ELSEVIER

Journal of Molecular Catalysis A: Chemical 112 (1996) 93–104

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

Enantioselective heterogeneous catalysis. 2. [1] Examination of the formation of the individual (R) and (S) lactates in the cinchonidine modified platinum hydrogenation of pyruvate

Robert L. Augustine *, Setrak K. Tanielyan

Department of Chemistry, Seton Hall University, South Orange, NJ 07079, USA

Received 15 November 1995; accepted 13 May 1996

Abstract

The formation of the individual (R) and (S) lactates was measured during the dihydrocinchonidine modified platinum catalyzed hydrogenation of ethyl pyruvate at atmospheric pressure in a methyl acetate solvent. It was found that the product ee increased during the initial phase of the reaction. Plotting the amount of each enantiomer formed in one minute intervals against reaction time showed clearly that, as previously suggested, this reaction proceeds through an initial stage characterized by a significant increase in ee followed by a period of essentially stable ee. When (R) methyl lactate was added as a co-modifier with the dihydrocinchonidine, the production of (R) ethyl lactate decreased somewhat and the incremental changes observed during the first ten minutes of the reaction were less than those seen in the absence of the (R) methyl lactate co-modifier. With (S) methyl lactate as the co-modifier, the production of (R) ethyl lactate decreased significantly and the incremental changes were markedly different from those observed in the absence of a co-modifier. The production of (S) ethyl lactate was affected only slightly by the presence of either (R) or (S) methyl lactate as the co-modifier.

Keywords: Enantioselective hydrogenation; Pyruvate hydrogenation; Cinchona alkaloid modifiers

1. Introduction

Enantioselective heterogeneous catalysis has received considerable attention in recent years because of its potential impact on the synthesis of chiral pharmaceuticals and agrochemicals. Most recently the enantioselective hydrogenation of α keto esters over cinchona alkaloid modified platinum catalysts has been extensively studied to try to develop an understanding of the catalyst–modifier–substrate interactions occurring during the reaction [1–12]. Such information is needed to produce effective chiral catalyst systems which can be used to promote other reactions.

Several important observations have emerged from this work. One of the earliest was that the cinchona alkaloid modifier not only promoted enantioselectivity in the reaction but it also increased the rate of the hydrogenation as compared to the unmodified reaction [3,10,13]. Some

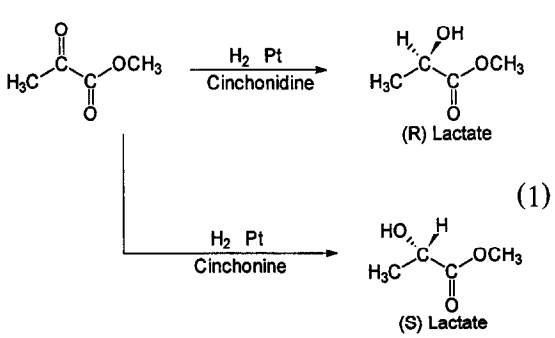
* Corresponding author.

[1] For Part 1, see [1].

1381-1169/96/$15.00 Copyright © 1996 Elsevier Science B.V. All rights reserved.

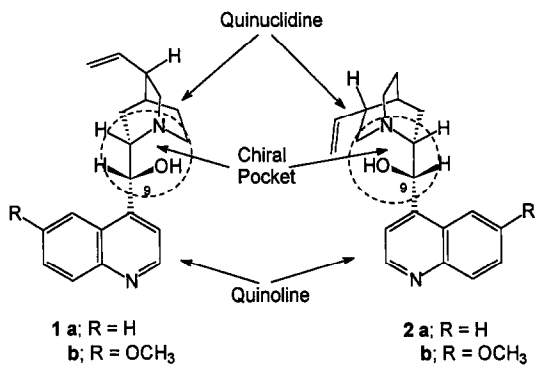
PII S1381-1169(96)00228-2

evidence has been reported for the interaction of the cinchonidine and pyruvate in solution before adsorption on the catalyst surface [14] but the generally accepted concept, at present, is that the alkaloid is adsorbed on the catalyst surface to provide a chiral environment near an active surface site and that there is an interaction between a molecule of the keto ester and an adsorbed alkaloid modifier which directs the addition of hydrogen to the keto group to give a specific lactate enantiomer [1,4,10]. The (R) lactate is produced using cinchonidine, **1a**, or quinine, **1b**, while (S) lactate is formed when cinchonine, **2a**, or quinidine, **2b**, is used as the modifier (Eq. (1)). That this interaction is also responsible for the increase in hydrogenation rate is also generally accepted. It has been proposed that the rate increase is caused by stabilizing the half-hydrogenated species by hydrogen-bonding to the quinuclidine nitrogen of the alkaloid [13]. Others have suggested that the rate increase is the result of an interaction between the quinuclidine nitrogen and the electron deficient carbonyl carbon which would weaken the C–O double bond and, thereby, accelerate the hydrogenation [1,10]. This later view has been supported by ab initio and semiempirical calculations of the 'complex' between pyruvate and either ammonia or the quinuclidine nitrogen of cinchonidine [15–17]. These calculations show that such an interaction can be taking place. The hydrogen-bonding concept, however, cannot be dismissed since its presence is logical once the transfer of the first hydrogen atom from the catalyst to the keto-oxygen takes place.



(1)

In any event, as depicted in structures **1** and **2**, the 'chiral pocket' of the cinchona alkaloid centers on the quinuclidine nitrogen but the C_9 oxygen is also involved to some extent. When the C_9–OH was replaced by an $-OCH_3$ group the enantioselectivity of the reaction was essentially unchanged, but removal of this oxygen resulted in a near 50% decrease in product ee [18].



We had originally proposed a working model for the catalyst–modifier–substrate interaction which involved an edge-on adsorption of the alkaloid molecule onto the platinum surface through the quinoline nitrogen [1]. Recent work, however has shown that chiral modifiers having an amino-alcohol function similar to that in cinchonidine but which were attached to either a naphthalene or a quinoline ring, were also effective. Little difference was noted between species containing the naphthalene or the quinoline ring [19–22]. Further, energy minimum calculations on cinchonidine indicate that the preferred conformation of this molecule is one in which the chiral pocket is nearly perpendicular to the plane of the quinoline ring so a planar adsorption on the catalyst surface can still provide a chiral environment around the active sites [4]. This latter information is particularly important since it has been shown that the hydrogenation of pyruvates, with or without the alkaloid modifier, takes place on the coordinately unsaturated corner atoms or adatoms on the metal surface [1].

We have recently reported that with reactions run under the more commonly used conditions of higher reaction pressure and higher alkaloid concentrations the product ee is not constant throughout the entire reaction [23]. In the dihydrocinchonidine modified platinum catalyzed hydrogenation of ethyl pyruvate the product ee increased considerably during the first 25–30% of the reaction and then remained relatively constant until the reaction was completed [23]. It appears that the overall reaction is composed of two regimes. One, in the early stages of the reaction, is distinguished by this increase in product ee while the second, in the later stages of the reaction, has a more constant product ee. We felt that this initial change in product ee could possibly be used to understand the interactions taking place between the modifier and substrate on the catalyst surface. We were also interested in the fact that at higher hydrogen pressures and cinchonidine concentrations a steady product ee was not observed until the reaction was more than 25% completed while in reactions run under one atmosphere of hydrogen and lower substrate and alkaloid concentrations the product ee was essentially constant from 10% completion through the rest of the reaction [1].

With these factors in mind we decided to examine the formation of the individual (R) and (S) lactates produced on hydrogenation of ethyl pyruvate over cinchonidine modified platinum catalysts to see whether this information might provide a better understanding of the various aspects of this reaction.

2. Experimental

The experimental details of the reaction procedure have been described. The catalyst used was a 4.9% Pt/SiO_2 prepared by ion exchange [24]. The standard reaction conditions involved placing 10 mg of the catalyst in 15 mL of purified methyl acetate into a 25 mL Erlenmeyer flask which was used as a reactor. This mixture was stirred under one atmosphere of hydrogen for 15 min with the temperature held at 25 ± 0.1°C. A standard solution containing 2 mg of purified dihydrocinchonidine in methyl acetate was then injected into the reactor through a septum and stirring under hydrogen was continued for another 15 min. Ethyl pyruvate (0.25 mL, 2.25 mmol) was then added through a septum and measurement of hydrogen consumption was begun using an automated apparatus [25]. Samples (0.05 mL) of the reaction mixture were extracted after every 1.2 mL of hydrogen uptake (about 2% conversion) and analyzed by gas chromatography using a Chiraldex B–TA chiral column as previously described [1]. All components of the reaction mixture were completely separated under the conditions used. At higher conversions the samples were taken at longer intervals.

The enantiomeric excess (ee) of each sample was calculated using the equation

$$ee = ((R - S)/(R + S))^{*} 100.$$

The incremental changes in the (R) and (S) lactates were calculated from data points generated from the equation obtained using a curve fit algorithm.

When used as co-modifiers, (R) or (S) *methyl* lactate (0.45 mmol) was added to the reaction mixture after the catalyst had been stirred with the alkaloid but before the introduction of the *ethyl* pyruvate. The gc analytical procedure permitted the complete separation of the *methyl* lactate and *ethyl* lactate enantiomers so the calculated product ee was only that of the *ethyl* lactate produced by the hydrogenation of *ethyl* pyruvate.

The effect of agitation on the reaction rate and product ee was determined using a 1/4″ × 7/8″ magnetic stirring bar inside a 25 mL Erlenmeyer. The stirring bar was driven by a variable speed 1/10 hp motor with a magnetic head. The speed of the motor was measured using a digital tachometer.

3. Results and discussion

Most of the previous work in this area used reaction conditions and catalyst pretreatment procedures which were designed primarily for optimizing product ee [2–10]. We felt, however, that many of these reaction parameters were not those which would be effective for understanding the catalyst–modifier–substrate interaction that is critical to any rational development of alternate catalyst systems. In the first place most of the earlier work involved the hydrogenation of high concentrations of substrate, usually about 2 M but frequently higher and, at times, even neat pyruvate. With this high substrate concentration, the reaction kinetics are almost certainly in the saturation region as shown by the near zero order in substrate which has been reported for reactions run using these high concentrations [26]. In our standard procedure we used a 0.15 M pyruvate concentration, one that is about ten times more dilute than those commonly reported.

Others have commonly used higher hydrogen pressures, usually at least ten atmospheres, since it has been shown that product ee increases with increasing hydrogen pressure. However, we found it more convenient to sample the reaction mixture when the hydrogenation was run at atmospheric pressure.

A third deviation from the commonly used procedure involved the solvent used in the reaction. Other workers have used alcohols, benzene and toluene as solvents [2–10]. These materials, however, have been shown to have a strong interaction with platinum and palladium [27,28] so they could interfere with the adsorption of the substrate and/or modifier on the catalyst surface. A better indication of the nature of the catalyst–modifier–substrate interaction would probably be obtained by using a solvent which had a minimal ability to adsorb on the catalyst and, thus, not compete with the adsorption of the modifier or the substrate. The ideal solvent would be a hydrocarbon as these species have been shown to have virtually no interaction with platinum or palladium at room temperature, [27,28] but these materials do not readily dissolve the alkaloid modifier. Methyl acetate was selected as our standard solvent because it dissolves both the alkaloid modifiers and the pyruvate and it was shown to adsorb only slightly on the catalyst [28] and, thus, would have little tendency to interfere with the adsorption of the substrate and/or the modifier.

In our previous paper describing the more mild reaction conditions we showed that the enantioselective hydrogenation of ethyl pyruvate was first order in catalyst [1]. This and the apparent activation energy data established that the reactions reported there were not run under any hydrogen diffusion limitation. It has been shown that with other reaction conditions the product ee was lowered for reactions run under mass transport limiting conditions [23,29]. To be more certain of our rate and ee data we first had to establish conditions which were outside the diffusion regime. Increasing the stirring rate in the reactor resulted in an increase in the rate of hydrogen uptake during pyruvate hydrogenation up to about 800 rpm. With faster stirring the reaction rate remained constant. The product ee did not change when the reaction was run using stirring speeds of 600 rpm and higher. With these data in hand we selected a stirring speed of 900 rpm for all reactions.

The next parameter needing standardization was the optimum dihydro-cinchonidine–platinum ratio for the 4.9% Pt/SiO_2 catalyst. We found that the reaction rate went through a maximum at a dihydrocinchonidine–platinum ratio of 0.4 molecule of alkaloid per platinum atom in the catalyst sample. This value was selected as the standard for this study. Since the catalyst had a dispersion of 0.4, this corresponded to a 1:1 molar ratio between the cinchonidine molecules and the surface atoms on the catalyst. However, the large size of the modifier precludes this stoichiometry so some of the alkaloid must also be adsorbed on the catalyst support. UV examination of the supernatant liquid showed that the cinchonidine, if

present in solution, was there in a concentration too low to be detected. This would seem to preclude any appreciable contribution to the reaction from a modifier–substrate species formed in solution and then adsorbing on the catalyst [14].

The presence of oxygen on the catalyst was also shown to have an effect on the reaction rate and product ee [30] so the hydrogenations were run using a catalyst which had been re-reduced in flowing hydrogen at 380°C for two hours.

Small aliquots of the reaction mixture were extracted at intervals corresponding to about a two percent increase in conversion in the initial stages of the hydrogenation and at longer intervals during the later phases of the reaction. Chiral gc analysis of these aliquots gave the exact amounts of the (R) and (S) lactates and the starting pyruvate which were present in each sample. The hydrogen uptake data corresponded with the decrease in pyruvate concentration and the increase in lactate formation. Fig. 1a (curve 1) shows the hydrogen uptake for a pyruvate hydrogenation run over dihydrocinchonidine modified freshly reduced Pt/SiO_2. (R) Ethyl lactate was preferentially formed with an ee of 55% at 50% conversion. Curves showing the extent of formation of both the (R) and (S) lactates with time are also shown in Fig. 1a. The change in product ee with the extent of hydrogenation [23] is shown in Fig. 1b. It was considered that such a change could have been caused by the initial formation of a significant amount of (S) lactate followed by the formation of the product at a constant R–S ratio. To determine whether this may be happening, the incremental amounts of both the (R) and (S) lactates which were formed over one minute intervals were calculated using equations derived from curve fit algorithms (Fig. 2a). These data clearly show the two stages of this reaction. Initially, (R) lactate production increases significantly, goes through a maximum and then, eventually levels off in a steady decline in the second stage. The (S) lactate, on the other hand, shows a somewhat steeper decline in the initial state than is

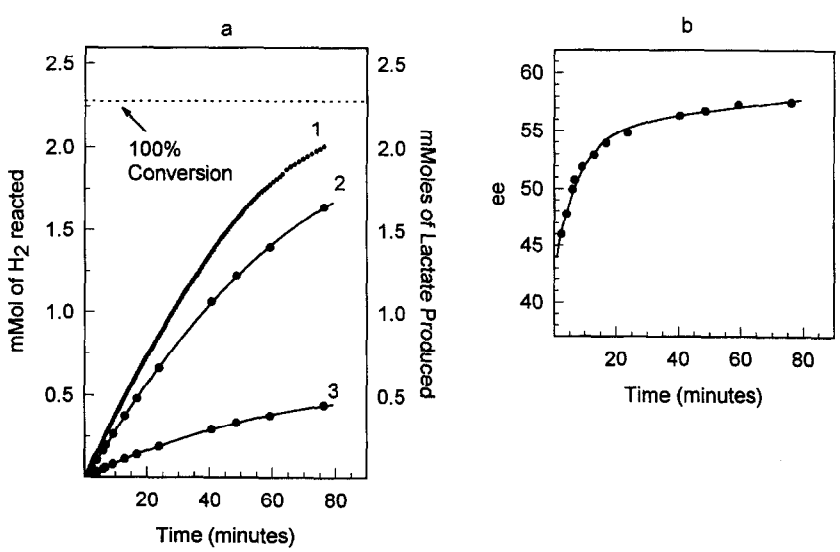


Fig. 1. (a) Hydrogen uptake for the ethyl pyruvate hydrogenation over a dihydrocinchonidine modified platinum catalyst (curve 1); extent of formation of (R) ethyl lactate (curve 2); extent of formation of (S) ethyl lactate (curve 3). The solid lines represent the fitted curve from which the incremental data in Fig. 2a were calculated. (b) Changes in ee observed during the course of ethyl pyruvate hydrogenation over a dihydrocinchonidine modified platinum catalyst.

observed in the final stage of the reaction. The combination of these changes produce the initial rise in product ee. Fig. 2b shows the incremental ee's calculated from the data in Fig. 2a. This shows that the initial changes in product ee take place somewhat earlier than is indicated by the data in Fig. 1b. The rise in the incremental ee toward the end of the reaction is due to the non-proportional decrease in the incremental (R) and (S) lactate formation during the second stage of the reaction. Over the last sixty minutes of the reaction the size of the (R) lactate increments decrease by 59% while the size of the (S) lactate increments decrease by 65%.

It has been reported that the addition of racemic methyl lactate to the reaction mixture before the pyruvate was introduced resulted in a reduction of the hydrogenation rate of nearly 50% [26] but inhibition by the individual enantiomers was not reported. In order to examine this inhibition more fully, samples of (R) or (S) lactate were added to the reaction mixture during the catalyst pretreatment procedure. To avoid complications in product analysis, (R) and (S) methyl lactates were used as the auxiliary modifiers. The gas chromatographic procedure used completely separated both the enantiomeric methyl lactates and the ethyl lactates so the ee data obtained was clearly only that produced by the hydrogenation of ethyl pyruvate.

The hydrogen uptake curves for those reactions in which (R) or (S) methyl lactate were added to the reaction mixture are depicted in Fig. 3a. For comparison Fig. 3a also depicts the hydrogen uptake curve for the reaction run without the initial addition of lactate. The reaction having (R) methyl lactate as the co-modifier takes place with about the same initial rate as the standard reaction but after about 30–40% conversion, the rate drops off appreciably. However, when (S) methyl lactate was used as a co-modifier, the reaction rate was slower from the very beginning. Fig. 3b shows the extent of (R) and (S) ethyl lactate formation for hydrogenations run in the presence of (R) or (S) methyl lactate (curves 2 and 3) along with the corresponding data for the hydrogenation run without the initial addition of lactate (curve 1).

As shown by the data in Fig. 4 the changes observed in the product ee's during the course of the reactions were essentially the same for the hydrogenation run in the presence of (R)

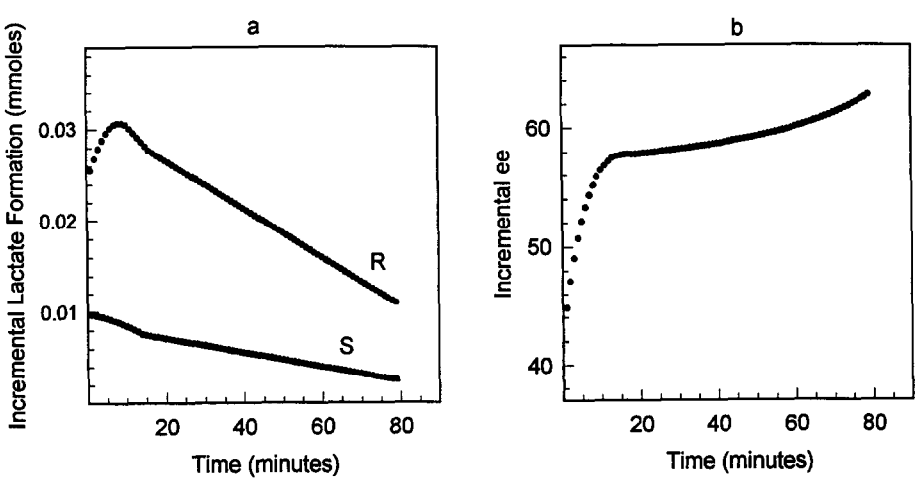


Fig. 2. (a) Incremental amounts of (R) and (S) ethyl lactates formed in one minute intervals. (b) Incremental product ee's calculated from the data in Fig. 2a.

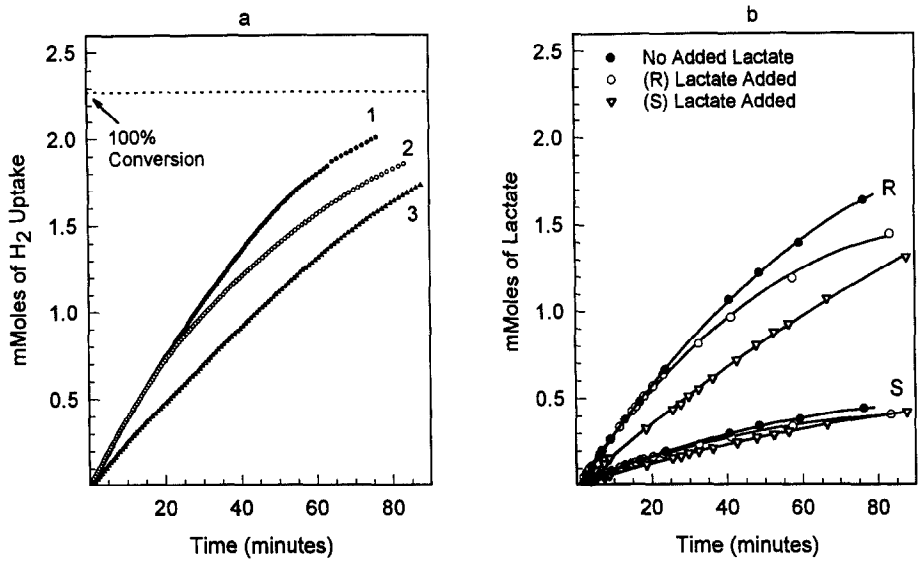


Fig. 3. (a) Hydrogen uptake curves for ethyl pyruvate hydrogenations over dihydrocinchonidine modified platinum catalysts with no added lactate (curve 1), with (R) methyl lactate added as a co-modifier (curve 2) and with (S) methyl lactate added as a co-modifier (curve 3). (b) Formation of (R) and (S) lactates during ethyl pyruvate hydrogenations run over a dihydrocinchonidine modified platinum catalyst with no added lactate, with (R) methyl lactate added as a co-modifier and with (S) methyl lactate added as a co-modifier.

methyl lactate and that run in the absence of any lactate co-modifier. When (S) methyl lactate was added at the start of the reaction the product ee curve was significantly lower.

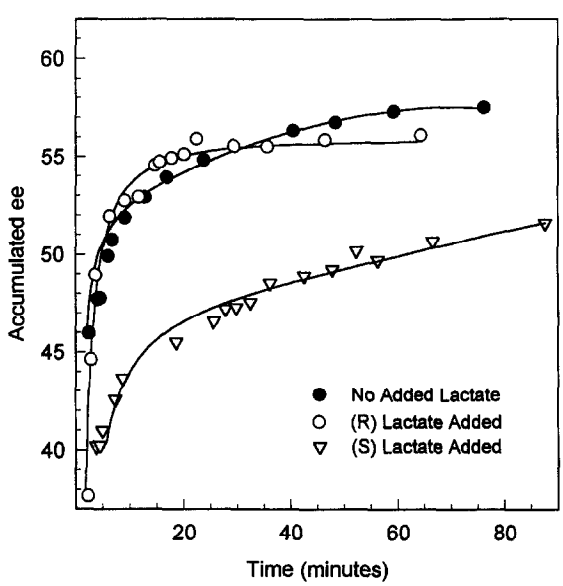


Fig. 4. Changes in ee observed during the course of ethyl pyruvate hydrogenation over dihydrocinchonidine modified platinum catalysts with no added lactate, with (R) methyl lactate added as a co-modifier and with (S) methyl lactate added as a co-modifier.

Fig. 5 depicts the incremental changes in both (R) and (S) ethyl lactate formation with time for the first ten minutes of the reactions run in the absence of any added lactate (Fig. 5a), with the initial addition of (R) methyl lactate (Fig. 5b) and with added(S) methyl lactate (Fig. 5c). Each data point represents the amount of product formed in a one minute interval. The data in Fig. 5a correspond to the first ten data points of Fig. 2a. These data show that with the initial addition of (R) methyl lactate the reaction began with larger increments of (R) ethyl lactate than were observed in the absence of added (R) lactate (Fig. 5a). The incremental changes in (S) ethyl lactate formation were also larger at the beginning of the reaction than those observed in Fig. 5a. The initial addition of (S) methyl lactate (Fig. 5c), however, had a significant effect on the formation of the (R) ethyl lactate but about the same effect on the incremental (S) ethyl lactate formation as did the initial addition of (R) methyl lactate. The results depicted in Figs. 3 and 5 show that the presence of a lactate co-modifier has a significantly greater effect on (R) lactate

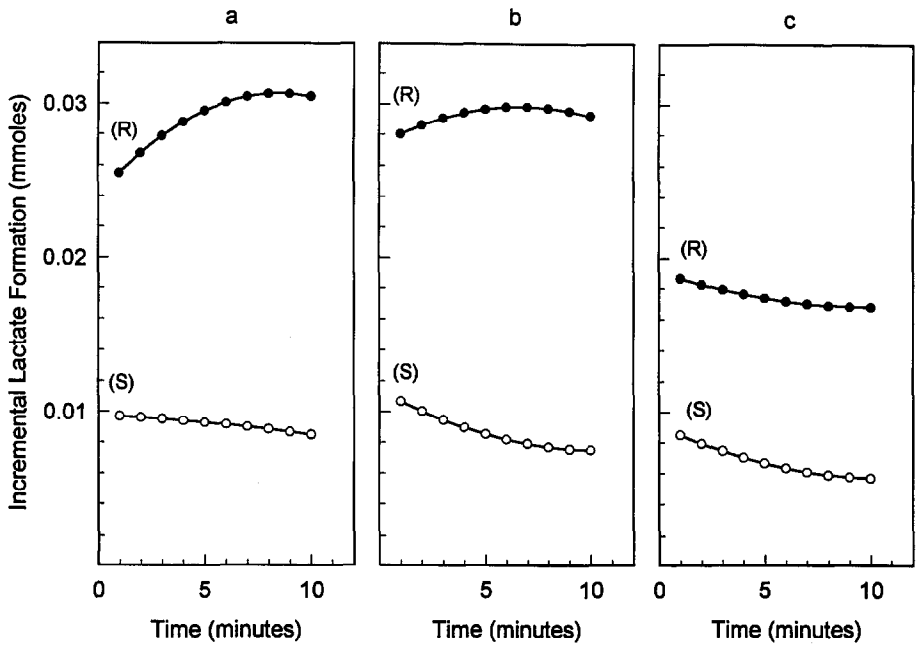
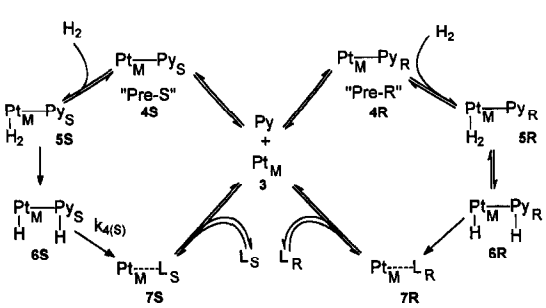


Fig. 5. Incremental changes in (R) and (S) ethyl lactate production over the first ten minutes of the reaction; (a) with no added lactate as a co-modifier, (b) with (R) methyl lactate added as a co-modifier and (c) with (S) methyl lactate added as a co-modifier.

production than on the formation of the (S) enantiomer.

There remains, then, the problem of explaining these observations within a reasonable reaction scheme. This hydrogenation is an example of a kinetically coupled reaction [31–33] in which the intermediates for the formation of both the (R) and (S) lactates are produced from a common chirally modified site as depicted in Scheme 1. The active site, Pt_M, **3**, in this scheme is composed of an active surface platinum atom and the cinchonidine modifier. The pyruvate can adsorb on this site in two ways with one



Scheme 1.

mode leading to the formation of the (R) lactate (Pre-R), **4R**, and the other to the (S) lactate (Pre-S), **4S**. Hydrogen is then adsorbed on the platinum giving **5R** and **5S** followed by hydrogen transfer to the pyruvate to give the half-hydrogenated species, **6R** and **6S**. The second hydrogen transfer produces the adsorbed lactates, **7R** and **7S**. Finally, desorption of the lactates regenerates the modified active site, Pt_M, **3**.

Rationalizing the effect of added (R) or (S) methyl lactate is not straightforward. In both cases (R) ethyl lactate formation is affected much more than the production of (S) ethyl lactate. The preferential impact on (R) ethyl lactate formation could arise from some type of preferred interaction with the Pre-R intermediate, **4R**, or by some reversal of the **7R** ⇌ **3** equilibrium. It is not apparent from the data at hand exactly what is taking place on the catalyst surface during these reactions. It also has to be recognized that Scheme 1 is still only a partial representation of all of the reactions taking place during the cinchonidine modified platinum hy-

drogenation of pyruvate. Obviously, not all active sites on the surface have been modified so there will be some formation of equal amounts of the (R) and (S) lactates on these sites [34,35].

Some proposals have been made concerning the nature of the modified active site on the metal surface. In these the quinoline portion of the alkaloid is considered to be adsorbed in a planar manner on the metal surface with the quinuclidine portion of the molecule forming a chiral pocket into which the pyruvate fits in an enantioselective manner [3,4,22,36]. However, these proposals have the modifier adsorbed on the 111 plane of the platinum with no discussion of how the hydrogen is transferred from the metal to the pyruvate. We have shown, though, that as in the hydrogenation of alkenes and a number of other reactions [37], the hydrogenation of pyruvate over either modified or unmodified platinum takes place on the more coordinately unsaturated corner atoms or adatoms on the platinum surface [1]. Frontier molecular orbital considerations [38,39] indicate that both the hydrogen and the substrate are adsorbed on the same platinum atom [40]. Thus, the alkaloid must be adsorbed on the metal surface in such a way as to provide a chiral environment around these coordinately unsaturated active sites. It has been fairly well established that the quinoline ring is adsorbed on the metal in a planar mode [19–22] and not through the heterocyclic nitrogen as we previously proposed [1]. At first it was thought that this would place the chiral pocket too close to the metal surface to be of influence around an adatom on the face. However, it has been reported that the internuclear C–Pt distance for benzene adsorbed in a planar mode on a 111 platinum surface was about 0.23 nm [41]. As depicted in Fig. 6, this separation between the quinoline ring and the metal surface places the chiral pocket of the alkaloid at the correct height for the pyruvate to adsorb on the active adatom site and still be associated with the alkaloid. The cinchonidine is pictured having the calculated minimum energy conformation [4].

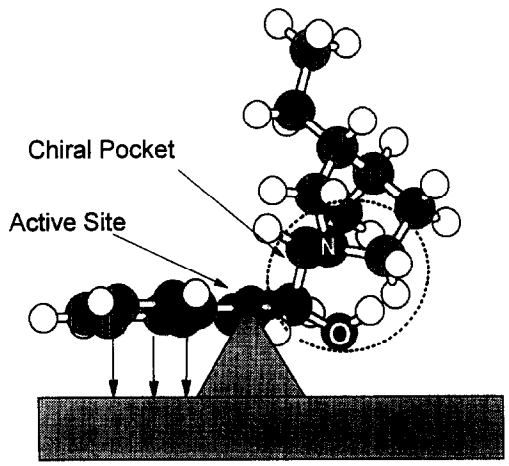


Fig. 6. Depiction of the planar adsorption mode for the quinoline portion of dihydrocinchonidine showing the proximity of the chiral pocket to an adatom active site.

To complete this picture it is necessary to describe the Pre-R and Pre-S interactions between the cinchonidine and the pyruvate. It is widely accepted that this association incorporates some interaction between the quinuclidine nitrogen and the ketone carbonyl group of the pyruvate. One such interaction is between the electron pair on the nitrogen and the electron deficient carbon atom of the carbonyl group, which, as discussed above would account for the observed increase in hydrogenation rate in these reactions [3,13]. Two other facts are also important here. First, the preferred conformation of the pyruvate is that in which the two carbonyl groups are *trans* to each other. Second, the oxygen of the C_9–OH group of the cinchonidine has an effect on product ee as discussed in the Introduction [18]. This latter aspect can be accommodated by invoking a weak interaction between the electrons on the oxygen and the carbon of the ester carbonyl group (denoted by Y in the right hand structure in Fig. 7), an interaction which occurs during transesterification reactions. This and the interaction between the quinuclidine nitrogen and the carbon of the keto group (denoted by X) form a favorable *pseudo*-six-membered ring between the pyruvate and the alkaloid as depicted in Fig. 7. When this arrangement is present inside the

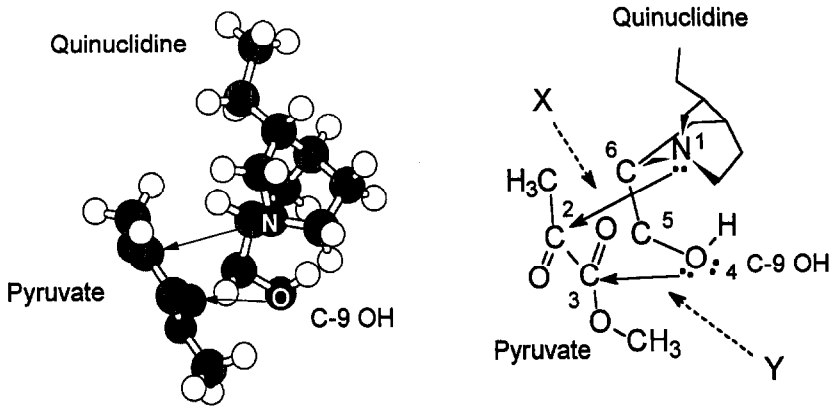


Fig. 7. Depiction of the proposed interaction between dihydrocinchonidine and pyruvate illustrating the formation of a six-membered ring in the intermediate. The quinoline ring of the alkaloid has been omitted for clarity.

chiral pocket shown in Fig. 6, adsorption of the carbonyl group on the active site of the metal can take place.

The orientation of the keto carbonyl group with respect to the metal is also of importance. In Fig. 8 are shown the four possible orientations of the pyruvate which retain the N–C interaction (X). In two of these, the oxygen atom of the carbonyl group is pointing toward the metal surface (Fig. 8a and b) and in the others it is pointing away from the metal (Fig. 8c and d). Examination of models shows, however, that with an adsorption distance between the quinoline ring and the platinum face of about 0.2 nm, [41] those modes having the carbonyl oxygen atom pointing away from the metal surface will place the C–O double bond too far above the active site so adsorption on the metal (denoted by Z) and hydrogen transfer cannot take place. This leaves those configurations (Fig. 8a and b) in which the carbonyl oxygen is facing the metal surface as viable alternatives.

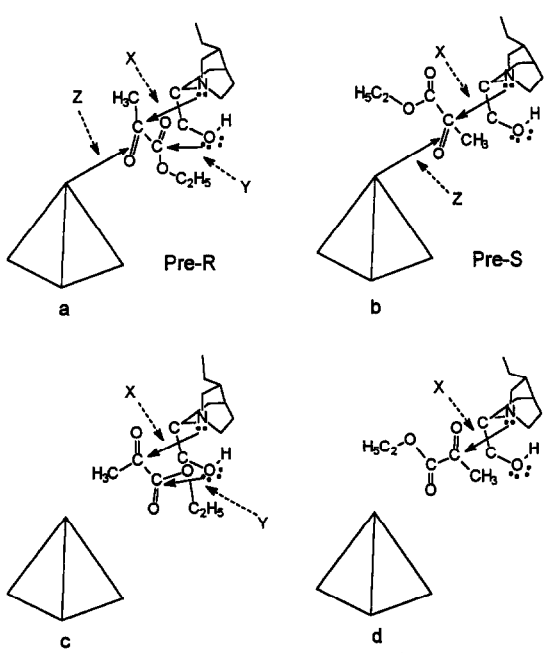


Fig. 8. Four possible modes of interaction between dihydrocinchonidine and pyruvate showing the relationship with an adatom active site. The dihydrocinchonidine structure was simplified as in Fig. 7.

The structure shown in Fig. 8a, with both the N–C and O–C interactions forming a *pseudo*-six-membered ring species, is expected to be formed more favorably than the structure that shown in Fig. 8b in which only the N–C interaction is present. Further hydrogen addition from the active site to the pyruvate in configuration (a) leads to (R) lactate formation while hydrogen addition to configuration (b) gives the (S) enantiomer. Fig. 8a is, thus the Pre-R, **4R**, and Fig. 8b is the Pre-S, **4S**. Fig. 9 shows a depiction of (R) lactate formation using these structural representations for the symbols used in Scheme 1. Hydrogen addition to Pre-R, **4R**, gives the reactive entity, **5R**. The transfer of the first hydrogen produces a half-hydrogenated

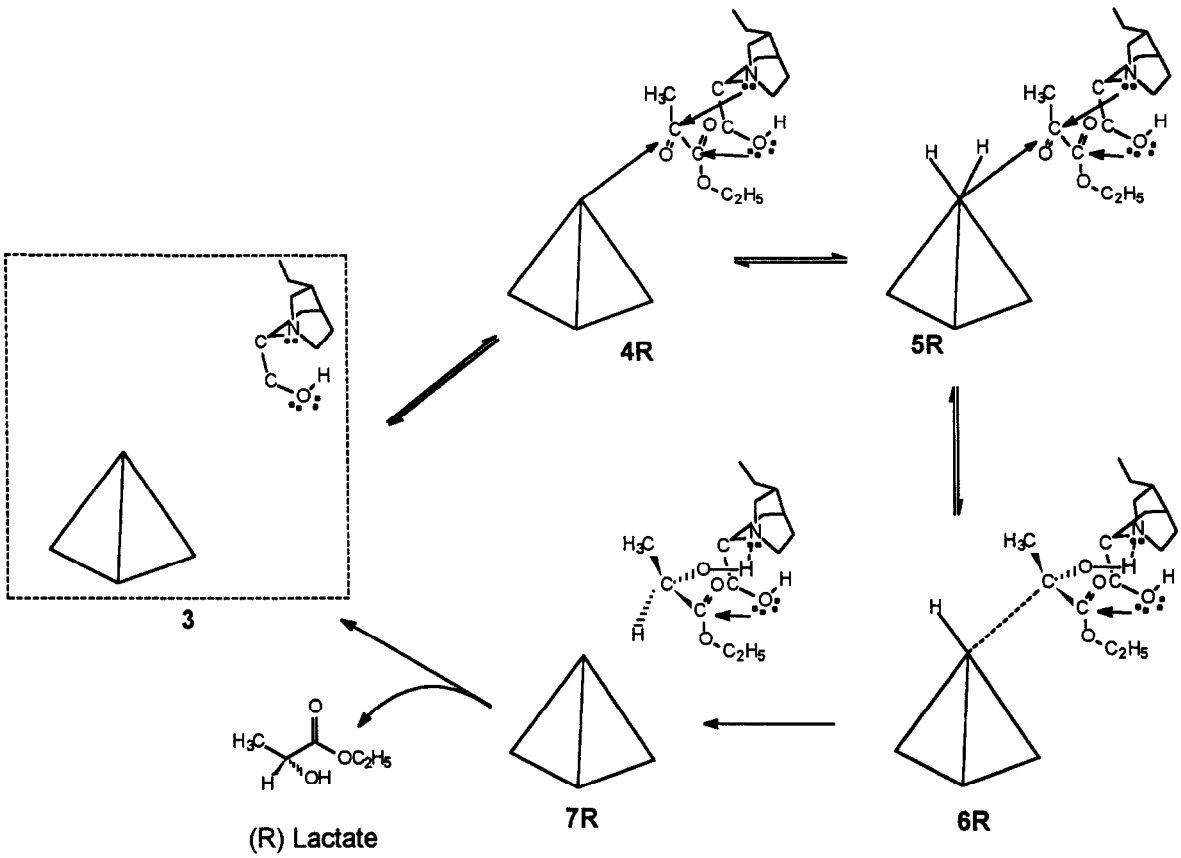


Fig. 9. Proposed mechanism for the formation of (R) lactate over an adatom active site using molecular representations for dihydrocinchonidine and pyruvate.

species, **6R**, in which hydrogen bonding can take place between the quinuclidine nitrogen and the newly formed hydroxy group. Similar hydrogen bonding is also possible with the half-hydrogenated intermediate in the formation of the (S) lactate, but with the (R) intermediate, the O–C interaction provides additional stability to the intermediate, **6R**. Transfer of the second hydrogen gives the adsorbed lactate, **7R**, which then desorbs the (R) lactate and regenerates the active site, **3**.

This proposal explains most of the experimental observations made here and reported in the literature and the molecular representations in Figs. 8 and 9 appear to be reasonable. We are unable at the present time, however, to suggest any molecular arrangements which might be present when either (R) or (S) lactate is added to the reaction mixture as a co-modifier. Obviously, further work is needed to understand this aspect of the reaction.

4. Conclusions

The formation of the individual (R) and (S) lactates was measured during the dihydrocinchonidine modified platinum catalyzed hydrogenation of ethyl pyruvate at atmospheric pressure in a methyl acetate solvent. It was found that the product ee increased during the initial phase of the reaction. Plotting the amount of each enantiomer formed in one minute intervals against reaction time showed clearly that, as previously suggested [23], this reaction proceeds through an initial stage characterized by a sig-

nificant increase in ee followed by a period of essentially stable ee. When (R) methyl lactate was added as a co-modifier with the dihydrocinchonidine, the production of (R) ethyl lactate decreased somewhat and the incremental changes observed during the first ten minutes of the reaction were less than those seen when the co-modifier was absent. With (S) methyl lactate as the co-modifier, the production of (R) ethyl lactate decreased significantly and the incremental changes were markedly different from those observed in the absence of a co-modifier. The production of (S) ethyl lactate was affected only slightly by the presence of either (R) or (S) methyl lactate as a co-modifier.

Acknowledgements

This work was supported by the National Science Foundation under grant No. CTS-9312533. The salt used to prepare the catalyst was supplied by Johnson Matthey through their precious metal loan program.

References

[1] R.L. Augustine, S.K. Tanielyan and L.K. Doyle, Tetrahedron Asymmetry 4 (1993) 1803.
[2] S. Niwa, S. Imai and Y. Orito, Nippon Kagaku Kaishi (1982) 137.
[3] G. Webb and P.B. Wells, Catal. Today 12 (1992) 319.
[4] K.E. Simons, P.A. Meheux, S.P. Griffiths, I.M. Sutherland, P. Johnston, P.B. Wells, A.F. Carley, M.K. Rajumon, M.W. Roberts and A. Ibbotson, Recl. Trav. Chim. Pays-Bas 113 (1994) 465.
[5] K.E. Simmons, A. Ibbotson and P.B. Wells, Spec. Publ. R. Soc. Chem. 114 (Catalysis and Surface Characterisation) (1992) 174.
[6] G. Bond, K.E. Simons, A. Ibbotson, P.B. Wells and D.A. Whan, Catal. Today 12 (1992) 421.
[7] J.T. Wehrli, A. Baiker, D.M. Monti, H.U. Blaser and H.P. Jalett, J. Mol. Catal. 57 (1989) 245.
[8] H.U. Blaser, S.K. Boyer and U. Pettlekow, Tetrahedron Asymmetry, 2 (1991) 721.
[9] H.U. Blaser and M. Muller, Stud. Surf. Sci. Catal. 59 (Heterog. Catal. Fine Chem., II) (1991) 73.
[10] H.U. Blaser, J.P. Jalett, D.M. Monti, J.F. Reber and J.T. Wehrli, Stud. Surf. Sci. Catal. 41 (Heterog. Catal. Fine Chem.) (1988) 153.
[11] J.L. Margetfalvi and M. Hegedus, J. Catal. 156 (1995) 175.
[12] P. Johnston and P.B. Wells, J. Catal. 156 (1995) 180.
[13] G. Bond, P.A. Meheux, A. Ibbotson and P.B. Wells, Catal. Today 10 (1991) 371.
[14] J.L. Margetfalvi, Chem. Ind. (Dekker) 62 (Catal. Org. React.) (1995) 189.
[15] O. Schwalm, J. Weber, J. Margitfalvi and A. Baiker, J. Mol. Struct. 297 (1993) 285.
[16] O. Schwalm, J. Weber, B. Minder and A. Baiker, Int. J. Quantum Chem. 52 (1994) 191.
[17] O. Schwalm, B. Minder, J. Weber and A. Baiker, Catal. Lett. 23 (1994) 271.
[18] H.U. Blaser, H.P. Jalett, D.M. Monti, A. Baiker and J.T. Wehrli, Stud. Surf. Sci. Catal. 67 (Struct.-Act. Sel. Relat. Heterog. Catal.) (1991) 147.
[19] G. Wang, T. Heinz, A. Pfaltz, B. Minder, T. Mallat and A. Baiker, J. Chem. Soc. Chem. Commun. (1994) 2047.
[20] B. Minder, M. Schurch, T. Mallat and A. Baiker, Catal. Lett. 31 (1995) 143.
[21] B. Minder, T. Mfallat, A. Baiker, G. Wang, T. Heinz and A. Pfaltz, J. Catal. 154 (1995) 371.
[22] K.E. Simons, G. Wang. T. Heinz, T. Giger, T. Mallat, A. Pfaltz and A. Baiker, Tetrahedron Asymmetry 6 (1995) 505.
[23] U.K. Singh, R.N. Landau, Y. Sun, C. LeBlond, D.G. Blackmond, S.K. Tanielyan and R.L. Augustine, J. Catal. 154 (1995) 91.
[24] R.L. Augustine, K.P. Kelly and Y.M. Lay, Appl. Catal. 19 (1985) 87.
[25] R.L. Augustine, S.K. Tanielyan and G. Wolosh, Chem. Ind. (Dekker) 53 (Catal. Org. React.) (1994) 547.
[26] I.M. Sutherland, A. Ibbotson, R.B. Moyes and P.B. Wells, J. Catal. 125 (1990) 77.
[27] R.L. Augustine, R.W. Warner and M.J. Melnick, J. Org. Chem. 49 (1984) 4853.
[28] R.L. Augustine and P. Techasauvapak, J. Mol. Catal. A 87 (1994) 95.
[29] M. Garland, H.P. Jallet and H.U. Blaser, Stud. Surf. Sci. Catal. 59 (Heterog. Catal. Fine Chem., II) (1991) 177.
[30] P.A. Meheux, A. Ibbotson and P.B. Wells, J. Catal. 128 (1991) 387.
[31] J. Halpern, Chem. Ind. (Dekker) 22 (Catal. Org. React.) (1985) 1.
[32] C.R. Landis and J. Halpern, J. Am. Chem. Soc. 109 (1987) 1746.
[33] M. Boudart and G. Dhega-Mariadassou, Catal. Lett. 29 (1994) 7.
[34] M. Garland and H.U. Blaser, J. Am. Chem. Soc. 112 (1990) 7048.
[35] H.U. Blaser, M. Garland and H.P. Jallet, J. Catal. 144 (1993) 569.
[36] A.F. Carley, M.K. Rajumon, M.W. Roberts and P.B. Wells, J. Chem. Soc. Faraday Trans. 91 (1995) 2167.
[37] R.L. Augustine, Catal. Today 12 (1992) 139.
[38] R.L. Augustine and K.M. Lahanas, Stud. Surf. Sci. Catal. 75 (New Frontiers in Catalysis, Pt. C) (1993) 1567.
[39] R.L. Augustine and K.M. Lahanas, Chem. Ind. (Dekker) 53 (Catal. Org. React.) (1994) 279.
[40] R.L. Augustine, Heterogeneous Catalysis for the Synthetic Chemist (Marcel Dekker, Inc., New York, 1996) chs. 3–4.
[41] G.A. Somorjai, Phil. Trans. R. Soc. Lond. A. 318 (1986) 81.