

# The Use of Platinum Metal Complexes in Asymmetric Catalysis

CONTINUING DEVELOPMENTS WILL INCREASE POTENTIAL

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*Since the original demonstrations of homogeneous organometallic catalysis under mild conditions in the 1960s there has been much progress. A central focus for development has been asymmetric synthesis, through the use of optically active ligands. Chiral chelating biphosphines have played a key role in these advances, which have led to: asymmetric hydrogenation as a route to amino-acids and Vitamin E precursors, kinetic resolution in directed hydrogenation, asymmetric isomerisation of olefins in a route to citronellol, and asymmetric catalytic C-C bond formation. This review highlights recent developments.*

The organic chemistry of the noble metals is literally unique, since it has no counterpart in biology. This means investigations have to start without the guidelines provided by enzymology, which have contributed so much to the development of synthesis. It makes asymmetric catalysis a very significant feature of noble metal chemistry, since it affords competition with natural sources for optically active materials by an approach which is completely different in concept. The current level of interest in asymmetric synthesis in both the pharmaceutical and chemical industries, for the production of optically pure drugs, agrochemicals, chiral smectic C liquid crystals and polymers of controlled helicity, gives the topic a vigorous present and a secure future.

At the moment, the most substantial contributions lie in the formation of C-H and C-C bonds. It is a curious fact that all the examples of highly effective asymmetric catalysis involve low-valent complexes of ruthenium, rhodium and palladium; the lower block platinum metals are much less important in this area of catalysis. To some extent this is because they tend to form more stable complexes, and stability is counter productive in catalysis. However, when the correct procedures are learned iridium and

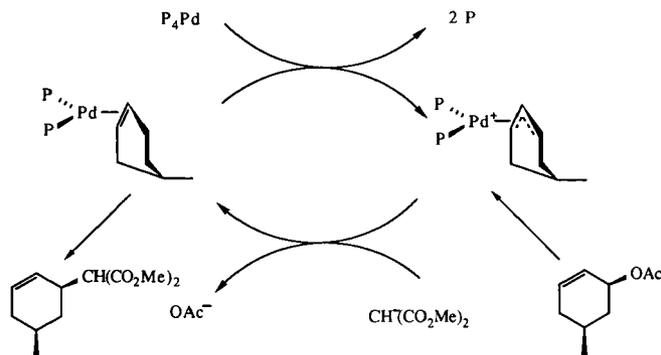
platinum complexes can be highly effective, as is demonstrated by platinum hydroformylation and iridium hydrogenation, the latter pioneered by R. H. Crabtree (1). But the application of these complexes in asymmetric catalysis is not advanced.

In the remainder of this article, the various methods for asymmetric synthesis of C-C and then C-H bonds are described. Due emphasis is given to methods providing an enantiomer excess of  $\geq 95$  per cent.

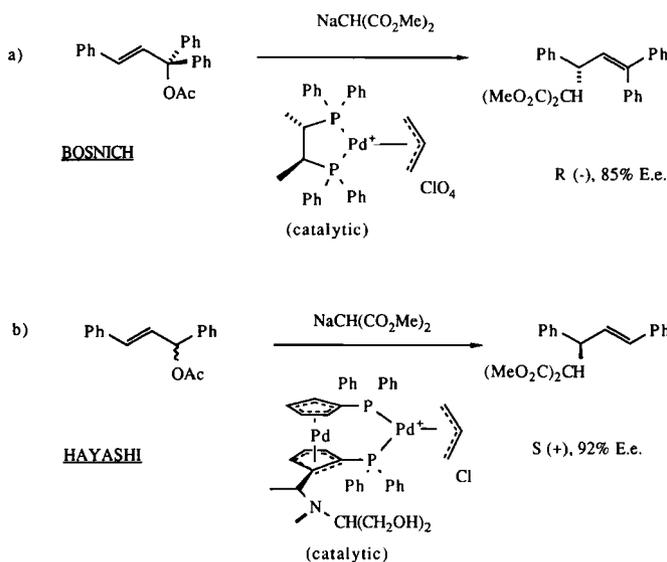
## Asymmetric Catalysis in C-C Bond Formation

Palladium chemistry is pre-eminent in catalytic C-C bond formation, as a result of its early applications in both cross-coupling reactions and allylic alkylation. The development of asymmetric synthesis in this area is much newer, with recent breakthroughs from the research group of Hayashi in Japan being pre-eminent.

Almost single-handedly, Trost made catalytic allylic alkylation part of the essential repertoire of synthetic organic chemistry (2). His reaction sequence is illustrated in Figure 1, and it should be noted that the key step involves reaction between a cationic palladium allyl and a soft nucleophile such as malonate ion. With an



**Fig. 1** Catalytic allylic alkylation; note the configurational relationship between the starting material and the product



**Fig. 2** High enantiomer excess in catalytic allylic alkylation

optically active biphosphine such as CHIRAPHOS, asymmetric synthesis can occur. Because the new bond is formed some distance from the metal and its chiral ligand, optical yields were modest in most early studies. Bosnich and co-workers found that diphenylallyl derivatives were better (Figure 2(a)) because their bulkiness elicited a stronger interaction with the ligand, so that one of the two possible intermediates was strongly favoured

(3). The best examples to date are due to Hayashi's group (4). They use a rather unusual ferrocenyl-phosphine, with a polar side-arm. This acts so as to bias the reaction towards one end of a symmetrical or near-symmetrical intermediate. Although the details are not properly understood the effect is dramatic, leading to allylic products with high optical purity, as shown in Figure 2(b).

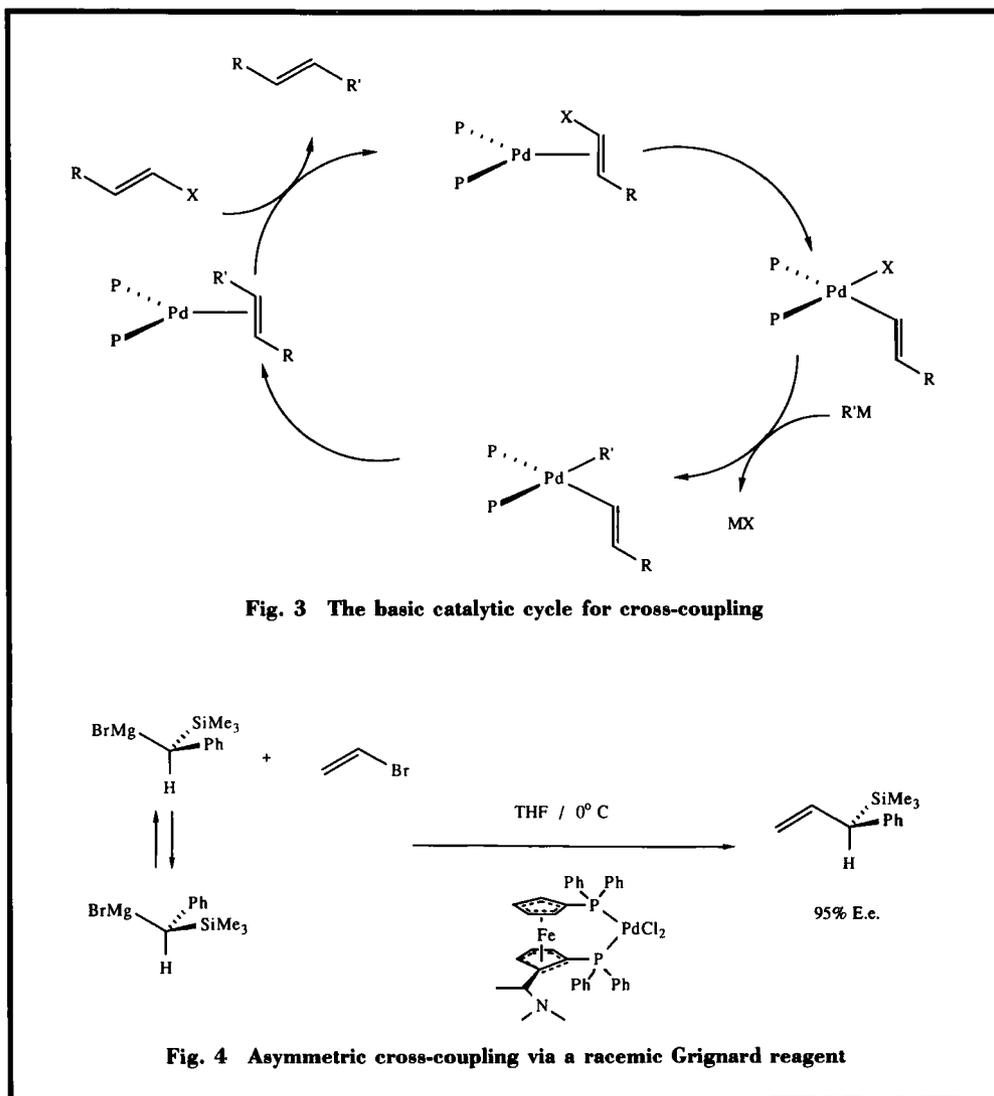
Cross-coupling is the enigma of asymmetric

catalysis. This straightforward reaction, whereby a carbon-carbon bond is assembled within the co-ordination sphere, seems a perfect arrangement for stereochemical control (5), see Figure 3. The intrinsic limitations of existing procedures, particularly incompatibility towards polar substituents, have yet to be overcome and few good examples of asymmetric synthesis with high enantiomer excess are available. Again the best work comes from Hayashi's group, and makes optically active allylsilanes available (6), as illustrated below in

Figure 4. A feature of their approach is the clever use of ferrocene as a template for designing asymmetric ligands. The allylsilanes have a well-developed organic chemistry and can be converted into many other chiral products.

### Asymmetric Catalysis in C-H Bond Formation

Wilkinson's classic work on rhodium catalysed homogeneous hydrogenation encouraged many other groups to make optically active phosphines; hydrogenation is widely utilised in



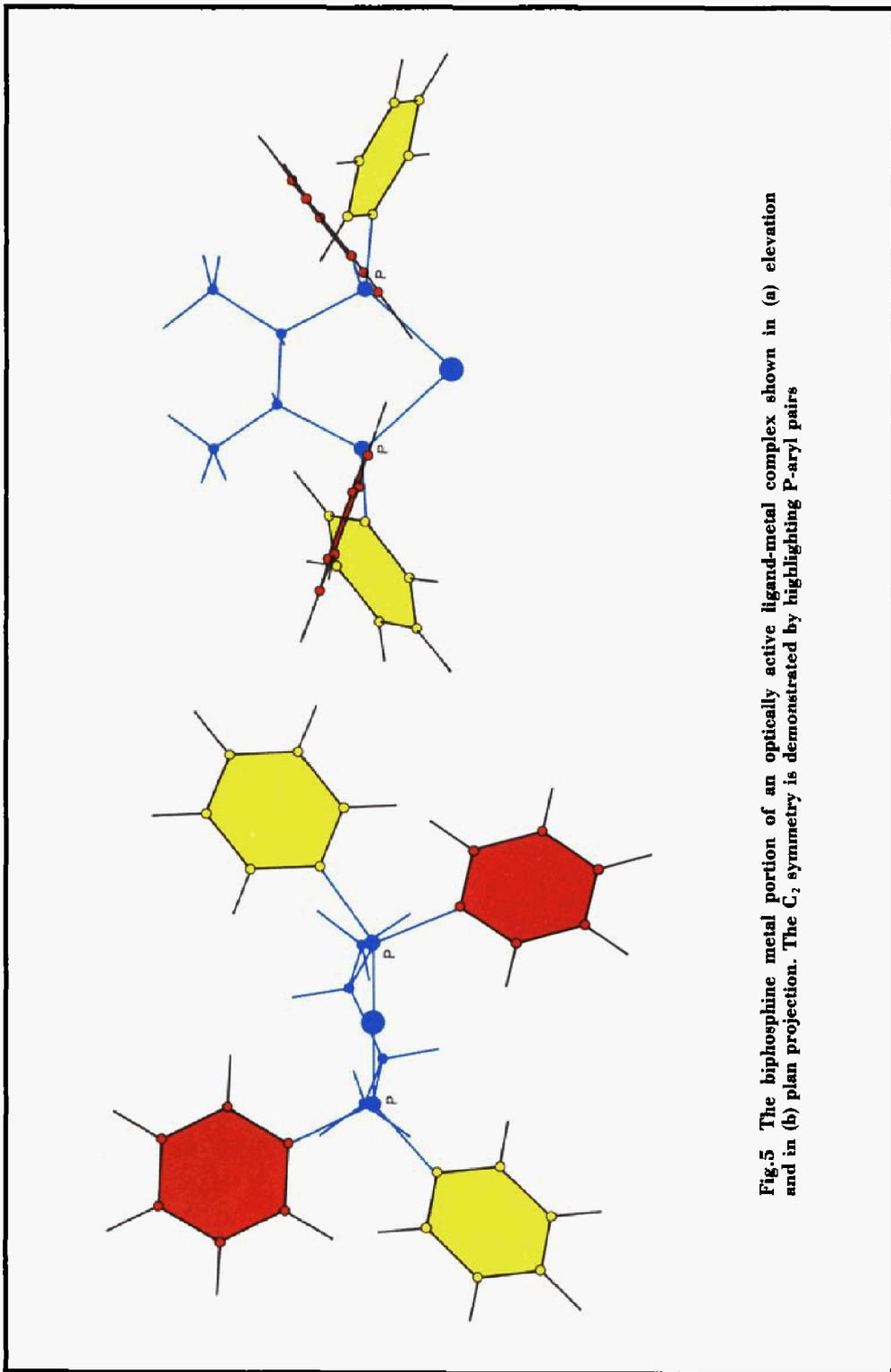
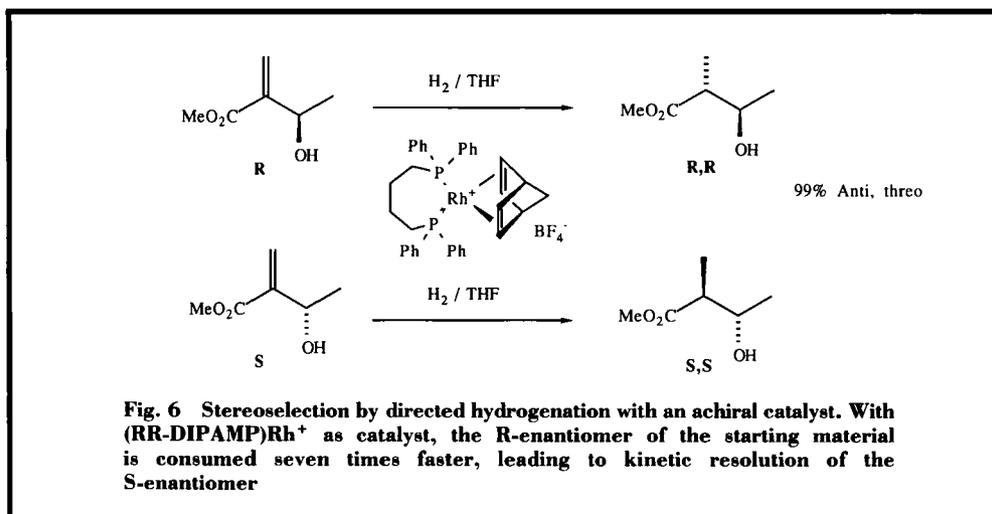


Fig.5 The biphosphine metal portion of an optically active ligand-metal complex shown in (a) elevation and in (b) plan projection. The  $C_2$  symmetry is demonstrated by highlighting P-aryl pairs



synthesis, and the potential for introducing optical activity seemed highly attractive. Progress only became rapid when Kagan showed that the important step was to employ bi-phosphines, and now there are upwards of fifty ligands which give good results in asymmetric hydrogenation (7). Application tends to be limited to dehydroamino acids and related compounds where a substituent on the olefin provided the necessary "bite" by occupying a co-ordination site throughout the catalytic cycle. The source of chiral recognition is still not fully understood, despite much effort (8), but the role of the biphosphine has been clarified by X-ray studies on a rigid biphosphine rhodium complex, see Figure 5. The asymmetric centres enforce a chiral conformation on aryl groups bound to phosphorus. This permits a discrimination between the reaction channels leading to "left-hand" and "right-hand" products because of the way that the catalytic reactant is bound to rhodium during the catalytic cycle. For dehydroamino acids, it appears that the interactions involving the  $-\text{CO}_2\text{H}$  group are the most critical. By analogy with enzymology, asymmetric hydrogenation works because this substituent operates as a key on the arylphosphine lock, but only when one prochiral face of the olefin is bound to rhodium. For the other face, there is a mismatch which

makes the addition of hydrogen energetically unfavourable.

One recent development widens the scope of asymmetric hydrogenation (9). When the olefin being reduced includes a neighbouring chiral centre there can be two possible isomeric products, depending on which face accepts hydrogen. For example, the  $\beta$ -hydroxyacrylate of Figure 6 can give rise to *syn*- and *anti*-hydrogenation products, and it turns out that the latter is strongly predominant. With a simple chelate rhodium catalyst both enantiomers of racemic starting material are reduced with equal facility; the most interesting experiment involves an optically active catalyst such as DIPAMP-Rh<sup>+</sup>. Here the reactivity of the two enantiomeric forms of starting material is quite different, and one is efficiently drained off in a fast hydrogenation. This leads to kinetic resolution of the slow reacting enantiomer. It may be recovered in 90 to 95 per cent optical purity at  $\geq 65$  per cent reaction. In similar manner,  $\beta$ -carboxyacrylates and acylaminoacrylates can be subjected to kinetic resolution. The sequence of two hydrogenation steps, one with an optically active catalyst and the second with a simple chelate rhodium catalyst leads to  $\beta$ -hydroxyesters and  $\beta$ -aminoesters or to 2,3-dialkylsuccinic acid derivatives in a state of high optical purity. This represents the first

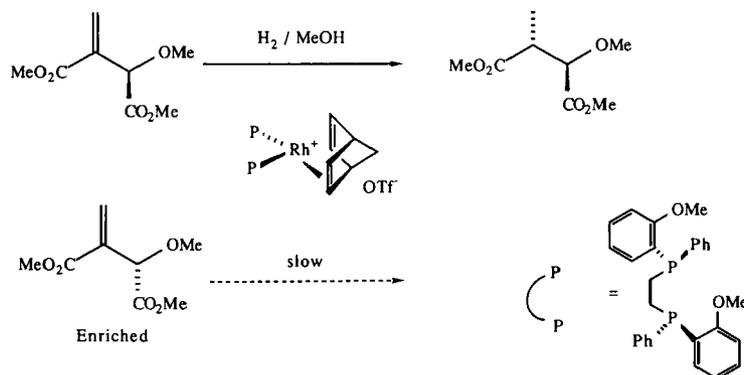


Fig. 7 Kinetic resolution of racemic itaconates

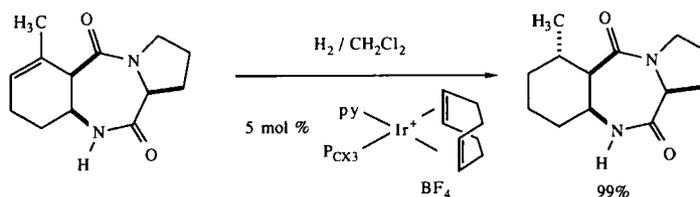
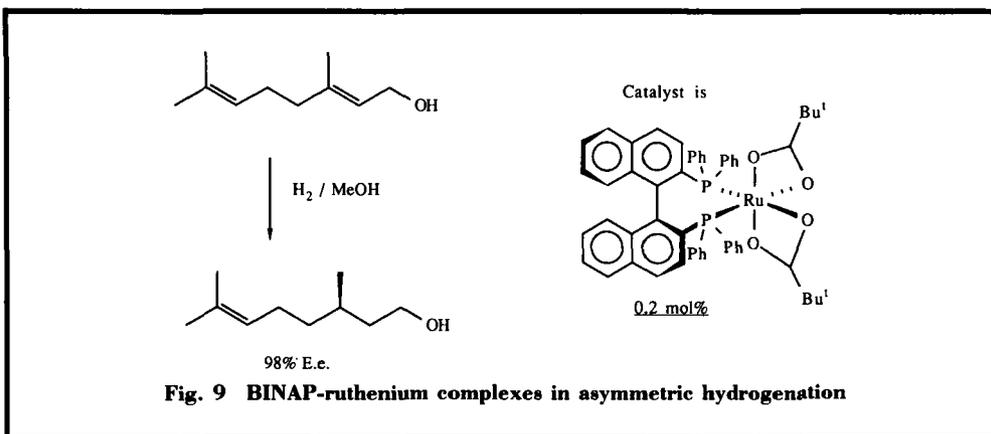


Fig. 8 Face selectivity in directed hydrogenation

case of a catalytic kinetic resolution which does not require enzymes or micro organisms, as is shown in Figure 7.

The secret of success is to find reactants possessing a functional group in proximity to the olefin which can bind to the metal and control the stereochemical course of hydrogenation. In a cyclic compound, this can lead to face-selectivity, where the functionality directs hydrogen to the double bond in a constrained way. Some of the best examples involve iridium catalysts, which work well for cyclic systems. It is of interest that the alcohol or amide group which controls reaction stereochemistry can be quite remote from the double bond undergoing hydrogenation, see Figure 8. The stereo-selectivity can exceed the limits of conventional measurement by g.c. or h.p.l.c. techniques, and product discrimination of >1000:1 has been reported (9).

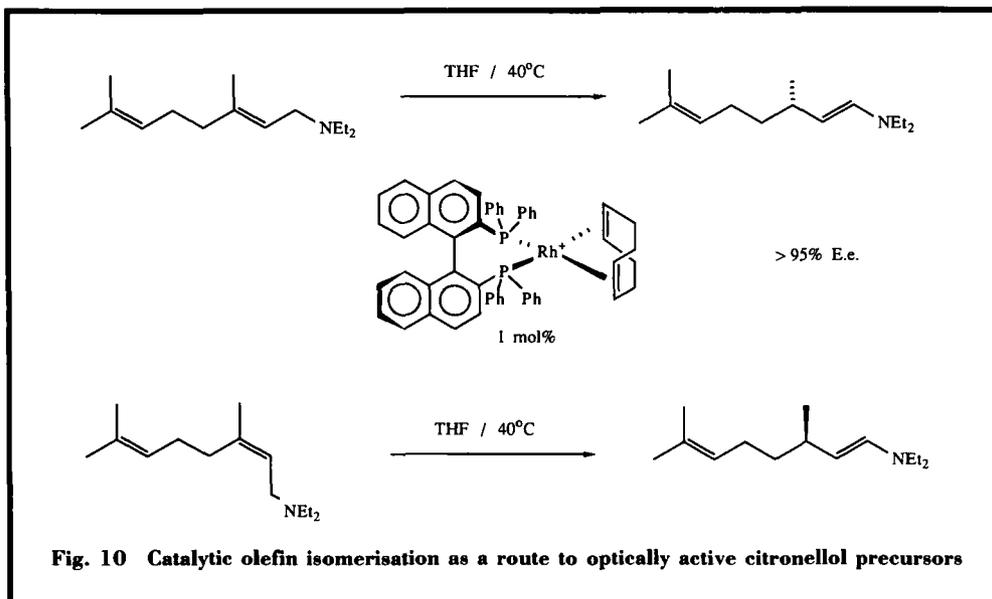
Over a period of twenty years, rhodium catalysts have dominated homogeneous hydrogenation, so it was natural for asymmetric catalysts to be closely related. Their dominance has been challenged in recent Japanese work, particularly that emanating from Noyori's laboratory. He developed the binaphthyl-derived ligand, BINAP, which made a useful but not outstanding contribution to the asymmetric hydrogenation of dehydroamino acids (10a). When the corresponding ruthenium complexes were prepared, they were also found to be active in hydrogenation, but in the opposite stereochemical sense to their rhodium counterparts. More recent applications to the production of enantiomerically pure isoquinoline alkaloids are impressive (10b). Even more so is the hydrogenation of trisubstituted allylic alcohols, for it solves a long-standing problem in organic chemistry and provides a route to



enantiomerically pure compounds in the Vitamin E series (10c) shown in Figure 9. This takes the field of asymmetric hydrogenation one stage further, and closer to being a completely general method for the asymmetric synthesis of tertiary centres.

The final example again comes from Noyori's group and involves catalytic isomerisation in the generation of a new asymmetric centre (11). This brings the discussion full circle, since the reactive intermediate in the catalytic cycle is presumably an allylrhodium hydride, quite

closely related to the allylpalladium intermediates in allylic alkylation. The rhodium complex is prepared from BINAP and is an efficient catalyst for olefin isomerisation in the absence of hydrogen around 40°C; olefin isomerisation has long been known as a competing side-reaction in some homogeneous hydrogenations. The most successful case (Figure 10) is with dimethylgeranylamine and dimethylnerylamine, which were converted into opposite enantiomers of the same enamine, with high optical purity. The product can be



hydrolysed in acid to citronellol, providing an elegant and commercially viable route to this important perfumery intermediate.

## Summary and Future Trends

These examples demonstrate that asymmetric catalysis has become a significant contributor to the "chiral economy" over the last ten years and promises to provide further developments. There is a conspicuous gap in our knowledge at the present time. Most industrial chemists think first of hydroformylation or hydrocarboxylation in the context of homogeneous catalysis, but here the problems associated with

the asymmetric induction have not been satisfactorily solved. Optical yields in rhodium hydroformylation have been uniformly low; platinum-tin complexes give better results, but under rather forcing conditions (12). Clearly much work remains to be done but the future of platinum metal complexes as asymmetric catalysts looks most encouraging, for both industrial and academic applications.

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## A Fast Response Platinum-Iridium Thermocouple

The use of thermocouples made from platinum group metals and their alloys for the measurement of high temperatures is long established and widespread, and is based upon their reproducible thermoelectric properties, their accuracy over a wide temperature range and their resistance to corrosion. Now it is possible to fabricate thin-film thermocouples using integrated circuit technology and a recent paper from the IBM Thomas J. Watson Research Center describes a process for producing thin-film platinum-iridium thermocouples

with the same thermoelectric behaviour as bulk couples (H. M. Tong, G. Arjavalingam, R. D. Haynes, G. N. Hyer and J. J. Ritsko, *Rev. Sci. Instrum.*, 1987, **58**, (5), 875-877).

The thicknesses of the platinum and iridium films were 0.51 and 0.29  $\mu\text{m}$ , respectively, which ensured continuity on the alumina substrate. The thermocouple has been calibrated up to 790°C. With a fast response time and low thermal capacity the thermocouple is very suitable for monitoring instantaneous temperatures during device processing.