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Transfer of Chirality in Complexes with D_3 Symmetry: Kinetics of the Formation Reaction of Chiral Tris[*O*,*O′*-bis(2-methylbutyl)-dithiophosphato]chromium(III) Complexes (Λ,Δ)-[Cr{(±)-Mebdtp}$_3$], Δ-(+)$_{589}$- and Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$]

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Dedicated to Prof. Stephen F. Mason on the occasion of his 85th birthday

Keywords: Chirality / Circular dichroism kinetics / UV/Vis spectroscopy / Dithiophosphate / Chromium complexes

The formation reaction of chiral racemic and diastereoisomeric title complexes, (Λ,Δ)-[Cr{(±)-Mebdtp}$_3$] and Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$], was monitored by absorption, UV/Vis, and circular dichroism, CD, spectroscopy, in the presence of either an excess of the racemic, (±)-Mebdtp$^-$, or the enantiopure ligand, (+)-(*S*)(*S*)-Mebdtp$^-$ = *O*,*O′*-bis[(+)-(*S*)-2-methylbutyl] dithiophosphate ion, at 25 °C in various solvents (ethanol, tetrahydrofuran, chloroform/ethanol, 9:1) and at various pH values and reactant concentrations. The kinetics of the formation reaction of the racemic complex, (Λ,Δ)-[Cr{(±)-Mebdtp}$_3$], shows three consecutive reaction steps. The relative pseudo first-order rate constants depend in different ways on the ligand and H$^+$ concentrations. Circular dichroism measurements during the formation reaction using the enantiopure ligand, as well as in the final equilibrium state, show a prevalence of the Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] over the Δ-(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] diastereoisomer in all solvents used. A mechanism is proposed which involves two parallel pathways each consisting of three consecutive reactions of solvent substitution by a chiral chelated ligand, interconnected by some reversible inversion reactions to obtain in solution the thermodynamic and kinetic Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] as the major diastereoisomeric compound. From the equilibrated solution the more stable solid (Λ,Δ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] crystallizes as a ca. 1:1 compound of a pair of the two diastereoisomers, undergoing a crystallization-induced second-order asymmetric transformation. Δ-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] is the thermodynamically stable diastereoisomer in the solid state, though in solution this inverts to the more stable Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$].

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Introduction

Transfer of chirality from a chiral ligand to a coordination centre is an interesting probe to follow in the field of asymmetric catalysis, as well as in supramolecular and bioinorganic chemistry.[1] Intrinsic chirality at the metal centre can be determined by an enantiopure A[*R*] or A[*S*] ligand forming a tris-chelated octahedral OC-6 metal complex of D_3 symmetry, resulting as a left- or right-handed helical coordination, i.e. Λ-M(A[*R*]^A[*R*])$_3$ or Δ-M(A[*R*]^A[*R*])$_3$.[2–4] Chiral discrimination in the formation of diastereoisomeric octahedral tris-chelate complexes can be considered as the difference in the interaction of the chiral ligand molecules with the two chiral forms of intermediate complexes.

In the past, circular dichroism, CD, has been very useful to study the kinetics of the configurational inversion reaction, Λ-M(A[*R*]^A[*R*])$_3$ ⇄ Δ-M(A[*R*]^A[*R*])$_3$, of optically labile diastereoisomeric complexes, as well as to follow qualitatively the formation reaction of Λ- or Δ-M[(*R*,*R*)-bdtp]$_3$ diastereoisomers in various solvents, M^{III} = Cr, Co, Rh, Ir.[3,4] Chiroptical spectroscopy is a sensitive probe for studying electronic transitions and stereochemistry of chiral transition-metal complexes. CD spectra of chiral tris-(bidentate chelate) metal complexes having octahedral coordination can show the intrinsic configurational chirality of the coordinating metal ion. Chiral octahedral complexes of D_3 symmetry give positive or negative differential optical density, ΔOD, during the formation reaction with enantiomeric ligands, so the kinetic of these reactions can be observed.

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The aim of this work is to show the influence of the chiral ligand *O*,*O'*-bis[(+)-(*S*)-2-methylbutyl]dithiophosphate, (+)-(*S*)(*S*)-Mebdtp$^-$ (**1**) on the kinetics and thermodynamics of the formation reaction of diastereoisomeric coordination compounds, showing, if possible, the chirality transfer mechanisms from the ligand (**1**) to the metal centre. Our current interest is also to reveal the influence of the solvent on the formation reaction of the diastereoisomers, as well as on the configurational inversion reaction during the crystallization, to predetermine chirality on the coordination centre.

The addition of the ligand to solvated metallic ions in solution may occur in a typical three-step mechanism for octahedral tris-bidentate complexes. Two- or three-chelate ligands coordinated to a metal ion form a left-handed (Λ) or a right-handed (Δ) helix. Two-chelate ligands form a segment of helices if the two bidentate ligands do not form a common mean plane. With the title chiral ligand **1** the preferential formation of the Λ-(*S*,*S*)(*S*,*S*)(*S*,*S*) diastereoisomer in solution has been shown by CD spectroscopy.[3a]

Here we report the results of a kinetic study on the formation reaction of the title complexes, as followed by absorption (OD) and by circular dichroism (CD) to clarify the mechanism of transfer of chirality from the ligand to the metal centre and the solvent effect in this type of coordination compound.

Results and Discussion

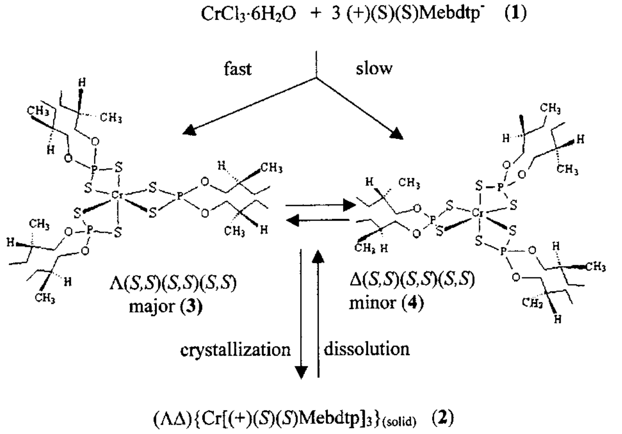
Formation Reaction

The formation reaction of the chiral octahedral complex was carried out at 25 °C using either the enantiomeric dithiophosphinic acids, (+)-(*S*)(*S*)-MebdtpH or the racemic form, (±)-MebdtpH, as well as their lithium salts, as bidentate ligands, to react with Cr^{3+} solvated ion in three different solvents [ethanol (EtOH), chloroform/ethanol ($CHCl_3$/EtOH, 90:10), and tetrahydrofuran (THF)] following Equation (1) and Scheme 1.

$$Cr^{3+}_{(sol)} + 3\ (\pm)\text{-Mebdtp}^-_{(sol)} \rightarrow Cr[(\pm)\text{-Mebdtp}]_{3(sol)} \qquad (1)$$

This reaction was studied using an enantiopure chiral ligand by CD and UV/Vis spectroscopy to determine the influence of absolute ligand configuration and of the solvent on the kinetics and thermodynamics of diastereoselective octahedral complex formation.[3a] A faster formation of the tris{*O*,*O'*-bis[(+)-(*S*)-2-methylbutyl]dithiophosphato}chromium(III) complex, Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**3**), than Δ-(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**4**), was observed in solution, but in the solid phase a chiral complex (ΛΔ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**2**), is formed as a ca. 1:1 crystalline mixture of diastereoisomers **3** and **4** (Scheme 1).

Chiral discrimination occurs during formation of complexes in solution and also during their crystallization, as characterized by CD spectroscopy.



Scheme 1.

In solution the major diastereoisomer is the Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**3**), which is in equilibrium with the minor Δ-(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**4**).

Preferential crystallization of Δ- (**4**) together with Λ- (**3**) resulted in the formation of the hetero-chiral 1:1 complex (ΛΔ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$]$_{(solid)}$ (**2**). This complex is evidently less soluble than the single diastereoisomers Λ- (**3**) or Δ- (**4**). We deduce that an inversion reaction of the major Λ-(**3**) towards the minor Δ-(**4**) complex of the equilibrium occurs during crystallization, undergoing a crystallization-induced second-order asymmetric transformation, which finally yields crystals of (ΛΔ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$]$_{(solid)}$ (**2**), due to more stable hetero-chiral diastereoisomeric crystal packing as known also for some enantiomers and racemates.[2,5,6] As seen in the past, changing the stereochemical arrangement of the ligand groups and atoms causes various different dispersion forces or hydrogen bonding and different chiral discrimination forces between the molecules, in solution as well as in the solid state.[4a]

To clarify the nature of compound **2** we examined CD and absorbance spectra in solution and in the solid state (nujol, KBr pellets, thin film) or as microcrystalline powder by diffuse reflectance circular dichroism, DRCD.[7] When the solid complex **2** was dissolved in CH_2Cl_2, the absorption spectrum of the solution showed two bands in the range 500–700 nm. OD measures the total concentration of the complex in solution and did not change over time.[3a] In contrast, its CD spectra changed drastically: it showed a very weak almost flat spectrum at the time of dissolution, but the intensity of a positive Cotton effect at ca. 675 nm increased substantially to reach a maximum after 5–23 h (Figure 1, A). This corresponds to an equilibrium state between the major (**3**) and the minor (**4**) in CH_2Cl_2 solution reached through a Δ-(**4**) → Λ-(**3**) configurational inversion (Figure 1, A). This indicates the formation in the solid state of intermolecular weak interactions between hetero chiral diastereoisomers. Until now crystals suitable for X-ray structural investigation have not been obtainable, but hetero-chiral packing of a pair of octahedral enantiomeric complexes has been established in the crystalline racemic

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compound (ΛΔ)-[Cr{ddtp}$_3$] with ddtp$^-$ = diethyl dithiophosphate ion, when the enantiomers are more soluble than the racemic compound.[2,3a,6] Hetero-chiral packing of a pair of octahedral diastereoisomeric complexes are also known.[2] The solubility of the two diastereoisomers is very high and ΛΔ-(**2**) is the less soluble complex. During crystallization the Λ-(**3**)–Δ-(**4**) packing-energy or the temperature favour the Λ → Δ configurational inversion and formation of the less soluble solid ΛΔ-(**2**).

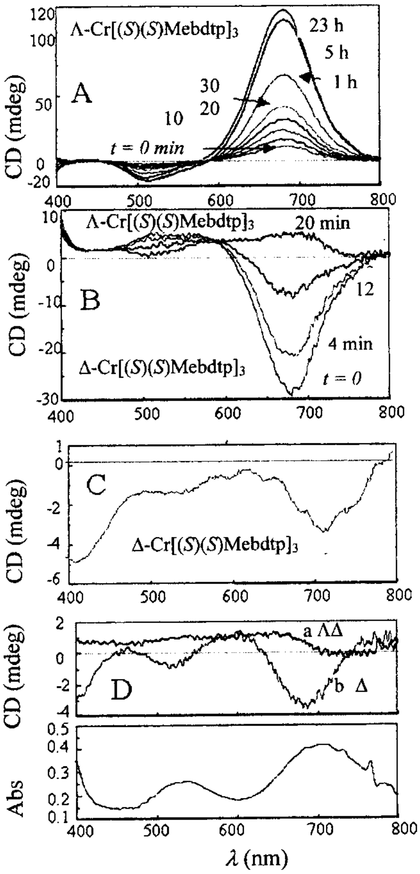

Figure 1. (A) CD spectra of ΔΛ-Cr[(*S*)(*S*)-Mebdtp]$_3$ (**2**) dissolved in CH_2Cl_2, positive at 678 nm at $t = 0$ and inverted to Λ-Cr[(*S*)(*S*)-Mebdtp]$_3$ after 5–23 h. (B) CD spectra of Δ-Cr[(*S*)(*S*)-Mebdtp]$_3$ (**4**) obtained maintaining the solid ΔΛ-Cr[(*S*)(*S*)-Mebdtp]$_3$ (**2**) under vacuum at 100 °C for 3 h. The compound after dissolution in CH_2Cl_2 inverts from Δ to Λ showing changes at 678 nm from a negative CD at $t = 0$, 4, 12 min to a positive CD after 20 min and over up to 5 h. (C) CD spectrum in nujol mull of solid Δ-Cr[(*S*)(*S*)-Mebdtp]$_3$ (**4**) obtained under vacuum at 100 °C for 3 h. (D) CD and UV/Vis spectra of a film over quartz: (a) ΔΛ-Cr[(*S*)(*S*)-Mebdtp]$_3$ (**2**) and (b) Δ-Cr[(*S*)(*S*)-Mebdtp]$_3$ (**4**) obtained after fast evaporation of a solution in CH_2Cl_2.

CD spectra of the solid **2** in nujol, KBr pellet and as a solid film (Figure 1, D, a) show a flat line in the 400–800 nm range, proving that the crystallized complex **2** is optically inactive as a ca. 1:1 solid mixture of the two diastereoisomers Λ-(**3**) and Δ-(**4**). DRCD of **2** also shows no Cotton effect in the same region as a result of the heterochiral equimolecular composition of the complex.

Heating of the solid **2** causes the thermodynamic Δ-(**4**) solid diastereoisomer to form. So the last complex **2**, maintained 3 h under vacuum at 100 °C, shows an inversion of configuration Λ → Δ of the inherent chiral coordination centre in the solid diastereoisomeric mixture **2**. Δ-Cr[(+)-(*S*)(*S*)-Mebdtp]$_3$ (**4**) is the major component in the new solid mixture. CD spectra of this mixture with major (**4**) and minor (**3**) diastereoisomers in nujol mull (Figure 1, C) and as a film (Figure 1, D, b) clearly show a stable negative Cotton effect in the range 680–710 nm, compared with the flat spectrum of (ΛΔ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$]$_{\text{(solid)}}$ (**2**) (Figure 1, D, a).

The CD spectrum of the solution of the major (**4**) and minor (**3**) mixture shows a negative Cotton effect at 678 nm at $t = 0$ min, immediately after dissolution in CH_2Cl_2; this is caused by the presence of the diastereoisomer Δ-(*S*,*S*)(*S*,*S*)(*S*,*S*) (**4**) as the major component (Figure 1, B). The CD spectrum is opposite and about enantiomeric to that of the major diastereoisomer Λ-(*S*,*S*)(*S*,*S*)(*S*,*S*) (**3**) in solution (Figure 1A). In a solution of CH_2Cl_2, EtOH, $CHCl_3$, or THF, the major diastereoisomer Δ- (**4**) inverts the absolute configuration of the coordination metal centre from Δ to Λ (Figure 1B) and the equilibrium between major (**3**) and minor (**4**) is once again established. In the solid state the complex Δ- (**4**) is thermodynamically more stable, but after 5 h in solution it reaches an equilibrium between the kinetic and thermodynamic major Λ- (**3**) and minor Δ- (**4**), diastereoisomeric complexes (Scheme 1, Figure 1A, B).

The less soluble complex **2** is characterized by different interconversion equilibria between the **3** and **4** diastereoisomeric species, depending on the different conditions of temperature, pressure and solvent.[3]

The preferential formation of kinetic and thermodynamic Λ-(–)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] complex (**3**) in solution, or of thermodynamic Δ-Cr[(+)-(*S*)(*S*)-Mebdtp]$_3$ (**4**) in the solid state, can be achieved by kinetically diastereoselective steps and/or equal formation of the two Λ-(**3**), and Δ- (**4**) diastereoisomers with a parallel or consecutive Δ → Λ or Λ → Δ inversion reaction.

Absorption and Circular Dichroism Spectra

The absorption spectra of the formation reaction solution in EtOH show two bands at ca. 675 and 530 nm, which increase with the reaction time (Figure 2). Two points in the spectra near 450 nm look somewhat like isosbestic points. However, accurate examination shows that as time increases the spectra shifts to higher wavelengths, excluding the presence of real isosbestic points and suggesting the presence of some reaction steps in the formation mechanism (see enlargement in the small window reported in Figure 2).

In the CD spectra at the beginning of the reaction a weak positive Cotton effect, growing with time, is observed, and attributed to the $^4A_{2g} \rightarrow {}^4T_{2g}$ transition corresponding to the absorbance at ca. 675 nm. Figure 3 reports the variation with time of the differential absorbance, ΔOD, in the CD spectrum in ethanol.

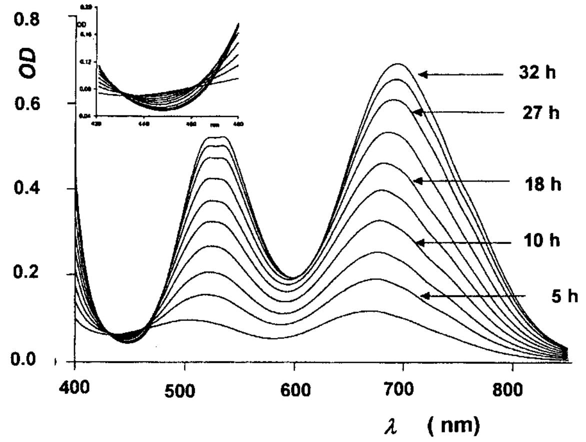

Figure 2. Variation of the OD spectra during the formation reaction of Cr[(±)-Mebdtp]$_3$. Initial concentrations: Cr(ClO$_4$)$_3$ 0.002 mol dm^3, LH 0.1 mol dm^3, EtOH as the solvent.

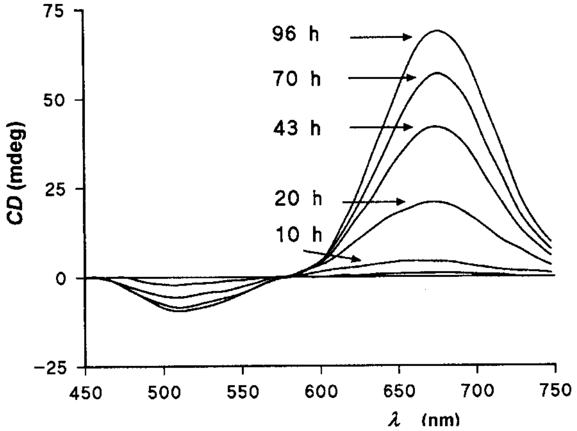

Figure 3. Variation of the CD during the formation reaction of Λ-Cr[(*S*)(*S*)-Mebdtp]$_3$ (**3**). Initial concentrations: Cr(ClO$_4$)$_3$ 0.002 mol dm^3, LH 0.1 mol dm^3, EtOH as the solvent.

Kinetics by Absorption Spectra

The kinetics of the formation reaction [Equation (1) and Scheme 1] have been studied by UV/Vis and CD spectroscopy in an attempt to understand the reaction pathway of the stereoselective formation of the Λ- (**3**) diastereoisomer in solution, as well as the configuration inversion of diastereoisomeric compounds in solution and in the solid state.

Kinetic measurements of very high accuracy can offer reliable information on the formation mechanism in complex systems. OD measurements can give information on the total stoichiometric reaction. CD contributes information on the presence and reactivity of intermediate stereoisomers.

Figure 4 reports the variation in optical density with time, at 675 nm, and shows the influence on the reaction rate of three different solvents. Experimentally we measured and stored in a binary file one point OD/time every minute, so in the figure the results appear as continuous lines. OD values for the three runs at the beginning and at the end of the reactions are nearly equal, so the plot affords direct comparison of the reaction rates in the three solvents.

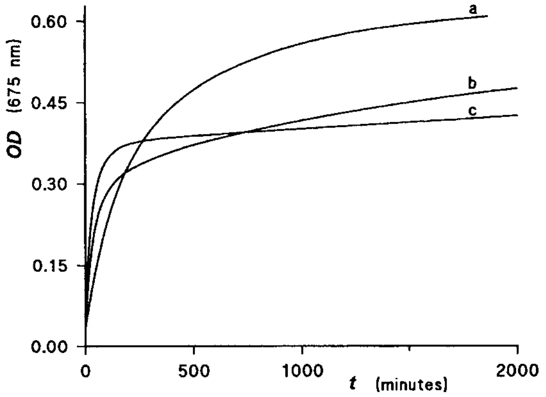

Figure 4. Increase of the optical density at 675 nm with reaction time in different solvents. (a) EtOH; (b) CHCl$_3$/EtOH, 90:10; (c) THF, initial concentrations: Cr(ClO$_4$)$_3$ 0.002 mol dm^3, LH 0.1 mol dm^3.

At the beginning of the reaction the OD signals in various different solvents increase with time, showing that the initial rate values differ according to the solvent in the sequence: THF > (CHCl$_3$/EtOH, 90:10) > EtOH. In the last part of the reaction the sequence is inverted, showing a lower reaction rate for THF and a higher one for EtOH.

The rate of a reaction between two ions of opposite charges, i.e. Cr^{3+}, CrL^{2+}, CrL$_2^+$ and L$^-$, should decrease with an increase in the dielectric constant of the solvent ($\varepsilon_{\text{EtOH}} = 25.1$, $\varepsilon_{\text{THF}} = 7.6$, $\varepsilon_{\text{CHCl3}} = 4.8$), because the electrostatic interactions are lowered.[8] The measured rates in the solvents used do not agree well with this statement and thus, we cannot attribute the rate difference to the dielectric constants of the solvents. The more important reason for the solvent-dependent reaction rates is probably due to at least partial substitution of the water molecules in the hydration sphere of Cr$^{\text{III}}$(H$_2$O)$_6$ by solvent molecules, changing the characteristics of the activated complexes and of the reaction intermediates.

The experimental results were analyzed by applying a method of minimization of bi- or tri-exponential equations, similar to that used by N. W. Alcock et al.[9]

There are two types of mechanism, I and II, that can be hypothesized. The three rate constants, k_a, k_b, k_c, and the extinction coefficients, ε_B and ε_C, of the intermediates CrL(sol)$_4^{2+}$ and CrL$_2$(sol)$_2^+$ were considered as adjustable parameters. The extinction coefficients ε_A and ε_D of the first Cr(sol)$_6^{3+}$ and the last CrL$_3$ species are accessible from the observed optical density at the beginning and at the end of the reaction.

The experimental data of the reaction in THF of Figure 4 (c) are reported in Figure 5 and Figure 6. Similar plots were obtained for reactions in other solvents.

Figure 5 shows a first-order plot, $-\log(\text{OD}_{\text{inf}} - \text{OD})$ as a function of time. The curve only becomes linear after a rather long reaction time, while the first part of the reaction, by the nonlinearity of the curve, suggests the presence of consecutive steps.

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$$\underset{\varepsilon_A}{Cr(sol)_6^{3+}} + 3\,L^- \xrightarrow{k_a} \underset{\varepsilon_B}{CrL(sol)_4^{2+}} + 2\,L^- \xrightarrow{k_b} \underset{\varepsilon_C}{CrL_2(sol)_2^{+}} + L^- \xrightarrow{k_c} \underset{\varepsilon_D}{CrL_3} \qquad \text{(I)}$$

$$\text{and} \qquad Cr(sol)_6^{3+} + 3\,L^- \xrightarrow{k'_a} CrL_2(sol)_2^{+} + L^- \xrightarrow{k'} CrL_3 \qquad \text{(II)}$$

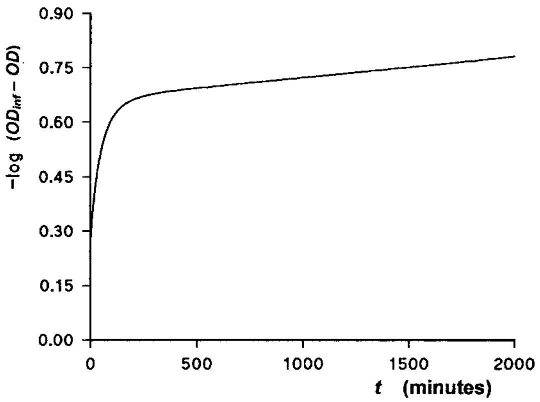

Figure 5. First-order plot of the formation reaction of Cr[(±)-Mebdtp]$_3$ in THF as the solvent. Cr(ClO$_4$)$_3$ 0.002 mol·dm^{-3}, LH 0.1 mol dm^3.

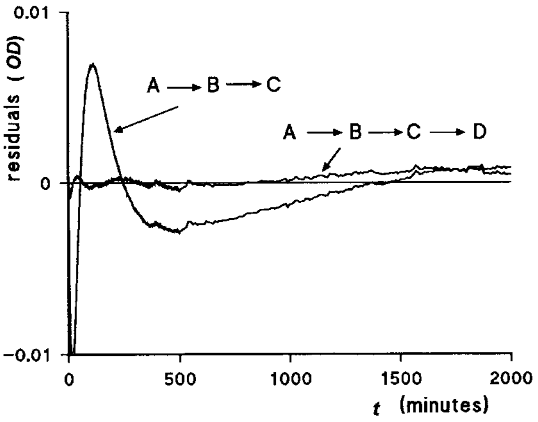

Figure 6. Differences between the observed optical density at 675 nm and that calculated according to mechanisms (I) and (II). Cr(ClO$_4$)$_3$ 0.002 mol dm^3, LH 0.1 mol dm^3, THF as the solvent.

Figure 6 reports the residuals (differences between the observed and calculated OD values) obtained applying the method of minimization to the three- and two-step mechanism, (I) and (II) respectively.

There is a much better agreement with mechanism (I), particularly in the first part of the reaction, the residuals being about 0.001 OD units, ca. 0.2%, of a total absorbance variation of about 0.6 OD units. The optical density varia-

Table 1. Pseudo-first-order rate constants (s^{-1}) for the formation reaction of Cr[(+)-(*S*)(*S*)-Mebdtp]$_3$ in different solvents and different reactant concentrations (mol dm^3). [CrCl$_3$·6H$_2$O] = 0.002 mol dm^3.

Solvent	Reaction number	[LH][a]	[LLi][b]	[H$^+$]	$10^5\,k_a$	$10^5\,k_b$	$10^5\,k_c$
C$_2$H$_5$OH	1	*0.050[c]	0	0.20	5.87	1.93	1.05
	2	*0.075	0	0.20	10.1	3.12	1.60
	3	*0.10	0	0.20	13.9	4.08	1.85
	4	*0.15	0	0.20	23.5	7.98	2.33
	5	*0.20	0	0.20	46.8	13.3	2.57
	6	*0.10	0	0.025	63.5	18.9	1.84
	7	*0.10	0	0.05	38.6	12.1	2.35
	8	*0.10	0	0.075	36.2	9.10	1.96
	9	*0.10	0	0.10	27.7	7.97	1.97
	10	*0.10	0	0.15	20.7	6.15	1.83
	11	*0	0.10	**[c]	1050	61	2.17
	12	*0.05	0.05	0.05	39.5	9.7	2.55
	13	0.10	0	0.10	43.3	12.1	2.49
	14	0.05	0	0.05	30.2	9.75	2.0
THF	15	*0	0.20	**	3470	178	2.3
	16	*0.20	0	0.20	192	40	0.55
	17	0.10	0	0.10	72	25	0.23
	18	0	0.050	**	2200	38	2.1
	19	0	0.10	**	3000	43	3.9
CHCl$_3$/C$_2$H$_5$OH, 90:10	20	0	0.05	**	877	43	7.2
	21	0	0.20	**	983	42	6.3
	22	0.10	0	0.10	50	9.0	0.58

[a] LH = (+)-(*S*)(*S*)-MebdtpH. [b] LLi = (+)-(*S*)(*S*)-MebdtpLi. [c] * Measurement done at ionic strength I = 0.212 mol dm^{-3}. ** Reaction solution about neutral.

tion as a function of time, in all runs made in THF and $CHCl_3$/EtOH (90:10), is in agreement with mechanism (I) comprehending three consecutive pseudo first-order reactions to Cr^{III}.

By contrast, some of the runs performed in EtOH as the solvent show a good agreement with the two-step mechanism II. Nonlinear least-square calculations, according to mechanism (I), afford poor accuracy, different results being obtained if one changes the initial set of adjustable parameters.

This discrepancy can be attributed to the too small differences between the values of the rate constants of the first and second step. To improve the reliability of the results for runs in EtOH, supposing that the reaction always occurs in three steps, the extinction coefficient, ε_b, of the first intermediate, CrL^{2+}, was measured, performing some runs with an excess of Cr^{3+} over the ligand, L^-. The value obtained, $\varepsilon_{CrL^{2+}} = 46.7\ dm^3 mol^{-1} cm^{-1}$, was then imposed as a nonadjustable parameter in mechanism I. The extinction coefficient, ε_c, of the second intermediate, CrL_2^+, was calculated as an adjustable parameter for the runs more in agreement with mechanism II. The mean value obtained, $\varepsilon_{CrL^{2+}} = 186.9 \pm 5.8\ dm^3 mol^{-1} cm^{-1}$ was imposed as a nonadjustable parameter for all the runs made in EtOH following mechanism I. In every case the k_c calculated values were nearly equal to the obtainable values from first-order diagrams in the last part of the reaction. We inferred that the three steps observed do correspond to the complexation of one, two and three molecules of the ligand to chromium ion, as shown in mechanism I.

In Table 1 pseudo first-order rate constants for the formation reaction of $[Cr\{(+)\text{-}(S)(S)\text{-Mebdtp}\}_3]_{(sol)}$ following the three-step mechanism I are reported. Where possible the ionic strength was maintained constant at $0.212\ mol dm^{-3}$, by adding tetrabutylammonium trifluoromethanesulfonate. The H^+ concentration was adjusted with tetrabutylammonium hydroxide or perchloric acid or using lithium salt as the ligand. The ligand LH was considered to be a strong acid, as shown by pH measurements. From the results obtained at constant ionic strength in ethanol as the solvent, it is possible to derive some information as to the reaction orders with respect to the ligand and to the H^+ ion.

Reaction Order with Respect to the Ligand

The reaction order with respect to the ligand (proves 1–5 of Table 1) is bigger than one for k_a and k_b and smaller than one for k_c, in good agreement with Equations (2), (3), and (4).

$$k_a = a\,[L] + b\,[L]^2 \tag{2}$$

$$k_b = a'\,[L] + b'\,[L]^2 \tag{3}$$

$$k_c = a''\,[L]/(1 + b''\,[L]) \tag{4}$$

From the values of rate constants measured at constant $[H]^+$, $0.200\ mol dm^{-1}$, and a ligand concentration ranging from 0.05 and $0.2\ mol dm^{-1}$, values of $a = (7.49 \pm 1.70) \times 10^{-4}\ mol^{-1} dm^3 s^{-1}$, $b = (7.08 \pm 1.34) \times 10^{-3}\ mol^{-2} dm^6 s^{-1}$, $a' = (2.65 \pm 0.32) \times 10^{-4}\ mol^{-1} dm^3 s^{-1}$, $b' = (1.88 \pm 0.25) \times 10^{-3}\ mol^{-2} dm^6 s^{-1}$, $a'' = (2.7 \pm 2.9) \times 10^{-4}\ mol^{-1} dm^3 s^{-1}$ and $b'' = 4.8 \pm 1.3\ mol^{-1} dm^3$ were calculated. A mechanism for the third reaction step in agreement with Equation (4) could involve a fast pre-equilibrium followed by a slow reaction, as in equations Equations (5) and (6).

$$CrL_2^+ + L^- \rightleftarrows CrL_2^+\cdots L^- \tag{5}$$

$$CrL_2^+\cdots L^- \rightarrow CrL_3 \tag{6}$$

In the intermediate $CrL_2^+\cdots L^-$, where we have not indicated the solvent molecules, ligand L^- could be bonded to the metal by a single bond and the slow step should be a ring closure with solvent substitution. Similar mechanisms should be present in the first and second reaction steps too. The presence of a quadratic term in Equations (2) and (3) suggests parallel reaction paths of a second order with respect to the ligand. These second-order paths could be attributed to the possibility, forbidden for the third step, of forming intermediates with more than one mono-bonded ligand, followed by slow ring closure.

Alternatively these intermediates, $Cr^{3+}\cdots L^-$, $CrL^{2+}\cdots L^-$, $CrL_2^+\cdots L^-$, could be ionic pairs with the ligands and the metal somehow linked between them through the solvent molecules of the coordination sphere of the metal. In this case the rate-determining step should be substitution of a solvent molecule by the ligand, followed by a fast ring closure. The value of b'' seems to support the last hypothesis. In fact in the mechanism we propose, b'' is the formation constant of the $CrL_2^+\cdots L^-$ and corresponds, according to the Fuoss theory,[10] to a distance between the metal and the ligand in the ionic pair of 10.1 Å, a value that seems to be of the right order of magnitude.

Reaction Order with Respect to the H^+ Ion

The rate constants for the first and second steps, k_a and k_b, depend inversely on the hydrogen ion concentration in all the solvents used, taking very large values when $[H^+]$ is almost absent (proves 6–10, Table 1). Probably at the beginning of the reaction not all the water molecules in the coordination sphere of the Cr^{3+} ion are substituted by the solvent and the mechanism could involve de-protonated species as shown for the first step of the reaction in Equations (7), (8) and (9).

$$Cr(OH_2)^{3+} \overset{K_a}{\rightleftarrows} Cr(OH)^{2+} + H^+ \tag{7}$$

$$k'\text{: } Cr(OH_2)^{3+} + L^- \rightarrow CrL^{2+} + H_2O \tag{8}$$

$$k''\text{: } Cr(OH)^{2+} + L^- \rightarrow CrL^{2+} + OH^- \tag{9}$$

The deprotonated species, $Cr(OH)^{2+}$ and analogously $CrL(OH)^+$ for the second step, are normally more reactive

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than nondeprotonated species in substitution reactions.[11] The observed pseudo-first-order rate constants k_{obs} should depend on the hydrogen ion concentration as in Equation (10).

$$k_{\mathrm{obs}} = (k'\ K_a + k''\ [H^+])/([H^+] + K_a) \qquad (10)$$

The experimental results of Table 1, (proves 3, 6–10, $[L^-]$ constant, 0.100 mol dm^{-3}, and $[H^+]$ varying from 0.025 and 0.200 mol dm^3) are qualitatively in agreement with Equation (10). The attempt to test Equation (10) quantitatively, however, leads to values of the acid ionization constants for $Cr(OH_2)^{3+}$, $K_a = 0.026 \pm 0.020$ mol dm^{-3}, and for $Cr(OH_2)$-L^{2+} of the second step, $K_a = 0.018 \pm 0.008$ mol dm^3, that are too high compared to the value of $1.4 \cdot 10^{-4}$ mol dm^3 measured in aqueous solution for $Cr(OH_2)_6^{3+}$.[12] The rate constants of the third step depend very little on the hydrogen ion concentration, probably because of the low charge of the complex ion CrL_2^+.

Kinetics by CD

Kinetic measurements performed by optical density cannot distinguish between Λ and Δ configuration. We then repeated the same runs as shown in Figure 4 recording the CD signal at 675 nm against time, as shown in Figure 7. The positive Cotton effect observed throughout the reaction and in all solvents used indicates a higher production in solution of the Λ-(–)$_{589}$- (**3**) than the Δ(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**4**) complex; see Figure 1 (A), 3 and 7.

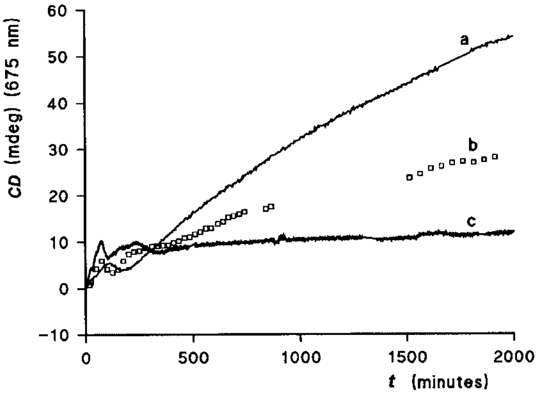


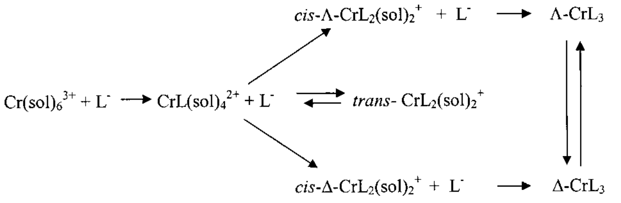
Figure 7. Variation of the CD signal at 675 nm with formation reaction time in different solvents: (a) EtOH; (b) $CHCl_3$/EtOH, (c) THF. Initial concentrations: $Cr(ClO_4)_3$ 0.002 mol dm^3, LH 0.1 mol dm^3.

The Λ-(–)$_{589}$-(**3**) is present at the final equilibrium as a major complex being stabilized by the solvent in the order: EtOH > ($CHCl_3$/EtOH, 90:10) > THF. In the first part of the reaction the positive curve is not monotonic, but shows some oscillations, with the formation of one maximum and one minimum in the case of EtOH as the solvent (Figure 7, a) and two maxima and two minima in the other two cases (Figure 7b, c). Afterwards the CD signal grows quite regularly to the end of the reaction. These oscillations can be attributed to the formation of Equilibria (11) and (12) between the Λ and Δ forms of CrL_2^+ (1:2) and CrL_3 (1:3).

$$\Lambda\text{-}CrL_2^+ \rightleftarrows \Delta\text{-}CrL_2^+ \qquad (11)$$

$$\Lambda\text{-}CrL_3 \rightleftarrows \Delta\text{-}CrL_3 \qquad (12)$$

Taking into account, (i) the profile of reaction (Figure 7), (ii) the three consecutive reaction steps of mechanism (I), supported by the OD measurements, and (iii) Λ and Δ, *cis* and *trans* stereoisomery of intermediates CrL_2^+ and final CrL_3 complexes, a probable mechanism of the reaction studied could be that reported in Scheme 2.



Scheme 2.

The free octahedral coordination positions, are occupied by the solvent molecules. Every reaction step, indicated by an arrow, should be of pseudo-first order with respect to Cr^{III}, which is very complicated because of the presence of metal complex ions that are differently solvated, protonated and forming ion pairs. The planar *trans*-intermediate $CrL_2(sol)_2^+$ in this Scheme was hypothesized as having to go back to the diastereoisomer 1:1, $CrL(sol)_4^{2+}$, to form the *cis*-Λ- or the *cis*-Δ-CrL_2^+, 1:2 diastereoisomer. Considering Equations (5)–(12), moreover, Scheme 2 must be considered as a simplified version of more complicated ones.

The number of parameters of Scheme 2, that influence the CD signal, e.g. rate constants and CD values, is too large for any quantitative evaluation, because of the formation of various chiral species during the reaction. Nevertheless many computer simulations have been performed to test the compatibility of the proposed reaction mechanism with the CD values oscillating in the first part of the reaction (Figure 7). We compared the experimental results of the three runs reported in Figure 7 during the first 700 min of reaction also with some other mechanisms with different numbers of intermediates and reaction steps. Every simulation used CD values of Λ-Cr[(+)-(*S*)(*S*)-Mebdtp]$_3$, (**3**) measured at the end of the reactions as a known value, and assumed approximated values for all the other parameters. The differential equations involved were resolved numerically and the theoretical values of the CD signals were compared with experimental ones. The calculation was repeated many times, alternately and by small amounts changing the values of all the parameters, until it reached the minimum possible value of the standard deviation.

Numerical values of the parameters thus obtained are not reliable because they strongly depend on the initial values used in the calculations. However, the standard deviation and the shape of the CD signal/time curve obtained with different sets of adjustable initial parameters were practically identical. One can always obtain better agreement between observed and calculated values, if more intermediate species are used, even if some levelling effect has been noted. However, we think that these calculations could be useful for selecting the simplest mechanism of the hypothetical ones, which could be in sufficiently good agreement with the experimental results. Figure 8 uses continuous lines to report the calculated runs according to Scheme 2. In EtOH (Figure 8, a) the agreement is better than was the case in other solvents, though simulation cannot really reproduce the nonmonotonic behaviour of CD with time. It is interesting to note that this agreement gets worse if we try to compare the experimental results with a mechanism with only two consecutive paths instead of one with three consecutive paths. This fact supports the choice of mechanism (I) over mechanism (II) in the kinetic runs in EtOH deduced by absorbance measurements.

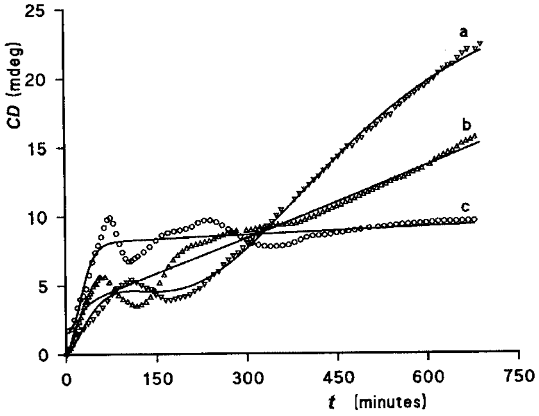
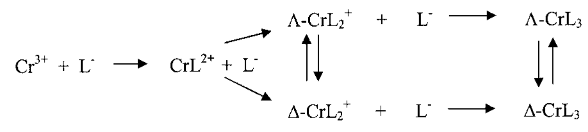


Figure 8. Simulated curves (continuous lines) CD/time, for Scheme 2 compared with experimental ones: (a) in EtOH (triangles); (b) in $CHCl_3$/EtOH, 90:10 (delta symbols); (c) in THF (circles).

The other two runs performed in the other two solvents are not in agreement with Scheme 2 and must be compared with some more complicated Schemes. Similar computer simulations were carried out for Schemes 3–5.



Scheme 3.

The oscillations of CD observed in THF as the solvent are more complicated and difficult to resolve but they should contain a greater amount of information about the mechanism. As the complexity of the mechanism increases, so does the agreement between the experimental points and the calculated line.

Simulated curves (see 2 in Figure 9) obtained following Scheme 2 does not agree with the experimental curve in THF (see 1 in Figure 9).

In Scheme 3 we do not consider the intermediate *trans*-CrL_2^+, but, instead, we suppose an interconnecting direct equilibrium between Λ- and Δ-$CrL_2(sol)_2^+$. The little improvement in respect of calculations with Scheme 2, where there is one more intermediate as *trans*-CrL_2^+, suggests that the new equilibrium is an important responsible factor in the oscillations observed (see 3 in Figure 9).

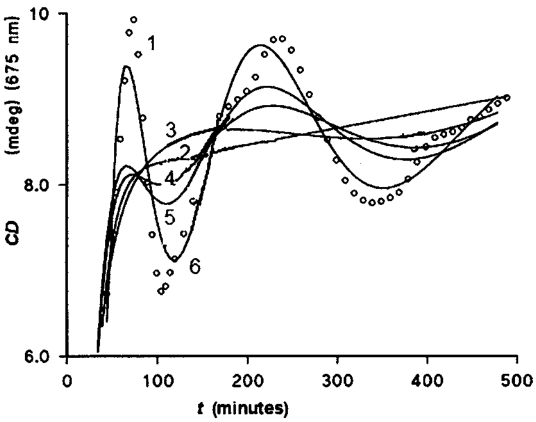


Figure 9. Experimental curve CD/time, in THF (1, line of circles), compared with simulated curves (2–6, continuous lines), obtained from various schemes of formation reaction: Scheme 2; Scheme 3, without the intermediate *trans*-CrL^{2+}; Scheme 4, with all intermediates and equilibria; Scheme 5, where the *cis*- and *trans*-$CrL^{2+}\cdots L^-$ intermediates were considered kinetically important; curve 6 refers to a scheme not reported here, but similar to Scheme 5, where the Λ- and Δ-$CrL^{2+}\cdots L^-$ were also considered.

In Scheme 4 it is suggested that the *trans*-CrL_2^+ intermediate could react further, forming equilibria with Λ- and Δ-$CrL_2(sol)_2^+$ diastereoisomers as well. The agreement grows and the two maxima and minima observed experimentally begin to appear (Figure 9 and Figure 4).

On increasing the number of direction routes (arrows) in Scheme 4, we did not obtain a much better agreement, so we have tried to increase the number of intermediates alone.

Scheme 5 supports the hypothesis, just suggested in Equations (2)–(6) of the kinetic importance of intermediates $CrL^{2+}\cdots L^-$, which should be present under two forms, one with L^- mono-bonded in the *cis* position with respect to the plane of the first chelated ligand, the other linked in the *trans* position. The *cis* species should form Λ- or Δ-$CrL_2(sol)_2^+$, while the *trans* species should form Λ-$CrL_2(sol)_2^+$, Δ-$CrL_2(sol)_2^+$, or planar *trans*-$CrL_2(sol)_2^+$ (see 5 in Figure 9)

If we suppose that ion pairs of the type $CrL_2^+\cdots L^-$ are also present in the third reaction step, the agreement between calculated and experimental data increases (Figure 9, 6). However, increasing the number of intermediates we can obtain better agreement between observed and calculated values, but some levelling effect has been noted.

The experimental results point to a more complicated mechanism in THF than in EtOH. The solvent confirms its effect on the kinetic and in the thermodynamic stabilization of the various diastereoisomers formed during the reaction. All our experimental results strongly hint at the last tested mechanisms. However, Scheme 4 must be considered as a good exemplification of some more complicated mechanisms that we cannot evaluate quantitatively. For every step shown in Scheme 4 there may be a corresponding reaction path and various intermediates, as in Scheme 5 or more complicated Schemes.

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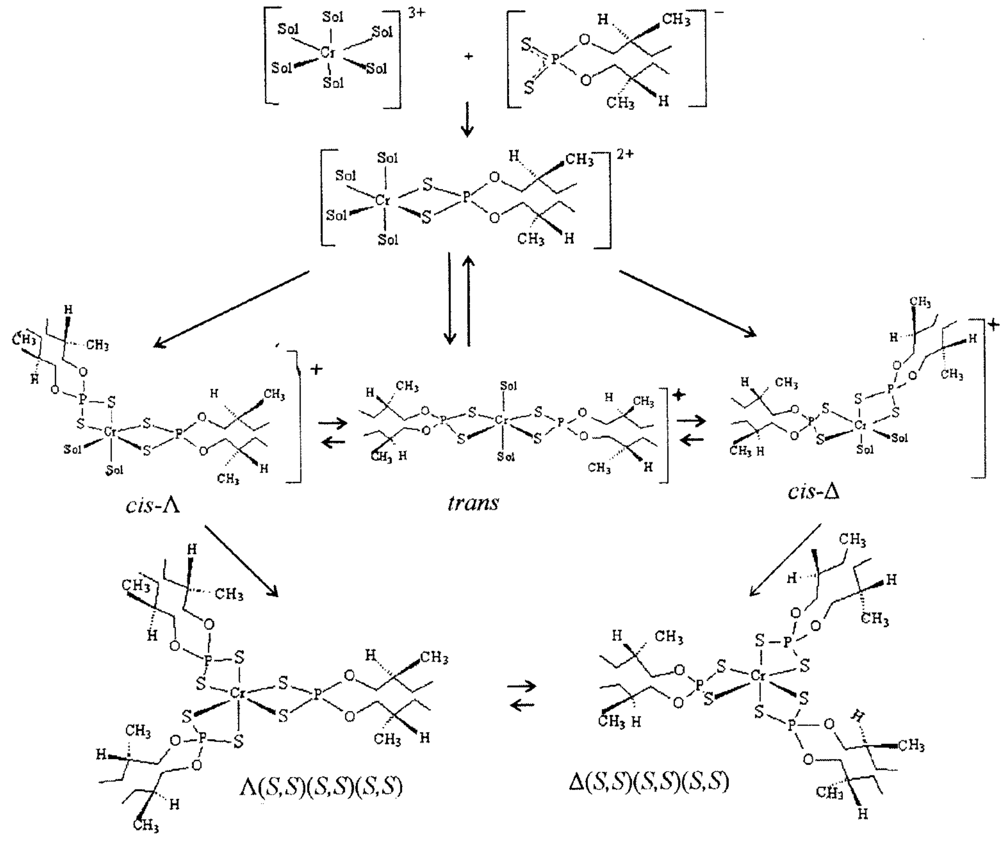
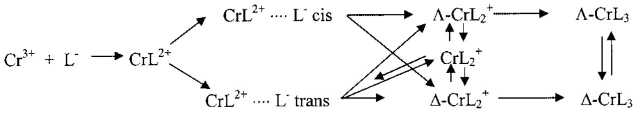


Scheme 4.



Scheme 5.

In the formation of diastereoisomeric octahedral tris-chelate complexes, chiral discrimination is active because of the difference in the interaction of the chiral chelating ligand molecules with the pro-chiral metal centre of the 1:1 ion, CrL^{2+} and/or with the two chiral intermediate 1:2, *cis* bis-chelated complexed ions, Λ- or Δ-CrL_2^+, forming Λ- or Δ-CrL_3 diastereoisomeric helical complexes 1:3.

The shape and stereochemical features of the ligand molecules lead to diastereoselectivity in the formation reaction of complexes. The structure of the resulting complex and the interactions with the solvent causes thermodynamic stability of the diastereoisomers as well as chiral discrimination/recognition between molecules.

We are currently trying quantitative analysis of the configurational inversion reactions from Λ-CrL_3 to Δ-CrL_3 shown in all Schemes proposed.[13,14]

Conclusions

This paper reports the kinetic study of the formation reaction of chiral octahedral coordination compounds by isotropic and chiroptical spectroscopy. The diastereoselective synthesis of the complex was followed kinetically by UV/Vis and CD measurements. The OD spectra suggest a three-step consecutive mechanism for tris-chelate complex formation. However, a mono-bonded ligand or ion pair could be formed before chelation and substitution of the solvent. CD spectroscopy shows new observables and adds a remarkable new contribution to the knowledge of the chirality transfer and stereoselective synthesis mechanism of chiral inorganic diastereoisomeric coordination compounds, when an enantiopure ligand is used. The CD spectra show preferential formation of Λ-(**3**) diastereoisomer in solution, and of Δ-(**4**) in the solid state. The mechanisms hypothesized on the basis of the kinetic measurements enable one to show the formation in solution of the kinetic and thermodynamic Λ-(–)$_{589}$-[Cr{(*S*)(*S*)-Mebdtp}$_3$] (**3**) complex in equilibrium with Δ-(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**4**) through two parallel three-step consecutive pathways interconnected by some configurational inversion reactions at the metal centre.

Our experimental results show that diastereoselective synthesis of Λ-(*S*,*S*)(*S*,*S*)(*S*,*S*) or Δ-(*S*,*S*)(*S*,*S*)(*S*,*S*) can be achieved using the chiral enantiopure dithiophosphate ligand (+)-(*S*)(*S*)-Mebdtp$^-$ (**1**). The diastereoselective reaction of chiral enantiopure ligand **1** with a Cr^{III} ion occurs through kinetically diastereoselective steps during the formation reaction of 1:2 metal/ligand complex, Λ-Cr[(*S*)(*S*)-Mebdtp]$_2^+$ or Δ-Cr[(*S*)(*S*)-Mebdtp]$_2^+$, and of 1:3 complex,

3 or **4**. A hetero-chiral recognition occurs during crystallization, giving (ΛΔ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$]$_{\text{(solid)}}$ (**2**) which by configurational inversion gives the thermodynamic complex Δ-(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**4**) in the solid phase. Crystal packing favours a crystallization-induced second-order asymmetric transformation, shifting all equilibria towards formation of the more stable and less soluble (ΛΔ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$]$_{\text{(solid)}}$ diastereoisomer.

The transfer of chirality from the enantiomeric ligand (+)-(*S*)(*S*)-Mebdtp$^-$ to the Cr$^{\text{III}}$ centre is achieved during the formation process by stereoselecting the kinetic and thermodynamic diastereoisomer Λ-(+)$_{589}$-[Cr{(*S*)(*S*)-Mebdtp}$_3$] in all the solvents used and the thermodynamic complex Δ-(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] in the solid phase. The (*S*)(*S*) configuration of the chiral ligand predetermines Λ configuration on the chromium(III) centre in solution and Δ configuration in the solid state.

Experimental Section

Preparation of the Compounds

Hydrated chromium(III) chloride, 2-methyl-1-butanol, and phosphorus pentasulfide (Carlo Erba and Aldrich) were used without further purification. Solvents were purified by standard methods and dehydrated to a spectroscopic degree.

Lithium *O,O'*-bis[(*S*)-(+)-2-methyl butyl]dithiophosphate, (+)-(*S*)(*S*)-MebdtpLi, and MebdtpLi were obtained as described, using lithium carbonate to neutralize the acid formed.[3]

(ΛΔ)-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**2**) and the diastereoisomers Λ-(–)$_{589}$- (**3**) and Δ-(+)$_{589}$-[Cr{(+)-(*S*)(*S*)-Mebdtp}$_3$] (**4**) were prepared as described.[3]

Measurement of Formation Reaction Rates

Kinetics of the formation reaction of the complexes were analyzed by absorption, UV/Vis, and CD spectroscopy, through measurement of optical density OD and ellipticity, ψ, or differential absorption, ΔOD, at 675 nm, with various concentrations in different solvents at 25.00 ± 0.01 °C. The ligand was always in great excess so as to maintain pseudo first-order conditions for the Cr^{3+} ion.

Solutions of hydrated chromium ion, $CrCl_3 \cdot 6H_2O$ ($2 \cdot 10^{-3}$ mol dm^3), containing a minimum of water (ca. 10^{-2} mol dm^3), were mixed with solutions of the other reagents, in a thermostatted cell (l = 1 cm), controlled by a thermocouple in contact with the same cell. In chloroform solutions it was necessary to add 10% of absolute ethanol to dissolve the chromium trichloride. Formation reactions were followed up to a state of equilibrium between the two diastereoisomers formed, and many days later a stable absorption band at 675 nm and a correspondingly stable Cotton effect were observed. The total concentration of the complexes formed, C_{tot}, was determined by isotropic absorbance spectra. The concentration of the major diastereoisomer formed, C_{Λ}, was determined by the intensity of the relative Cotton effect in CD spectra.

Spectroscopic Measurements

The kinetics were followed at a fixed wavelength (675 nm) with a Cary/4 spectrophotometer and with a Jasco J-500 A spectropolarimeter using a 1-cm cell. UV/Vis spectra were measured with a Jasco UVIDEC 650 spectrophotometer in various solvents, between 750 and 200 nm. Circular dichroism spectra were obtained in freshly prepared solutions and in nujol mull, KBr pellets, and film between 750 and 200 nm on a Jasco J-810 spectropolarimeter.

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