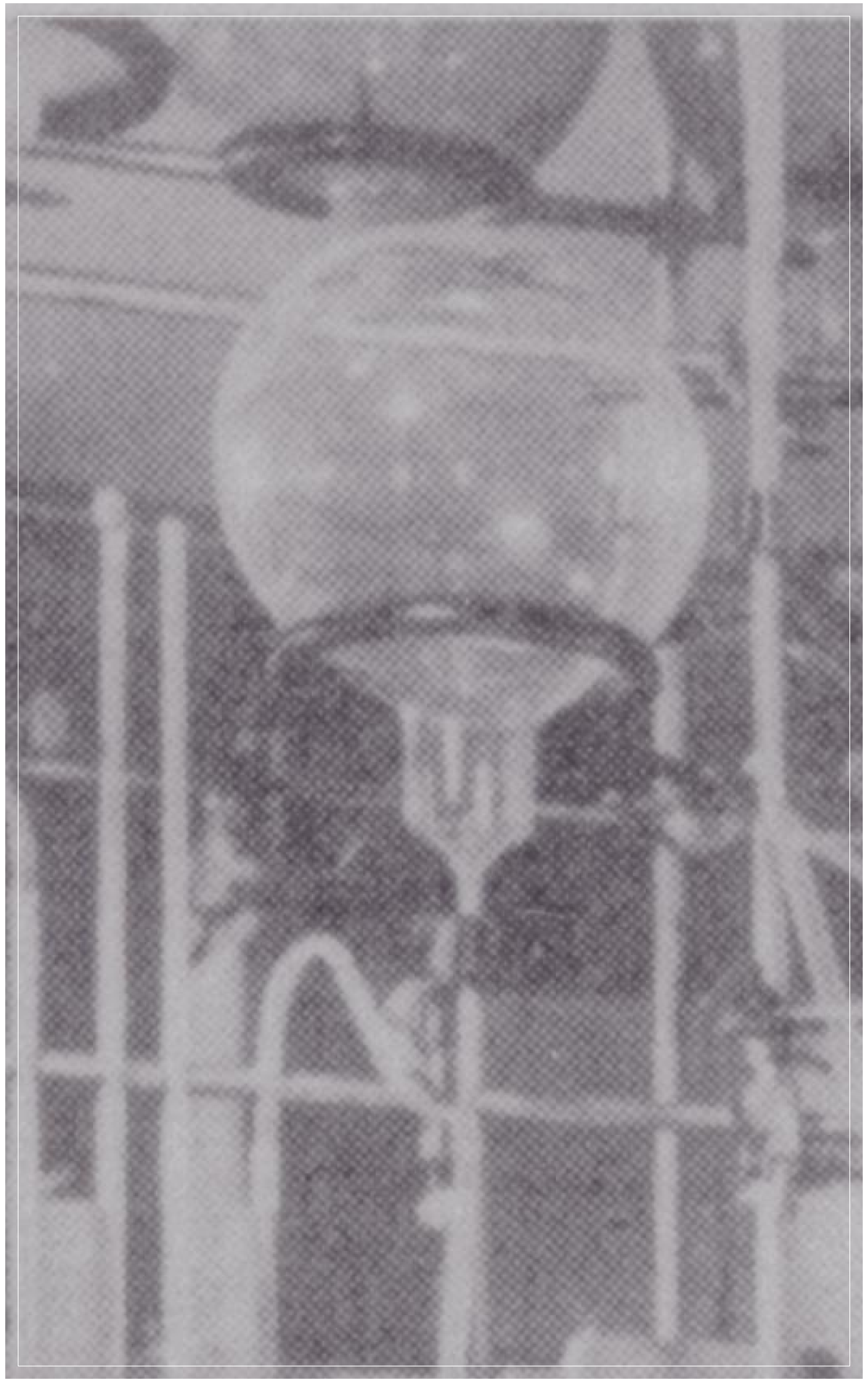


(1975 - 1999)

Chiral reactions in heterogeneous catalysis

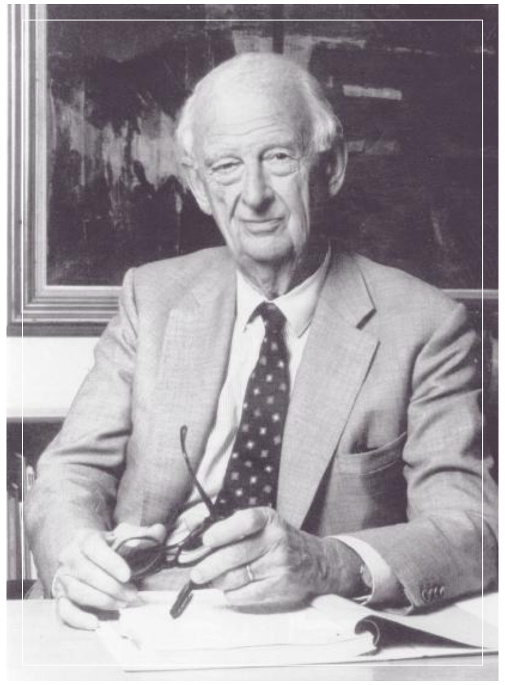
"Creativity is the endless pursuit of a seemingly unsolvable problem"

Hisao Yamada

The preparation of pure chemical compounds has been one of the most rapid growth areas in chemistry over the last decade with heterogeneous catalysis being recognised as providing new possibilities. A number of different strategies have been developed to obtain enantioselectivity through heterogeneous catalysis: the use of chiral species to modify the solid surface; the grafting of a chiral catalytic complex on a solid - the so called heterogenised homogeneous catalyst - and homogeneous formation of a chiral complex before reaction at the solid surface. Because the interaction between functional groups is complex, the influence the surface has on reaction mechanisms is, so far, not well developed.

Hydrogenation reactions have dominated the field with α- or β-ketoesters being the preferred substrates and nickel modified by tartaric acid and platinum modified by cinchona alkaloids as preferred catalytic systems with modified zeolites playing a crucial role. Some examples of the leading groups are in Switzerland (Blaser and Baiker), Japan (Nitta, Osawa, Izumi and Harada), USA (Sachtler, Augustine), United Kingdom (Webb, Wells, Thomas, Catlow, Hutchings and Whyman) and the Netherlands (Sheldon). In spite of the present hyper-activity the use of metal catalysts to effect asymmetric reactions is not new with Schwab in Germany and Lipkin and Stewart in the USA active in the 1930s. In 1995 at the ChiCat Symposium both Reisse and Ghosez suggested that those in catalysis should "not reinvent wheels that organic chemists had laboured over many years" and "that goals already achieved by organic chemists will not be easy to obtain through heterogeneous catalysis". We await future developments with much anticipation!

Heterogeneous catalysts were first used by Schwab and Lipkin and Stewart in the 1930s to facilitate asymmetric reactions. A pre-requisite for asymmetric activity is the presence of a chiral environment on the catalyst surface; there have been in the main two approaches to this, first by supporting the (metal) catalyst on a chiral support and second by the adsorption of a chiral modifier on the active phase of a conventional catalyst. Although Izumi reported enantioselective activity for the hydrogenation of β-keto esters in 1956, interest in chiral reactions increased dramatically after Orito reported in 1978 the enantioselective hydrogenation of α-ketoesters catalysed by a cinchona alkaloid modified supported platinum catalyst. Since then extensive research by Wells at Hull, Blaser at Ciba-Geigy AG, Webb in Glasgow and Baiker in Zurich has endeavoured to obtain a consistent all-embracing



Haldor Topsøe

model for the mechanism and in 1993 the First European Symposium on Chiral Reactions in Heterogeneous catalysis was held in Brussels. At this meeting there were (for example) contributions by Osawa and Harada from Japan concerning the hydrogenation of 2-butanone using a nickel catalyst modified by tartaric acid; Whyman from Liverpool of cinchona modified platinum; Ghosez from Louvain who discussed strategies for asymmetric synthesis; Reschetilowski from Germany who reported results for platinum containing zeolites; Bethell (Liverpool), Hutchings (now at Cardiff) King (Synetix) and Page (Loughborough) who established that modifying zeolite Y with chiral sulfoxides gave enhancement of both reactivity and selectivity for the dehydration of butan-2-ol to but-2-ene, and Tungler from Budapest who reviewed the use of chiral auxiliaries for producing enantiomers in excess.

The overall message from this conference was that it is not easy to distinguish between the role of a chiral additive as an auxiliary (reaction with the substrate in solution) and as a modifier (reaction with the catalyst at the surface). The hydrogenation of ethyl pyruvate is a good example of the difficulty; does the cinchonidine act as an adsorbed modifier on the surface of the platinum catalyst or as an auxiliary dissolved in the reaction mixture and interacting also with the substrate?

The Dutch group, led by Sachtler, had prior to the platinum-cinchonidine results, studied during the period 1972-1976 the enantioselective hydrogenation of methyl acetoacetate to methyl 3-hydroxybutyrate at nickel surfaces modified by tartaric and α-amino acids. Reproducible results were difficult to obtain but they proposed the perpendicular chelation of modifier molecules to nickel sites which interpreted the chiral sense of the experimentally observed enantioselectivity. The "template model" proposed by Wells in Hull was put to the test in a collaborative project making use of the surface science facilities at Cardiff. No evidence was obtained from LEED for ordered structures of dihydrocinchonidine at Pt(111) surfaces, furthermore although multilayers of the alkaloid could be adsorbed at room temperature, in the presence of ethanol only the chemisorbed monolayer was stable. The possible role of the solvent (C_2H_5OH) was also investigated; hydrocarbon species were shown to be formed readily at the atomically clean Pt(111) surface which had identical spectroscopic characteristics (XPS and UPS) to that of propene. When oxygen (= 0.1) was present at Pt(111) both hydrocarbon and oxygenated species are present. One of the most recent and significant contributions to the area of heterogeneous asymmetric catalysis is that of Gellman and Attard who drew attention to the inherent chiral characteristic of kink sites present at platinum surfaces - contrary to the view that had been previously widely held that metal surfaces were themselves non-chiral. Anchoring a chiral catalyst within the inner walls of a mesoporous support (MCM-41) and co-ordinated to a Pd^{II} centre has been shown recently by a Cambridge-Royal Institution group to exhibit a degree of regioselectivity and enantiomeric excess in the allylic animation of cinnamyl acetate far superior to that of its homogeneous counterpart. This emphasises that improvements are indeed possible through judicious use of carefully chosen materials as supports - although the scepticism of Reisse and Ghosez should also be kept in mind!

It has been estimated that within the chemicals and pharmaceutical industries the market for chiral molecules is growing at such a pace that by the year 2000 the market value will be close on $30bn with an annual growth of 25%. At present inorganic homogeneous catalysts are very much at the forefront of industrial processes aimed at inducing chirality during addition or ring opening reactions.

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