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COMPETITIVE PRODUCT INHIBITION IN A CLAY-CATALYSED DIELS–ALDER REACTION

CHRISTINE COLLET AND PIERRE LASZLO*
Université de Liège, Laboratoire de Chimie Fine aux Interfaces, Institut de Chimie B6, Sart-Tilman, 4000 Liège, Belgium and Département de Chimie, Ecole Polytechnique, 91128 Palaiseau, France

The normal electron-demand Diels–Alder cycloaddition between cyclopentadiene and methyl vinyl ketone is inhibited by the cycloadduct, when catalyzed by kaolinite-supported zinc chloride. This inhibition stems from occupation of the catalytic sites by both the cycloadduct and methyl vinyl ketone. Catalysis occurs in this case exclusively by a decrease in the enthalpy of activation.

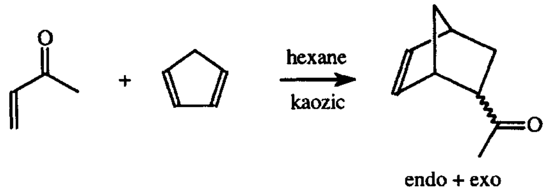
INTRODUCTION

Earlier work from this laboratory has shown the great promise of clay microreactors. Such catalytic systems are inexpensive, regenerable and 'user friendly' in their simplicity of operation, such as set-up and work-up. Further, they show turnovers and catalytic accelerations of such magnitudes as to make possible reactions under mild conditions, at ambient pressure and temperature. Clay microreactors are 'environment friendly', in contrast to noble metal catalysts. Also, they are capable of enzyme-like selectivities, such as between closely related reactants. A case at hand is discrimination by 'clayzic' between benzene and toluene'.[1]

Our continuing investigation of kaolinites (china clays) and of modified kaolinites as catalysts for organic reactions led us to test such catalysts in the Diels–Alder reaction. Kaolinites[2] are 1 : 1 clays associating one octahedral alumina layer and one tetrahedral silica layer. Individual platelets stack owing to a strong hydrogen-bonding network between alanol groups as hydrogen-bond donors and silyloxy groups as hydrogen-bond acceptors on neighbouring platelets. The hydrogen-bond network can also stabilize highly polar molecules, such as formamide or dimethyl sulphoxide, as intercalates[3] between the clay platelets. Such a utility, we surmised, might be turned to advantage in stabilising also the transition state of a Diels–Alder reaction: some Diels–Alder cycloadditions have a strong zwitterionic component, according to theoretical analyses.[4]

OBSERVATION OF PRODUCT INHIBITION

We elected to study the cycloaddition between cyclopentadiene and methyl vinyl ketone (MVK). We chose it as a model Diels–Alder reaction of the normal electron-demand type: the reaction partners are an electron-rich (or activated) diene and an electron-poor dienophile. Our choice of experimental conditions was motivated to a large extent by environmental criteria, to which we shall return later. Thus, we chose *n*-hexane as solvent.



We studied the uncatalysed reaction in the temperature range 273–309·2 K and obtained the results given in Table 1. As expected, the uncatalysed reaction is sluggish, with a half-life of hours at room temperature, and unselective, with an *endo* preference of a mere factor 3. Although the *endo* and *exo* transition states differ in their (negative) volumes of activation ($\delta\Delta V^{*} \approx 0{\cdot}5\ \mathrm{cm^3\,mol^{-1}}$),[5] a solvent with a low internal pressure does not discriminate between these two transition states, and cannot serve as a reaction accelerator.[6]

When the same reaction is catalysed by 'kaozic' (kaolinite-supported zinc chloride) (Table 2), the

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* Author for correspondence.

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Table 1. Rates and product distribution for the uncatalysed reaction

T (K) (±0·5)	k (l mol^{-1} s^{-1}) (±9 × 10^{-7})	*endo/exo* (±0·1)
275·2	$0{\cdot}99\times10^{-5}$	3·7
289·1	$3{\cdot}50\times10^{-5}$	3·5
290·6	$4{\cdot}60\times10^{-5}$	3·4
298·5	$7{\cdot}48\times10^{-5}$	3·4
305·5	$12{\cdot}1\times10^{-5}$	3·3

kinetics become markedly different (Figure 1). The pseudo-first-order treatment shows a large discrepancy between the calculated curve and the experimental points. Another striking observation is an anomalously low apparent log A value (in the Arrhenius formalism) of about 4, instead of the expected value of about 6.

The simplest way to account for the slowdown of the kinetics as the reaction proceeds is competitive inhibition by the reaction products, *endo*- and *exo*-2-acetyl-5-norbornene. Indeed, to a first approximation, one may consider the *endo* stereoisomer as the lone product since in this catalysed reaction the *endo* preference is about a factor of 20.

Table 2. Rates and product distribution for the catalysed reaction

T (K) (±0·5)	k (l mol^{-1} s^{-1}) (±0·05)	*endo/exo* (±0·3)
248·7	3·32	37·0
253·2	3·97	32·5
263·2	6·63	27·3
273·2	10·80	22·1
289·2	17·81	17·1
291·4	19·30	16·5
298·5	25·03	14·7
305·9	31·50	12·7

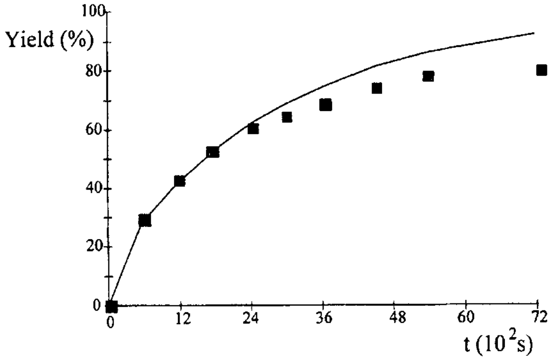

Figure 1. Time evolution of the product yield (%) for the catalysed Diels–Alder reaction at 290·6 K

THEORETICAL MODELS

We treat the adsorbed phase as a two-dimensional fluid. Let us denote by θ the fraction of the clay surface occupied by a monomolecular layer of adsorbed molecules. This parameter is defined as $\theta = n/n_{\max}$, where n is the number of adsorbed molecules and $n_{\max}$ is the number of molecules corresponding to complete coverage of the surface; θ is given by

$$\theta = \frac{a[\mathrm{MVK}]}{b + a[\mathrm{MVK}]} = \frac{\lambda[\mathrm{MVK}]}{1 + \lambda[\mathrm{MVK}]} \tag{1}$$

where $\lambda = a/b$ is a parameter characteristic of each adsorbed chemical species. For the reaction studied, the two polar components are methyl vinyl ketone (**1**) and *endo*-2-acetyl-5-norbornene (**2**), and this equation can be rewritten as

$$\theta_1 = \frac{\lambda_1[\mathbf{1}]}{1 + \lambda_1[\mathbf{1}] + \lambda_2[\mathbf{2}]} \quad \text{and}$$

$$\theta_2 = \frac{\lambda_2[\mathbf{2}]}{1 + \lambda_1[\mathbf{1}] + \lambda_2[\mathbf{2}]} \tag{2}$$

In order to obtain reaction rates, we apply Rideal's model.[7] The reaction is assumed to take place between one molecule in the fluid phase, cyclopentadiene, and one molecule in the adsorbed phase, methyl vinyl ketone. Since

$$-\frac{\mathrm{d}[\mathbf{1}]}{\mathrm{d}t} = k[\mathbf{1}]_{\mathbf{a}}[\mathrm{Cp}] \tag{3}$$

or

$$-\frac{\mathrm{d}[\mathbf{1}]}{\mathrm{d}t} = k[\mathrm{sites}]_0[\mathrm{Cp}] \cdot \frac{\lambda_1[\mathbf{2}]}{1 + \lambda_1[\mathbf{1}] + \lambda_2[\mathbf{2}]} \tag{4}$$

Cyclopentadiene (Cp) is used in large excess with respect to methyl vinyl ketone so that its concentration remains invariant throughout the reaction. The concentration of catalytic sites, $[\mathrm{sites}]_0$, is defined by

$$[\mathrm{sites}]_0 = \frac{S}{Vs} \tag{5}$$

where S is the specific surface area of the catalyst accessible to reactant molecules, s is the surface associated with an individual site and V is the total volume of the solution.

In order to bypass the difficulties in the determination of the two unknowns S and s (for instance, the BET specific surface area depends on the choice of the probe molecule,[8] dinitrogen or argon), we used a direct method. We determined by UV spectrophotometry the number of MVK molecules ($\lambda_{\max} = 294$ nm) adsorbed on the surface of the catalyst, as $[\mathrm{sites}]_0 = 1{\cdot}6\times10^{-5}$ mol g^{-1}. The 2-acetyl-5-norbornene product led to the same result.

QUANTITATIVE ANALYSIS

In a first series of experiments, we established separately adsorption isotherms for methyl vinyl ketone and *endo*-2-acetyl-5-norbornene (Figure 2) on kaozic at various temperatures. The thermodynamic values were $\Delta H^\circ = -4{\cdot}36 \pm 0{\cdot}5$ and $-9{\cdot}5 \pm 0{\cdot}6\ \mathrm{kJ\,mol^{-1}}$ and $\Delta S^\circ = 49{\cdot}1 \pm 3$ and $39 \pm 1{\cdot}8\ \mathrm{J\,mol^{-1}\,K^{-1}}$, respectively.

In the temperature range studied (253–307 K), the reaction product adsorbs more strongly than the

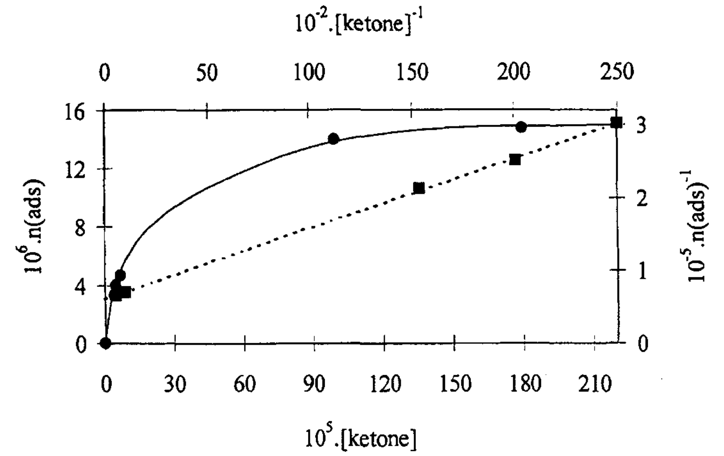

Figure 2. Adsorption isotherm of 2-acetyl-5-norbornene at 32·8 °C. The curve is $n(\mathrm{ads}) = \lambda[\mathrm{ketone}]/(1 + \lambda[\mathrm{ketone}])$ and the straight line $1/n = 1/n_{\mathrm{max}} + (1/n_{\mathrm{max}}\,\lambda)(1/[\mathrm{ketone}])$

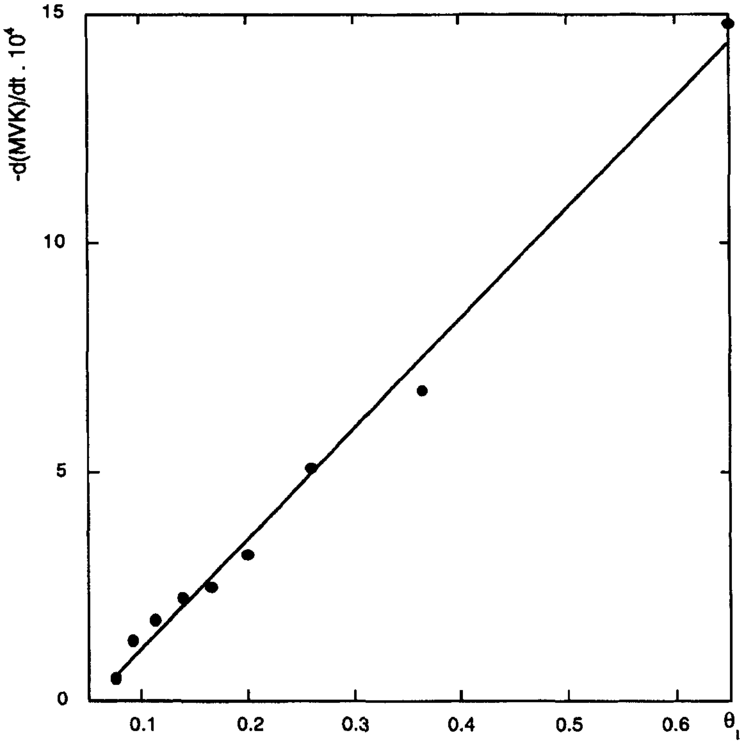

Figure 3. Plot of the reaction rate, measured by the disappearance of the methyl vinyl ketone reactant (ordinate), versus the Rideal θ_I parameter

polar (Lewis basic) reactant methyl vinyl ketone: $\lambda_2 > \lambda_1$. Introducing these experimentally determined values of λ_i ($i = 1, 2$) in equation (4) allows the determination of the rate constant k. This leads to excellent agreement between the calculated curve and the data points (Figure 3). The Arrhenius and Eyring parameters for the catalysed Diels–Alder reaction were as follows: $\log A = 5{\cdot}78 \pm 1{\cdot}2$; $E_a = 25 \pm 0{\cdot}6\ \mathrm{kJ\,mol^{-1}}$; $\Delta H^{*} = 22{\cdot}8 \pm 0{\cdot}9\ \mathrm{kJ\,mol^{-1}}$; and $\Delta S^{*} = -142 \pm 3\ \mathrm{J\,mol^{-1}\,K^{-1}}$.

DISCUSSION

As regards the uncatalysed reaction, we were able to calibrate our results against an independent determination of the kinetic parameters for the same reaction.[9] The Arrhenius and Eyring parameters for the uncatalysed reaction were as follows: $\log A = 6{\cdot}0 \pm 1{\cdot}5$; $E_a = 58 \pm 9\ \mathrm{kJ\,mol^{-1}}$; $\Delta H^{*} = 61 \pm 12\ \mathrm{kJ\,mol^{-1}}$ ($54\ \mathrm{kJ\,mol^{-1}}$ in isooctane solvent[9]); and $\Delta S^{*} = -117 \pm 50\ \mathrm{J\,mol^{-1}\,K^{-1}}$ ($-160\ \mathrm{J\,mol^{-1}\,K^{-1}}$ in osppctane solvent[9]).

The applicability of the Rideal model to the present set of data is clear from the outstanding fit between the calculated and observed values. Such agreement supports a mechanism with the methyl vinyl ketone reactant adsorbed on the solid surface, in close proximity to nearby catalytic sites, and with cyclopentadiene molecules, the reactant used in large excess, in the adjoining solution.

The thermodynamic parameters descriptive of adsorption on the solid catalyst by the methyl vinyl ketone reactant and by the *endo*-2-acetyl-5-norbornene product include negative enthalpies of adsorption, as one would expect. The adsorption entropies are large and positive, in consonance with release of solvation molecules. For instance, when methyl vinyl ketone binds to the kaozic catalyst, *n*-hexane solvent molecules are released in the bulk.

Turning now to the activation parameters, the strongly negative entropy of activation is about the same for the catalysed and uncatalysed reactions. This finding is at variance with other observations from this laboratory on a Wittig reaction that derived its catalytic acceleration exclusively from the reduction of the activation entropy. In the present reaction, the catalysis stems exclusively from reduction, by a factor of about 3, of the enthalpy of activation.

Solvent molecules that had been solvating both methyl vinyl ketone and the binding sites of attachment on the catalyst gain translational degrees of freedom. One may assert that for each molecule of methyl vinyl ketone (or 2-acetyl-5-norbornene) that binds to the catalyst, at least two solvent molecules are released.

The next point is more puzzling. The zinc chloride loading that leads to the best results (acceleration and stereoselectivity), when compared with the measured specific surface of the china clay (*ca* $10\ \mathrm{m^2\,g^{-1}}$), points to an average number of one zinc catalytic centre per Å^2. Comparison with the number of UV-determined adsorption sites indicates that a minute fraction (*ca* 0·7%) of the impregnated zinc is catalytically active, at least when compared with the adsorption equilibrium determination. A variety of factors may be responsible. It may well be that during calcination, when zinc chloride species shed their ether solvation, only a fraction of these attain sufficient coordinative unsaturation to offer adequate binding sites to substrate molecules. These most active sites may be also the most exposed catalytic sites, on the edges of platelets, or on the periphery of mesopores within tactoid aggregates of the clay platelets. Another consideration to be kept in mind is that the surface element associated with each site may differ significantly from the above roughly calculated figure if calcination produces a highly divided powder with a fractal dimension significantly exceeding 2·0.

These clear results obtain, as will be recalled, for a reaction run in *n*-hexane solution. Since such an environmentally friendly solvent (also with no leaching) is likely to gain in use, especially for industrial applications, and because of the central importance to organic synthesis of the Diels–Alder reaction, we deem the present quantitative study important for future reference.

EXPERIMENTAL

Preparation of kaozic. A 2·2 M solution of zinc chloride etherate in dichloromethane (10 ml) is mixed with kaolin (10 g). The solvent is evaporated with a Rotavapor and then in a vacuum oven (12 h, 120 °C, 10 mmHg).

Determination of adsorption constants and number of sites. Kaozic (1·2 g) is mixed with solutions of ketone in n-hexane (4×10^{-5}, 5×10^{-5}, 6×10^{-5}, 1×10^{-4} and 2×10^{-3} M; 25 ml). The concentrations of ketone in the solution at equilibrium are measured by gas chromatography (GC) and UV spectrophotometry ($\lambda_{\max} = 294$ nm) at several temperatures.

Kinetic studies. Methyl vinyl ketone (5 mmol) and kaozic (1·2 g) are mixed in n-hexane (100 ml) at the temperature of the reaction. Cyclopentadiene (4 g) is added and the reaction is followed by UV spectrophotometry ($\lambda_{\mathrm{MVK}} = 294$ nm) and GC (2-acetyl-5-norbornene).

Control without kaozic. The kinetic and thermodynamic parameters are given with their experimental uncertainties, assuming that the systematic error is not greater than three times the standard deviation, i.e. ±3 s.

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