table 1 lists the group leaders that have left the Institute since 2000 to accept academic positions elsewhere in Germany or abroad. Furthermore, many of the Mülheim postdocs obtained academic positions as well.



Scheme 23. Recycling of the OrganoTexCat in a desymmetrization reaction for over 300 cycles.[104]

Table 1: Group leaders who have left the MPI to accept an academic position elsewhere (some of whom have since filled other positions).

Name	Year	University
W. F. Maier	2000	University of Saarbrücken, Germany
W. Leitner	2002	RWTH Aachen, Germany
G. Veser	2002	University of Pittsburgh, USA
F. Glorius	2004	University of Marburg (then Münster U.), Germany
L. Gooßen	2004	University of Kaiserslautern, Germany
S. Kaskel	2004	Technical University Dresden, Germany
D. Belder	2005	Regensburg University (then Leipzig U.), Germany
S. Hecht	2006	Humboldt University Berlin, Germany
M. Bühl	2007	University of St. Andrews, UK
C. Nevado	2007	University of Zürich, Switzerland
A. H. Lu	2009	Dalian University, China
R. Palkovits	2010	RWTH Aachen, Germany
N. Maulide	2013	University of Vienna, Austria

11. Summary and Future Prospects

The last two decades have witnessed sweeping changes in the organizational form of the Max-Planck-Institut für Kohlenforschung coupled with the establishment of new research directions headed by five Directors. The new era is characterized by research encompassing all essential types of catalysis and their applications under one roof. These include such diverse areas as natural-product syntheses utilizing transition-metal complexes, chiral compound preparation catalyzed by novel organocatalysts or evolved enzymes, transformations mediated by heterogeneous catalysts,[105] reversible hydrogen storage, biomass transformation, and the synthesis of novel solid materials. The Theory Department, which is strong in method development while also engaging in collaborative efforts with the other four Departments, forms an integral part of the Institute. With the four present directors and the successor to Manfred T. Reetz soon to arrive, the Institute is well positioned for future challenges.

The Max-Planck-Institut für Kohlenforschung is not the only MPI in Mülheim. Located on the same campus, the Mülheim Chemistry Campus, is also the Max-Planck-Institute for Chemical Energy Conversion (MPI CEC). The origin of this Institute goes back to 1957, when Günther O. Schenck joined the MPI für Kohlenforschung as a Scientific Member of the Max Planck Society, heading an independent group dedicated to photochemistry. This group was later transformed into the independent Max Planck Institute for Radiation Chemistry, with a separate building adjacent to the Kohlenforschung and with Schenck as founding director. Subsequently Dietrich Schulte-Frohlinde, Oskar E. Polansky, and Kurt Schaffner joined the MPI for Radiation Chemistry as Scientific Members and Directors. In the 1990s, the research focus of this Institute shifted towards bioinorganic chemistry with the appointment of Karl Wieghardt in 1994 (emeritus since 2010) and Wolfgang Lubitz in 2000, leading to the change in its name to Max Planck Institute for Bioinorganic Chemistry.

Most recently, the direction of this Institute took yet another turn to become the MPI CEC, with Robert Schlögl of the Fritz Haber Institute[4] as provisional founding Director. Together with Wolfgang Lubitz and Frank Neese, he forms the board of directors of the new MPI CEC, the mission being the exploration of the basic physical and chemical phenomena underlying chemical energy conversion processes. Four departments are planned, which means that the Mülheim Chemistry Campus will eventually feature a total of nine Directors. The re-direction of the research in the MPI CEC is enthusiastically supported by the scientific community and by the state of Nordrhein-Westfalen, which is pledging financial support for the construction of new buildings to house four departments.

It is evident that the two Max Planck Institutes on the Mülheim Chemistry Campus share some common goals. In the future, they will benefit (even more so than today) from synergies in their research infrastructures and increasing collaborative scientific efforts. This will further strengthen the Mülheim Chemistry Campus as one of the focal points of chemistry research in the Max-Planck-Society.

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[105] Throughout this Essay, I have used the terms “homogeneous catalyst” and “heterogeneous catalyst” as internationally practiced, although strictly speaking they should be replaced by “molecular catalyst” and “solid catalyst”, respectively. A process can be performed heterogeneously, but the catalytically active species may not be heterogeneous; for example, homogeneous when utilizing a metal net. I thank Ferdi Schüth for pointing this distinction out.