Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron: Asymmetry
Tetrahedron: *Asymmetry* 19 (2008) 822–831

Potassium and silver chiral cobaltate(III) complexes as precatalysts for asymmetric C–C bond formation

Yuri N. Belokon,[a,*] Viktor I. Maleev,[a] Dimitri A. Kataev,[b] Ilya. L. Mal'fanov,[c] Alexander G. Bulychev,[c] Margarita A. Moskalenko,[a] Tat'yana F. Saveleva,[a] Tat'yana V. Skrupskaya,[a] Konstantin A. Lyssenko,[a] Ivan A. Godovikov[a] and Michael North[d]

[a]*A.N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 28, Vavilova Str., 119991 Moscow, Russian Federation*
[b]*Higher Chemical College, Russian Academy of Sciences, 9, Miusskaya pl., 125047 Moscow, Russian Federation*
[c]*Department of Chemistry, Kaliningrad State University, 2, Universitetskaya Str., 236000 Kaliningrad, Russian Federation*
[d]*School of Natural Sciences and University Research Centre in Catalysis and Intensified Processing, Bedson Building, University of Newcastle upon Tyne, Newcastle upon Tyne, NE1 7RU, United Kingdom*

Received 16 January 2008; accepted 10 March 2008
Available online 15 April 2008

Abstract—Chiral, coordinatively-saturated cobaltate(III) complexes of Schiff bases obtained from salicylaldehyde and the optically active amino acids, (*S*)-Val, (*S*)-Thr, and (*S*)-Trp, are formed as C_2-symmetrical, octahedral, anionic Λ(*S*,*S*)-, and Δ(*S*,*S*)-diastereoisomeric complexes, which are easily separable by chromatography. The complexes are stereochemically inert and, thus, are not transformed into each other under normal conditions. The counter-cations of the complexes can be easily interchanged and the sodium, potassium, and silver salts of some of the complexes were prepared. The structures of diastereoisomeric Λ-[(Sal-(*S*)-Val)$_2$Co(III)]$^-$Ag$^+$ and Δ-[(Sal-(*S*)-Val)$_2$-Co(III)]$^-$Ag$^+$ were established by single crystal X-ray analysis. All of the sodium and potassium complexes effectively catalyzed the reaction between benzaldehyde and Me_3SiCN, but only the Λ-[(Sal-(*S*)-Trp)$_2$Co(III)]$^-$K$^+$ complex gave rise to enantiomerically-enriched mandelonitrile with up to 77% ee. The silver salts catalyzed a Mukaiyama reaction with low enantioselectivity (ee in the range 6–27%).

1. Introduction

Positively charged complexes formed by chiral ligands strongly coordinated to metal ions, which serve as single center Lewis acid catalysts, are routine tools in asymmetric catalysis and are still intensively developed.[1] However, the chemistry of polynuclear catalysts, which are salts of chiral metal-complex anions with achiral cations, has only recently started being developed actively.[2–4] For instance, a family of bimetallic rare earth-alkali metal-tris(1,1′-bi-2-naphthoxide) catalysts with an element of asymmetry in the anion has recently been developed by Shibasaki et al.[2] Such catalysts have been used efficiently, particularly in asymmetric Michael additions and aldol condensations.[2]

Lacour et al. have elaborated upon a series of chiral octahedral phosphate anions for many purposes, including the enantiomeric purity determination of chiral cationic complexes and epimerization of ion pairs.[3] Asymmetric induction by a chiral anion in the Stevens[4a] and Carroll[4b] rearrangements is a sound indication of the viability of the chiral anion concept in asymmetric catalysis. A new class of chiral borate anions, namely, derivatives of optically active amino[5a] or hydroxy[5b] acids have been created. In the presence of copper salts, these compounds catalyze the enantioselective cyclopropanation of styrene[5a] or can be used as stereodifferentiating chiral ionic liquid media[5b] in an aza-Baylis–Hilman reaction. Chiral counteranions derived from BINOL-phosphates are also used as inducing agents in several reaction types.[6] These reactions include biomimetic reduction and epoxidation of enals,[6a,b] Pd-catalyzed allylation[6c] of aldehydes,[6c] silver catalyzed alkyne addition to imines,[6d] and gold ion catalyzed hydroalkoxylation.[6e]

An advantage of the achiral cation/chiral weakly coordinated anion ion-pair system is the ability to retain a greater

* Corresponding author. Tel./fax: +7 499 135 63 56; e-mail: yubel@ineos.ac.ru

0957-4166/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2008.03.010

Lewis acidity in the cation, when compared to the traditional metal complexes where the charge on the metal is compensated by the strong first-sphere ligand metal coordination. Thus, chiral metal cations such as Na^+ or K^+, which are not usually considered as likely candidates for Lewis acids in catalytic cycles, can become efficient asymmetric catalysts in combination with chiral weakly coordinated anions.

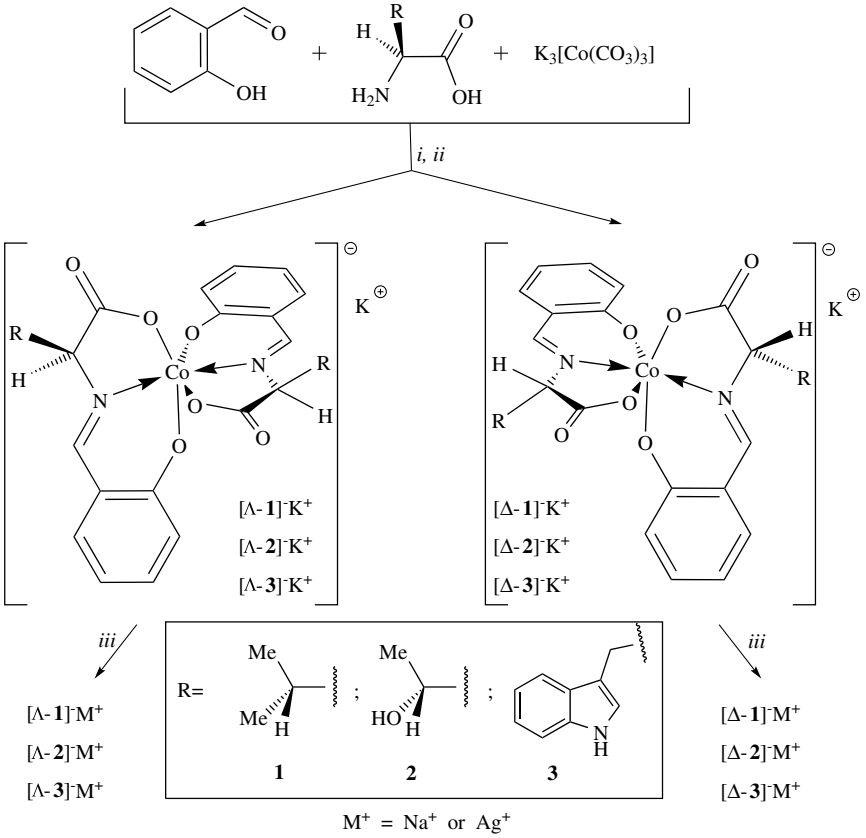
Herein, we report a proof of principle study of chiral anionic complexes of potassium and silver Λ- or Δ-bis-[*N*-salicylidene-(*S*)-aminoacidato]-cobaltates[7] as Lewis acid catalysts in asymmetric reactions involving C–C bond formation. Bis(*N*-salicylideneaminoacidato)cobaltates are coordinatively-saturated anionic cobalt complexes with two perpendicular tridentate ligands, which are the Schiff bases of salicylaldehyde and (*S*)-amino acids. These complexes have previously been used (by some of us) as chiral substrates for asymmetric ligand alkylation in syntheses of enantiomerically-enriched amino acids.[8] The chiral cobaltate anion is stereochemically inert and retained its chiral integrity during the amino acid synthesis.[8] The complexes were synthesized by a modified literature procedure[9] as shown in Scheme 1.

2. Results and discussion

The complexes exist as meridinal Δ- and Λ-stereoisomers, which are not interconverted under normal conditions (i.e., they are stereochemically inert) but can be separated chromatographically on Al_2O_3. The Λ(*S*,*S*)-complexes were always observed to have higher R_f values than the Δ(*S*,*S*)-diastereomers.[7] Thus, diastereoisomeric Δ(*S*,*S*)- and Λ(*S*,*S*)-Co(III) complexes of the Schiff bases of salicylaldehyde and the following amino acids: (*S*)-valine, [Δ-**1**]K and [Λ-**1**]K, (*S*)-threonine, [Δ-**2**]K, and (*S*)-tryptophan, [Δ-**3**]K and [Λ-**3**]K were prepared. The general stereoselectivity trend was that an excess of the Δ(*S*,*S*)-isomer always formed during the synthesis.[7] In the case of (*S*)-threonine, only the Δ(*S*,*S*)-isomer was obtained in significant amounts.

The corresponding sodium and silver salts [Δ-**1**]Na, [Λ-**1**]Na; [Δ-**2**]Na; [Δ-**3**]Na, [Λ-**3**]Na, and ([Δ-**1**]Ag, [Λ-**1**]Ag; [Δ-**2**]Ag) were prepared from the respective potassium salts by ion-exchange on a cation exchange resin. It was not possible to prepare and purify the silver salts of either [Δ-**3**] or [Λ-**3**]. The single crystal X-ray structure of [Δ-**2**]K has previously been reported.[8]

The X-ray analysis of two silver salts with the chiral anion—bis-[*N*-salicyliden-(*S*)-valinato]-cobaltate ([Δ-**1**]Ag, Fig. 1 and [Λ-**1**]Ag, Fig. 2)—has been carried out. Both salts contain solvate molecules: water ([Δ-**1**]Ag) and methanol ([Λ-**1**]Ag). In the crystal of [Λ-**1**]Ag the independent part of the unit cell contains two independent anions situated on the C_2-axis and one silver cation in the general position. In the crystal of ([Δ-**1**]Ag), the unit cell is more complex. The asymmetric unit cell contains ten cobaltate complexes. Four of these are situated on the C_2-axis,



Scheme 1. Reagents and conditions: (i) EtOH, reflux, 3 h; (ii) separation and purification by gel chromatography on Sephadex LH-20 (C_6H_6/EtOH, 3:1); (iii) ion-exchange and gel chromatography on Sephadex LH-20 (C_6H_6/EtOH, 3:1).

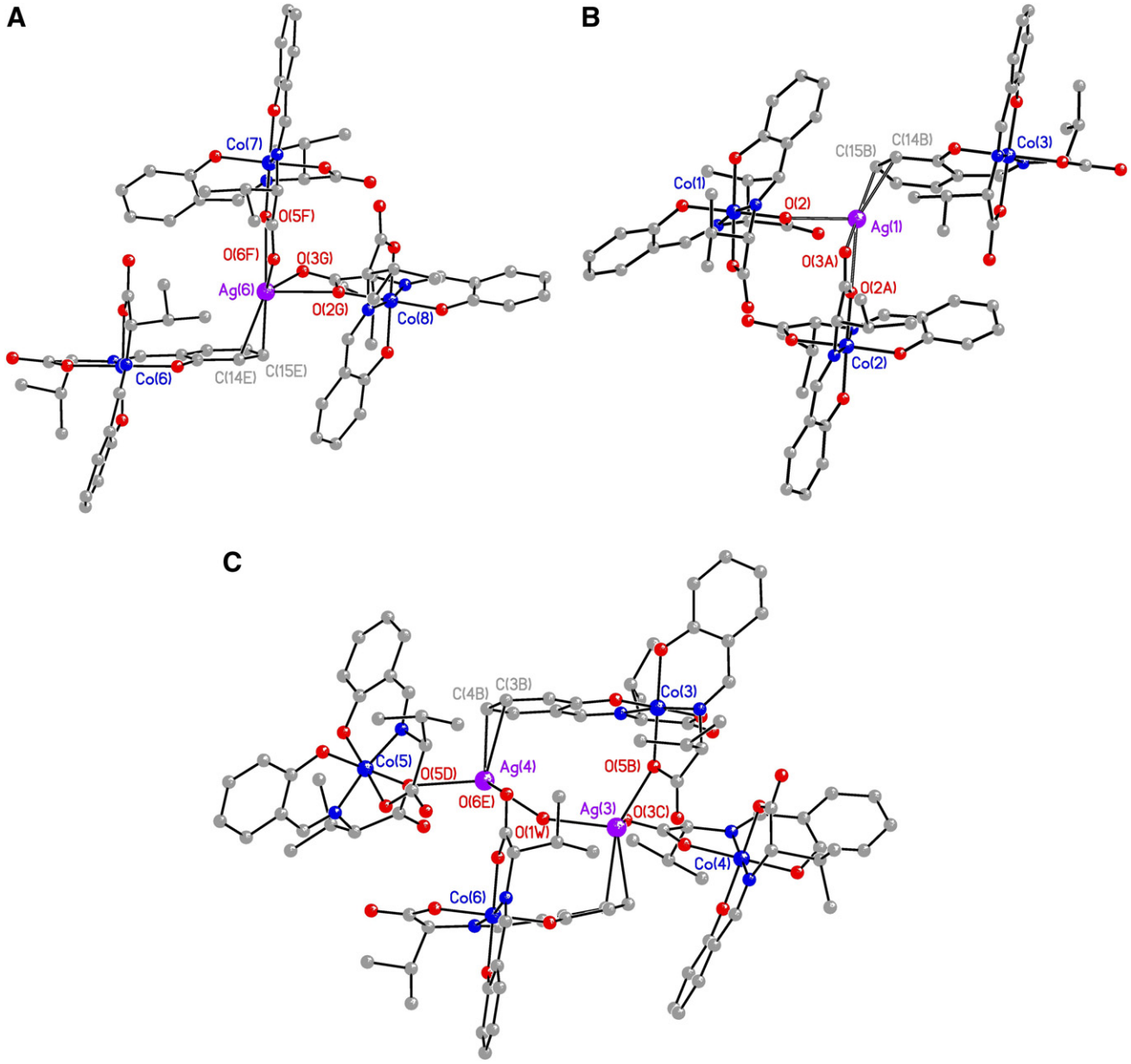


Figure 1. The different types of cation···anion interactions in [Δ-**1**]Ag: (A) bidentate/bidentate coordination of carboxyl groups; (B) bidentate/monodentate coordination of carboxyl groups; (C) monodentate/monodentate coordination of carboxyl groups.

similar to the structure of [Λ-**1**]Ag and the rest are in general positions. For all the independent cations, the formation of close ionic pairs is observed. On the basis of the X-ray diffraction data, an analysis of the interactions of the silver cations with the chiral anions was performed. The coordination polyhedron of the cations was formed by both oxygen atoms of the ligand and aromatic systems. Comparison of [Δ-**1**]Ag and [Λ-**1**]Ag revealed that a change of the complex configuration leads to significant modification of the close ion pairs and considerable weakening of the Ag···π interactions in the case of [Λ-**1**]Ag. It should be noted that the number of oxygen atoms in the coordination sphere of the cations was almost identical. However, in the case of [Δ-**1**]Ag, a set of carboxyl group oxygen atoms formed the coordination sphere, whilst in the case of [Λ-**1**]Ag there were also phenolic oxygen atoms present. This difference can be traced to a greater steric shielding of the carboxyl groups of the neighboring ligand by the amino acid side chain moiety of another ligand in [Λ-**1**]Ag, leaving the phenolic oxygen atoms exposed to possible coordination with the silver cation. The opposite situation occurred in [Δ-**1**]Ag where the side chain of one ligand shielded the phenolic oxygen atoms of another ligand, leaving the carboxyl groups available for coordination.

The complexes were tested as catalysts for the asymmetric addition of trimethylsilyl cyanide to benzaldehyde (Scheme 2). The reaction was carried out in methylene chloride under argon at 20 °C. No reaction was observed under the experimental conditions without a catalyst. The silver complexes did not catalyze the reaction.

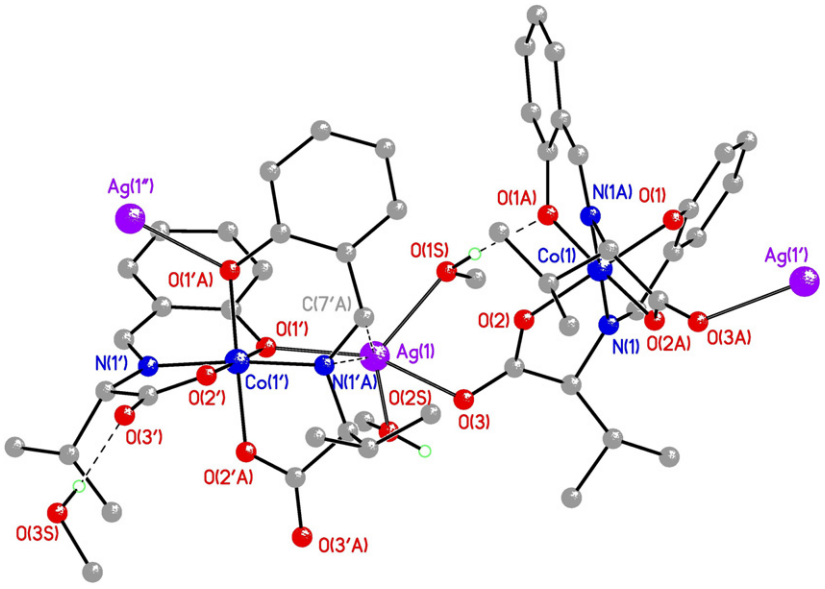
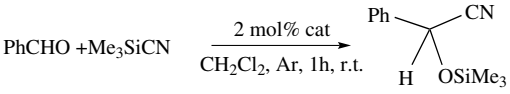


Figure 2. Cation···anion interactions in [Λ-**1**]Ag, assembling anions into chains.



Scheme 2.

Table 1. Synthesis of mandelonitrile trimethylsilyl ether catalyzed by the sodium and potassium complexes **1**–**3**[a]

Entry	Catalyst	$t_{1/2}$[b] (min)	ee (%) (configuration)[c]
1	[Ph_4B]K	112	0
2	[Δ-**1**]Na	5	0
3	[Λ-**1**]Na		0
4	[Δ-**1**]K ([Δ-**1**]Li)	6 (1.3)	0
5	[Λ-**1**]K		0
6	[Δ-**2**]Na		0
7	[Δ-**2**]K		23(*S*)
8	[Δ-**3**]Na		0
9	[Λ-**3**]Na	10	4(*S*)
10	[Δ-**3**]K	70	0
11	[Λ-**3**]K	2.5	60–65(*S*)
12[d]	[Λ-**3**]K		77(*S*)

[a] PhCHO 1 mmol, TMSCN 1.1 mmol, catalyst 0.02 mmol, CH_2Cl_2 1 mL, rt, under Ar within 1–3 h, the chemical yields were in the range of 80–95%.
[b] Half-reaction time, the value in the parentheses is that of a Li salt.
[c] Results of enantiomeric GLC analysis.
[d] 5 equiv of Ph_3P relative to the catalyst was added.

As can be seen from the data presented in Table 1 (entries 2–12), all of the sodium and potassium complexes exhibited high catalytic activity: the yields of the product were 80–95% after 1–3 h. The order of cation efficiency was the expected one Li > Na or K, as the data in entries 1, 2, and 4 indicated. Clearly, the chiral anions were adding to the catalytic efficiency. For example, the potassium tetraphenylborate was an order of magnitude less efficient relative to K[Δ-**1**]. In addition, the configuration of the anion was important, as the data in entries 10 and 11 showed that [Λ-3]**K** was more than 20 times more efficient than [Δ-**3**]**K**, the latter was more efficient than [Λ-**3**]**Na** (entries 9 and 11).

All (*S*)-valine based complexes ([Δ-**1**]Na, [Λ-**1**]Na, [Δ-**1**]K, [Λ-**1**]K, Table 1, entries 2–5) gave racemic mandelonitrile trimethylsilyl ether. Similarly, complexes of other amino acids, with a sodium cation as counterion, exhibited little to no stereoselectivity (Table 1, entries 6, 8, and 9). It was only when the (*S*)-threonine derived complex [Δ-**2**]K was used that an enantiomerically-enriched product (ee 23%, Table 1, entry 7) was obtained. Notably, (*S*)-tryptophan complex [Δ-**3**]K generated no asymmetric induction in this reaction whereas its [Λ-**3**]K diastereoisomer produced mandelonitrile trimethylsilyl ether with an enantiomeric excess of 60–65% (Table 1, entries 10 and 11). Thus, the results of the catalysis depended on the nature of the counter-cation, the presence of functional groups in the side chain of the amino acid moiety and the absolute configuration of the Co(III) complex.

There were no detectable changes in the ^{1}H NMR spectrum of complexes **1**–**3** after one to three hours in the presence of 10 equiv of trimethylsilyl cyanide. Thus, it appeared that the octahedral structure of the complex anion remained intact during the course of the reaction. Since the coordinatively-saturated and stable anionic Co(III) complexes possess no Lewis acidity, it is reasonable to assume that the potassium cation with some Lewis acidity catalyzed the reaction and the metal-complex anion created different chiral environments, providing asymmetric induction in some cases. This hypothesis was supported by a control experiment in the presence of achiral potassium tetraphenyl borate, which gave racemic cyanohydrin in high yield (Table 1, entry 1). Therefore, it can be concluded that the alkali cations are quite capable of serving as Lewis acids, catalyzing the reaction with the participation of the basic

anions, possibly serving as additional basic catalysts. Different types of cation coordination in [Δ-**1**]Ag and [Λ-**1**]Ag (see Figs. 1 and 2) provide sufficient grounds for ascribing the differences in asymmetric induction to alternative asymmetric surroundings of the potassium-ion in the complexes of different configuration.

We expected that the introduction of additional achiral 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, could affect the stereoselectivity of the reaction. It turned out that additives to the catalyst [Λ-**3**]K, which decompose the tight ion pairs (water, alcohols, and crown ethers), sharply decreased the stereodifferentiating ability of the catalyst. In contrast, triphenylphosphine exerted a positive effect on the efficiency of catalysis, and in this case, the enantiomeric excess of the product of trimethylsilylcyanation of benzaldehyde was 77% (Table 1, entry 12).

Table 2 summarizes the influence of the dilution of the reaction on the catalyst efficiency. Most likely, the complexes are catalytically active in both monomeric and associated forms, as the data summarized in Table 2 indicated. Thus, a 20-fold dilution of the reaction mixture (Table 2 entries 1 and 4) should be expected to result in an increase of the proportion of monomeric catalytic species, accompanied by a slowing of the reaction rate and a significant decrease in the chemical yield of the reaction within a 1 h period because of the reagent dilution. Unexpectedly, the dilution only slightly decreased the chemical yield of the reaction, probably indicating a compensating effect of a greater catalytic efficiency of the monomer, compared to the activity of the oligomeric species, predominant at higher concentrations. However, the dilution did have a dramatic effect on the enantioselectivity of the reaction (Table 2 entries 1–4). Thus, a 20-fold dilution of the reaction mixture (Table 2 entries 1 and 4) resulted in a complete loss of asymmetric induction. This observation might indicate that the catalytic species responsible for the asymmetric induction was an oligonuclear complex resembling the ones depicted in Figures 1 and 2.

To confirm the possible association of the complexes in the reaction conditions, the pseudo-2D diffusion 2D-DOSY method was used. For [Δ-**1**]Na, spectra in a mixture of $CDCl_3$ and CD_3OD (2:1) (Fig. 3) and DMSO-d_6 (Fig. 3) were recorded. The cross peaks (Fig. 3), corresponding to

Table 2. The influence of dilution on the performance of the [Λ-**3**]K catalyst in the addition of trimethylsilyl cyanide to benzaldehyde[a]

Entry	CH_2Cl_2 volume (mL)	Concentration (M) of			Yield (%)	ee (%)
		[Λ-**3**]K	PhCHO	Me_3SiCN		
1	0.5	0.04	2	2.20	95	76
2	1	0.02	1	1.10	91	77
3	4	0.005	0.25	0.28	80	5
4	10	0.002	0.10	0.11	70	0

[a] The experimental conditions are the same as in entry 12 (Table 1) with the exception of varying volumes of CH_2Cl_2.

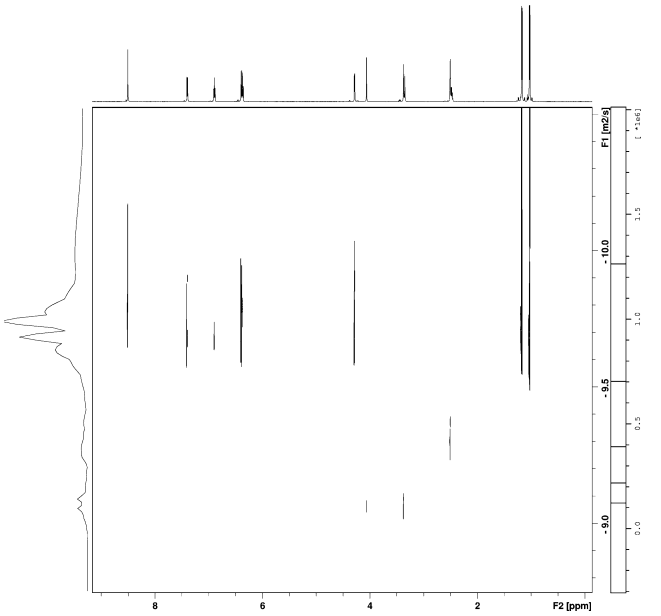


Figure 3. 2D-DOSY spectrum of [Δ-**1**]Na in $CDCl_3/CD_3OD$ mixture (2:1).

the complex, are sufficiently broad in the F1 log scale of diffusion coefficient D, to indicate that some association occurs in the solution (presumably containing three molecules, according to the number of maxima in the cross peaks) with different lability, easily interconverting with each other. On the other hand, in the spectrum in DMSO-d_6 solution (Fig. 4) the cross peaks (indicated by the red line) are narrower, supporting the theory that no association occurs in this solution.

The experiments conducted with other aldehydes under the optimal experimental conditions (Table 1, entry 12) were summarized in Table 3.

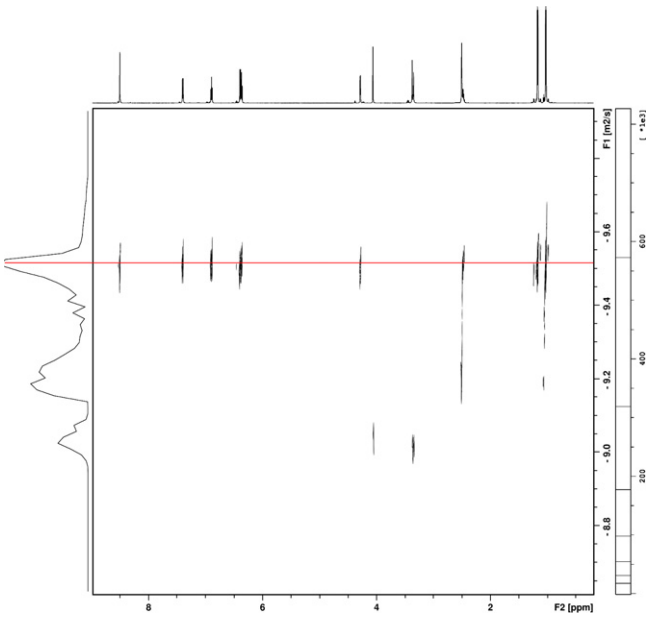
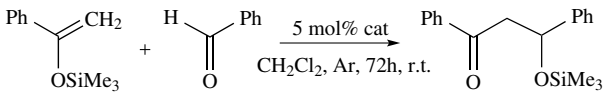


Figure 4. 2D-DOSY spectrum of [Δ-**1**]Na in DMSO-d_6.

Table 3. The addition of TMSCN to a series of aldehydes catalyzed by the [Λ-**3**]K catalyst[a]

Entry	Aldehyde	Yield (%)	ee (%)
1	4-F–C_6H_4–CHO	>90	6
2	4-MeO–C_6H_4–CHO	>90	45
3	Ph-CH=CH–CHO	>90	0
4	$(CH_3)_2$CH–CHO	>90	0

[a] The experimental conditions are the same as in entry 12 (Table 1) with the exception of varying aldehyde structures.



Scheme 3.

Table 4. Acetophenone enol Mukaiyama reaction with benzaldehyde (Scheme 3)[a]

Entry	Catalyst	Yield[b] (%)	ee[b] (%) (*S*)
1	[Λ-**1**]Ag	33	6
2	[Δ-**1**]Ag	31	19
3	[Δ-**2**]Ag	8	27

[a] Benzaldehyde (1 mmol), acetophenone enol (1 mmol), the catalyst (0.05 mmol), CH_2Cl_2 (1 mL), stirring under Ar, at room temperature, 72 h.

[b] Enantiomeric excess and chemical yield were established by chiral HPLC.

As can be seen from the data, the introduction of electronegative substituents into the benzaldehyde molecule resulted in a significant loss of the enantioselectivity of the reaction (compare Table 1, entry 12 with Table 3, entries 1 and 2). The addition of TMSCN to isobutanal and cinnamaldehyde resulted in racemic products (Table 3, entries 3 and 4).

Any sodium or potassium complexes prepared in this work did not catalyze the Mukaiyama reaction (Scheme 3). However, the silver complexes ([Δ-**1**]Ag, [Λ-**1**]Ag; [Δ-**2**]Ag) did catalyze the reaction, although with low chemical yield and enantioselectivity (Table 4, entries 1–3). The low chemical yields of the reaction might be, in part at least, a consequence of Ag-ion reduction by benzaldehyde, effectively eliminating the catalytic species.

3. Conclusion

A novel family of simple chiral Lewis acid catalysts has been developed. Their ease of preparation and assembly, the possibility of an almost infinite variation of their structures, and the introduction of different functional groups into their side chains make them interesting prospective systems for future exploration as catalysts in a host of Lewis acid catalyzed reactions. An apparent way of increasing both the catalytic efficiency and asymmetry inducing power of the catalysts seems to be the introduction of functional groups into the side chain of the amino acid moieties and/or salicylaldehyde. The groups could serve both as a general base catalyst in a host of C–C bond forming reactions and/or serve to improve the coordination of the achiral cations to the chiral anions. Another way of modification might be the substitution of amino alcohols for the amino acids and so forth.

4. Experimental

X-ray diffraction experiments were carried out with a Bruker SMART APEX II CCD area detector, using graphite monochromated Mo-K_α radiation ($\lambda = 0.71073$ Å) at 100 K. Reflection intensities were integrated using SAINT software and absorption correction was applied semi-empirically using a SADABS program.

The structures were solved by direct methods and refined by full-matrix least-squares against F^2 in anisotropic approximation for non-hydrogen atoms. The analysis of Fourier density synthesis revealed that in complex [Δ-**1**]Ag the *i*-propyl groups in the three independent anions, the cobalt atom in one independent anion and one of silver cations are all disordered. The refinement of self occupancy factors (sof) for disordered fragments was carried out with constraints on thermal parameters and led in all cases except the cobalt atom to equal sof values for disordered fragments. In the case of Co(9) and Co(10), the sof for the two positions were 0.75 and 0.25, respectively. The C–C bond lengths for some disordered fragments were refined to be equal using the free variable. In addition to the above fragments, the solvate water molecules are also disordered and their refinement was performed in the same manner. For some positions, partial occupancy by water was observed.

The positions of the hydrogen atoms of methanol molecules in the [Λ-**1**]Ag structure were located from Fourier density synthesis while for all other hydrogen atoms in anions, in both structures positions were calculated geometrically. For water molecules in [Δ-**1**]Ag, the hydrogen atoms were not located. Crystal data and structure refinement parameters for both complexes are given in Table 5. All calculations were performed using the SHELXTL software.[10]

^{1}H NMR spectra were recorded on Bruker Avance 300 (300 MHz), and Bruker Avance-400 (400 MHz) spectrometers. Chemical shifts are reported on the δ scale relative to the signal of residual protons of the deuterated solvent. 2D-DOSY experiment parameters: Bruker Avance 600 MHz spectrometer (600.22 MHz ^{1}H), $\Delta = 200$ ms, $\delta = 1$ ms. All spectra were obtained under thermostatically controlled conditions at 298 K.

Optical rotations were measured on a Perkin–Elmer 241 polarimeter in a thermostated cell (5 cm) at 25 °C. The solvent and concentration in grams per 100 mL of the solvent are given for all compounds. Circular dichroism curves were recorded on a Jasper J 700 dichrograph. Melting points were determined in open capillary tubes and are uncorrected. Elemental analyses were carried out by the laboratory of Microanalysis of INEOS RAS.

Table 5. Crystal data and structure refinement parameters for [Δ-**1**]Ag and [Λ-**1**]Ag complexes

Compound	[Δ-**1**]Ag	[Λ-**1**]Ag
Empirical formula	$C_{24}H_{29}AgCoN_2O_{7.50}$	$C_{27}H_{38}AgCoN_2O_9$
Formula weight	632.29	701.39
Crystal color, habit	Dark-brown	Dark-brown
Temperature (K)	100(2)	100(2)
Crystal system	Monoclinic	Monoclinic
Space group	*C*2	*C*2
a (Å)	36.058(7)	19.8020(8)
b (Å)	22.758(5)	13.5109(7)
c (Å)	25.826(5)	14.1523(10)
β (°)	108.47(3)	130.969(5)
V (Å^3)	20101(8)	2858.9(4)
Z(*Z*′)	32 (8)	4(1)
F(000)	10272	1440
D_{calc} (g cm^{-1})	1.671	1.630
Linear absorption, μ (cm^{-1})	14.88	13.20
T_{min}/T_{max}	0.664/0.755	0.685/0.768
Scan type	ω	ω
θ Range (°)	1.57–28.34	1.57–29.00
Completeness of dataset (%)	99.7	99.0
Reflections measured	195,104	8127
Independent reflections	50,036 ($R_{int} = 0.0663$)	6542 ($R_{int} = 0.0132$)
Observed reflections [$I > 2\sigma(I)$]	38055	6397
Parameters	2577	368
Final $R(F_{hkl})$: R_1	0.0555	0.0183
wR_2	0.1407	0.0428
GOF	0.974	1.015
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.919/−1.605	0.461/−0.508

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 used.

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 a DP-TFA-γ-cD chiral stationary phase (32 m × 0.20 mm). The standard for each compound was its racemic form.

4.1. Kinetic measurements

To a round bottom flask were added a catalyst (0.06 mmol), followed by CH_2Cl_2 (3 mL), benzaldehyde (0.3 mL, 1 mmol), and TMSCN (0.45 mL, 3.72 mmol) under Ar with stirring at 25 °C. After certain time intervals, aliquots (10 μL) of the solution was withdrawn and were immediately added to hexane (1 mL), then 50 μL of this solution were withdrawn and added to hexane (3.8 mL), thus effectively stopping the reaction. The optical density of the solution was recorded at 241 nm (benzaldehyde absorption maximum) to allow the progress of the reaction to be monitored.

4.2. Synthesis of $K_3[Co(CO_3)_3]$ (modified method[11])

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) was added dropwise with cooling to 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. The dark-green precipitate that formed was filtered off and washed with water and EtOH to give the title compound (8.9 g) as a dark green solid. Mp >300 °C.

4.3. Synthesis of potassium Δ- and Λ-bis-(*N*-salicylidene-aminoacidato)cobaltates (general procedure)

Salicylaldehyde (10 mmol) was added with stirring to a mixture of $K_3[Co(CO_3)_3]$ (5 mmol) and an aminoacid (10 mmol) in EtOH. The reaction mixture was refluxed for 3 h, then filtered. The filtrate was concentrated in vacuo, and the residue was washed with diethyl ether, and dissolved in EtOH. The isomers were separated and purified 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.

4.4. Exchange of counterions (general procedure)

A complex (100 mg) was dissolved in a mixture of H_2O and EtOH (5 mL each) and slowly passed through a DOWEX-50 × 8 ion-exchange resin filled column, containing ions of the required metal as counterions. The resulting solution was concentrated, and the target product was purified by gel chromatography on Sephadex LH-20 using an EtOH–benzene (1:3) mixture as eluent.

4.5. Potassium Λ-bis-[*N*-salicylidene-(*S*)-valinato]-cobaltate [Λ-1]K

86% yield. Mp >300 °C, $[\alpha]_D^{25} = -5965$ (*c* 0.031, MeOH). ^{1}H NMR (300 MHz, D_2O): δ 1.07–1.12 (m, 12H, CH_3-

Val); 2.57–2.62 (m, 2H, β-CH-Val); 4.20 (d, *J* 8.1 Hz, 2H, α-CH-Val); 6.60 (t, *J* 7.8 Hz, 2H, CH_{Ar}); 6.77 (d, *J* 13.2 Hz, 2H, CH_{Ar}); 7.09 (d, *J* 8.1 Hz, 2H, CH_{Ar}); 7.43 (d, *J* 11.7 Hz, 2H, CH_{Ar}); 8.40 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}CoKN_2O_6{\cdot}2H_2O$: C, 50.35; H, 5.28; N, 4.89. Found: C, 50.65; H, 4.80; N, 5.11.

4.6. Potassium Δ-bis-[*N*-salicylidene-(*S*)-valinato]-cobaltate [Δ-1]K

86% yield. Mp >300 °C, $[\alpha]_D^{25} = -3630$ (*c* 0.030, MeOH). ^{1}H NMR (300 MHz, D_2O): δ 1.26–1.31 (m, 12H, CH_3-Val); 2.60–2.66 (m, 2H, β-CH-Val); 4.53 (d, *J* 8.0 Hz, 2H, α-CH-Val); 6.53–6.61 (m, 4H, CH_{Ar}); 6.97 (t, *J* 10.2 Hz, 2H, CH_{Ar}); 7.47 (d, *J* 7.1 Hz, 2H, CH_{Ar}); 8.48 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}CoKN_2O_6{\cdot}0.16C_6H_6$: C, 54.64; H, 4.95; N, 5.10. Found: C, 54.61; H, 5.15; N, 5.09.

4.7. Sodium Λ-bis-[*N*-salicylidene-(*S*)-valinato]-cobaltate [Λ-1]Na

87% yield. Mp >300 °C. $[\alpha]_D^{25} = -6185$ (*c* 0.031, MeOH); ^{1}H NMR (300 MHz, CD_3OD): δ 1.21–1.31 (m, 12H, CH_3-Val); 2.57–2.67 (m, 2H, β-CH-Val); 4.31 (d, *J* 8.1 Hz, 2H, α-CH-Val); 6.60 (t, *J* 7.8 Hz, 2H, CH_{Ar}); 6.81 (d, *J* 13.2 Hz, 2H, CH_{Ar}); 7.09 (d, *J* 8.1 Hz, 2H, CH_{Ar}); 7.43 (d, *J* 11.7 Hz, 2H, CH_{Ar}); 8.39 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}N_2O_6CoNa{\cdot}0.75EtOH{\cdot}0.5H_2O$: C, 54.31; H, 5.63; N, 4.97. Found: C, 54.34; H, 5.14; N, 4.64.

4.8. Sodium Δ-bis-[*N*-salicylidene-(*S*)-valinato]-cobaltate ([Δ-1]Na)

84% yield. Mp >300 °C. $[\alpha]_D^{25} = -3660$ (*c* 0.034, MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 1.26–1.31 (m, 12H, CH_3-Val); 2.60–2.66 (m, 2H, β-CH-Val); 4.53 (d, *J* 8.0 Hz, 2H, α-CH-Val); 6.53–6.61 (m, 4H, CH_{Ar}); 6.97 (t, *J* 10.2 Hz, 2H, CH_{Ar}); 7.47 (d, *J* 7.1 Hz, 2H, CH_{Ar}); 8.48 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}N_2O_6CoNa{\cdot}0.5H_2O$: C, 54.45; H, 5.14; N, 5.29. Found: C, 54.42; H, 5.46; N, 5.46.

4.9. Silver Λ-bis-[*N*-salicylidene-(*S*)-valinato]-cobaltate [Λ-1]Ag

83% yield. Mp >300 °C. $[\alpha]_D^{25} = -5600$ (*c* 0.029 MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 1.19–1.29 (m, 12H, CH_3-Val); 2.50–2.68 (m, 2H, β-CH-Val); 4.30 (d, *J* 8.1 Hz, 2H, α-CH-Val); 6.57 (t, *J* 7.8 Hz, 2H, CH_{Ar}); 6.77 (d, *J* 13.2 Hz, 2H, CH_{Ar}); 7.08 (t, *J* 7.65 Hz, 2H, CH_{Ar}); 7.46 (d, *J* 7.8 Hz, 2H, CH_{Ar}); 8.39 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}N_2O_6CoAg$: C, 47.62; H, 4.33; N, 4.63. Found: C, 47.43; H, 4.41; N, 4.30.

4.10. Silver Δ-bis-[*N*-salicylidene-(*S*)-valinato]-cobaltate [Δ-1]Ag

81% yield. Mp >300 °C. $[\alpha]_D^{25} = -2770$ (*c* 0.026 MeOH). ^{1}H NMR (300 MHz, CD_3OD): δ 1.26–1.31 (m, 12H, CH_3-Val), 2.61–2.66 (m, 2H, β-CH-Val); 4.53 (d, *J* 8.0 Hz, 2H, α-CH-Val); 6.61 (t, *J* 7.2 Hz, 2H, CH_{Ar}); 6.82 (d, *J* 8.4 Hz, 2H, CH_{Ar}); 6.97 (t, *J* 10.2 Hz, 2H, CH_{Ar}); 7.47 (d, *J* 7.1 Hz, 2H, CH_{Ar}); 8.48 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}N_2O_6CoAg{\cdot}0.5H_2O$: C, 46.93; H, 4.43; N, 4.56. Found: C, 46.90; H, 4.26; N, 4.33.

4.11. Potassium Δ-bis-[*N*-salicylidene-(*S*)-threoninato]-cobaltate [Δ-2]K

70% yield. Mp >300 °C, $[\alpha]_D^{25} = -5995$ (*c* 0.0022, MeOH). ^{1}H NMR (300 MHz, D_2O): δ 1.30 (d, *J* 8.7 Hz, 6H, CH_3-Thr); 4.19–4.21 (m, 2H, β-CH-Thr); 4.51 (d, *J* 8.1 Hz, 2H, α-CH-Thr); 6.58–6.60 (m, 4H, CH_{Ar}); 7.20 (t, *J* 9.6 Hz, 2H, CH_{Ar}); 7.50 (d, *J* 9.9 Hz, 2H, CH_{Ar}); 8.60 (s, 2H, CH=N). Anal. Calcd for $C_{22}H_{22}CoKN_2O_8{\cdot}2EtOH$: C, 50.91; H, 5.80; N, 4.24. Found: C, 50.80; H, 5.67; N, 4.59.

4.12. Sodium Δ-bis-[*N*-salicylidene-(*S*)-threoninato]-cobaltate ([Δ-2]Na)

75% yield. Mp >300 °C. $[\alpha]_D^{25} = -6405$ (*c* 0.025, MeOH). ^{1}H NMR (300 MHz, D_2O): δ 1.30 (d, *J* 8.7 Hz, 6H, CH_3-Thr), 4.21 (t, *J* 9.0 Hz, β-CH-Thr), 4.49 (d, *J* 8.2 Hz, 2H, α-CH-Thr), 6.58–6.62 (m, 4H, CH_{Ar}), 7.18 (t, *J* 9.6 Hz, 2H, CH_{Ar}), 7.53 (d, *J* 9.9 Hz, 2H, CH_{Ar}), 8.62 (s, 2H, CH=N). Anal. Calcd for $C_{22}H_{22}N_2O_8CoNa{\cdot}H_2O{\cdot}1/3\ C_6H_6$: C, 50.71; H, 4.61; N, 4.93. Found: C, 50.80; H, 4.67; N, 4.59.

4.13. Silver Δ-bis-[*N*-salicylidene-(*S*)-threoninato]-cobaltate [Δ-2]Ag

83% yield. Mp >300 °C. $[\alpha]_D^{25} = -5978$ (*c* 0.031 MeOH). ^{1}H NMR (300 MHz, D_2O): δ 1.53 (d, *J* 5.4 Hz, 6H, CH_3-Thr); 4.34–4.47 (m, 2H, β-CH-Thr); 4.53–4.78 (m, 2H, α-CH-Thr); 6.69 (t, *J* 7.35 Hz, 2H, CH_{Ar}); 6.84 (d, *J* 8.4 Hz, 2H, CH_{Ar}); 7.18 (t, *J* 7.8 Hz, 2H, CH_{Ar}); 7.54 (d, *J* 7.5 Hz, 2H, CH_{Ar}); 8.49 (s, 2H, CH=N). Anal. Calcd for $C_{22}H_{22}AgCoN_2O_8$: C, 43.48; H, 3.74; N, 4.69. Found: C, 43.37; H, 3.64; N, 4.60.

4.14. Potassium Λ-bis-[*N*-salicylidene-(*S*)-tryptophanato]-cobaltate [Λ-3]K

86% yield. Mp >300 °C, $[\alpha]_D^{25} = -4060$, $[\alpha]_{578}^{25} = -3740$, $[\alpha]_{546}^{25} = -738$ (*c* 0.032, MeOH). ^{1}H NMR (300 MHz, $D_2O + CD_3COCD_3$ (1:1)): δ 3.14, 3.41 (AB part of ABX system, J_{AB} 14.0 Hz, J_{AX} 8.4 Hz, J_{BX} 11.4 Hz, 4H, CH_2-Trp); 4.81–4.84 (m, X part of ABX system, 2H, α-H-Trp); 6.03 (d, *J* 8.0 Hz, 2H, CH_{Ar}); 6.15 (s, 2H, CH_{Ar}); 6.50 (d, *J* 9.0 Hz, 2H, CH_{Ar}); 6.68 (s, 2H, CH_{Ar}); 6.90 (s, 2H, CH_{Ar}); 6.97 (s, 4H, CH_{Ar}); 7.26 (d, *J* 7.4 Hz, 2H, CH_{Ar}); 7.43 (d, *J* 7.2 Hz, 2H, CH_{Ar}); 7.83 (s, 2H, CH=N). Anal. Calcd for $C_{36}H_{28}CoKN_4O_6{\cdot}Et_2O$: C, 61.22; H, 4.88; N, 7.14. Found: C, 61.53; H, 4.74; N, 7.57.

4.15. Potassium Δ-bis-[*N*-salicylidene-(*S*)-tryptophanato]-cobaltate [Δ-3]K

80% yield. Mp >300 °C, $[\alpha]_D^{25} = -5280$, $[\alpha]_{578}^{25} = -5510$, $[\alpha]_{546}^{25} = -4890$ (*c* 0.032, MeOH). ^{1}H NMR (400 MHz, $D_2O + CD_3COCD_3$ (1:1)): δ 3.14, 3.40 (AB part of ABX system, J_{AB} 13.2 Hz, J_{AX} 9.2 Hz, J_{BX} 12.8 Hz, 4H,

CH_2-Trp); 4.78–4.82 (m, X part of ABX system, 2H, α-H-Trp); 6.00 (d, J 8.4 Hz, 2H, CH_{Ar}); 6.17 (s, 2H, CH_{Ar}); 6.63 (d, J 9.2 Hz, 2H, CH_{Ar}); 6.70 (s, 2H, CH_{Ar}); 6.92 (s, 2H, CH_{Ar}); 7.00 (s, 4H, CH_{Ar}); 7.25 (d, J 7.2 Hz, 2H, CH_{Ar}); 7.40 (d, J 7.2 Hz, 2H, CH_{Ar}); 7.90 (s, 2H, CH=N). Anal. Calcd for $C_{36}H_{28}CoKN_4O_6$·EtOH: C, 60.31; H, 4.53; N, 7.40. Found: C, 60.37; H, 4.81; N, 7.21.

4.16. Sodium Λ-bis-[*N*-salicylidene-(*S*)-tryptophanato]-cobaltate [Λ-3]Na

84% yield. Mp >300 °C, $[\alpha]_D^{25} = -4860$, (c 0.029, MeOH). ^{1}H NMR (400 MHz, $D_2O + CD_3COCD_3$ (1:1)): δ 3.00, 3.42 (AB part of ABX system, J_{AB} 13.2 Hz, J_{AX} 9.2 Hz, J_{BX} 12.7 Hz, 4H, CH_2-Trp); 5.98–6.02 (m, X part of ABX system, 2H, -H-Trp); 6.11 (s, 2H, CH_{Ar}); 6.62 (d, J 9.2 Hz, 2H, CH_{Ar},); 6.71 (s, 2H, CH_{Ar}); 6.90 (s, 2H, CH_{Ar}); 7.04 (s, 4H, CH_{Ar}); 7.27 (d, J 7.2 Hz, 2H, CH_{Ar}); 7.43 (d, J 7.2 Hz, 2H, CH_{Ar}); 7.75 (s, 2H, CH=N). Anal. Calcd for $C_{36}H_{28}CoNaN_4O_6$·2EtOH·H_2O: C, 59.70; H, 5.26; N, 6.96. Found: C, 59.62; H, 5.21; N, 6.90.

4.17. Sodium Δ-bis-[*N*-salicylidene-(*S*)-tryptophanato]-cobaltate [Δ-3]Na

79% yield. Mp >300 °C, $[\alpha]_D^{25} = -5590$ (c 0.032, MeOH). ^{1}H NMR (400 MHz, $D_2O + CD_3COCD_3$ (1:1)): δ 3.15, 3.42 (AB part of ABX system, J_{AB} 13.2 Hz, J_{AX} 9.2 Hz, J_{BX} 12.7 Hz, 4H, CH_2-Trp); 4.84–4.86 (m, X part of ABX system, 2H, α-H-Trp); 6.00 (d, J 8.4 Hz, 2H, CH_{Ar}); 6.11 (s, 2H, CH_{Ar}); 6.62 (d, J 9.2 Hz, 2H, CH_{Ar}); 6.71 (s, 2H, CH_{Ar}), 6,9 (s, 2H, CH_{Ar}); 7.04 (s, 4H, CH_{Ar}); 7.27 (d, J 7.2 Hz, 2H, CH_{Ar}), 7.40 (d, J 7.2 Hz, 2H, CH_{Ar}); 7.75 (s, 2H, CH=N). Anal. Calcd for $C_{36}H_{28}CoNaN_4O_6$: C, 62.25; H, 4.06; N, 8.07. Found: C, 62.29; H, 4.36; N, 7.97.

4.18. Trimethylsilylcyanation of aldehydes (general procedure)

A Schlenk flask was evacuated and filled with argon whilst being heated with a heatgun. Then the flask was cooled under a flow of argon, and a catalyst (0.02 mmol), an additive (see Table 3) (0.1 mmol), CH_2Cl_2 (1 mL), aldehyde (1 mmol), and trimethylsilyl cyanide (0.15 mL, 0.111 g, 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 composition of the product was determined by gas chromatography. No additive was used in several experiments.

4.19. Asymmetric Mukaiyama reaction (general procedure)

A Schlenk flask was evacuated and filled with argon, whilst being heated with a heatgun. The flask was then cooled to room temperature under a flow of argon. A catalyst (0.05 mmol) was added to the flask and benzaldehyde (0.1 mL, 1 mmol) solution in CH_2Cl_2 (1 mL) was added. Then the solution was stirred for 2 min and α-(trimethylsilyloxy)styrene (0.2 mL, 0.188 g, 0.98 mmol) was added. The reaction mixture was stirred for 72 h under an argon atmosphere. The catalyst was removed from the reaction mixture by column chromatography on silica gel (column 60 × 5 mm), using CH_2Cl_2 as an eluent. The enantiomeric purity of the product was determined by chiral HPLC.

4.20. Crystallographic data

The crystallographic data have been deposited with the Cambridge Crystallographic Data Center, CCDC 671992 for [Δ-**1**]Ag and CCDC 671991 for [Λ-**1**]Ag. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

Acknowledgments

This work was financially supported by an ISTC Grant G-1361. The authors thank Dr. N. Ikonnikov for conducting chiral GLC analyses of the cyanohydrins and Dr. M. Ilyin for HPLC analyses of the Mukaiyama adducts.

References

1. Some recent references: (a) Saito, S.; Tsubogo, T.; Kobayashi, S. *J. Am. Chem. Soc.* **2007**, *129*, 5364–5365; (b) Sibi, M.; Stanley, L.; Soeta, T. *Org. Lett.* **2007**, *8*, 1553–1556; (c) Jankowska, J.; Paradowska, J.; Rakiel, B.; Mlynarski, J. *J. Org. Chem.* **2007**, *72*, 2228–2231; (d) Ooi, T.; Ohmatsu, K.; Maruoka, K. *J. Am. Chem. Soc.* **2007**, *129*, 2410–2411; (e) Saito, B.; Egami, H.; Katsuki, T. *J. Am. Chem. Soc.* **2007**, *129*, 1978–1986; (f) Liu, D.; Canales, E.; Corey, E. *J. Am. Chem. Soc.* **2007**, *129*, 1498–1499; (g) Zeng, W.; Chen, G.; Zhou, Y.; Li, Y. *J. Am. Chem. Soc.* **2007**, *129*, 750–751, and references cited therein.
2. A review: Fritz, V.; Staddart, J.; Shibasaki, M. *Simulating Concepts in Chemistry*; Wiley-VCH: New York, 2000.
3. (a) Lacour, J.; Jodry, J.; Ginglinger, C.; Torche-Haldimann, S. *Angew. Chem., Int. Ed.* **1998**, *17*, 2379–2380; (b) Pasquini, C.; Desvergenes-Breuil, V.; Jodry, J.; Cort, A.; Lacour, J. *Tetrahedron Lett.* **2002**, *43*, 423–426; (c) Vial, L.; Lacour, J. *Org. Lett.* **2002**, *4*, 3939–3942; (d) Lacour, J.; Hebbe-Vton, V. *Chem. Soc. Rev.* **2003**, *32*, 373–382; (e) Lacour, J.; Hebbe-Vton, V. *Chem. Soc. Rev.* **2003**, *32*, 373–382; (f) Lacour, J.; Frantz, R. *Org. Biomol. Chem.* **2005**, *3*, 15–19.
4. (a) Gonsalves-Faebos, M.; Vial, L.; Lacour, J. *Chem. Commun.* **2008**, 829–831; (b) Constant, S.; Tortoioli, S.; Muller, J.; Linder, D.; Buron, F.; Lacour, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 8979–8982.
5. (a) Llewellyn, D.; Arndtsen, B. *Organometallics* **2004**, *23*, 2838–2840; (b) Llewellyn, D.; Arndsten, B. *Tetrahedron: Asymmetry* **2005**, *16*, 1789–1799; (c) Gausepohl, R.; Buskens, P.; Kleinen, J.; Bruckmann, A.; Lehman, G. W.; Klankermayer, J.; Leitner, W. *Angew. Chem., Int. Ed.* **2006**, *45*, 3689–3692.
6. (a) Mayer, S.; List, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 4393–4395; (b) Wang, X.; List, B. *Angew. Chem., Int. Ed.* **2008**, *487*, 1119–1122; (c) Mukherjee, S.; List, B. *J. Am. Chem. Soc.* **2007**, *129*, 11336–11337; (d) Rueping, M.; Antonchick, A. P.; Brinkmann, C. *Angew. Chem., Int. Ed.* **2007**, *46*, 6903–6906, and references cited therein; (e) Hamilton, G. L.; Kang, E. J.; Mba, M.; Toste, F. D. *Science* **2007**, *317*, 496–499.

7. Λ- or Δ-correspond respectively to left and right spiral arrangement of ligands in relation to the C_2 axis of the complexes according to: Legg, J.; Douglas, B. *J. Am. Chem. Soc.* **1966**, *88*, 2697–2699.
8. Belokon, Y.; Belikov, V.; Vitt, S.; Saveleva, T.; Burbelo, V.; Bakhmutov, V.; Alexandrov, G.; Struchkov, Y. *Tetrahedron* **1977**, *33*, 2551.
9. Burrows, R.; Bailar, J. *J. Am. Chem. Soc.* **1966**, *88*, 4150–4253.
10. Sheldrick G. SHELXTL-*97, Version 5.10*; Bruker AXS: Madison, **1998**, WI-53719, USA.
11. Ellis, J. E.; Winzenburg, P. T.; Warnock, G. F. *J. Organomet. Chem.* **1990**, *383*, 521–530.