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Research Note

Competition of chiral modifiers on platinum: A transient catalytic and in situ ATR-IR study in continuous reactors

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Abstract

Fundamental aspects of the competition of chiral modifiers on a metal surface were investigated in a continuous-flow fixed-bed reactor using the enantioselective hydrogenation of ethyl pyruvate on Pt/Al_2O_3 as an example. The "chiral switch" in the product composition was induced by replacing the modifier (cinchonidine, cinchonine, and quinidine) in the feed. The changes at the catalytic interface were followed by in situ ATR-IR spectroscopy under high-pressure conditions. These studies confirmed the replacement of the chiral modifiers on the metal surface and revealed differences in the adsorption strength and geometry ("flat" and "tilted" species).

Keywords: Cinchona alkaloids; Enantioselective hydrogenation; Ethyl pyruvate; Continuous reactor; Chiral switch; Adsorption mode; In situ ATR-IR spectroscopy

1. Introduction

Heterogeneous catalysts based on the concept of modification of a metal surface by a strongly adsorbing chiral compound are usually less effective than the homogeneous counterparts, but have advantages related to industrial production [1–4]. The easy separation and recycling of the catalyst, and the possibility of continuous operation [5–9], are attractive features for process intensification. In addition, it is possible to change the major enantiomer of the product from (R) to (S) and back by simply replacing the chiral modifier in the feed. The fundamental aspects of this "chiral switch" are analogous to the nonlinear behavior of modifier mixtures studied in batch reactors by using two modifiers that alone give the opposite enantiomers of the product [10–17]. This nonlinear phenomenon is commonly attributed to the different adsorption strengths of the chiral modifiers on the metal surface. However, the spectacular shifts in ee could not be explained satisfactorily solely by the different surface concentrations of the modifiers [18]. It has been speculated that the dominant adsorption geometries of the modifiers are also different [19].

To understand the competition of chiral modifiers on the metal surface at the molecular level, we analyzed the phenomenon in transient catalytic and in situ spectroscopic experiments in continuous-flow reactors. The hydrogenation of ethyl pyruvate to lactate on a cinchona-modified Pt/Al_2O_3 catalyst was chosen as a test reaction [20,21].

2. Experimental

2.1. Catalytic experiments

The experimental setup consisted of three feed lines for the dissolved chiral modifier, the dissolved substrate, and H_2. The rates of the two liquid flows were regulated by HPLC pumps. The three lines were mixed directly before the reactor. An 8-cm-long Swagelok stainless steel tube with an inner diameter of 1.8 mm (d_r) was used as a continuous-flow reactor. At the front end of the reactor, a quartz wool plug served to disperse the liquid phase and to hold the catalyst bed in place. Before use, the 5 wt% Pt/Al_2O_3 catalyst (Engelhard 4759) was reduced at 400 °C in flowing H_2 for 60 min, cooled to room temperate in H_2 in 30 min, and finally flushed with nitrogen. The activated catalyst was immediately transferred to the reactor. Typically, 75 mg of catalyst was used, yielding a bed length (L) of 28 mm. An average catalyst particle diameter of 70 μm (d_p) led to the

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following geometrical ratios of the catalyst bed: $L/d_p = 400$; $d_r/d_p = 25.7$.

The substrate (ethyl pyruvate, Acros, 98%) was carefully distilled under vacuum before use. The chiral modifiers and solvents (Fluka) were used as received. H_2 was delivered by PanGas (99.995 vol%). The reaction conditions were as follows: acetic acid (toluene) solvent, 736 mM ethyl pyruvate, 0.225 mM modifier, 15 bar H_2, 0.4 ml/min total liquid flow rate, 20 °C. Conversion and ee were determined with a Thermo Finnigan gas chromatograph equipped with a Chirasil-Dex CB (25 m × 0.25 mm × 0.25 μm) capillary column.

2.2. ATR-IR spectroscopy

ATR-IR spectra were collected using a Bruker Optics IFS-66/S spectrometer equipped with a liquid nitrogen-cooled MCT detector and a commercial ATR accessory (Optispec, Switzerland). Toluene (Fluka, 99.7 vol%) was dried over molecular sieves; N_2 was provided by PanGas (99.999 vol%). The Pt/Al_2O_3 catalyst was suspended in 1.5 ml of water, placed on a ZnSe internal reflection element (IRE; 52 × 20 × 2 mm, Crystran Ltd, England) and dried overnight. The catalyst powder film was reduced at 350 °C before the measurement with the activation procedure described previously. The Pt/Al_2O_3 thin film was prepared on a Ge IRE (52 × 20 × 2 mm; Komlas, Germany) by electron beam vapor deposition as described elsewhere [22]. The IRE was fixed in a stainless flow-through high-pressure ATR-IR cell, designed and manufactured in-house. The temperature in the cell was regulated by a thermostat. After mounting the cell, the sample compartment was purged with nitrogen for 3–4 h. Then, N_2-saturated toluene was flown over the coated IRE for 60 min, followed by H_2-saturated solvent to clean the surface for 10 min. The chiral modifier dissolved in toluene was then added for the next 30 min before being replaced by the second chiral modifier for another 30 min. All experiments were carried out at 10 bar. The total liquid flow (0.4 ml/min) was regulated using a HPLC pump, and the same concentrations of modifier and substrate were used as in the catalytic experiments. Spectra were acquired by co-adding 300 scans at a resolution of 4 cm^{-1}. Water vapor and CO_2 signals were subtracted when required.

3. Results and discussion

Three different cinchona alkaloids were applied as chiral modifiers in trace amounts, at a modifier-to-pyruvate molar ratio of 307 ppm. Platinum modified by quinidine (QD) and cinchonine (CN) gave the (*S*)-lactate in excess, and that modified by cinchonidine (CD) gave the (*R*)-lactate in excess. When QD was used, the ee in the effluent of the continuous-flow fixed-bed reactor stabilized at around 66% (Fig. 1). After QD was replaced by CD in the feed, the (*R*)-enantiomer formed in excess within 5 min and the ee increased gradually to 89%. (Note that under optimized conditions, both CD and QD afford up to 97–98% ee in batch reactors [18,23] and around 90% in continuous-flow reactors [5].) In the reverse case, CD was fed first (Fig. 1), and after switching to QD, the shift in ee was slow and incomplete even after 75 min.

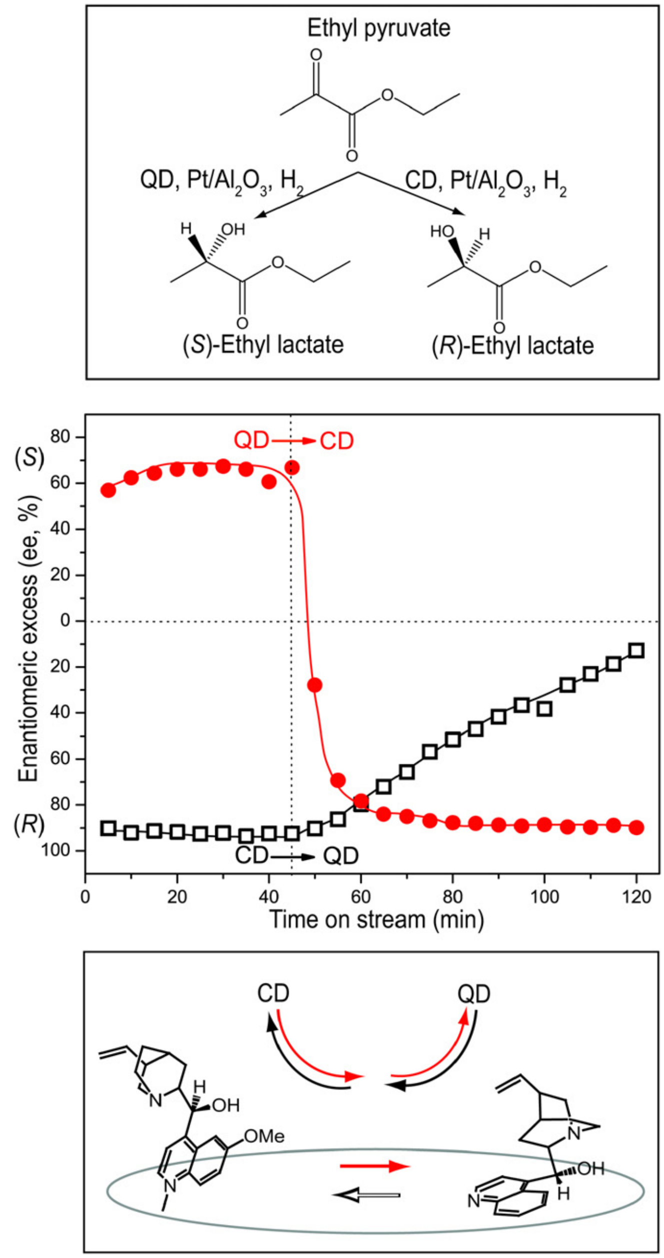

Fig. 1. Top: Major enantiomers in the hydrogenation of ethyl pyruvate on Pt/Al_2O_3 modified by cinchonidine (CD) or quinidine (QD). Middle: Switch of the major enantiomer by replacement of QD with CD (●) or CD with QD (□) in the continuous hydrogenation of ethyl pyruvate in acetic acid. The vertical dashed line indicates the time when the second modifier reached the catalytic bed. Bottom: Different adsorption geometries of the competing modifiers on the Pt surface.

In an analogous experiment, replacement of CN by the pseudoenantiomer CD resulted in a rapid chiral switch from 86% (*S*)-lactate to 82% (*R*)-lactate. Replacement of CD by CN was slower, but still faster than the switch from CD to QD (Fig. 1). It is very likely that the variations in the dynamics of the chiral switch can be traced to differences in the adsorption strength of the modifiers at the metal surface. Based on these experiments, a relative order of adsorption strength of CD > CN > QD may

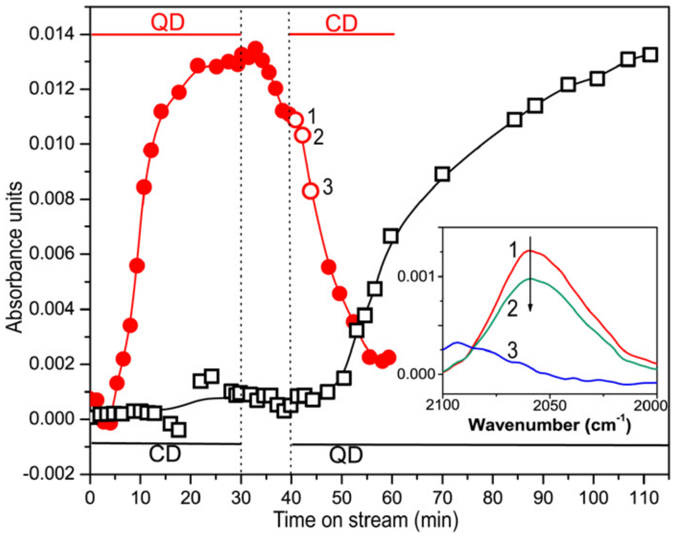

Fig. 2. Time-dependent intensity of the signal at 1622 cm^{-1} during the switch of the cinchona alkaloids on 5 wt% Pt/Al_2O_3 in H_2-saturated toluene. Vertical dashed lines mark the time regions when the modifiers were present in the ATR-IR cell. Inset: ATR-IR spectra for different times-on-stream belonging to points 1, 2, and 3 in the CO region. Conditions: 0.225 mM alkaloid concentration, 5 mg catalyst, 0.4 ml/min total liquid flow rate, 20 °C, 10 bar.

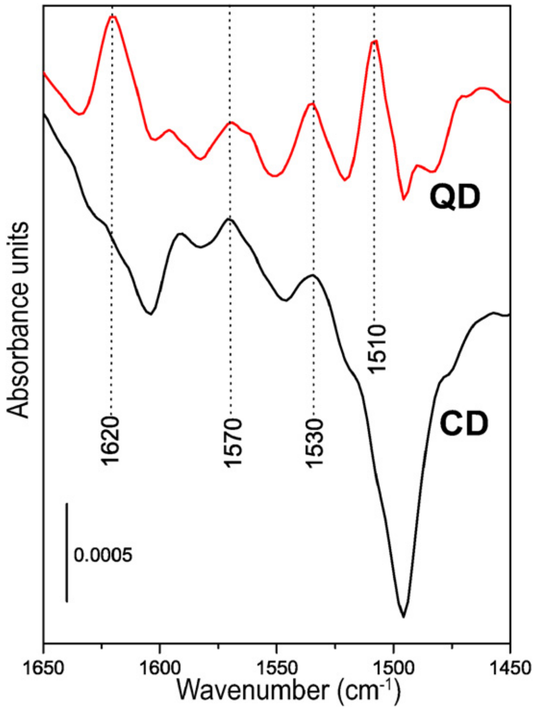

Fig. 3. ATR-IR spectra of QD (after 16 min on stream) and CD (18 min on stream after switching from QD), recorded on Pt/Al_2O_3 thin model film in H_2-saturated toluene. Conditions: 0.225 mM alkaloid concentration, 0.4 ml/min total flow rate, 20 °C, 10 bar.

be deduced, which is in good agreement with previous studies on the nonlinear behavior of modifier mixtures on Pt in the same reaction [10,18,24].

ATR-IR spectroscopy [25,26], a powerful surface-sensitive technique, was applied to provide molecular insight into the chiral switch at the catalyst–liquid interface. QD and CD were probed because they exhibit slightly different IR spectra due to the presence of the 6′-methoxy group in QD. The ATR-IR experiments were conducted in a specially designed high-pressure continuous-flow cell to mimic the conditions in the catalytic fixed-bed reactor. The 15-mg catalyst coating on the ZnSe crystal was activated in solution at 10 bar in H_2. Toluene was used as a solvent because it interferes less than acetic acid in the spectral region of interest. In a "bridging" experiment in the catalytic reactor using toluene instead of acetic acid, the ee changed from 13% (*S*) with QD to 85% (*R*) with CD (96% conversion with 25 mg of catalyst). In the analogous experiment in the ATR-IR reactor cell, continuous replacement of the modifiers induced a switch of ee from 21% (*S*) to 22% (*R*)-lactate at 4% conversion. We must reemphasize that the reaction rate and enantioselectivity strongly depend on the conditions, including the efficiency of mass transport [4].

The evolution of the lactate signal could be followed in situ by the increasing peak at 1221 cm^{-1}. Because the strong pyruvate signals cover most other signals of the product and modifier, additional experiments were carried out without substrate to focus on the exchange of modifier at the catalyst surface. Fig. 2 shows the time-dependent intensity of the signal at 1622 cm^{-1}, which is characteristic for QD (Fig. 3). This signal served as a tracer for the modifier replacement. As soon as CD reached the catalyst layer, it replaced adsorbed QD relatively rapidly, as indicated by attenuation of the signal intensity at 1622 cm^{-1} in Fig. 2. Fig. 2 also shows that the time required to replace CD by QD was remarkably longer in the control experiment, in good agreement with the experiments conducted in the catalytic reactor.

The spectra obtained with the commercial catalyst were dominated by the interaction of the alkaloids with Al_2O_3, probably via the quinuclidine N and the OH functions. Competition with CO adsorbed on the small Pt particles located on the large Al_2O_3 surface provides the sole evidence for the alkaloid–metal surface interaction. (CO is produced at the boundary sites on Pt by the slow reduction of CO_2 adsorbed on Al_2O_3 as carbonate [27].) The inset of Fig. 2 shows that when CD reached the catalyst, CO was rapidly displaced from Pt, but reappears with time on stream. The competitive adsorption of CO, H, and CD has been shown previously [28,29]. This detail indicates the chiral switch at Pt, which was, however, immediately masked by the replacement of QD by CD on Al_2O_3.

To uncover the molecular interaction of the modifiers with the metal surface, a Pt thin film deposited onto Al_2O_3 was used as a model catalyst. Fig. 3 shows the spectra of QD before the chiral switch and that of CD after the chiral switch. It can be seen that CD adsorbed preferentially parallel to Pt, as indicated by the signal at 1570 cm^{-1} [30,31]. In contrast, a dominantly tilted geometry of QD was displayed by the strong signals at 1510 and 1620 cm^{-1}. This binding mode, illustrated in the inset in Fig. 1, led to weaker modifier–Pt interaction.

As mentioned previously, CD and QD have the same ee when applied alone in pyruvate hydrogenation [18,23]. It is reasonable to assume that the reaction mechanism, including the adsorption geometry of the alkaloids (parallel to the Pt surface via the quinoline ring [21]), is similar with these two modifiers.

It was shown earlier that this "flat" adsorption mode is dominant for CD, although more weakly adsorbed tilted species are also present on Pt [30]. In contrast, the contribution of the flat adsorption mode is minor with QD, because this alkaloid adopts dominantly tilted adsorption geometry (Fig. 3), which is a spectator species that does not participate in enantioselection. As a result, in CD–QD mixtures, the former controls the enantioselection, which explains the large nonlinearity and different rates of their substitution on Pt.

4. Conclusion

The transient experiments in the continuous-flow reactor illustrate the feasibility of switching the major enantiomer in the product by simply changing the feed from one modifier to another. Besides the technical importance, this concept offers a new possibility for screening modifier libraries. With this approach, not only the efficiency of the modifiers, but also their relative adsorption strength can be estimated.

The ATR-IR experiments were carried out under true in situ conditions, as evidenced by the enantioselective transformation of ethyl pyruvate in the tiny high-pressure reactor cell. It has already been speculated [18] that the weaker adsorption of QD relative to CD is due to the dominantly tilted adsorption mode of the quinoline ring; our study provides the first experimental evidence for this assumption. Catalytic experiments on the kinetic aspects of the chiral switch and further ATR-IR studies regarding CN adsorption are in progress.

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