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Heterogeneous Enantioselective Hydrogenation of Hydroxy-substituted (*E*)-2,3-diphenylpropenoic Acids over Pd/Al_2O_3 Modified by Cinchonidine

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Abstract The enantioselective hydrogenation of (*E*)-2,3-diphenylpropenoic acids substituted by hydroxyl group has been studied over Pd/Al_2O_3 catalyst modified by cinchonidine. The effect of the acidic hydroxyl substituents was compared with that of the methoxy group in the same position. The *para*-hydroxyl substituent on the 3-phenyl ring had similar effect on the enantioselectivity as the methoxy group, whereas the *meta* positioned decreased the optical purity of the saturated acid. This was explained by different origin of the increase in the enantioselectivity obtained in the presence of electron releasing substituents in these positions. Although, the *para*-hydroxyl group on the 2-phenyl ring had beneficial influence on the enantioselectivity of the hydrogenation of the mono-substituted acid, in the presence of fluorine or hydroxyl group on the 3-phenyl ring the effect of the two substituents was not additive. This study demonstrated that the cinchonidine-modified Pd catalyst is appropriate for the preparation of several hydroxy-substituted 2,3-diphenylpropionic acids in good optical purities, extending the scope of this catalytic system to new types of versatile chiral building blocks.

Keywords Heterogeneous catalysis · Asymmetric hydrogenation · Enantioselectivity · Cinchonidine · 2,3-Diphenylpropenoic acid · Palladium · Hydroxyl substituent

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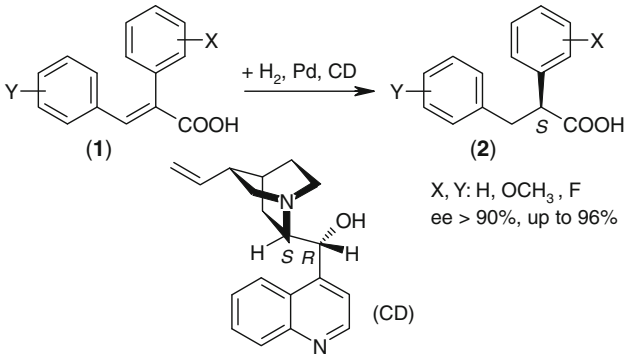
1 Introduction

Catalytic hydrogenations are widely applied processes for preparing fine chemicals, including optically pure intermediates used in the pharmaceutical and agrochemical industries [1–3]. Numerous industrially important hydrogenations are carried out in heterogeneous catalytic systems over metal catalysts [1]. The adsorption of optically pure compounds, so-called modifiers, on metal surfaces provided efficient heterogeneous catalysts for the asymmetric hydrogenation of several types of prochiral compounds [4–8]. Among these are α, β-unsaturated carboxylic acids, which were hydrogenated enantioselectively over Pd catalysts modified by cinchona alkaloids [6, 9]. The structure of the acid was found to have decisive influence on the enantiomeric excess (ee) [10–20]. Until now the best, over 90% ees were obtained in the hydrogenation of (*E*)-2,3-diphenylpropenoic acid and its methoxy and/or fluorine derivatives using Pd catalysts modified by cinchonidine (**CD**) (see Scheme 1) [21–25].

The enantioselectivities were influenced by the substituents position. Acids substituted in *para* position on the 3-phenyl ring and in *para* or *ortho* positions on the 2-phenyl ring were hydrogenated in the highest enantioselectivities [21–24]. The influence of the *para*-methoxy substituent on the 3-phenyl is due to its electron releasing mesomeric effect, which leads to increase in the basic character of the carboxylate ion, hence interacting stronger with the protonated **CD** when compared to the unsubstituted acid [26]. Few other alkoxy derivatives were also tested resulting in decreased ee by replacing the methyl group with *n*-octyl, but keeping the high ees in the presence of 3-phenyl-*n*-propyl or $Me(OCH_2CH_2)_3$ groups [24, 27]. In consequence, the optical purity of the alkoxy-substituted 2,3-diphenylpropionic acids prepared by this method was



Scheme 1 Enantioselective hydrogenation of (*E*)-2,3-diphenylpropenoic acids over Pd catalyst modified by cinchonidine (**CD**)

influenced by the substituent position as well as by the structure of the substituent.

A convenient method for obtaining alkoxy derivatives could be the preparation of the corresponding hydroxy-substituted compounds and their transformation following the enantioselective hydrogenations. Moreover, the presence of the free phenolic hydroxyl group provides additional possibilities for obtaining synthetically useful chiral intermediates. However, the enantioselective hydrogenation of hydroxy-substituted (*E*)-2,3-diphenylpropenoic acids was not yet attempted. The aim of the present study was the preparation of (*E*)-2,3-diphenylpropenoic acids substituted by hydroxyl group in various positions and examination of their enantioselective hydrogenation over Pd catalyst modified by **CD**, this way broadening the scope of this asymmetric heterogeneous catalytic system.

2 Experimental

2.1 Materials

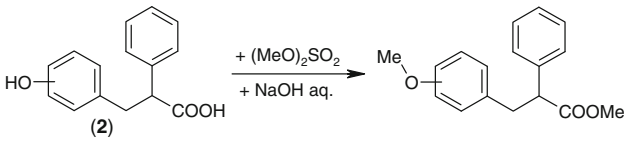
The catalyst used was 5% Pd/Al_2O_3 (Engelhard, 40692, BET 200 $m^2\ g^{-1}$, Pd dispersion 0.21 [28]) reduced in H_2 flow prior reactions as earlier described [22, 29]. Cinchonidine (**CD**, Alfa Aesar, 99%), benzylamine used as additive (**BA**, Fluka, ≥99.5%) and H_2 gas (Linde AG, 99.999%) were used as received. Benzaldehyde and phenylacetic acid derivatives for the preparation of (*E*)-2,3-diphenylpropenoic acids were purchased from Aldrich and used as received. The hydrogenations were carried out in *N*,*N*-dimethylformamide (DMF, Scharlau, Multisolvent grade) with 2.5 vol% distilled water. Solvents and reagents of analytical grade were used in the preparation of unsaturated acids and product derivatizations.

2.2 Preparation of Hydroxy-substituted (*E*)-2,3-diphenylpropenoic Acids

The substituted 2,3-diphenylpropenoic acids were prepared by Perkin condensation using the corresponding benzaldehydes and phenylacetic acids [22, 23]. A stirred mixture of the corresponding arylacetic acid (40 mmol), aldehyde (40 mmol), 12 cm^3 triethylamine and 8 cm^3 acetic anhydride was refluxed for 4–6 h. To the cooled mixture 12 cm^3 conc. HCl solution was added followed by 30–40 cm^3 cold water; the precipitate was filtered and washed with cold water. After drying the solid was dissolved in 1% NaOH aqueous solution, the alkaline solution was stirred with charcoal at room temperature and filtered. The solution was acidified with 1/1 conc. HCl/water solution, the precipitate was filtered and purified by several crystallization in ethanol–water mixtures. The isomer distribution of the crude reaction products and the purity of the *E* isomers after crystallizations were monitored by analytical TLC (Fluka Silica gel TLC cards) and GC-MSD (Agilent Techn. 6890 N GC-5973 MSD, HP-1MS, 60 m capillary column) analysis after methylation of both the carboxylic acid and the phenolic group in 20% NaOH solution using $(CH_3O)_2SO_2$. The acids were identified and their purities were checked by melting point measurements and by ^{1}H- and ^{13}C-NMR spectroscopy using BRUKER AVANCE DRX 400 NMR spectrometer (^{1}H at 400 MHz, ^{13}C at 100 MHz) in $(CD_3)_2SO$ solution. The *E* isomers were purified to 97–98% purities (for analytical data see the Supplementary material).

2.3 Hydrogenation Procedure and Product Analysis

The hydrogenations were carried out under atmospheric H_2 pressure at room temperature in a glass hydrogenation apparatus equipped with a gas-burette and magnetic stirrer. The initial hydrogenation rates (r_{um}, r_m, $r_{m,\mathbf{BA}\text{-}1}$, $r_{m,\mathbf{BA}\text{-}2}$; where the subscript annotations stand for unmodified, modified, modified with the addition of 1 or 2 equivalent (eq) **BA**) were determined from the H_2 up-take curves between 0.05 and 0.15 mmol H_2 consumption. In a typical run 0.025 g catalyst and 3 cm^3 DMF + 2.5 vol% H_2O were placed in the reactor, the apparatus was flushed with H_2, the catalyst was pretreated by stirring for 0.5 h under H_2 followed by addition of 0.025 mmol **CD** (except in hydrogenations over unmodified catalyst), 0.5 mmol unsaturated acid, the given amount of **BA** (when used) and another 2 cm^3 solvent. The system was flushed with H_2 and the slurry was stirred under 0.1 MPa H_2 pressure with 1,000 rpm. After the given time 5 cm^3 methanol was added, the catalyst was filtered and washed with 5 cm^3 methanol.



Scheme 2 Product derivatization for GC analysis

Portions of products were methylated using $(CH_3O)_2SO_2$ as follows (see Scheme 2). The methanol was evaporated from 0.5 cm^3 samples, 0.3 cm^3 40% NaOH was added to the product followed by addition of 0.1 cm^3 of $(CH_3O)_2SO_2$. The mixture was shaken for few minutes accompanied by increase in the temperature. The precipitated methoxy-substituted methyl esters were extracted in *tert*-butyl methyl ether. Identification and enantiomeric separation of the methylated products was described previously [23]. Conversions (X) and ees were calculated based on GC-FID analysis using chiral capillary column (Cyclosil-B, 30 m × 0.25 mm, J & W Sci. Inc.) according to the formulae: X (%) = 100 × ([*S*-**2**] + [*R*-**2**])/[$\mathbf{1_0}$]; ee (%) = 100 × |[*S*-**2**]-[*R*-**2**]|/([*S*-**2**] + [*R*-**2**]); where [*S*-**2**], [*R*-**2**] are the concentrations of the methylated product enantiomers and [$\mathbf{1_0}$] is the initial concentrations of the unsaturated acids. No other products than the saturated acids were detected in the resulting solutions and the reactions were reproducible within ±1%. The absolute configuration of the excess enantiomer was assigned to be *S* by GC based on the previously published results obtained using methoxy-substituted 2,3-diphenylpropionic acids (see the Supplementary material). Optical rotation measurements (Polamat A polarimeter) using the crude products showed the excess formation of the dextrorotatory enantiomers in each reaction except the racemic hydrogenations.

3 Results and Discussions

The influence of the hydroxyl group was studied under identical reaction conditions as applied for the hydrogenation of methoxy-substituted acids both in the absence and presence of **BA**. The base additive as well as decreasing the reaction temperature increases the ee in the hydrogenations of the latter acids [22, 30, 31]. The beneficial effect of the methoxy substituent was explained by decrease in the acidity of the substrate due to its strong electron releasing mesomeric effect. Accordingly, the hydroxyl group with even stronger mesomeric effect should give similar results. However, possible additional interactions of the acidic Ph–OH group with the modifier and/or the additive or alteration in the adsorption strength of the acid by adsorption of the –OH group make the results unpredictable. Compounds selected for the initial study are shown in Fig. 1. Results of hydrogenations were

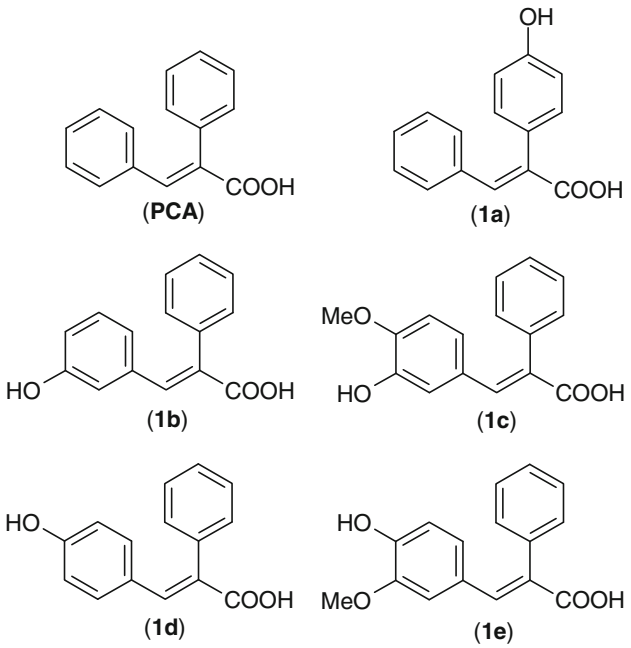


Fig. 1 Selected hydroxy-(*E*)-2,3-diphenylpropenoic acids **1a–e**

summarized in Table 1 and were compared with data obtained with the unsubstituted (**PCA**) and the corresponding methoxy-substituted acids (where available) [22].

The acid substituted on the 2-phenyl ring in *para* position (**1a**) was hydrogenated slower and provided higher ee than **PCA** and the corresponding methoxy derivative both in the absence and presence of 1 eq **BA**. Considering that the 2-phenyl ring is tilted when the (*E*)-2,3-diphenylpropenoic acids are adsorbed on flat metal surface [23, 32], the interaction of the hydroxyl group in **1a** with the metal is unlikely. In contrast with the unsubstituted and methoxy-substituted acids decrease in the temperature resulted in significant ee drop, as well as the use of 2 eq of **BA**. The temperature affects several crucial reaction parameters, such as the solubility of the reactants, the diffusion and surface reaction rates, the adsorption, desorption processes from unmodified and modified surface sites and the hydrogenation of the modifier [33], just to mention the most important [6, 9]. Thus, it is difficult to identify the main reason of the observed ee decrease without further kinetic studies. On the other hand the **BA** used in excess is able to interact with the acidic Ph–OH group, forming strongly basic phenoxide species. These may corrupt the stereocontrol of the reaction by interacting with the protonated **CD** or due to the steric effect of the phenoxide–benzylammonium ion pair. Further investigations are planned to elucidate the interactions occurring under these conditions, however, from practical point of view the results obtained using 1 eq **BA** at 295 K are more attractive.

Table 1 Hydrogenation of selected hydroxy-substituted (*E*)-2,3-diphenylpropenoic acid derivatives

Substrate	r_{um}; $X_t^{a,b,c}$	r_m; $X_t^{a,c,d}$	$r_{m,\mathbf{BA}\text{-}1}$; $X_t^{a,c,d}$	$r_{m,\mathbf{BA}\text{-}2}$; $X_t^{a,c,d}$	ee (%)[a]	$ee_{\mathbf{BA}\text{-}1}$ (%)[a,e]	ee_{BA-1}^{273} (%)[a,f]	$ee_{\mathbf{BA}\text{-}2}$ (%)[e]
PCA [16]	51; $100_{1.5}$	9; 99_6	12; 99_6	–	70	73	80	–
1a	36 (45); 100_2	7 (11); 99_6	9 (21); 99_6	8; 98_6	75 (70)	78 (77)	61 (80)	48
1b	8 (39); 100_5	4 (8); 92_6	5 (32); 94_6	3; 77_6	67 (77)	68 (87)	66 (90)	61
1c	14; 100_4	4; 95_8	3; 80_8	2; 72_8	70	73	70	71
1d	22 (42); 100_4	4 (6); 98_8	8 (18); 99_5	5; 99_8	75 (83)	90 (89)	82 (89)	87
1e	26; 100_3	7; 99_6	13; 100_6	7; 98_6	85	89	88	85

Reaction conditions: 25 mg 5% Pd/Al_2O_3, 5 cm^3 DMF + 2.5 vol% H_2O, 0.025 mmol **CD**, 0.5 mmol substrate, 0.1 MPa H_2, 295 K

[a] Values in brackets are previously published data obtained using the corresponding methoxy-substituted acids under identical conditions included for comparison [22]

[b] r_{um}: initial H_2 up-take rate (mmol h^{-1} g^{-1}) over unmodified catalyst

[c] X_t: conversions (%) reached in t (h) time

[d] r_m, $r_{m,\mathbf{BA}\text{-}1}$, $r_{m,\mathbf{BA}\text{-}2}$: initial H_2 up-take rates (mmol h^{-1} g^{-1}) over catalyst modified by **CD** in the absence, presence of 1 and 2 eq **BA**

[e] $ee_{\mathbf{BA}\text{-}1}$, $ee_{\mathbf{BA}\text{-}2}$: enantiomeric excesses obtained in the presence of 1 and 2 eq of **BA** additive

[f] ee_{BA-1}^{273}: enantiomeric excess obtained in the presence of 1 eq of **BA** at 275 K

Replacement of the methoxy group on the 3-phenyl ring by hydroxyl substituent either in *meta* or *para* position (**1b** and **1d**) resulted in significant decrease in the initial rates and ees, the former acid providing even lower ee than **PCA**. Addition of 1 eq **BA** had different effect on the hydrogenation of the above two compounds, that is had little influence on the hydrogenation of **1b**, whereas increased significantly both the initial rate and the ee value in the reaction of **1d**. Thus, the ee obtained in the hydrogenation of the latter compound exceeded that obtained with the corresponding methoxy derivative. The ee decreased in the reaction of both acids by decreasing the temperature or by using 2 eq of **BA**. It must be noted that in the hydrogenation of the methoxy analog of **1d** the ee was constant in the presence of 0.5–2 eq **BA** [24]. The two acids prepared from isovanillin and vanillin additionally substituted by methoxy group on the 3-phenyl ring (**1c** and **1e**) gave similar rate and ee trends as obtained with the acids bearing the hydroxyl substituent in the same positions, i.e. **1b** and **1d**, respectively. However, the presence of the additional methoxy group led to usually higher or at least similar ees when compared with the mono-substituted acids.

In contrast with the 2-phenyl ring the 3-phenyl moiety is adsorbed close to parallel on the flat metal surface [32], which implies the possible interaction of the substituents with the Pd surface. The adsorption of anisole was found to be stronger than that of benzene due to the effect of the substituent on the charge density of the aromatic ring. However, it was shown that the methoxy substituent does not interact directly with the metal surface [34]. On the contrary, phenol is adsorbed dissociatively on Pd surface and the resulted phenoxide species coordinate close to parallel to the surface interacting with the metal by the aromatic ring and the O lone electron pairs [35]. Thus, the anchoring effect of the phenolic group may cause a decrease in hydrogenation rate over modified surface sites leading to drop in the ee values when the methoxy substituent on the 3-phenyl ring is replaced by hydroxyl group. The decrease in the ee observed in the presence of 2 eq **BA** can be attributed to the interaction of the hydroxyl group with **BA**. This interaction results in further alteration of the acid adsorption and decrease in the number of the surface chiral sites, affecting unfavourably the ee and the initial rate.

Comparison of the results obtained using **1b** and **1d** clarify the still opened question of the surprisingly beneficial effect of the *meta* substituents on the ee. It is known that the *meta*-methoxy group affects in opposite way the acidity of the substrate as the *para*, still their effect on the ee is similar [22, 23]. According to the above results the *meta* substituents influence the enantioselection in a different way, possibly by affecting the interaction strength of the 3-phenyl ring with the surface. The electron donating substituents in *meta* position increase the electron density on the phenyl ring and consequently the adsorption strength of the acid. Differences in the effect of **BA** on the hydrogenation of *meta* and *para* substituted derivatives also support the different origin of the ee increase in the reactions of these compounds. Thus, the *para* substituents influence the ee mainly by their effect on the acidity, whereas the *meta* by affecting the adsorption strength of the 3-phenyl moiety.

The ee obtained in the hydrogenation of **1d** in the presence of 1 eq **BA** equalled that resulted in the hydrogenation of the corresponding methoxy derivative. This encouraged me to examine hydroxyl derivatives substituted on both phenyl rings, since the best ees were obtained in

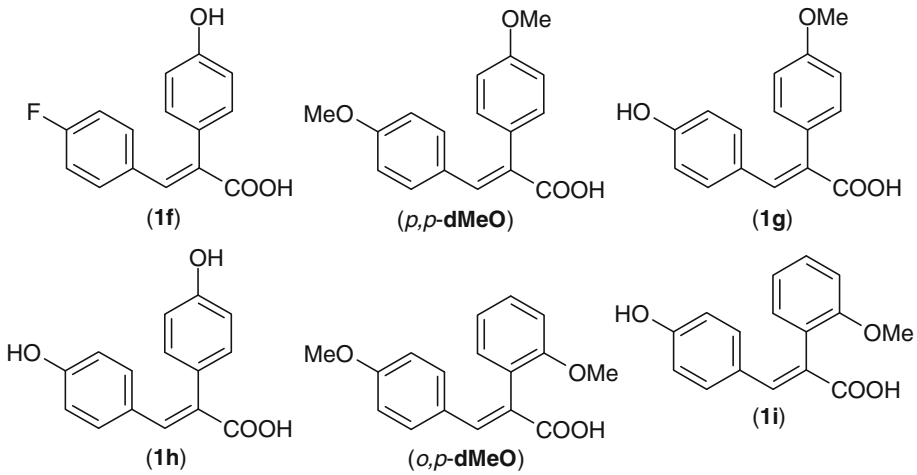


Fig. 2 The examined (*E*)-2,3-diphenylpropenoic acids **1f–i** substituted on both phenyl rings

Table 2 Results of hydrogenations of (*E*)-2,3-diphenylpropenoic acids substituted on both phenyl rings by methoxy or hydroxyl groups

Substrate[a]	r_{um}; $X_t^{b,c}$	r_m; $X_t^{c,d}$	$r_{m,BA-1}$; $X_t^{c,d}$	$r_{m,BA-2}$; $X_t^{c,d}$	ee (%)	ee_{BA-1} (%)[e]	ee_{BA-1}^{273} (%)[f]	ee_{BA-2} (%)[e]
1f	10; 100_5	6; 94_6	8; 97_6	5; 85_6	61	69	67	66
p,p-**dMeO**	29; 100_4	4; 99_6	8; 99_6	–	86	89	90	–
1 g	8; 100_5	2; 84_8	5; 99_8	4; 97_8	80	82	82	78
1 h	6; 97_5	3; 69_6	5; 92_6	5; 73_6, 3[g]; 66_6^g	78	83	81	69, 63[g]
o,p-**dMeO**	8; 75_5	4; 85_8	4; 90_8	–	83	90	92	–
1i	6; 93_6	1; 85_{20}	2; 93_{20}	1; 92_{20}	87	91	90	92

Reaction conditions: 25 mg 5% Pd/Al_2O_3, 5 cm^3 DMF + 2.5 vol% H_2O, 0.025 mmol **CD**, 0.5 mmol substrate, 0.1 MPa H_2, 295 K

[a] Results obtained with dimethoxy-derivatives (*p,p*-**dMeO** and *o,p*-**dMeO**) under identical reaction conditions [22]

[b] r_{um}: initial H_2 up-take rate (mmol h^{-1} g^{-1}) over unmodified catalyst

[c] X_t: conversions (%) reached in t (h) time

[d] r_m, $r_{m,BA-1}$, $r_{m,BA-2}$: initial H_2 up-take rates (mmol h^{-1} g^{-1}) over catalyst modified by **CD** in the absence, presence of 1 and 2 eq **BA**

[e] ee_{BA-1}, ee_{BA-2}: enantiomeric excesses obtained in the presence of 1 and 2 eq of **BA** additive

[f] ee_{BA-1}^{273}: enantiomeric excess obtained in the presence of 1 eq of **BA** at 275 K

[g] Results obtained in the presence of 3 eq **BA**

the hydrogenation of such compounds [21–24]. Structures of selected compounds and some of the corresponding methoxy derivatives are shown in Fig. 2. The results obtained in the hydrogenation of these acids are summarized in Table 2.

Disappointing ees were obtained in the hydrogenation of **1f**, either when compared with **1a** or with the corresponding methoxy substituted acid (not shown, see [23]). Thus, the beneficial effect of the fluorine substituent was suppressed by the presence of the hydroxyl group on the 2-phenyl ring. The discrepancies observed in the effect of the hydroxyl group on the 2-phenyl ring during the hydrogenation of the mono- and di-substituted derivatives (**1a** and **1f**), showed that the effects of the substituents on the two phenyl rings in this case are not additive as was suggested to be in the hydrogenation of dimethoxy-substituted compounds [15]. Further studies are needed to evidence the interactions in which the hydroxyl substituent on the 2-phenyl is involved.

Replacing either one or both methoxy substituent by hydroxyl group in the *para*, *para*-dimethoxy substituted acid (*p,p*-**dMeO**) had detrimental effect on both the ees and the initial rates. Both hydroxy-substituted acids (**1g** and **1h**) were hydrogenated in lower ee when compared with *p,p*-**dMeO**. Slightly lower ee values were obtained in the hydrogenation of **1h** with hydroxyl substituent on the 2-phenyl ring as compared with **1g**. Both acids were hydrogenated in similar optical purities at 294 and 275 K, whereas, the ee decreased significantly when more than 1 eq of **BA** was used. The best enantioselectivities were obtained in the hydrogenation of (*E*)-2-(2-methoxyphenyl)-3-(4-hydroxyphenyl)propenoic acid (**1i**), which exceeded those resulted in that of the corresponding dimethoxy-derivative (*o,p*-**dMeO**) both in the absence and presence of

BA. Although, the ee decreased by decreasing the reaction temperature, in the presence of 2 eq of **BA** up to 92% ee was obtained, value reached only at 275 K with *o,p*-**dMeO** under otherwise identical reaction conditions.

Finally, results obtained with the hydroxy-substituted acids showed that this group in *para* position on the 3-phenyl ring has a similar effect as the methoxy group. Thus, the ee increase observed with such acids has a common origin, i.e. due to their electron releasing effect the electron density on the conjugated acrylic acid moiety increases, leading to more efficient acid–modifier interaction on the surface. In contrast, the beneficial influence of the *meta* positioned electron releasing substituents is suggested to be due to their effect on the adsorption strength of the 3-phenyl ring, as these substituents increase the electron density only on this phenyl ring. Additionally the hydroxyl groups in either *para* or *meta* position also influence the acids adsorption by their anchoring effect thus affecting the stereochemical out-come of the hydrogenations. It was shown that the latter effect is more accentuated when the hydroxyl group is *meta* positioned, whereas is less significant when is in *para* position due to the extended conjugated system of the acid. The suggested effects of the substituents in these positions are illustrated schematically in Fig. 3.

Furthermore, results obtained in the presence of **BA** allowed drawing conclusions on the way this additive influences the enantioselection. It was demonstrated that **BA** increases the rate and ee by accelerating the desorption of the saturated acid from chiral surface sites [30, 31]. The hydroxy-substituted acids contain two acidic groups, though of different acidities (pKa -COOH $\approx$ 7; pKa -Ph-OH $\approx$ 10). In the hydrogenation of hydroxy-substituted acids in the presence of 2 eq **BA**, when the additive surely interacts with the phenolic hydroxyl group forming strongly basic phenolate anions, the ee decreased significantly (except **1i**). However, in the presence of 1 eq of **BA** the ee always increased (with up to 15% in case of **1d**). These observations indicate that the 5 mol % excess of additive (**1** eq BA + **5** mol % CD) was not interacting with the phenolic group, otherwise a small decrease in the ee should be observed. Accordingly, one may assume that the excess **BA** will continue to be bonded to the cinchonidinium-carboxylate species and will participate in the formation of the surface intermediate complex during the enantioselective hydrogenation.

4 Conclusions

The effect of replacement of the methoxy by hydroxyl group in substituted (*E*)-2,3-diphenylpropenoic acids on their enantioselective hydrogenation over Pd catalyst modified by cinchonidine was examined. The hydrogenation of mono-substituted acids bearing *para*-hydroxyl group on the 2-phenyl or 3-phenyl ring provided similar or better ee than the corresponding methoxy substituted acids. It was shown that in the hydrogenation of acids substituted on both phenyl rings the beneficial effect of the substituents is not always additive, thus, only in the hydrogenation of the (*E*)-2-(2-methoxyphenyl)-3-(4-hydroxyphenyl)propenoic acid the ee reached the value obtained with the corresponding dimethoxy derivative. However, this asymmetric heterogeneous catalytic method was found to be appropriate for the preparation of several hydroxy-substituted (*S*)-2,3-diphenylpropenoic acids in good yields and optical purities (see Fig. 4).

The results obtained with the hydroxy-substituted acids also shed light on the different origin of the influence of the electron releasing substituents situated in *meta* or *para*

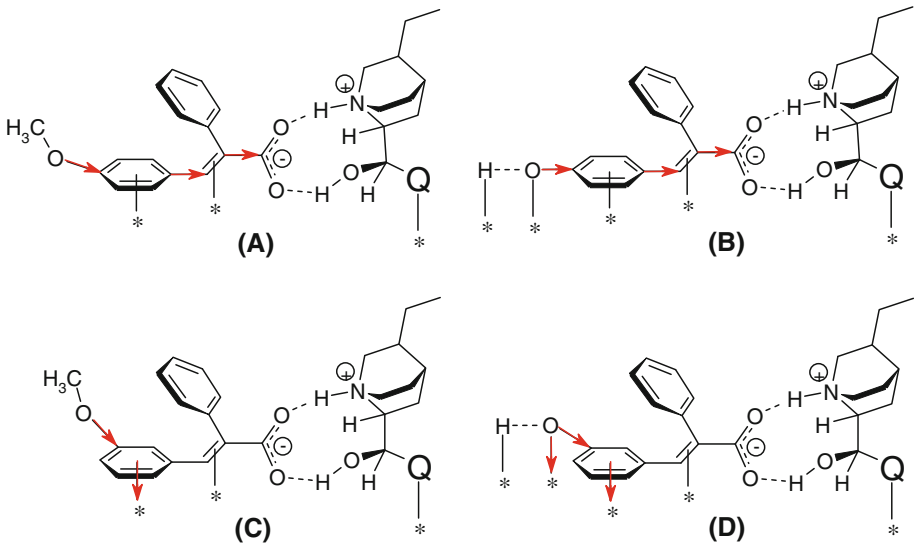


Fig. 3 Schematic illustration of the substituent electronic effect in the suggested surface intermediate complexes: (*E*)-2-phenyl-3-(4-methoxyphenyl)propenoic acid-**CD** (**a**), **1d**-**CD** (**b**), (*E*)-2-phenyl-3-(3-methoxyphenyl)propenoic acid-**CD** (**c**) and **1b**-**CD** (**d**); (Q = 4-quinolyl)

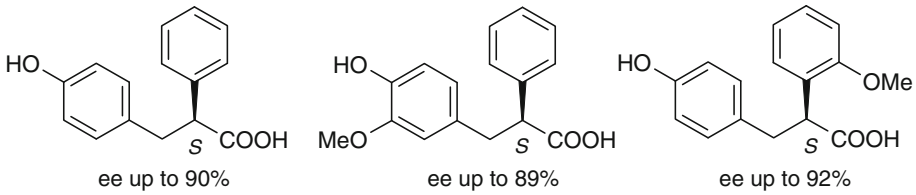


Fig. 4 Hydroxy-substituted (*S*)-2,3-diphenylpropionic acids obtained in over 90% yield and high optical purity

position on the 3-phenyl ring, the former increasing the adsorption strength of the acids, whereas the latter affecting favourably the acidity of the substrate and consequently the interaction strength with the modifier.

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