ASYMMETRIC SYNTHESIS OF THREONINE AND RETRORACEMIZATION OF AMINO ACIDS USING Ni(II) COMPLEXES OF SCHIFF BASES WITH S-2-N-(N'-BENZYLPROLYL)AMINOBENZALDEHYDE

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Chiral Cu(II) complexes of Schiff bases of amino acids (AA) with S-2-N-(N'-benzylprolyl)aminobenzaldehyde (S-BPAB) were made previously in [1, 2] with the aim of designing regenerating reagents and catalysts for enantiomeric conversions of AA. The enantioselective effects in these complexes were used for partial fission and asymmetric synthesis of α-AA. Thus the use of (S-BPAB—AA)·Cu(II) made it possible to effect the asymmetric synthesis of L-threonine with an enantiomeric purity of 60% and a threo:allo ratio = 6:1 and also the conversion of the R enantiomer into an S enantiomer for racemic AA (a retroracemization process), achieving an enantiomeric purity of 12-54% [2].

Larger enantioselective effects may seemingly be expected for Ni(II) complexes since on going from Cu(II) (d^9) to Ni(II) (d^8) a growth is observed in the metal—N and metal—O bond energies with increasing strength of the ligand. This leads to shortening of bond lengths and an increase in the rigidity of the complex [3].

In the present work we have studied the CH acidity of the amino acid fragment and enantioselective effects in complexes (S-BPAB—AA)·Ni(II) and have carried out a comparison with the analogous complexes (S-BPAB—AA)·Cu(II). The obtained results were used for the retroracemization of racemic α-AA and the asymmetric synthesis of threonine.

In the work we extended the retroracemization process described by us previously in [1-2] to Trp and other difficult AA. For these AA there is no possibility of a reliable GLC enantiomer analysis due to the resinification of Trp in the process of making derivatives and the low vapor tension of derivatives of the difficult AA.

In connection with this we have developed analytical methods for determining the enantiomeric composition of reaction mixtures containing difficult AA which are based on the use of liquid chromatography and on the use of a new enantioselective high-temperature chromatographic phase, viz. the tert-butylamide of N-heptadecanoyl-S-Val.

DISCUSSION OF RESULTS

Preparation and Structure of Complexes (S-BPAB—AA)·Ni(II). A convenient method of synthesis of S-BPAB has been developed by us which permits a more than twofold improvement in the yield of product in comparison with the method proposed previously in [2] (scheme 1).

Scheme 1

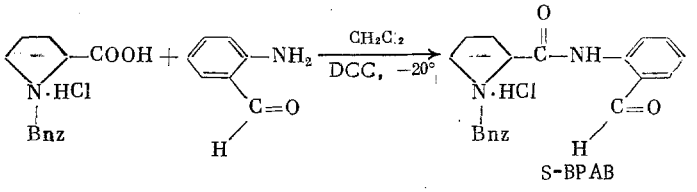

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TABLE 1. Properties of (S-BPAB—AA)·Ni(II) Complexes

Complex	Ratio [AA]:[BPAB] under conditions of forming complex	Yield, %	Empirical formula	Found/calculated, %			mp, °C	λmax (log ε), nm	$[M]_\lambda^{25}$			
				C	H	N			578	546	436	365
									nm			
(S-BPAB – Gly)·Ni(II)	1:1	45	$C_{21}H_{21}N_3NiO_3$	59,91 / 59,75	5,43 / 5,02	9,40 / 9,95	116–122	260(4,17)	+7273	+3776	+4160	−3147
	5:1	91						332(3,68)				
								408(3,46)				
								533(2,06)				
(S-BPAB – S-Val)·Ni(II)*	1:1	40	$C_{24}H_{27}N_3NiO_3$	62,48 / 62,10	5,92 / 5,86	9,38 / 9,05	150–154	260(4,07)	+10549	+2954	−1899	+11392
	5:1	78						327(3,67)				
								408(3,48)				
								524(2,19)				
(S-BPAB – R-Val)·Ni(II)*	1:1	6	$C_{24}H_{27}N_3NiO_3$	62,44 / 62,10	5,57 / 5,86	9,25 / 9,05	180–186	263(4,12)	+4772	+5682	+10682	−15455
	5:1	11						338(3,63)				
								412(3,39)				
								522(2,02)				

*(S-BPAB—S-Val)·Ni(II) and (S-BPAB—R-Val)·Ni(II) were obtained from R,S-Val with subsequent separation of the mixture of diastereoisomers on silica gel in the system $CHCl_3$:acetone (5:1).

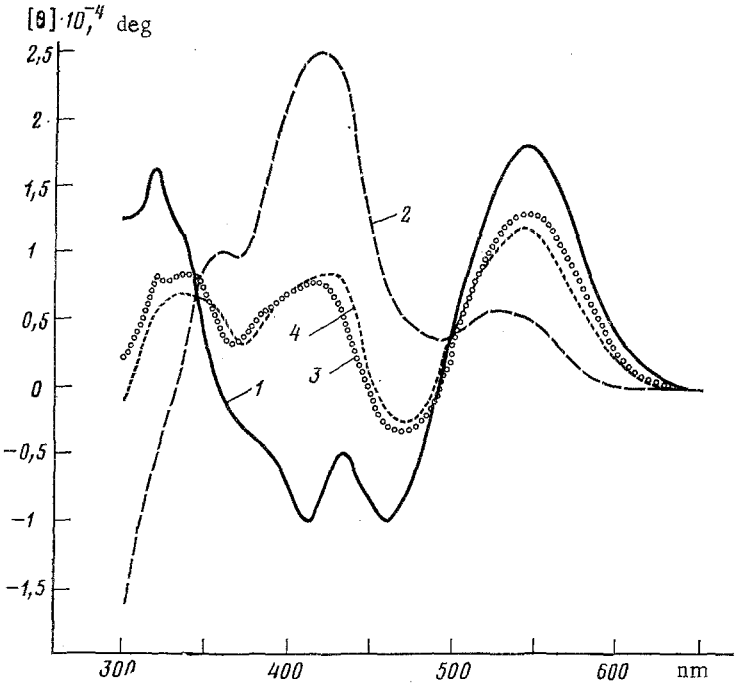


Fig. 1. CD spectra in MeOH: 1) (S-BPAB—S-Val)·Ni(II); 2) (S-BPAB—R-Val)·Ni(II); 3) (S-BPAB—Gly)·Ni(II); 4) (S-BPAB—Gly)·Ni(II) calculated from the CD spectra of the (S-BPAB—S-Val)·Ni(II) and (S-BPAB—R-Val)·Ni(II) diastereomers.

The interaction of S-BPAB with racemic Val or Gly and $Ni(NO_3)_2$ in MeOH in the presence of MeONa led is represented in scheme 2 to the formation of red-colored complexes insoluble in water and readily soluble in $CHCl_3$ and CH_2Cl_2. The chemical yield of the reaction increased with a rise in the [AA]:[BPAB] ratio (Table 1).

Scheme 2

$$\text{S-BPAB} + R,\text{S-AA} \xrightarrow[\text{MeONa, } 40^\circ]{\text{Ni(II)·MeOH}} (\text{S-BPAB}-S\text{-AA}) + (\text{S-BPAB}-R\text{-AA})$$

R,S-Val formed two diastereomeric complexes which were readily separated on silica gel, Gly formed one complex.

These complexes were diamagnetic and had a broad absorption maximum at 500-550 nm in the region for d—d transitions of flat square Ni(II) complexes [4]. Elemental analysis of complexes (see Table 1), their molecular weights, and PMR spectra (see Experimental) were in agreement with the structure indicated in scheme 3 where the Ni(II) ion is coordinated with the ionized carboxyl group, the N atoms of the aldimine group, the ionized amide group, and with the tertiary N atom of the proline fragment.

By analogy with the isostructural Cu(II) complexes of [1, 2] it may be proposed that the N atom of the pyrrolidine ring also takes up an R configuration.

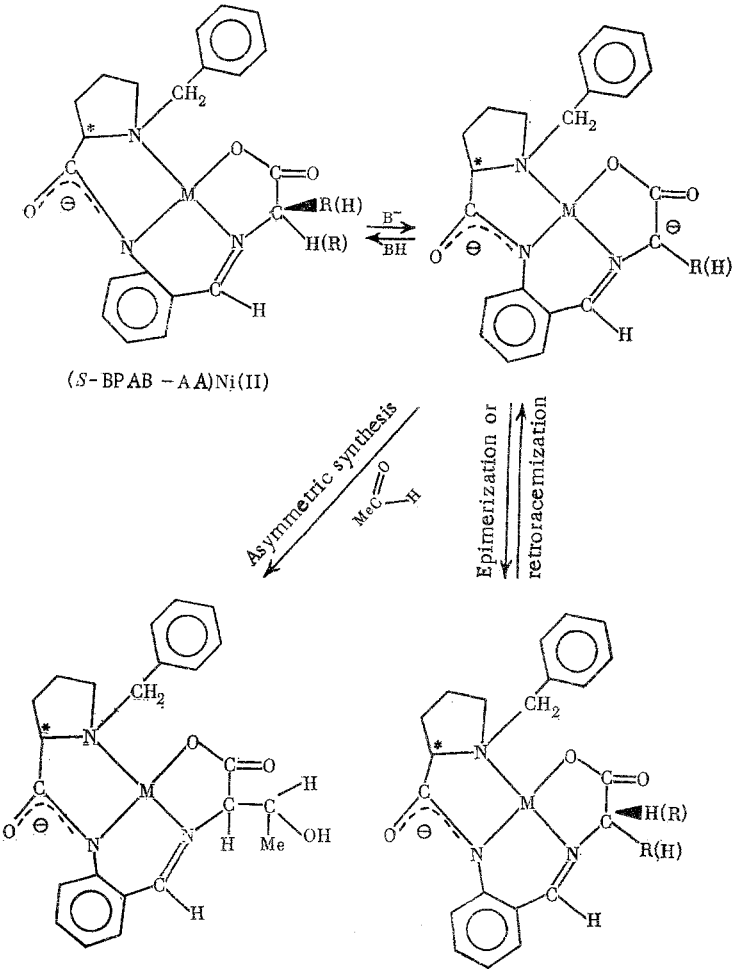
The diastereomeric complexes of Val, as might have been expected, differed from one another in the chemical shifts of signals in the PMR spectra and in the shapes of the circular dichroism (CD) spectra (Fig. 1) having practically identical IR and electronic spectra (see Table 1).

The diastereomer possessing the greatest mobility on silica gel in the system $CHCl_3$—acetone contained S-Val and S-BPAB in a ratio 1:1 while the more slowly moving diastereomer contained R-Val and S-BPAB in the same ratio.

The CD spectrum of (S-BPAB—Gly)·Ni(II) calculated allowing for the additivity of the vicinal conformational and configurational components of the CD spectra [5, 6] of the diastereomeric Val complexes was practically in agreement with that found experimentally (see Fig. 1). Thus all the obtained results confirmed the structure of the complexes represented in scheme 3.

Epimerization of (S-BPAB—R-Val)·Ni(II) and (S-BPAB—S-Val)·Ni(II). Retroracemization of Amino Acids. The enantiomeric composition of amino acids obtained after decomposition of the equilibrium mixtures of diastereomeric complexes were determined by GLC on a high-temperature chromatographic phase and by high-pressure liquid chromatography (see Experimental section).

Scheme 3



The epimerization of the individual complexes (S-BPAB—S-Val)·Ni(II) or (S-BPAB—R-Val)·Ni(II) at 25°C under the action of MeONa complied with first-order kinetic rules. It is evident from Fig. 2 that the equilibrium mixture of diastereomeric complexes obtained both from (S-BPAB—S-Val)·Ni(II) and from (S-BPAB—R-Val)·Ni(II) had the same specific optical rotation. The character of the change of specific optical rotation indicated that only one of the two chiral fragments of the complex was subject to epimerization.

In reality the proline ligand isolated on decomposition of the equilibrium diastereomeric mixture of complexes had a specific optical rotation identical with that of the initial S-BPAB.

The optical rotatory dispersion (ORD) curve of the equilibrium mixture of diastereomers was in agreement with that calculated theoretically on the basis of data of enantiomer analysis by GLC of the isolated R- and S-Val (see Experimental).

Epimerization of Val occurred even during the making of the Ni(II) complexes from R,S-Val at 25°C in 0.2 N MeONa and the ratio of diastereomers in a preparative synthesis (see Table 1) agreed with the composition of the equilibrium diastereomeric mixture obtained during epimerization of the individual complexes with R- or S-Val.

It is evident from Table 2 that the unreacted AA remained practically racemic; consequently the main reason for the generation of an excess of the diastereomer containing S-Val was epimerization of diastereomers formed during the reaction leading to the conversion of R-Val into S-Val under the action of MeONa, i.e., retroracemization [2, 8].

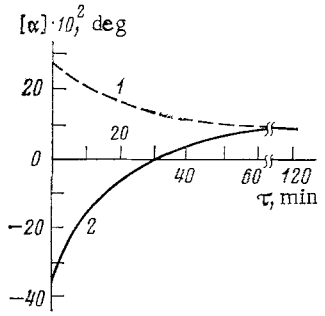


Fig. 2

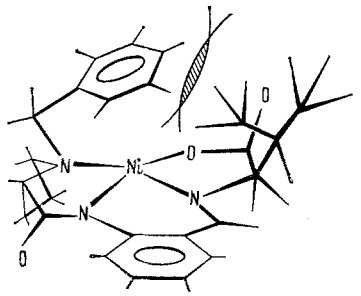


Fig. 3

Fig. 2. Change with time of the specific optical rotation at 365 nm of 1) (S-BPAB—S-Val)·Ni(II) and 2) (S-BPAB—R-Val)·Ni(II) under the action of 0.005 N MeONa in abs. MeOH at 25°C.

Fig. 3. Schematic representation of nonbonding interaction of substituents of the amino acid fragment and the phenyl group screening the apical position in the complex (S-BPAB—R-Val)·Ni(II).

TABLE 2. Enantiomer Composition and Chemical Yield of Amino Acids after Retroracemization*

Amino acid	Molar ratio AA:BPAB	Enantiomeric purity of amino acids obtained after decomp. of mixtures of diastereomeric complexes, %†		Yield, %‡	Enantiomer excess for unreacted amino acids
		Ni(II)	Cu(II) [2]		
Ala	1:1	15(*S*)	0	4	Racemate
Phe	1:1	40(*S*)	42(*S*)	51	8% (*R*)
Trp	1:1	64(*S*)		26	3% (*R*)
Val	1:1	72(*S*)	54(*S*)	46	16% (*R*)
Val	5:1	78(*S*)		94	Racemate
NVa	3:1	42(*S*)	12(*S*)	91	The same
PhGly	3:1	39(*S*)	35(*S*)	67	" "

*Retroracemization was carried out under the action of 0.2 N MeONa in the presence of a stoichiometric amount of $Ni(NO_3)_2$ at 40°C, 20 h, under Ar.
†Determined by enantiomer GLC analysis. Results differed by less than 5% in parallel experiments.
‡Determined by quantitative GLC analysis after decomposition of complexes [7].

Under the same experimental conditions NVa, Phe, PhGly, and Trp were subject to retroracemization. In all cases equilibrium was established between the diastereomers and was followed in the course of the reaction by TLC for the absence of change of diastereomer ratio.

In difference to the Cu(II) complexes which decomposed under the action of 1 N HCl at ∿20°C more drastic conditions were required for the decomposition of Ni(II) complexes. Boiling in 10% HCl was required but even under these conditions the decomposition did not always proceed quantitatively.

It is evident from Table 2 that the enantiomeric purity of the obtained AA increased in parallel with the bulk of their side chains reaching a maximum value in the case of Val (78% S) and a minimum in the case of Ala (15% S).

Asymmetric synthesis of Thr by condensation of acetaldehyde with (S-BPAB—Gly)·Ni(II) with AcH in MeOH under the action of bases at ∿20°C gave a mixture of diastereomeric complexes as in Scheme 4.

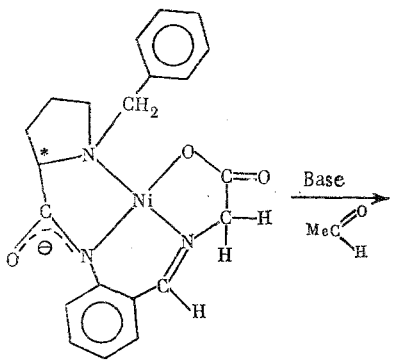
The course of the experiment was conveniently followed using TLC for the disappearance of the initial glycine complex. After the end of the reaction and decomposition of the mixture of diastereomeric complexes the AA were isolated by a standard method separating out S-BPAB which may be used once again in the reaction. As in the case of the isostructural Cu(II) complexes [2], the enantiomeric purity and absolute configuration of the Thr enantiomer

TABLE 3. Enantiomeric Purity and Chemical Yield of Threonine Obtained on Condensing (S-BPAB—Gly)·Ni(II) with Acetaldehyde

[AA]:[AcH] ratio	Reaction conditions	Enantiomeric purity, %*		Ratio [threo] † / [allo]	Yield, % †
		Thr	allo-Thr		
1:50	Et_3N	86(*S*)	76(*S*)	1:2,1	84
1:50	0,2 *N* MeONa	18(*R*)	7(*R*)	5:1	68

*From data of GLC enantiomer analysis [7].
†From data of quantitative GLC analysis [7].

Scheme 4



→ [Mixture of diastereomeric complexes]

HCl

H_2O

S-BPAB + *R*- and *S*-Thr + R- and *S*-allo-Thr + $NiCl_2$.

formed in excess depended on the basicity of the medium and stopped changing 30 min after the start of the experiment. This indicated that at any pH value an equilibrium was established between the diastereomeric complexes the position of which depended on the basicity of the medium. Thus on catalysis by Et_3N in excess, S-Thr and S-allo-Thr were formed with an enantiomeric purity of 90 and 80% respectively. The Thr:allo-Thr ratio was 1:2 (Table 3). Further increase in the basicity of the medium on catalysis by MeONa led to practically racemic Thr and allo-Thr with a ratio of 5:1.

A similar dependence of enantiomer yield and allo:threo ratio on basicity of the medium was also observed for complexes of Cu(II) in [2].

Comparison of Enantioselective Effects in Isostructural Complexes of Cu(II) and Ni(II). Data on the retroracemization of AA under the action of S-BPAB in the presence of Ni(II) and Cu(II) ions are collated in Table 2. As is evident from these data the formation of the diastereomer with an excess of S-AA is thermodynamically favored for both Ni(II) and Cu(II). The overall tendency towards an increase in enantioselectivity on going from a complex (S-BPAB—AA)·Cu(II) to a complex (S-BPAB—AA)·Ni(II) was preserved. Thus, retroracemization of Val in the case of Ni(II) complexes gave an enantiomeric excess of 72-78% S-Val; for Cu(II) the excess was 54%.

The rate constant for epimerization of the R-Val fragment in the Ni(II) complex under the action of $^-OCH_3$ was $1.4 \cdot 10^{-1}$ liter/mole·sec and exceeded somewhat the rate constant for the epimerization of R-Val in the Cu(II) complex ($0.9 \cdot 10^{-1}$ liter/mole·sec) [2]. The enantiometric excess of S-Thr and S-allo-Thr obtained under conditions of Et_3N catalysis was 80-90% for complexes of Ni(II) and 51% for complexes of Cu(II).

We propose that in the case of complexes of both Cu(II) and Ni(II) the observed enantioselectivity of the processes is explained sterically by a nonbonding interaction of the AA side chain and the phenyl fragment of the benzyl group in the (S-BPAB—R-AA)·M(II) isomer as represented in Fig. 3. The conformation with the phenyl ring screening the apical position of the metal ion is encountered fairly frequently in complexes of transition metals [9]

including the complex of S-N-benzylproline with Cu(II) in [10]. One of the reasons for the stability of such a conformation is seemingly the nonbonding interaction of the phenyl group with the protons of the proline fragment which should displace the phenyl ring into the space above the metal ion although it is also impossible to exclude the presence of some bonding interactions of phenyl with the metal ion [9].

It is obvious that the interaction of the amino acid side chain with the phenyl ring in the isomer containing an R-AA must lead to a growth in steric hindrance absent in the isomer with the S-AA.

Thus some increase in enantioselective effects has been observed on going from Cu(II) to Ni(II). An increase took place in the kinetic stability of the complex expressed as the requirement of the Ni(II) complexes for a more acidic medium and higher temperature for decomposition in comparison with the Cu(II) complexes.

EXPERIMENTAL

Amino acids used in the work were of pure grade from Reanal (Budapest) and Reakhim. The MeONa was prepared by adding metallic Na to abs. MeOH under Ar while cooling.

PMR spectra were taken on Tesla NMP-BS-467A (60 MHz) and Brucker WP-200 (200 MHz) instruments and electronic spectra on a Specord UV-VIS instrument. CD spectra were taken on a Jasco 1-20 instrument. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. ORD curves were taken on a Jasco ORD/NV-5 instrument.

The enantiomeric compositions of AA were determined by GLC using a new enantioselective high-temperature phase, viz., N-heptadecanoyl-S-Val tert-butylamide of mp 77-78°C, which was obtained from L-valine tert-butylamide hydrochloride and the hydroxysuccinimide ester of heptadecanoic acid by the method described for the corresponding N-stearoyl derivative in [11]. Amino acids were analyzed as the N-trifluoroacetyl isopropyl esters on a steel capillary column of length 30 m of internal diameter 0.25 mm. The flame ionization detector was from Hitachi, carrier gas He, and the system for dividing the test sample was all glass.

Enantiomer analysis of tryptophan was carried out using a Perkin-Elmer 601 high-pressure liquid chromatograph with a flow microphotometric cuvette and a Perkin-Elmer L-55 spectrophotometer as detector. Measurements were made of absorption at 260 nm. Separation was effected on a column of size 25 × 0.46 cm with sorbent applied to the silica gel surface, N = 2500 theoretical plates [12]. Elution was isocratic using aqueous organic solvent H_2O:MeCN = 70:30 with added 0.01 M NH_4OAc, 10^{-4} M $Cu(OAc)_2$ and AcOH to pH 4. Elution rate was 2 ml/min, column temperature 70°C. Test samples of weight about 1 μg were introduced with a Rheodyne-702 loop dosing apparatus.

o-Aminobenzaldehyde was obtained according to [13], mp 37-38°C (cf. [13]).

N-Benzyl-S-proline was obtained by the procedure in [2], mp 165-166.5°C, $[\alpha]_{578}^{20}$ −28.24 (MeOH, c = 0.01 g/ml) (cf. [2]).

N-Benzyl-S-proline Hydrochloride. N-Benzyl-S-proline was dissolved in 10% HCl and evaporated. The residue was dried in vacuum over P_2O_5.

S-2-N-(N'-Benzylprolyl)aminobenzaldehyde (S-BPAB). A solution of o-aminobenzaldehyde (0.2 g: 1.6 mmole) in anhydrous CH_2Cl_2 (2 ml) was added dropwise with stirring at −20°C to a suspension of N-benzyl-S-proline hydrochloride (0.39 g: 1.6 mmole) in anhydrous CH_2Cl_2 (1 ml). Dicyclohexylcarbodiimide (0.4 g: 1.9 mmole) was then sprinkled in portionwise. The reaction mixture was stirred at −20°C for 30 min and glacial AcOH (0.1 ml) added. The solid was filtered off and washed on the filter with CH_2Cl_2 (10 ml). The filtrate was washed with 5% Na_2CO_3 solution (3 × 20 ml), dried over anhydrous Na_2SO_4, and evaporated. The solid was chromatographed on a column of LH-20 in the system benzene:EtOH (2:1), collecting the second fraction absorbing at 254 nm. The solvent was evaporated and the residue recrystallized from hexane. S-BPAB (0.28 g: 56%) was obtained having mp 98-99°C. Found: C 73.96; H 6.57; N 9.34%. $C_{19}H_{20}N_2O_2$. Calculated: C 74; H 5.54; N 9.08%. $[\alpha]_{578}^{20}$ −186.33; $[\alpha]_{546}^{20}$ −217.39; $[\alpha]_{436}^{20}$ −310.55 ($CHCl_3$, c $1.6 \cdot 10^{-3}$ g/ml). UV spectrum ($CHCl_3$, λ_{max}, nm): 226 (log ε 4.02), 273 (4.00), 338 (3.68). PMR spectrum (in $CDCl_3$, δ, ppm): 1.5-2.6 m [6 H, CH_2 (Pro)], 3.29 m [1 H, α-H (Pro)), 7.10-7.39 m (7 H, Ar), 9.75 s (1 H, HCO), 12.0 s (1 H, HC=O). AB system for CH_2 group: 3.47, 3.86; AB system for H^3H^6 fragment of o-aminobenzaldehyde: 7.45, 8.65.

Ni(II) Complexes of Schiff Bases of S-BPAB with R- and S-Valine. $Ni(NO_3)_2 \cdot 6H_2O$ (0.58 g: 2 mmole) and 1 N MeONa (4 ml) were added to S-BPAB (0.62 g: 2 mmole) in MeOH (32

ml) and the mixture stirred for 15 min. A solution of racemic valine (1.17 g: 10 mmole) in 1 N MeONa (4 ml) was then added and stirred at 40°C for 20 h. At the end of stirring, water (100 ml) was poured in, and the complex and extracted with $CHCl_3$. The extract was washed with water, dried over Na_2SO_4, and evaporated. The residue was chromatographed on a column of SiO_2 in the system $CHCl_3$:acetone (5:1) separating the diastereomeric complexes as fraction I (S-BPAB—S-Val)·Ni(II) and fraction II (S-BPAB—R-Val)·Ni(II). The complexes were purified additionally on an LH-20 column in the system benzene: EtOH (2:1) and dried in vacuum over P_2O_5. In this way (S-BPAB—S-Val)·Ni(II) (0.72 g: 78%) was obtained having mp 150-154°C. PMR spectrum ($CDCl_3$, δ, ppm): 1.23 and 1.38 d [3 H, CH_3 (Val), J = 7.5 Hz), 2.0-2.5 m [4 H, β- and γ- CH_2 (Pro)], 2.15 m [1 H, β-CH (Val), 3.33 m [1H, α-H-(Pro)], 3.51 m [2H, δ-CH_2 (Pro)], 3.66 d [1H, α-H (Val), J = 3.5 Hz], 6.8-8.4 m (9 H, Ar), 7.38 s (1 H, HC=N). AB system of the benzyl CH_2 group, 3.42 and 4.35, J = 15 Hz.

In addition (S-BPAB—R-Val)·Ni(II) (0.1 g: 11%) was obtained having mp 180-185°C. PMR spectrum ($CDCl_3$, δ, ppm): 1.17 and 1.20 d [3 H, CH_3 (Val), J = 7 Hz], 2.1-2.7 m [4 H, β- and γ-CH_2 (Pro)], 2.40 m [1 H, β-CH (Val)], 3.40 m [1 H, α-H (Pro)], 3.75 d [1 H, α-CH (Val), J = 4 Hz], 3.87 m [2 H, δ-CH_2 (Pro)], 6.8-8.6 m (9 H, Ar), 7.53 s (1 H, HC=N). AB system of benzyl CH_2 group, 3.57, 4.50, J = 14 Hz.

Ni(II) complex of the Schiff base of S-BPAB and glycine (S-BPAB—Gly)·Ni(II) was obtained similarly to (S-BPAB—Val). Yield was 0.764 g (91%) of mp 116-122°C. PMR spectrum ($CDCl_3$, δ, ppm): 1.9-2.23 [β- and γ- CH_2 (Pro)], 3.30 [δ-CH_2 (Pro)], 3.60 [α-CH (Pro)], 6.78-8.37 m (9 H, Ar), 7.41 s (1 H, CH=N). AB system of benzyl CH_2 group 3.45, 4.32, J = 14 Hz. AB system of glycine CH_2 group 4.02, 4.20, J = 18 Hz.

Isolation of S-BPAB and Amino Acids from Their Complexes. Complexes were decomposed by a general procedure. Complex (∿0.2 mmole) in MeOH (5 ml) was added dropwise to boiling 10% HCl solution (10 ml) containing S-Ala as internal standard. The solution was neutralized with 25% NH_4OH solution to pH 8-9 and S-BPAB extracted with $CHCl_3$. Yield of S-BPAB determined spectrophotometrically by the absorption at 338 nm was from 75 to 80% in different experiments. An aqueous solution was liberated from the salt on Dowex 50 (H^+ form) resin.

Retroracemization of amino acids was carried out by a general procedure. A 0.4 N MeONa solution (2 ml) was added in a stream of Ar to a mixture of racemic AA (0.2 mmole), S-BPAB (0.2 mmole), and $Ni(NO_3)_2 \cdot 6H_2O$ (0.2 mmole) in MeOH (2 ml) and stirred at 40°C for 24 h. Water (10 ml) was added, the complex extracted with $CHCl_3$, evaporated, and decomposed as described above. The internal standard S-Ala was added to the aqueous solution and unreacted AA isolated on a column of Dowex 50 (H^+ form).

Epimerization of (S-BPAB—S-Val)·Ni(II) and (S-BPAB—R-Val)·Ni(II) under the action of MeONa. A 0.005 N solution of MeONa (1 ml) was added under Ar to complex (S-BPAB—S-Val)·Ni(II) or (S-BPAB—R-Val)·Ni(II) ($1.15 \cdot 10^{-3}$ mmole) and the mixture placed in a polarimeter cuvette (l = 0.5 cm) thermostatted at 25°C. The change in angle of rotation at 365 nm was followed. At the end of the reaction (end of change in angle of optical rotation) the complex was decomposed as described above.

Asymmetric Synthesis of Threonine in the Presence of Et_3N. A solution of acetaldehyde (0.46 g: 10.5 mmole) in MeOH (3.5 ml) and Et_3N (0.5 ml) was added under Ar to (S-BPAB—Gly)·Ni(II) (0.09 g: 0.21 mmole). The mixture was kept for 1 h at ∿20°C, neutralized with 10% HCl solution, and evaporated. Further processing was the same as on decomposition of complexes. The enantiomer composition and chemical yield of Thr and allo-Thr were determined by GLC (see Table 3) [7].

Asymmetric Synthesis of Threonine in the Presence of MeONa. A solution of acetaldehyde (0.46 g: 10.5 mmole) in MeOH (3.2 ml) and 1 N MeONa (0.8 ml) was added under Ar to (S-BPAB—Gly)·Ni(II) (0.09 g: 0.21 mmole). The reaction mixture was kept at ∿20°C for 1 h, neutralized with 1 N HCl, and evaporated. Further processing was the same as on decomposition of complexes. The enantiomer composition and chemical yield of Thr and allo-Thr were determined by GLC (see Table 3) [7].

CONCLUSIONS

1. Complexes of Ni(II) with Schiff bases of 2-N-(2'-S-N-benzylpyrrolidin-2-carbonyl)-aminobenzaldehyde (S-BPaB) with glycine and valine have been synthesized in which the Ni ion is coordinated with the N atoms of the proline fragment, of the aldimine group, of the ionized amide, and with the carboxyl group.

2. The presence has been shown of enantioselective effects in complexes of Schiff bases of S-BPAB with R,S-amino acids with Ni(II) which increase with an increase in volume of the amino acid side chain. The enantiomer excess for the complex with S-Val was 78%.

3. The retroracemization of alanine, valine, norvaline, phenylalanine, phenylglycine, and tryptophan was carried out using S-BPAB and Ni(II) with enantiomer yields of 15, 78, 42, 40, 39, and 64% respectively.

4. The asymmetric synthesis of S-threonine has been effected by condensing acetaldehyde with (S-BPAB—Gly)·Ni(II) on catalysis with Et_3N with a S-Thr and S-allo-Thr ratio of 1:2 and enantiomer yield of 86 and 76% respectively. An increase in pH led to a reduction in enantiomer yield and reversal of the sign of the enantioselective effect.

5. A method has been developed for enantiomer analysis of tryptophan using high-pressure liquid chromatography as has a GLC method for difficult amino acids using a high-temperature chiral chromatographic phase, viz., N-heptadecanoyl-S-Val tert-butylamide.

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