Anionic chiral cobalt(III) complexes as catalysts of asymmetric synthesis of cyanohydrins

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Chiral coordinatively saturated cobalt(III) complexes with Schiff bases of enantiopure amino acids are formed as Λ- and Δ-isomers, which are not transformed into each other under normal conditions. These complexes catalyze the formation of enantiomerically enriched cyanohydrins from aldehydes and Me_3SiCN under homo- and heterogeneous catalysis.

Key words: enantioselective phase transfer catalysis, chiral cobalt(III) complexes, cyanohydrins, aldehydes, trimethylsilyl cyanide, amino acids, salens.

Catalysts containing chiral elements in the cationic part are widely used in asymmetric catalysis.[1] However, the chemistry of polynuclear catalysts, which are salts of chiral anions with achiral cations, has started to develop actively in the recent time.[1—3] For instance, a family of bimetallic catalysts based on chiral binaphthol with an element of asymmetry in the anionic part has recently been developed.[1] Such catalysts are used, in particular, in the aldol condensation and Michael addition. Chiral octahedral phosphates are used to shift the equilibrium in solutions of mutually transforming enantiomers toward one of them with enantiomeric excess up to 98%.[2] A new class of chiral borate anions, *viz.*, derivatives of enantiomerically pure amino acids, was created.[3] In the presence of copper salts, these compounds catalyze the enantioselective cyclopropanation of styrene. We have previously[4] synthesized potassium bis(*N*-salicylideneaminoacidato)cobaltates, which are coordinatively saturated cobalt complexes with two perpendicular tridentate ligands, the latter being the Schiff bases of salicylaldehyde and (*S*)-amino acids. These complexes were used as chiral substrates for asymmetric alkylation in syntheses of enantiomerically enriched amino acids.[4]

Results and Discussion

In the present work, we report the use of the chiral anionic* complexes, *viz.*, potassium Λ-bis[*N*-salicylidene-(*S*)-aminoacidato]cobaltates,[4] as catalysts in the syntheses of enantiomerically enriched cyanohydrins. These complexes were synthesized according to the somewhat modified literature procedure[5] (Scheme 1).

The isomers were separated and purified by column chromatography. The complexes exist as meridian Λ- and Δ-stereoisomers, which are not transformed into each other under normal conditions (*i.e.*, they are stereochemically inert) and can be separated chromatographically. Thus, we prepared individual Λ- and Δ-stereoisomeric cobalt complexes of the Schiff bases of salicylaldehyde and the following amino acids: glycine**, (*S*)-valine, (*S*)-phenylalanine, (*S*)-tryptophan, and

* The electrophoresis data that confirm the ionic structure of the complexes are given in Experimental.

** In the case of glycine, two enantiomeric complexes are formed, which were separated by the crystallization of the diastereomeric salts with brucine.[6]

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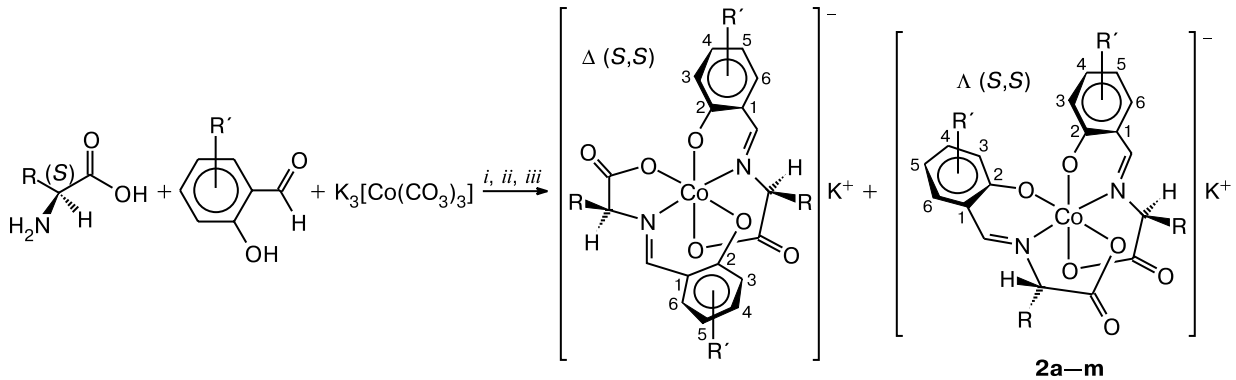
Scheme 1



1, 2	R	R´	1, 2	R	R´	1, 2	R	R´
a	H	H	**f**	$(CH_2)_2C(O)NH_2$	H	**j**	3-Indolylmethyl	4-OH
b	Pr^i	H	**g**	$CH_2C(O)NH_2$	H	**k**	3-Indolylmethyl	4-CH_2OPh
c	$(CH_2)_2SMe$	H	**h**	3-Indolylmethyl	H	**l**	3-Indolylmethyl	3,5-Bu^t_2
d	Bn	H	**i**	3-Indolylmethyl	3-OMe	**m**	3-Indolylmethyl	5-Br
e	(*S*)-CH(OH)Me	H						

Reagents and conditions: *i*. EtOH, reflux, 3 h. *ii*. Chromatographic separation on Al_2O_3 (EtOH). *iii*. Additional purification by gel chromatography on Sephadex LH-20 (C_6H_6—EtOH, 3 : 1).

(*S*)-asparagine. We failed to separate completely diastereomers of the complex synthesized from (*S*)-glutamine and, therefore, a mixture of the Λ- and Δ-isomers in a ratio of 1 : 4 was used. In the case of (*S*)-threonine and (*S*)-methionine, we succeeded in isolating only the Δ-isomer. The complexes were assigned to Λ- and Δ-isomers by a comparison of the characteristic regions of the circular dichroism (CD) curves (λ = 316—600 nm) with the CD curves obtained for isomers of the (*S*)-threonine complex (Fig. 1). The absolute configurations of the isomers of the (*S*)-threonine complex have been determined previously[7] by X-ray diffraction analysis along with the possibility to assign configurations of the Λ- and Δ-complexes of (*S*)-amino acids using CD spectra. The CD curves for the Δ-isomer of (*S*)-threonine complex **1e** and the Δ-isomer of (*S*)-tryptophan complex **1h** are shown in Fig. 1.

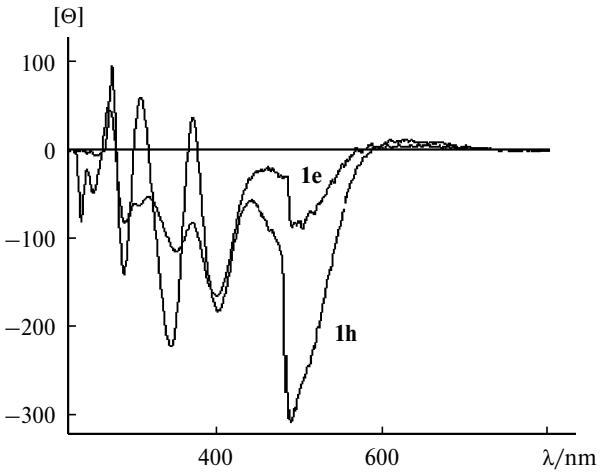
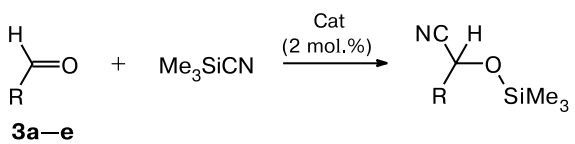


Fig. 1. Circular dichroism curves for complexes **1e,h** (solvent EtOH, concentrations of the substances were 0.032 g in 10 mL of solvent).

It can be seen that the CD curves of the synthesized complexes (see Fig. 1) do not differ by sign of the Cotton effect in the region of λ = 316—600 nm, which makes it possible to assign the Δ-configuration to complexes **1** regardless of the character of the substituent in the amino acid fragments. The replacement of substituents affects only the value but not the sign of the Cotton effect in this region, which allows one to unambiguously assign the Δ- or Λ-configuration of the complex.

For testing of complexes **1a—h** and **2a—h** as catalysts of asymmetric C—C bond formation, we chose the addition of trimethylsilyl cyanide to benzaldehyde (**3a**) (Scheme 2). The reaction was carried out in dichloromethane under argon at 20 °C. In the absence of catalyst only traces of the product were found.

Scheme 2



3a—e

Cat is catalyst

R = Ph (**a**), 4-FC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), PhCH=CH (**d**), Pr^i (**e**)

Table 1. Yield and enantiomeric purity of *O*-trimethylsilylmandelonitrile after the trimethylsilylcyanation of benzaldehyde catalyzed by complexes **1a—h** and **2a,b,d,g,h**[a]

Complex	Yield[b]	*ee*[b] (*S*)	Complex	Yield[b]	*ee*[b] (*S*)
	%			%	
1a	85	0	**1h**	90	6
1b	87	0	**2a**	80	0
1c	95	0	**2b**	84	0
1d	90	0	**2d**	75	0
1e	90	23	**2g**	87	0
1f[c]	85	0	**2h**	87	60
1g	87	0			

[a] Reaction conditions: benzaldehyde (1 mmol), Me_3SiCN (1.1 mmol), catalyst (0.02 mmol), CH_2Cl_2 (1 mL), stirring, argon atmosphere, ~20 °C, reaction time 1 h.
[b] Here in Tables 2—5, the yield and enantiomeric purity were determined by chiral GLC.
[c] A mixture of diastereomers with 75% diastereomeric excess of the Δ-isomer was used as the catalyst.

The results of the addition of Me_3SiCN to benzaldehyde are given in Table 1. All complexes exhibit high catalytic activity: the yield of the product is 75—95%. In the case when complex **2h** is used, the enantiomerically enriched product (*ee* 60%) was formed, whereas complex **1h** performs no asymmetric induction in this reaction. Thus, we found that the results of catalysis depends on both the nature of the alkyl substituent in the amino acid fragment and stereochemistry of the complex.

Since the coordinatively saturated and stable anionic Co^{III} complexes possess no Lewis acidity, it is reasonable to assume that just the potassium cation with some Lewis acidity performs catalysis of the reaction, and the metal-complex anion only creates the chiral environment providing asymmetric induction.

To verify this assumption, we replaced the potassium cation in complex **1b** by a silver cation possessing no Lewis acidity toward carbonyl compounds.[8] The resulting complex **1n** was catalytically inactive in the trimethylsilylcyanation of benzaldehyde. In addition, the control experiment in the presence of achiral potassium tetraphenyl borate gave racemic cyanohydrin in high yield (90%). Therefore, it can be concluded that the potassium cation catalyzes the reaction acting as the Lewis acid, while the chiral anion determines the configuration of the product that formed.

It seemed reasonable to study the influence of the cation nature in complexes similar to **2h** on the stereodifferentiating ability in the trimethylsilylcyanation of benzaldehyde. Using ion-exchange chromatography, we obtained complexes **2o—r** containing lithium, sodium, cesium, and rubidium cations, respectively.

All of them exhibited high catalytic activity (Table 2, entries *3—6*) but their stereodifferentiating ability was low:

Table 2. Yield and enantiomeric purity of *O*-trimethylsilylmandelonitrile after the trimethylsilylcyanation of benzaldehyde catalyzed by complexes **1n** and **2h,o—r***

Entry	Complex	Counter-cation	Yield	*ee* (*S*)
			%	
1	**1n**	Ag^+	0	0
2	**2h**	K^+	87	60
3	**2o**	Li^+	87	6**
4	**2p**	Na^+	90	4
5	**2q**	Cs^+	87	0
6	**2r**	Rb^+	90	0

* Reaction conditions: benzaldehyde (1 mmol), Me_3SiCN (1.1 mmol), catalyst, (0.02 mmol), CH_2Cl_2 (1 mL), stirring, argon atmosphere, ~20 °C, reaction time 1 h.
** Enantiomeric excess of the (*R*)-form.

in the best case, benzaldehyde was trimethylsilylcyanated with 6% enantiomeric excess (see Table 2, entry *3*). We assumed that the introduction of additional ligands capable of interacting with the potassium cation (thus changing its Lewis acidity) and creating additional steric hindrance for the interaction of the substrate with the catalyst can affect the stereoselectivity of the reaction. It turned out that additives to catalyst **2h**, which decompose the tight ion pair (compounds containing the mobile hydrogen atom and crown ethers), decrease sharply the stereodifferentiating ability of the catalyst, and the enantiomeric purity of the product in these cases is low (Table 3; entries *2*, *3*, and *13*). On the contrary, triphenylphosphine, triphenylphosphine selenide, and indole exert a positive

Table 3. Yield and enantiomeric purity of *O*-trimethylsilylmandelonitrile after the trimethylsilylcyanation of benzaldehyde catalyzed by complex **2h** in the presence of various additives*

Entry	Additive	Yield	*ee* (*S*)
		%	
1	—	87	60
2	H_2O	90	0
3	*tert*-Butanol	99	5
4	Bis(diphenylphosphino)ethane	93	60
5	Triphenylphosphine	89	77
6	Triphenylphosphine selenide	89	70
7	Triphenylphosphine oxide	95	11
8	Diphenylphosphine	78	0
9	Methyl(diphenyl)phosphine	90	0
10	Indole	97	74
11	Pyridine	85	40
12	Imidazole	87	17
13	18-Crown-6	80	0

* Reaction conditions: benzaldehyde (1 mmol), $(Me)_3SiCN$ (1.1 mmol), catalyst (0.02 mmol), additive (0.1 mmol), CH_2Cl_2 (1 mL), stirring, argon atmosphere, ~20 °C, reaction time 1 h.

Table 4. Yield and enantiomeric purity of *O*-trimethylsilylcyanohydrins after the trimethylsilylcyanation of aldehydes **3a—e** catalyzed by complex **2h** in the presence of triphenylphosphine*

Aldehyde	R	Yield	*ee* (*S*)
		%	
3a	Ph	90	77
3b	4-FC_6H_4	99	5
3c	4-$MeOC_6H_4$	93	45
3d	PhCH=CH	89	0
3e	Pr^i	89	0

* Reaction conditions: benzaldehyde (1 mmol), $(Me)_3SiCN$ (1.1 mmol), complex **2h** (0.02 mmol), CH_2Cl_2 (1 mL), PPh_3 (0.1 mmol), stirring, argon atmosphere, ~20 °C, reaction time 1 h.

effect on the efficiency of catalysis, and in these cases the enantiomeric excess of the product is 77, 70, and 74%, respectively (see Table 3; entries *5*, *6*, and *10*).

The most efficient catalytic system **2h**—PPh_3 was tested in the trimethylsilylcyanation of a series of aromatic and aliphatic aldehydes **3b—e** (see Scheme 2 and Table 4). The highest enantiomeric excess was observed for benzaldehyde; aliphatic aldehydes produced the racemic product.

It seemed reasonable to study the influence of substituents in the salicylidene fragments on the stereodifferentiating ability of potassium Λ-bis[*N*-salicylidene-(*S*)-tryptophanato]cobaltate (**2h**). For this purpose, we synthesized complexes **2i—m** (see Scheme 1). The results obtained with these complexes are presented in Table 5.

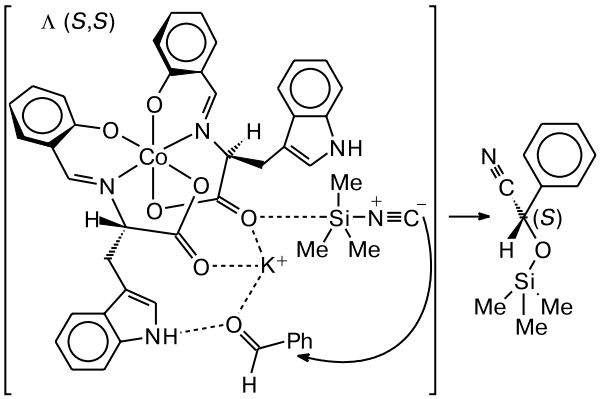
Summarizing the aforesaid, we can propose the most probable mechanism of catalysis of the trimethylsilylcyanation of benzaldehyde by complex **2h** (Scheme 3). Trimethylsilyl cyanide activated due to the interaction with the carboxyl group of amino acid attacks benzaldehyde, which, in turn, is also activated due to the interaction with the potassium cation and NH group of the indole fragment of tryptophan. In this case, the Si attack predominates, which results in the enantiomerically enriched product with the (*S*)-configuration.

Table 5. Yield and enantiomeric purity of *O*-trimethylsilylmandelonitrile after the trimethylsilylcyanation of benzaldehyde catalyzed by complexes **2i—m***

Entry	Complex	Yield	*ee* (*S*)
		%	
1	**2i**	87	45
2	**2j**	80	0
3	**2k**	90	65
4	**2l**	98	0
5	**2m**	87	65

* Reaction conditions: benzaldehyde (1 mmol), $(Me)_3SiCN$ (1.1 mmol), catalyst (0.02 mmol), CH_2Cl_2 (1 mL), additive PPh_3 (0.1 mmol), stirring, argon atmosphere, ~20 °C, reaction time 1 h.

Scheme 3



Assuming that water-soluble complex **2h** can transfer benzaldehyde from the organic phase into water, we tested this catalyst in the phase transfer synthesis of *O*-acetylcyanohydrins in a two-phase toluene—water medium (Scheme 4). In fact, this complex catalyzes the reaction of benzaldehyde with potassium cyanide and acetic anhydride (yield 93%, enantiomeric excess 4%). In the absence of the catalyst, the reaction practically does not occur.

Scheme 4

Reagents and conditions: *i*. Catalyst **2h** (2 mol.%), H_2O—toluene, 2.5 h, argon, yield 93%, *ee* 4%. *ii*. Without catalyst, H_2O—toluene, 2.5 h, argon, yield 3%, *ee* 0%.

It is most likely that in this case the catalyst performs the transfer of benzaldehyde into water, where its reaction with the cyanide anion occurs. The cyanohydrin that formed is transferred to the organic phase where its interaction with acetic anhydride gives *O*-acetylcyanohydrin.

We hope that further studies devoted to optimization of the conditions and catalyst structure will provide higher values of asymmetric induction and yields in stereoselective homo- and heterogeneous catalyses in the synthesis of enantiomerically enriched cyanohydrins.

Experimental

^1H NMR spectra were recorded on Bruker WP-200-SY (200 MHz), Bruker Avance 300 (300 MHz), and Bruker

AMX-400 (400 MHz) spectrometers. Chemical shifts were measured in the δ scale relatively to the signal of residual protons of the deuterated solvent.

Optical rotation was measured on a Perkin—Elmer 241 polarimeter in a temperature-controlled cell (5 cm) at 25 °C. The solvent and concentration in grams per 10 mL of the solvent are given for all compounds. Circular dichroism curves were detected on a Jasco J 700 dichrograph.

Silica gel Kieselgel 60 (Merck), Al_2O_3 (Chemapol), and Sephadex LH-20 were used. Solvents were purified by standard procedures. Freshly distilled aldehydes and trimethylsilyl cyanide were applied

Enantiomeric analysis of the synthesized trimethylsilyl ethers of cyanohydrins was carried out on a gas chromatograph (model 3700-00) equipped with a flame-ionization detector on the DP-TFA-γ-cD chiral stationary phase (32 m × 0.20 mm). The standard for each compound was its racemic form.

Synthesis of $K_3[Co(CO_3)_3]$. A solution of $Co(NO_3)_2 \cdot 6H_2O$ (7.27 g, 0.025 mol) in H_2O (12.5 mL) and 30% H_2O_2 (5 mL) were added dropwise at 0 °C to a suspension of K_2CO_3 (17.4 g, 0.126 mol) in H_2O (12.5 mL). The reaction mixture was stirred for 20 h at ~20 °C. A green precipitate that formed was filtered off and washed with water and EtOH. The dark green substance (8.9 g) was obtained, m.p. >300 °C.

Synthesis of potassium Δ- and Λ-bis(*N*-salicylideneaminoacidato)cobaltates 1a—m and 2a—m, respectively (general procedure). Unsubstituted salicylaldehyde or its substituted derivative (0.01 mol) was added with stirring to a mixture of $K_3[Co(CO_3)_3]$ (0.005 mol) and amino acid (0.01 mol) in EtOH. The reaction mixture was refluxed for 3 h using a reflux condenser and then filtered. The filtrate was concentrated *in vacuo*, and the residue was washed with diethyl ether and dissolved in EtOH. The isomers were purified and separated by column chromatography on Al_2O_3 (EtOH as eluent). An additional purification was carried out by gel chromatography on Sephadex LH-20 using an EtOH—benzene (1 : 3) mixture as eluent.

Potassium Δ-bis(*N*-salicylideneglycinato)cobaltate (1a). The yield was 90%, m.p. >300 °C, $[\alpha]_D^{25}$ −93.3 (*c* 0.003, MeOH). ^{1}H NMR (300 MHz, D_2O), δ: 4.65 (s, 4 H, H_2O); 5.03 (m, 4 H, CH_2); 6.78 (t, 2 H, *J* = 5.4 Hz); 6.88 (t, 2 H, *J* = 6.3 Hz); 7.23 (m, 2 H); 7.60 (d, 2 H, *J* = 5.7 Hz); 8.70 (s, 2 H, CH=N).

Potassium Δ-bis[*N*-salicylidene-(*S*)-valinato]cobaltate (1b). The yield was 86%, m.p. >300 °C, $[\alpha]_D^{25}$ −3215.0 (*c* 0.0030, MeOH). Found (%): C, 54.61; H, 5.15; N, 5.09. $C_{24}H_{26}CoKN_2O_6 \cdot 0.16C_6H_6$. Calculated (%): C, 54.64; H, 4.95; N, 5.10. ^{1}H NMR (300 MHz, D_2O), δ: 1.11 (m, 12 H, Me); 2.50 (m, 2 H, CH); 4.2 (d, 2 H, CH, *J* = 8.1 Hz); 6.32 (t, 2 H, CH_{Ar}, *J* = 8.4 Hz); 6.83 (t, 2 H, CH_{Ar}, *J* = 13.2 Hz); 7.10 (d, 2 H, CH_{Ar}, *J* = 8.1 Hz); 7.21 (s, 1 H, CH_{Ar} (C_6H_6)); 7.50 (d, 2 H, CH_{Ar}, *J* = 11.7 Hz); 8.40 (s, 2 H, CH=N).

Potassium Δ-bis[*N*-salicylidene-(*S*)-methioninato]cobaltate (1c). The yield was 80%, m.p. 195—197 °C, $[\alpha]_D^{25}$ −438.7 (*c* 0.0031, MeOH). Found (%): C, 45.39; H, 4.32; N, 3.89. $C_{24}H_{26}CoKN_2O_6S_2 \cdot 2H_2O$. Calculated (%): C, 45.28; H, 4.75; N, 4.40. ^{1}H NMR (300 MHz, D_2O), δ: 2.10 (m, 6 H, Me); 2.30 (m, 8 H, CH_2); 4.65 (s, 4 H, H_2O); 5.12 (s, 2 H, CH); 6.44 (d, 2 H, CH_{Ar}, *J* = 5.7 Hz); 6.60 (d, 2 H, CH_{Ar}, *J* = 6.0 Hz); 7.02 (d, 2 H, CH_{Ar}, *J* = 9.0 Hz); 7.31 (d, 2 H, CH_{Ar}, *J* = 8.7 Hz); 7.50 (d, 2 H, CH_{Ar}, *J* = 8.4 Hz); 8.50 (s, 2 H, CH=N).

Potassium Δ-bis[*N*-salicylidene-(*S*)-phenylalaninato]cobaltate (1d). The yield was 79%, m.p. >300 °C, $[\alpha]_D^{25}$ −4204.5 (*c* 0.0032, MeOH). Found (%): C, 57.41; H, 3.94; N, 4.26. $C_{32}H_{26}CoKN_2O_6 \cdot 2H_2O$. Calculated (%): C, 57.48; H, 4.52; N, 4.19. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.31 (s, 2 H, CH); 3.53 (d, 2 H, CH, *J* = 7.5 Hz); 4.55 (s, 4 H, H_2O); 4.74 (s, 2 H, CH); 6.34 (t, 2 H, CH_{Ar}, *J* = 9.3 Hz); 6.86 (t, 4 H, CH_{Ar}, *J* = 8.3 Hz); 7.19 (t, 2 H, CH_{Ar}, *J* = 9.0 Hz); 7.29 (s, 2 H, CH_{Ar}); 7.41 (m, 8 H, CH_{Ar}); 7.54 (s, 2 H, CH=N).

Potassium Δ-bis[*N*-salicylidene-(*S*)-threoninato]cobaltate (1e). The yield was 70%, m.p. >300 °C, $[\alpha]_D^{25}$ −5995.2 (*c* 0.0022, MeOH). Found (%): C, 50.80; H, 4.67; N, 4.59. $C_{22}H_{22}CoKN_2O_8 \cdot 2EtOH$. Calculated (%): C, 50.91; H, 5.80; N, 4.24. ^{1}H NMR (300 MHz, D_2O), δ: 1.30 (d, 6 H, Me, *J* = 8.7 Hz); 4.20 (t, 2 H, CH, *J* = 9.0 Hz); 4.5 (d, 2 H, CH, *J* = 8.1 Hz); 6.60 (m, 4 H, CH_{Ar}); 7.20 (t, 2 H, CH_{Ar}, *J* = 9.6 Hz); 7.50 (d, 2 H, CH_{Ar}, *J* = 9.9 Hz); 8.60 (s, 2 H, CH=N).

Mixture of potassium Δ- and Λ-bis[*N*-salicylidene-(*S*)-glutaminato]cobaltates (1f : 2f = 4 : 1). The yield was 68%, m.p. >300 °C, $[\alpha]_D^{25}$ −2088.2 (*c* 0.0032, MeOH). Found (%): C, 40.74; H, 3.43; N, 3.80. $C_{24}H_{24}CoKN_4O_8 \cdot 5H_2O$. Calculated (%): C, 41.03; H, 5.16; N, 8.18. ^{1}H NMR spectrum of predominant isomer (300 MHz, D_2O), δ: 2.40, 3.01 (both d, 4 H each, CH_2, *J* = 9.3 Hz); 4.64 (s, 10 H, H_2O); 5.00 (t, 2 H, CH, *J* = 12.6 Hz); 6.50 (d, 2 H, CH_{Ar}, *J* = 9.9 Hz); 6.60 (t, 2 H, CH_{Ar}, *J* = 12.2 Hz); 7.30 (t, 2 H, CH_{Ar}, *J* = 12.9 Hz); 7.55 (d, 2 H, CH_{Ar}, *J* = 9.3 Hz); 8.50 (s, 2 H, CH=N).

Potassium Δ-bis[*N*-salicylidene-(*S*)-asparaginato]cobaltate (1g). The yield was 80%, m.p. >300 °C, $[\alpha]_D^{25}$ −273.3 (*c* 0.003, MeOH). Found (%): C, 39.90; H, 4.12; N, 8.64. $C_{22}H_{20}CoKN_4O_8 \cdot 5H_2O$. Calculated (%): C, 40.25; H, 4.61; N, 8.53. ^{1}H NMR (300 MHz, D_2O), δ: 2.90 (d, 4 H, CH_2, *J* = 9.6 Hz); 4.65 (s, 10 H, H_2O); 5.20—5.30 (t, 2 H, CH, *J* = 12.0 Hz); 6.32 (d, 2 H, CH_{Ar}, *J* = 11.2 Hz); 6.64 (t, 2 H, CH_{Ar}, *J* = 12.0 Hz); 7.00 (t, 2 H, CH_{Ar}, *J* = 12.3 Hz); 7.50 (d, 2 H, CH_{Ar}, *J* = 12.0 Hz); 8.40 (s, 2 H, CH=N).

Potassium Δ-bis[*N*-salicylidene-(*S*)-tryptophanato]cobaltate (1h). The yield was 80%, m.p. >300 °C, $[\alpha]_D^{25}$ −5281, $[\alpha]_{578}^{25}$ −5506, $[\alpha]_{546}^{25}$ −4893 (*c* 0.0032, MeOH). Found (%): C, 60.37; H, 4.81; N, 7.21. $C_{36}H_{28}CoKN_4O_6 \cdot EtOH$. Calculated (%): C, 60.31; H, 4.53; N, 7.40. ^{1}H NMR (400 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 1.15 (t, 3 H, Me (EtOH)); 3.14 (t, 2 H, CH, *J* = 13.2 Hz); 3.40 (d, 2 H, CH, *J* = 12.8 Hz); 3.61 (q, 2 H, CH_2 (EtOH)); 4.80 (d, 2 H, CH, *J* = 9.2 Hz); 6.00 (d, 2 H, CH_{Ar}, *J* = 8.4 Hz); 6.17 (s, 2 H, CH_{Ar}); 6.63 (d, 2 H, CH_{Ar}, *J* = 9.2 Hz); 6.70, 6.92 (both s, 2 H each, CH_{Ar}); 7.00 (s, 4 H, CH_{Ar}); 7.25, 7.40 (both d, 2 H each, CH_{Ar}, *J* = 7.2 Hz); 7.90 (d, 2 H, CH=N, *J* = 7.8 Hz).

During the syntheses of the complexes containing substitutents in salicylidene fragments, only Λ-isomers **2i—m** were isolated from the reaction mixture.

Potassium Λ-bis(*N*-salicylideneglycinato)cobaltate (2a). The yield was 90%, m.p. >300 °C. ^{1}H NMR (300 MHz, D_2O) δ: 4.65 (s, 2 H, H_2O); 5.00 (m, 4 H, CH_2); 6.78 (t, 2 H, CH_{Ar}, *J* = 5.4 Hz); 6.88 (t, 2 H, CH_{Ar}, *J* = 6.3 Hz); 7.23 (m, 2 H, CH_{Ar}); 7.60 (d, 2 H, CH_{Ar}, *J* = 5.7 Hz); 8.70 (s, 2 H, CH=N).

Potassium Λ-bis[*N*-salicylidene-(*S*)-valinato]cobaltate (2b). The yield was 86%, m.p. >300 °C, $[\alpha]_D^{25}$ −3400.0 (*c* 0.0029, MeOH). Found (%): C, 50.65; H, 4.80; N, 5.11. $C_{24}H_{26}CoKN_2O_6 \cdot 2H_2O$. Calculated (%): C, 50.35; H, 5.28; N, 4.89. ^{1}H NMR (300 MHz, D_2O), δ: 1.10 (m, 12 H, Me); 2.60 (m, 2 H, CH); 4.20 (d, 2 H, CH, *J* = 8.1 Hz); 4.55 (s, 4 H, H_2O); 6.60 (t, 2 H, CH_{Ar}, *J* = 7.8 Hz); 6.77 (d, 2 H, CH_{Ar},

J = 13.2 Hz); 7.09 (d, 2 H, CH_{Ar}, *J* = 8.1 Hz); 7.43 (d, 2 H, CH_{Ar}, *J* = 11.7 Hz); 8.40 (s, 2 H, CH=N).

Potassium Λ-bis[*N*-salicylidene-(*S*)-phenylalaninato]cobaltate (2d). The yield was 79%, m.p. >300 °C, $[\alpha]_D^{25}$ –3793.6 (*c* 0.0031, MeOH). Found (%): C, 60.41; H, 4.31; N, 4.29. $C_{32}H_{26}CoKN_2O_6$. Calculated (%): C, 60.76; H, 4.14; N, 4.43. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.30 (s, 2 H, CH); 3.50 (d, 2 H, CH, *J* = 7.2 Hz); 4.71 (s, 2 H, CH); 6.36 (t, 2 H, CH_{Ar}, *J* = 9.0 Hz); 6.80 (t, 4 H, CH_{Ar}, *J* = 8.1 Hz); 7.13 (t, 2 H, CH_{Ar}, *J* = 9.3 Hz); 7.20 (s, 2 H, CH_{Ar}); 7.45 (m, 8 H, CH_{Ar}); 7.54 (s, 2 H, CH=N).

Potassium Λ-bis[*N*-salicylidene-(*S*)-asparaginato]cobaltate (2g). The yield was 80%, m.p. >300 °C, $[\alpha]_D^{25}$ –0.004 (*c* 0.0032, MeOH). Found (%): C, 39.81; H, 3.61; N, 8.79. $C_{22}H_{20}CoKN_4O_8 \cdot 5H_2O$. Calculated (%): C, 40.25; H, 4.61; N, 8.53. ^{1}H NMR (300 MHz, D_2O), δ: 3.00 (d, 4 H, CH_2, *J* = 9.8 Hz); 4.65 (s, 10 H, H_2O); 5.29 (t, 2 H, CH, *J* = 12.2 Hz); 6.30 (d, 2 H, CH_{Ar}, *J* = 11.0 Hz); 6.64 (t, 2 H, CH_{Ar}, *J* = 12.2 Hz); 6.90 (t, 2 H, CH_{Ar}, *J* = 12.3 Hz); 7.40 (d, 2 H, CH_{Ar}, *J* = 12.3 Hz); 8.40 (s, 2 H, CH=N).

Potassium Λ-bis[*N*-salicylidene-(*S*)-tryptophanato]cobaltate (2h). The yield was 86%, m.p. >300 °C, $[\alpha]_D^{25}$ –4062.5, $[\alpha]_{578}^{25}$ –3737.5, $[\alpha]_{546}^{25}$ –737.5 (*c* 0.0032, MeOH). Found (%): C, 61.53; H, 4.74; N, 7.57. $C_{36}H_{28}CoKN_4O_6 \cdot Et_2O$. Calculated (%): C, 61.22; H, 4.88; N, 7.14. ^{1}H NMR (200 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 1.13 (t, 3 H, Me (Et_2O)); 3.14 (t, 2 H, CH, *J* = 14.0 Hz); 3.41 (d, 2 H, CH, *J* = 11.4 Hz); 3.50 (q, 2 H, CH_2 (Et_2O)); 4.83 (d, 2 H, CH, *J* = 8.4 Hz); 6.03 (d, 2 H, CH_{Ar}, *J* = 8.0 Hz); 6.15 (s, 2 H, CH_{Ar}); 6.50 (d, 2 H, CH_{Ar}, *J* = 9.0 Hz); 6.68 (s, 2 H, CH_{Ar}); 6.90 (s, 2 H, CH_{Ar}); 6.97 (s, 4 H, CH_{Ar}); 7.26 (d, 2 H, CH_{Ar}, *J* = 7.4 Hz); 7.43 (d, 2 H, CH_{Ar}, *J* = 7.2 Hz); 7.83 (d, 2 H, CH=N, *J* = 7.0 Hz).

Potassium Λ-bis[*N*-3-methoxysalicylidene-(*S*)-tryptophanato]cobaltate (2i). The yield was 89%, m.p. >300 °C, $[\alpha]_D^{25}$ –4613.3 (*c* 0.0030, MeOH). Found (%): C, 55.07; H, 4.67; N, 5.73. $C_{38}H_{32}CoKN_4O_8 \cdot 3H_2O$. Calculated (%): C, 55.34; H, 4.64; N, 6.79. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 2.90 (s, 6 H, OMe); 3.60, 4.00 (both s, 2 H each, CH); 4.65 (s, 6 H, H_2O); 5.00 (br.s, 2 H, CH); 6.20 (s, 4 H, CH_{Ar}); 6.50, 6.90 (both s, 2 H each, CH_{Ar}); 7.20 (s, 4 H, CH_{Ar}); 7.30 (s, 2 H, CH_{Ar}); 7.50 (d, 2 H, CH_{Ar}, *J* = 7.8 Hz); 8.00 (br.s, 2 H, CH=N).

Potassium Λ-bis[*N*-4-hydroxysalicylidene-(*S*)-tryptophanato]cobaltate (2j). The yield was 76%, m.p. >300 °C, $[\alpha]_D^{25}$ –3967.7 (*c* 0.0031, MeOH). Found (%): C, 52.19; H, 4.89; N, 6.17. $C_{36}H_{26}CoK_3N_4O_8 \cdot 0.5H_2O$. Calculated (%): C, 52.23; H, 3.29; N, 6.77. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.34 (t, 2 H, CH, *J* = 12.0 Hz); 3.60 (d, 2 H, CH, *J* = 12.0 Hz); 4.12 (s, 1 H, H_2O); 5.00 (d, 2 H, CH, *J* = 9.3 Hz); 5.70 (s, 2 H, CH_{Ar}); 5.80 (d, 2 H, CH_{Ar}, *J* = 7.5 Hz); 6.40 (d, 2 H, CH_{Ar}, *J* = 7.8 Hz); 6.70 (s, 2 H, CH_{Ar}); 7.10 (m, 6 H, CH_{Ar}); 7.50 (d, 2 H, CH_{Ar}, *J* = 6.9 Hz); 7.80 (d, 2 H, CH=N, *J* = 6.9 Hz).

Potassium Λ-bis[*N*-4-benzyloxysalicylidene-(*S*)-tryptophanato]cobaltate (2k). The yield was 70%, m.p. 207—209 °C, $[\alpha]_D^{25}$ –2969.7 (*c* 0.0033, MeOH). Found (%): C, 59.71; H, 5.07; N, 5.19. $C_{50}H_{40}CoKN_4O_8$. Calculated (%): C, 60.36; H, 5.25; N, 5.61. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.43 (t, 2 H, CH, *J* = 12.0 Hz); 3.86 (d, 2 H, CH, *J* = 12.4 Hz); 4.94 (d, 2 H, CH, *J* = 8.8 Hz); 6.00 (d, 2 H, CH_{Ar}, *J* = 8.8 Hz); 6.20 (s, 2 H, CH_{Ar}); 6.72 (d, 2 H, CH_{Ar}, *J* = 8.4 Hz); 7.26—7.42 (m, 8 H, CH_{Ar}); 7.43—7.50 (m, 10 H, CH_{Ar}); 7.60 (d, 2 H, CH_{Ar}, *J* = 6.4 Hz); 7.90 (d, 2 H, CH=N, *J* = 6.4 Hz); 10.39 (s, 2 H).

Potassium Λ-bis[*N*-3,5-di-*tert*-butylsalicylidene-(*S*)-tryptophanato]cobaltate (2l). The yield was 76%, m.p. 190—192 °C, $[\alpha]_D^{25}$ –726.7 (*c* 0.0030, MeOH). Found (%): C, 67.21; H, 7.01; N, 5.38. $C_{52}H_{60}CoKN_4O_6$. Calculated (%): C, 66.79; H, 6.47; N, 5.99. ^{1}H NMR (200 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 1.42 (d, 36 H, Me, *J* = 16.0 Hz); 3.50 (m, 4 H, CH); 3.14 (t, 2 H, *J* = 14.0 Hz); 3.41 (d, 2 H, *J* = 11.4); 4.83 (d, 2 H, CH, *J* = 8.4 Hz); 6.03 (d, 2 H, CH_{Ar}, *J* = 8.0 Hz); 6.15 (s, 2 H, CH_{Ar}); 6.50 (d, 2 H, CH_{Ar}, *J* = 9.0 Hz); 6.68, 6.90, 6.97 (all s, 2 H each, CH_{Ar}); 7.26 (d, 2 H, CH_{Ar}, *J* = 7.4 Hz); 7.44 (d, 2 H, CH_{Ar}, *J* = 7.2 Hz); 7.66 (d, 2 H, CH=N, *J* = 7.0 Hz).

Potassium Λ-bis[*N*-5-bromosalicylidene-(*S*)-tryptophanato]cobaltate (2m). The yield was 69%, m.p. >300 °C, $[\alpha]_D^{25}$ –3280.0 (*c* 0.0030, MeOH). Found (%): C, 46.97; H, 3.40; N, 5.87. $C_{36}H_{26}Br_2CoKN_4O_6 \cdot 3H_2O$. Calculated (%): C, 46.87; H, 3.50; N, 6.07. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.52 (t, 2 H, CH, *J* = 10.8); 3.75 (d, 2 H, CH, *J* = 15.2 Hz); 4.64 (s, 6 H, H_2O); 4.86 (d, 2 H, CH, *J* = 12.0 Hz); 6.36 (d, 2 H, CH_{Ar}, *J* = 9.0 Hz); 6.84 (m, 4 H, CH_{Ar}); 7.05 (m, 8 H, CH_{Ar}); 7.44 (d, 2 H, CH_{Ar}, *J* = 7.8 Hz); 7.82 (d, 2 H, CH=N, *J* = 7.8 Hz).

Exchange of counterions (general procedure). Complex **1b** or **2h** (100 mg) was dissolved in a mixture of H_2O and EtOH (5 mL each) and passed through the DOWEX-50x8 ion-exchange resin containing ions of the corresponding metals as counterions. The resulting solution was concentrated, and the residue was purified by gel chromatography on Sephadex LH-20 using an EtOH—benzene (1 : 3) mixture as the eluent.

Silver Δ-bis[*N*-salicylidene-(*S*)-valinato]cobaltate (1n). M.p. >300 °C. Found (%): C, 46.25; H, 4.53; N, 4.49. $C_{24}H_{26}AgCoN_2O_6 \cdot H_2O$. Calculated (%): C, 46.24; H, 4.40; N, 4.23. ^{1}H NMR (300 MHz, D_2O), δ: 1.29 (m, 12 H, Me); 2.55 (m, 2 H, CH); 4.20 (br.s, 2 H, CH_2); 4.50 (s, 2 H, H_2O); 6.50 (br.s, 4 H, CH_{Ar}); 6.97 (br.s, 2 H, CH_{Ar}); 7.40 (br.s, 2 H, CH_{Ar}); 8.40 (br.s, 2 H, CH=N).

Lithium Λ-bis[*N*-salicylidene-(*S*)-tryptophanato]cobaltate (2o). M.p. >300 °C, $[\alpha]_D^{25}$ –5346 (*c* 0.0030, MeOH). Found (%): C, 59.41; H, 4.34; N, 7.44. $C_{36}H_{28}CoLiN_4O_6 \cdot 2.5H_2O$. Calculated (%): C, 59.76; H, 4.60; N, 7.74. ^{1}H NMR (200 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.09, 3.50 (both s, 2 H each, CH); 4.54 (s, 5 H, H_2O); 4.90 (d, 2 H, CH, *J* = 11.2 Hz); 6.17 (m, 2 H, CH_{Ar}); 6.32 (m, 4 H, CH_{Ar}); 6.50 (d, 2 H, CH_{Ar}, *J* = 7.4 Hz); 6.90 (s, 2 H, CH_{Ar}); 7.17 (m, 4 H, CH_{Ar}); 7.41 (s, 2 H, CH_{Ar}); 7.60 (d, 2 H, CH_{Ar}, *J* = 7.4 Hz); 7.90 (d, 2 H, CH=N, *J* = 7.8 Hz).

Sodium Λ-bis[*N*-salicylidene-(*S*)-tryptophanato]cobaltate (2p). M.p. >300 °C, $[\alpha]_D^{25}$ –4856.2 (*c* 0.0029, MeOH). Found (%): C, 59.62; H, 5.21; N. 6.90. $C_{36}H_{28}CoN_4NaO_6 \cdot 2H_2O$. Calculated (%): C, 59.18; H, 4.41; N, 7.67. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.00, 3.58 (both s, 2 H each, CH); 4.57 (s, 4 H, H_2O); 4.81 (d, 2 H, CH, *J* = 12.0 Hz); 6.17 (m, 4 H, CH_{Ar}); 6.50 (d, 2 H, CH_{Ar}, *J* = 7.2 Hz); 6.68, 6.90 (both s, 2 H each, CH_{Ar}); 7.10 (m, 4 H, CH_{Ar}); 7.41 (s, 2 H, CH_{Ar}); 7.53 (d, 2 H, CH_{Ar}, *J* = 7.8 Hz); 7.95 (d, 2 H, CH=N, *J* = 7.5 Hz).

Cesium Λ-bis[*N*-salicylidene-(*S*)-tryptophanato]cobaltate (2q). M.p. >300 °C, $[\alpha]_D^{25}$ –3142.0, $[\alpha]_{578}^{25}$ –2838.7, $[\alpha]_{546}^{25}$ –509.7 (*c* 0.0031, MeOH). Found (%): C, 54.38; H, 4.31; N, 6.78. $C_{36}H_{28}CoCsN_4O_6$. Calculated (%): C, 53.75; H, 3.51;

N, 6.96. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.45 (t, 2 H, CH, J = 10.2 Hz); 3.61 (d, 2 H, CH, J = 9.9 Hz); 5.10 (d, 2 H, CH, J = 12.0 Hz); 6.51 (d, 2 H, CH_{Ar}, J = 11.7 Hz); 6.90 (s, 2 H, CH_{Ar}); 7.01 (t, 2 H, CH_{Ar}, J = 8.7 Hz); 7.20 (s, 2 H, CH_{Ar}); 7.35 (m, 8 H, CH_{Ar}); 7.20 (d, 2 H, CH_{Ar}, J = 10.5 Hz); 8.20 (d, 2 H, CH=N, J = 11.1 Hz).

Rubidium Λ-bis[*N*-salicylidene-(*S*)-triptophanato]cobaltate (2r). M.p. >300 °C, $[\alpha]_{578}^{25}$ −2838.7, $[\alpha]_D^{25}$ −3578.0 (*c* 0.0030, MeOH). Found (%): C, 53.20; H, 4.43; N, 6.40. $C_{36}H_{28}CoN_4O_6Rb \cdot 3H_2O$. Calculated (%): C, 53.31; H, 4.23; N, 6.91. ^{1}H NMR (300 MHz, D_2O + CD_3COCD_3 (1 : 1)), δ: 3.67 (t, 2 H, CH, J = 10.8 Hz); 3.87 (d, 2 H, CH, J = 9.6 Hz); 4.53 (s, 6 H, H_2O); 5.20 (d, 2 H, CH, J = 7.8 Hz); 6.44, 6.80 (both m, 4 H each, CH_{Ar}); 7.00 (t, 2 H, CH_{Ar}, J = 12.0 Hz); 7.35 (m, 4 H, CH_{Ar}); 7.50 (s, 2 H, CH_{Ar}); 7.60 (d, 2 H, CH_{Ar}, J = 12.0 Hz); 8.10 (s, 2 H, CH=N).

Trimethylsilylcyanation of aldehydes 3a—e (general procedure). A Schlenk flask was vacuumed and filled with argon while heating with the flame of a gas burner. Then the flask was cooled by passing an argon flow, and a catalyst (0.02 mmol), an additive (see Table 3) (0.1 mmol), CH_2Cl_2 (1 mL), aldehyde **3a—e** (1 mmol), and trimethylsilyl cyanide (0.15 mL, 111 mg, 1.24 mmol) were introduced into the flask. The reaction mixture was stirred for 1 h at ~20 °C under argon and then passed through a thin Al_2O_3 layer, eluting the reaction product with CH_2Cl_2. The enantiomeric purity of the product was determined by gas chromatography on the chiral phase. No additive was used in several experiments.

Addition of potassium cyanide to benzaldehyde. A catalyst (0.02 mmol), H_2O (0.5 mL), toluene (4.5 mL), benzaldehyde (0.1 mL, 100 mg, 1 mmol), KCN (200 mg, 3 mmol), and acetic anhydride (0.17 mL, 111 mg, 1.8 mmol) were placed into a flask. The reaction mixture was stirred for 1 h and then passed through a thin Al_2O_3 layer. The enantiomeric purity of the product was determined by gas chromatography on the chiral phase.

Electrophoresis of complexes 1a and 2b,h was carried out in the buffer with pH 9.5 (glycine, NaOH, NaCl), I = 10 mA, V = 400 V, t = 45 min; run 21, 23, and 10 mm for **1a**, **2b**, and **2h**, respectively. All compounds moved to the cathode.

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