JOURNAL OF CATALYSIS **144**, 569–578 (1993)

Enantioselective Hydrogenation of Ethyl Pyruvate: Kinetic Modeling of the Modification of Pt Catalysts by Cinchona Alkaloids

H. U. BLASER,* M. GARLAND,† AND H. P. JALLET*

**Central Research Services, CIBA-GEIGY AG, R-1055.6, CH-4002 Basel, Switzerland; and*
†Department of Chemical Engineering, Swiss Federal Institute of Technology,
Universitätstrasse 6, CH-8092 Zürich, Switzerland

Received January 4, 1993; revised May 5, 1993

The effect of modifier concentration on rate and optical yield is described for the enantioselective hydrogenation of ethyl pyruvate using 5% Pt/Al_2O_3 catalysts in the presence of cinchona alkaloids. Results are reported for three systems using two commercial catalysts, 10,11-dihydrocinchonidine (HCd) and O-methyl-HCd as modifiers, and ethanol, toluene, and acetic acid as solvents. The modifier concentration was varied between 0 and 6 mmol/liter and the reactions were carried out at room temperature at 20 and 100 bar hydrogen pressure. The fully modified catalysts displayed enantioselectivities up to 95%. A simple kinetic model was developed which is able to describe the observed dependence of both rate and enantioselectivity on the modifier concentration. The main feature of the model is the reversible formation of modified active sites by adsorption of single cinchona molecules on the Pt surface whereby the modified sites display high enantioselectivity and an enhanced catalytic activity. The scope and limitations of the simple two-site model together with the underlying assumptions are discussed and a three-site model is proposed in order to rationalize the effects observed at high modifier concentrations.

INTRODUCTION

The observation that the addition of a ligand or modifier affects not only the enantioselectivity of a metallic catalyst but also enhances its activity was first described for the dihydroxylation of alkenes catalyzed by osmium complexes in the presence of cinchona alkaloids and was termed "ligand-accelerated catalysis" (*1*). In this reaction, a chiral auxiliary is added to a solution containing OsO_4 and alkene, resulting in both the preferential formation of one enantiomer of the diol as well as a marked increase in the reaction rate. Later, similar observations were reported for the heterogeneous hydrogenation of α-keto esters, catalyzed by cinchona-modified Pt/Al_2O_3 or Pt/SiO_2 catalysts (*2, 3*). Subsequent studies were carried out with trace quantities of cinchona alkaloids (modifier/$Pt_{surf} \leq 1$) (*4–6*). These experiments confirmed that both ee and rate were continuous functions of the cinchona concentration. With Pt/Al_2O_3, the maximum optical yields were obtained with a modifier/Pt_{surf} ratio as low as 0.25 in toluene (*4*) or less than 0.1 in acetic acid (*5*). For a Pt/SiO_2 catalyst in toluene, maximum ee and rate were reached at a modifier/Pt_{surf} ratio of about 0.2 (*6*).

For the 10,11-dihydrocinchonidine-Pt/Al_2O_3 system, the dependence of ee and rate on the modifier concentration as well as their interdependence was successfully analyzed in the context of a two-site mechanistic scheme (*4*). For experiments conducted in toluene and ethanol, it was shown that a linear relationship exists between ee and 1/rate. The results described by Bond *et al.* (*6*) for their cinchonidine-Pt/SiO_2 system were slightly different, especially in the region of maximum ee and rate. This was taken as experimental support for the template mechanism proposed earlier by the same

0021-9517/93 $5.00

authors (*3*). Spencer has developed a mathematical description for the analysis of this template model (*7*).

In this contribution, we present further analyses of the cinchona-modified system in the context of our two-site model for the hdyrogenation of ethyl pyruvate. It is shown that under reaction conditions at trace level modifier concentrations a simple Langmuir adsorption isotherm describes the behavior of different catalysts and modifiers in several solvents. At higher cinchona concentrations, some phenomena are observed which can no longer be explained with a simple two-site model (*8*).

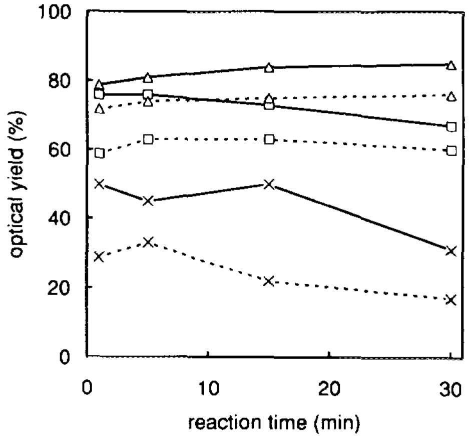

FIG. 1. Effect of reaction time on optical yield. 100 mg E 4759, 20°C, 20 bar H_2. (×) 0.01 mg, (□) 0.10 mg, (△) 2 mg HCd; (—) toluene, and (---) EtOH. Conversions after 30 min: 0.01 mg HCd, ca. 20%; 0.10 mg HCd, 45–55%; 2 mg HCd, > 95%.

EXPERIMENTAL

Two 5% Pt/Al_2O_3 catalysts were used in this study: Engelhard E 4759 (particle size 50–120 μm, BET surface area 168 m^2/g, mean pore radius 20 Å, pore volume 0.27 ml/g, dispersion 0.24) and Johnson Matthey 5R94 (particle size 10–30 μm, BET surface area 131 m^2/g, mean pore radius 70 Å, pore volume 0.93 ml/g, dispersion 0.22) (*9*).

A 50-ml batch reactor with cooling jacket, baffles, a 3-cm magnetic stirring bar, a thermocouple, and a capillary sampling line was used for all experiments. A 49-ml reservoir, pressure regulators, pressure transducers, and a cryostat were connected to the reactor. The reactor could be maintained isothermal and isobaric for the duration of the experiment. Typically, 100 mg catalyst (pretreated for 2 h in H_2 at 400°C), variable amounts of the cinchona alkaloid [10,11-dihydrocinchonidine (HCd) or O-methoxy-HCd (MeOHCd)], 10 ml ethyl pyruvate, and 20 ml solvent were charged to the reactor. The system was then purged five times with argon while stirring. In the absence of stirring, the reservoir and reactor were pressurized with hydrogen. After 2–3 min, both the stirrer and data acquisition were started. The reaction was stopped after 5–10 min. In all cases, the reactions were zero order in ethyl pyruvate and initial rate data were analyzed after the 30-s saturation period with an estimated accuracy of ±10%. Conversion was estimated via hydrogen consumption or checked with GLC. Optical yields were determined after derivatization with isopropylisocyanate followed by GLC (Chirasil-L-Val).

There were some indications that the modifier might not be completely stable under reaction conditions (*4*). Therefore, the optical yields were measured as a function of reaction time. The results depicted in Fig. 1 show that the optical yields started to decline after 5–10 min of reaction if the modifier concentration was very low. It is thus essential to consider initial rates and initial optical yields in mechanistic analyses.

RESULTS

Three series of experiments with various modifier concentrations are described and analyzed for the hydrogenation of ethyl pyruvate at room temperature. In the first series, catalyst E 4759 was used in ethanol as solvent (0–2 mg HCd, 20 bar) (*4*). The second series was conducted in toluene with the same catalyst E 4759 (0–50 mg HCd, 20 bar), and, finally, preliminary data are reported for the reaction in acetic acid using catalyst 5R94 (0–50 mg MeOHCd, 100 bar). The experimental results are tabulated in Table 1 and depicted in Figs. 2–5.

TABLE 1

Dependence of Initial Rate and Optical Yield on Modifier Concentration in Different Solvents

EtOH, HCd, E4759			Tol, HCd, E4759			AcOH, MeOHCd, 5R94		
[mod] (mmol/liter)	Rate (10^{-6} mol/s)	ee (%)	[mod] (mmol/liter)	Rate (10^{-6} mol/s)	ee (%)	[mod] (mmol/liter)	Rate (10^{-6} mol/s)	ee (%)
0.000	7.5	0	0.000	4.5	1.5	0.0	5.7	0.5
0.002	10.5	17.4	0.001	11	31	6.5×10^{-5}	6.2	47
0.006	15.0	44.7	0.002	13	42	1.3×10^{-4}	7.1	48
0.010	29.3	57.6	0.006	21	61	2.6×10^{-4}	11	81
0.028	35.3	66.1	0.011	28	70	6.5×10^{-4}	21	85
0.068	56.3	70.7	0.023	36	73	9.0×10^{-4}	25	86
0.113	71.3	76.5	0.056	47	77	1.3×10^{-3}	38	91
0.169	65.0	74.6	0.113	51	79	2.6×10^{-3}	51	92
0.225	78.8	77.5	0.169	51	80	6.5×10^{-3}	72	93
			0.225	51	79	1.3×10^{-2}	82	94
			0.563	51	81	2.6×10^{-2}	93	94
			1.126	48	81	6.5×10^{-2}	93	94
			2.252	48	78	0.13	110	94
			5.631	45	79	0.26	116	94
						0.65	124	94
						1.3	136	94
						2.6	141	94
						6.5	141	94

Temperature 20°C; pressure 20 bar (toluene, EtOH) and 100 bar (AcOH).

Several features of the dependence of rate and optical yield on cinchona concentration are noteworthy. In all three cases, increasing the amount of modifier leads to a steady increase of both rate and ee at low modifier concentration. The small optical yields observed for the unmodified catalyst in toluene and acetic acid might be due either to the inaccuracy of the ee determination (±1%) or some residual modifier. At higher cinchona concentrations, the pattern changes. In toluene, both rate and optical yield start to decrease when the concentration of HCd is increased beyond 2 mmol/liter. For the reaction in ethanol, a similar behavior has been reported in a preliminary study with high modifier concentrations (*2*). In acetic acid, the optical yield reaches a plateau at 94% while the rate clearly shows an inflection point around 0.1 mmol/liter of MeOHCd. These results are reproducible and indicate that the choice of the solvent, catalyst, and/or the modifier has an effect on the general form of the ee and rate curves.

Derivation of Expressions for Optical Yield (ee), Rate (r), and Modifier Coverage (x) in the Context of a "Two-Site Model"

For our model we assume that the modifier is reversibly adsorbed on unmodified surface platinum atoms, Pt_u, thereby creating modified Pt atoms, Pt_m. Furthermore, it is assumed that the large cinchona alkaloid occupies and/or blocks ν platinum atoms on the metal surface. In other words, in this model an asymmetric site consists of ν *modified Pt atoms and one adsorbed cinchona molecule (CIN).*

$$\nu \mathrm{Pt_u} + \mathrm{CIN} \overset{K_m}{\rightleftharpoons} \nu\, \mathrm{Pt_m} \qquad (1)$$

Racemic hydrogenation of the α-ketoester occurs on the unmodified sites, enantioselective hydrogenation on the modified sites.

Expressions for rate and optical yield. The observed rate of product formation, r_{obs}, can be written as the sum of the rates for unmodified and modified catalyst. By introducing pseudo first order rate constants, k_{u} and k_{m}, a mass balance for the platinum surface atoms (determined from CO adsorption), $\mathrm{Pt_{surf}} = \mathrm{Pt_u} + \mathrm{Pt_m}$, and by defining the degree of surface modification, $x_{\mathrm{m}} = \mathrm{Pt_m}/\mathrm{Pt_{surf}}$, Eq. (4) is obtained:

$$r_{\mathrm{obs}} = r_{\mathrm{u}} + r_{\mathrm{m}} \tag{2}$$

$$r_{\mathrm{obs}} = k_{\mathrm{u}}\mathrm{Pt_u} + k_{\mathrm{m}}\mathrm{Pt_m} \tag{3}$$

$$r_{\mathrm{obs}} = [(1 - x_{\mathrm{m}})k_{\mathrm{u}} + x_{\mathrm{m}}k_{\mathrm{m}}]\mathrm{Pt_{surf}} \tag{4}$$

Expressions can be written for the rate of formation of the R and S enantiomers by introducing an intrinsic selectivity $s = [\mathrm{R}]/([\mathrm{R}] + [\mathrm{S}])$ for the modified sites and by assuming racemic hydrogenation on unmodified sites:

$$r_{\mathrm{R}} = 0.5k_{\mathrm{u}}\mathrm{Pt_u} + sk_m\mathrm{Pt}_m \tag{5}$$

$$r_{\mathrm{S}} = 0.5k_{\mathrm{u}}\mathrm{Pt_u} + (1 - s)k_{\mathrm{m}}\mathrm{Pt_m} \tag{6}$$

Using only the variables defined above, and the definition of the enantiomeric excess, $\mathrm{ee} = 100([\mathrm{R}] - [\mathrm{S}])/([\mathrm{R}] + [\mathrm{S}])$, a new expression for $\mathrm{ee_{obs}}$ is obtained (Eq. (8)). It is essential that initial reaction data are used since Eq. (7) is only valid if the degree of modification, x_{m}, remains constant during the experiment so that the formation of the two enantiomers is proportional to $\mathrm{r_R}$ and $\mathrm{r_S}$, respectively:

$$\mathrm{ee_{obs}} = 100(r_{\mathrm{R}} - r_{\mathrm{S}})/(r_{\mathrm{R}} + r_{\mathrm{S}}) \tag{7}$$

$$\mathrm{ee_{obs}} = [100(2s - 1)x_{\mathrm{m}}k_{\mathrm{m}}\mathrm{Pt_{surf}}]/r_{\mathrm{obs}} \tag{8}$$

Expressions for the equilibrium isotherm. Equation (8) can be rearranged to give Eq. (9) which shows that the product of $\mathrm{ee_{obs}}$ and $\mathrm{rate_{obs}}$ is proportional to the degree of surface modification x_{m}. This can provide information concerning the form of the adsorption isotherm between cinchona molecules and the modifiable platinum surface:

$$\mathrm{ee_{obs}} \cdot \mathrm{r_{obs}} = x_{\mathrm{m}}100(2s - 1)k_{\mathrm{m}}\mathrm{Pt_{surf}} \tag{9}$$

In order to further analyze the form of the adsorption isotherms, we define an equilibrium adsorption constant, K_{m}, for the modifier/Pt surface complex (Eq. (10)) and a mass balance for the alkaloid where $[\mathrm{CIN}]_{\mathrm{soln}}$ and $[\mathrm{CIN}]_{\mathrm{ads}}$ represent the concentration of the cinchona modifier in solution and adsorbed on platinum, respectively. Equation (11) is only valid if secondary adsorption of modifier (i.e., on the support) is negligible. By substituting $\mathrm{Pt_m}$ and $\mathrm{Pt_u}$ by $x_{\mathrm{m}}\mathrm{Pt_{surf}}$ and $(1 - x_{\mathrm{m}})\mathrm{Pt_{surf}}$, respectively, and allowing for the stoichiometry of adsorption (see Eq. (1)), Eq. (13) is obtained with x_{m} and K_{m} as the only variables. K_{m} can thus be estimated from experimental x_{m} values (using Eq. (9)) or it is possible to calculate x_{m} after assuming K_{m}:

$$K_{\mathrm{m}} = [\mathrm{Pt_m}]/([\mathrm{CIN}]_{\mathrm{soln}}[\mathrm{Pt_u}]) \tag{10}$$

$$\mathrm{CIN_{soln}} = \mathrm{CIN_{tot}} - \mathrm{CIN_{ads}} \tag{11}$$

$$\mathrm{CIN_{ads}} = \mathrm{Pt_m}/\nu = x_{\mathrm{m}}\mathrm{Pt_{surf}}/\nu \tag{12}$$

$$K_{\mathrm{m}}^{-1} = [\mathrm{Pt_{surf}}](x_{\mathrm{m}} - 1)/\nu + [\mathrm{CIN}]_{\mathrm{tot}}(1 - x_{\mathrm{m}})/x_{\mathrm{m}} \tag{13}$$

We can now consider the degree of modification as a function of modifier concentration. In Fig. 2, both the experimental and calculated values for $\mathrm{ee_{obs}} \cdot \mathrm{rate_{obs}}$ are depicted for the three series of experiments at low modifier concentration. A fairly good fit is obtained using for our calculations the values for s and k_{m} tabulated in Table 2. Note that for the different catalytic systems, the scale of the modifier concentration is not the same, indicating that the [CIN] necessary for reaching a similar degree of modification is quite different.

Modeling of reaction data. For the calculation of ee and rate as a function of modifier concentration, Eqs. (4), (8), and (9) are used, containing the adjustable parameters k_{u}, k_{m}, s, ν, and K_{m}. The rate constant k_{u} can be obtained from an experiment with unmodified catalyst. In the simplest case (Pt surface entirely modifiable, $(x_{\mathrm{m}})_{\max} = 1$; no further adsorption effects), it is possible to determine k_{m} and s from the rate and ee obtained at full coverage. If k_{m} and s are

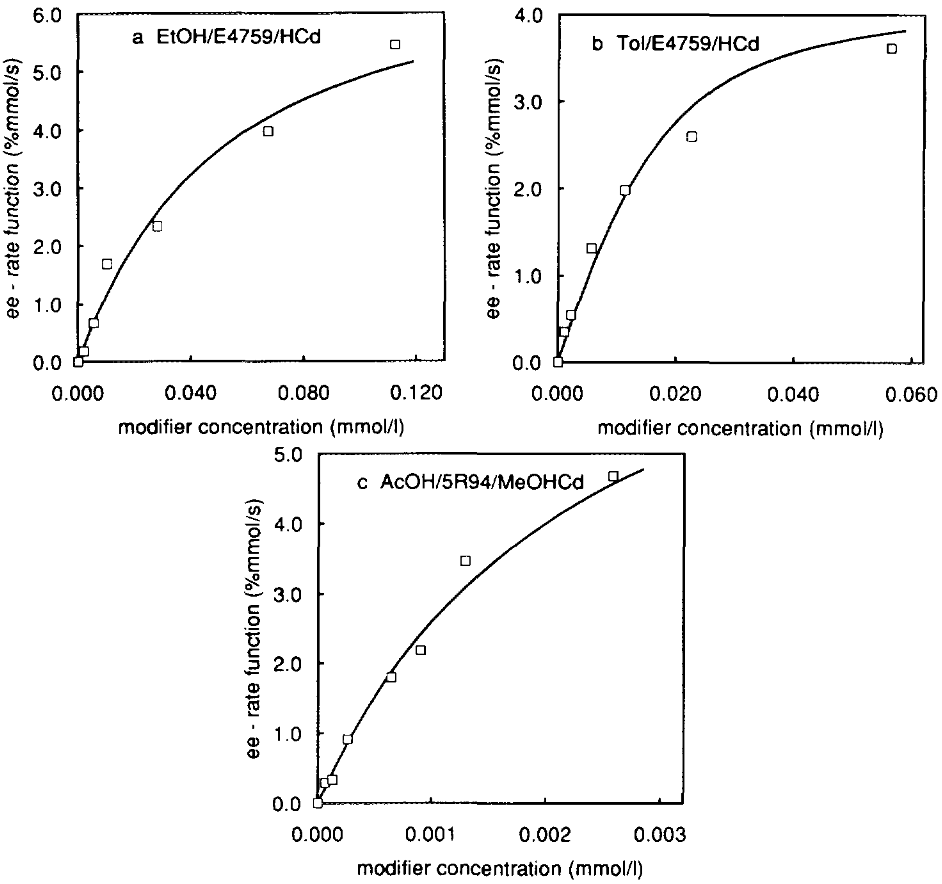

FIG. 2. The function $ee_{obs} \cdot r_{obs}$ versus $[CIN]_{tot}$ for data taken at low modifier concentration for the systems (a) EtOH, E4759, HCd; (b) Tol, E4759, HCd; and (c) AcOH, 5R94, MeOHCd. Experimental data, see Table 1; choice of parameters for the calculated curves, see Table 2.

known, then x_m can be calculated (Eq. (9)) and by assuming a value for ν, the equilibrium constant K_m is obtained (Eq. (13)).

As an example, the initial reaction data obtained in ethanol as solvent at low HCd concentrations are modeled. Figure 3 shows a plot of ee and rate versus the modifier concentration. Clearly, the results for the HCd/E4759 system in ethanol at low HCd concentration are in good agreement with a simple two-site mechanism. However, for the other two data series a good fit is obtained only at very low modifier concentrations. At higher modifier concentrations, the experimental points start to deviate from the predicted curve.

Calculation of the Dependence of Rate and Optical Yield on the Modifier Concentration in the Context of a "Three-Site Model"

As pointed out above, at high modifier concentrations the observed rate and ee values are no longer in agreement with a simple two-site catalytic model. This could be due to the occurrence of a second mode of adsorption of the modifier, i.e., the formation of a second type of modified site with different catalytic properties. Models are developed for two simple cases. In the first case, we assume that all sites are modifiable, i.e., $(x_m)_{max} = 1$, and that a second cinchona molecule can adsorb on an already modified site

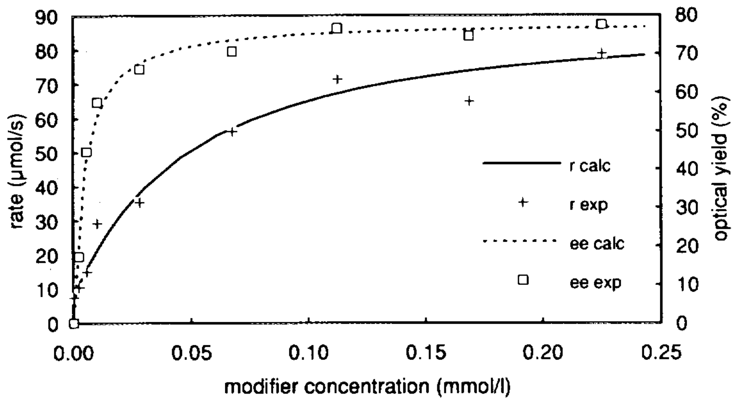

FIG. 3. Plot of optical yield and rate versus modifier concentration for the system EtOH, HCd, E4759. Experimental data, see Table 1; choice of parameters, see Table 2.

(multilayer adsorption). In the second case, it is assumed that the platinum surface is composed of two types of Pt atoms with different adsorption constants and different catalytic properties. The following nomenclature is used. The modified active sites are Pt_m and Pt_{m_2}, with adsorption constants K_m and K_{m_2}, rate constants k_m and k_{m_2} and selectivities s and s_2, respectively. The mass balance for surface Pt is $Pt_{surf} = Pt_u + Pt_m + Pt_{m_2}$ and the degree of modification is defined as $x_m = Pt_m/Pt_{surf}$ and $x_{m_2} = Pt_{m_2}/Pt_{surf}$. Then it is possible to calculate r_{obs} and ee_{obs} using

$$r_{obs} = [(1 - x_m - x_{m_2})k_u + x_m k_m + x_{m_2} k_{m_2}]Pt_{surf} \quad (14)$$

$$ee_{obs} = [(100(2s - 1)x_m k_m + 100(2s_2 - 1)x_{m_2} k_{m_2})Pt_{surf}]/r_{obs} \quad (15)$$

TABLE 2

Value of Parameters Used for Calculating the Theoretical Curves in Figs. 2–5

	EtOH, HCd, E4759	Tol, HCd, E4759	AcOH, MeOHCd, 5R94
s	0.89	0.905	0.98
s_2	—	0.825	0.97
k_u (s^{-1})	1.3	0.9	1.1
k_m (s^{-1})	14.6	8.0	345
k_{m_2} (s^{-1})	—	5.9	25
K_m (mol^{-1})	25,000	170,000	450,000
K_{m_2} (mol^{-1})	—	500	4000
$(x_m)_{max}$	1	1	0.1
$(x_{m_2})_{max}$	—	1	0.9

The constraints for the two cases differ. In the first case, Pt_{m_2} represents doubly modified sites and therefore x_m decreases as x_{m_2} increases. The two equilibria are coupled but it is plausible to assume that further adsorption occurs only when most of the Pt surface has been modified. In the second case, x_m and x_{m_2} are independent of each other and asymptotically reach their maximum values, albeit at different modifier concentrations. The two equilibria are separable and defined as $K_m = x_m/[(x_m)_{max} - x_m][CIN]_{soln}$ and $K_{m_2} = x_{m_2}/[(x_{m_2})_{max} - x_{m_2}][CIN]_{soln}$. Both models can describe the changes observed for the optical yields and also the increases in rate as more and more modifier is present. However, a decrease in rate can only be understood if we assume that the number of the sites with high activity decreases.

We have applied the assumption of double modification to the experiments with the HCd/E4759 system in toluene. Figure 4 shows that it is indeed possible to simulate the experimental results using a three-site model. Due to the large variation of the modifier concentration a better representation of the fit between observed points and the calculated curve is achieved plotting r_{obs} and ee_{obs} vs log[CIN].

In acetic acid, the second model charac-

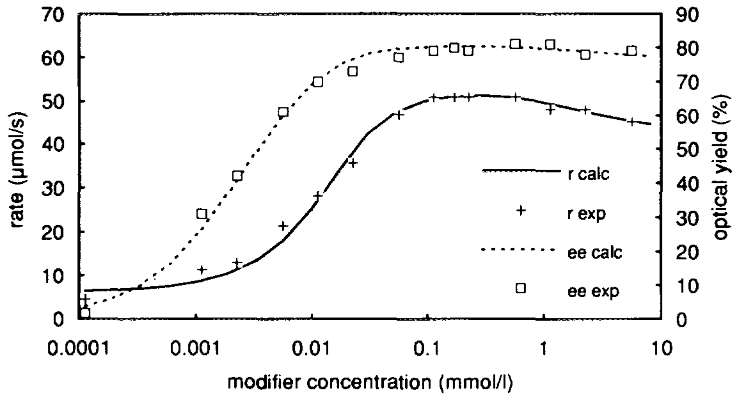

FIG. 4. Plot of optical yield and rate versus the logarithm of the modifier concentration for the system Tol, HCd, E4759. Experimental data, see Table 1; choice of parameters, see Table 2.

terized by two types of Pt_{surf} was used. In this system, quite high r_{obs} and ee_{obs} are obtained with extremely small amounts of modifier, far too little modifier if every Pt_{surf} were modifiable. Therefore, in order to calculate a meaningful equilibrium constant K_m and obtain a reasonable fit of the data (see Fig. 5), we have assumed that $(x_m)_{max} \leq 0.2$. It is possible to obtain a similar fit using a variant of the first case, by assuming $(x_m)_{max} \leq 0.2$ and double modification of these sites at higher modifier concentration.

DISCUSSION

As pointed out in our previous communication (*4*), the concept of ligand-accelerated catalysis which was originally proposed for homogeneous catalysts (*1*) can also be used when the catalytically active site is part of a metal surface. In the following discussion some additional aspects concerning the development of kinetic models for the modification of heterogeneous catalysts are examined.

Dependence of the degree of surface modification on modifier concentration. For the case of a chiral modifier it is possible to show that there exists a simple linear relationship between the degree of modification, i.e., the fraction of active sites covered by modifier, and the product of ee and rate *as long as we accept the assumption that only*

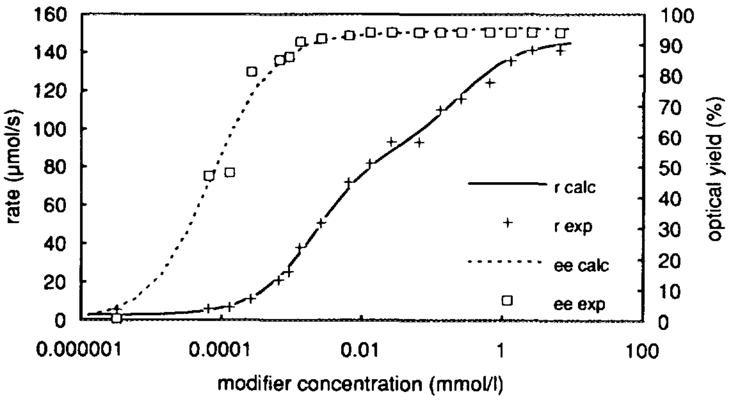

FIG. 5. Plot of optical yield and rate versus the logarithm of the modifier concentration for the system AcOH, MeOHCd, 5R94. Experimental data, see Table 1; choice of parameters, see Table 2.

modified sites can induce chirality. The fact that a simple Langmuir-type adsorption isotherm describes the behavior of all three systems is in excellent agreement with the proposed reversible adsorption of the cinchona modifiers. This hypothesis receives further support from the observation that the absolute configuration of the produced lactate can be influenced by the addition of a cinchona modifier of opposite inducing power to the reaction solution of an already modified catalyst (*10*). Irreversible adsorption of the modifier would lead to a linear dependence of the degree of modification on modifier concentration. In this case, addition of a different modifier to the reaction solution with an already modified catalyst would not affect the resulting ee. Still another dependence of the degree of modification on modifier concentration would be predicted if well ordered arrays (*11*, *12*) of adsorbed modifier were responsible for enantioselectivity. A simple statistical analysis shows that the probability of array formation is very low at low coverage and then increases rapidly when more and more sites are occupied. Assuming a reversible adsorption, an S-shaped curve for the function of x_{array} vs [mod] would result.

Relationship between the degree of modification and surface coverage. In the simplest case, when every surface platinum atom is active and modifiable, the degree of modification x is equal to the classical surface coverage θ; this means that $(x_{\text{m}})_{\text{max}} = 1$. Simple geometrical considerations with respect to the dimensions of pores, crystallites and modifier molecules and also the heterogeneous nature of the Pt surface make this simple case improbable. Since it is not possible in general to determine $(x_{\text{m}})_{\text{max}}$, all surface platinum atoms are considered equally accessible for CO (determination of Pt surface area) and for modification by the cinchona modifier. It is important to note that the true intrinsic selectivity of the modified catalyst can only be determined if $(x_{\text{m}})_{\text{max}}$ can be established independently. As described above, for the case of the third series it is no longer feasible to assume that $(x_{\text{m}})_{\text{max}} = 1$. The observed ee and rate curves can only be modeled correctly if we assume that at most 20% of the surface Pt atoms are accessible to the modifier. At the moment it is not clear whether this difference is due to the modifier, the solvent or the catalyst used. In a previous investigation, a large number of supported platinum catalysts were tested for the enantioselective hydrogenation of ethyl pyruvate using HCd as modifier (*13*). These catalysts differed in their metal loading, dispersion, the support used, the method of reduction, etc. The resulting rates and ee values showed a distinct if somewhat weak interrelationship, in agreement with our two-site model, and it was proposed that this might be due to a difference in $(x_{\text{m}})_{\text{max}}$.

The three-site model. The phenomena observed at very high modifier concentrations were at first somewhat puzzling. However, it is possible to describe the behavior of the catalytic system also for this concentration region with a very simple extension of the two-site model. A decrease of the optical yields at high modifier concentration has also been described for the enantioselective hydrogenation of β-ketoesters using alanine-modified Ni catalysts (*12*) and for enantioselective electrochemical reductions using Hg electrodes modified with various alkaloids (*14–16*). Whereas for the Ni catalyst a different mode of action was proposed, the phenomena observed for modified electrodes were analogously explained in terms of reversible adsorption. Applying our three-site model, it is indeed possible to calculate theoretical curves for the dependence of the observed ee values on the alkaloid concentration with a rather good fit.

Comments concerning our modeling assumptions. For the sake of simplicity, we have carried out most calculations assuming that the Pt surface is entirely modifiable, $(x_{\text{m}})_{\text{max}} = 1$, that all Pt atoms are active for hydrogenation, and that no further adsorption effects occur. Applying simple geometrical considerations, the stoichiometric factor ν, which cannot be determined experimentally, was estimated to be 15. If any of these assumptions are modified, the values for k_u and k_m, and for K_m will change accordingly. For example, it has been shown that the hydrogenation activity of a Pt/Al_2O_3–HCd system was suppressed when about 6% of the surface was blocked by Sn-alkyl species (*17*). If we assume that only 6% of the surface Pt atoms are active for hydrogenation, k_u would increase by a factor of 16.6. Assuming only 6% of the surface to be modifiable would similarly affect the values of k_m and K_m.

In both toluene and acetic acid, the adsorption phenomena occur in two distinct concentration regions. Therefore, it was possible to obtain good initial estimates of k_m, s, and K_m from the data at low modifier concentration. It was then relatively straightforward to fit the curves for the entire concentration region by varying k_{m_2}, s_2, and K_{m_2}. In both cases, the second adsorption constant is a factor of about 500–2000 smaller than K_m. The introduction of a second mode of adsorption does not change our basic mechanistic picture concerning surface modification.

Some mechanistic considerations. Any mechanistic model must be able to explain the observed behavior of reaction rate and enantioselectivity under varying modifier concentration. The fact that full modification is reached at very low modifier concentation strongly suggests that the critical activated complex is formed on the Pt surface. This argues against an important effect of interactions between ethyl pyruvate and modifier in solution on rate and enantioselectivity as proposed by Margitfalvi *et al.* (*10*). The interdependence observed for ee and rate can best be explained if under the present reaction conditions the rate and selectivity determining steps are the same. From the values of r_{obs} and ee_{obs} it is trivial to calculate the rate of formation of the R and S enantiomer, respectively ($r_R = (r \cdot ee/100 + r)/2$). If the values for the unmodified and modified catalysts are compared, we note that with the exception of case 3 at high [CIN], it is only the formation of the R-enantiomer that is accelerated by the modifier. It follows that there is a very specific interaction between the adsorbed cinchona alkaloid and the α-ketoester (or a reaction intermediate). An unspecific acceleration by hydrogen bonding as discussed by Webb and Wells (*12*) cannot explain the observed enantioselectivity. It must be stressed that for the platinum cinchona system there is no structural information available that would allow the proposal of a detailed mechanism which is more than educated speculation.

CONCLUSIONS

The present study contributes to the understanding of the modification of heterogeneous catalysts by organic modifiers (or promoters, inhibitors), an important strategy to influence the selectivity of a given catalyst. The application of a *chiral* modifier allows the study of some aspects of modification which are otherwise difficult to assess. The results for the enantioselective hydrogenation of ethyl pyruvate are in excellent agreement with the notion that the modifier must be adsorbed on the metal surface of the catalyst in order to be effective. It is generally agreed that enantiodiscrimination is only possible if the modifier is in very close proximity to the reactants in the product determining step. From this we infer that the *direct interaction of the reactants and the modifier at the active site* is an important mode of action for inhibitors and promoters.

ACKNOWLEDGMENT

We thank Dr. Martin Studer for helpful discussions and a critical review of the manuscript.

REFERENCES

1. Jacobsen, E. N., Marko, I., Mungall, W. S., Schröder, G., and Sharpless, K. B., *J. Am. Chem. Soc.* **110,** 1968 (1988); Jacobsen, E. N., Marko, I., France, M. B., Svendsen, J. S., and Sharpless, K. B., *J. Am. Chem. Soc.* **111,** 737 (1989).

2. Blaser, H. U., Jalett, H. P., Monti, D. M., Reber, J. F., and Wehrli, J. T., *Stud. Surf. Sci. Catal.* **41,** 153 (1988).

3. Sutherland, I. M., Ibbotson, A., Moyes, R. B., and Wells, P. B., *J. Catal.* **125,** 77 (1990).
4. Garland, M., and Blaser, H. U., *J. Am. Chem. Soc.* **112,** 7048 (1990).
5. Blaser, H. U., Jalett, H. P., and Wiehl, J., *J. Mol. Catal.* **68,** 215 (1991).
6. Bond, G., Simons, K. E., Ibbotson, A. Wells, P. B., and Whan, D. A., *Catal. Today* **12,** 421 (1992).
7. Spencer, M. S., personal communication
8. A preliminary account of part of this work has appeared: Garland, M., Jalett, H. P., and Blaser, H. U., *Prepr. Pap. Am. Chem. Soc. Div. Fuel Chem.* **37,** 320 (1992).
9. Blaser, H. U., Jalett, H. P., Monti, D. M., Baiker, A., and Wehrli, J. T., *Stud. Surf. Sci. Catal.* **67,** 147 (1991).
10. Margitfalvi, J. L., Marti, P., Baiker, A., Botz, L., and Sticher O., *Catal. Lett.* **6,** 281 (1990); Margitfalvi, J. L., Minder, B., Talas, E., Botz, L. and Baiker, A., *in* "Proceedings, 10th International Congress on Catalysis, Budapest, 1992" (L. Guczi, F. Solymosi, and P. Tétényi, Eds.), p. 2471. Akadémiai Kiadó, Budapest, 1993.
11. Thomas, J., *Angew. Chem. Adv. Mater.* **101,** 1105 (1989).
12. Webb, G., and Wells, P. B., *Catal. Today* **12,** 319 (1992).
13. Wehrli, J. T., Baiker, A., Monti, D. M., and Blaser, H. U., *J. Mol. Catal.* **61,** 207 (1990).
14. Schoo, N., and Schäfer, H. J., *in* "Dechema-Monographien," Vol. 125, p. 815. VCH Verlagsgesellschaft, 1992.
15. Kopilov, J., Kariv, E., and Miller, L. L., *J. Am. Chem. Soc.* **99,** 3450 (1977).
16. Joubault, M., *J. Chem. Soc. Chem. Commun.*, 953 (1980).
17. Margitfalvi, J. L., Jalett, H. P., Talas, E., Baiker, A., and Blaser, H. U., *Catal. Lett.* **10,** 325 (1991).