STEREOSELECTIVITY OF HETEROGENEOUS CATALYSTS, MODIFIED BY OPTICALLY ACTIVE POLYELECTROLYTES

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UDC 541.128:541.135

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Metal-containing macromolecular catalysts are assuming constantly increasing practical and theoretical importance as models of biological systems [1]. One of the traits of macromolecular catalysis is its stereoselectivity [2]. The successful use of heterogeneous and homogeneous catalytic systems, including optically active natural and synthetic polymers, for the asymmetric hydrogenation of unsaturated compounds is known [3]. A strong dependence of the conformation of the polymer chain both on the conformation of the individual units and on the medium is characteristic for polymeric catalysts.

We studied the asymmetric synthesis of phenylalanine (PAL) by the hydrogenation of the methyl ester of α -acetamidocinnamic acid (MEAA) over skeletal Ni and Pd-black, modified by the optically copolymers of styrene with the L- and D-alanine maleimides (SPL-L and SPL-D)



In the study we used the amorphous SPL-L and SPL-D, which were obtained by the reaction of L- and Dalanine with the copolymer of styrene and maleic anhydride, and the partially crystalline SPL-L, which was obtained by the radical copolymerization of styrene with L-alanine maleamide [4]. The hydrogenation of the MEAA was run in organic solvents at atmospheric H₂ pressure and ~20°C. The catalysts were modified with 1% solutions of the copolymers, after which they were washed well to remove excess modifier.

The results of the asymmetric synthesis of PAL over Pd-black and skeletal Ni, modified by solutions of optically active polymers in organic solvents, are given in Table 1. From Table 1 it can be seen that both over Pd-black and skeletal Ni, modified by amorphous and partially crystalline SPL-L, independent of the modification and hydrogenation solvents used, D-(+)-PAL is formed with an optical purity of 1-2%. Here a good reproducibility is observed in parallel experiments (1-3) in the degree of asymmetry of the synthesis p_{λ} , calculated from the $[\alpha]_{\lambda}$ values of PAL [5] for two wavelengths. Based on the amino acid analysis data, a chemically pure PAL, devoid of other amino acids, was obtained in all of the experiments.

In the asymmetric hydrogenation of MEAA in dioxane over Pd-black, modified by aqueous solutions of the amorphous SPL-L and SPL-D (Fig. 1), not only the optical purity of the formed PAL, but also the sign of its rotation, changes in a complex manner as a function of the modification pH. Modification with SPL-L at pH 4-9 gives the predominant formation of D-PAL, in which connection the maximum specific rotation is observed at pH 7, while L-PAL is formed predominantly at pH > 9. When SPL-D is used the optical yield as a function of the modification pH represents a mirror image of the curve that was obtained for SPL-L. The formation of L- and D-PAL in the asymmetric hydrogenation of MEAA over Pd-black, modified by SPL-D and SPL-L at pH 7, is also corroborated by the optical rotation dispersion (ORD) curves in the 300-230 nm region (Fig. 2), which are characteristic for PAL [6].

Institute of Heteroorganic Compounds, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 12, pp. 2764-2770, December, 1973. Original article submitted May 7, 1973.

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čxpt. No.	Catalyst	Modification-hy- drogenation sol- vents	Yield of PAL, %	[α] _D , deg., at		pλ,%, optical purity of PAL at	
				589 nm	436 nm	589 nm	436 nm
1 2 3 4 5 6 7	Pd-black " Skeletal Ni Pd-black "	Dioxane-dioxane The same """ Dioxane-CHCl ₃ Methanol-metha-	99 89 94 85 80 96 91	$\begin{array}{ c c c } +0,61 \\ +0,43 \\ +0,55 \\ +0,55 \\ +0,48 \\ +0,38 \\ +0,40 \end{array}$	$ \begin{vmatrix} +1,29 \\ +1,01 \\ +1,24 \\ - \\ +1,41 * \\ +0,94 * \end{vmatrix} $	1,80 1,27 1,62 1,62 1,41 1,12 1,18	$ \begin{array}{c} 1,94\\ 1,52\\ 1,87\\ -\\ 1,43\\ 0,96\\ \end{array} $
8	Skeletal Ni	The same	83	+0,39	+1,29*	1,15	1,31

TABLE 1. Asymmetric Synthesis of D-PAL by Hydrogenation of MEAA over Pd-Black and Skeletal Ni, Modified by Solutions of Amorphous (Experiments 1-4) and Partially Crystalline SPL-L (Experiments 5-8)

*Determined at λ 335 nm (Jasco ORD/UV-5 spectropolarimeter).

At the present time the concepts of complex formation attract much attention in heterogeneous catalysis [2, 7, 8]; asymmetric synthesis in the presence of modified catalysts is explained by the formation of an optically active intermediate mixed complex: substrate-catalyst-modifier. Due to the stereoselective effect of the optically active modifier the substrate is coordinated with the catalyst preferably in one of possible conformations, and one of the antipodes of the reaction products is predominantly formed during subsequent transformations [2].

Apparently, the complex relation observed by us between the stereoselective effect and the modification pH is associated with the formation of various types of complexes on the catalyst surface. In order to elucidate this we studied the complexes of SPL-D with Na_2PdCl_4 as a function of the pH of the solution as being models of complex formation on the Pd-black surface. The formation of optically active complexes was shown by the ORD method in aqueous-alcohol solution at pH 4-10 (Fig. 3). Two Cotton effects can be seen on the ORD curves in the 300-500 nm region, which are characteristic for the d-d transitions of optically active Pd(II) complexes [9]. A noticeable change in the character of the ORD curves with increase in the pH can be associated with a change in the structure of the complexes. The curves for the potentiometric titration of SPL-D in the presence of Na_2PdCl_4 , and without it, in 0.1 N aqueous-alcohol NaCl solution (Fig. 4) lead to more definite conclusions. With a degree of dissociation (α) of the COOH groups of ~ 0.5 , the relative acidity of the carboxyl groups of the complexes changes when compared with the acidity of the COCH groups of the starting copolymer. When $\alpha > 0.5$ the acidity of the complexes is higher than that of the starting copolymer, which is characteristic for the carboxylate complexes of the polyvalent ions of the transition metals [10, 11]. A decrease in the relative acidity of the complexes is observed when α < 0.5, which can be caused by the formation of complexes in this region in which the COOH groups of the copolymer are not the ligands. It is most probable that the complexes of the Pd(II) ions with the CO groups of the imide rings are formed at $\alpha < 0.5$, since it is known that PdCl₂ readily forms complexes with amides under mild conditions, for example, with DMF at the CO group [12]. The concentration effect also testifies in support of this, which is manifested in the fact that the macromolecule enters into the role of a stronger complexing agent than a low-molecular analog, since each macromolecule is in essence a concentrated solution of the ligands [1]. The insertion of the Pd(II) ion into the polymeric matrix evidently leads to a decrease in the acidity of the COOH groups of the polyelectrolyte, mainly due to the electrostatic effect of the negatively charged complex ion.

As a result, it is possible to assume the formation of the following complexes: the imide complexes (I) are formed predominantly in acid and neutral media (when $\alpha < 0.5$), while the carboxylate complexes (II) are formed predominantly in alkaline medium ($\alpha > 0.5$). These two types of complexes have a different stereochemical environment of the Pd, which leads to a different coordination of the substrate with the catalytic complex





Fig. 1. Values and sign of rotation of the PAL that is formed in the asymmetric hydrogenation of MEAA over Pd-black, modified by aqueous solutions of SPL-L and SPL-D, as a function of the modification pH.

Fig. 2. ORD curves in UV region of the L- (1) and D-PAL (2) obtained in the asymmetric hydrogenation of MEAA over Pd-black, respectively modified by aqueous solutions of SPL-D and SPL-L at pH 7.

If in the carboxylate complex (II) the stereochemistry of the environment of the Pd(II) ion, rigidly attached by a chelate bond, is determined only by the configuration of the α -carbon atom of the alanine moiety, then in the case of the imide complex (I) we can speak of the preferred conformation of the α -carbon atom of the alanine moiety only due the possibility of free rotation around the C-N bond. It is possible to assume that the conformation of the α -carbon atom of the alanine molecular hydrogen bond when $\alpha = 0$ (I), and it is stabilized to a greater degree by the formation of the more stable hydrogen bond of the COOH group of the alanine molecular of the succinimide ring, which forms a complex with the adjacent carboxylate anion in the chain (Ia)



The indicated structure of unit (Ia) can probably arise when $\alpha = 0.5$, if the macromolecule is stretched out in the chain and, due to electrostatic repulsion, bears alternate dissociated and undissociated COOH groups. This is confirmed by the potentiometric titration curves, from which it can be seen that the process for unrolling the macromolecule, both for the complexes and for SPL-D, ends when $\alpha \sim 0.5$.

Starting with the theory of carboxylic polyelectrolytes [13], with increase in α the macromolecule, which represents a disordered rolled coil when $\alpha = 0$, gradually unrolls and assumes the conformation of a stretched chainlet. This process is caused by the electrostatic repulsion of the negatively charged groups, the accumulation of which leads to an increase in the energy that is needed for a further ionization of the COOH groups, and a decrease in their acidity occurs. The unrolling of the macromolecule partially compensates for the increase in the energy of proton cleavage due to changes in the free energy of the polymeric matrix, as a result of which the electrostatic potential value of the chainlet practically does not change in the region of the coil-stretched chain region, which is expressed in a slight change of the acidity in this region with increase in α . In the case of SPL-D the process of unrolling the macromolecule in the absence of NaCl begins at $\alpha \sim 0.1$, and ends at $\alpha \sim 0.4$ (see Fig. 4, curve 6). A confirmation of the coil-stretched chain transition region is shifted toward greater α values (0.2-0.5) in the presence of NaCl, since an increase in the concentration of Na ions leads to a decrease in the electrostatic repulsion of the indicated conformation of unit (Ia), and consequently, also the maximum stereoselective effect of the catalytic complex, are realized



Fig. 3. ORD curves of complexes of SPL-D and Na_2PdCl_4 at pH: 1) 4.9; 2) 6.0; 3) 10.0, and of SPL-D at pH: 4) 7.0; 5) 10.0.

Fig. 4. Potentiometric titration curves of SPL-D $(1.71 \cdot 10^{-3} \text{ equiv/liter})$ in 0.1 N NaCl solution; $[Na_2PdCl_4]$ (equiv/liter $\cdot 10^{-4}$): 1) 0; 2) 2.14; 3) 4.28; 4) 8.56; 5) 17.1; 6) SPL-D without NaCl and Na_2PdCl_4 .

at $\alpha = 0.5$, which corresponds to a pH of 6.5-7.0 for the modifying solution (curve 6) and the maximum stereoselectivity of the modified Pd-black (see Fig. 1). A further increase in the pH leads to a constantly greater predominance of the (II) complex, and an inversion in the sign of rotation of the formed PAL is observed at pH > 9.

The linear sections of the titration curves of the complexes (see Fig. 4, curves 2 and 3), in the range $\alpha \sim 0.5$ -0.7, intersect the titration curve of the starting SPL-D, and reflect the transition of complex (Ia) to (II), which is accompanied by a change in the electrostatic potential of the polymeric matrix, which partially compensates for the increase in the dissociation energy of the carboxyl groups. As a cooperative process, the indicated transition, which is a reaction of substitution in Pd(II) complexes, should proceed with time. Actually, during the titration of the complexes in this range of α the maximum time of establishing the pH, after adding an alternate portion of NaOH, reached 30 min. The middle of this transition ($\alpha \sim 0.6$), where complex (II) begins to predominate over (Ia), corresponds to a modification pH of ~9, especially for the complex with a 1:4 ratio of the Pd(II) ions to the COOH groups of SPL (curves 3 and 6), which is close to the pH for inversion of the sign of the formed PAL (see Fig. 1).

A decrease in the catalyst activity during modification (time for hydrogenation of MEAA over Pd-black ~1 h, and 1.5-2.5 h over modified Pd-black) and the progress of asymmetric synthesis both indicate the formation of the mixed complex: substrate-catalyst-modifier, while the obtained p_{λ} values of the formed PAL apparently reflect the stereoselective effects during asymmetric hydrogenation over modified Pd-black. The small p_{λ} values are apparently not caused as much by the low stereoselectivity of the catalytic complexes as by the low degree of filling the active centers of the catalyst by the optically active modifier due to the steric hindrance that arises during the modification of the catalyst surface by cumbersome and rigid polymeric molecules. The chain effect that is manifested as steric hindrance in the complexing of the macromolecule with the ions of the transition metals in solution [1] should have even greater importance during complex formation on the surface of a heterogeneous catalyst.

EXPERIMENTAL METHOD

To modify the catalysts we used the following copolymers of styrene with the maleimides of L- and D-alanine ($[\eta]$, dl/g, in dioxane at 25°C; $[\alpha]_D$, in dioxane at 25°): amorphous SPL-L, $[\eta] 0.31$, $[\alpha]_D - 8.10^\circ$, amorphous SPL-D, $[\eta] 0.41$, $[\alpha]_D + 11.36^\circ$, and partially crystalline SPL-L, $[\eta] 0.064$, $[\alpha]_D - 8.94^\circ$. The Pd-black was obtained as described in [14], while the sketetal Ni was obtained by the leaching of Ni-Al alloy. The methyl ester of α -acetamidocinnamic acid was obtained by the esterification of α -acetamidocinnamic acid azlactone with methanol in the presence of NaOH [15], mp 120-121.5°. Found: C 65.97; H 6.15; N 6.36%. C₁₂H₁₃NO₃. Calculated: C 65.74; H 5.98; N 6.39%. All of the solvents were made absolute employing conventional procedures.

Modification of Catalysts and Hydrogenation. To 0.5 g of skeletal Ni or ~0.25 g of Pd-black was added 15 ml of a 1% solution of SPL in either an organic solvent or in water at a definite pH, and the mixture was kept in the refrigerator for 2 h, with periodic shaking. Then the catalyst was washed by decantation of the organic solvent or water 5 times, and in the case where the hydrogenation solvent differed from the modification solvent, it was also washed several times with the solvent used in the hydrogenation. The modified catalyst was charged into the hydrogenation vessel (duck), 10 ml of the solvent was added, and the mixture was saturated with H_2 for ~10 min. After this a solution of 0.5 g of MEAA in 15 ml of the solvent was charged into the vessel and the hydrogenation was run at room temperature using a high-speed shaker that operated at 400-500 turns/min. The hydrogenation over the catalysts that had been modified by aqueous SPL solutions was run in dioxane. The hydrogenation was stopped when the theoretical amount of H_2 had been absorbed, the catalyst was filtered, and the solution was evaporated to dryness, after which the methyl ester of N-acetylphenylalanine was hydrolyzed by refluxing with 15 ml of 2 N HCl solution for 10 h. After evaporation of the hydrolyzate the PAL hydrochloride was dissolved in 15 ml of water, the solution was filtered, and the PAL was separated on a Dowex-50 column using 30 ml of 1 N NH₄OH solution. After evaporation of the aqueous solution to dryness the PAL was dried over P2O5 in vacuo at 40-50°. A KLA-3B amino acid analyzer was used for the amino acid analysis of the PAL. The specific rotation of the PAL was determined in aqueous solutions at a concentration of 1-2 g/100 ml, at 20-25°, in a cell with a length of 0.5-0.7 dm, on a Roussel-Jouan polarimeter, at 589 and 436 nm, with an accuracy of $5 \cdot 10^{-4} \text{ deg}$ in which connection the $\alpha_{observed}$ in most cases was $0.5-2.0\cdot 10^{-2}$ deg. The ORD curves of the PAL in the UV region were taken on a Jasco, Model ORD/UV-5 spectropolarimeter, at a concentration of 0.1 g/100 ml, in a cell with a length of 0.1 dm, at 20-25°.

Method of Determining the ORD. To 5 ml of an alcohol solution of SPL-D were added 5 ml of water and $1 \cdot 10^{-2}$ M aqueous Na₂PdCl₄ solution (obtained by dissolving equivalent amounts of NaCl and PdCl₂ in water, and the amount of Pd was determined as described in [16]) in such an amount as to give a molar ratio of COOH groups :Pd(II) = 1:1. The obtained solutions were titrated with 0.1 N NaOH solution to the appropriate pH, allowed to stand overnight, and then water was added to bring the solution volume up to 15 ml, the pH was determined again, and the mixture was analyzed. The SPL-D solutions without the Na₂PdCl₄ were prepared in a similar manner. The obtained solutions of the complexes contained 0.07-0.11 g/100 ml of SPL-D; this concentration was used to calculate $[\alpha]_{\lambda}$. The ORD curves of the solutions of the complexes and of SPL-D were taken on a Jasco, Model ORD/UV-5 spectropolarimeter, in cells with a length of 0.1-0.2 dm, at 20-25°.

Potentiometric Titration. To 1 ml of an alcohol solution of SPL-D, containing $2.56 \cdot 10^{-5}$ equiv/liter of COOH groups, were added 1.5 ml of aqueous 1 N NaCl solution and the appropriate amount of $1 \cdot 10^{-2}$ M aqueous Na₂PdCl₄ solution to give the following COOH :Pd(II) ratios: 1:1 (2.56 ml), 2:1 (1.28 ml), 4:1 (0.64 ml), and 8:1 (0.32 ml). Then the solution volume was brought up to 15 ml with water to give SPL-D solutions with a concentration of $1.71 \cdot 10^{-3}$ equiv/liter of COOH groups, and 17.1, 8.55, 4.28, and $2.14 \cdot 10^{-4}$ equiv/liter of Pd(II) ions in 0.1 N NaCl solution. The titration was run on a Radiometer TTT-1c (SBU-1a)SBR-2c titrator with 0.1 N NaOH solution in 0.1 N NaCl solution. The subsequent NaOH portions were added after a stable pH had been established, which required 2-30 min. The titration of the SPL-D without adding NaCl was done in a similar manner. The agreement of parallel titrations was 0.03-0.05 pH units in the pH region <7, and ~0.1 in the pH region >7.

CONCLUSIONS

1. The hydrogenation of the methyl ester of α -acetamidocinnamic acid over Pd-black and sketetal Ni, modified by optically active copolymers of styrene with alanine maleimide, gives an optically active phenyl-alanine with an optical purity of 1-2%.

2. The modification of Pd-black by aqueous solutions of optically active copolymers revealed that the modification pH affects not only the value, but also the sign of rotation of the formed phenylalanine.

3. The value and character of the catalyst stereoselectivity as a function of the modification pH is explained by the formation of various types of complexes on the catalyst surface, due to the configurational and conformational changes in the optically active polyelectrolyte as a function of its degree of dissociation.

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