

ADVANCES IN THE MODELLING OF LIGAND-ACCELERATED HETEROGENEOUS REACTIONS

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INTRODUCTION

The term ligand-accelerated catalysis first appeared in conjunction with the osmium catalyzed dihydroxylation of alkenes.¹ In this reaction, a chiral auxiliary, normally a natural occurring cinchona alkaloid, is added to a solution containing OsO₄ and alkene. The resulting homogeneous system, leads to both the enantiomeric excess of one diol as well as a marked increase in reaction rate.

In addition to a dramatic 1-2 orders of magnitude increase in reaction rate, a remarkable interdependence between the optical yield (ee) and rate at low concentrations of chiral modifier is observed.² This interdependence can be easily recognized by examining simultaneous plots of ee and rate versus modifier concentration. Such plots exhibited a strong increase in rate, but an even more spectacular increase in ee, as a function of modifier. Indeed, such characteristic plots give the impression that a maximum ee is reached long before the maximum rate for the system is attained.

The heterogeneous and enantioselective hydrogenation of α -keto esters, catalyzed by cinchona modified Pt/Al₂O₃ was first reported by Orito et al.^{3,4} Initial studies with both the unmodified (racemic) and

fully modified (enantioselective) Pt/Al₂O₃ systems showed that the rate of hydrogenation for the latter was roughly 1 order of magnitude higher.⁵ Indeed, at 20°C and 10.0 MPa hydrogen the measured turnover frequency for the fully modified system approaches 50 s⁻¹.⁶ However, mass transfer control can be avoided by using a powdered catalyst, low loadings and a proper level of agitation.⁶

Subsequent studies were carried out with trace quantities of cinchona (modifier/Pt_T \leq 1).⁷ These experiments confirmed that both ee and rate were continuous functions of the cinchona concentration. Moreover, these functions yielded the characteristic types of curves indicative of a ligand accelerated reaction. With a modifier to Pt_T concentration as low as 0.25 in toluene,⁷ or less than 0.10 in acetic acid,⁸ maximum optical yields can be obtained.

The interdependence of ee and rate for the cinchona modified Pt/Al₂O₃ systems, were successfully analyzed in the context of a two-cycle mechanistic scheme. After imposing a mass balance constraint on the total platinum in the system, a simple relationship between ee and rate arises (Eq 1). This slope-intercept form correctly describes the interdependence of ee and rate for experiments conducted in toluene and ethanol as solvents.⁷

$$ee_{obs} = a + b/r_{obs} \quad 1$$

$$a = 100(2s-1)k_m/(k_m - k_u)$$

$$b = 100(2s-1)k_u k_m Pt_T / (k_m - k_u)$$

In the following, Eq 1 is modified to include a stoichiometry for the modified platinum sites. The data from toluene experiments are then re-examined. Emphasis is given to (i) the turnover frequency based on the number of modified sites and (ii) the form of the adsorption isotherm.

EXPERIMENTAL

The 5% Pt/Al₂O₃ catalyst used in this study (Engelhard 4759) had a mean particle size of 55 μm, a BET surface area of 140 m²/g, a mean pore radius of 50 Å, a real density of 5.0 g/ml, and a dispersion of 0.28.⁶

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 kinetic experiments. A 45 ml reservoir, pressure regulators, pressure transducers and a cryostat were connected to the reactor. The reactor could be maintained isothermal ΔT = 0.3°C, and isobaric ΔP = 0.1 MPa for the duration of an experiment.

Typically, 100 mg catalyst (pretreated 2 hours in H₂ at 400°C), 0.2 mg 10,11-dihydrocinchonidine (HCD), 10 ml ethyl pyruvate and 20 ml solvent were charged to the reactor. The system was then purged 5 times with argon under stirring.

In the absence of stirring, the reservoir and reactor were pressurized with hydrogen. After 2-3 minutes, both the stirrer and data acquisition were started. Initial rate data was analyzed after the 30 second saturation period. Optical yields were determined after derivatization followed by glc.⁶

RESULTS AND DISCUSSION

Basic Derivation for EE and Rate First, consider a mass balance for the total platinum surface atoms Pt_T in an experiment, in terms of unmodified and modified platinum atoms and also the degree of surface modification x_m.

$$Pt_T = Pt_u + Pt_m \quad 2$$

$$x_m = Pt_m/Pt_T \quad 3$$

The observed rate of product formation can then be written (i) in terms of the modified and unmodified rates (ii) by including pseudo first order rate constants k_u and k_m (iii) by including the variable x_m.

$$r_{obs} = r_u + r_m \quad 4$$

$$r_{obs} = k_u Pt_u + k_m Pt_m \quad 5$$

$$r_{obs} = [(1-x_m)k_u + x_mk_m]Pt_T \quad 6$$

By introducing an intrinsic selectivity s for the modified sites, expressions can be written for the rate of formation of the R and S enantiomers as well.

$$r_R = 0.5k_u Pt_u + sk_mk_m Pt_m \quad 7$$

$$r_S = 0.5k_u Pt_u + (1-s)k_mk_m Pt_m \quad 8$$

Using only the variables defined above, and the definition of ee, two new expressions can be written for the observed optical yields ee_{obs}.

$$ee_{obs} = 100(r_R - r_S)/(r_R + r_S) \quad 9$$

$$ee_{obs} = 100(r_R - r_S)/r_{obs} \quad 10$$

$$ee_{obs} = [100(2s-1)x_mk_m Pt]/r_{obs} \quad 11$$

Further, rearranging Eq 6 gives:

$$x_m = [(r_{obs}/Pt_T) - k_u]/(k_m - k_u) \quad 12$$

Finally, elimination of x_m from Eq 11 leads to the interdependence between ee and rate (or TOF).

$$ee_{obs} = a + b/TOF \quad 13$$

$$a = 100(2s-1)k_m/(k_m - k_u)$$

$$b = 100(2s-1)k_u k_m/(k_m - k_u)$$

Comment I. For data which conforms to the slope-intercept form of Eq 13, the condition m < 0 represents a ligand

accelerated reaction, whereas the condition $m > 0$ represents a ligand decelerated reaction.

The numerical value of k_u can always be obtained from an unmodified experiment or from the relationship $k_u = b/a$. Further, if the system is entirely modifiable, or if one explicitly assumes ($x_{m,max} = 1$), then it is possible to solve for k_m and s . Otherwise k_m and s remain undetermined.

Comment II. The above derivation avoids a number of potential problems. Foremost, the exact relationship between the quantity of modifier and the number of modified platinum sites is unknown, and may well differ from system to system. For example, we don't know if the system obeys a simple Langmuir adsorption isotherm, and there may well be some adsorption on the support. (See Comment IV)

The final expression for a two-cycle system Eq 13, involving just e and rate, and free from both $[HCd]$ and x_m , was tested on the toluene system.⁷ A very good linear correlation was obtained, namely, $s = 0.93 \pm 0.02$, $k_u = 1.03 \pm 0.07 \text{ s}^{-1}$ and $k_m = 10.0 \pm 0.7 \text{ s}^{-1}$.

Inclusion of Stoichiometries. Clearly, it is an oversimplification to assume that each platinum atom is a site. This is particularly true for modified sites Pt_m , where adsorption of modifier ($MW \approx 300$) certainly requires an ensemble of platinum atoms. Accordingly, we define a modified site Pt^* in terms of a stoichiometry ν_m of modified atoms. Additionally, a new consistent rate constant k^* for a modified site can be defined.

$$Pt^* = Pt_m / \nu_m \quad 14$$

$$k^* = \nu_m k_m \quad 15$$

$$r_m = k^* Pt^* \quad 16$$

Next, let us assume that a modified site consists of a single cinchona molecule and an ensemble of platinum atoms. The quantity of adsorbed modifier $[HCd]_{ad}$ can be defined in terms of the number of modified sites, and in terms of an appropriate equilibrium constant.

$$[HCd]_{ad} = Pt^* \quad 17$$

$$[HCd]_{ad} = K_{eq} [HCd]_{soln} Pt_u \quad 18$$

Finally, there is the implicit assumption that all platinum atoms are modifiable. This is almost certainly not the general case. As a very simple example, consider platinum crystallites in very narrow pores ($< 10 \text{ \AA}$). Such atoms are almost certainly inaccessible to the modifier.

Accordingly, the total number of surface platinum atoms which are potentially modifiable, is considerably less than the number of surface platinum atoms i.e. $Pt_T \leq Pt_{surf}$, and we can write:

$$Pt_T = \xi Pt_{surf} \quad 19$$

$$0 \leq \xi \leq 1 \quad 20$$

Comment III. If the adsorption of a cinchona molecule is very strong, i.e. the equilibrium constant is very large, then the number of modified platinum atoms and the fraction modification are simply:

$$Pt_m = \nu_m [HCd]_T \quad 21$$

$$x_m = \nu_m [HCd]_T / Pt_T \quad 22$$

At this point, the rate of reaction can be rearranged, and its derivative with respect to $[HCd]_T$ can be taken. This provides a very good estimate of the magnitude of the pseudo first order rate constant k^* for a modified site when the condition $k_u \ll k_m$ is fulfilled.

$$r_{obs} = [k_u + x_m(k_m - k_u)] Pt_T \quad 23$$

$$r_{\text{obs}} = (k_v/Pt_T) + v_m[\text{HCd}]_T(k_m - k_u)$$

$$dr_{\text{obs}}/d[\text{HCd}]_T = v_m(k_m - k_u) \quad 25$$

$$dr_{\text{obs}}/d[\text{HCd}]_T \approx k^* \quad 26$$

The minimum value of the rate constant k^* for experiments conducted in toluene as solvent at 20°C is $k^* \approx 130 \text{ s}^{-1}$. If the above assumptions concerning strong adsorption and stoichiometry are correct, then k^* is the effective turnover frequency per molecule of dihydrocinchonidine!

Comment IV. The product of ee and TOF is a very interesting function because it serves as a measure for the fraction modification x_m . Such a measure can suggest an appropriate form for an adsorption isotherm between dihydrocinchonidine molecules and the platinum surface.

$$ee \cdot \text{TOF} = 100(2s-1)k_m x_m \quad 27$$

A plot of (ee•TOF) versus $[\text{HCd}]_T/Pt_{\text{surf}}$ is shown in Figure 1. Clearly, the results for the cinchona and $\text{Pt}/\text{Al}_2\text{O}_3$ system are in agreement with a simple Langmuir adsorption isotherm, with no further complication or qualifications.

The above result is interesting because it has been suggested that enantioselection in the cinchona system arises due to a *well ordered array* of adsorbed modifier.^{9,10} The results presented in Figure 1 strongly argue against such a suggestion. Indeed, the formation of a well ordered array or even the statistically random aggregation of 3 or 4 modifier molecules, as the source of enantioselection, would not lead to the simple, continuous and asymptotically increasing form shown in Figure 1.

This latter result strongly suggests that an enantioselective site consists of *one cinchona alkaloid molecule and an ensemble of platinum atoms*.

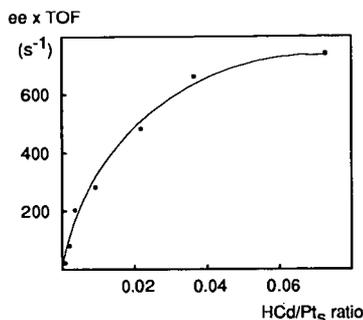


Figure 1. The function (ee•TOF) versus $[\text{HCd}]_T/Pt_{\text{surf}}$ for data taken in ethanol as solvent. (See Eq 27)

A considerably more complex relationship exists between ee and rate at yet higher loadings of chiral modifier in both toluene and ethanol as solvent and at high loadings in acetic acid.

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