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Stereodifferentiation in heterogeneous catalytic hydrogenation. Kinetic resolution and asymmetric hydrogenation in the presence of (*S*)-proline: Catalyst-dependent processes

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ABSTRACT

The kinetic resolution of 3,5,5-trimethyl cyclohexanone (TMCH) and asymmetric hydrogenation of isophorone (3,5,5-trimethyl cyclohex-2-enone, IP) were investigated on different Pd catalysts in the presence of (*S*)-proline (Pr). It could be proven that in isophorone hydrogenation the optically active TMCH was formed not only by kinetic resolution but also through asymmetric C=C hydrogenation. The activity and stereoselectivity of different Pd catalysts depended on the support material, preparation method, and reaction conditions as well, confirming our assumption that enantiodifferentiation takes also place on the catalyst surface and not only in the homogeneous liquid phase condensation reaction.

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1. Introduction

Heterogeneous catalytic asymmetric hydrogenation of isophorone (3,5,5-trimethyl cyclohex-2-enone, IP, **2**) in the presence of (*S*)-proline (Pr, **1**) was first reported more than 20 years ago [1–3]. IP was the only substrate among several α,β-unsaturated ketones which afforded significant *ee* (60% at 55% chemical yield of trimethyl cyclohexanone, TMCH, **3**) in this reaction [4]. Continuing this work, asymmetric hydrogenation of acetophenone [5,6], diastereoselective reductive alkylation of Pr with ethyl pyruvate [7,8], asymmetric hydrogenation of benzylidene benzosuberone [9], synthesis of chiral modifiers based on (*S*)-proline, and their use in the enantioselective hydrogenation of IP [10–14] were also investigated.

Detailed circular dichroism, NMR and IR spectroscopy measurements, and preparative experiments resulted in the conclusion that asymmetric hydrogenation of IP can proceed through carbonylamine (**4**) and oxazolidinone-type intermediate (**5**), which was verified on the basis of the work of Joucla and Mortier [15]. Recently, Seebach et al. [16] studied these compounds and their reactivity in detail, stressing their role in proline catalysis. List et al. [17] tried to find out which intermediate compounds play significant role in the proline-catalyzed aldol reaction of different ketones, using O^{18}-labeled water. Based on these results they suggest a covalent, enamine intermediate (**8**).

In IP hydrogenation [4], the optical purity of TMCH depended on the catalytic metal. Pd and Rh gave higher *ee*, but only alkylated proline was formed with Pt. The product *ee* changed also with the solvent, methanol proved to be the best one. The effect of IP/Pr molar ratio on *ee* was tested too, 1:1 ratio gave the best result.

Török and co-workers [18] initiated the revival of the Pd-mediated asymmetric hydrogenation of IP with Pr, they regarded Pr as a catalyst modifier, not as a chiral auxiliary. Two years later Török and co-workers [19] proposed another mechanism for IP/Pr hydrogenation on different Pd catalysts. The participation of kinetic resolution in the formation of optically active TMCH was stressed. They emphasized the role of Pr-modified catalyst surface in IP hydrogenation, contradicting Lambert and co-workers [20], who claimed that enantiodifferentiation takes place only in solution.

Lambert and co-workers tested the IP hydrogenation extensively [20,21]. They claimed on the basis of spectroscopic and kinetic measurements that optically active TMCH was formed solely in the kinetic resolution of this compound, namely with reductive alkylation of Pr and in complete contrast to the case of ketoester asymmetric hydrogenation, the metal surface was not involved in the crucial enantiodifferentiation step.

Li et al. [22] tested Pd supported on Al_2O_3–K_2CO_3 and concluded that the main source of optically active TMCH was kinetic resolution.

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It was pointed out in our recent paper [23] that (i) on Pd/C even at small conversions (0.12–0.2 mol hydrogen consumption) optically active TMCH was formed in significant amounts, due, likely to the asymmetric hydrogenation of IP, rather than to kinetic resolution of the saturated ketone only; (ii) at high conversions a mixture of the two alkylated proline products could be obtained which shows that Pr reacts also with (*S*)-TMCH.

An apparent analogy of our Pr chiral auxiliary-assisted asymmetric hydrogenation could be the palladium-induced domino reaction of benzyl β-ketoesters, where after the Pd-mediated hydrogenolysis of the protecting benzyl group, asymmetric decarboxylation occurs catalyzed by a chiral amine, the result being optically active ketones [24–27]. In the second step two reaction routes are possible, the homogeneous route catalyzed by chiral amino alcohol and the heterogeneous route, Pd^0 metal surface plus the adsorbed amino alcohol catalyzed asymmetric decarboxylation. Baiker and co-workers pointed out that the first, homogeneous reaction mechanism dominates, high enantioselectivity needs at least a twofold chiral auxiliary:substrate molar ratio, which can be ensured by slow deprotonation reaction, with small intermediate ketoacid concentration [27]. The analogy is really virtual in the IP/Pr and TMCH/Pr systems in contrast with the aforementioned, the role of the Pd surface, the importance of the heterogeneous reaction in stereocontrol should be proven.

Another debated issue is the role of Pr, whether it is a chiral auxiliary [4,20,21] or a chiral modifier [18,19]. The auxiliary added to the reaction mixture in commensurable amount to the substrate, can react with it, the asymmetric induction takes place within a usually covalent adduct of the auxiliary and the substrate, which contains chiral and prochiral part alike. Finally the heterogeneous catalyst Pd distinguishes between the enantiomers of this adduct, reacting faster with one isomer. Contrarily the chiral modifier [28–32] is effective even in small ratio to the substrate (1:10–$1:10^5$). It adsorbs strongly on the metal surface (for example, cinchonidine), determining the adsorption geometry of the substrate, which is bound to the modifier with second order interactions, like H-bonding. The IP/Pr system from the point of view of both quantitative and qualitative features belongs to the chiral auxiliary-governed reactions. In this respect, we agree with Lambert and co-workers [21], who pointed out the much stronger adsorption of IP than that of Pr on metallic Pt surfaces.

In order to ascertain the details of these Pr-mediated reactions, the kinetic resolution of TMCH and the asymmetric hydrogenation of IP were studied with different Pd catalysts.

2. Experimental

2.1. Materials

Pd/C catalyst Selcat Q, 10% metal content, was purchased from Fine Chemical Company. Its support is a high surface area-activated carbon (BET surface area 1200 m^2/g). Pd black catalyst was prepared according to the following procedure: 18 mmol (6.0 g) K_2PdCl_4 was dissolved in 50 ml water and reduced at boiling point with 74 mmol (5.0 g) Na(HCOO) dissolved in 20 ml water. When the reduction was complete, the pH of the suspension was basic (pH 9). The catalyst was filtered, washed several times with distilled water, and then dried in air at ambient temperature. Its BET surface area is 8 m^2/g.

Catalysts, 5 wt%, Pd/TiO_2 and Pd/Al_2O_3, were prepared as follows: the calculated amount of the catalyst precursor (K_2PdCl_4) was added to the aqueous suspension of 10 g support (nonporous TiO_2, BET surface area 40 m^2/g, or powdered alumina, surface area 50 m^2/g). The pH value of the solution was adjusted to 10–11 by adding KOH. The suspension was boiled for 1 h, and then Na(HCOO) in 2.5 molar excess with respect to palladate was added to the boiling mixture. After 30 min, the suspension was cooled, and the catalyst was filtered, washed with distilled water, and dried.

Catalysts, 5 wt%, $Pd/BaCO_3$ and Pd/MgO, were prepared as follows: the calculated amount of the catalyst precursor (H_2PdCl_4 in 5 cm^3 water) was added to the 15 cm^3 aqueous suspension of 2 g support (nonporous powdered materials), after mixing for half an hour. Na(HCOO) in 10 cm^3 aqueous solution in 2.5 molar excess with respect to palladate was added to the boiling mixture. The suspension was cooled after 30 min, and the catalyst was filtered, washed with distilled water, and dried.

Methanol, *n*-hexanol, (*S*)-proline, and isophorone were supplied by Sigma–Aldrich. The latter was distilled in vacuum before use. TMCH was prepared in our laboratory by hydrogenating isophorone without solvent, using Pd/C catalyst at ambient temperature and 10 bar hydrogen pressure. TMCH content was >99%, determined with GC.

2.2. Catalysts characterizations

Adsorption measurements were made in an atmospheric flow system [33] in order to determine the active surface of Pd catalysts samples. O_2 titration and H_2 titration were carried out after each other several times.

Prior to the first adsorption of O_2, the sample was treated in 1.2% H_2/Ar for 15 min and then in Ar gas to remove absorbed hydrogen, to avoid the hydrogen absorption in the bulk phase of the metal.

$(Pd–H)_s$ was titrated with O_2 injections via a calibrated loop (0.1 ml each). Next $(Pd–O)_s$ was titrated with H_2. After decomposition of beta-PdH, O_2 was adsorbed again.

The stoichiometry of the calculations was based on [34]:

- for titration with O_2

$$(Pd{-}H)_s + 0.75O_2 = (Pd{-}O)_s + 0.5H_2O$$

- for titration with H_2

$$(Pd{-}O)_s + 1.5H_2 = (Pd{-}H)_s + H_2O$$

2.3. Hydrogenation

Hydrogenations were carried out at 25 °C, under hydrogen pressures of 10–60 bar in a 250 cm^3 stainless steel autoclave (Technoclave) equipped with a magnetic stirrer. The solvent was methanol, with 3.5 vol% *n*-hexanol content, which served as internal standard for GC measurements. Before hydrogenation, the reaction mixtures were boiled for 5 min, then cooled, catalyst was added, and finally stirred under nitrogen for 10 min in the reaction vessel.

2.4. Analysis

Reaction mixtures were analyzed with a Chrompack 9001 gas chromatograph equipped with a β-cyclodextrine capillary column (temperature-programed analysis: 90 °C (10 min) – 10 °C/min to 160 °C) and FID. Chromatograms were recorded and the peak area was calculated with Chromatography Station for Windows V1.6 (DataApex Ltd., Prague). As internal standard, *n*-hexanol was used. The peak area of TMCH enantiomers and isophorone (the FID detector signals for same amount of TMCH and isophorone are identical) was correlated with that of *n*-hexanol, in order to determine the amount converted to alkylated proline, which cannot be detected with GC. Enantiomeric excess was defined as:

$$ee(\%) = ([R] - [S])/([R] + [S]) \times 100$$

Table 1
Results of chemisorption measurements.

Catalyst	Nominal Pd content (w%)	Final hydrogen adsorption (mol/g)	Final oxygen adsorption (mol/g)	Active surface area (m^2/g catalyst)		Active surface area (m^2/g Pd)	
				Hydrogen	Oxygen	Hydrogen	Oxygen
Pd/C Selcat Q	10	57	23	1.8	1.4	18	14
Pd/Al_2O_3	5	98	26	3.1	1.6	62	32
Pd/TiO_2	5	89	36	2.8	2.3	56	46
Pd black	100	760	350	23.9	22.0	23.9	22.0
$Pd/BaCO_3$	5	39	13	1.2	0.8	24	16
Pd/MgO	5	66	26	2.1	1.6	42	32

Table 2
Results of TMCH + Pr hydrogenations.

Catalyst (mg)	$p(H_2)$ (bar)	Reaction time (h)	Conv. (%)	*ee* (%)	Missing *S* isomer (%)	Rate[a]		Activity in period I	
						Period I	Period II	Act.[b]	Spec. act.[c]
Pd/C									
5	10	15	61	100	24	10	4.1	2	20
10	10	10	62	100	23	14	6.2	1.4	14
20	10	3.7	79	100	54	44	21	2.2	22
Pd/TiO_2									
10	10	30	40	44	15	2	1.3	0.2	4
40	10	7.5	73	100	57	17	10	0.4	8
Pd black									
5	60	24	60	89	21	5	2.5	1	1
5	10	140	47	68	12	0.6	0.34	0.12	0.12
10	10	80	51	60	20	6	0.4	0.6	0.6
Pd/Al_2O_3									
20	10	20	53	100	7	6	2.5	0.3	6
10	10	116	63	92	31	5.4	0.48	0.54	10.8
$Pd/BaCO_3$									
40	60	26	33	43	8	8	0.79	0.2	4
10	10	3	3	3	0	0	0	0	0
Pd/MgO									
40	60	19	74	92	51	11	0.3	0.28	5.6
10	10	47	58	95	19	4	1.0	0.4	8

[a] Ratio of conversion (%) and reaction time (h).
[b] Reaction rate/catalyst amount.
[c] Reaction rate/Pd amount.

3. Results and discussion

3.1. Properties of Pd catalysts

In order to prove the involvement of Pd surface in the enantiodifferentiation process, Pd on different support materials were prepared, characterized, and used, including the basic supports used by Török and co-workers [18,19]. The supported catalysts have similar active surface area; see Table 1, the small value of the high surface area carbon-supported Pd can be attributed to the smaller β-hydride formation. Pd black has been added to the series of supported catalysts as it turned to be the best in the enantioselective hydrogenation of IP with dihydroapovincaminic acid [35], (*S*)-α,α-diphenyl-2-pyrrolidinemethanol modifiers [10–14], and of benzylidene benzosuberone with cinchonidine modifier [36].

3.2. Results of hydrogenation of TMCH–proline

The amount of the catalysts was usually varied between 2 and 40 mg. The data in Table 2 represent reactions of measurable activity. The reaction rate and stereoselectivity of reductive alkylation of Pr, namely the kinetic resolution of TMCH, change substantially with the properties of Pd catalyst, with the catalyst/substrate ratio as well as with the hydrogen pressure. Value of *ee* and conversion vs. time curves for 5 mg Pd/C catalyst are shown in Fig. 1. The amount of consumed TMCH enantiomers vs. time curves for 5 and 20 mg Pd/C catalyst is depicted in Fig. 2. Increasing the amount of Pd/C catalyst from 5 to 20 mg, the consumption of both TMCH enantiomers becomes much faster, the selectivity becomes smaller, corresponding to expectations.

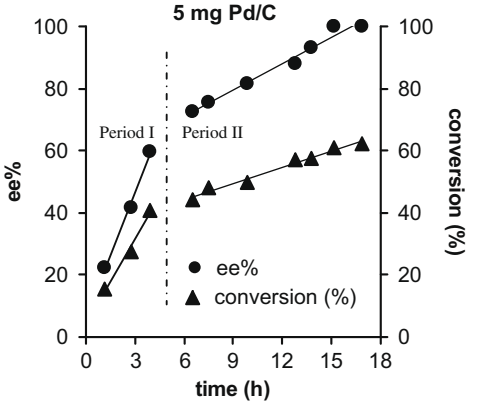


Fig. 1. *ee* and conversion vs. time. (Conditions: Pd/C catalyst, 5 mg, 20 cm^3 methanol (hexanol) solvent, 700 mg TMCH, 575 mg (*S*)-proline, hydrogen pressure 10 bar, temperature 25 °C, mixing speed 700 rpm.)

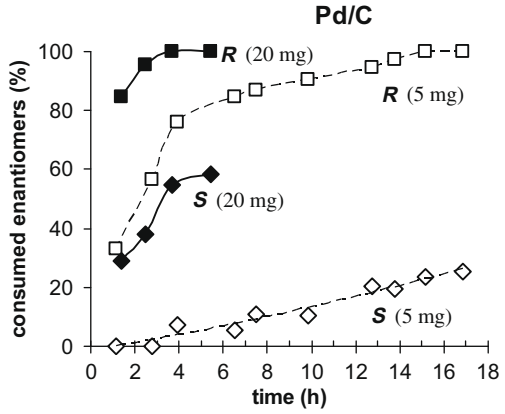


Fig. 2. Consumed TMCH enantiomers vs. time, 5 mg Pd/C, 20 mg Pd/C. (Conditions: same as before, with 5 mg catalyst.)

It is obvious that both TMCH enantiomers participate in reductive alkylation as early as the start of the reaction. The stereoselectivity of the process depends largely on the catalyst/substrate ratio. With 5 mg catalyst the consumption of the (*S*)-TMCH, (the enantiomer in excess), is only 24% until reaching 100% *ee*. With 20 mg catalyst, however, the corresponding value is 54%.

In all hydrogenations with different catalysts there are two periods with respect to reaction rate: initially approximately until 40% conversion it is faster, followed by a significantly slower section (see Fig. 1). The reaction parameters and results together with the calculated reaction rate and specific activity values are summarized in Table 2. The specific activities were calculated for the first period of the hydrogenations, they can be handled as initial rates. $Pd/BaCO_3$ catalyst could only be tested at 60 bar hydrogen pressure. It had negligible activity at 10 bar.

The activity order of the catalysts follows the sequence of active surface area, exception is Pd/C:

$$Pd/C > Pd/Al_2O_3 \cong Pd/TiO_2 \cong Pd/MgO > Pd/BaCO_3 \cong \text{Pd black}$$

With respect to stereoselectivity, Pd on alumina is superior, at 100% *ee* the amount of missing *S* enantiomer is only 7%, second is Pd/C, with 23% loss of *S*-TMCH. But even on the best catalyst the hydrogenation of the minor diastereoisomer condensate takes place, especially after the consumption of the major one (see Fig. 3).

The observed stereoselectivity order of the catalysts, based on the missing *S* isomer values at high *ee*, is:

$$Pd/Al_2O_3 > Pd/C > Pd/MgO > \text{Pd black} > Pd/BaCO_3 > Pd/TiO_2$$

With a less selective catalyst and at high pressure (Fig. 4), the consumption of both diastereoisomers is more evident from the beginning of the hydrogenation. This confirms that both diastereoisomers of the proline–TMCH condensate are present in the reaction mixture and they are hydrogenated with different relative rates depending on the catalyst used and on the reaction conditions. This proves that enantiodifferentiation occurs in the (*S*)-proline–TMCH reaction both in the homogeneous phase, i.e. in the solution at adduct forming and on the Pd surface in heterogeneous hydrogenation. The explanation of the stereoselectivity order of the different Pd catalysts needs further investigation.

3.3. Hydrogenation of isophorone in the presence of proline

The debate about the mechanism of IP/Pr asymmetric hydrogenation [19,20,22] can be summarized in one question: whether the optically active ketone was formed (i) exclusively by kinetic resolution of the saturated ketone or (ii) by the partial hydrogenation of the IP–Pr condensate resulting also in enantiomeric excess of TMCH. The possible reaction pathways (Scheme 1 and Scheme 2), were reviewed. On Scheme 1 the oxazolidinone (**5**) is the key intermediate [4,16], the formation of its precursor, a carbinolamine is accompanied already with the formation of a new asymmetric carbon. In the other reaction route, the key intermediate is an enamine (**8**) [3,17], which has a *syn* and *anti* isomer, depending on the relative position of the proline carboxylate and the two methyl groups on the cyclohexane ring. The adsorption geometry of the stereo- and diastereoisomers of both key intermediates can significantly differ in the preliminary adsorption before C=C hydrogenation, this explains the enantiodifferentiation in the hydrogenation.

The reaction routes which consume IP and the TMCH enantiomers are the alkylated proline producing reaction routes: $r_2 + r_4$, $r_1 + r_3$. If optically active TMCH is formed only through kinetic resolution, the molar amount of consumed or missing IP + TMCH would be always greater than the molar amount of the excess TMCH enantiomer (*S*). That is why hydrogenations with different catalysts, under different conditions were followed; the molar amounts of the ketones were measured as a function of time and conversion, by means of the internal standard *n*-hexanol. If our assumption is correct, r_2, the chemoselective C=C hydrogenation of the oxazolidinones (**5**), or of enamines (**8**) produces (after hydrolysis) optically active TMCH. In this case, the value of molar amount of TMCH *ee* could be greater than the moles of missing ketones obviously only in the first period of the reaction, when the kinetic resolution is marginal.

The results with Pd/C catalyst, the IP conversions, and amounts of TMCH enantiomers vs. time are represented in Fig. 5. In Fig. 6, the missing IP + TMCH vs. conversion for Pd/C and $Pd/BaCO_3$ cata-

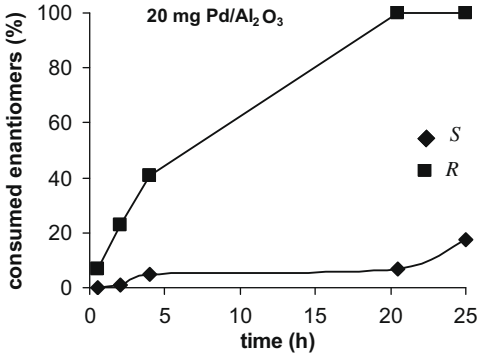


Fig. 3. Consumed TMCH enantiomers vs. time, 20 mg Pd/Al_2O_3. (Conditions: Pd/Al_2O_3 catalyst, 20 mg, 20 cm^3 methanol (hexanol) solvent, 700 mg TMCH, 575 mg (*S*)-proline, hydrogen pressure 10 bar, temperature 25 °C, mixing speed 700 rpm.)

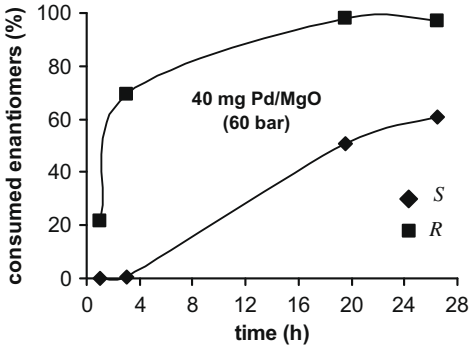
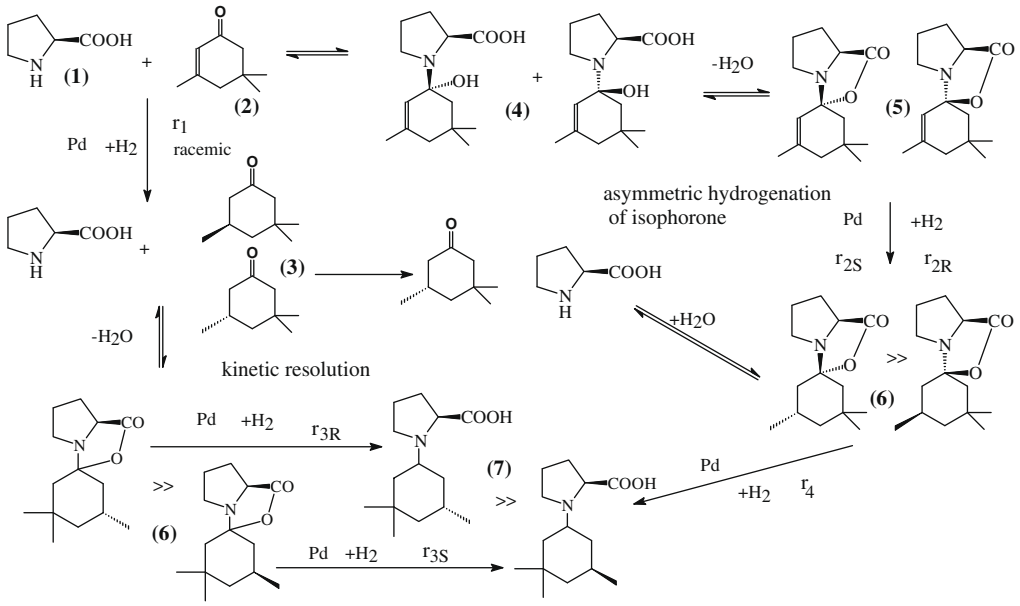
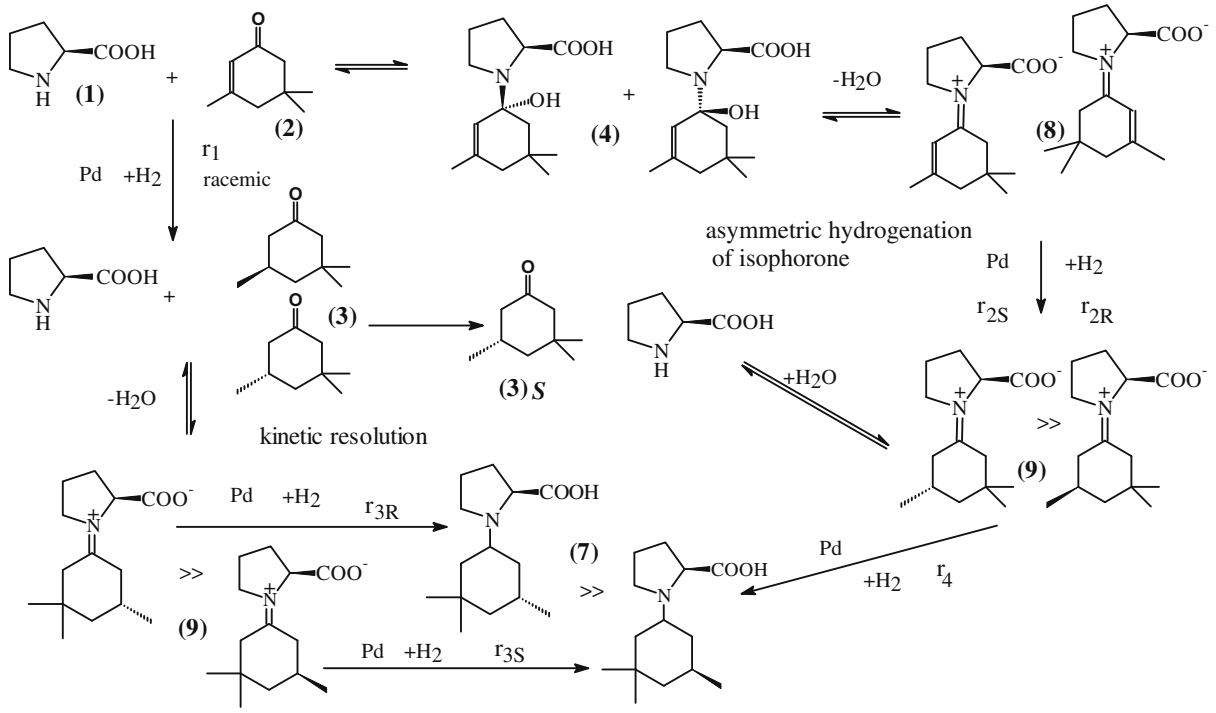


Fig. 4. Consumed TMCH enantiomers vs. time, 40 mg Pd/MgO. (Conditions: Pd/MgO catalyst, 40 mg, 20 cm^3 methanol (hexanol) solvent, 700 mg TMCH, 575 mg (*S*)-proline, hydrogen pressure 60 bar, temperature 25 °C, mixing speed 700 rpm.)



Scheme 1. The reaction scheme of the hydrogenation of the IP–Pr 1:1 mixture, key intermediate is oxazolidinone. (**1**) *S*-proline, (**2**) isophorone, (**3**) trimethyl cyclohexanone, (**4**) carbinolamine, (**5**) unsaturated oxazolidinone, (**6**) saturated oxazolidinone, and (**7**) *N*-(trimethyl cyclohexyl) proline.



Scheme 2. The reaction scheme of the hydrogenation of the IP–Pr 1:1 mixture, key intermediate is enamine. (**1**) *S*-proline, (**2**) isophorone, (**3**) trimethyl cyclohexanone, (**4**) carbinolamine, (**7**) *N*-(trimethyl cyclohexyl) proline, (**8**) unsaturated enamine, and (**9**) saturated enamine.

lysts is shown. The values are negative in the conversion range up to 60%, meaning that during this period the TMCH *ee* did not arise exclusively from kinetic resolution.

IP hydrogenation was tested with all catalysts in order to find out their activity and enantiodifferentiating ability. The results are summarized in Table 3. The activity order in IP hydrogenation was similar to that of the TMCH reductive alkylation:

$$Pd/C > Pd/Al_2O_3 > Pd/TiO_2 \approx Pd/MgO > Pd/BaCO_3 > \text{Pd black}$$

Among supported catalysts, the activity of Pd on basic supports was smaller. In Fig. 6, data characterizing the enantioselectivity of two catalysts are depicted, giving answer to the debated question about the sources of TMCH *ee*. The negative values of [missing IP + TMCH] − [*S* excess] on some catalysts indicate that, up to a particular conversion, the asymmetric C=C hydrogenation of the IP–Pr condensate takes place. The ratio of the two processes producing excess (*S*)-TMCH, namely kinetic resolution and asymmetric C=C hydrogenation cannot be established on the basis of the data in Table 3. The consecutive hydrogenation (C=C saturation + reductive alkylation without desorption, $r_2 + r_4$) cannot be excluded either. This consumes the ketone, but does not result in optically active TMCH.

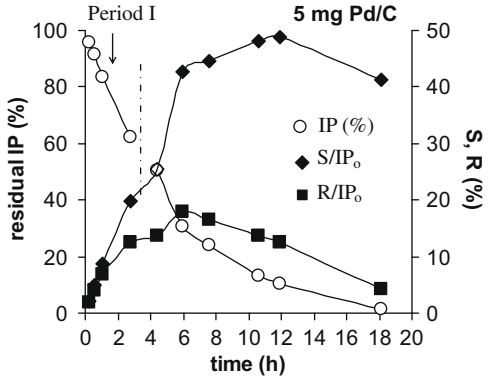


Fig. 5. The amount of residual IP and TMCH enantiomers vs. time, 10 mg Pd/C. (Conditions: Pd/C catalyst, 10 mg, 20 cm^3 methanol (hexanol) solvent, 700 mg IP, 575 mg Pr, hydrogen pressure 2 bar, temperature 25 °C, mixing speed 700 rpm.)

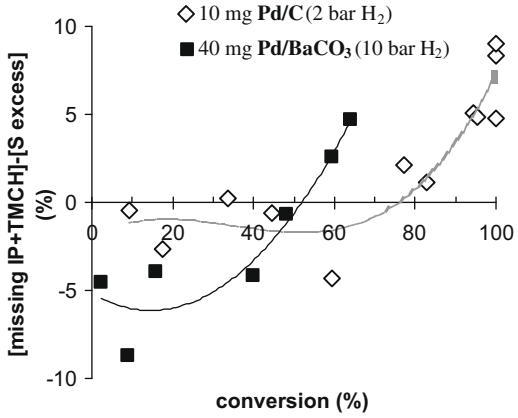


Fig. 6. The amount of [missing IP + TMCH] – [*S* excess] correlated with molar amount of starting IP$_o$ vs. conversion, 10 mg Pd/C, 40 mg Pd/BaCO$_3$. (Conditions: Pd/C catalyst, 10 mg, 20 cm^3 methanol (hexanol) solvent, 700 mg IP, 575 mg Pr, hydrogen pressure 2 bar, temperature 25 °C, mixing speed 700 rpm. Pd/BaCO$_3$ catalyst, 40 mg, 20 cm^3 methanol (hexanol) solvent, 700 mg IP, 575 mg Pr, hydrogen pressure 10 bar, temperature 25 °C, mixing speed 700 rpm.)

Data in the last column of Table 3 can be used also for characterizing the stereoselectivity of the catalyst. The less is the relative amount of missing ketones minus TMCH *ee* at the highest enantiomeric excess in the given reaction, the better is the catalyst stereoselectivity with respect to both enantiomeric excess producing processes, kinetic resolution + C=C saturation.

Pd/C at low hydrogen pressure, Pd/MgO, and Pd/Al_2O_3 have the best stereoselectivity with *ee* values of ~90%. The explanation of the chemo- and stereoselectivity differences of the Pd catalysts on different supports needs further investigation.

4. Conclusions

The kinetic resolution of TMCH with (*S*)-proline gave (*S*)-TMCH in excess, the final *ee* approached 100%, but the rate of the reductive alkylation and the yield of the optically active ketone depended substantially on the Pd catalyst used. Pd on activated carbon support was most active, when applied in small catalyst substrate ratio (5/700). Even its selectivity was acceptable: at 100% *ee*, the amount of missing (*S*)-TMCH was only 24%. With respect to both activity and stereoselectivity, Pd on alumina catalyst proved to be the best, at 100% *ee* the amount of missing (*S*)-TMCH was only 7%. The catalysts on basic supports ($BaCO_3$, MgO) had no special advantages. Their basicity and greater proline adsorption ability, supposed by Török and co-workers [18] did not act in the reductive alkylation.

The consumption of the TMCH enantiomers and their rate of hydrogenation in the reductive alkylation depended on the catalyst and on the reaction conditions (hydrogen pressure and catalyst/substrate ratio). The second enantiodifferentiating step, the hydrogenation of the condensated products of (S)-proline and the TMCH

Table 3
IP hydrogenation results with different Pd catalysts.

Catalyst (mg)	p(H_2) (bar)	Reaction time (h)	Conv. (%)	*ee* (%)	Reaction rate[a]		Activity in period I		∗ (%)	∗∗ (%)	∗∗∗ (%)
					Period I	Period II	Act.[b]	Spec. act.[c]			
Pd/C											
5	10	18.1	99	81	11.6	2.4	2.3	23	0–80	−13	18.7
10	2	20	100	87	14.9	2.5	1.5	15	0–60	−4.3	9
	10	12.7	99	93	24.4	3.7	2.4	24	–	–	29.9
20	10	4.3	100	92	77.4	6.8	3.9	39	0–80	−3.3	31
Pd/TiO_2											
20	10	19.7	78	51	9.1	3.0	0.35	7	–	–	5.3
Pd black											
5	50	16	93	76	13.7	2.2	2.7	2.7	0–40	−6.7	14.7
20	10	80	20	10	1	0.14	0.05	0.05	–	–	–
Pd/Al_2O_3											
20	10	30	100	91	12.7	1.8	0.64	12.7	–	–	25.8
Pd/$BaCO_3$											
40	50	51	64	43	4.6	1.0	0.12	2.4	0–50	−8.7	4.7
	10	49	64	22	2.5	1.0	0.06	1.2	0–60	−15	−7.5
20	10	95	25	25	1.1	0.1	0.06	1.2	0–60	−12	−10
Pd/MgO											
40	10	49	98	92	12.9	1.2	0.32	6.4	0–40	−3.1	19.9
	50	27.5	100	100	14.6	2.3	0.37	7.4	0–45	−5	47.6
20	10	100	70	65	3	0.4	0.15	3.0	0–40	−3	20

∗Conversion range of IP asymmetric hydrogenation. ∗∗The biggest negative value of [missing (IP + TMCH)] – [*S* excess]/IP$_o$. ∗∗∗[missing IP + TMCH] – [*S* excess]/IP$_o$ measured at the highest *ee* value in the reaction.

[a] Conversion (%)/reaction time (h).

[b] Reaction rate/catalyst amount.

[c] Reaction rate/Pd amount.

enantiomers takes place at the metal surface of the Pd catalysts with different rates, depending largely on the catalyst properties, resulting in different optically active TMCH yields at 100% *ee*.

Asymmetric hydrogenation of IP in the presence of Pr was investigated also with different Pd catalysts. The exact amount of IP and TMCH enantiomers during the reaction was followed, so it could be proven that the optically active TMCH was formed not only by kinetic resolution but also through asymmetric C=C hydrogenation. The activity and stereoselectivity of the different Pd catalysts depended on the support material, preparation method, and reaction conditions as well, confirming our assumption that enantiodifferentiation takes also place on the catalyst surface, not only in the homogeneous liquid phase reaction between TMCH and Pr. The key intermediate in this reaction route can be an oxazolidinone (**5**) or an enamine (**8**), the literature and the present data do not allow to select between them. The explanation of the activity and selectivity differences of the tested Pd catalysts needs also further study.

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