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Highly asymmetric heterogeneous catalytic hydrogenation of isophorone on proline modified base-supported palladium catalysts

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Abstract

A highly effective asymmetric heterogeneous catalytic hydrogenation of isophorone (3,5,5-trimethyl-2-cyclohexenone) by proline-modified base-supported Pd catalysts is described. Effective combination of enhanced proline adsorption and secondary kinetic resolution resulted in very high enantioselectivities (*ee* up to 99%). Using (*S*)- and (*R*)-proline enantiomers as chiral auxiliaries, both enantiomers of the product were obtained with excellent optical yields.

Keywords: Chiral hydrogenation; Pd catalysts; Isophorone; Proline; Support effect; Secondary kinetic resolution

1. Introduction

The special importance of chiral molecules in numerous domains of modern life provides extraordinary potential for asymmetric synthesis [1]. Heterogeneous asymmetric catalytic hydrogenation is one of the most versatile methods for synthesizing chiral compounds [2]. Currently, tartaric acid-modified Raney-Ni and cinchona alkaloid-modified Pt catalysts are the most prominent systems for the hydrogenation of β and α-ketoesters, respectively [3]. Continuous improvements have followed the original discoveries by Izumi et al. (Raney-Ni-tartaric acid) [4] and Orito et al. (Pt-cinchona) [5]. Several reviews and books have summarized the developments in this field [3]. Due to significant interest in practical applications, the field of chiral heterogeneous hydrogenations has undergone an explosive development in recent years. Numerous new feasible applications with *ee* > 90% have been published [6]. In addition to new applications, extensive efforts have been made to interpret the mechanisms of these reactions [7].

Despite the significant advancement in heterogeneous chiral C=O hydrogenation, no comparable, effective, and practical processes are available for the equally important C=C double-bond hydrogenation. The most prominent example is chiral hydrogenation of 4-methoxypyrone and 4-hydroxypyrone on cinchona-modified Pd/TiO_2 catalysts. Under optimized conditions, very high enantioselectivity has been achieved (up to 94% *ee*) [8]. These results were the first to demonstrate that the potential of chirally modified heterogeneous Pd catalysts is much broader than considered before. This study unambiguously indicates that Pd catalysts can be as useful and practical in heterogeneous enantioselective applications as the well-known Pt-cinchona or Ni-tartrate systems. Other promising examples include hydrogenation of 2-methyl-2-pentenoic acid (*ee* up to 66%) [9], α-phenylcinnamic acid (*ee* up to 72%) [10], and itaconic acid (*ee* up to 71%) [11]. In addition to tartaric acid and cinchona alkaloids, (*S*)-proline has also been found to initiate chiral induction in C=C double-bond hydrogenation of isophorone [12]. The system was extensively studied, and the highest enantioselectivity obtained was 56% [13]. Several recent reviews have summarized the latest developments [14,15].

Continuing our efforts to develop new selective chiral heterogeneous hydrogenation catalysts and applications, herein we report the highly asymmetric hydrogenation of isophorone on

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Table 1
Effect of catalyst support on the hydrogenation of isophorone on (*S*)-proline modified Pd catalysts at RT and 5 bar hydrogen pressure (50 mg catalyst, 1.0 mmol of (*S*)-proline, 1.0 mmol isophorone, 5 ml of EtOH, the *ee* values were determined after 1 h reaction time, (*S*) product formed in excess)

Catalyst	Supplier, catalyst no.	Conversion (%)	**4** selectivity (%)	*ee* (%)
5% Pd/C	Engelhard Selcat 103	100	33	8
5% Pd/Al_2O_3	Engelhard 40692	100	30	34
5% $Pd/BaCO_3$	Aldrich 23,752-3	37	85	68
5% $Pd/BaCO_3$	Alfa-Aesar 11721	65	82	72
5% $Pd/CaCO_3$	Alfa- Aesar 11723	76	55	84
5% Pd/SrCO	Alfa-Aeasar 39819	57	84	74

proline modified base-supported Pd catalysts. We illustrate the advantages of using these catalytic systems and propose some interpretations of our results.

2. Experimental

2.1. Materials

Isophorone used was of analytical grade (Aldrich), and solvents with minimum purity of 99.5% were Fisher products. (*S*)- and (*R*)-prolines (minimum purity >99.5%) were purchased from Fluka. The Pd catalysts used in this study are commercially available; catalysts were purchased from Aldrich (5% $Pd/BaCO_3$), Engelhard (5% Pd/C-Selcat103, 5% Pd/Al_2O_3-E40692), and Alfa-Aesar (5% $Pd/BaCO_3$, 5% Pd/CaO_3, 5% $Pd/SrCO_3$). Catalyst sources and codes are given in Table 1. Because each catalyst is commercially available, we determined the metal particle size of only four carbonate-supported catalysts, which play a major role in the present study. Mean metal particle sizes were determined by high-resolution transmission electron microscopy (JEOL 4000FX electron microscope) as described earlier [16]. The following mean particle sizes were obtained: 5% $Pd/BaCO_3$ (Aldrich, 237523), 4.3 nm; 5% Pd/BaO_3 (Alfa-Aesar, 11721), 6.9 nm; 5% Pd/CaO_3 (Alfa-Aesar, 11723), 3.9 nm; 5% Pd/SrO_3 (Alfa-Aesar, 39819), 3.3 nm.

2.2. General procedure for asymmetric hydrogenation of isophorone on proline-modified Pd catalysts

The hydrogenations were performed at room temperature (25 °C) in a Berghof HR-100 autoclave equipped with a Teflon liner. The catalytic system including catalyst, solvent, and modifier [50 mg of 5% Pd catalyst, 114 mg (1.0 mmol) of (*S*)-proline, and 5 ml of EtOH] was activated under 20 bar of hydrogen pressure with continuous stirring for 30 min. The reactant (150 μL [1.0 mmol]) was introduced, then the autoclave was flushed with hydrogen several times and filled to the desired pressure and stirred (at 1000 rpm) for the required reaction time (usually 2 h). Alterations from this general procedure are noted in tables and figures.

2.3. General procedure for kinetic resolution of racemic dihydroisophorone on proline modified Pd catalyst

Racemic dihydroisophorone was prepared at room temperature (25 °C) using a Berghof HR-100 autoclave with a Teflon liner by the hydrogenation of isophorone (20 mmol) on 100 mg of Pd/Al_2O_3 in 15 ml of ethanol, at 20 bar of hydrogen pressure. The catalyst was removed by membrane filtration, and the solvent was evaporated in *vacuo*. The obtained product *rac*-dihydroisophorone was of 99% purity (GC).

Then 1 mmol of *racemic* dihydroisophorone was added to a pretreated mixture (see Section 2.2) of 50 mg of 5% $Pd/BaCO_3$ catalyst, 114 mg (1.0 mmol) of (*S*)-proline, and 5 ml of EtOH. The mixture was hydrogenated at room temperature (25 °C) and at 5 bar of hydrogen pressure in a Berghof HR-100 autoclave with a Teflon liner. Samples were withdrawn periodically and analyzed by GC and GC–MS for selectivity determination and product identification, respectively.

2.4. Analysis

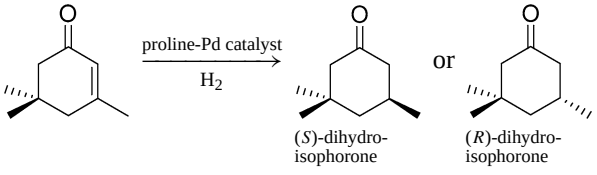
Product identification was monitored by GC–MS (Shimadzu QP 5050 System), whereas enantiomeric excess ($ee\ (\%) = |[R] - [S]| \times 100/([R] + [S])$) was determined by chiral gas chromatography (HP 5890 GC-FID, 30-m-long Betadex [Supelco] capillary column). The absolute configuration of products was determined through a comparison with an authentic sample [12,13]. The *ee* values were reproducible within 1%.

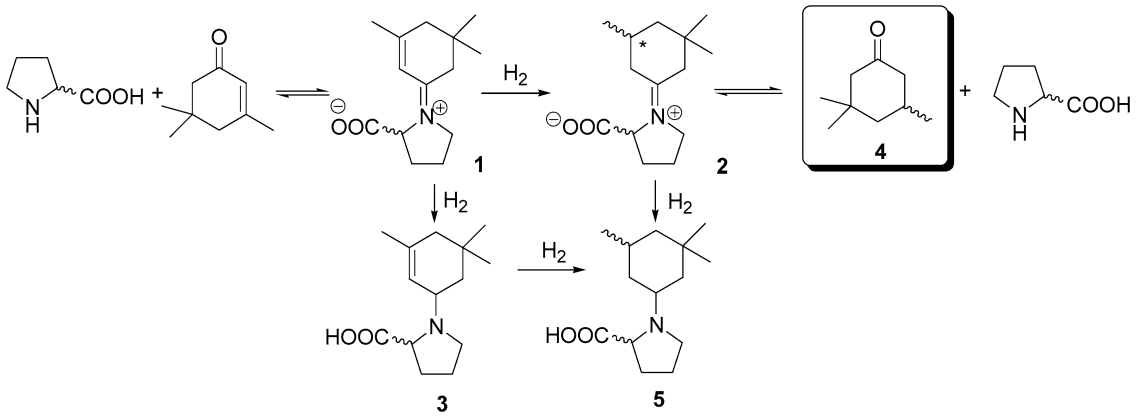
2.5. Determination of adsorbed proline amount

The proline-catalyst-solvent mixture [50 mg of Pd catalyst, 114 mg of (*S*)-proline, and 5 mL of CD_3OD] was stirred for various times (5, 10, 20, and 30 min), after which the catalyst was removed by membrane filtration and the supernatant was analyzed. The proline content of the supernatant was determined by ^1H NMR after calibration, with ethanol as an internal standard, using a Varian Innova400 (400 MHz) NMR spectrometer.

3. Results and discussion

(*S*)-Proline has been applied as modifier in heterogeneous enantioselective hydrogenations (*ee* up to 56%) [12,13,15]. Recent publications on proline as a chiral catalyst sparked renewed interest in this "old–new" chiral auxiliary [17]. Proline has induced very high enantioselectivity (>90% *ee*) in several new applications, including aldol condensation, Diels–Alder reaction, and Claisen rearrangement. For the present study, asymmetric hydrogenation of isophorone was selected as the test reaction:





Scheme 1. General pathway of proline-modified hydrogenation of isophorone.

This mechanism involves formation and hydrogenation of intermediate (**1**) to dihydroisophorone (**4**) (Scheme 1) [12,13,15]. Fully hydrogenated stereoisomeric proline–isophorone adducts (**5**) also form as undesired byproducts. These adducts (including **1**) were characterized previously and confirmed by our GC–MS investigations [12,13]. No other byproducts have been observed.

Our recent investigations on the test reaction using presonicated proline-modified Pd/Al_2O_3 catalysts indicated the importance of modifier adsorption in obtaining high enantioselectivity [18]. Presonicated catalysts gave 20–25% higher *ee* values than their nonsonicated counterparts. As this pretreatment method improves modifier adsorption [19]; the *ee* increase has been explained by a similar effect [18]. These findings suggest the use of catalysts that improve proline adsorption. One possible way to do this is to anchor proline through ionic interaction–namely, acid–base surface bonding. Because proline has multiple functional groups, it is capable of reacting under such conditions. Therefore, the use of both acidic and basic supports is promising. However, the specific C=O–NH interaction requires the nitrogen of modifier (Scheme 1). Thus, we have selected four commercially available base-supported catalysts. These catalysts have been characterized by transmission electron microscopy [16]. The following mean particle sizes were obtained: 5% $Pd/BaCO_3$ (Aldrich, 237523), 4.3 nm; 5% Pd/BaO_3 (Alfa-Aesar, 11721), 6.9 nm; 5% Pd/CaO_3 (Alfa-Aesar, 11723), 3.9 nm; 5% Pd/SrO_3 (Alfa-Aesar, 39819), 3.3 nm. These particle sizes are similar to those of platinum or palladium catalysts commonly used in asymmetric hydrogenations (e.g., 5% Pd/Al_2O_3 [Engelhard 40692], also used in this study, 4.1 nm; 5% Pt/Al_2O_3 [Engelhard 4759], 3.5 nm).

To test our hypothesis, we investigated these four alkaline earth metal carbonate-supported Pd catalysts. For comparison, we also tested two catalysts with considerably neutral supports. The results are summarized in Table 1.

The data clearly indicate that nature of the support strongly affects the reaction. Although the activity of alkaline earth metal carbonate-supported catalysts is lower than that of carbon- and alumina-supported samples, they provide higher enantioselectivity. Their use resulted in a minimum two-fold increase in *ee* values. In addition, chemoselectivity toward formation of **4** was also significantly better using these catalysts.

Based on our intention to demonstrate a generally applicable character of our idea, we carried out further investigations with each carbonate-supported sample. As a next step, we decided to test the effect of solvents to determine the most beneficial media for hydrogenation. A wide variety of solvents was applied, starting with methanol and extending to completely nonpolar solvents, such as toluene. The results are summarized in Table 2.

As the data indicate, MeOH and EtOH result in significantly higher *ee* values than any other solvent. Nonpolar and polar nonprotic solvents tend to not be advantageous for hydrogenation. It is worth noting that conversion is relatively low in ethanol; however, optical yields are practically equal to those obtained in methanol at close to 100% conversion. Because enantioselectivity is a kinetic phenomenon in these systems, at higher conversion values, optical yields should also be higher. Accordingly, ethanol was chosen as a solvent for further study.

Due to the critical importance of hydrogen pressure to hydrogenation, the effect of this variable on enantioselectivity and product accumulation rates was determined for each alkaline-earth metal carbonate-supported catalyst. The results are summarized in Fig. 1.

As Fig. 1a shows, hydrogen pressure has no significant effect on enantioselectivity values in the presence of $BaCO_3$-supported samples (*ee* up to 97%); however, $CaCO_3$- and $SrCO_3$-supported catalysts lose enantioselectivity (to 85% *ee*) at higher hydrogen pressures. Hydrogen pressure mainly affects reaction rates; reaction occurs with significantly lower rates at lower hydrogen pressures (Fig. 1b).

Enantioselectivity is usually a kinetic phenomenon in these systems; therefore, the best optical yields are expected at higher conversion values. To verify this expectation, we determined the conversion versus reaction time and optical yield versus conversion functions for each catalyst (Fig. 2). It is worth noting that formation of **5** could significantly affect these and other kinetic curves, depending on the rate of formation on an individual catalyst. Although in product mixtures only the formation of **5** has been observed, this compound can form through three pathways (with **1**, **2**, and **4** as possible precursors). Be-

Table 2
Effect of solvents on the enantioselective hydrogenation of isophorone (50 mg catalyst, 114 mg (1.0 mmol) of (*S*)-proline, 150 µL (1.0 mmol) isophorone and 5 ml of solvent, RT, 80 bar hydrogen pressure). (*S*)-Dihydroisophorone formed in excess in each case

Solvent	Catalysts	Conversion	Reaction time (h)	*ee* (%)
Methanol	$Pd/BaCO_3^A$	100	1.5	64
	$Pd/BaCO_3^{AA}$	96	1	55
	$Pd/CaCO_3$	100	1	47
	$Pd/SrCO_3$	96	1	56
Ethanol	$Pd/BaCO_3^A$	23	1.5	60
	$Pd/BaCO_3^{AA}$	20	1	54
	$Pd/CaCO_3$	90	1	83
	$Pd/SrCO_3$	45	1	56
Isopropanol	$Pd/BaCO_3^A$	16	1.5	32
	$Pd/BaCO_3^{AA}$	34	1	26
	$Pd/CaCO_3$	42	1	23
	$Pd/SrCO_3$	60	1	16
Acetonitrile	$Pd/BaCO_3^A$	20	1.5	20
	$Pd/BaCO_3^{AA}$	75	1	14
	$Pd/CaCO_3$	57	1	20
	$Pd/SrCO_3$	80	1	14
DMF	$Pd/BaCO_3^A$	25	1.5	15
	$Pd/BaCO_3^{AA}$	84	1	10
	$Pd/CaCO_3$	64	1	18
	$Pd/SrCO_3$	60	1	16
Ethyl acetate	$Pd/BaCO_3^A$	75	1.5	20
	$Pd/BaCO_3^{AA}$	100	1	32
	$Pd/CaCO_3$	65	1	19
	$Pd/SrCO_3$	100	1	13
Ether	$Pd/BaCO_3^A$	54	1.5	14
	$Pd/BaCO_3^{AA}$	98	1	40
	$Pd/CaCO_3$	56	1	12
	$Pd/SrCO_3$	73	1	30
Toluene	$Pd/BaCO_3^A$	77	1.5	22
	$Pd/BaCO_3^{AA}$	100	1	24
	$Pd/CaCO_3$	75	1	18
	$Pd/SrCO_3$	100	1	40

A, Aldrich; AA, Alfa-Aesar.

cause the rate of these secondary reactions could be reasonably different for diverse catalysts, hydrogen pressures, or solvents, these curves are suitable only for illustration, not for quantitative analysis.

The conversion versus reaction time curves demonstrate a typical saturation-type tendency. The *ee* versus conversion functions, however, show a monotonous increase that turns to saturation only at around 100% conversion, providing excellent enantioselectivity on each catalyst (85–96%). The shapes of these curves are significantly different than those seen in cinchona-modified systems [20]. These features, together with decreased selectivity toward formation of dihydroisophorone (**4**), indicate a secondary reaction. The data suggest that formation of product **5** (Scheme 1) predominantly consumes the minor (*R*)-dihydroisophorone [(*R*)-**4**] in the presence of (*S*)-proline. This phenomenon increases *ee* values of **4** to virtually 100% (99.5% *ee*) on $BaCO_3$- and $SrCO_3$-supported catalysts.

This phenomenon has been verified in separate experiments. Catalytic hydrogenation of isophorone on (nonmodified) Pd/Al_2O_3 catalyst readily provided an authentic sample of

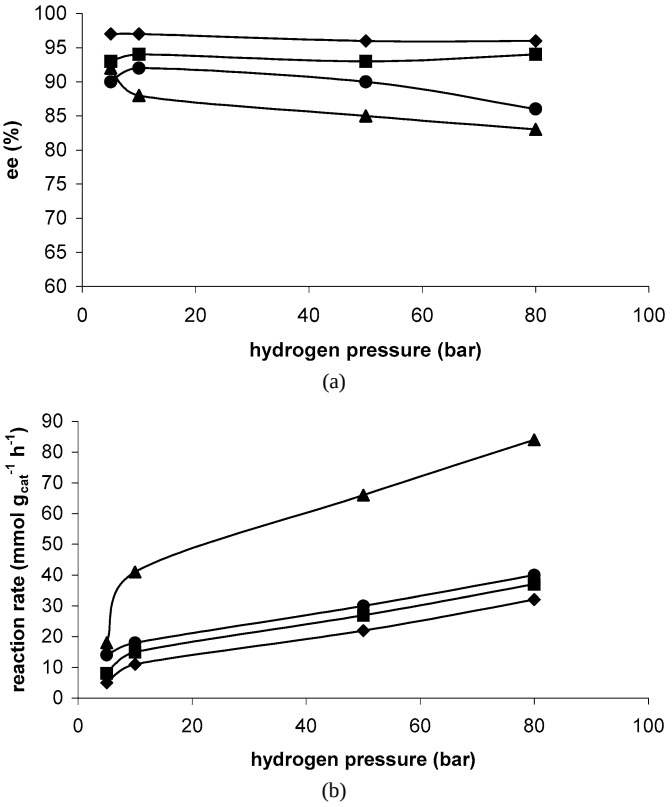


Fig. 1. Effect of hydrogen pressure on enantiomeric excesses (a); and reaction rates (b) in enantioselective hydrogenation of isophorone at room temperature (50 mg catalyst, 1.0 mmol of (*S*)-proline, 1.0 mmol isophorone and 5 ml of EtOH. ◆, $Pd/BaCO_3$(Aldrich); ■, $Pd/BaCO_3$(Alfa-Aesar); ▲, $Pd/CaCO_3$; ●, $Pd/SrCO_3$). (*S*)-Dihydroisophorone formed in excess in each case.

racemic dihydroisophorone (**4**). Then chiral hydrogenation of *rac*-**4** was carried out by (*S*)-proline-modified $Pd/BaCO_3$ catalyst. After the usual catalyst pretreatment (see Experimental section), 1 mmol of dihydroisophorone was added, the mixture was hydrogenated at room temperature for several hours, and samples were withdrawn and analyzed. For comparison, this experiment was also carried out using (*S*)-proline-modified commercial Pd/C and Pd/Al_2O_3 catalysts. The results are summarized in Fig. 3.

As the data clearly show, a change in enantiomeric excess is exactly opposite to the change in selectivity. According to Scheme 1, proline reacts with dihydroisophorone (**4**) and either decomposes to form equilibrium or undergoes hydrogenation on the Pd surface to form **5**, which is stable and does not decompose. As this process progresses, the selectivity for dihydroisophorone decreases considerably (Fig. 3b). In parallel, the originally *racemic* sample becomes chiral, and within minutes a significant increase in enantiomeric excess can be observed (Fig. 3a). (*S*)-Proline-modified catalysts consume (*R*)-dihydroisophorone in a fast reaction, resulting in the formation of (*S*)-dihydroisophorone-enriched mixtures. Using (*R*)-proline-modified catalysts, the enantioselection is the opposite, and (*R*)-dihydroisophorone-enriched product forms. The extent of kinetic resolution varies with different catalysts. Whereas $Pd/BaCO_3$ catalyst results in virtually enantiopure (*S*)-dihydroisophorone, the *ee* values turn to saturation on

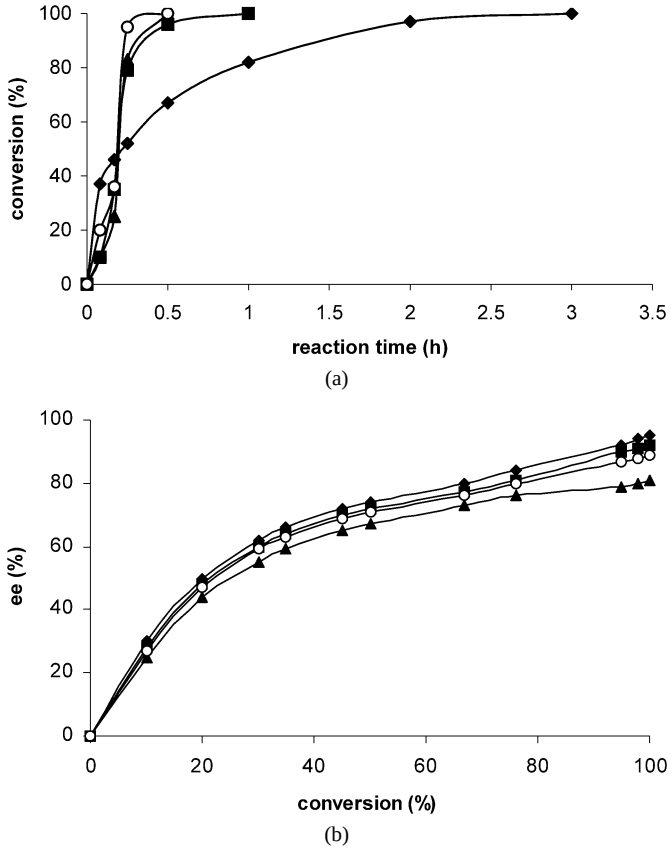


Fig. 2. Effect of reaction time on conversion (a); and conversion on enantiomeric excess (b) in the enantioselective hydrogenation of isophorone at room temperature in ethanol at 80 bar hydrogen pressure (50 mg catalyst, 1.0 mmol of (*S*)-proline, 1.0 mmol isophorone, 5 ml of solvent. ◆, $Pd/BaCO_3$(Aldrich); ■, $Pd/BaCO_3$(Alfa-Aesar); ▲, $Pd/CaCO_3$; ○, $Pd/SrCO_3$). (*S*)-Dihydroisophorone formed in excess in each case.

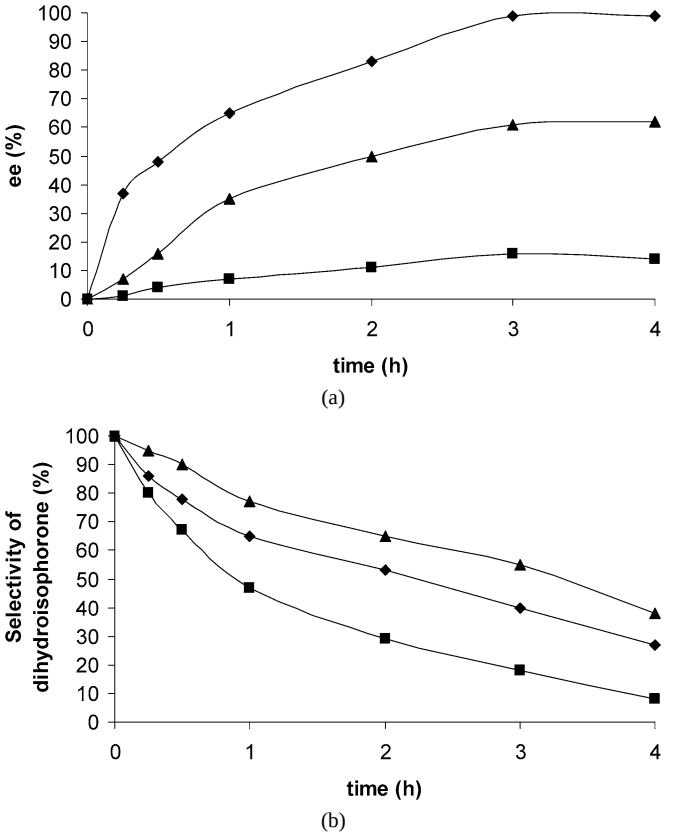


Fig. 3. Kinetic resolution of *racemic* dihydroisophorone in the presence of (*S*)-proline modified-supported Pd catalysts at 5 bar hydrogen pressure: ◆, $Pd/BaCO_3$ (Aldrich); ■, Pd/C (Engelhard); ▲, Pd/Al_2O_3 (Engelhard). (a) Enantiomeric excess as a function of reaction time (b) selectivity of dihydroisophorone as a function of reaction time at room temperature (50 mg catalyst, 1.0 mmol of (*S*)-proline, 1.0 mmol dihydroisophorone, and 5 ml of EtOH, RT). (*S*)-Dihydroisophorone formed in excess in each case.

Pd/Al_2O_3 (at 62% *ee*) and Pd/C (at 12% *ee*). These results are in agreement with the data given in Table 1 and indicate that enantiodifferentiation is more effective when using base-supported Pd catalysts. Comparing Figs. 2b and 3a reveals curves of similar shape for enantiodifferentiation, clearly suggesting that secondary kinetic resolution plays a crucial role in determining the final enantiomeric excess.

Accordingly, we optimized the process for each carbonate-supported catalyst. The results including both (*S*)- and (*R*)-proline modified reactions are tabulated in Table 3. These catalysts produce excellent enantioselectivity under optimized conditions. Each catalyst provides *ee* values ⩾94% using either of the proline enantiomers. It is worth mentioning that both enantiomers of dihydroisophorone (**4**) can be synthesized with selection of appropriate proline enantiomer as a modifier. Chemoselectivity values toward formation of dihydroisophorone (**4**) are moderate, due to secondary kinetic resolution, but are still significantly better than those obtained on other catalysts (Tables 1 and 3).

Our earlier results on presonicated catalysts suggested the importance of enhanced proline adsorption. This has been key idea in using carbonate-supported Pd catalysts. To test this hypothesis, we studied proline-catalyst-EtOH mixtures under the usual pretreatment conditions (see Experimental section).

Table 3
Optimized asymmetric hydrogenation of isophorone on proline-modified Pd catalysts at RT and 5 bar hydrogen pressure (100% conversion) in EtOH (50 mg catalyst, 1.0 mmol of (*S*)-proline, 1.0 mmol isophorone, 5 ml of solvent)

Catalyst[a]	Chiral auxiliary	Product	**4** selectivity (%)	*ee* (%)
5% $Pd/BaCO_3$-A	(*S*)-Proline	(*S*)	45	99
5% $Pd/BaCO_3$-A	(*R*)-Proline	(*R*)	51	94
5% $Pd/BaCO_3$-AA	(*S*)-Proline	(*S*)	50	99
5% $Pd/BaCO_3$-AA	(*R*)-Proline	(*R*)	51	94
5% $Pd/CaCO_3$-AA	(*S*)-Proline	(*S*)	45	99
5% $Pd/CaCO_3$-AA	(*R*)-Proline	(*R*)	47	98
5% $Pd/SrCO_3$-AA	(*S*)-Proline	(*S*)	52	99
5% $Pd/SrCO_3$-AA	(*R*)-Proline	(*R*)	53	97

[a] A, Aldrich; AA, Alfa-Aesar.

These experiments were designed to detect changes in proline concentration on contact with the catalysts. A similar approach has been proven useful in characterizing presonicated cinchona-modified Pt catalysts [19]. Mixtures were stirred, and samples were withdrawn at specified times. Then the solids were removed by membrane filtration, and the proline concentration of the liquid was determined by ^{1}H NMR after calibration. We studied $Pd/BaCO_3$ (Aldrich), Pd/C (Engelhard Selcat 103), and

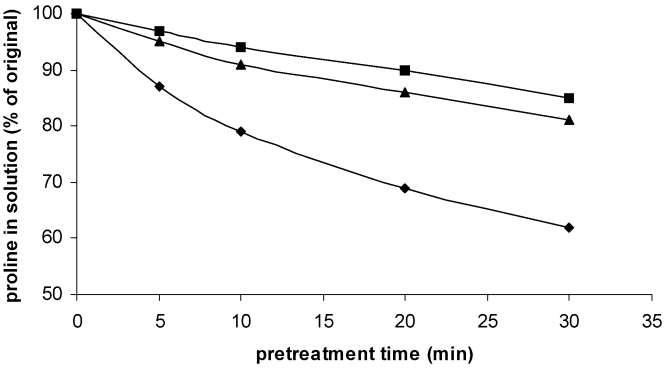


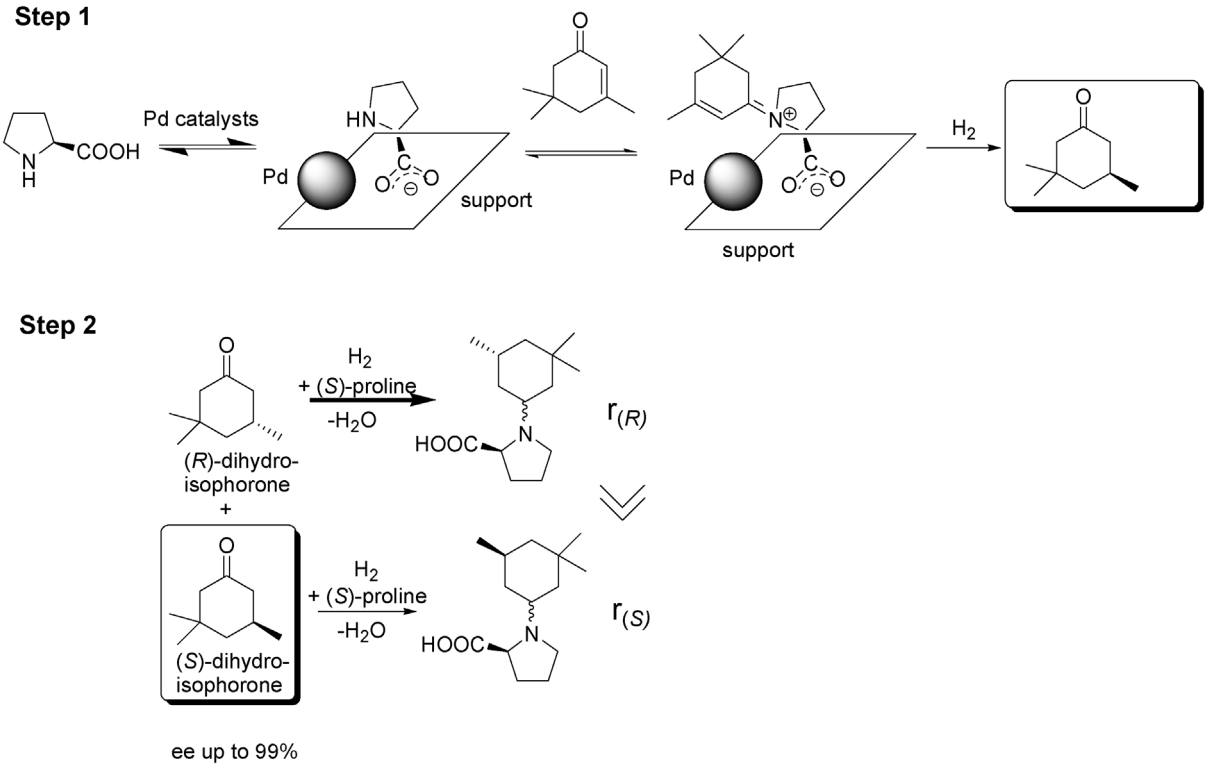
Fig. 4. Effect of modifier-catalyst contact time on the proline concentration in the supernatant of a typical catalytic system (50 mg catalyst, 1.0 mmol of (*S*)-proline, 5 ml of MeOH). ◆, Pd/$BaCO_3$ (Aldrich); ■, Pd/C (Engelhard); ▲, Pd/Al_2O_3 (Engelhard).

Pd/Al_2O_3 catalysts (Engelhard 40692). The results are illustrated in Fig. 4.

As shown, the amount of proline decreased significantly on contact with the $BaCO_3$-supported catalyst. In contrast, only a minor decrease occurred in the presence of the C- and Al_2O_3-supported samples. The maximum decrease in proline concentration was observed after 30 min of contact time. (Because a 30-min pretreatment was applied before hydrogenation, the effect of longer contact times was not studied.) This phenomenon can be explained by more pronounced proline adsorption on the surface of the Pd/$BaCO_3$ catalyst. Comparison with the carbon- and alumina-supported samples indicates a significant contribution of the $BaCO_3$ support in enhancing proline adsorption. These experiments show that basic supports considerably enhance proline adsorption on the catalyst including both metal and support. As such, these catalysts provide a better chiral environment for hydrogenation, in accordance with enhanced *ee* values.

The foregoing results suggest that the excellent enantioselectivity can be explained by synergism of two phenomena. First, our earlier results on presonicated Pd/Al_2O_3 catalysts [18] suggest that strong proline adsorption is needed to obtain high *ee* values. In the present case, the use of basic supports enhances proline adsorption by providing a suitable chemical environment through ionic interaction (i.e., acid–base reaction). The present catalytic system is a new, effective example of the support effect in heterogeneous catalysis. It is known (in, e.g., chemoselective hydrogenation) that the chemical nature of a support can significantly affect selectivity [21]. This is exactly what we have observed in the present work. High proline coverage on the catalyst surface provides a sufficient, effective chiral environment for enantioselection. We propose that first step of the mechanism is the proline adsorption occurring during pretreatment. Carbonate-supported catalysts most likely promote proline adsorption on their basic support. Therefore, it is reasonable to suggest that proline covers metal–support interfaces and thereby blocks *racemic* hydrogenation. The adsorbed amount suggests that the modifier practically covers the surface, leaving only a limited number of active sites unmodified.

Second, as observed, decreasing chemoselectivity accompanies increasing *ee* values due to secondary kinetic resolution. It is clear that strong proline adsorption makes this resolution step successful on carbonate-supported catalysts. In contrast, catalysts with neutral support (C or alumina) result in only



Scheme 2. Proposed mechanism of isophorone hydrogenation on (*S*)-proline modified carbonate supported Pd catalysts.

negligible (carbon) or moderate (Al_2O_3) enantiodifferentiation during kinetic resolution. Our proposed mechanistic scheme is illustrated on Scheme 2.

4. Conclusions

In conclusion, our investigations using different catalyst supports clearly indicate that modifier adsorption is crucial factor in asymmetric hydrogenation of α,β-unsaturated carbonyl compounds, such as isophorone, on proline-modified Pd catalysts. Using alkaline earth metal carbonate-supported catalysts produces significant secondary kinetic resolution. These catalysts successfully enhance enantiodifferentiation and provide unprecedented high *ee* values (up to 99% *ee*). Similar application of chemical adsorption of chiral auxiliaries may open up wide range of new practical application possibilities for heterogeneous catalytic asymmetric hydrogenation.

Acknowledgments

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