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Quantification of rate acceleration in asymmetric catalytic hydrogenation

Dmitry Yu. Murzin*

Laboratory of Industrial Chemistry and Reaction Engineering, Process Chemistry Centre, Åbo Akademi University, Biskopsgatan 8, FIN-20500 Turku, Finland

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ABSTRACT

A quantitative model is advanced for asymmetric catalytic hydrogenation allowing estimation of the ratio between the rate constants in the absence and presence of the modifier. Comparison between the model and experimental data for 1,2-phenyl-propanedione is given.

1. Introduction

The origin of the rate acceleration in asymmetric heterogeneous catalysis, i.e. enhancement of the reaction rate in the presence of a chiral modifier was recently debated [1–3]. Ligand acceleration, readily observed in homogeneous catalysis, in the case of enantioselective hydrogenation over heterogeneous catalysts is mainly associated with ethyl pyruvate (EP) hydrogenation over cinchonidine (CD)-modified Pt catalysts (Orito reaction) [4–7]. Hydrogenation of some other α-ketoesters [8], activated ketones [9], α-keto acids [10], trifluoromethyl ketones [11,12] and α-keto acetals [13,14] was reported to be enhanced by the presence of a modifier, and at the same time for other reactants the reaction rate did not differ too much in racemic and enantioselective reactions and sometimes even rate deceleration is observed [15].

Thus ligand acceleration is not necessarily an intrinsic feature of enantioselective hydrogenation, but is dependent on the substrate and even substrate concentration. For instance dramatic rate acceleration in the case of ethyl pyruvate hydrogenation was explained [2] by taking into account catalyst deactivation, which is less prominent in the domain of low concentrations and is more profound at the elevated concentrations of the substrate.

Although asymmetric catalysis does not lead necessarily to a significant rate increase, the intrinsic catalyst activity could be in principle altered by the modifier–reactant interactions. It was noted in Ref. [3] that the observations of the overall reaction rate cannot give "any reliable information on the relation between the intrinsic rates on modified and unmodified sites", since "the number of sites involved in racemic and enantioselective hydrogenation is not known".

In the present contribution we would like to present a kinetic framework, allowing for quantification of intrinsic rate acceleration in case it exists. Since this is one of the first attempts to make a rigorous kinetic treatment of the rate acceleration the potential influence of deactivation is not considered here.

2. Kinetic model

In the case of racemic hydrogenation it can be assumed that the substrate is adsorbed on the catalyst surface, followed by a catalytic transformation to a racemic mixture with the racemic rate

$$r_{rac} = k_u \theta_S \quad (1)$$

where k_u is the apparent rate constant when there is no modifier present (so-called the case of unmodified sites). This constant includes also hydrogen pressure dependence; θ_s is the coverage by substrate.

When a modifier is adsorbed on the surface it is supposed that in the elementary reaction, which leads to enantiodifferentiation, not only the substrate but also the modifier is involved

$$r_{mod} = k_{mod} \theta_s^e \theta_M \quad (2)$$

Here K_{mod} and θ_s^e are, respectively, the apparent rate constant and the coverage of substrate. When the reaction is carried out in the presence of the modifier, θ_M is the coverage of modifier. It is also reasonable to consider that not all sites are covered, thus even in the presence of the modifier the racemic hydrogenation is possible,

* Corrresponding author: Tel.: +358 2 2154985; fax: +358 2 2154479.
E-mail address: dmurzin@abo.fi.

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which gives an expression for the enantioselective rate

$$r_{\text{enantio}} = k_{\text{mod}}\theta_s^e\theta_M + k_u\theta_s^e \quad (3)$$

In Eqs. (1) and (2) for the sake of simplicity the hydrogen pressure dependence is included in the rate constants. More rigorous treatment should consider hydrogen coverage as well; moreover according to the experimental procedure used in asymmetric hydrogenation, the catalyst is usually pre-treated with hydrogen and then the substrate is added to the slurry. Such a procedure implies that at least at the initial reaction period changes in hydrogen coverage are possible, if competition between bulky organic molecules and small hydrogen atoms for the surface sites is assumed.

The justification for the simplified treatment could be found, however, in experimental observations reported for 1-phenyl-1,2-propanedione hydrogenation [16]. The effect of hydrogen pressure was found to be negligible in this reaction as the hydrogen pressure was varied from 1.2 to 6.5 bar. The reaction order with respect to hydrogen was found to be close to zero and neither regioselectivity nor enantioselectivity was seen to be dependent on hydrogen pressure. These observations indicate that hydrogen adsorption is mainly of a non-competitive nature, meaning that coverage of hydrogen does not depend on the concentration of bulky organic molecules (substrate, products and modifier), which is consistent with Eqs. (1) and (2).

The experimentally observed rate acceleration l is defined as the ratio of enantioselective and racemic rates

$$l = \frac{k_{\text{mod}}\theta_s^e\theta_M + k_u\theta_s^e}{k_u\theta_S} = \frac{\theta_s^e}{\theta_S}\left(1 + \frac{k_{\text{mod}}\theta_M}{k_u}\right) \quad (4)$$

where the ratio k_{mod}/k_u could be defined as the intrinsic kinetic acceleration. When no modifier is present $\theta_M = 0$, the coverage rate θ_s^e degenerates into θ_s and the rate acceleration is equal to unity.

Coverage of adsorbed species could be elucidated by assuming the quasi-equilibria for adsorption of the substrate and the modifier. In the case of racemic hydrogenation one arrives at

$$\theta_S = \frac{K_S C_S}{1 + K_S C_S} \quad (5)$$

while for enantioselective hydrogenation it holds that

$$\theta_s^e = \frac{K_S C_S}{1 + K_S C_S + K_M C_M} \quad (6)$$

and

$$\theta_M = \frac{K_M C_M}{1 + K_S C_S + K_M C_M} \quad (7)$$

where K_M and K_S are respective adsorption coefficients for the modifier and the substrate.

Combining Eqs. (4)–(7) the observable rate acceleration becomes

$$l = \frac{1 + K_S C_S}{1 + K_S C_S + K_M C_M}\left(1 + \frac{k_{\text{mod}}}{k_u}\frac{K_M C_M}{1 + K_S C_S + K_M C_M}\right) \quad (8)$$

which gives a possibility to obtain an expression showing the relationship between the intrinsic kinetic acceleration and observable rate acceleration

$$k_a = \frac{k_{\text{mod}}}{k_u} = \frac{1 + K_S C_S + K_M C_M}{K_M C_M}\left(l\frac{1 + K_S C_S + K_M C_M}{1 + K_S C_S} - 1\right) \quad (9)$$

It follows from Eq. (8) that if there is no modifier present in the system, the observable rate acceleration is equal to unity, whatever is the intrinsic kinetic acceleration.

2.1. Analysis of intrinsic kinetic acceleration

Analysis for the observable rate acceleration, described by Eq. (8), could be performed. Let us start with some special cases. In the low concentration region for both the modifier and the substrate the reaction rate follows the first order dependence on their concentrations and the following is valid: $1 \gg K_s C_s, 1 \gg (K_S C_s + K_M C_M)$. Then the expression for the rate acceleration gives

$$l = 1 + k_a K_M C_M \quad (10)$$

which is in line with the increase in the reaction rate as a function of the modifier concentration in the lower concentration region.

When the concentration of the substrate increases, the observable rate acceleration starts to be dependent on the substrate concentration

$$l = 1 + k_a\frac{K_M C_M}{K_S C_S} \quad (11)$$

With further increase in the modifier concentration Eq. (8) is transformed into

$$l = \frac{1}{K_M C_M}(1 + k_a) \quad (12)$$

showing that the observed rate declines with the increase in the modifier concentration.

Numerical analysis can be performed for Eq. (8), which is rewritten in a slightly different form

$$l = \frac{1}{1 + ((K_M C_M)/(1 + K_S C_S))}\left(1 + k_a\frac{(K_M C_M)/(1 + K_S C_S)}{1 + ((K_M C_M)/(1 + K_S C_S))}\right)$$
$$= \frac{1}{1 + aC_M}\left(1 + k_a\frac{aC_M}{1 + aC_M}\right) \quad (13)$$

where $a = K_M/(1 + K_S C_S)$. Fig. 1 displays several simulations for different sets of parameters (kinetic acceleration and a).

Note that the observed rate acceleration is not very significant, even when kinetic constant is several times higher in the presence of the modifier. When the parameter a is diminished by the increase in the substrate concentration or by the decrease in the adsorption strength of the modifier, the decrease in the rate acceleration with the increase in the modifier concentration becomes less sharp (Fig. 2). Note that the maximum value of the observed rate acceleration does not change.

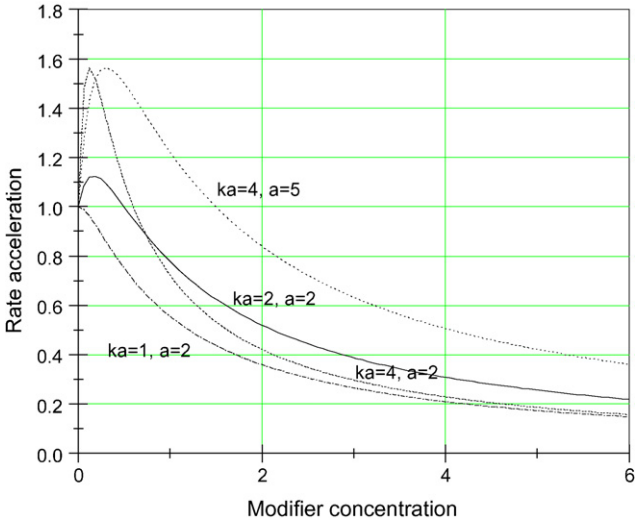

Fig. 1. Simulations for the observed rate acceleration as a function of the modifier concentration for various values of intrinsic kinetic acceleration and parameter a.

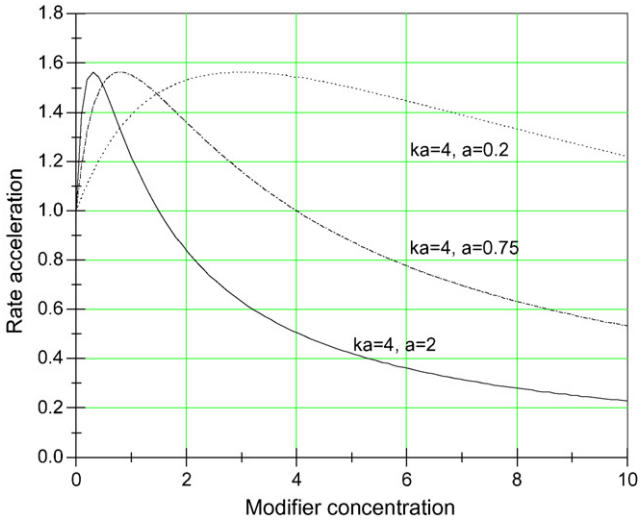

Fig. 2. Simulations for the observed rate acceleration as a function of the modifier concentration for various values of parameter *a*.

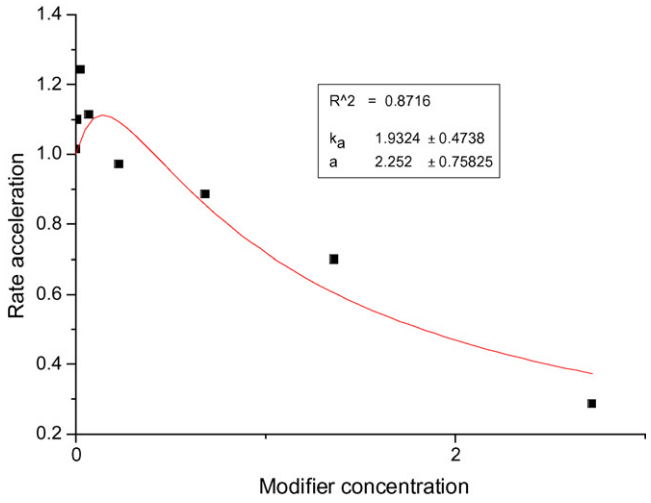

Fig. 4. Comparison between experimental and calculated values for the observed rate acceleration as a function of the modifier concentration (C_M in mmol/L, k_a dimensionless, a in L/mmol) in case of 1,2-phenylpropanedione hydrogenation in ethylacetate at 15° C and 5 bar.

As could be seen from Fig. 3, in order to obtain the value of observable rate acceleration of ca. 25, the intrinsic kinetic acceleration, e.g. the ratio of the rate constants in the presence and the absence of the modifier, should be around 100. This in turns implies that the difference in activation energies between enantioselective and racemic hydrogenation is close to 11.4 kJ/mol. If the ratio of the rate constants is equal to 10, ΔE is close to 5.7 kJ/mol. These considerations assume that the values of pre-exponential factors for enantioselective and racemic hydrogenations are the same; e.g. the transition states of these reactions are close to each other. This is valid for the case of limited mobility of the transition states, when the values of the vibrational and rotational partition functions are equal to unity. It should be noted, however, that in general partition functions of the transition states for racemic and enantioselective catalysis are not necessarily the same.

Analysis of Eq. (13) could be performed to calculate the value of the modifier concentration at which the reaction rate is maximal. To this end the minimum of the reciprocal function of l, given by the following equation

$$\frac{1}{l} = \frac{1 + 2aC_M + a^2(C_M)^2}{1 + aC_M + ak_aC_M} \tag{14}$$

should be 0.

Taking the derivative of Eq. (14) and setting it equal to zero one arrives at the quadratic equation

$$a^3(1 + k_a)(C_M^{max})^2 + 2a^2(C_M^{max}) + a(1 - k_a) = 0 \tag{15}$$

which can be easily solved leading to the value of the modifier concentration at maximum observed rate acceleration

$$C_M^{max} = \frac{k_a}{a(1 + k_a)} - 2a^2 \tag{16}$$

and finally substituting the modifier concentration in Eq. (13) with its value from Eq. (16) leads to the maximum value of the rate acceleration

$$l^{max} = \frac{1}{1 + (k_a/(1 + k_a)) - 2a^3}\left(1 + k_a\frac{(k_a/(1 + k_a)) - 2a^3}{(k_a/(1 + k_a)) - 2a^3}\right). \tag{17}$$

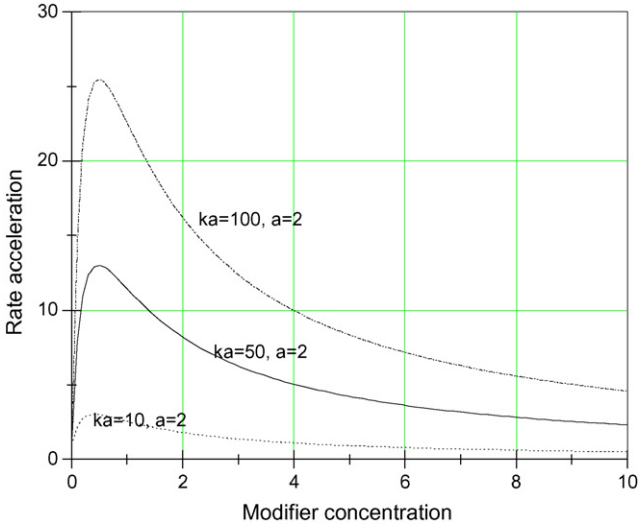

Fig. 3. Simulations for the observed rate acceleration as a function of the modifier concentration for various values of intrinsic kinetic acceleration.

2.2. Modeling of 1,2-phenylpropanedione hydrogenation data

Experimental data on hydrogenation of 1,2-phenylpropanedione over a supported platinum catalyst modified with chinconidine [16] were used to test the applicability of Eq. (13). The results of numerical data fitting are presented in Fig. 4. As can be seen from the figure the model is able to capture the essential features of the rate acceleration behavior. The value of kinetic acceleration is close to two, which implies that when transition states of enantioselective and racemic hydrogenation are similar, the difference in activation energies between them is ca. 1.7 kJ/mol, e.g. in the range which cannot be determined with high precision by experimental methods. It should be also noted that precision in calculations for computational methods based of stabilization of keto-orbitals for racemic and enantioselective hydrogenations is in the same range.

3. Conclusions

The mathematical framework for the calculation of intrinsic kinetic acceleration (e.g. the ratio of kinetic constants for enantios-

elective and racemic reactions) in enantioselective hydrogenation is provided. Simulation results reveal the relationship between this parameter, the experimentally observed rate acceleration, and the substrate and modifier concentrations. Numerical data fitting is performed for 1,2-phenylpropanedione hydrogenation over Pt/Al_2O_3 catalyst, showing that the value of intrinsic kinetic acceleration in this case is close to 2.

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