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Alternative cocrystallization of "almost" enantiomers and true enantiomers in some *cis*-β-organocobalt salen-type complexes with α-amino acids

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Abstract

The reaction of a chiral *cis*-β-organocobalt salen-type complex, **1**, racemic mixture of *Δ* and *Λ* enantiomers, with enantiomerically pure L-histidine and a non-chiral monocationic cobalt complex, **3**, resulted quite unexpectedly in the cocrystallization of diastereomers. Each diastereomer is a dicobalt monocationic complex, where four positions around one metal center are occupied by the tetradentate ligand in a *cis* fashion, the remaining two positions being occupied by L-histidinate. Histidinate further axially coordinates the other Co atom through the nitrogen of the imidazole residue. The two diastereomers are related by a quasi-symmetry center. In this case, the opposite helical chirality of the metal complex **1** prevails over the identical configuration of the asymmetric carbon in the crystallization process and the diastereomers behave as if they were enantiomers.

The reaction of the same cobalt complexes **1** and **3** with DL-histidine led to the formation of two pairs of enantiomers, which crystallized separately as racemic compound. Therefore, in this case, the chirality of the asymmetric center is the property that allows the mutual selective recognition of the "true" enantiomers and drives their cocrystallization.

Keywords: Organocobalt; Salen; *cis*-Configuration; Diastereomers cocrystallization

1. Introduction

Metal complexes with tetradentate Schiff base ligands derived from salicylaldehyde and diamines (salen-type ligands) generally adopt a *trans* planar geometry but, in some instances, the quadridentate ligand may assume a *cis*-β-configuration [1]. In the last years, the interest in *cis*-β metal Schiff base complexes has been renewed, as they are well suited, in principle, for enantioselective catalysis, being chiral and having two labile mutually *cis* coordination sites. Quite recently, some *cis*-β-cobalt (III) salen type derivatives proved to be efficient catalysts for the enantioselective Baeyer–Villiger oxidation [2] and in the asymmetric sulfoxidation [3].

We have reported the synthesis and the characterization of the diastereomers obtained from the reaction between the *cis*-β folded organocobalt salen complex **1** (Chart 1), present as racemic mixture of *Δ* and *Λ* enantiomers, with enantiomerically pure α-L amino acids [4]. In fact, α-amino acids are able to chelate the two labile *cis* coordination positions of **1** with the amino and the carboxylate groups. The reaction with L-tyrosine afforded a mixture of the two diastereomers (Δ_{Co}L-tyr)-**2**

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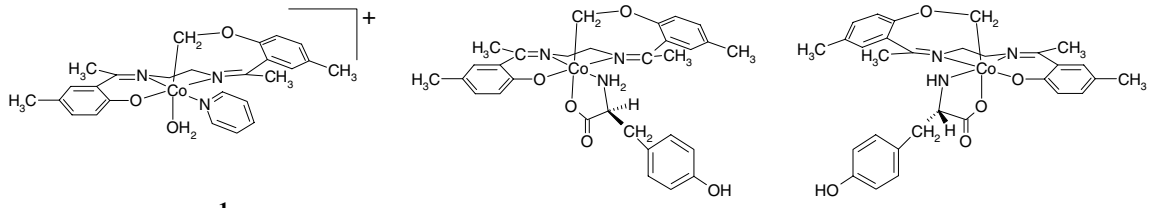


1 (Δ_{Co}L-tyr)-**2** (Λ_{Co}L-tyr)-**2**

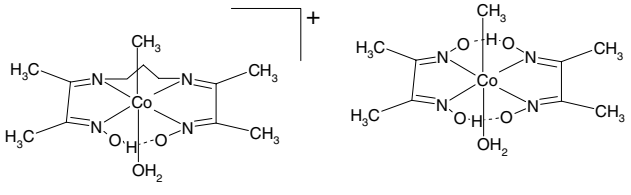
Chart 1.

and (Λ_{Co}L-tyr)-**2** (Chart 1), which could be separated by fractional crystallization owing to the lower solubility of the diastereomer (Δ_{Co}L-tyr)-**2** [4].

Unlike tyrosine and other previously tested amino acids [4], L-histidine has a further binding site, which can be used to coordinate a second metal center, giving a dinuclear complex containing two chiral centers. Therefore, we have extended our investigation to the reaction among racemic **1**, a second non-chiral organocobalt (III) complex (**3** or **4**, Chart 2), and either L-histidine or DL-histidine. Quite unexpectedly, the reaction with L-histidine resulted in the cocrystallization of the diastereomers, whereas the reaction with DL-histidine resulted in the cocrystallization of the enantiomers. The cocrystallization of enantiomers is well known [5], but there are few examples of cocrystallization of diastereomers of metal complexes [6]. Furthermore, to our knowledge, no examples are reported in which a chiral complex, which cocrystallizes with a diastereomer in the absence of the "true" enantiomer, is able to recognize selectively the latter, if present in solution, to form exclusively the racemic compound.

2. Experimental

General information. ^{1}H NMR spectra were recorded on a Jeol EX-400 (^{1}H at 400 MHz) and were referenced to residual solvent protons. Electrospray mass spectra were recorded in positive mode by using an API 1 mass spectrometer (Perkin–Elmer). CD spectra were obtained with a Jasco J-170 spectropolarimeter. The complexes **1** [7], **3** [8], and **4** [9] were synthesized as previously described. All the reagents and the solvents were commercially obtained and were used without further purification.



Cation of **3** **4**

Chart 2.

Caution: Perchlorate salts of metal complexes with organic ligands are potentially explosive. Only small amounts of material should be prepared, and these should be handled with great care.

2.1. Synthesis of 5

A solution of L-histidine (13 mg, 0.084 mmol in 1 mL of H_2O) and a solution of **3** (36 mg, 0.084 mmol in 2 mL of MeOH) were added subsequently to a solution of racemic **1** (0.050 g, 0.084 mmol in 8 mL of MeOH). After the addition of 4 mL of water, the pH was adjusted to 9 with NaOH 1 M. The solution was filtered and set aside for evaporation. An orange solid, equimolar diastereomeric mixture of ($\Delta_{Co}L_{his}$)-**5** and ($\Lambda_{Co}L_{his}$)-**5**, was collected by filtration. The recrystallization from CH_2Cl_2/*n*-heptane afforded single crystals of **5** suitable for X-ray analysis.

Yield: 52 mg (64%). Anal. Calc. for $C_{39}H_{54}N_9O_{10}Co_2Cl \cdot H_2O$: C, 47.8; H, 5.76; N, 12.9. Found: C, 47.6; H, 5.67; H, 12.6%. ESI-MS (90 V, CH_2Cl_2): *m*/*z*+ calcd: 962.2. Found: 862.2 (**5** − ClO_4^-, 100%).

^{1}H NMR spectrum of **5** (400 MHz, DMSO-d_6, see Chart 3 for the numbering scheme). ($\Delta_{Co}L_{his}$)-**5**: δ (ppm) = 0.28 (m, 1H, H-N1ha), 0.60 (s, 3H, H-C29a), 1.53 (m, 1H, H-C27a), 1.60 (m, 1H, H-N1ha), 1.94 (m, 1H, H-C27a), 2.15 (s, 3H, H-C4ma), 2.14 (s, 3H, H-C1ma), 2.24 (s, 3H, H-C18a or H-C25a), 2.30 (s, 3H, H-C18a or H-C25a), 2.36 (s, 3H, H-C3ma), 2.38 (s, 3H, H-C21a or H-C22a), 2.42 (s, 3H, H-C21a or H-C22a), 2.49 (s, 3H, H-C2ma), 2.50–2.70 (m, 2H, H-C2ha and H-C3ha), 2.85 (m, 1H, H-C3ha), 3.15–3.35 (m, 1H, H-C8a), 3.61–3.68 (m, 4H, H-C26a and H-C28a), 3.80 (m, 1H, H-C8a), 4.03 (m, 1H, H-C9a), 4.38 (m, 1H, H-C9a), 5.92 (d, 1H, H-C17a), 6.05 (s, 1H, H-C5ha), 6.39 (d, 1H, H-C2a), 6.62 (d, 1H, H-C17a), 6.80 (dd, 3H, H-C3a), 7.14 (d, 1H, H-C15a), 7.18–7.24 (m, 3H, H-C14a, H-C12a, H-C6ha), 7.32 (bs, 1H, H-C5a), 12.42 (bs, 1H, H-N3ha), 19.04 (s, 1H, O3a$^{\cdot\cdot}$ H$^{\cdot\cdot}$O4a). ($\Lambda_{Co}L_{his}$)-**5**: δ (ppm) = 0.62 (s, 3H, H-C29b), 0.91 (m, 1H, H-N1hb), 1.53 (m, 1H, H-C27b), 1.94 (m, 1H, H-C27b), 2.13 (s, 3H, H-C1mb), 2.16 (s, 3H, H-C4mb), 2.27 (s, 3H, H-C18b or H-C25b), 2.33 (s, 3H, H-C18b or H-C25b), 2.40 (s, 3H, H-C3mb), 2.40 (s, 3H, H-C21b or H-C22b), 2.44 (s, 3H, H-C21b or H-C22b), 2.40–2.50 (m, 1H, H-N1hb),

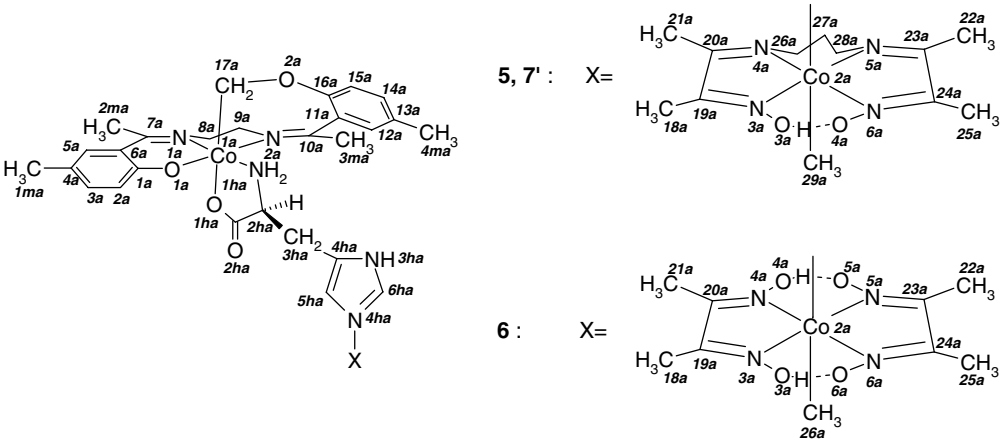


Chart 3. Numbering scheme for the cations of **5** and **7′** and for **6**.

2.45 (s, 3H, H-C2mb), 2.45–2.7 (m, 2H, H-C3hb), 3.14 (m, 1H, H-C2hb), 3.20–3.25 (m, 1H, H-C8b), 3.61–368 (m, 4H, H-C26b and H-C28b), 3.86 (m, 1H, H-C8b), 4.03 (m, 1H, H-C9b), 4.57 (m, 1H, H-C9b), 6.00 (s, 1H, H-C5hb), 6.32 (d, 1H, H-C17b), 6.35 (d, 1H, H-C2b), 6.65 (d, 1H, H-C17b), 6.73 (dd, 3H, H-C3b), 6.91 (bs, 1H, H-C12b), 7.14 (d, 1H, H-C15b), 7.18–7.24 (m, 2H, H-C14b and H-C6hb), 7.29 (bs, 1H, H-C5b), 13.02 (bs, 1H, H-N3hb), 19.07 (s, 1H, O3b··H··O4b).

2.2. Synthesis of *6*

The reaction was performed as described above using **4** (27 mg, 0.084 mmol in 2 mL of MeOH) instead of **3**. An orange solid, equimolar diastereomeric mixture of ($\Delta_{Co}L_{his}$)-**6** and ($\Lambda_{Co}L_{his}$)-**6**, was collected by filtration. The recrystallization from CH_2Cl_2/*n*-heptane afforded single crystals suitable for X-ray analysis. Unfortunately, the very small dimensions and the poor quality of the single crystals prevented a complete X-ray structural determination.

Yield: 37 mg (40%). Anal. Calc. for $C_{36}H_{49}N_9O_8Co_2$ (M_r = 853.7): C, 50.6; H, 5.79; N, 14.77. Found: C, 50.0; H, 5.85; H, 14.1%. ESI-MS (90 V, CH_2Cl_2): *m*/*z*+ calcd for **6**: 853.7. Found: 854.5(88%).

^{1}H NMR spectrum of **6** (400 MHz, DMSO-d_6, see Chart 3 for the numbering scheme). ($\Delta_{Co}L_{his}$)-**6**: δ (ppm) = 0.35 (m, 1H, H-N1ha), 0.39 (s, 3H, H-C26a), 1.71 (m, 1H, H-N1ha), 2.08 (s, 3H, H-C4ma), 2.14 (s, 3H, H-C1ma), 2.08, 2.10, 2.10, 2.16 (each of them, s, 3H, H-C18a, H-C21a, H-C22a, and H-C25a, not separately assigned), 2.36 (s, 3H, H-C3ma), 2.48 (s, 3H, H-C2ma), 2.42 (m, 1H, H-C3ha), 2.58 (m, 1H, H-C2ha), 2.85 (m, 1H, H-C3ha), 3.30–3.40 (m, 1H, H-C8a), 3.80 (m, 1H, H-C8a), 4.02 (m, 1H, H-C9a), 4.35 (m, 1H, H-C9a), 5.95 (d, 1H, H-C17a), 6.32 (s, 1H, H-C5ha), 6.38 (d, 1H, H-C2a), 6.61 (d, 1H, H-C17a), 6.78 (dd, 3H, H-C3a), 7.12 (d, 1H, H-C15a), 7.19–7.25 (m, 3H, H-C14a, H-C12a, and H-C6ha), 7.31 (bs, 1H, H-C5a), 12.16 (bs, 1H, H-N3ha), 18.61 (s, 2H, O·· H··O). (Λ_{Co}- L_{his})-**6**: δ (ppm) = 0.41 (s, 3H, H-C26b), 0.91 (m, 1H, H-N1b), 2.09, 2.10, 2.13, 2.13 (each of them, s, 3H, H-C18b, H-C21b, H-C22b, and H-C25b, not separately assigned), 2.12 (s, 3H, H-C1mb), 2.20 (s, 3H, H-C4mb), 2.31 (m, 1H, H-N1hb) 2.37 (s, 3H, H-C3mb), 2.46 (m, 4H, H-C2mb and H-C3hb), 2.60 (m, 1H, H-C3hb), 3.10 (m, 1H, H-C2hb), 3.20–3.30 (m, 1H, H-C8b), 3.82 (m, 1H, H-C8b), 4.02 (m, 1H, H-C9b), 4.57 (m, 1H, H-C9b), 6.17 (s, 1H, H-C5hb), 6.27 (d, 1H, H-C17b), 6.33 (d, 1H, H-C2b), 6.64 (d, 1H, H-C17b), 6.73 (dd, 3H, H-C3b), 7.02 (bs, 1H, H-C12b), 7.12 (d, 1H, H-C15b), 7.19–7.25 (m, 2H, H-C14b and H-C6hb), 7.28 (bs, 1H, H-C5b), 12.45 (bs, 1H, H-N3hb), 18.59 (s, 2H, O···H···O).

2.3. Synthesis of 7

The reaction was carried out as described above for the synthesis of **5** using racemic DL-histidine instead of enantiomerically pure L-histidine.The product collected by filtration was a diastereomeric mixture of the enantiomers ($\Delta_{Co}L_{his}$)-**7**, ($\Lambda_{Co}D_{his}$)-**7** and of the enantiomers ($\Delta_{Co}D_{his}$)-**7**, ($\Lambda_{Co}L_{his}$)-**7** in the ratio 1:0.7.

Yield: 37 mg (46%). Anal. Calc. for $C_{39}H_{54}N_9O_{10}Co_2Cl$ (M_r = 962.2): C, 48.7; H, 5.66; N, 13.1. Found: C, 49.8; H, 4.87; N, 12.9%. ESI-MS (60 V, CH_2Cl_2): *m*/*z*+ calcd: 962.2. Found: 862.3 (**7** − ClO_4^-, 100%). The ^{1}H NMR spectrum of **7** shows the same peaks as that of **5**, the two sets of signals having intensity ratio 1:0.7.

The less soluble diastereomer, formed by the enantiomers ($\Delta_{Co}L_{his}$)-**7**, ($\Lambda_{Co}D_{his}$)-**7** (**7′**),was isolated in almost pure form (>90%) by fractional crystallization from CH_3OH/H_2O. The ^{1}H NMR spectrum of **7′** (400 MHz, DMSO-d_6) is identical to that of ($\Delta_{Co}L_{his}$)-**5**. The recrystallization of **7′** from CH_2Cl_2/*n*-heptane afforded single crystals suitable for X-ray analysis.

2.4. Structure determination

Single crystals, suitable for X-ray data collections, were obtained as described above. The intensities of compound **5** were collected at 200 K, using a rotating copper-anode generator working at 45 kV and 80 mA, equipped with a Enraf Nonius KCCD diffractometer. Three hundred and sixty nine images were collected (crystal-to-detector distance of 42 mm) with 6° oscillation and 20 s/deg exposure time for CCD image. The data were processed, scaled and merged with the programs DENZO and SCALE-PACK [10].

The structure was solved by Patterson method [11], followed by Fourier syntheses and refined by full-matrix least-squares (on F^2) cycles [12]. The H atoms were not refined but were included at calculated positions in the final refinements. The refinement of **5** was troublesome, due the high parameter correlation resulting from the approximate centrosymmetry between the two crystallographically independent molecules. In fact, the structure can be accurately solved in the $P\bar{1}$ space group ($R_1 = 0.099$), except for the position of the asymmetric C atom of the histidinate, which is found statistically disordered. Very small single crystals of **6** and **7′** were obtained in several crystallization attempts. Therefore, data collection for both the structures was carried out at the X-ray diffraction beam-line of the Elettra Synchrotron, Trieste (Italy), using the rotating crystal method with the monochromatic wavelength of 1.0 Å. Data were collected on a CCD MAR detector. Single crystals, suitable for X-ray data collection, were mounted in a loop with a drop of Paratone and the measurements were performed at 100 K using a nitrogen stream cryocooler. Sixty frames were collected with rotation of 3° about ϕ axis, fixed dose of radiation, and the detector positioned at 40 mm from the crystal. The DENZO and SCALE-PACK programs were used to integrate, scale and merge the diffraction data. The structures were solved by direct methods [13] and difference-Fourier techniques. The full-matrix least squares technique was used to refine **7′** structure. For **7′**, all the non-H atoms with full occupancy were refined with anisotropic thermal parameters; the oxygen of the water and the C atom of CH_2Cl_2 were refined isotropically. All H atoms were placed in idealized positions and refined as riding atoms with the relative isotropic parameters.

A suite of programs [14] was also used for the geometrical and final calculations for both structures. The program PLATON [15] was used to examine the solvent-containing cavities. Crystal and refinement data are given in Table 1. CCDC 255592 (5) and CCDC 255593 (7′) contain the supplementary crystallographic data for this paper.

Table 1
Crystallographic data for **5** and **7′**

Identification code	**5**	**7′**
Empirical formula	$(C_{78}\ H_{108}Co_4N_{18}O_{12})$ $(ClO_4)_2.2H_2O$	$(C_{39}\ H_{54}Co_2N_9O_6)$ $(ClO_4).CH_2Cl_2.\ 2.5H_2O$
Formula weight	1960.48	1092.19
Temperature (K)	200(2)	100(2)
Wavelength (Å)	1.5418	1.0000
Crystal system, S.G.	Triclinic $P1$ Flack parameter 0.042	Tetragonal $P\bar{4}2_1c$
Unit cell dimensions		
a (Å)	11.519(5)	30.804(5)
b (Å)	11.986(5)	30.804(5)
c (Å)	17.305(5)	11.665(5)
α (°)	79.213(5)	90
β (°)	78.200(5)	90
γ (°)	74.112(5)	90
V (Å^3)	2227.5(15)	11069(5)
Z, ρ_{calc} (mg/m^3)	1, 1.462	8, 1.311
μ (mm^{-1})	6.964	1.979
F (000)	1020	4552
Crystal size (mm)	$0.3 \times 0.2 \times 0.2$	$0.3 \times 0.1 \times 0.05$
θ range for data collection (°)	5.18–58.92	6.39–33.18
Reflections unique/refl. with $[I > 2\sigma(I)]$	10916/7719	6720/5595
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/parameters	10,916/1096	6720/610
Goodness-of-fit on F^2	1.031	1.086
Final R indices $[I > 2\sigma(I)]$	R_1[a] = 0.0889, wR_2[b] = 0.2369	R_1[a] 0.079, wR_2[b] = 0.2071
R indices (all data)	$R_1 = 0.1228$, $wR_2 = 0.2741$	$R_1 = 0.0971$, $wR_2 = 0.2457$
Largest different peak and hole (e Å^{-3})	0.729 and −0.572	0.880 and −0.691

[a] $R_1 = \sum \| F_o | - | F_c \| / \sum | F_o |$.
[b] $wR_2 = [\sum w(|F_o|^2 - F_c|^2)^2 / \sum w|F_o^2|^2]^{1/2}$.

3. Results and discussion

3.1. Reaction of racemic 1 with L-histidine and either 3 or 4

The reaction of racemic **1** with L-histidine resulted in an untractable mixture of products, likely due to the different possibilities of coordination of the amino acid to **1** and to the consequent multiple equilibria in solution. The addition of the second non-chiral Co complex **3**, which coordinates the imidazole residue of L-histidine, allowed to isolate the orange microcrystalline product **5**. The ^{1}H NMR spectrum of **5** in DMSO-d_6 showed two sets of signals of equal intensity, suggesting that **5** is formed by the diastereomers ($\Delta_{Co}L_{his}$)-**5** and ($\Lambda_{Co}L_{his}$)-**5** in the ratio 1:1 (Figure S1 in Supporting Information). The assignment of the signals to the diastereomers was carried out by comparison with the spectrum of the isolated pair of enantiomers ($\Delta_{Co}L_{his}$)-**7**, ($\Lambda_{Co}D_{his}$)-**7** (**7′**, see below). The spectra of the fractions collected by filtration at different time during the evaporation process did not show any enrichment in one of the two diastereomers. The CD spectrum in CH_2Cl_2 is reported in Fig. 1.

The reaction of racemic **1** with L-histidine and **4** led to the isolation of **6**, whose ^{1}H NMR and CD spectra showed the same features as those of **5**, suggesting that **6** is formed by the diastereomers ($\Delta_{Co}L_{his}$)-**6** and ($\Lambda_{Co}L_{his}$)-**6** in equimolar ratio (Figures S2 and S3). Again, the separation of the diastereomers by fractional crystallization could not be achieved.

The recrystallization from CH_2Cl_2/*n*-heptane afforded single crystals of **5** and **6** suitable for X-ray analysis. The crystal of **5** contains the two diastereomers ($\Delta_{Co}L_{his}$)-**5** and ($\Lambda_{Co}L_{his}$)-**5**. A view of the species in the asymmetric unit is given in Fig. 2(a). Each diastereomer is a dicobalt monocationic complex, where four positions around one metal center are occupied by the tetradentate ligand in a *cis* fashion, the remaining two positions being occupied by the chelated L-histidinate, as previously found in the analogous mononuclear Λ and Δ species containing tyrosinate [4]. Histidinate further axially coordinates the Co atom of **3** through the N4ha atom of imidazole, giving a dinuclear species (Fig. 2(a)). The two diastereomers are related by a ''quasi'' symmetry center, due to the predominance of the chirality of the helical arrangement of the salen-type ligand about the Co center with respect to that of the asymmetric C atom of histidine. The ''quasi'' centrosymmetry of the crystal extends also to the crystallisation water molecules (two in the *P*1 asymmetric unit), each making two H-bonds with the O atom of histidine coordinated to Co of one diastereomer and with the N3ha atom of imidazole of the other.

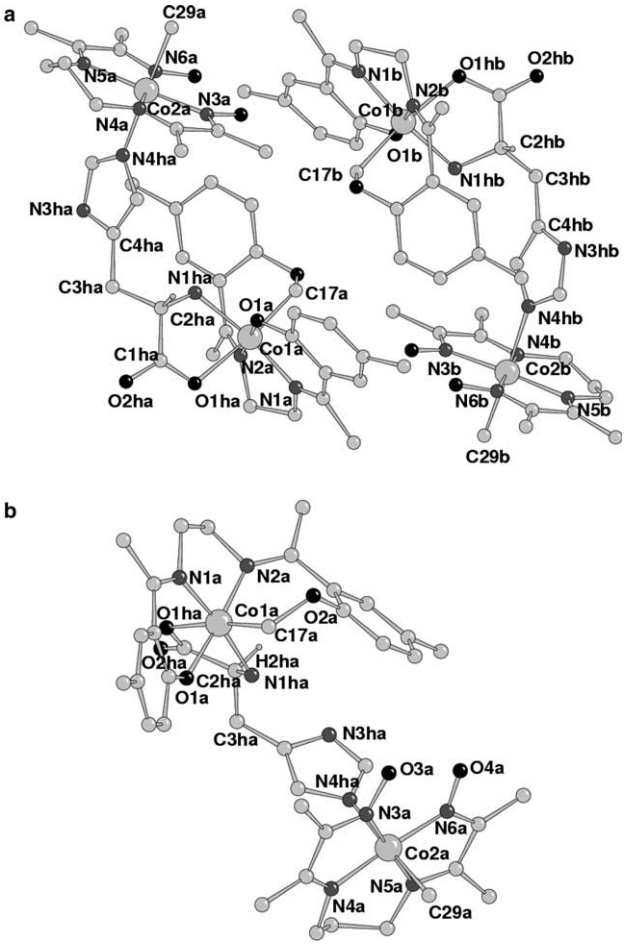


Fig. 2. (a) Crystal structure of **5** showing the independent monocationic diastereomers in the cell. (b) Crystal structure of **7′** (independent unit). Only the significant labels are reported for clarity.

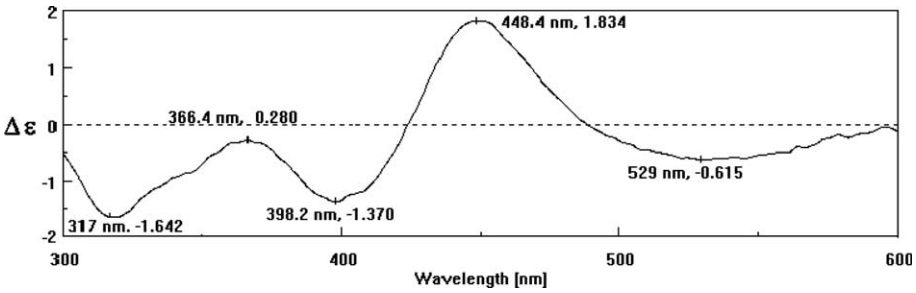


Fig. 1. Circular dichroism spectrum of **5** in CH_2Cl_2.

Similar dinuclear species were found in the crystal structure of **6**. Unfortunately, only single crystals of very small dimensions and poor quality were obtained. Nevertheless, the crystal structure clearly shows that four independent dinuclear units, with two pairs of diastereomers ($\Delta_{Co}L_{his}$)-**6** and ($\Lambda_{Co}L_{his}$)-**6** cocrystallize in the cell [16].

3.2. Reaction of racemic 1 with DL-histidine and 3

In the reaction among racemic **1**, DL-histidine, and **3**, the stereogenic metal center and the asymmetric carbon give rise to two pairs of enantiomers ($\Delta_{Co}L_{his}$)-**7**, ($\Lambda_{Co}D_{his}$)-**7** and ($\Delta_{Co}D_{his}$)-**7**, ($\Lambda_{Co}L_{his}$)-**7**. The ^{1}H NMR spectrum in DMSO-d_6 of the reaction product showed the same two sets of signals as that of **5**, but the relative intensity of the sets varied for fractions collected at different time during the evaporation process, owing to the different solubility of the diastereomers. The spectrum of a mixture is reported in Figure S4. A CH_2Cl_2 solution of the same product is CD silent, indicating that mixture is racemic. Therefore, both the pairs of enantiomers are formed in the synthesis, but, in the presence of the ''true enantiomers'', the precipitate consists in a mixture of the racemic compounds and the cocrystallization of the diastereomers does not occur. Repeated crystallization from CH_3OH/H_2O allowed the isolation of the less soluble pair of enantiomers (**7′**) in almost pure form (>90%), as it was evidenced by the presence of only one set of signals in the ^{1}H NMR spectrum (Figure S5). The assignment of signals was carried out through 2-dimensional NMR experiments (COSY, ROESY), as previously described [7]

X-ray quality crystals of **7′** have been obtained from CH_2Cl_2/*n*-heptane (Fig. 2b). The compound **7′** crystallizes in the tetragonal system space group $P\bar{4}2_1$ and contains the two enantiomers ($\Delta_{Co}L_{his}$)-**7**, ($\Lambda_{Co}D_{his}$)-**7** related by the crystallographic $\bar{4}$ axis. The geometry of the *cis*-β-cobalt salen type units in **5** and **7′** is comparable with that previously found in (Δ_{Co}L-tyr)-**2** and (Λ_{Co}L-tyr)-**2** [4]. In the *Λ*-diastereomer of **5** and **7′**, two short distances Co1a–O1a = 1.81(1) Å, 1.847(7) Å and Co1a–C17a = 1.90(1) Å, 1.881(11) Å, respectively, are observed. The imidazolate ring is oriented in such a way as to nearly bisect the five-membered ring of **3**, with similar dihedral angles around the C3ha–C4ha single bond in **5** and **7′**. The five-membered ring of histidinate in **5** appears more distorted in the *Λ* form with respect to the *Δ* form, the N4ha atom being displaced from the mean plane of the other four atoms of the cycle by 0.61(2) Å for *Λ* and 0.33(2) Å for *Δ* derivative, respectively. In **7′**, a mean value of 0.43(1) Å for the analogous N4ha displacement is observed. Comparable figures are also observed in the two diastereomers (Δ_{Co}L-tyr)-**2** [0.36(1) Å] and (Λ_{Co}L-tyr)-**2** [0.53(1) Å] [4].

The formation of crystals of **7′** agrees with the widespread notion that racemic crystals occur more frequently than conglomerates (the so-called Wallach's rule) [5a]. The reason has often been ascribed to a more efficient packing in racemic crystals, even if also kinetic factors dealing with nucleation and growth of crystals from racemic solutions may be involved [5b]. It is noteworthy that in the present case the analysis of the packing shows that the crystal packing in **5** is closer than that in **7′** (Fig. 3), the percent filled space being 67% in **5** and 61% in **7′**.

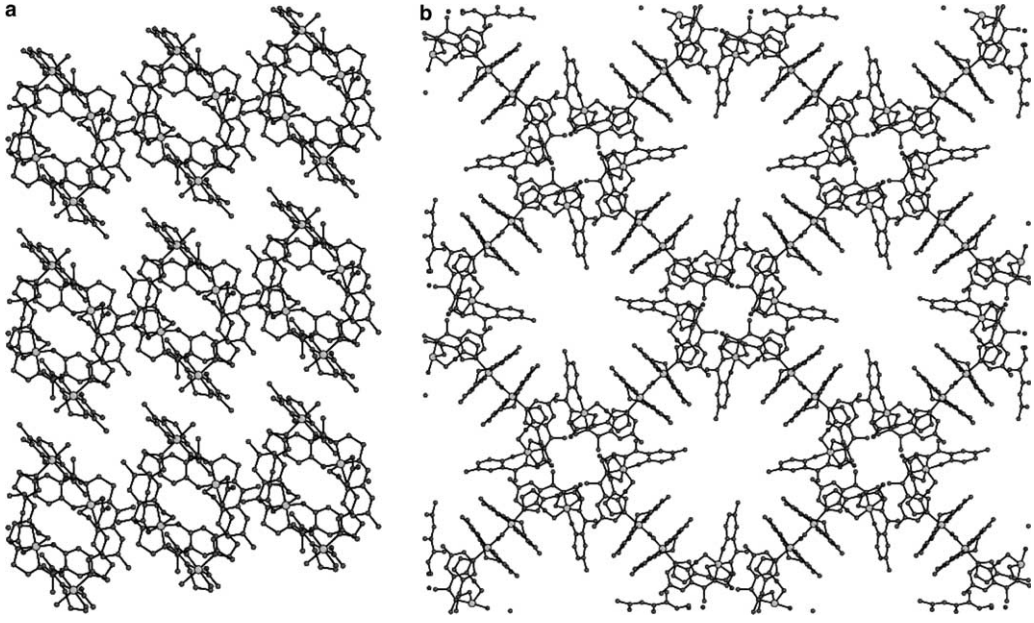


Fig. 3. (a) Crystal packing view along the *b*-axis of **5**. (b) Crystal packing with the channels formed along the *c*-axis of **7′**. In both cases H atoms, all solvent molecules and perchlorate ions are omitted.

4. Conclusion

The reactions of **1** with L-histidine and either **3** or **4** result in the cocrystallization of the diastereomers, built up from the enantiomers of **1** joined through the L-histidine to the non-chiral cobalt complex. To our knowledge, few similar cases are known [6b,6h,6i]. We have previously reported that the cocrystallization does not occur in the reaction of **1** with L-tyrosine, where the two diastereomers crystallize separately [4]. We suppose that, with increasing the size of the molecule by the addition of a second metal center, the opposite helical chirality of the metal complex **1** prevails over the identical L configuration of the asymmetric C in the crystallization process and the diastereomers behave as if they were enantiomers.

The reaction of **1** with DL-histidine and **3** leads to the formation of two pairs of enantiomers, which crystallize separately as racemic compounds. Therefore, in this case, the chirality of the asymmetric center is the property that allows the mutual selective recognition of the true enantiomers and drives their cocrystallization.

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Appendix A. Supplementary data

Two X-ray crystallographic files (**5** and **7′**) in CIF format and Figures S1–S5 presenting ^{1}H NMR and CD spectra. Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.jorganchem.2005.05.017.

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