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# Achiral amine additives in the enantioselective hydrogenation of aliphatic α,β-unsaturated acids over cinchonidine-modified $Pd/Al_2O_3$ catalyst

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ABSTRACT

The effect of the achiral amine additive structure was studied on the enantioselective hydrogenation of (*E*)-2-methyl-2-butenoic acid and (*E*)-2-methyl-2-hexenoic acid over $Pd/Al_2O_3$ catalyst modified by cinchonidine. It was found that secondary amines are similarly or even more efficient in increasing the enantioselectivity as primary amines. The right basicity of the amine, which may vary in a rather wide range, should be coupled with appropriate steric properties to be effective in increasing the enantioselectivity. The best performing amines was the earlier widely used benzylamine and *N*-methylbenzylamine. The influence of these amines on the effect of the catalyst amount, $H_2$ pressure and reaction temperature was studied. The effect of the amine amount on the hydrogenation of the two acids was also investigated. Based on the results the involvement of the amine additive in the formation of surface intermediates responsible for enantioselection is proposed.

Decrease of the reaction temperature to 273 K increased the enantiomeric excess in the presence of amines, resulting in the hydrogenation of (*E*)-2-methyl-2-hexenoic acid in up to 71% enantioselectivity in favour of the *S* product enantiomer, the highest value obtained until now in the enantioselective hydrogenation of aliphatic unsaturated carboxylic acids over chirally modified heterogeneous catalyst.



## 1. Introduction

Catalytic asymmetric processes are convenient methods for the synthesis of optically pure chiral pharmaceutical intermediates [1]. Following the development of a large variety of chiral metal complexes able to assure enantiodifferentiation in the hydrogenation of a wide range of prochiral unsaturated compounds, enantioselective hydrogenations are preferred options for inserting chirality in fine chemicals [2,3]. Promotion of green and environmental benign processes initiated the development of heterogeneous catalytic systems as alternatives of chiral complexes [4]. A simple approach to obtain catalytically active chiral materials for hydrogenation is the modification of metal surfaces with adsorbed optically pure organics. Among such catalysts the most successful are the tartaric acid modified Ni and the cinchona alkaloid modified Pt and Pd [5–8].

Supported Pd catalysts modified by cinchona alkaloids were found to provide high enantioselectivities in the hydrogenation of prochiral olefins, such as 2-pyrone derivatives [8,9] and α,β-unsaturated acids [8,10]. The hydrogenation of unsaturated acids in this catalytic system was sensitive to the structure of the acid [11]. Excellent enantiomeric excesses (ee) were obtained in reactions of (*E*)-2,3-diphenylpropenoic acids [12–17], whereas acids having aliphatic substituents in both α and β positions provided the saturated compounds in moderate, up to 67% ee [18–26]. Several aspects of the reaction mechanism, including the structure of the surface intermediate complex responsible for enantiodifferentiation, are not yet clarified. Based on the effect of the reaction conditions, it was ascertained that the active surface intermediates are different when the two types of acids, i.e. bearing aliphatic or aromatic substituents, are hydrogenated. The enantioselective hydrogenation of aliphatic unsaturated acids resulted in the best ee when carried out in apolar solvents under high $H_2$ pressure. It was shown by spectroscopic and computational studies that under these conditions the most stable cinchona alkaloid–acid adducts contained two or three acid molecules interacting via hydrogen bonds [27–29].

Despite the differences in reaction conditions necessary for obtaining high ee and consequently in the composition and structure of intermediate complexes, the use of an achiral base additive increased the ee in the hydrogenation of both acid types [15,21,24,30]. However, the amine additive had different effect on the rate of hydrogenations; rate increase was observed in reactions of diphenylpropenoic acids [31], whereas hydrogenations of

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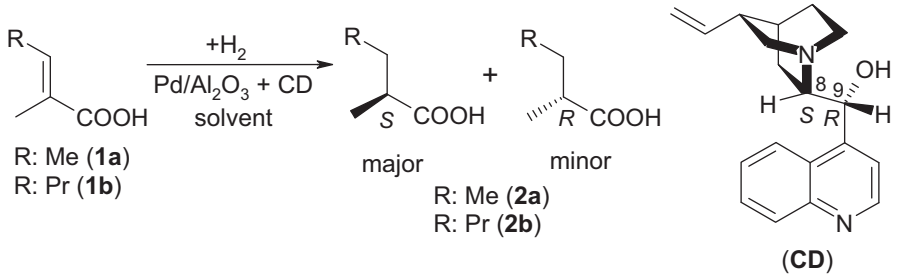


**Scheme 1.** Hydrogenation of selected aliphatic α,β-unsaturated acids over $Pd/Al_2O_3$ catalyst modified by cinchonidine.

aliphatic acids were decelerated by amines [26]. Up to now among achiral amines benzylamine (**3a**) was found the most efficient in increasing the ee. In a recent study Kim and Sugimura obtained high ee values in the hydrogenation of diphenylpropenoic acids in toluene without using amine additive [16]. Moreover, the addition of **3a** decreased the ee in the hydrogenation of several derivatives in this solvent. The authors included the hydrogenation of an aliphatic acid obtaining also decrease in the ee in the presence of **3a**, in contrast with our report [26]. It should be noted that the two studies were carried out over different catalysts, i.e. Pd/C STD-type vs. $Pd/Al_2O_3$ that could be the reason of the opposite tendencies. The former catalyst performed excellently in hydrogenations of diphenylpropenoic acid derivatives in polar-aqueous solvents, whereas apparently is far from being ideal for aliphatic unsaturated acids, possibly as concerns the properties of the support, which is crucial for reaching good enantioselection [32]. However, up to now in the hydrogenation of aliphatic α,β-unsaturated carboxylic acids only primary amines were tested [26]. It is known that the use of secondary and tertiary amine additives were less efficient in increasing the ee in the hydrogenation of itaconic acid [23].

Our present study reports the examination of the effect of the structure and amount of the achiral amine additive including primary, secondary and tertiary amines on the hydrogenation of two aliphatic prochiral unsaturated acids, i.e. (*E*)-2-methyl-2-butenoic acid and (*E*)-2-methyl-2-hexenoic acid (Scheme 1) over $Pd/Al_2O_2$ modified by cinchonidine. We have also investigated the influence of amines on the effect of some crucial reaction parameters such as the $H_2$ pressure and reaction temperature. The primary goal of these investigations was to obtain further increase in the optical purities of the saturated acids in this heterogeneous catalytic system in order to make the method more attractive for practical application. However, the results were also used to gain novel mechanistic insights into this reaction, particularly as concerns the composition of the surface intermediate responsible for enantioselection in the presence of amine additives.

## 2. Experimental

### 2.1. Materials

Commercial 5% $Pd/Al_2O_3$ (Engelhard, 40692) having BET surface area 200 $m^2\,g^{-1}$ and metal dispersion 0.21 [27] was used as received. Cinchonidine (CD, Alfa Aesar, 99%), (*E*)-2-methyl-2-butenoic acid (**1a**, 98%, Aldrich), (*E*)-2-methyl-2-hexenoic acid (**1b**, 98%, Alfa Aesar) were used without purification. The amine additives: benzylamine (**3a**), (*R*)-α-methylbenzylamine (**3b**), *N*-methylbenzylamine (**3c**), (*R*)-*N*,α-dimethylbenzylamine (**3d**), *N*,*N*-dimethylbenzylamine (**3e**), dibenzylamine (**3f**), 2-phenylethylamine (**3g**), methylamine, 33 wt% in ethanol (**3h**), dimethylamine, 33 wt% in ethanol (**3i**), diethylamine (**3j**), triethylamine (**3k**), isopropylamine (**3l**), diisopropylamine (**3m**), hexylamine (**3n**), dihexylamine (**3o**), dicyclohexylamine (**3p**) and piperidine (**3q**) were purchased from Fluka or Aldrich. High purity $H_2$ gas (Linde AG, 99.999%) and Multisolvent grade toluene (Scharlau) were used.

### 2.2. Hydrogenation procedure and product analysis

Hydrogenations were carried out in stainless steel autoclaves equipped with a pressure transmitter (P40, PMA GmbH) and with glass liner. Under typical conditions 15 mg 5% $Pd/Al_2O_3$, 10 $cm^3$ toluene, 0.05 mmol CD, 1 mmol acid and 1 mmol amine additive were loaded into reactor, the autoclave was flushed with $H_2$, filled to 5 MPa $H_2$ and the reaction was commenced by stirring the slurry using magnetic agitation (1000 rpm) at room temperature (295 K). Initial $H_2$ uptake rates ($R_{Hi}$) were calculated from the recorded pressure drops up to 40 ± 5% conversions corrected with the uptake registered in the absence of the acid. After the given time (t) the $H_2$ was released, the slurry was filtered, the solution was treated with 10% HCl aq solution, dried over $NaSO_4$ and analyzed.

Products were identified by GC–MS analysis using Agilent Techn. 6890 N GC–5973 MSD equipped with 60 m HP-1MS capillary column. Conversions (X (%)) and enantioselectivities (ee (%)) were calculated from gas chromatographic analysis using Agilent Techn. 6890 N GC–FID equipped with HP-Chiral (30 m × 0.25 mm, J & W Sci. Inc.,) chiral capillary column with the formulae:

$$X(\%) = 100 \times \frac{[(S)-\mathbf{2}] + [(R)-\mathbf{2}]}{[1_0]} \text{ and}$$

$$ee(\%) = 100 \times \frac{|[(S)-\mathbf{2}] - [(R)-\mathbf{2}]|}{([(S)-\mathbf{2}] + [(R)-\mathbf{2}])}$$

where [(*S*)-**2**] and [(*R*)-**2**] are the concentrations of the product enantiomers and [$\mathbf{1}_0$] is the initial concentration of the unsaturated acid **1a** or **1b**. The analysis conditions were: head pressure 135 kPa He; column temperature: 358 K (**1a**) or 388 K (**1b**), retention times (min): (*S*)-**2a** 13.0, (*R*)-**2a** 13.9, **1a** 21.2; (*S*)-**2b** 20.2, (*R*)-**2b** 21.8, **1b** 26.8. The absolute configuration of excess enantiomers were determined by GC analysis using commercially available optically pure products and based on published data [11]. Repeating some experiments three times resulted in product compositions reproducible within ±1%.

## 3. Results and discussion

The enantioselective hydrogenation of (*E*)-2,3-diphenylpropenoic acid over Pd catalyst modified by CD resulted in increased ee in the presence of various achiral amine additives. The most effective was found to be **3a**, however, other additives including secondary and tertiary amines also increased the ee [30,31]. Similarly, in the enantioselective hydrogenation of the aliphatic dicarboxylic itaconic acid, the best ee was obtained in the presence of **3a** and the efficiency of the additive decreased in the order: primary > secondary > tertiary amines [23]. Our previous study on the hydrogenation of **1a** in the presence of a series of primary

**Table 1**
Effect of the achiral amine additive structure on the enantioselective hydrogenation of the aliphatic α,β-unsaturated acids over $Pd/Al_2O_3$ modified by CD.[a]

| Entry | Additive, ($pK_a$)[b] | Hydrogenation of **1a** | | Hydrogenation of **1b** | |
|---|---|---|---|---|---|
| | | $t$ (min)/$R_{Hi}$[c] | ee (%)[d] | $t$ (min)/$R_{Hi}$[c] | ee (%)[d] |
| 1[e] | – | 20/307[f] | – | 30/348 | – |
| 2 | – | 30/260[f] | 47[f] | 30/297 | 54 |
| 3 | **3a** (9.49) | 45/190[f] | 62[f] | 40/207 | 66 |
| 4 | **3b** | 45/179[f] | 64[f] | 40/200 | 66 |
| 5 | **3c** (9.71) | 30/239 | 63 | 60/238 | 66 |
| 6 | **3d** | 30/235 | 59 | 60/240 | 63 |
| 7 | **3e** (9.03) | 30/251 | 51 | 60/258 | 57 |
| 8 | **3f** (7.70) | 30/260 | 55 | 60 (99)/252 | 58 |
| 9 | **3g** (10.08) | 45/230[f] | 59[f] | 60 (93)/220 | 61 |
| 10 | **3h** (10.63) | 40/233 | 48 | – | – |
| 11 | **3i** (10.94) | 40/233 | 58 | – | – |
| 12 | **3j** (11.02) | 60/239 | 59 | 60 (98)/244 | 64 |
| 13 | **3k** (10.68) | 30/237 | 55 | 60 (99)/220 | 57 |
| 14 | **3l** (10.63) | 45/245[f] | 58[f] | 60/206 | 64 |
| 15 | **3m** (11.50) | 60/255 | 58 | 60/214 | 63 |
| 16 | **3n** (10.85) | 45 (99)/210[f] | 57[f] | 60 (86)/n.d. | 60 |
| 17 | **3o** (11.01) | 60 (98)/n.d. | 61 | 60 (96)/208 | 60 |
| 18 | **3p** (10.80) | 30 (99)/260 | 55 | 60 (90)/229 | 62 |
| 19 | **3q** (11.30) | 60/260 | 58 | 60 (97)/258 | 56 |

[a] *Reaction conditions*: 15 mg 5% $Pd/Al_2O_3$, 10 $cm^3$ toluene, 0.05 mmol CD, 1 mmol acid, 1 mmol additive, 5 MPa $H_2$, 295 K.
[b] For amines annotations see the experimental section, $pK_a$ values from [33–36].
[c] Reaction time needed to reach complete transformation or the conversion (%) given in brackets/initial $H_2$ uptake rate (mmol $h^{-1}$ $g^{-1}$); n.d. = not determined.
[d] The (*S*)-**2a** or (*S*)-**2b** enantiomers were formed in excess.
[e] Reactions over unmodified catalyst.
[f] The results obtained with these primary amines were recently published [26].

amines showed a combined effect of the basicity, the steric hindrances and the adsorption characteristics of additives, **3a** having optimal properties among achiral primary amines [26]. To test the efficiency of other amines we have chosen to investigate the hydrogenation of two aliphatic prochiral unsaturated acids (**1a** and **1b**) in the presence of a series of primary, secondary and tertiary amines of different structures.

### 3.1. Effect of the amine additive structure

Selected results obtained in the hydrogenations of acids **1a** and **1b** over CD-modified $Pd/Al_2O_3$ using amine additives are collected in Table 1.

All amines tested increased the ee and decreased the $R_{Hi}$ in the hydrogenation of both acids when compared with reactions in the absence of additives. Interestingly, besides the optically pure primary amine **3b**, the secondary amine **3c** also gave higher or the same ee as **3a**. The basic strength of amines could not be correlated directly with the increase in the ee; this increase was slightly dependent also on the length of the β alkyl chain of the acid. Thus, when benzylamine derivatives are considered, one may reach to the conclusion that amines having $pK_a$ = 9.5–10 have the ideal basicity. However, only slightly lower ees were obtained by using **3o**, **3 g** or **3j** in the hydrogenation of **1a** and **3j**, **3l** or **3 m** in that of **1b** when compared with **3a** or **3c**. Among these are primary and secondary amines having the $pK_a$ in the range 10–11.5. Thus, the basicity of the amine additive may vary in a relatively wide range (9.5–11.5) and other factors also have role in determining the efficiency of the additive. This is confirmed when one considers that the $pK_a$ of the quinuclidine N in CD has a value in this range (∼10 [37]). Interestingly, the optically pure amines **3b** and **3d** had opposite behaviour when compared with **3a** and **3c**, i.e. **3d** gave lower ee than **3c**.

As a general rule we observed that tertiary amines (**3e** and **3k**) were the least efficient in increasing the optical purity of the products. Similarly low ees were obtained in the presence of **3f**, **3q** and **3h**. While the poor efficiency of **3f** may be explained by the low basicity of this amine, the performance of other amines could be traced back to steric reasons. Thus, tertiary amines may hinder the adsorption on modified surface sites of the acid-amine salt formed in the solution. Similar reason may explain the behaviour of the cyclic **3q**. On the contrary the insufficient steric hindrance of one methyl group could be the reason of the lower ee obtained in the presence of **3h**. The steric effect of additives on the ee was also indicated by comparing results obtained using amines having similar basicities, such as **3h**, **3k** and **3l**, respectively.

It must be noted that the slightly higher ee observed with **3c** when compared with **3a** was valid for other primary–secondary amine pairs of similar structure. Thus, secondary amines gave similar or higher ee as primary ones when the **3h**–**3i**, **3l**–**3m** or **3n**–**3o** pairs are considered. A general tendency is that in the presence of secondary amines the $R_{Hi}$ is also higher when compared with their primary amine pairs, though these values are lower than those obtained in the absence of additive. The performance of secondary amines confirmed the assumption that not solely the basicity of the amine additive is responsible for its effect on the stereochemical outcome of the reaction, steric effects are probable to play also significant role. However, these results also confirmed that the presence of one benzyl group favours high ees.

The above observations on the effect of secondary amine additives urged us to examine the influence of the additive structure on the effect of the reaction conditions.

### 3.2. Influence of amine additives on the catalyst amount dependence

An important requirement of reactions over heterogeneous catalysts is to fully exploit the activity of the catalyst. To ascertain whether the reaction is not controlled by diffusion phenomena the hydrogenation of **1a** was studied using various amounts of catalyst in the absence of additive and using two amines (**3a** and **3c**). Results obtained are illustrated in Fig. 1.

An important difference obtained in the absence of additive when compared with the use of either of amines was the more significant decrease in the ee by increasing the catalyst amount (over 25 mg). The $R^*_{Hi}$ deviated from the linearity over 25 mg catalyst, indicating that over higher amounts the reaction is not kinetically controlled irrespective of the presence of amines. The slopes of the $R^*_{Hi}$ curves at low catalyst amounts were different due to changes

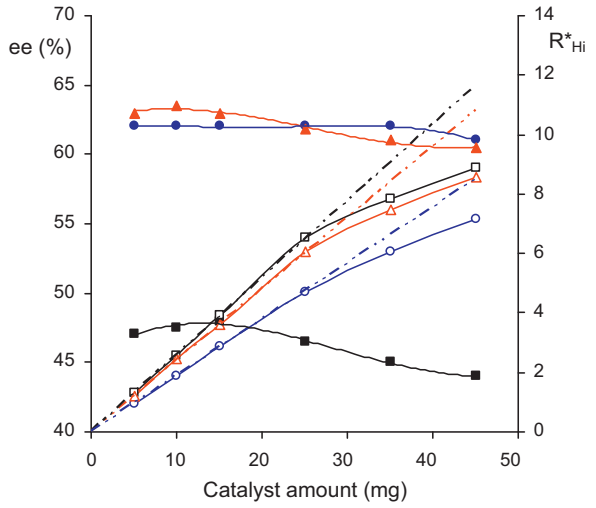


**Fig. 1.** Effect of the catalyst amount on $H_2$ uptake rate ($R^*_{Hi}$, mmol $h^{-1}$, open symbols) and ee (%, closed symbols) in the enantioselective hydrogenation of **1a** in the absence of amine additive (□, ■), in the presence of **3a** (○, ●) and **3c** (△, ▲). *Reaction conditions*: see Table 1. Dashed lines are $H_2$ uptake rates corresponding to lack of mass transfer control.

either in the number of the active sites or in the activation energy in the presence of the amines. When the diffusion became rate determinant, the slopes of the three curves were similar, maintaining the rate differences, which imply similar diffusion coefficients in the three reactions (without amine, with **3a** or with **3c**). Over higher amount of catalyst mass transfer control occurred at lower rates in the presence of amines and $R^*_{Hi}$ remained lower in the presence of amines when compared with reactions in absence of additives. This indicated that the structure or composition of the migrating chemical species is different, i.e. amines are incorporated in these species.

In consequence, under conditions assuring surface reaction control in the presence of amine additives the number of surface active sites decreased when compared with the amine free hydrogenation. It must be also noted that the amount of CD used is sufficient to maintain a complete modification of the active surface, thus alterations in the CD/surface Pd ratio by increasing the catalyst amount should not have significant effect on results obtained over low amounts of catalyst. Accordingly, we consider the above observations as confirmation of the participation of amine additives in the formation of the surface intermediate during the hydrogenation of aliphatic unsaturated carboxylic acids over catalyst modified by CD.

### 3.3. Effect of the achiral amine amount

The effect of the amine amount was studied in the hydrogenation of both **1a** and **1b**. The results using the selected amines (**3a** and **3c**) are presented in Fig. 2.

Significant differences were detected by using these amines. Although, under 1 equivalent (eq., as compared with the acid) of either amines the ee increased continuously by increasing the amine amount, the maxima in the presence of **3a** was obtained at 1 eq. of amine, whereas with **3c** the ee increased up to 1.5 eq. in the hydrogenation of both acids. Moreover, over 1 eq. of the latter amine ees surpassed those obtained with **3a**. $R_{Hi}$ decreased by increasing the amine amount up to ~0.7 eq. followed by practically constant values at higher additive amounts. The amine amount affected less the rate of the hydrogenation of **1a** than that of **1b** especially when **3c** was used, which implied a larger difference in the effects of the two amines on the $R_{Hi}$ of the former acid.

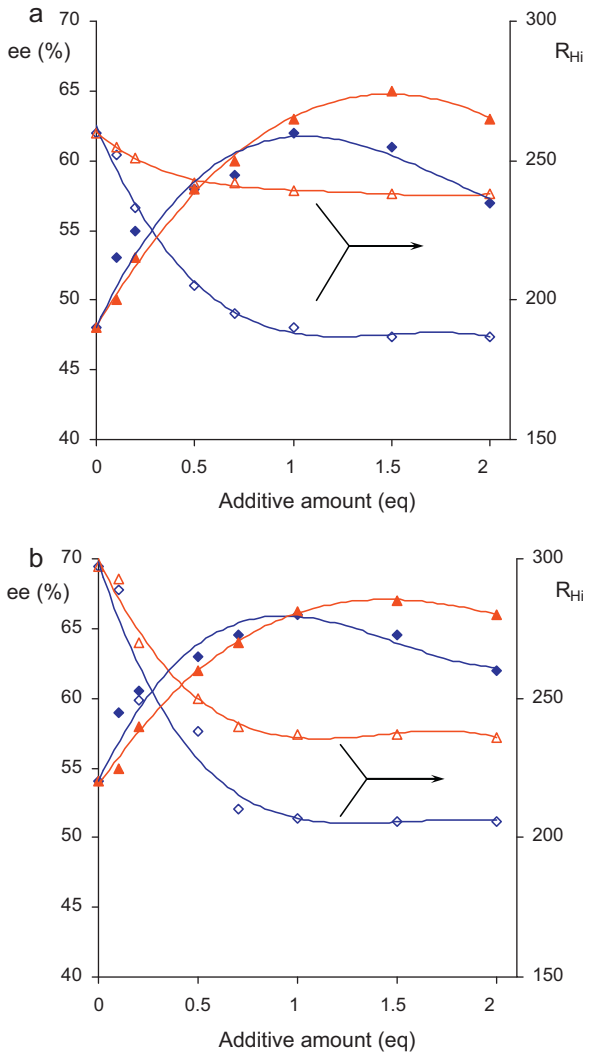


**Fig. 2.** Influence of **3a** (◇, ◆) or **3c** (△, ▲) amount on $H_2$ uptake rate ($R_{Hi}$, mmol $h^{-1}$ $g^{-1}$, open symbols) and ee (%, closed symbols) in the enantioselective hydrogenation of **1a** (a) and **1b** (b). *Reaction conditions*: see Table 1.

Accordingly, the effect of amines was proved to be slightly dependent on the size of the β substituent of the unsaturated acid, and the influence of the amine amount was different when secondary amine was used instead of primary ones. The difference obtained especially in $R_{Hi}$ in the presence of these amines can be accounted for alterations in the structure of the surface intermediate complex due to participation of the additive.

### 3.4. $H_2$ pressure and temperature effect in presence of amines

Increase in the $H_2$ pressure or decrease in hydrogenation temperature below room temperature increased the ee in the hydrogenation of aliphatic α,β-unsaturated carboxylic acids over Pd catalyst modified by CD [18,26]. The effect of the $H_2$ pressure on the hydrogenation of **1a** was studied in the presence of **3a** and **3b** (see Fig. 3).

Decreasing the pressure from the typically applied 5 MPa decreased both the $R_{Hi}$ and ee independently on the absence or presence of amine additives. However, the deceleration obtained by decreasing the pressure was higher in the absence of additives when compared with the use of either of selected amines. Less significant differences were obtained in the slopes of the ee decrease resulted in the absence or presence of amines. Nevertheless, in the

**Table 2**
Effect of decreasing the reaction temperature on the enantioselective hydrogenation of aliphatic α,β-unsaturated acids **1a** and **1b**.[a]

| Entry | Additive[b] | Hydrogenation of **1a** | | Hydrogenation of **1b** | |
|---|---|---|---|---|---|
| | | $X$ (%)/$t$ (min)[c] | ee (%)[d] | $X$ (%)/$t$ (min)[c] | ee (%)[d] |
| 1 | – | 100/90 | 47/48 | 100/90 | 54/56 |
| 2 | **3a** | 100/90 | 62/67 | 95/90 | 66/68 |
| 3 | **3b** | 100/90 | 63/67 | 96/90 | 66/71 |
| 4[e] | **3b** | 100/90 | 65/66 | 96/120 | 67/71 |

[a] *Reaction conditions*: 15 mg 5% $Pd/Al_2O_3$, 10 $cm^3$ toluene, 0.05 mmol CD, 1 mmol acid, 1 mmol additive, 5 MPa $H_2$.
[b] For amines annotations see the experimental section.
[c] Conversion/hydrogenation time at 273 K.
[d] Enantiomeric excesses obtained at 295 K/273 K; the *S* enantiomers formed in excess.
[e] Using 1.5 eq. additive.

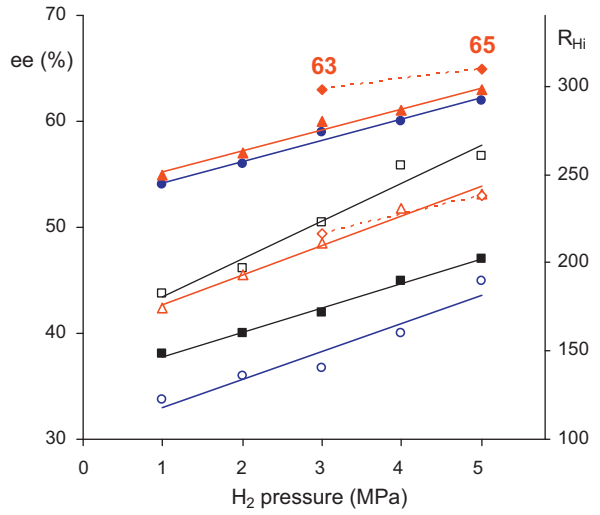


**Fig. 3.** $H_2$ pressure dependence of the hydrogenation of **1a** in the absence of achiral amine (□, ■), using 1 eq. of **3a** (○, ●) or **3c** (△, ▲) or 1.5 eq. **3c** (◇, ◆) ($R_{Hi}$, mmol $h^{-1}$ $g^{-1}$, open symbols; ee, %, closed symbols). *Reaction conditions*: see Table 1.

presence of 1.5 eq. **3c** under 3 MPa $H_2$ the ee was only 2% smaller when compared with that obtained in the reaction under 5 MPa. Hence, the presence of amines had also effect on the $R_{Hi}$ and ee decrease resulted by decreasing the pressure. The effect of the $H_2$ pressure was explained by decrease of the surface hydrogen concentration [18]. Thus, the presence of amines led to less significant effect of this parameter on both the $R_{Hi}$ and the ee. Decrease in the number of the catalytically active sites in the presence of amine additives may lead to such behaviour.

Decreasing the reaction temperature to 273 K increased the ee in this catalytic system [18,20]. In the present study we attempted to reach a better stereocontrol of the hydrogenation by combining the beneficial effect of the presence of an achiral amine with decreasing the hydrogenation temperature (see Table 2).

Indeed decreasing the temperature to 273 K led to higher increase in the ee in the hydrogenation of **1a** in presence of either **3a** or **3c** than in reactions carried out without additive. However, at low reaction temperature there was no difference in ees obtained with the two amines. On the contrary in the hydrogenation of **1b** the amine **3c** was more efficient in increasing the ee at 273 K, obtaining with 1 or 1.5 eq. of additive 71% ee. One explanation of the higher ee obtained at 273 K compared to that at room temperature was given in early studies of this catalytic system [18], i.e. the increase of the $H_2$ solubility and consequently the surface hydrogen concentration. However, the effect of the $H_2$ pressure showed that variations in the surface hydrogen concentration have less effect in the presence of the amines. Thus, the temperature effect on the ee should be traced back to different reason(s). A possibility is the involvement of the amine in the formation of the hydrogenation intermediate, however, the effect of the slower hydrogenation of the modifier's anchoring quinoline moiety [38] or the effect of the temperature on the conformational behaviour of the modifier on the surface [29] cannot be excluded.

## 4. Conclusions

The effect of the achiral amine additive structure was studied on the enantioselective hydrogenation of two aliphatic α,β-unsaturated carboxylic acids, i.e. (*E*)-2-methyl-2-butenoic acid and (*E*)-2-methyl-2-hexenoic acid, over $Pd/Al_2O_3$ catalyst modified by CD. We have found that secondary amines are similarly or even more effective in increasing the enantioselectivity as primary ones. It was shown that the basic strength of the additive may be varied in relatively wide range (from $pK_a$ 9.5 to 11.5). However, the amines beside the right basicity must also fulfil steric requirements in order to provide high enantioselectivities. The most efficient were found the earlier widely used benzylamine and the newly found *N*-methylbenzylamine. Using these two amines the effect of the catalyst and the amine amount was studied complemented by studies on the influence of the additive on the effect of the $H_2$ pressure and reaction temperature. The use of various catalyst amounts indicated kinetically controlled reaction under the typical conditions. Based on the decrease in the number of active sites in presence of amines we assumed that these take part in the formation of the surface intermediate. This assumption was confirmed by the effect of the amine amount on the hydrogenation, also affected by the alkyl chain length of the acid. Recently, it was demonstrated that the most stable CD-acid complexes are formed by interacting three unsaturated acid molecules with distorted open (3) CD conformer [29]. We propose that the amines interfere in the H-bond network on the surface, being incorporated in the intermediate complex. This may justify the effect of the amine structure and amount on the hydrogenation of these acids.

The above explanation can rationalize the influence of amines on the effect of the $H_2$ pressure, which showed less significant effect of the surface hydrogen concentration on the rate and the ee when additives are used. The decrease of the reaction temperature to 273 K increased more the ee in the presence of amines when compared with amine free hydrogenations. In consequence (*S*)-2-methylhexanoic acid could be prepared in up to 71% optical purity, unprecedented in enantioselective hydrogenations of aliphatic unsaturated carboxylic acids over chirally modified heterogeneous catalyst.

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