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Chiral ion pairs in catalysis: lithium salts of chiral metallocomplex anions as catalysts for asymmetric C–C bond formation

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ABSTRACT

A series of Co(III) anionic complexes of Schiff bases obtained from substituted salicylaldehydes and optically active amino acids has been synthesized. The ion pairing of these anions to a lithium cation can be used to induce asymmetry into lithium-catalyzed trimethylsilylcyanation of aldehydes and Michael reactions. The influence of the temperature, solvent polarity and structural modification of the chiral anion on the enantioselectivity of the catalysis has been investigated.

1. Introduction

Asymmetric synthesis using metal catalysts with the source of chirality residing in their cations has been the focus of great interest for many years.[1] However, little attention has been paid to complexes with chiral counteranions, although they have great potential as a novel type of asymmetric metal-based catalysts. In these complexes, the achiral cation can activate substrates and the chiral counteranion, being positioned away from the metal centre, is incorporated into the stereodetermining step.[2] The Lewis acidity of the cation in combination with the chiral, weakly coordinated anion should be enhanced in comparison with traditional metal complexes. Therefore, even alkali metal cations which are usually considered as weak Lewis acids, might become efficient catalysts in asymmetric transformations if chiral counteranions with delocalized charges were employed.

The strategy of chiral anion-mediated catalysis has only recently started to be explored.[3–5] A few examples exist of asymmetric reactions catalyzed by salts of alkali metal cations with chiral counteranions.[6–9] Shibasaki et al. reported the synthesis of bimetallic rare earth-alkali metal BINOL complexes and their successful application in catalytic asymmetric Michael additions and aldol reactions.[6] A mono-lithium BINOL salt in organic solvent was used in the asymmetric trimethylsilylcyanation of aldehydes by Kagan and Holmes.[7a] Ishihara et al. studied the same reaction in water as a cosolvent[7b] and described the enantioselective cyanosilylation of ketones in the presence of chiral lithium salts of phosphoric acids.[8] Nakajima et al. reported the use of the dilithium salt of 3,3′-dichlorobinaphthol in asymmetric aldol reactions.[9] Among other alkali metal cations, the lithium cation is considered to have the highest Lewis acidity.[10] For example, the lithium cation is a well-known catalyst for pericyclic reactions.[11] The group of Michl showed that a solution of the lithium salt of the permethylated icosahedral monocarbododecaborate, $LiCB_{11}Me_{12}$, in benzene is a much more effective catalyst than the usual solution of lithium perchlorate in diethyl ether.[11] A practically important application of $LiCB_{11}Me_{12}$ is catalysis of the radical polymerization of alkenes also reported by Michl.[12]

In previous work[13] we demonstrated that chiral anionic complexes of potassium and silver Λ- or Δ-bis[*N*-salicylidene-(*S*)-aminoacidato]cobaltates[14] can be used as Lewis acid catalysts in asymmetric trimethylsilylcyanation of aldehydes and Mukayama aldol reaction. It was deemed interesting to extend this approach to examine C–C bond-forming reactions catalyzed by lithium Λ- or Δ-bis[*N*-salicylidene-(*S*)-aminoacidato]cobaltates.

2. Results and discussion

Bis(*N*-salicylideneaminoacidato)cobaltates are coordinatively saturated anionic cobalt^{3+} complexes with two perpendicular tridentate ligands, which are the Schiff bases of salicylaldehyde and (*S*)-amino acids. These complexes were used earlier (by some of us) as chiral substrates for anionic Co^{3+} ligand alkylation in the syntheses of enantiomerically enriched amino acids.[15] The chiral cobaltate anion is stereochemically stable and retained its chiral integrity during the amino acid synthesis.[15] The complexes were synthesized by a modified literature procedure[16] as shown in Scheme 1.

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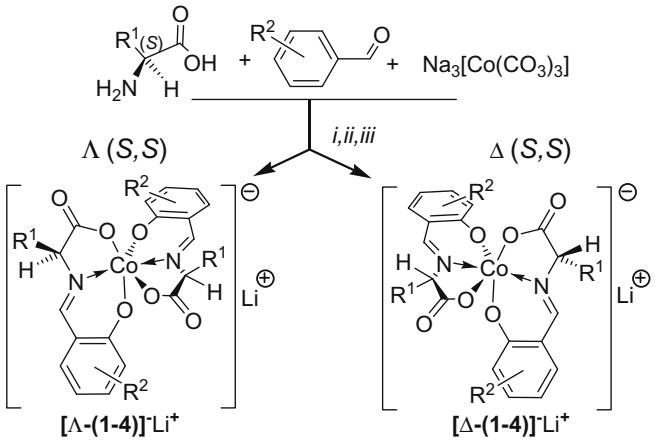


complex	1	2	3	4
R^1	^{i}Pr	^{i}Pr	^{t}Bu	^{i}Pr
R^2	H	3,3′-OMe	3,3′-OMe	3,3′-allyl

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).

The complexes exist as meridional Δ- and Λ-stereoisomers,[14] which are not interconverted under normal conditions (i.e., they are stereochemically inert) and 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. The general stereoselectivity trend was that an excess of the Δ(*S*,*S*)-isomer always formed during the synthesis.[15] The X-ray analyses of lithium salt with the chiral anion, bis[*N*-(3-methoxysalicyliden)-(*S*)-*tert*-leucinato]cobaltate [Λ-**3**]Li (Fig. 1) and its sodium analogue [Λ-**2**]Na (Fig. 2) have been carried out. Although both salts crystallize in the same space group (C2) and have very similar unit cell parameters (see Table 8), the binding of the cation to the complex anion is different. The coordination sphere of the alkali metal in [Λ-**3**]Li is filled by four oxygen atoms (Li···O 1.877(5)–2.119(12) Å): two of which belong to the methoxysalicylidene fragment of the ligand, while the others are from water molecules (Fig. 1). In the case of the [Λ-**2**]Na salt (Na···O 2.330(3)–2.415(3) Å) an additional M–O bond of 2.223(3) Å is formed with the carboxylate group of the neighbouring cobaltate anion. The crystal structure of [Λ-**2**]Na is actually a superimposition of the complex with two water molecules in the first coordination sphere of the sodium cation and one with H_2O(2W) replaced by methanol (Na···O 2.645(7) Å).

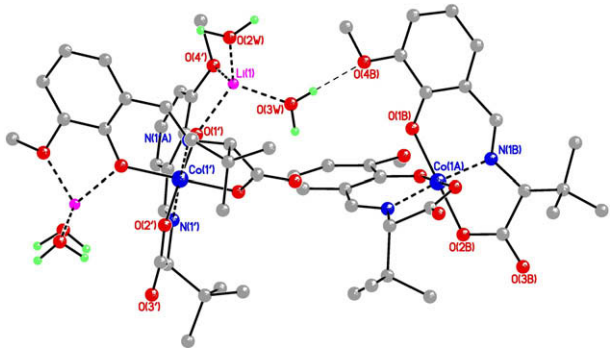


Figure 1. General view of compound [Λ-**3**]Li illustrating lithium to anion binding. Hydrogen atoms of the ligand as well as unbound water and ethanol molecules are omitted for clarity. Green spheres represent the remaining hydrogen atoms.

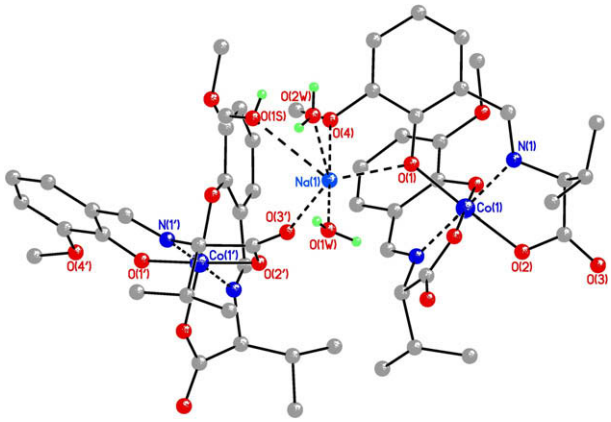
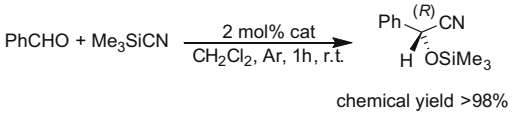


Figure 2. General view of compound [Λ-**2**]Na illustrating sodium to anion binding. Both the components of the superimposed solvent molecule, that is, water (shown as O(2W)) and methanol (shown as O(1S)) molecules, are given. Hydrogen atoms of the ligand are omitted for clarity. Green spheres represent the remaining hydrogen atoms.

The lithium salt also crystallizes as a solvate with one ethanol molecule per five complex species, but the ethanol does not bind to a cation. Although the exchange of lithium by sodium atom has only a small effect on the geometry of the complex anion, it leads to a variation of the supramolecular patterns in the corresponding crystals. Thus, the [Λ-**3**]Li salt has a typical isle structure. There are two independent moieties in its crystal: the cobaltate anions of the first type are connected with two alkali metal cations, while methoxysalicylidene fragments of the other species remain unbound, and thus the whole system is neutral. These structural units are held together by various H-bonds of intermediate strength (O···O 2.714(4)–3.032(4) Å), which, with a number of weak C–H···O and C–H···π contacts, result in the formation of the 3D framework. In contrast, the cobaltate anions in [Λ-**2**]Na are assembled into infinite chains through the sodium cations. The latter link the neighbouring complexes in such a way that species with two Na–OC bonds per anionic ligand and those with only one Na–OC bond alternate. These supramolecular associates are also interconnected with each other by means of H-bonds (O···O 2.818(3)–3.265(5) Å) and weaker C–H···O and C–H···π contacts.

Comparison of the Li and Na complexes indicates that the coordination of the Li cation is much more clearly defined and its stereochemical surrounding is easily predicted. In addition, the crystal structure of the Li complex has an alternation of separate $[LiALi]^+$ and $[A]^-$ moieties. One could envisage the anion [A] substituted by another anion, for example, a strongly basic one. This would constitute the typical catalytic pair of a Lewis acid and basic component of most nucleophilic additions of CH-acids to electrophiles. In addition, a water molecule coordinates to the Li cation in the structure, supporting the notion of the cation possessing Lewis acidity and modelling substrate coordination. Evidently, the lithium salts held the promise of becoming efficient chiral Lewis acids in a set of C–C forming reactions.

The asymmetric addition of trimethylsilyl cyanide to benzaldehyde was chosen as the first model reaction (Scheme 2). The reaction was carried out in methylene chloride under argon at 20 °C. No reaction was observed under these experimental conditions without a catalyst.



Scheme 2.

Table 1
Enantiomeric purity of (*R*)-mandelonitrile trimethylsilyl ether[a] in the reaction catalyzed by lithium complexes **1**–**4**[b]

Catalyst	**1**-Li	**2**-Li	**2**-Na[c]	**3**-Li	**4**-Li
Product ee (%) with catalyst of Δ configuration	23	24	9	0	0
Product ee (%) with catalyst of Λ configuration	22	40	16	12[d]	50 (60[e])

[a] For details of chiral GLC analysis see Section 4.
[b] Reaction conditions: PhCHO (1 mmol), TMSCN (1.1 mmol), catalyst (0.02 mmol), CH_2Cl_2 (1 mL), rt, under Ar, 1 h.
[c] 90% chemical yield.
[d] (*S*)-Mandelonitrile trimethylsilyl ether was formed.
[e] Reaction was carried out for 24 h at −20 °C.

Catalyst screening (Table 1) revealed that all the lithium complexes were catalytically active in this reaction. The chemical yield determined by NMR spectroscopy was >98% in the case of lithium salts and was 90% in the case of sodium salts (Table 1). The reaction proceeded quantitatively, but no chiral induction was observed, when [Δ-**3**]Li, or [Δ-**4**]Li complexes were used (Table 1).

The general trend was that low enantioselectivities were observed when complexes with a Δ configuration were used (Table 1, row 1). Complexes with a Λ-configuration showed moderate enantioselectivity (Table 1, row 2). Notably, (*S*)-valine-derived complex [Λ-**2**]Na generated a product with 16% enantiomeric excess, whereas its [Λ-**2**]Li analogue produced mandelonitrile trimethylsilyl ether with an enantiomeric excess of 40%. Increasing the steric bulk of the amino acid substituent (catalyst **3**) inverted the absolute configuration of trimethylsilylmandelonitrile into the (*S*)-form. Only one complex, [Λ-**4**]Li-containing allyl groups in the salicylidene fragment, afforded an enantioselectivity of 50%. A slightly better enantioselectivity (60%) was observed with [Λ-**4**]Li at −20 °C.

Increasing the amount of catalyst to 5 mol % or decreasing it to 0.5 mol % did not affect the enantioselectivity significantly (Table 2, entries 1–4). The stereoselectivity fell to only 19% when 0.1 mol % of [Λ-**2**]Li was used, but the yield was still high (Table 2, entry 5). Decreasing the amount of catalyst to 0.05 mol % further resulted in a relatively small change in ee (from 19% to 18%), but the chemical yield was only 78% (Table 2, entry 6). The catalyst (2 mol %) efficiently catalyzed the reaction without any added solvent, giving *O*-trimethylsilylmandelonitrile in quantitative yield and with 36% ee (Table 2, entry 7).

Table 2
Influence of the amount of catalyst on the enantioselectivity of benzaldehyde trimethylsilylcyanation with [Λ-**2**]Li as a catalyst[a]

Entry	Catalyst (mol %)	Yield (%)	ee[b] (%)
1	5	99	40
2	2	99	40
3	1	99	36
4	0.5	99	35
5	0.1	99	19
6	0.05	78	18
7[c]	2	99	36

[a] Reaction conditions: PhCHO (1 mmol), TMSCN (1.1 mmol), CH_2Cl_2 (1 mL), rt, under Ar, 1 h.
[b] Results of chiral GLC analysis, (*S*)-configuration.
[c] Reaction was carried out without solvent.

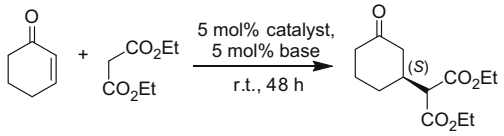
To evaluate the scope of the [Λ-**4**]Li catalyst system, the trimethylsilylcyanation of various aldehydes and acetophenone was examined (Table 3).

With aldehyde substrates, total conversion was observed after 24 h at −20 °C. The reaction of acetophenone occurred in the lowest yield. The introduction of electronegative substituents onto the aromatic ring of benzaldehyde resulted in a significant loss of enantioselectivity (Table 1, Table 3, runs 1 and 2). Cinnamaldehyde also gave lower asymmetric induction than benzaldehyde (Table 3, entry 3).

Table 3
The addition of TMSCN to a series of aldehydes catalyzed by [Λ-**4**]Li catalyst[a]

Run	Carbonyl compounds	Yield (%)	ee[b] (%)
1	4-F–C_6H_4CHO	>90	32
2	2-Cl–C_6H_4CHO	>90	42
3	PhCH=CHCHO	>90	37
4	PhCOMe	53	27

[a] Reaction conditions: carbonyl compounds (1 mmol), TMSCN (1.1 mmol), catalyst (0.02 mmol), CH_2Cl_2 (1 mL), under Ar, 24 h at −20 °C.
[b] Results of chiral GLC analysis, (*S*)-configurations.



Scheme 3.

The next reaction studied with our catalyst system was the asymmetric Michael reaction. The addition is an efficient method for enantioselective carbon–carbon bond formation.[17] An initial reaction of cyclohex-2-enone with diethyl malonate (Scheme 3) catalyzed by all the Li-complexes without any additional bases added failed to give the desired product after 48 h at ambient temperature.

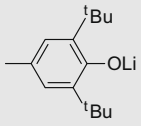
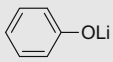
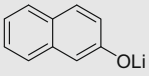
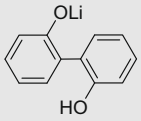
As expected (vide infra), Li salts of phenols were efficient co-catalysts of the reaction. Thus, premixing [Δ-**1**]Li with lithium 2,6-di-(*tert*-butyl)-4-methylphenolate in Et_2O, followed by addition of cyclohex-2-enone and diethyl malonate, afforded the desired product in 99% yield with 24% ee after 48 h. It should to be noted that there were no changes in the ^{1}H NMR spectrum of complex [Δ-**1**]Li after the addition of the phenolate. Thus, it appeared that the octahedral structure of the complex anion remained intact during the course of the reaction. Different solvents (Table 4), bases (Table 5) and temperatures were screened. Entries 2–9 in Table 4 show the effect of the solvent on the reaction catalyzed by [Δ-**1**]Li at room temperature. The solvent was seen to play a role in

Table 4
Asymmetric Michael addition catalyzed by [Δ-**1**]Li and lithium 2,6-di(*tert*-butyl)-4-methylphenolate[a]

Run	Solvent	Yield (%)	ee[b] (%)
1	Ether	99	24
2	CH_3CN	40	0
3	CH_2Cl_2	30	2
4	Toluene	72	1
5	Bu_2O	83	7
6	MeO^{t}Bu	58	31
7	THF	40	39
8	Dioxane	96	65–69
9	Dimethoxyethane	98	37

[a] Reaction conditions: cyclohex-2-enone (0.3 mmol), diethyl malonate (0.3 mmol), solvent (1 mL), under Ar, 48 h.
[b] Results of chiral HPLC analysis, (*S*)-configuration.

Table 5
Asymmetric Michael addition catalyzed by [Δ-**1**]Li and a number of lithium phenolates in dioxane[a]

Run	Base	Yield (%)	ee (%)[b]
1		96	65
2		87	69
3		97	52
4		20	55

[a] Reaction conditions: cyclohex-2-enone (0.3 mmol), diethyl malonate (0.3 mmol), dioxane (1 mL), under Ar, 48 h.
[b] Results of chiral HPLC analysis.

both the activity and the enantioselectivity, and dioxane gave the best results (Table 4, run 8). The variation of base led to PhOLi as the base of choice (Table 5, run 2). Finally, different Li-salts of bis-[*N*-salicyliden-(*S*)-valinato]cobaltates were tested as catalysts for the reaction (Table 6).

The results are summarized in Table 6. When the temperature was lowered to −20 °C, the enantioselectivity dropped significantly (Table 6, run 7). Raising the temperature to 50 °C also led to a significant decrease in enantioselectivity (Table 6, entry 8). Table 7 summarizes the influence of the dilution of the reaction on the catalyst efficiency. When the concentration of the catalyst was decreased to 0.015 M from 0.03 M, better enantioselectivity could be obtained (Table 7, entry 1 vs entry 2). Further decrease in the concentration of the catalyst and reagents led to less satisfying enantioselectivities (Table 7, entry 3). It seems that the catalytically active species might involve both dimeric and monomeric species, the relative amounts of which depend on the concentration of the catalyst. The dilution of the reaction mixture was found to result in an increase in enantioselectivity. This might indicate that the catalytically active species responsible for the asymmetric induction is a monomeric complex.

Table 6
Asymmetric Michael addition catalyzed by lithium complexes **1**, **2** and **4** with lithium phenolate as cocatalyst[a]

Entry	Catalyst	Yield (%)	ee (%) (configuration)[b]
1	[Δ-**1**]Li	96	69(*S*)
2	[Λ-**1**]Li	11	4(*R*)
3	[Δ-**2**]Li	57	58(*S*)
4	[Λ-**2**]Li	17	10(*R*)
5	[Δ-**4**]Li	68	56(*S*)
6	[Λ-**4**]Li	80	0
7[c]	[Δ-**1**]Li	98	0
8[d]	[Δ-**1**]Li	97	49(*S*)

[a] Reaction conditions: cyclohex-2-enone (0.3 mmol), diethyl malonate (0.3 mmol), dioxane (1 mL), under Ar, 48 h.
[b] Results of chiral HPLC analysis.
[c] Reaction was carried out at −20 °C.
[d] Reaction was carried out at 50 °C for 7 h.

3. Conclusion

The strategy described in the present work has demonstrated the ability of a chiral lithium ion-pair catalyst to promote the enantioselective cyanation of aldehydes and ketones, and an asymmetric Michael reaction, which might provide a new direction for the design of chiral catalysts for asymmetric catalysis. The ease of preparation and structural modification of the metallocomplex anions may improve the performance of the catalytic systems. Studies directed toward this are currently underway.

4. Experimental

X-ray diffraction experiments for [Λ-**3**]Li and [Λ-**2**]Na were carried out with a Bruker SMART APEX2 CCD diffractometer [Λ(Mo Kα) = 0.71072 Å, ω-scans] at 100 K.

Structures were solved by the direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. The hydrogen atoms of water molecules and those of the methanol molecule in [Λ-**2**]Na were located from the Fourier synthesis of the electron density and refined in the isotropic approximation. The hydrogen atoms of the O3W water molecule in [Λ-**2**]Na and that of the OH group of the ethanol molecule in [Λ-**3**]Li were not localized due to their strong disorder. The H(C) atom positions were calculated. The hydrogen atoms H(C) were refined in the isotropic approximation in riding model. Crystal data and structure refinement parameters for [Λ-**3**]Li and [Λ-**2**]Na are given in Table 8. All calculations were performed using the SHELXTL software.[18]

^{1}H NMR spectra were recorded on a Bruker Avance 300 (300 MHz) spectrometer. Chemical shifts are reported in ppm on the δ scale relative to the signal of residual protons of the deuterated solvent, spin-coupling constant in Hertz.

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. Melting points were determined in open capillary tubes and are uncorrected. Elemental analyses were carried out by the laboratory of Microanalysis of INEOS RAS.

Silica Gel Kieselgel 60 (Merck), Al_2O_3 (Chemapol) and Sephadex LH-20 were used. Solvents were purified by standard procedures. Freshly distilled reagents were used for chromatographic separations.

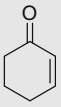
Enantiomeric analysis of the synthesized trimethylsilyl ethers of cyanohydrins was carried out on a gas chromatograph (model 3700-00) equipped with a flame-ionization detector on a DP-TFA-γ-cD chiral stationary phase (32 m × 0.20 mm). The standard for each compound was its racemic form. The absolute configuration of the major product was determined by comparison with the reported value of the specific rotation.[13]

The enantiomeric purity of the synthesized Michael adducts was determined by chiral HPLC analysis (Chiralpak AS-H chiral stationary phase, *i*PrOH–hexane/1:9, 210 nm). The absolute configuration of the major product was determined by comparison with the reported value of the specific rotation.[19]

4.1. Synthesis of $Na_3[Co(CO_3)_3]$ (modified method[20])

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 Na_2CO_3 (13.4 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 (7.5 g) as a dark green solid with mp >300 °C.

Table 7
The influence of dilution on the performance of the [Δ-**1**]Li catalyst in the addition of diethyl malonate to cyclohex-2-enone[a]

Run	Dioxane volume (mL)	Concentration (M) of			Yield (%)	ee (%)
		[Δ-1]Li		$CH_2(COOEt)_2$		
1	0.5	0.03	0.6	0.6	99	55
2	1	0.015	0.3	0.3	99	65
3	2	0.0075	0.15	0.15	99	62

[a] The experimental conditions are the same as in run 1 (Table 6) with the exception of varying volumes of dioxane.

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

Salicylaldehyde (10 mmol) was added with stirring to a mixture of $Na_3[Co(CO_3)_3]$ (5 mmol) and an amino acid (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.

A resulted sodium complex (100 mg) was dissolved in 10 mL 50% aqueous solution of EtOH and slowly passed through a DOWEX-50 × 8 ion-exchange resin filled column, containing lithium cations 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.

4.2.1. Sodium Λ-bis[*N*-(3-methoxysalicylidene)-(*S*)-valinato] cobaltate [Λ-2]Na

90% Yield. Mp >300 °C. $[\alpha]_D^{25} = -3697$ (*c* 0.035, MeOH). ^{1}H NMR (CD_3OD): 1.24–1.27 (m, 12H, CH_3-Val); 2.45–2.58 (m, 2H, β-H-Val); 3.28 (s, 6H, OMe); 4.49 (d, *J* 7.5, 2H, α-H-Val); 6.41 (t, 2H, *J* 7.8, CH_{Ar}); 6.56 (d, *J* 7.8, 2H, CH_{Ar}); 7.03 (d, *J* 7.8 Hz, 2H, CH_{Ar}); 8.31 (s, 2H, CH=N). Anal. Calcd for $C_{26}H_{30}N_2O_8CoNa$: C, 53.80; H, 5.21; N, 4.83. Found: C, 53.5; H, 5.45; N, 4.42.

4.2.2. Sodium Δ-bis[*N*-(3-methoxysalicylidene)-(*S*)-valinato] cobaltate [Δ-2]Na

84% Yield. Mp >300 °C. $[\alpha]_D^{25} = -8046$ (*c* 0.035, MeOH). ^{1}H NMR (CD_3OD): 1.16–1.27 (m, 12H, CH_3-Val); 2.79–2.89 (m, 2H, β-H-Val); 3.61 (s, 6H, OMe); 4.13 (d, *J* 8.1, 2H, α-H-Val); 6.47 (t, 2H, *J* 7.8, CH_{Ar}); 6.69 (d, 2H, *J* 7.5, CH_{Ar}); 7.06 (d, *J* 8.1, 2H, CH_{Ar}); 8.29 (s, 2H, CH=N). Anal. Calcd for $C_{26}H_{30}N_2O_8CoNa$: C, 53.80; H, 5.21; N, 4.83. Found: C, 53.75; H, 5.34; N, 4.62.

4.2.3. Lithium Λ-bis[*N*-salicylidene-(*S*)-valinato]cobaltate [Λ-1]Li

89% Yield. Mp >300 °C. $[\alpha]_D^{25} = -4031$ (*c* 0.032, MeOH); ^{1}H NMR (CD_3OD): 1.17–1.29 (m, 12H, CH_3-Val); 2.50–2.65 (m, 2H, β-H-Val); 4.49–4.6 (d, *J* 7.2, 2H, α-H-Val); 6.49–6.60 (m, 4H, CH_{Ar}); 6.85 (t, 2H, *J* 6.9, CH_{Ar}); 7.48 (d, *J* 7.1, 2H, CH_{Ar}); 8.43 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}N_2O_6CoLi{\cdot}2H_2O$: C, 53.34; H, 5.60; N, 5.18. Found: C, 53.15; H, 5.66; N, 5.11.

4.2.4. Lithium Δ-bis[*N*-salicylidene-(*S*)-valinato]cobaltate [Δ-1]Li

84% Yield. Mp >300 °C. $[\alpha]_D^{25} = -8631$ (*c* 0.032, MeOH). ^{1}H NMR (CD_3OD): 1.21–1.27 (m, 12H, CH_3-Val); 2.52–2.65 (m, 2H, β-H-Val); 4.27 (d, *J* 6.6, 2H, α-H-Val); 6.56 (t, *J* 6.9, 2H, CH_{Ar}); 6.77 (d, *J* 8.4, 2H, CH_{Ar}); 7.07 (t, *J* 6.9, 2H, CH_{Ar}); 7.43 (d, 2H, *J* 7.8, CH_{Ar}); 8.39 (s, 2H, CH=N). Anal. Calcd for $C_{24}H_{26}N_2O_6CoLi{\cdot}2H_2O$: C, 53.34; H, 5.60; N, 5.18. Found: C, 53.11; H, 5.72; N, 5.09.

4.2.5. Lithium Λ-bis[*N*-(3-methoxysalicylidene)-(*S*)-valinato] cobaltate [Λ-2]Li

90% Yield. Mp >300 °C. $[\alpha]_D^{25} = -3458$ (*c* 0.031, MeOH). ^{1}H NMR (CD_3OD): 1.26–1.27 (m, 12H, CH_3-Val); 2.43–2.54 (m, 2H, β-H-Val); 3.26 (s, 6H, OMe); 4.47 (d, *J* 7.3, 2H, α-H-Val); 6.38 (t, 2H, *J* 7.8, CH_{Ar}); 6.56 (d, *J* 7.6, 2H, CH_{Ar}); 6.97 (d, *J* 7.8, 2H, CH_{Ar}); 8.32 (s, 2H, CH=N). Anal. Calcd for $C_{26}H_{30}N_2O_8CoLi{\cdot}3.5H_2O$: C, 49.77; H, 5.94; N, 4.46. Found: C, 49.78; H, 5.93; N, 4.3.

4.2.6. Lithium Δ-bis[*N*-(3-methoxysalicylidene)-(*S*)-valinato] cobaltate [Δ-2]Li

86% Yield. Mp >300 °C. $[\alpha]_D^{25} = -6982$ (0.034, MeOH). ^{1}H NMR (CD_3OD): 1.18–1.28 (m, 12H, CH_3-Val); 2.75–2.86 (m, 2H, β-H-Val); 3.56 (s, 6H, OMe); 4.16 (d, *J* 8.3, 2H, α-H-Val); 6.48 (t, 2H, *J* 7.8, CH_{Ar}); 6.64 (d, 2H, *J* 7.5, CH_{Ar}); 7.04 (d, *J* 8.1, 2H, CH_{Ar}); 8.32 (s, 2H, CH=N). Anal. Calcd for $C_{26}H_{30}N_2O_8CoLi{\cdot}H_2O$: C, 53.62; H, 5.54; N, 4.81. Found: C, 54.10; H, 5.54; N, 4.92.

Table 8
Crystal data and structure refinement parameters for [Λ-**3**]Li and [Λ-**2**]Na complexes

Compound	[Λ-**3**]Li	[Λ-**2**]Na
Empirical formula	$C_{56.80}H_{82}Co_2Li_2N_4O_{22.40}$	$C_{52.70}H_{69.40}Co_2N_4Na_2O_{20.36}$
Formula weight	1311.00	1248.36
Temperature (K)	100	100
Crystal system	Monoclinic	Monoclinic
Space group	*C*2	*C*2
Z	2	2
a (Å)	21.0102(10)	19.1457(10)
b (Å)	14.6857(8)	14.0064(8)
c (Å)	14.4266(8)	13.7010(7)
β (°)	132.654(5)	129.359(5)
V (Å^3)	3273.8(4)	2840.8(3)
F(0 0 0)	1380	1305
D_{calc} (g cm^{-1})	1.330	1.459
Linear absorption, μ (cm^{-1})	5.83	6.79
$2\theta_{max}$ (°)	57	58
Completeness of dataset (%)	100	99.6
Reflections measured	20,065	16,341
Independent reflections	8661	7484
Observed reflections [$I > 2\sigma(I)$]	7692	6813
Parameters	384	389
R_1	0.0560	0.0373
wR_2	0.1535	0.0882
GOF	1.007	0.998
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.006/−1.375	0.659/−0.448

4.2.7. Lithium Λ-bis[*N*-(3-methoxysalicylidene)-(*S*)-*tert*leucinato]cobaltate [Λ-3]Li

84% Yield. Mp >300 °C. $[\alpha]_D^{25} = -4500$ (*c* 0.027, MeOH). ^{1}H NMR (D_2O): 1.13 (s, 18H, Me_3C); 3.08 (s, 6H, OMe); 4.52 (s, 2H, α-H-Val); 6.43-6.54 (m, 4H, CH_{Ar}); 6.99 (d, *J* 6.4, 2H, CH_{Ar}); 8.24 (s, 2H, CH=N). Anal. Calcd for $C_{28}H_{34}N_2O_8CoLi{\cdot}3H_2O$: C, 52.02; H, 6.24; N, 4.33. Found: C, 51.89; H, 6.51; N, 4.39.

4.2.8. Lithium Δ-bis[*N*-(3-methoxysalicylidene)-(*S*)-*tert*leucinato]cobaltate [Δ-3]Li

82% Yield. Mp >300 °C. $[\alpha]_D^{25} = -5763$ (*c* 0.027, MeOH). ^{1}H NMR (D_2O): 1.17 (s, 18H, Me_3C); 3.62 (s, 6H, OMe); 4.29 (s, 2H, α-H-Val); 6.22 (t, *J* 7.3, 2H, CH_{Ar}); 6.84 (d, *J* 7.9, 2H, CH_{Ar}); 7.14 (d, *J* 7.9, 2H, CH_{Ar}); 8.34 (s, 2H, CH=N). Anal. Calcd for $C_{28}H_{34}N_2O_8CoLi{\cdot}3H_2O$: C, 52.02; H, 6.24; N, 4.33. Found: C, 52.19; H, 6.37; N, 4.10.

4.2.9. Lithium Λ-bis[*N*-(3-allylsalicylidene)-(*S*)-valinato] cobaltate [Λ-4]Li

84% Yield. Mp >300 °C. $[\alpha]_D^{25} = -4633$ (*c* 0.06, MeOH). ^{1}H NMR (CD_3OD): 1.18–1.28. (m, 12H, CH_3-Val); 2.55 (m, 2H, β-H-Val); 2.76 (AB part of ABX, J_{AB} 15.0, J_{AX} 8.0, J_{BX} 6.6, 4H, CH_2-Allyl); 4.38 (m, 2H, α-H-Val); 4.64–4.72 (m, 4H, H_2C=); 5.32 (m, 2H, X part of ABX, =CH–); 6.41 (t, *J* 7.4, 2H, CH_{Ar}); 6.74 (d, *J* 6.5, 2H, CH_{Ar}); 7.22 (d, 2H, *J* 7.7, CH_{Ar}); 8.33 (s, 2H, CH=N). Anal. Calcd for $C_{30}H_{34}N_2O_6CoLi{\cdot}4H_2O$: C, 54.88; H, 6.45; N, 4.27. Found: C, 55.08; H, 5.72; N, 3.90.

4.2.10. Lithium Δ-bis[*N*-(3-allylsalicylidene)-(*S*)-valinato] cobaltate [Δ-4]Li

84% Yield. Mp >300 °C. $[\alpha]_D^{25} = -732$ (*c* 0.044, MeOH). ^{1}H NMR (CD_3OD): 1.22–1.38 (m, 12H, CH_3-Val); 2.86 (m, 2H, β-H-Val); 2.92, 3.18 (AB part of ABX, J_{AB} 15.1, J_{AX} 5.0, J_{BX} 7.2, 4H, CH_2-Allyl); 4.46 (m, 2H, α-H-Val); 4.60–4.73 (m, 4H, H_2C=); 5.46 (m, 2H, X part of ABX, =CH–); 6.48 (t, *J* 7.2, 2H, CH_{Ar}); 6.89 (d, *J* 7.2, 2H, CH_{Ar}); 7.34 (d, 2H, *J* 7.9, CH_{Ar}); 8.50 (s, 2H, CH=N). Anal. Calcd for $C_{30}H_{34}N_2O_6CoLi{\cdot}1.25H_2O$: C, 59.36; H, 6.06; N, 4.62. Found: C, 59.25; H, 6.12; N, 4.29.

4.3. Syntheses of lithium phenolates were conducted according to the literature procedure.[21]

4.3.1. Lithium 2,6-di-(*tert*-buthyl)-4-methylphenolate

Anal. Calcd for $C_{15}H_{23}OLi{\cdot}1.25H_2O$: C, 72.41; H, 10.33. Found: C, 72.35; H, 9.90.

4.3.2. Lithium phenolate

Anal. Calcd for $C_6H_5OLi{\cdot}2H_2O$: C, 52.96; H, 6.67. Found: C, 52.81; H, 6.70.

4.3.3. Lithium 2-naphtholate

Anal. Calcd for $C_{10}H_7OLi{\cdot}2H_2O$: C, 64.53; H, 5.96. Found: C, 64.04; H, 5.91.

4.3.4. Mono lithium salt of biphenyl-2,2′-diol

Anal. Calcd for $C_{12}H_9OLi{\cdot}2H_2O$: C, 68.58; H, 5.28. Found: C, 69.01; H, 5.91.

4.4. 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), (0.1 mmol), CH_2Cl_2 (1 mL), aldehyde (1 mmol) and trimethylsilyl cyanide (0.14 mL, 0.11 g, 1.1 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 SiO_2 layer, eluting the reaction product with CH_2Cl_2. The enantiomeric composition of the product was determined by gas chromatography.

4.5. Asymmetric Michael reaction (general procedure)

A Schlenk flask was evacuated and filled with argon, whilst being heated with a heatgun. Then the flask was cooled to room temperature under a flow of argon. A catalyst (0.015 mmol) and a base (0.015 mmol) were added to the flask and cyclohex-2-enone (0.03mL, 0.3 mmol) solution in dioxane (1 mL) was added. Then the solution was stirred for 2 min and diethyl malonate (0.046 mL, 0.049 g, 0.3 mmol) was added. The reaction mixture was stirred for 48 h under an argon atmosphere. The catalyst was removed from the reaction mixture by column chromatography on silica gel (column 60 × 5 mm), using EtOAc as an eluent. The enantiomeric purity of the product was determined by chiral HPLC.

4.6. Crystallographic data

The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre, CCDC 729876 for [Λ-**3**]Li and CCDC 729877 for [Λ-**2**]Na. 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).

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