TRANSITION METAL COMPLEXES – A NEW CLASS OF CATALYSTS OF INTERFACIAL ALKYLATION FOR THE ASYMMETRICAL SYNTHESIS OF α-AMINO ACIDS

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A new class of catalysts of interfacial asymmetrical alkylation is suggested for the synthesis of α-amino acids – positively charged complexes of the transition metals Cu(II), Ni(II), and Pd(II). These complexes consist of several fragments, by variation of which the structure of the catalysts can readily be modified. The complexes are chiral on account of (S)proline derivatives contained in them as one of the fragments. The catalyst complexes (C) were used in the alkylation of amino acid fragments of Ni(II) complexes of the Schiff base of glycine with N-(2-pyridinecarbonyl)-o-aminobenzophenone (Ni-PBP-Gly) and the Schiff base of alanine with N-(2-pyridinecarbonyl)-o-aminobenzaldehyde (Ni-PBA-Ala) under interfacial conditions. After decomposition of the alkylated complexes, phenylalanine and α-methyl-phenylalanine were isolated with yields of 33-87% and optical purity (o.p.) from 3 to 21%, depending on the C used.

Among the methods of organic synthesis, synthesis under conditions of interfacial catalysis (IFC) are taking on increasing practical significance [1-4]. The most frequently used interfacial catalysts are crown ethers, cryptands, quaternary ammonium and phosphonium salts. Only a limited number of examples are known in which C-alkylation under conditions of IFC with catalysis by chiral quaternary ammonium salts can occur asymmetrically with a sufficiently high optical purity [5-8]. The idea of using the method of asymmetrical IFC for the synthesis of amino acids was first implemented in [9], where quinine and cinchonine derivatives were used as catalysts. We first implemented the method of synthesizing amino acids by C-alkylation under conditions of asymmetrical IFC in [10] (N-benzylcinchonidinium chloride as the catalyst). An article that reported on conducting analogous reactions but with different substrates [11] appeared almost simultaneously. Phase transfer catalysts based on natural alkaloids possess a vital shortcoming – they are characterized by narrow specificity for the substrate molecule, and their modification is coupled with substantial difficulties.

Any compound possessing a positive charge can be considered as a formal analog of onium salts. We have suggested that positively charged complexes of transition metals with rather voluminous hydrophobic organic ligands, possessing a vacant place either in the main coordination sphere or in the apical position, may prove to be catalysts of interfacial reactions, in particular, in the alkylation of C–H acids. Only one attempt to use positively charged complexes of transition metals as catalysts of phase transition in reactions is known [12]. However, up to this time the possibility of using positively charged chiral complexes of transition metals as catalysts of asymmetrical synthesis under conditions of interfacial catalysis had not been discussed.

RESULTS AND DISCUSSION

In this article we reported the results of the use of positively charged complexes of Ni(II), Cu(II), Pd(II) as catalysts of the asymmetrical synthesis of α-amino acids by alkylation with alkyl halides under conditions of IFC of glycine and alanine fragments in Ni(II) complexes of their Schiff bases. The complex catalysts C-1 to C-11 represent positively

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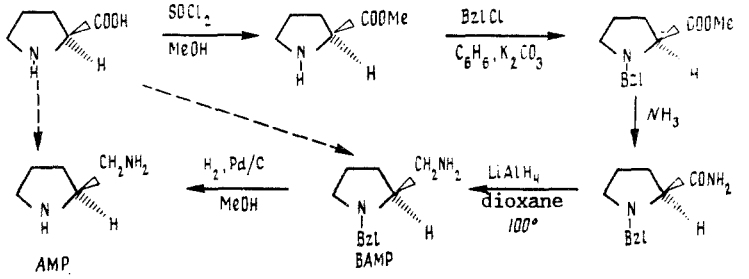
charged compounds, in which the metal ion is coordinated with a chiral ligand consisting of several fragments. The Schiff base (S)-2-aminomethylpyrrolidine (AMP) or (S)-1-benzyl-2-aminomethylpyrrolidine (BAMP) with the corresponding carbonyl compound was used as a ligand. Modification of such complexes is easily accomplished by varying the composition and structure of the individual fragments. The amino component of the ligand (AMP and BAMP) was synthesized as presented in Scheme 1.

Scheme 1



The catalysts C-1 to C-11 were produced by mixing equimolar amounts of a metal salt, carbonyl compound, and AMP (BAMP) with an addition of 2 equiv. of the base, as shown in Scheme 2. Subsequently, they were used as alkylation catalysts. Considering the PMR data [with the exception of complexes of Cu(II)] and the UV spectra of these compounds, we suggest that C-1 to C-11 have a planoquadratic or pyramidal structure. On the basis of the structural characteristics, all the catalysts can be subdivided into two groups. The first group includes C-2 to C-5, C-7, and C-10, in which the endo-hydrogen atoms of the pyrrolidine fragment of the ligand shield one apical position of the metal ion. Such shielding was also observed previously in analogously constructed neutral complexes [13-15]. The second group of catalysts includes C-1, C-6, C-8, C-9, and C-11, in which both apical positions of the metal ion are shielded: one by the benzyl group bonded to the nitrogen atom of the pyrrolidine ring (a well-known phenomenon [16]), the other by the hydrogen atom of the pyrrolidine fragment.

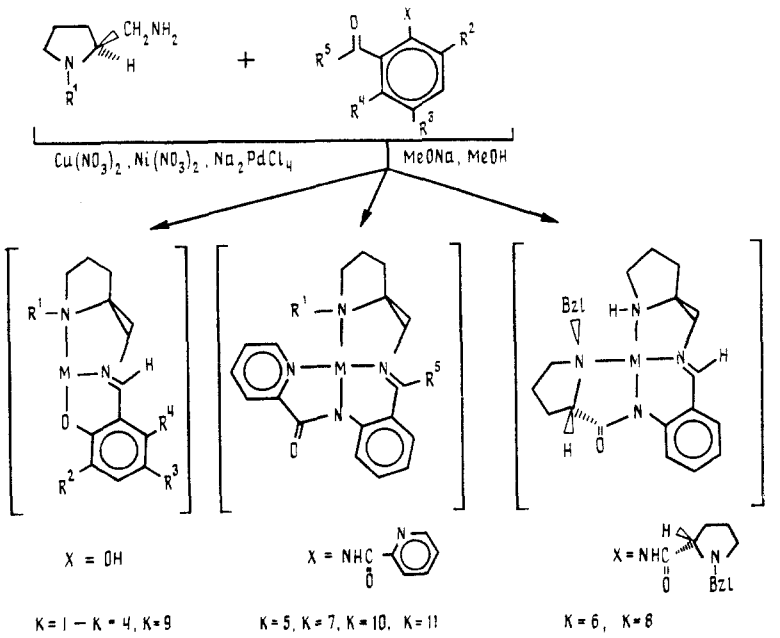
The substrates for the alkylation reactions were selected on the basis of the requirement of the greatest possible conformational rigidity. This condition is well satisfied by Ni(II) complexes of the Schiff bases of amino acids (glycine or alanine) with 2-[(N-pyridinecarbonyl)amino]benzophenone (PBP) or 2-[(N-pyridinecarbonyl)amino]benzaldehyde (PBA). The carbonyl compounds PBA and PBP were produced according to the procedures described in [17] and [10], respectively. The procedure of synthesis of the complexes of the substrate was taken from [10] and [15].

The alkylation reaction was conducted at ~20°C in CH_2Cl_2 in the presence of catalytic amounts of C-1 to C-11 (the usual substrate:catalyst ratio, 10:1) and a fivefold excess of solid alkali. At the end of the reaction, the product was purified chromatographically; the optical purity of the products was determined polarimetrically: for optically pure Ni-PBP-(S)-Phe $[\alpha]_D^{25}$ = +3940° (0.4 g/liter, $CHCl_3$–MeOH, 1:1, ℓ = 5 mm) and for Ni-PBP-(S)-α-Me-Phe $[\alpha]_D^{25}$ = +750° (0.02 g/liter, $CHCl_3$–MeOH, 1:1, ℓ = 1 cm). In the case of alkylation of the glycine complex, the amino acid was isolated, and its optical purity was additionally established by the method of gas–liquid chromatography [18].

The results obtained in the alkylation of the complexes Ni-PBP-Gly and Ni-PBA-Ala are cited in Table 1. Benzyl bromide was used as the alkylating agent in the model reaction. In addition, we investigated the influence of the nature of the alkyl halide on the stereoselective effects in the alkylation reaction on the example of alkylation of the complex Ni-PBP-Gly, catalyzed by C-2. The results are presented in Table 2.

In this work we studied the change in the optical yield as a function of the reaction time. The reaction of alkylation of Ni-PBP-Gly and Ni-PBP-Ala by benzyl bromide in the presence of C-2 was used as a model. The results of the alkylation are presented in Table 3, from the data of which it is evident that C-2 is virtually unchanged in 20-30 min (the reaction time), since for α-Me-Phe obtained as a result of the reaction, which does not epimerize in this case, the optical purity of the reaction product does not depend on the degree of conversion during this period of time. We should mention that the rate of alkylation of the alanine complex is lower than that of the glycine complex.

Scheme 2

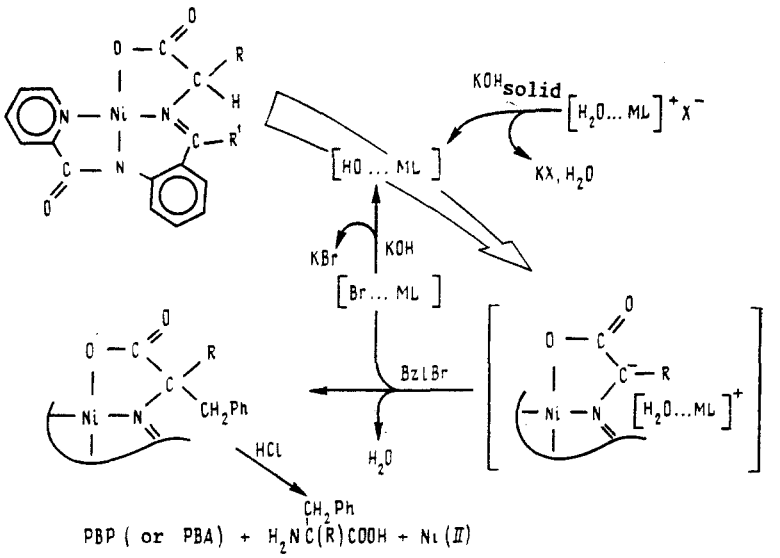


M = Cu, R^1 = Bzl, $R^2 = R^3 = R^4$ = H (K-1); $R^1 = R^2 = R^3 = R^4$ = H (K-2); $R^1 = R^4$ = H, $R^2 = R^3$ = Cl (K-3); $R^1 = R^2$ = H, $R^3 + R^4$ = —(CH—)$_4$— (K-4); M = Pd, R^1 = Bzl, $R^2 = R^3 = R^4$ = H (K-9).

$R^1 = R^5$ = H, M = Cu (K-5), Ni (K-7), Pd (K-10); R^1 = H, R^2 = Ph, M = Pd (K-11). M = Cu, (K-6), Ni (K-8).

The mechanism of the reactions of alkylation of C—H acids, occurring under conditions of interfacial catalysis by quaternary ammonium salts under the action of bases, has been investigated in rather great detail. The key step of these reactions in the overwhelming majority of cases is the formation of a carbanion from the C—H acid under the action of the base at the interface. In the case of catalysis by positively charged metal complexes, the mechanism of alkylation can be represented as follows (Scheme 3).

Scheme 3



At the first step a proton is stripped from a water molecule in the complex catalyst at the interface under the action of KOH, forming a neutral lipophilic complex [HO—ML] (as shown in Scheme 2, in all the complexes there is a possibility of incorporation of a water molecule into the coordination sphere: either in the main coordination plane or in the apical position). The basicity of the hydroxyl in the complexes C-1 to C-11 is rather high (in analo-

TABLE 1. Asymmetrical Alkylation of Ni(II) Complexes of Schiff Bases of Gly and Ala under Conditions of Interfacial Catalysis (CH_2Cl_2/KOH_{sol}, 20°C; BzlBr:substrate:catalyst, 5:1:0.1; reaction time 10-15 min)

Catalyst	Ni-PBP-Gly			Ni-PBA-Ala		
	yield, %	o.p., %	product	yield, %	o.p., %	product
C-1	58	0.6	(*R*)-Phe	33	0	(*R*, *S*)-Me-Phe
C-2	80	22	(*R*)-Phe	85	10	(*R*)-Me-Phe
C-3	62	5.4	(*R*)-Phe	33	3.6	(*R*)-Me-Phe
C-4	66	21	(*R*)-Phe	18	17	(*R*)-Me-Phe
C-5	68	3.0	(*R*)-Phe	61	13	(*S*)-Me-Phe
C-6		Traces	Phe	34	3	(*S*)-Me-Phe
C-7	90	0	(*R*, *S*)-Phe	87	4	(*R*)-Me-Phe
C-8		Traces	Phe	33	7	(*R*)-Me-Phe
C-9	14	0	(*R*, *S*)-Phe	95	0	(*R*, *S*)-Me-Phe
C-10	95	2.3	(*R*)-Phe	70	9.6	(*S*)-Me-Phe
C-11	64	7.2	(*S*)-Phe	95	1.7	(*S*)-Me-Phe
NBC *	88	9.4	(*S*)-Phe	48	31	(*R*)-Me-Phe

*Reaction time 30-40 min. NBC) N-benzylcinchonidinium chloride.

TABLE 2. Results of Alkylation of Ni-PBP-Gly by Various Alkyl Halides under Interfacial Conditions (CH_2Cl_2/KOH_{sol}; RX:substrate:catalyst, 5:1:0.1)

RX	C-2		NBC	
	yield, %	o.p., % (configuration)	yield, %	o.p., % (configuration)
$C_6H_5CH_2Br$	80	22(*R*)	88	13(*S*)
$2\text{-}C_{10}H_7CH_2Br$	96	6(*R*)	42	6(*S*)
$CH_2{=}CHCH_2Br$	96	0	30	0

TABLE 3. Dependence of the Yield and Optical Purity on the Time in the Alkylation of Ni-PBP-Gly and Ni-PBA-Ala by Benzyl Bromide under the Action of the Catalyst C-2*

t, min	Ni-PBP-(*R*)-Phe		Ni-PBA-(*R*)-MePhe	
	yield, %	o.p., %	yield, %	o.p., %
10	1.3	19	0.7	17
20	8.8	22	1.3	18
30	13.3	20	3.2	11
40	20.7	15	4.1	11
50	26.0	12	–	–
60	–	–	4.8	12
90	42.0	7	–	–
120	–	–	10.8	8

*Substrate:catalyst ratio 50:1.

gous complexes pK_a in water is equal to 9.36-9.66 [19]), and at the following step of the reaction these complexes strip a proton from the amino acid fragment of Ni-PBP-Gly or Ni-PBA-Ala. Diastereomeric ion pairs are formed, in which a chiral, positively charged complex C-1 to C-11 in the form of $[H_2O{-}ML]^+$ serves as the counter-ion. At the following stage alkylation of the carbanion of the amino acid fragment of the complex Ni-PBP-Gly or Ni-PBA-Ala by benzyl bromide occurs with the formation of an alkylation product and a complex catalyst containing a bromide ion in the coordination sphere. Subsequently, under the action of KOH, there is an exchange of bromine in C-1 to C-11 for hydroxyl, and the cycle is repeated. Judging by the chemical yield in alkylation, the catalyst may complete up to nine cycles of alkylation.

The distinction of complexes C-1 to C-4 and C-9 from the complexes C-5 to C-8, C-10, and C-11 is that in the latter case the hydroxyl ion (H_2O) is in an apical position, while

in the former case it occupies one of the four places in the main coordination plane of the complex. On account of such nonequivalent coordination, substantial differences in the transition states may also arise.

As can be seen from the data of Table 1, some of the new catalysts prove more effective than the representative of traditional quaternary ammonium salts – N-benzylcinchonidinium chloride (NBC). For example, in alkylation reactions catalyzed by NBC, the chemical yield 48-88% is reached in 1.5-2 h, whereas in C-2 and C-7 alkylation occurred to an extent of 80-87% in only 20-30 min of reaction.

As can be seen from Table 1, the most effective catalysts are C-2, C-5, C-7, and C-10. It can be suggested that the effectiveness of these catalysts is due to the fact that in addition to the unhindered side, at which coordination with the anion of the substrate is possible, these complexes are able to form hydrogen bonds with a substrate molecule through coordination of the NH group of the pyrrolidine fragment with the carbanion fragment in the intermediate ion pair (see Fig. 1). The most sterically hindered complexes (C-6 or C-8) are the least effective as catalysts in these reactions.

Evidently asymmetrical induction occurs at the stage of alkylation, and in this case there is a kinetic control of stereoselectivity. Thus, the case of the chirality is probably shielding of one side of the intermediate prochiral carbanion by a positively charged catalyst molecule closely bound to it in an ion pair. The presumed structure of the ion pair in the alkylation of the complex Ni-PBA-Ala during catalysis by C-5 is presented in Fig. 1. The formation of dimer or polymer particles of the coordination sphere of the complexes with polycyclic aromatic ligands was described in [20]. A certain π-interaction between the catalyst and the substrate and the hydrogen bonds that arise between the hydrogen of the NH group and the carbonyl of the complex to be alkylated may stabilize the ion pair in an organic solvent.

It is important that when hydrogen at the nitrogen atom of the pyrrolidine fragment is replaced by a benzyl group, the stereoselectivity drops (Table 1, C-1 and C-2). This fact confirms our hypothesis that the structure of the ion pair in the transition state is determined to a significant degree by the presence of a hydrogen bond, in the formation of which this hydrogen atom participates.

The increase in the lipophilicity of the catalyst in the sequence from C-2 to C-4 (Table 1) does not affect the chemical and asymmetrical yields in the alkylation of Ni-PBA-Gly; however, when Ni-PBA-Ala is used as a substrate, the rate of the alkylation reaction drops substantially (the yield in the same time falls from 85 to 18%), and asymmetrical induction, at the same time, rises from 10 to 17%.

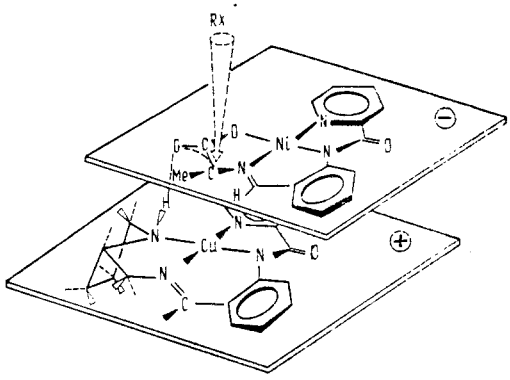
The introduction of electron acceptor groups into the molecule (transition from C-2 to C-3) substantially decreases the asymmetrical induction (from 22 down to 5.4% in alkylation of a glycine complex and from 10 to 3.6% in alkylation of an alanine complex), and the rate of alkylation falls simultaneously (Table 1).

For C-5 only apical coordination of the hydroxyl ion can occur, whereas in C-1 the coordinated hydroxyl ion, which we believe conducts the reaction, is situated in the main coordination plane of the complex. Transition to a complex with apical coordination causes a slight decrease in the rate of alkylation and a substantial drop (from 20 to 3%) in the stereoselectivity in the alkylation of Ni-PBP-Gly and a reversal of stereoselectivity [from 10% (R) to 13% (S)] in the alkylation of Ni-PBA-Ala. The hypothetical transition state that can ensure such a result is cited in Scheme 4.

The transition from catalysts based on Cu(II) to complexes of Ni(II) and Pd(II) leads to an increase in the rate of alkylation and to a drop in the asymmetrical induction in the series Cu > Pd > Ni (Table 1). As we go from catalysts based on Cu(II) (C-5 and C-6) to isostructural catalysts based on Ni(II) (C-7 and C-8), the configuration of the amino acid obtained in alkylation is reversed (Table 1). We must emphasize that the configuration of the chiral pyrrolidine fragment of the catalyst remains unchanged in this case. In catalysis by C-10 based on Pd(II), the configuration of the amino acid fragment produced by alkylation is analogous to that obtained with the use of C-5 [based on Cu(II)]. As yet we have no explanation for this fact.

Thus, a new class of catalysts of asymmetrical alkylation under interfacial conditions has been found. The chemical catalysts described have a structure far from optimum but, as

Scheme 4



shown in the article, the structure of the complexes is readily modified. We might hope that it will be possible to select a structure of the catalyst such as to obtain a sufficiently high asymmetrical induction. The elucidation of the principles of the influence of the structure of the catalyst on asymmetrical induction in alkylation reactions is the approach in which we hope to move further.

EXPERIMENTAL

In the work we used (S)-alanine and glycine from Reanal (Budapest) and Reakhim (Moscow), the resins Sephadex LH-20 Pharmacia Fine Chemicals, Toyopearl HW-60 Toyo soda MFG CO LTD, and KPC-12 produced by Reakhim (Moscow). The NMR spectra were taken on Tesla NMR-BS-467 (60 MHz) and Bruker WP-200 (200 MHz) instruments.

The electron spectra were recorded on a Specord M-40 spectrophotometer. A Jasco ORD/UV-5 instrument was used to measure the ORD spectra. The specific rotation was determined on a Perkin–Elmer 241 polarimeter.

Synthesis of (S)-N-Benzyl-2-aminomethylpyrrolidine (BAMP). Production of the Methyl Ester of (S)-N-Benzylproline. A stream of dry HCl was passed through a solution of 1.25 g (0.01 mole) of (S)-proline in 4 ml of abs. MeOH for 3 h. Then 3 ml of benzene and 3 g of Na_2CO_3 were added to the reaction flask. After this, 1.5 ml (0.13 mole) of benzyl chloride was added slowly with mixing, and the mixture was boiled with mixing for 9 h. The reaction mixture was decomposed with water, the organic layer was removed, and the aqueous layer was extracted with benzene. The organic extracts were combined, benzene evaporated, and the residue redistilled. Bp 100-102°C (2 mm). Yield of the methyl ester of (S)-N-benzylproline 1.82 g (0.0083 mole), 83%. Found, %: C 71.20; H 7.79; N 6.54. $C_{13}H_{17}NO_2$. Calculated, %: C 71.23; H 7.76; N 6.39. PMR spectrum ($CDCl_3$, δ, ppm): 1.7-2.2 m (5H, 2β, 2γ, δ-Pro), 3.0-3.3 m (2H, α, δ-Pro), 3.50, 4.02 (AB, 2H, $-C\underline{H}_2-Ar$), 3.7 s (3H, –OMe), 7.15-7.40 m (5H, Ar). $[\alpha]_D^{25} = -89.5°$ ($CHCl_3$, C = 4.24 g/100 ml, ℓ = 2 cm).

Production of the Amide of (S)-N-Benzylproline. The methyl ester of (S)-N-benzylproline (5.3 g, $2.42 \cdot 10^{-2}$ mole) was dissolved in 15 ml of MeOH, the solution was cooled to 0°C, and a stream of dry NH_3 was passed through for 4 h. The mixture was left for 15 h at 0°C, and a stream of dry NH_3 was again passed through for 4 h at 0°C. The solution was evaporated, and the amide of (S)-N-benzylproline was recrystallized twice from heptane. Yield 2.52 g ($1.23 \cdot 10^{-2}$ mole), 51%, mp 65-66°C. Found, %: C 70.60; H 8.00; N 13.70. $C_{12}H_{16}N_2O$. Calculated, %: C 70.59; H 7.84; N 13.73. PMR spectrum ($CDCl_3$, δ, ppm): 1.5-2.6 m (5H, 2β, 2γ, δ-Pro), 2.8-3.3 m (2H, α, δ-Pro), 7.0-7.5 m (5H, Ar), 6.3 s (2H, NH_2), 3.45, 4.00 (AB, 2H, $-C\underline{H}_2-Ar$, J_{AB} = 13 Hz).

Reduction of the Amide of (S)-N-Benzylproline. To a solution of 0.3 g ($7.5 \cdot 10^{-3}$ mole) lithium aluminum hydride in 10 ml of abs. THF a solution of 0.4 g ($2.1 \cdot 10^{-3}$ mole) of the amide of (S)-N-benzylproline in 10 ml of abs. THF was added with vigorous mixing and boiled for 8 h. After this 0.6 ml of an 8% aqueous solution of KOH was decomposed, the precipitate filtered off, the solution evaporated, and the (S)-N-benzyl-2-aminomethylpyrrolidine (BAMP) obtained was redistilled, bp 95-97°C (2 mm). Yield 0.15 g ($8.15 \cdot 10^{-4}$ mole, 41%). Found, %: C 75.85; H 9.50; N 14.60. $C_{12}H_{17}N_2$. Calculated, %: C 75.75; H 9.54; N 14.72. PMR spectrum ($CDCl_3$, δ, ppm): 1.4-1.8 m (5H, 2β, 2γ, δ-Pro), 2.18 s (2H, NH_2), 2.0-2.3 m (1H, δ-Pro), 2.5-3.0 m (2H, $-C\underline{H}_2-NH_2$), 3.5 m (1H, α-Pro), 3.18, 3.83 (AB, 2H, $-C\underline{H}_2-Ar$, J_{AB} = 13.5 Hz). $[\alpha]_D^{25} = -55.0°$ ($CHCl_3$, C = 9.97 g/100 ml, ℓ = 5 mm).

TABLE 4. Characteristics of Complex Catalysts

Catalyst	Formula	Mp, °C	Yield, %	Found/Calculated, %			UV spectrum λ_{max} (log ε) ℓ = 1 mm, C, g/liter	$[\alpha]_{\lambda}^{25*}$ (MeOH, l=10 mm)
				C	H	N		
C-1	$C_{19}H_{21}N_2OCu \cdot OH^-$	56–57	42	60,72 / 61,03	6,05 / 5,93	7,58 / 7,48	370(3,42); 615(2,44) C=0,43	$[\alpha]_{400}$=−125,6° $[\alpha]_{334}$=+25,6°
C-2	$C_{12}H_{15}N_2OCu \cdot Cl^- \cdot {}^1/_3H_2O$	147–150	31	46,55 / 47,75	4,88 / 5,12	9,37 / 9,08	285(3,38 sh); 368(3,59) C=0,44	$[\alpha]_{410}$=+55°
C-3	$C_{12}H_{13}N_2OCl_2Cu \cdot NO_3^-$	256–259	46	36,90 / 36,24	3,74 / 3,30	10,58 / 10,56	264(4,03 sh); 383(3,63) C=0,46	$[\alpha]_{410}$=+53°
C-4	$C_{16}H_{17}N_2OCu \cdot NO_3^- \cdot {}^1/_3H_2O$	238–240	70	50,19 / 49,93	4,28 / 4,62	10,05 / 10,91	285(3,95 sh); 386(3,75) C=0,36	$[\alpha]_{410}$=+78,5°
C-5	$C_{18}H_{19}N_4OCu \cdot OH^- \cdot 3H_2O$	91–93	51	49,51 / 48,91	4,91 / 5,93	11,53 / 12,67	271(4,0 sh); 377(3,64) C=0,215	$[\alpha]_{450}$=+197° $[\alpha]_{550}$=+197°
C-6	$C_{24}H_{29}N_4OCu \cdot {}^1/_2OH^- \cdot {}^1/_2NO_3^- \cdot H_2O$	94–96	64	56,34 / 56,45	6,24 / 6,21	12,43 / 12,34	280(4,04 sh); 360(3,63) C=0,4	$[\alpha]_{450}$=−90,4°
C-7	$C_{18}H_{19}N_4ONi \cdot NO_3^-$	175–174	53				254(4,10); 330(3,51); 392(3,34) C=0,3	$[\alpha]_{480}$=+154° $[\alpha]_{560}$=−82,2°
C-8	$C_{24}H_{29}N_4ONi \cdot NO_3^- \cdot {}^3/_2H_2O$	110–114	68	53,84 / 53,66	5,86 / 6,00	13,03 / 12,17	290(3,93 sh); 345(3,71); 360(3,64); 424(3,50) C=0,44	$[\alpha]_{456}$=−283,7° $[\alpha]_{552}$=+283,7°
C-9	$C_{19}H_{21}N_2OPd \cdot Cl^-$	117–120	52	53,07 / 52,47	4,80 / 4,83	5,50 / 6,44	288(3,98); 352(3,51); 390(3,55) C=0,4	$[\alpha]_{400}$=−220°
C-10	$C_{18}H_{19}N_4OPd \cdot Cl^-$	85–87	45				272(4,13 sh); 413(3,54) C=0,46	$[\alpha]_{360}$=+96°
C-11	$C_{31}H_{29}N_4OPd \cdot OH^- \cdot {}^3/_2CHCl_3$	217–219	47	50,98 / 50,30	3,75 / 4,06	6,22 / 7,22	292(4,04 sh); 343(3,81); 357(3,76 sh); 423(3,62) C=0,56	$[\alpha]_{376}$=+214° $[\alpha]_{460}$=−136°

*The concentration corresponds to the concentration cited for the UV spectra.

Production of (S)-2-Aminomethylpyrrolidine (AMP) by Removal of the Benzyl Group from BAMP. In a vessel for hydrogenation we placed 100 mg (0.526 mole) of BAMP and 10 ml of MeOH, added 40 mg of the catalyst 10% Pd/C and 3 ml of formic acid, and turned on the stirrer. After 20 min the stirrer was turned off, the reaction mixture was filtered off from the catalyst, evaporated, and the product was redistilled. Bp 57-59°C (9 mm). Yield 14.73 mg ($1.47 \cdot 10^{-4}$ mole, 28%). Found, %: C 59.79; H 11.92; N 28.02. $C_5H_{12}N_2$. Calculated, %: C 60.0; H 12.0; N 28.0. PMR spectrum ($CDCl_3$, δ, ppm): 1.4-1.8 m (5H, 2β, 2γ, δ-Pro), 2.18 s (2H, NH_2), 2.0-2.3 m (1H, δ-Pro), 2.5-3.0 m (2H, $-C\underline{H}_2-NH_2$), 3.5 m (1H, α-Pro), 3.18, 3.83 (AB, 2H, $-C\underline{H}_2Ar$; J_{AB} = 13.5 Hz). $[\alpha]_D^{25}$ = +298.16° ($CHCl_3$; C = 0.109 g/100 ml; ℓ = 1 cm).

Production of Complex Catalysts (on the example of the synthesis of C-5). To a mixture of 0.036 g (0.37 mmole) AMP, 0.09 g (0.37 mmole) $Cu(NO_3)_2$ and 0.83 g (0.37 mmole) 2-[(N-pyridinecarbonyl)amino]benzaldehyde (PBA) in 5 ml of MeOH we added 0.3 ml of 1.5 N MeONa with mixing in a stream of Ar. The mixing was continued for 20 h, then the reaction mixture was neutralized with 0.1 M AcOH and evaporated. The reaction product (C-5) was isolated chromatographically on the resin Toyopearl HW-60 in the system ethanol:water (1:1) and additionally purified on the resin LH-20 in the system benzene:ethanol (3:1). Yield of the complex 0.09 g (0.24 mmole, 64.8%). The characteristics of the complexes are presented in Table 4.

Alkylation Procedure. We dissolved 0.1 mmole of Ni-PBP-Gly (or Ni-PBA-Ala) and 0.01 mmole of the complex catalyst in 2 ml of CH_2Cl_2, cooled to −70°C, and added 0.2 mmole (22.4 mg) KOH, 0.15 mmole (0.012 ml) of BzlBr in the case of a glycine substrate and 0.3 mmole (0.024 ml) in the case of an alanine substrate. The air was evacuated, the flask was filled with argon, cooling was selected, and the stirrer was turned on. The reaction occurred at ~20°C in 20-30 min. The reaction mixture was decomposed with an aqueous solution of AcOH, the layers were separated, and the organic layer was evaporated and purified chromatographically on silica gel in the system acetone:$CHCl_3$ (1:5). In the case of alkylation of the glycine complex, the amino acid was isolated according to the procedure described in [15].

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