Catalytic Activity Enhancement of a Cyclodextrin/Water-Soluble-Rhodium Complex System Due to its Gradual Supramolecular Organization in the Interphase

Michel Dessoudeix,[a] Martine Urrutigoïty,[a] and Philippe Kalck*[a]

Keywords: Biphasic catalysis / Cyclodextrins / Hydroformylation / Rhodium

Heavy terminal alkenes can be hydroformylated at a significant rate by using the water-soluble catalyst precursor [$Rh_2(\mu\text{-}StBu)_2(CO)_2(TPPTS)_2$] and β-cyclodextrin or its dimethylated form as phase-transfer agent. A study of the recycling has shown that the aqueous phase can be directly reintroduced into catalysis and also that each new run presents a slightly higher level of activity. Careful examination of the parameters of this catalysis leads us to propose that a gradual supramolecular organization in the interphase occurs for the rhodium complex, its solvation sphere and cyclodextrin which should involve at least two molecules in a head-to-tail or head-to-head arrangement.

Introduction

Homogeneous catalysts continue to play a prominent role as efficient tools to produce fine chemicals in enantioselective catalysis.[1,2] However, the separation of the catalyst from the reaction products is still one of the main concerns of chemists.[3] Among the various methods described in the literature,[3] the use of water soluble complexes with hydrophobic organic products, needing only a decantation step for the separation and the recycling of the catalyst, is increasingly popular. Nevertheless, for heavy substrates, the contact with the catalyst in the aqueous phase becomes the rate limiting step so that the use of cyclodextrins (CD's) as inverse phase-transfer agents appears to be an elegant way which preserves some economical viability.[4] Since the first report of the use of α-cyclodextrin in the hydroformylation reaction,[5] several studies have appeared to show that the transfer phenomenon is significantly enhanced between the organic phase and the aqueous phase where the catalyst is maintained.[6] In fact, it has been shown that CD — which is soluble in water but has poor solubility in polar solvents — forms inclusion complexes with both the substrate and the products transferring them into the aqueous phase. More recently, the efficiency of this process has been attributed to the greater complexation coefficient of the CD with the substrate than with the product.[7]

We have investigated the role of β-cyclodextrin and dimethyl-β-cyclodextrin in the biphasic low-pressure hydroformylation reaction of heavy alkenes catalyzed by the water-soluble complex [$Rh_2(\mu\text{-}StBu)_2(CO)_2(TPPTS)_2$]. Various alkenes have been used as representative elements of heavy molecules and they range from C_8 to C_{18}. All the parameters of this reaction have been considered and their influence on the conversion rate and the regioselectivity analyzed. Moreover, the recycling of the aqueous phase containing both the catalyst and the cyclodextrin has been studied.

Results and Discussion

The general procedure adopted in the present experiments is 5 bar for the total pressure of a 1:1 H_2/CO mixture, a temperature of 80 °C and a stirring rate, for the mechanical stirrer of the autoclave, of 1870 rpm, i.e. in a chemical regime where the conversion rate does not depend on the stirring. Thus, the mass transfer of the substrate from the organic phase to the aqueous phase in which catalysis occurs remains constant. The stirring rate was adjusted to the same value from one experiment to another so that this parameter is not involved in the following discussion and does not affect the parameters which are analyzed.

We can recall[8] that, in the absence of cyclodextrin, oct-1-ene, whose solubility in water is only 2.07×10^{-3} g/L, is slowly transformed into the corresponding C_9 aldehydes since the yield is 11% in 20 h; the selectivity of *n*-nonanal vs. 2-methyloctanal is as high as 98% and is characteristic of a catalysis in pure water. After the addition of cyclodextrin in a oct-1-ene/cyclodextrin molar ratio of 28 and a β-CD/rhodium molar ratio of 18.4, the conversion rate reaches 26%, as shown in Table 1, and the linearity decreases to 88.5%. Such a lowering of the regioselectivity indicates that the medium where the catalytic activity of the system occurs is no longer completely aqueous and is, in fact, intermediate between aqueous and purely organic, since in a pure toluene phase previous experiments have shown a 75% selectivity. In Table 1 we have examined the effects of the chain length on the conversion. For dec-1-ene, the yield decreases to 6.2%, whereas the selectivity for the linearity is 90.2%. However, for higher alkenes, the reactivity is very modest and lies between 1 and 2% for C_{18} to C_{12} alkenes.

In order to improve significantly the mass transfer, we have used dimethylated-β-cyclodextrin (DM-β-CD) which

---

[a] Laboratoire de Catalyse, Chimie Fine et Polymères, Ecole Nationale Supérieure de Chimie de Toulouse,
118, route de Narbonne, 31077 Toulouse Cédex 04, France
E-mail: pkalck@ensct.fr

1434−1948/01/0707−1797 $ 17.50+.50/0

Table 1. Evolution of the yield and the linearity as a function of the number of carbon atoms of the alkene; reaction conditions: P_T = 5 bar, T = 80 °C, time = 18 h, catalyst = 0.25 mmol, P/Rh = 10, H_2O = 40 mL, alkene = 64 mmol, β-CD = 2.3 mmol, DM-β-CD = 2.6 mmol

Number of carbon atoms	β-CD		DM-β-CD	
	Yield (%)	Linear aldehyde (%)	Yield (%)	Linear aldehyde (%)
8	26.2	88.5	59.1	88.7
10	6.2	90.2	50.7	90.2
12	2.1	n. d.	30.1	93.2
14	1.6	n. d.	8.3	85.5
16	1.4	n. d.	5.3	79.1

is much more soluble in water than β-CD itself (590 and 18.5 g/L, respectively). These results are displayed in Table 1. For oct-1-ene the conversion is greatly improved since it reaches 59.1%, instead of 26% for β-CD, the linearity being unchanged. In addition dec-1-ene and dodec-1-ene are readily transformed whereas the C_{14} and C_{16} alkenes are still converted but at a lower rate. In fact, the distinct behavior between β-CD and its dimethylated form stems mainly from the differences which exist in the hydrogen-bond network and in their steric hindrance, β-CD being rigid and DM-β-CD showing a significant flexibility. In fact, it seems that the height of the CD's and the size of the cavity play a dramatic effect along the chain length for its inclusion inside the cavity to a greater or lesser extent by minimizing the hydrophobic effect. Such a fitting allows the aliphatic chain to be coiled up with mainly the carbon−carbon double bond emerging from the torus. These results show that DM-β-CD rapidly transforms various heavy alkenes as opposed to β-CD which cannot convert an alkene heavier than oct-1-ene. We have checked that, in an equimolar mixture of C_8, C_{10} and C_{12} alkenes, β-CD discriminates in favor of oct-1-ene since 70% is converted.

The influence of the quantities of the two cyclodextrins introduced has been investigated in a wide range. Table 2 displays the yields, the selectivities in linear aldehyde and the turnover frequencies when β-CD is progressively added. β-CD begins to precipitate at 2.3 mmol. Of course, beyond this value the yields remain constant.

Table 2. Influence of the quantity of β-cyclodextrin on the yield and the linearity during the hydroformylation of oct-1-ene; reaction conditions: P_T = 5 bar, T = 80 °C, time =18 h, catalyst = 0.25 mmol, P/Rh = 10, H_2O = 40 ml, oct-1-ene = 64 mmol

β-CD (mmol)	Yield (%)	Linearity (%)	TOF (h^{-1})	TOF/β-CD ($h^{-1} \times mmol^{-1}$)
0	2	98	0.6	–
0.44	6	98	1.8	4.1
0.88	10.2	97	3.0	3.4
1.32	14.1	95	4.2	3.2
1.76	19.2	93	5.7	3.3
2.20	26.2	88.5	7.8	3.5
4.41	30.1	87.2	9.0	2.0

As shown in Figure 1, variation of the yield with the amounts of added cyclodextrin occurs almost linearly until a plateau is reached beyond 2.3 mmol. Similarly, the linearity decreases slowly from 98% (in the absence of β-CD) to 88% near to the 2.3 mmol point. It occurred to us to investigate the turnover frequencies calculated per mol of CD versus the quantities of β-CD, thus expressed in h^{-1} per mol (last column in Table 2). Instead of the expected straight line, we observed that the curve decreases until it reaches a minimum near 1.5 mmol (Figure 2), then increases to a local optimum value of 2.3 mmol.

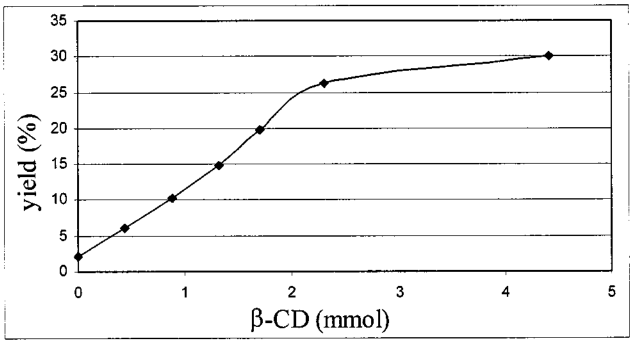

Figure 1. Variation of the yield versus quantity of β-CD

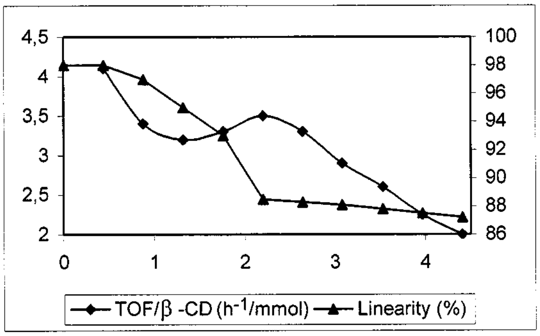

Figure 2. Curves of the TOF/β-CD and the linearity as a function of the quantity of β-CD

This phenomenon seems to be directly connected to the concentration of β-CD in the medium. An organization of the solvation sphere of the cyclodextrin should give a regular effect. We suggest that the observed effect could result from a particular arrangement of several cyclodextrin units. First, a decrease of the curve is consistent with an inhibiting effect which could be due to two CD's encapsulating one guest in a head-to-head manner.[9,10] The optimum value

Table 3. Evolution of the yield, the linearity and the TOF during recycling; reaction conditions: P_T = 5 bar,; T = 80 °C, time = 18 h, catalyst = 0.25 mmol, P/Rh = 10, H_2O = 40 mL, alkene = 64 mmol, DM-β-CD = 3.05 mmol

Recycling		Oct-1-ene			Dec-1-ene	
Yield (%)	Nonanal (%)	TOF (h^{-1})	Yield (%)	Undecanal (%)	TOF (h^{-1})	
0	65.9	85.0	19.7	65.5	89.7	19.6
1	80.0	88.6	23.9	69.1	89.3	20.6
2	87.5	86.8	26.1	73.0	88.8	21.8
3	91.1	85.7	27.2	84.7	87.6	25.3

should correspond to a peculiar arrangement of two or three β-CD's giving rise to a kind of tunnel, as already mentioned in the literature for the head-to-tail encapsulation of very large molecules.[11,12] The further decrease in the curve is due to the precipitation of β-CD (in the calculations the full quantity of β-CD has been introduced).

When the regioselectivity is considered, it is clear that the selectivity in linear aldehyde decreases dramatically for increasing amounts of β-CD. This unexpected decrease of the selectivity curve shows the role of the steric hindrance of the β-CD on the C=C double bond: in our opinion it is more and more included in the CD cavity thus providing preferential access of the terminal carbon to the hydride ligand in the step where the rhodium-alkyl species is formed (Figure 3). If the aim is to obtain the better yields of linear aldehydes, an examination of Figure 2 shows that a good compromise between the yield and the linearity lies in the range 1.76−2.20 mmol of β-cyclodextrin.

DM-β-CD shows similar trends, but for oct-1-ene, due to its too short chain length, only the inhibiting effect is observed, whereas for dec-1-ene and dodec-1-ene, the TOF/DM-β-CD versus the quantity of DM-β-CD remains constant, although a slight increase can be noted in the latter case. Here, the chain length is more adapted to the depth imposed by the arrangement of the two CD's. Except for oct-1-ene, which becomes more included inside the organophilic cavity and for which the linearity decreases as expected for an organic environment,[13] the linearity of the aldehydes formed from dec-1-ene and dodec-1-ene remains almost invariant showing once again the mutual adaptation of the two DM-β-CD's framework and these two alkenes.

Whereas recycling a catalyst produces generally either no variation in the yield or a decrease in the catalytic activity, we observed, on four successive runs, an important enhancement of the yield, with the linearity being almost the same (Table 3 and Figure 2).

Such an increase in the catalytic activity along the recycling means that the system keeps a sort of a local organization which improves the contact between the reactants. Indeed, from one run to the next, after decantation, the aqueous phase is directly recycled with no further work up. Thus, as this phase contains the cyclodextrin and the water-soluble rhodium complex, such a direct reintroduction does not disrupt the arrangement gained by the catalyst/cyclodextrin/substrate/solvent system during the previous run. The association of two cyclodextrin units, head-to-head or head-to-tail, is consistent with this hypothesis. We need also to consider how the organic/aqueous volume around the DM-β-CD/ $[Rh_2(\mu\text{-S}t\text{Bu})_2(CO)_2(TPPTS)_2]$ couple is organized. Indeed, the internal secondary alcohol groups inside the DM-β-CD torus are considered as hydrophobic whereas the external primary alcohol functions are compatible with the approach of water molecules. However, near the entrance of the cavity a mixed volume should be present containing toluene and water, especially at 80 °C, a temperature for which we are near the heteroazeotropic composition; the relative concentration of both solvents should vary, of course, inside this volume. The arrangement should associate the rhodium complex and the external part of the cyclodextrin(s) in the water-rich area and the alkene in the organic-rich part of this volume. Thus, such an organization could improve the transfer phenomenon from one run to the next. This system could possibly migrate more rapidly near the interface giving rise to a more efficient transfer of the alkene from the organic phase to the so-called aqueous phase. Such a view is not inconsistent with the association of two cyclodextrin units.

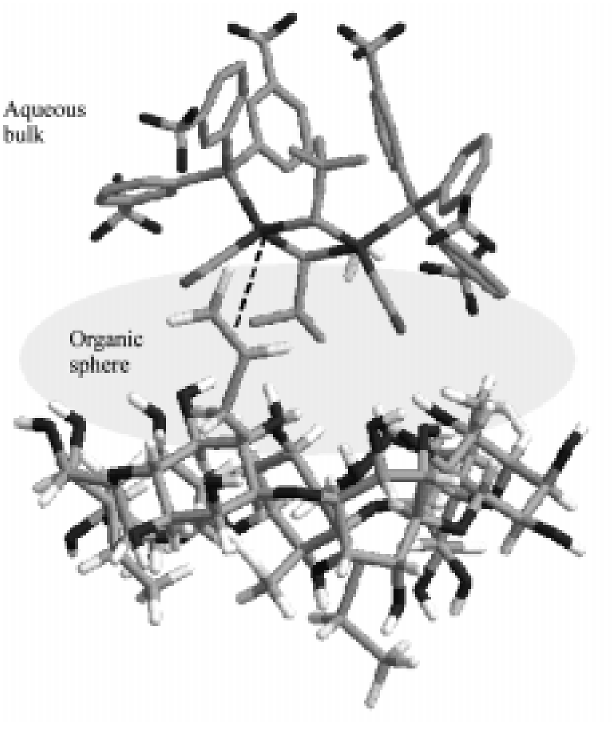

Figure 3. Scheme of the hydroformylation of oct-1-ene, using cyclodextrin, in the organic sphere

Conclusion

We can conclude that a solvation sphere is gradually organized in the volume where the cyclodextrin improves the contact between the carbon-carbon double bond and the rhodium center of the catalyst (Figure 3). This specific volume can be viewed as a supramolecular microreactor.

Experimental Section

Starting Materials: All reagents were purchased from Aldrich and used without further purification. Cyclodextrins are a generous gift from Wacker Chimie S.A. and tris(*m*-sodiumsulfonatophenyl)phosphane (TPPTS) a gift from Hoechst (Ruhrchemie). Rhodium trichloride trihydrate is a generous loan from Engelhardt-Comptoir-Lyon-Alemand-Louyot. The complex $[Rh_2(\mu\text{-S}t\text{Bu})_2(CO)_2(TPPTS)_2]$ was prepared as previously described.[14]

Biphasic Catalysis: In a typical run, $[Rh_2(\mu\text{-S}t\text{Bu})_2(CO)_2(TPPTS)_2]$ (0.25 mmol, 0.42 g) and TPPTS (4.5 mmol, 2.8 g) were dissolved in 40 mL of deaerated water in a Schlenk tube, and then 64 mmol of alkene was added. The reactor was evacuated and the solution introduced by suction. The reactor was then heated to 80 °C (preheated oil bath) under mechanical stirring (1870 rpm). When the temperature of 80 °C was reached, the autoclave was pressured with 5 bar of an equimolar CO/H_2 mixture. During the catalytic test, the pressure was kept constant and equal to 10 bar inside the reactor. After 18 h, the gas mixture feed was stopped and the reactor cooled to room temperature. The gas present inside the reactor was then slowly evacuated. After opening the reactor the biphasic solution was transferred by suction into a round-bottom flask and placed under nitrogen.

GPC: After catalysis the organic phases were analyzed by gas phase chromatography on a Carlo Erba HRGC 5160 apparatus equipped with a flame ionization detector and a capillary column Alltech Econocap FFAP (30m; 0.53 mm; 1.2μm), $T_{\text{det}} = 200$ °C, $P_{H_2} = 0.5$ bar.

Infrared Spectroscopy: Infrared spectra were recorded on a Perkin−Elmer 1710 FTIR apparatus.

---

[1] B. Cornils and W. A. Herrmann, in *Applied Homogeneous Catalysis with Organometallic Compounds − A Comprehensive Handbook in Two Volumes*, John Wiley & Sons, Chichester, **1996**.

[2] A. N. Collins, G. N. Sheldrake and J. Crosby, in *Chirality in Industry*, John Wiley & Sons, Chichester, **1997**.

[3] B. Cornils and W. A. Herrmann, in *Aqueous-Phase Organometallic Catalysis − Concept and Application*, John Wiley & Sons, Chichester, **1996**.

[4] W. Saenger, *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 344−362; K. A. Connors, *Chem. Rev.* **1997**, *97*, 1325−1357.

[5] J. R. Anderson, E. M. Campi, W. R. Jackson, *Catal. Lett.* **1991**, *9*, 55−58.

[6] E. Monflier, E. Blouet, Y. Barbaux, A. Mortreux, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2100−2102.

[7] E. Monflier, G. Fremy, Y. Castanet, A. Mortreux, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 2269−2271.

[8] P. Kalck, L. Miquel, M. Dessoudeix, *Catal. Today* **1998**, *42*, 431−440.

[9] P. M. Ivanov, D. Salvatierra, C. Jaime, *J. Org. Chem.* **1996**, *61*, 7012−7018.

[10] J. Velasco, P. Guardado, C. Carmona, M. A. Muñoz, M. Balón, *J. Chem. Soc., Faraday Trans.* **1998**, *94*, 1469−1476.

[11] H. Asanuma, M. Kakazu, M. Shibata, T. Hishiya, M. Komiyama, *Chem. Commun.* **1997**, 1971−1972.

[12] M. Ceccato, P. Lo Nostro, C. Rossi, C. Bonechi, A. Donati, P. Baglioni, *J. Phys. Chem. B* **1997**, *101*, 5094−5099.

[13] Ph. Kalck, in *Organometallics in Organic Synthesis. Aspects of a Modern Interdisciplinary Field* (Eds.: A. de Meijere, H. tom Dieck), Springer, Heidelberg, **1987**, 297−320.

[14] Ph. Kalck, P. Escaffre, F. Serein-Spirau, A. Thorez, B. Besson, Y. Coleuille, R. Perron, *New J. Chem.* **1988**, *12*, 687−690.

Received June 22, 2000
[I00247]