JOURNAL OF CATALYSIS 128, 387–396 (1991)

Enantioselective Hydrogenation

II. Variation of Activity and Optical Yield with Experimental Variables in Methyl Pyruvate Hydrogenation Catalyzed by Cinchona-Modified Platinum/Silica (EUROPT-1)

P. A. MEHEUX, A. IBBOTSON,* AND P. B. WELLS[1]

*School of Chemistry, The University, Hull, HU6 7RX, United Kingdom; and *ICI Fine Chemicals Manufacturing Organisation, P.O. Box No. 42, Hexagon House, Blackley, Manchester, M9 3DA, United Kingdom*

Received June 13, 1990

The enantioselective hydrogenation of methyl pyruvate, MeCOCOOMe, to methyl lactate, MeCH(OH)COOMe, preferentially in the *R*-(+)-form has been catalyzed in a stirred reactor over the temperature range 253 to 348 K and over the pressure range 10 to 110 bar by 6.3% Pt/silica (EUROPT-1) modified by cinchonidine and dihydrocinchonidine. Variations of activity and of optical yield are reported as a function of (a) modification procedure, (b) reaction procedure, and (c) temperature. The dependence of optical yield on conversion and hydrogen pressure is also reported. The achievement of high optical yield (ca. 74 to 80%, i.e., 87 to 90% R-(+)-, 13 to 10% *S*-(−)-ester) is critically dependent on the choice of modifier, the modification procedure, and temperature, whereas conversion, hydrogen pressure, and the presence or absence of solvent are of lesser importance. The observations are interpreted in terms of the mechanism proposed in Part I. Preliminary experiments with a flow reactor show unexpectedly high optical yields.

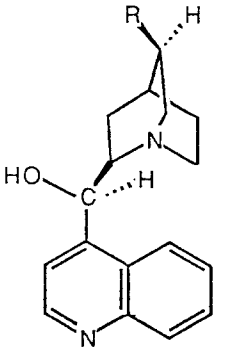
INTRODUCTION

This series of papers constitutes a study of the reaction first reported by Orito *et al.* in 1979 (*1*) in which Pt modified by the deposition of a cinchona alkaloid on its surface is used to achieve the hydrogenation of α-ketoesters to give optically active products. Part I (*2*) records our investigation of the surface conditions prevailing during the hydrogenation of methyl pyruvate, MeCO COOMe, to methyl lactate, MeCH(OH) COOMe, over a 6.3% Pt/silica (EUROPT-1) modified by cinchonidine (Scheme 1, **Ia**) and its diastereoisomer cinchonine. Modification by these alkaloids provided predominantly the *R*-(+)- and *S*-(−)- esters, respectively, the optical yields being in the range 64 to 77%. A mechanism was proposed, based on (i) measurements of isotherms for the adsorption of cinchonidine and of methyl pyruvate, (ii) mesurements of kinetics, and (iii) deuterium tracer information.

According to this mechanism, cinchonidine achieves high surface coverage on the Pt surface (and on the support) and leaves exposed to the fluid phase restricted or "shaped" groups of Pt atoms of such a configuration that molecules of methyl pyruvate are themselves restricted as to the conformations in which they can adsorb. This restriction as to adsorption mode leads to a corresponding restriction in the configuration of the product formed by the simple addition of two hydrogen atoms. The preferential formation of *R*-(+)-methyl lactate when cinchonidine is used as modifier, and of *S*-(−)-ester when cinchonine is used as modifier, is thereby interpreted. This work

[1] To whom correspondence should be addressed.

0021-9517/91 $3.00



SCHEME 1. (**1a**) R = vinyl, (**1b**) R = ethyl.

established the role of alkaloid molecules as surface templates for this reaction; the possibility that these modifiers have an additional role involving specific chemical direction of the reaction will be explored in a later paper in which we describe the effect on enantioselectivity of variations in alkaloid structure.

In the present paper we investigate the dependence of optical yield on experimental variables. For reasons set out in the Discussion, the modifier chiefly examined is dihydrocinchonidine (Ib); however, a few experiments have been conducted with cinchonidine (Ia) to provide a direct comparison with results presented in Part I.

EXPERIMENTAL

Materials

Experiments were conducted using 0.1- or 0.2-g samples of the 6.3% Pt/silica EUROPT-1 for which a detailed characterization has been reported (*3–7*). The catalyst was used in State 3 as defined in Part I (*2*); i.e., the as-received material (reduced by the manufacturer, but subsequently oxidized by the action of air) was evacuated at 293 K for 0.5 h, rereduced at 373 K in 1-bar static hydrogen for 0.5 h and cooled to ambient temperature in hydrogen before modification by the alkaloid.

Methyl pyruvate (Fluka), cinchonidine (Aldrich), ethanol (AnalaR), and hydrogen were used as received. 10,11-Dihydrocinchonidine was prepared from cinchonidine by reaction with 1 bar H_2 over 5% Pd/carbon in 0.5 M sulfuric acid at 293 K (*8*). The resulting solution was filtered to remove catalyst and neutralized with sodium hydroxide solution whereupon dihydrocinchonidine precipitated. The product was separated, washed, dried at 353 K, and recrystallized from an ethanol/water mixture; it contained no impurities detectable by ^1H NMR or by thin-layer chromatography (mp 502–504 K; lit. 504 K).

Static Reactors

Hydrogenations at 10-bar pressure were carried out in the liquid phase in a Fischer-Porter reactor of volume 200 ml fitted with a magnetic stirrer (*2*). Hydrogen pressure was maintained to within ±0.1 bar by microcomputer control. Hydrogen consumption as a function of time was displayed on the data processor.

The effect of pressure over the range 10 to 110 bar was studied at the ICI laboratories at Blackley using (i) a glass-lined Bergius reactor and (ii) a stirred constant-pressure autoclave. Samples of catalyst were reduced and modified at Hull (see below) and were used at Blackley up to a fortnight later.

Reaction Procedures

Procedure A. For reactions in the Fischer-Porter reactor each sampled at various conversions, the mixture consisted of 0.2 g modified catalyst, 20 ml methyl pyruvate, and hydrogen at 10-bar pressure. No solvent was used.

*Procedure B.*For reactions conducted in the Fischer-Porter reactor and analyzed at one conversion only, the mixture consisted of 0.1 g modified catalyst, 10 ml methyl pyruvate, 20 ml ethanol solvent, and hydrogen at 10 bar pressure.

Procedure C. The mixture for reactions in the Bergius reactor consisted of 0.2 g modified aged catalyst, 20 ml methyl pyruvate, 40 ml ethanol solvent, and various pressures of hydrogen. Reactions were analyzed once at high conversion. For reactions

in the stirred autoclave the same mixture was used except that the volume of solvent was 100 ml.

Procedure D. When the catalyst was modified anaerobically in the Fischer-Porter reactor, Procedure D was used and is described below.

Catalyst Modification (Treatment with Alkaloid)

Normal modification. Five milliliters of a 1% wt/wt solution of alkaloid in ethanol was introduced via a septum into a low-pressure static reactor which contained the sample of rereduced catalyst under hydrogen. This was always achieved without exposure of the catalyst to air. Catalyst and modifier solution were then transferred to an open beaker which contained a further 35 ml of the modifier solution and stirred magnetically in air for 1 h, after which the solution was decanted and discarded and the wet catalyst was washed into the Fischer-Porter reactor with a further 20 ml ethanol.

Normal modification with aging. Normal modification (above) was followed to the point where the catalyst and modifier solution had been stirred in air for 1 h. The catalyst and solution were then stored in a sealed glass container and transported from Hull to ICI Blackley where, after a period of days, the solution was decanted and the wet catalyst transferred to the Bergius reactor or the autoclave.

Extended modification. Normal modification (above) was followed except that the catalyst and modifier solution were stirred in air for 18 h before the wet catalyst was loaded into the Fischer-Porter reactor. Of our procedures, this resembles most closely that described in the original literature where a stirring time of 20 h is recommended (*1*).

Anaerobic modification. In this modification process the catalyst was not exposed to air at any stage. The catalyst was rereduced under normal conditions (see above) in the Fischer-Porter reactor which, for the purpose, was fitted with a septum. A shut-off valve capable of sustaining 20-bar pressure was located between the reactor and the septum. The modifier solution (0.1 g alkaloid in 20 ml ethanol) was admitted to 0.1 g EUROPT-1 under 1-bar hydrogen and the mixture stirred magnetically for 1 h. Ten milliliters methyl pyruvate was then added, the shut-off valve closed, hydrogen pressure raised to 10 bar, and reaction proceeded. Clearly, reactions of this type occurred in the presence of a considerable concentration of free alkaloid.

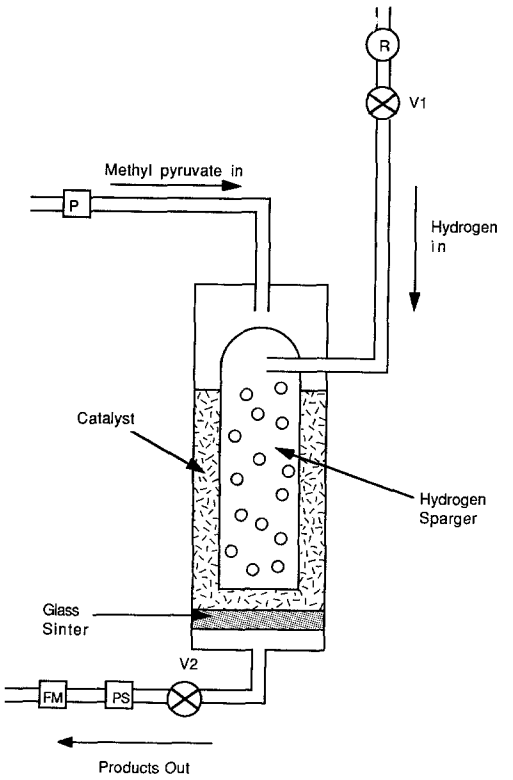


FIG. 1. Schematic diagram of the flow reactor and ancillary equipment. P, high pressure liquid pump; R, hydrogen regulator; V1, nonreturn value; V2, fine metering value; PS, product separator; FM, flow meter.

The Flow Reactor

This reactor consisted of a stainless-steel tube 100 mm long and with a 10-mm internal diameter fitted with an internal steel sparger of 8-mm outside diameter and a glass sinter at the exit (Fig. 1). The cylindrical cavity

between the sparger and the reactor wall was charged with 0.4 g EUROPT-1 which had previously been modified by cinchonidine using the normal modification procedure. Methyl pyruvate and hydrogen at 10-bar pressure were admitted as shown; the respective flow rates were 12 ml h^{-1} and 60 liters (measured at 290 K and 1-bar pressure) h^{-1}. Successive 3-ml samples of product were removed from the collection device for analysis.

Analysis

Reactions conducted by Procedures B, C, and D, i.e., those in which a solvent was used, were analyzed as described fully in Part I (*2*). Briefly, after filtration to remove catalyst and glc analysis to determine conversion, the filtrate was distilled to separate solvent and remove any traces of modifier. The optical rotation of the resultant mixture of methyl pyruvate and methyl lactate was measured and a second glc analysis was carried out to check the methyl lactate concentration.

For reactions conducted by Procedure A (i.e., those in which no solvent was used) the solutions were filtered, the first analysis and the distillation were omitted, the optical rotation was measured, and the conversion determined by glc. This procedure did not remove traces of modifier; the consequent effects are discussed below.

Optical yields determined by polarimetry were compared with those measured by capillary gas chromatography using the chiral stationary phase Chirasil-Val-L. Since enantiomeric resolution on this column relies primarily on H-bonding between an amide-NH function in the sample and carbonyl groups in the stationary phase it was necessary to derivatize the methyl lactate. This was achieved by aminolysis of the ester in *n*-propylamine at 383 K followed by acylation with heptafluorobutyric anhydride at the same temperature to give the 2-heptafluorobutyroxycarboxamide $C_3F_7CO \cdot OCH(CH_3) \cdot CONHC_3H_7$. This material in methylene dichloride solution was injected into the chromatograph. Values of optical yield obtained by chromatography and by polarimetry are compared in Table 1; the zero optical yield recorded for the racemic mixture establishes internal consistency.

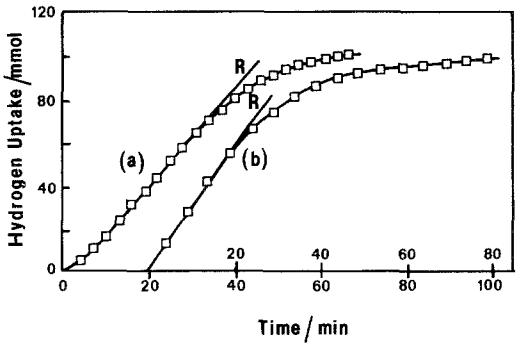


FIG. 2. Variation of hydrogen uptake with time for reactions conducted using Procedure B (temp. = 293 K, 0.1 g catalyst, normal modification, H_2 = 10 bar; for other details see Experimental). The gradients shown provide values for the constant rate, *R*. (a) Modifier = cinchonidine; (b) modifier = dihydrocinchonidine. Complete reaction corresponds to an uptake of 113 mmol.

RESULTS

Variation of Activity with Catalyst Modification Procedure

Hydrogen uptake versus time curves for reactions catalyzed by EUROPT-1 modified by cinchonidine and by dihydrocinchonidine are shown in Fig. 2. As reported in Part I (*2*) cinchonidine-modified Pt provided curves which showed an initial acceleratory region (curve a) followed by a constant rate; at about 70% conversion the rate dropped due to inhibition by product. The initial acceleratory region was less marked or absent when dihydrocinchonidine was used as modifier (Fig. 2, curve b).

Table 2 presents values of the constant rate measured at 293 K. Unmodified EUROPT-1 exhibited a low activity for methyl pyruvate hydrogenation of ca. 40 mmol h^{-1} (g. cat)$^{-1}$ irrespective of whether a solvent was used or not (entries 1 and 2). By contrast, catalysts normally modified by either alkaloid gave 30-fold higher rates provided a solvent was used (entries 3 and 4). Even higher rates were achieved when the

TABLE 1

Comparison of Optical Yields Determined by Chromatography and Polarimetry

Sample	Chromatographic analysis[a] (%)		Optical yield[b] (%)	
	R-(+)-ML[c]	*S*-(−)-ML[c]	Chromatography	Polarimetry
Racemate	50	50	0	—
Product	62	37	25	24
Product	75	25	50	52
Product	85	15	70	70

[a] Values expressed to nearest %.
[b] Values by chromatography ± 1%; values by polarimetry ± 2%.
[c] ML = methyl lactate.

extended modification procedure was used (entry 5), whereas aging reduced activity (entry 6), and much lower rates were observed when the solvent was omitted (entry 7). When catalysts were modified anaerobically, the rates were hardly faster than those obtained over unmodified catalyst.

Dependence of Optical Yield on Modifier, Modification Procedure and Conversion

Figure 3 shows the conversion-dependence of optical yield at room temperature; modifiers, modification procedures, and reaction procedures are detailed in the legend.

Curves 1 and 3 show that Pt modified by dihydrocinchonidine exhibited a markedly higher enantioselectivity than that modified by cinchonidine. Thus, the majority of the present work concentrates on the behavior of dihydrocinchonidine-modified Pt.

The relative effectiveness of normal modification and extended modification (as recommended in the original literature) is compared by means of curves 1 and 2. Since our values of optical yield are uncertain to ±2%, these reactions are closely similar and show that modification time can be reduced from 18 h to 1 h with no deleterious effect on enantioselectivity.

The open symbols on curves 1, 2, and 3 refer to experiments carried out without solvent (see Procedure A) whereas the solid symbols indicate use of solvent (see Procedure B). Distillation to remove traces of modifier was incorporated in Procedure B but not in Procedure A (see Experimental). Thus, the lower optical yields determined by Procedure A (open points, Fig. 3) are probably depressed by the presence of traces of modifier, and the higher optical yields determined by Procedure B (filled points) are expected to be correct. On this basis, the best optical yields obtained at about 20% conversion probably exceeded 80%.

Curves 1 and 4 compare the performance of catalysts prepared by normal (aerobic) modification and by anaerobic modification. Because of the procedures used, the open symbols on curve 1 represent one reaction conducted without solvent and sampled at five conversions, whereas the solid symbols on curve 4 represent six individual reactions conducted in a solvent each being analyzed once. Despite these differences, it is clear that anaerobic modification results not only in low rates (Table 1) but also in inferior optical yields. Thus, exposure of the catalyst to air during modification is crucial to its achievement of high enantioselectivity.

Variation of Optical Yield with Hydrogen Pressure

Reactions were carried out in the Bergius reactor and in the autoclave using catalyst samples modified by dihydrocinchonidine and reaction Procedure C (see Experimental). Over the range 10 to 110 bar the optical

TABLE 2

Dependence of the Constant Hydrogenation Rate, R, on Modification and Reaction Conditions

Entry	Modifier[a]	Modification procedure	Modification time (h)	Aging time (h)	Solvent	R^b (mmol h^{-1} g^{-1})
1	None	—	—	—	None	50
2	None	—	—	—	Ethanol	35
3	C	Normal	1	0	Ethanol	1100–1300
4	DHC	Normal	1	0	Ethanol	1100–1300
5	DHC	Extended	18	0	Ethanol	1490
6	DHC	Normal with aging	1	890	Ethanol	715
		Normal				
7	DHC		1	0	None	275
8	DHC	Anaerobic	1	0	Ethanol	66

[a] C, cinchonidine; DHC, dihydrocinchonidine.
[b] Hydrogen pressure = 10 bar; temperature = 293 K.

yield showed a weak maximum at about 50 bar (Table 3). Optical yields obtained at 9 bar using the Bergius reactor and the autoclave agreed closely with that obtained at the same pressure using the Fischer-Porter reactor (compare Table 3 and Fig. 3). Thus, aging had no effect on optical yield.

Variation of Activity and of Optical Yield with Temperature

Constant rates, R, and optical yields were measured over the range 253 to 348 K (Fig. 4). The temperature-dependence of the rates over unmodified Pt (curves (a) and (b)) is not well described by the Arrhenius equation, whereas that for the faster reactions over modified Pt obey the equation over a limited range for which the apparent activation energies are 41 ± 4 kJ mol^{-1} (cinchonidine-modified Pt) and 33 ± 4 kJ mol^{-1} (dihydrocinchonidine-modified Pt). The separately determined value reported in Part I for cinchonidine-modified Pt was 38 kJ mol^{-1}. The catastrophic loss of activity of cinchonidine-modified Pt at 313 K, reported in Part I, is again observed, and similar behavior is observed when dihydrocinchonidine is used as modifier.

TABLE 3

Dependence of Optical Yield on Hydrogen Pressure[a]

Reactor	Hydrogen pressure (bar)	Optical yield (%)
Autoclave	10	64
Bergius	10	64
Autoclave	30	68
Bergius	48	67
Bergius	50	69
Bergius	90	63
Bergius	110	60

[a] Temp. = 293 K; conversions >90%; normal modification; reaction Procedure C.

The close correspondence of the rates observed when these modifiers were used in the range 253 to 313 K suggests that similar hydrogenation conditions obtain at the two surfaces. However, Fig. 5 shows that optical yield decreased with increasing temperature over this range with cinchonidine as modifier, whereas it was temperature independent when dihydrocinchonidine was used.

Preliminary Experiment with the Flow Reactor

We were concerned to know whether the alkaloid would remain adsorbed to the platinum active phase under flow reactor conditions, or whether it would be eluted rapidly

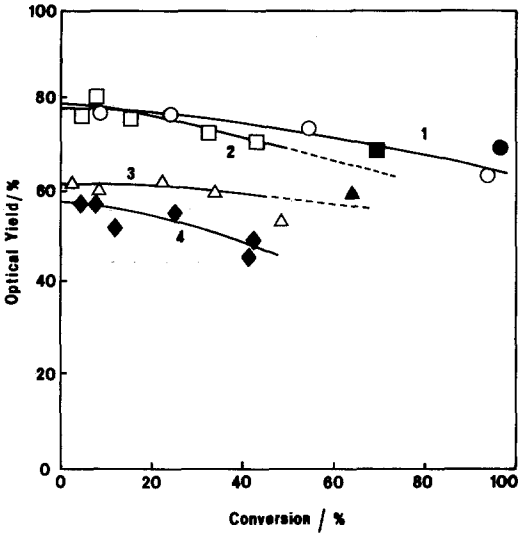


FIG. 3. Variation of optical yield with conversion in reactions at 10-bar pressure and 293 K. Curve 1 = normal modification with dihydrocinchonidine (open circles, no solvent (Procedure A); filled circle, with solvent (Procedure B)). Curve 2 = extended modification with dihydrocinchonidine (open squares, no solvent (Procedure A); filled square, with solvent (Procedure B)). Curve 3 = normal modification with cinchonidine (open triangles, no solvent (Procedure A); filled triangle, with solvent (Procedure B)). Curve 4 = anaerobic modification with dihydrocinchonidine: (filled diamonds, with solvent (procedure D)).

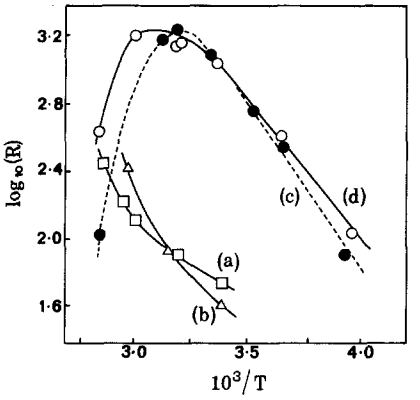


FIG. 4. Variation of the constant rate, R/mmol h^{-1} g^{-1}, on temperature T for reaction over EUROPT-1 at 10-bar hydrogen pressure for (a) unmodified catalyst, no solvent (Procedure A); (b) unmodified catalyst, solvent used (Procedure B); (c) catalyst normally modified by cinchonidine, solvent used (Procedure B); (d) catalyst normally modified by dihydrocinchonidine, solvent used (Procedure B).

resulting in lower optical yield that would deteriorate further with time on stream. Accordingly, the flow reactor was loaded with 0.4 g cinchonidine-modified EUROPT-1 (normal modification) and operated under the conditions described in the Experimental Section and about 7% conversion. The optical yields obtained are shown in Fig. 6; remarkably, they were some 20% higher than those obtained from the static reactor (compare Fig. 3) and, despite a minor disturbance in the reactor after half an hour on stream, the optical yield remained high. Product from the reactor contained cinchonidine that was detected spectrophotometrically; the rate of alkaloid loss from the catalyst was highest over the first 15 min, and had dropped to only a slight loss after 1 h. In Part I we established that the majority of cinchonidine adsorbed on EUROPT-1 was physisorbed on the silica support, and we conclude that it was alkaloid held on the support that was eluted in this experiment with the flow reactor. The unexpectedly high optical yield was achieved at a surprisingly low reaction rate of 40 mmol h^{-1} g^{-1}.

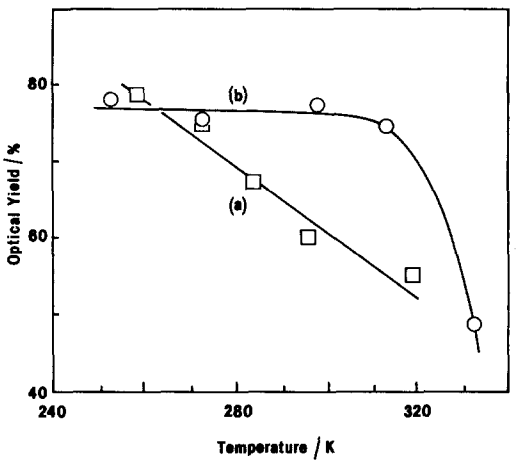


FIG. 5. Variation of optical yield with temperature for reaction over EUROPT-1 at 10-bar hydrogen pressure. (a) Catalyst normally modified by cinchonidine, solvent used (Procedure B); (b) catalyst normally modified by dihydrocinchonidine, solvent used (Procedure B).

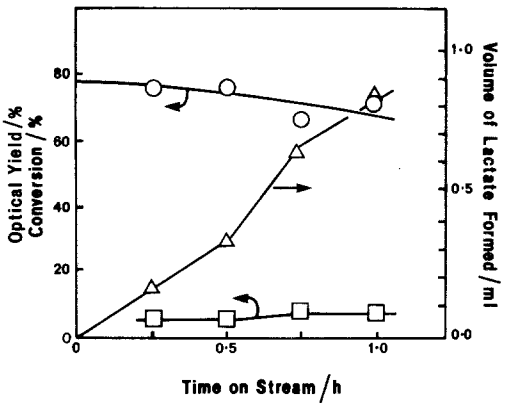


FIG. 6. Characteristics of the operation of the flow reactor for the hydrogenation of methyl pyruvate at 293 K and 10-bar hydrogen pressure. Catalyst weight = 0.4 g. Catalyst modified by cinchonidine using the normal procedure. No solvent used. Circles = optical yield; squares = conversion; triangles = volume of product formed.

The performance of this reactor merits further study.

DISCUSSION

Recently, Blaser and co-workers have reported an optical yield in ethyl pyruvate hydrogenation catalyzed by cinchonidine-modified EUROPT-1 (*9*) of 65% which concurs with our values recorded in Fig. 3. These workers also record that dihydrocinchonidine is a more efficient modifier than cinchonidine (*8*). Their experiments show highly variable optical yields between 10% and almost 90%; their best value of 89% exceeds our best, and was achieved in methyl pyruvate hydrogenation in methanol or toluene as solvent over Pt/alumina modified by dihydrocinchonidine (*8*).

Physical Architecture of the Modifier

The property of enantioselectivity is conferred on EUROPT-1 by the presence of the cinchona alkaloid at the Pt surface. In Part I we presented a model for cinchonidine adsorption and a mechanism for methyl pyruvate hydrogenation which together interpreted the observed preferential formation of *R*-(+)-methyl lactate (*2*). Briefly, it was noted that the conformation of the free cinchonidine molecule having the lowest energy was one which could be adsorbed at a low-index platinum surface via the quinoline ring system without steric hindrance. Such molecules in the adsorbed state possess L-shaped adsorption shadows, such that in a non-close-packed assembly they leave "shaped" ensembles of surface platinum atoms exposed to the fluid phase. These ensembles and their environment are of such a geometry that the conformation in which methyl pyruvate molecules may adsorb is largely restricted to that which, on hydrogenation, gives the observed optically active product.

The greatly enhanced hydrogenation rate observed in the presence of modifier was attributed to a high concentration of adsorbed-H, such as might be achieved by noncompetitive adsorption of hydrogen at sites not available to methyl pyruvate, e.g., those beneath the quinuclidine ring system of the adsorbed modifier.

Studies of ethanol adsorption on EUROPT-1 showed that C_2H_5O(ads) was formed along with adsorbed alkaloid during modification. This, and the expectation that atmospheric oxygen may adsorb on the platinum surface during normal modification, led to the view that the modified Pt surface probably consists of an ordered coadsorption of alkaloid and O-containing entities (C_2H_5O(ads) and/or O(ads)). The poor performance of anaerobically modified Pt reported here supports this model.

Chemical Architecture of the Modifier

In this paper we are mostly concerned with the chemical architecture of the modifier and with the implications for activity and enantioselectivity of changes in experimental variables.

Activity of Pt normally modified by cinchonidine and by dihydrocinchonidine was the same (Table 1, entries 3 and 4) as is expected if the high rates are indeed attributable to enhanced hydrogen coverages achieved by noncompetitive adsorption at

sites partially obscured by or adjacent to the L-shaped templates.

The higher optical yield provided by dihydrocinchonidine as modifier (Fig. 3, curves 1 and 3) is simply interpreted. The geometry of cinchonidine is such that it may adsorb on Pt by the quinoline ring system, or by the vinyl group, but not by both functions simultaneously. Thus we may expect that the random approach of cinchonidine molecules to the Pt surface during modification results in two modes of adsorption, one which provides the L-shaped template for successful enantioselective hydrogenation, and one which does not. By comparison, dihydrocinchonidine, which has had the vinyl function removed by hydrogenation, can adsorb only by the quinoline ring system as the L-shaped template. Thus, the proposed mechanism simply interprets the better performance of dihydrocinchonidine as a catalyst modifier.

We reported in Part I that some saturation of the vinyl group in cinchonidine occurs during enantioselective hydrogenation, and speculated that this initiates a rearrangement of the ad-layer of modifier molecules, thus contributing to the small acceleration in rate observed during the early stages of reaction (Fig. 1a). We now note that little or no acceleratory phase is observed with dihydrocinchonidine as modifier (Fig. 2b) and equate this with the fact that no such rearrangement can occur in an ad-layer of this modifier.

Finally, this chemistry also interprets the different temperature dependencies of the optical yield observed with cinchonidine and dihydrocinchonidine as modifier (Fig. 5). In a situation where the modifier (cinchonidine) adsorbs in two states, the relative populations of these two states will be temperature dependent if the free energies of adsorption of the two states are different. Hence, if only one state templates the surface toward enantioselective hydrogenation, the optical yield will vary with temperature. On this model, the observed fall of optical yield with increasing temperature is associated with cinchonidine adsorbed by the vinyl group being the state having the higher free energy of adsorption.

Modification: A Consideration of O-Containing Coadsorbents

Figure 3 (curve 4) and Table 1 (entry 8) show unequivocally that EUROPT-1 not exposed to air during modification exhibited an impaired enantioselectivity and a greatly reduced activity. This supports our view (*2*) that the formation of adsorbed-O is the process that spaces out adsorbed alkaloid molecules so that they adopt a non-close-packed configuration. Clearly, C_2H_5O(ads) does not function as efficiently as O(ads) for this purpose.

On this basis, the depressed optical yields and rates obtained with anaerobically modified Pt arise from a more closely or less advantageously packed ad-layer of alkaloid molecules and the presence of a smaller number of adsorption sites for methyl pyruvate.

Finally, although C_2H_5OH does not substitute efficiently for O_2 in the modification process, it clearly performs a positive role as a solvent because reactions with solvent proceeded more rapidly than those without solvent by a factor of 4 or 5 (Table 1). Since the solubility of these alkaloids in ethanol is higher than that in methyl pyruvate, it is likely that a small fraction of adsorbed alkaloid is removed by ethanol to provide an increased rate of hydrogen adsorption without substantially impairing the templating effect of the modifier.

Performance at High Hydrogen Pressure

High optical yields were maintained up to 110-bar pressure of hydrogen (Table 3). This is to be expected in that the mechanism involves simple addition of two hydrogen atoms across the carbon–oxygen double bond with no secondary reactions involving hydrogen (with D_2 the product is entirely $CH_3CD(OD)COOCH_3$ (*10*)). Increased hydrogen coverage at higher pressures should result in the same optical yields being

achieved at higher rates. Unfortunately, it was not possible to measure values of the constant rate in either of the very high pressure reactors. What is unexpected is that the adsorbed alkaloid remains an efficient modifier under these high pressures of hydrogen. In Part I we demonstrated that the quinoline system in cinchonidine was susceptible to hydrogenation at very low coverage of the modifier, but resistant to hydrogenation in the context of normally modified EUROPT-1 exposed to 10-bar hydrogen pressure. It appears that dihydrocinchonidine remains resistant to hydrogenation at 293 K at hydrogen pressures up to the highest value used of 110 bar.

Performance at Elevated Temperatures

By contrast, this reaction is particularly sensitive to temperature. The enantioselectivity and activity collapse above about 313 K. This was attributed in Part I to a change in the manner of alkaloid adsorption above this temperature, the suddenness of the change suggesting a phase-change in the adsorbed state of the modifier. The present work confirms and extends the original observation but does not advance its interpretation.

Future Work

This detailed discussion supports the view that cinchona alkaloids adsorb by interaction of the quinoline system at the Pt surface and that variations in reaction rate reflect changes in hydrogen or methyl pyruvate coverage as experimental conditions are varied. In a future paper we shall report (a) studies of H/D exchange in the modifier in an attempt to determine the orientation of the adsorbed modifier and (b) studies of the rate of dihydrogen/dideuterium exchange during enantioselective hydrogenation in an attempt to monitor relative changes in hydrogen coverage under experimental conditions. Studies are also underway to refine our model of the modified surface by use of molecular graphics, treating the adsorption of the methyl pyruvate molecule at a shaped site as a docking problem.

ACKNOWLEDGMENTS

The authors thank ICI Fine Chemicals Manufacturing Organisation for financial and material support and SERC for the award of a postgraduate studentship to P.A.M. under the CASE Scheme.

REFERENCES

1. Orito, Y., Imai, S., Niwa, S., and Nguyen, G-H., *J. Synth. Org. Chem. Japan* **37,** 173 (1979).
2. Sutherland, I. M., Ibbotson, A., Moyes, R. B., and Wells, P. B., *J. Catal.* **125,** 77 (1990).
3. Bond, G. C., and Wells, P. B., *Appl. Catal.* **18,** 221 (1985).
4. Bond, G. C., and Wells, P. B., *Appl. Catal.* **18,** 225 (1985).
5. Geus, J. W., and Wells, P. B., *Appl. Catal.* **18,** 231 (1985).
6. Frennet, A., and Wells, P. B., *Appl. Catal.* **18,** 243 (1985).
7. Wells, P. B., *Appl. Catal.* **18,** 259 (1985).
8. Blaser, H. U., Jalett, H. P., Monti, D. M., Reber, J. F., and Wehrli, J. T., *Stud. Surf. Sci. Catal.* **41,** 153 (1988).
9. Blaser, H. U., Jalett, H. P., Monti, D. M., and Wehrli, J. T., *Appl. Catal.* **52,** 19 (1989).
10. P. A. Meheux and P. B. Wells, unpublished work.