ISOMERIZATION STUDIES OF Δ,Λ-[Ni(1,10-phen)$_2$(S-aa)]$^+$ SYSTEMS

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ABSTRACT

The Δ-Λ isomerization of partially resolved [Ni(1,10-phen)$_2$(S-aa)]$^+$ systems, where S-aa is S-phenylalaninate, S-isoleucinate, S-leucinate, S-valinate, or S-alaninate, has been studied at 15, 20 and 25 °C in methanol as solvent. Kinetic parameters have been obtained by means of optical rotation measurements. The first-order rate constants for the isomerization process follow the order S-leu > S-ala > S-phe > S-ileu > S-val, whereas $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are in the sequence S-phe > S-ala > S-val > S-ileu > S-leu. These results are discussed in relation to the possible influences of intramolecular noncovalent interactions on the activation parameters.

KEY WORDS: Nickel, phenanthroline, aminoacidate, isomerization, optical rotation.

RESUMEN

Se estudia la isomerización Δ-Λ en sistemas [Ni(1,10-fen)$_2$(S-aa)] parcialmente resueltos, en que S-aa es S-fenilalaninato, S-isoleucinato, S-leucinato, S-valinato o S-alaninato, a 15, 20 y 25°C, en metanol como disolvente. Los parámetros cinéticos se determinan a partir de mediciones de rotación óptica. Las constantes de primer orden obtenidas para el proceso de isomerización siguen la secuencia S-leu > S-ala > S-fenala > S-ileu > S-val, en tanto que $\Delta H^{\ddagger}$ y $\Delta S^{\ddagger}$ siguen la secuencia S-fenala > S-ala > S-val > S-ileu > S-leu. Estos resultados se discuten en relación con las posibles influencias de las interacciones no covalentes intramoleculares en los parámetros de activación.

PALABRAS CLAVES: Níquel, 1,10-fenantrolina, S-aminoacidato, isomerización, rotación óptica.

INTRODUCTION

Ligand-ligand noncovalent interactions play a significant role in a variety of processes involving metal ion-biomolecule systems. Hydrophobic interactions, for instance, contribute as structure determining factors for M^{n+}/ATP dimeric reactive species in the *in vitro* metal ion promoted

dephosphorylation of adenosine 5'-triphosphate[1]. Steric interactions may also influence the kinetics of the hydrolytic cleavage of peptide promoted by transition metal complexes[2,3]. Studies on simple mixed-chelate systems, such as ternary complexes involving aminoacidate ligands, have provided a great deal of information concerning ligand-ligand noncovalent interactions, with a natural emphasis on structural aspects and thermodynamic stability[4-6]. We have previously reported the optical activity and conductance properties of the diastereoisomeric system, Δ,Λ-[Ni(phen)$_2$(S-ala)]$^+$ $(X^{q-})_{1/q}$, where phen is 1,10-phenanthroline and S-ala is S-alaninate, in the presence of different counteranions (X^{q-}), in methanolic solution[7]. When freshly prepared, the above optically labile system undergoes a counteranion-dependent decrease in optical activity which can be ascribed to a $\Lambda \rightarrow \Delta$ isomerization process. On the other hand, the position of [Λ]/[Δ] diastereoisomeric equilibrium of nonresolvable Δ,Λ-[M(phen)$_2$(S-aa)]$^+$ $(X^{q-})_{1/q}$ systems, where M is Zn or Cd and S-aa is a S-aminoacidate ligand, is apparently dependent upon ligand-ligand noncovalent interactions involving the side chains of the chiral ligands[8,9]. Hence, it should be expected that these interactions may also exert some influence upon the isomerization processes of analogous nickel systems. In this work the possible effects of non-covalent ligand-ligand interactions on the $\Lambda \rightarrow \Delta$ isomerization rates of partially resolved Δ,Λ-[Ni(phen)$_2$(S-aa)]$^+$$(SO_4^{2-})_{1/2}$ systems has been studied in methanolic solution, at 15, 20, and 25°C, for the series: S-alaninate, S-valinate, S-leucinate, S-isoleucinate, and S-phenylalaninate.

EXPERIMENTAL

Preparation of [Ni(phen)(S-aa)]$^+$ stock solutions[10].

Δ,Λ-[Ni(phen)(S-aa)] $(SO_4)_{1/2}$ stock solutions were prepared by means of the reaction[7]: $NiSO_4 \cdot 6H_2O$ + phen$\cdot H_2O$ + S-aaH + (1/2)$Ba(OH)_2 \cdot 8H_2O \rightarrow \Delta,\Lambda$-[Ni(phen) (S-aa)] $(SO_4)_{1/2}$ + (1/2)$BaSO_{4(s)}$ + 12H_2O. Stoichiometric amounts of A.R. grade chemicals were weighed on an analytical balance and mixed in methanol (*pro analysis*) as solvent. Magnesium sulfate heptahydrate was added (in the Mg^{2+}: Ni^{2+} = 1:1 mole ratio) because, according to previous observations, it prevents the coprecipitation of nickel(II) with barium sulfate in methanolic solution. Such effect could be ascribed to a more preferable adsorption of the Mg^{2+} ions on the surface of the $BaSO_4$ precipitate[11]. The resulting mixtures were ultrasonically stirred and allowed to stand at room temperature in stoppered flasks until complete reaction of the aminoacid took place. Barium sulfate was removed by vacuum filtration. The resulting solutions were concentrated by boiling and standardized in volumetric flasks to 0.007 M at 20°C.

Preparation of partially resolved Δ,Λ-[Ni(phen)$_2$(S-aa)]$^+$ systems.

The solutions for the kinetic experiments were freshly prepared by mixing aliquots of 0.007 M 1,10-phenanthroline monohydrate in methanol (pro analysis) and Δ,Λ-[Ni(phen) (S-aa)]$^+$ stock solution, in the 1:1 volume ratio, at room temperature. An instantaneous color change from pale blue to very pale purple-pink is then observed.

Measurements

Isomerization rates were studied at 15, 20, and 25°C by measuring the changes in optical rotation at 450 nm with time. These measurements were made on a modified Perkin Elmer 141 polarimeter using thermostated closed 5 cm cells. The rather restricted range of temperatures mentioned above was considered appropriate in view of both the optical rotation decay rates observed and the volatility of the solvent. CD in the UV-visible region and absorption spectra in the UV region were recorded on a Jobin Yvon CD 6 spectrometer. Absorption spectra in the visible region were measured on a Unicam UV3 spectrophotometer. Water contents of the systems Δ,Λ-[Ni(phen)$_2$(S-aa)]$^+$ were determined by means of the Karl-Fischer method. The water concentrations were found to be in the range 0.42-0.66%.

RESULTS AND DISCUSSION

Absorption and CD spectra

Absorption spectra in the visible region of the Δ,Λ-[Ni(phen)$_2$(S-aa)]$^+$ systems are very similar to those previously reported for analogues with S-alaninate[7]. However, some small but significant changes with time are observed in these spectra. Thus, the $^3A_{2g} \rightarrow {}^3T_{1g}$ band[12] appears bathochromically shifted by 100 cm^{-1} at time zero and by 50 cm^{-1} after two hours with respect to its position at equilibrium. This effect was found to be quite reproducible, in spite of taking place within the range of variation of the position of the above mentioned band for similar systems at equilibrium (546-550 nm)[7]. This fact suggests that the freshly prepared solutions would contain a slight excess of NiN_4O_2 chromophore. The above assumption agrees with the view that Ni^{2+} should become harder by chelation with two diimine ligands[13]. As will be seen in the discussion on the activation parameters, such NiN_4O_2 chromophore could correspond to the system Δ,Λ-Ni(phen)$_2$(S-aa) (SO$_4$)]$^-$, in which the aminoacidate would behave as a monodentate ligand through an oxygen donor[14]. Accordingly, the reactions involved in the preparative procedure could be summarized through the following scheme[10]:

$$\Delta,\Lambda\text{-[Ni(phen)(S-aa)]}^+ + SO_4^{2-} \underset{}{\overset{K}{\rightleftharpoons}} \Delta,\Lambda\text{-[Ni(phen)(S-aa) (SO}_4\text{)]}^-$$

where $K > 1$, and $[\Lambda] > [\Delta]$.

$$\Delta\text{-[Ni(phen)(S-aa)]}^+ \text{ (blue)} + \text{phen} \xrightarrow{k_\Delta} \Delta\text{-[Ni(phen)}_2\text{(S-aa)]}^+ \text{ (purple-pink)}$$

$$\Lambda\text{-[Ni(phen)(S-aa)]}^+ \text{ (blue)} + \text{phen} \xrightarrow{k_\Lambda} \Lambda\text{-[Ni(phen)}_2\text{(S-aa)]}^+ \text{ (purple-pink)}$$

where $k_\Lambda > k_\Delta$.

$$\Delta\text{-[Ni(phen)(S-aa) (SO}_4\text{)]}^- + \text{phen} \xrightarrow{k_\Delta'} \Delta\text{-[Ni(phen)}_2\text{(S-aa) (SO}_4\text{)]}^-$$

$$\Lambda\text{-[Ni(phen)(S-aa) (SO}_4\text{)]}^- + \text{phen} \xrightarrow{k_\Lambda'} \Lambda\text{-[Ni(phen)}_2\text{(S-aa) (SO}_4\text{)]}^-$$

where $k_\Lambda' > k_\Delta'$.

The assumption $[\Lambda] > [\Delta]$ for the [Ni(phen) (S-aa)]$^+$ species is based on the fact that the preparation of the systems Δ,Λ-[Ni(phen)$_2$(S-aa)]$^+$ by means of the reaction:

$$\Delta,\Lambda\text{-[Ni(phen)}_2\text{]}^{2+} + \text{[Mg(S-aa)]}^+ \longrightarrow \Delta,\Lambda\text{-[Ni(phen)}_2\text{(S-aa)]}^+ + Mg^{2+}$$

leads to diastereoisomeric mixtures whose initial optical rotations are much smaller than those herein reported. Moreover, the study of molecular models suggests that the isomers Λ-fac-[Ni(phen)(S-aa)]$^+$ should predominate in the Δ,Λ-[Ni(phen)(S-aa)]$^+$ systems[15].

The CD spectra in the visible region agree with the D_{2h} holohedrized microsymmetry of the $[Ni(phen)_2(S\text{-}aa)]^+$ species. E.g. for the S-valinate system at time 2 min the following sign pattern appears in the region of the $^3A_{2g} \rightarrow {}^3T_{1g}$ band: 503 nm (+0.0092); 548 nm (-0.0031); 595 nm (+0.0113), whereas only one CD band is observed in the region of $^3A_{2g} \rightarrow {}^1E_g$: 770 nm (-0.0446)[12]. Significant changes with time in the CD spectra in the visible region, other than a decrease in the intensities, are not observed.

Figure 1 shows the circular dichroism spectra in the 1,10-phenanthroline $\pi \rightarrow \pi^*$ transition (β' and α bands) at 2 min and at equilibrium for a selected system. Exciton patterns which indicate a predominance in concentration of Λ isomer are observed in both spectra. Accordingly, the optical rotation of the systems under study would mainly arise from an excess of Λ-$[Ni(phen)_2(S\text{-}aa)]^+$.

Kinetic treatment

As it can be noticed from the data of Figure 1 and Table I, the decrease in optical rotation with time runs fairly parallel to the decrease in the intensity of the exciton CD bands; e.g. at 25°C:

$\alpha_{eq}/(\alpha_o + \alpha_o') = 0.54$, at 450 nm, and $\Delta\varepsilon_{eq}/\Delta\varepsilon_o = 0.56$, at 275 nm

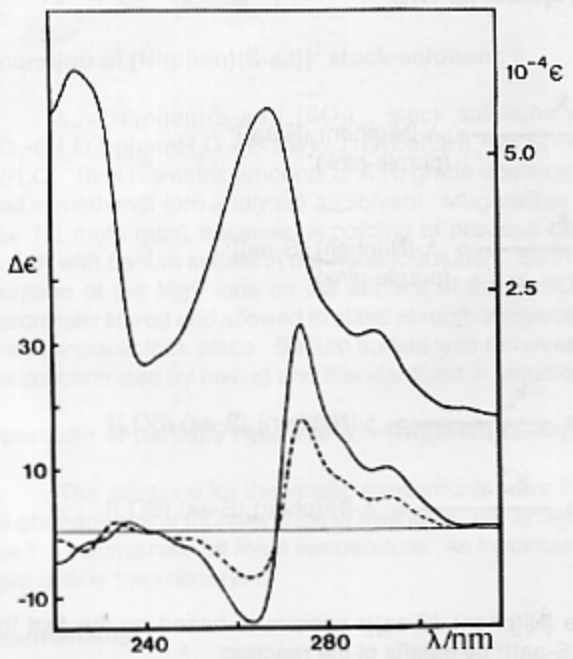

FIG. 1. Absorption and circular dichroism spectra in the UV region of the system Δ,Λ-$[Ni(phen)_2(S\text{-}val)]^+$, at time 2 min and at equilibrium.

Hence, changes in optical rotation at 450 nm with time would reflect the decrease in concentration of the Λ isomer on account of the reaction:

$$\Lambda\text{-}[Ni(phen)_2(S\text{-}aa)]^+ \rightarrow \Delta\text{-}[Ni(phen)_2(S\text{-}aa)]^+$$

The molecular rotation of the diastereoisomeric mixture would be:

$$[\phi] = \{ [\Lambda] [\phi]_{\Lambda} + [\Delta] [\phi]_{\Delta} \} / \{ [\Lambda] + [\Delta] \}$$

where $[\Lambda]$ and $[\Delta]$ are the concentrations of the isomers at time t, or at equilibrium, and $[\phi]_{\Lambda}$ and $[\phi]_{\Delta}$ are the respective molecular rotation.

TABLE I. Optical rotation parameters for the Δ,Λ-$[NI(PHEN)_2(S\text{-}AA)]^+$ SYSTEMS[a].

S-aa	Temp. (°C)	α_o (degrees)	α_{eq} (degrees)	α_o' (degrees)	Time range[b] (hours)
S-val	15	1.022	0.577	0.052	3.2-6.1
	20	0.944	0.540	0.079	2.5-4.5
	25	0.887	0.531	0.113	1.7-5.5
S-ileu	15	0.976	0.556	0.052	3.3-6.0
	20	0.914	0.526	0.080	2.5-5.3
	25	0.834	0.502	0.109	1.9-5.8
S-phe	15	0.625	0.317	0.050	2.9-5.9
	20	0.598	0.309	0.054	2.2-4.9
	25	0.570	0.289	0.074	1.4-4.1
S-ala	15	0.604	0.306	0.053	3.1-6.2
	20	0.574	0.288	0.062	2.2-4.7
	25	0.537	0.275	0.077	1.3-3.3
S-leu	15	0.624	0.309	0.065	2.9-6.0
	20	0.570	0.281	0.079	2.0-4.3
	25	0.509	0.266	0.108	1.4-4.9

[a]The mean deviations of the optical rotations are of ±0.002 degrees for α_o and α_{eq}, and ±0.004 degrees for α_o'.
[b]Time range for the determination of α_o and k.

From the above relationships:

$$[\phi] = [\Lambda] \{ [\phi]_{\Lambda} - [\phi]_{\Delta} \} / \{ [\Lambda] + [\Delta] \} + [\phi]_{\Delta}; \quad \text{and}$$

$$[\phi]_{eq} = [\Lambda]_{eq} \{ [\phi]_{\Lambda} - [\phi]_{\Delta} \} / \{ [\Lambda] + [\Delta] \} + [\phi]_{\Delta}$$

By subtraction and subsequent rearrangement:

$$[\Lambda] - [\Lambda]_{eq} = \{ [\phi] - [\phi]_{eq} \} \{ [\Lambda] + [\Delta] \} / \{ [\phi]_{\Lambda} - [\phi]_{\Delta} \}$$

Similarly:

$$[\Lambda]_o - [\Lambda]_{eq} = \{ [\phi]_o - [\phi]_{eq} \} \{ [\Lambda] + [\Delta] \} / \{ [\phi]_{\Lambda} - [\phi]_{\Delta} \}$$

where $\{ [\Lambda] + [\Delta] \} / \{ [\phi]_{\Lambda} - [\phi]_{\Delta} \}$ is constant for a given experiment. In terms of the directly measured optical rotations the above expressions become:

$$[\Lambda] - [\Lambda]_{eq} = (\alpha - \alpha_{eq}) \{ [\Lambda] + [\Delta] \} / \{ [\phi]_{\Lambda} - [\phi]_{\Delta} \} l_d \text{ and}$$

$$[\Lambda]_o - [\Lambda]_{eq} = (\alpha_o - \alpha_{eq}) \{ [\Lambda] + [\Delta] \} / \{ [\phi]_{\Lambda} - [\phi]_{\Delta} \} l_d$$

where l_d is the path of the cuvette in decimeters. If a first-order kinetics is assumed for the isomerization process[16,17]:

$$\ln (\alpha - \alpha_{eq}) = -kt + \ln(\sigma_o - \alpha_{eq}) \quad (1)$$

The decrease in optical rotation of the systems here studied obeys the above rate equation at times of reaction greater than 1.4, 2 and 3 hours, at 25, 20 and 15°C, respectively. Thus, k and α_o were determined by plotting $\ln(\alpha - \alpha_{eq})$ against t over the appropriate time ranges (Table I). The overall rate expression is:

$$\alpha - \alpha_{eq} - \alpha_{eq}' = (\alpha_o - \alpha_{eq})\ e^{-kt} + (\alpha_o' - \alpha_{eq}')\ e^{-k't} \quad (2)$$

The term $(\alpha_o' - \alpha_{eq}')\ e^{-k't}$, which means in all cases a rather small contribution, would arise from the presence of an additional fast-isomerizing optically active system. As previously suggested, such system could correspond to:

$$\Lambda\text{-}[Ni(phen)_2(S\text{-}aa)\ (SO_4)]^+ \rightleftharpoons \Delta\text{-}[Ni(phen)_2(S\text{-}aa)\ (SO_4)]^+$$

where both aminoacidate and sulfate are acting as monodentate ligands[14,18-20].

The occurrence of an initial excess of $[Ni(phen)_2(S\text{-}aa)\ (SO_4)]^+$ species would be a consequence of the preparative procedure. A rather low stereoselectivity should be expected for the above system on account of the monodentate behavior of the chiral ligand. Hence $\alpha_{eq}' \approx 0$, and the parameters α_o' and k' can be determined by plotting $\ln[\alpha(exp) - \alpha]$ against t over the appropriate time ranges, i.e., from 0 up to 1.4, 2 and 3 hours, at 25, 20 and 15°C, respectively. From the above approximations the expression (2) becomes:

$$\alpha - \alpha_{eq} + (\alpha_o - \alpha_{eq})\ e^{-kt} + \alpha_o' e^{-k't} \quad (3)$$

This rate equation was employed to perform the theoretical curves of variation of optical rotation with time, at 20°C, included in Figure 2. Similar agreement between the theoretical curves and the experimental data were obtained for the kinetic determinations at 15 and 25°C. The values of the parameters involved in equation (3) are listed in Tables I, II and III. Activation parameters calculated by means of the transition-state theory[21] are also included in Tables II and III. Such parameters were computed by using the pre-exponential factor $kT/h = 3{,}6656 \cdot 10^{14}\ min^{-1}$, i.e. at

TABLE II. First-order rate constants and activation parameters for Λ-Δ isomerization of $[Ni(phen)_2(S\text{-}aa)]^+$ systems[a].

S-aa	10^3k, min^{-1} 15°C	20°C	25°C	ΔH‡ (kcal/mol)	ΔS‡ (e.u.)	(H_2O) (%)
S-val	1.14±0.05	2.07±0.07	3.25±0.07	17.4±1.1	-19.8±3.7	0.66
S-ileu	1.21±0.05	2.11±0.06	3.40±0.07	17.0±1.1	-20.9±3.8	0.42
S-phe	1.20±0.07	2.24±0.09	3.81±0.11	19.1±1.5	-13.5±5.3	0.61
S-ala	1.42±0.07	2.54±0.14	4.17±0.15	17.8±1.5	-17.9±5.2	0.51
S-leu	1.57±0.07	2.80±0.11	4.37±0.09	16.9±1.1	-20.9±4.2	0.54

[a]Errors in rate constants and activation parameters were estimated from the mean deviation of the optical rotation measurements.

T = 293,15 °K, and the relationship $\Delta H^{\ddagger} = E_a - RT$, which rules for reactions in solution[21]. Small differences in water content of the systems had not significant effects on the values of the kinetic parameters. Hence, the data of Tables I, II and III would be considered appropriate for comparative purposes.

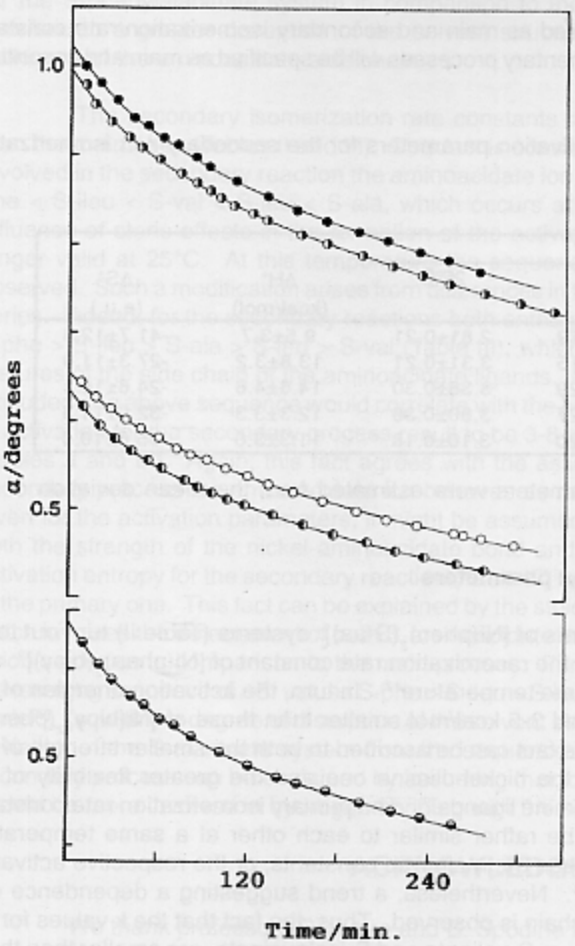

FIG. 2. Variation of optical rotation at 450 nm with time for the Λ-Δ isomerization of $[Ni(phen)_2(S\text{-}aa)]^+$ systems at 20°C. $[Ni^{2+}]_{total}$ = 0.0035 M. l_d = 0.05 m. (●) S-valinate; (◑) S-isoleucinate; (○) S-phenylalaninate; (◐) S-alaninate: (◒) S-leucinate: (——) computed with equation (3) and parameters of Tables I, II and III.

A dissociative path for the racemization of similar mixed ligand nickel systems has been already established[16,17]. Thus, in view of the kinetics observed for the systems under study, the following scheme can be proposed for the isomerization process:

$$\Lambda\text{-}[Ni(phen)_2(S\text{-}aa)]^+ \xrightarrow{k} \Lambda\text{-}[Ni(phen)_2]^{2+} + S\text{-}aa^-$$

$$\Lambda\text{-}[Ni(phen)_2(S\text{-}aa)\ (SO_4)]^- \xrightarrow{k'} \Lambda\text{-}[Ni(phen)_2]^{2+} + S\text{-}aa^- + SO_4^{2-}$$

$$\Lambda\text{-}[Ni(phen)_2]^{2+} \xrightarrow{\text{fast}} \Delta\text{-}[Ni(phen)_2]^{2+}$$

$$\Lambda\text{-}[Ni(phen)_2]^{2+} + S\text{-}aa \xrightarrow{\text{fast}} \Delta\text{-}[Ni(phen)_2(S\text{-}aa)]^{+}$$

The constants k and k' will be hereafter referred as main and secondary isomerization rate constant, respectively. Likewise, the corresponding elementary processes will be specified as main and secondary reaction.

TABLE III. First-order rate constants and activation parameters for the secondary Λ-Δ isomerization process[a].

S-aa	10^2k', min^{-1}			ΔH‡ (kcal/mol)	ΔS‡ (e.u.)
	15°C	20°C	25°C		
S-val	1.55±0.22	2.12±0.19	2.81±0.21	9.5±3.7	-41.7±12.6
S-ileu	1.43±0.17	2.08±0.15	3.31±0.21	13.8±3.2	-27.3±11.0
S-phe	1.39±0.18	2.05±0.29	3.38±0.30	14.6±4.6	-24.6±16.1
S-ala	1.79±0.18	2.83±0.27	3.80±0.36	12.3±3.3	-32.0±11.3
S-leu	1.55±0.19	2.46±0.20	3.10±0.18	11.3±3.0	-35.6±10.4

[a]Errors in rate constants and activation parameters were estimated from the mean deviation of the optical rotation measurements.

Isomerization rate constants and activation parameters

The main isomerization rate constants of $[Ni(phen)_2(S\text{-}aa)]^+$ systems (Table II) turn out to be approximately two or three times as large as the racemization rate constant of $[Ni(phen)_2(bipy)]^{2+}$ and similar to that of $[Ni(bipy)_2(phen)]^{2+}$, at the same temperature[17]. In turn, the activation energies of the main reactions are found to be about 2-4 and 3-5 kcal/mol smaller than those of $[Ni(bipy)_2(phen)]^{2+}$ and $[Ni(phen)_2(bipy)]^{2+}$, respectively[17]. This fact can be ascribed to both the smaller strength of the nickel-aminoacidate binding with regard to the nickel-diimine one and the greater flexibility of the aminoacidate ligands in comparison to the diimine ligands[17]. The primary isomerization rate constants of the systems $[Ni(phen)_2(S\text{-}aa)]^+$ result to be rather similar to each other at a same temperature (Table II). No correlation is observed between the main rate constants, or the respective activation parameters, and the hydrophobicity scale[22]. Nevertheless, a trend suggesting a dependence of k upon the features of the aminoacidate side chain is observed. Thus, the fact that the k values for the systems with C-3 branched amino-acidates, i.e. S-valinate and S-isoleucinate, are smaller than those of the remaining systems suggests that steric effects contribute to decrease the isomerization rate. In fact, the k values are in the same sequence as the optical rotations at the equilibrium. However, the enthalpies of activation do not account for the above order (Table II). Both enthalpies and entropies of activation follow the order: S-phe > S-ala > S-val > S-ileu > S-leu. The activation enthalpy for the main reaction seems to depend in a complex manner on the structure of the chiral ligand. Probably, the main determining factors of the $\Delta H^{\ddagger}$ values are the strength of nickel-aminoacidate binding (ligation energy) and the conformational changes involved in the formation of the activated complex. Thus, it could be assumed that the greater value of $\Delta H^{\ddagger}$ for the S-phenylalaninate system is mainly due to the prevalence of steric effects which hinder the conformational changes involved in the transition state. Whereas for the S-alaninate system, which exhibits a relatively high $\Delta H^{\ddagger}$ value, in spite of the less bulky side chain of the chiral ligand, the strength of the nickel-aminoacidate binding would prevail as determining factor. Accordingly, if the S-alaninate system is excluded, the resulting

order of $\Delta H^{\ddagger}$ values seems to vary inversely to the flexibility of the aminoacidate side chain: S-leu ≈ S-ileu < S-val < S-phe. The values of activation entropy for the primary process result to be much more negative than those of $[Ni(bipy)_2(phen)]^{2+}$ and $[Ni(phen)_2(bipy)]^{2+}$ [17] (Table II). This fact would be ascribed to the detachment of the aminoacidate ligand in the transition state, which involves an increase in the number of ionic species and, hence, an increase in the extent of solvation. The less negative $\Delta S^{\ddagger}$ value for the S-phenylalaninate system in comparison to those of the remaining ones (Table II) would be ascribed to a greater disruption of the solvent structure in the transition state, owing to the greater bulkiness of the aminoacidate side chain.

The secondary isomerization rate constants turn out to be approximately ten times greater than the main ones (Tables II and III). This fact is consistent with the assumption that in the complexes involved in the secondary reaction the aminoacidate ion acts as monodentate ligand. The sequence S-phe < S-ileu < S-val < S-leu < S-ala, which occurs at 15 and 20°C, might appear ascribable to the influence of steric effects in the formation of the activated complex. However, the above order is no longer valid at 25°C. At this temperature the sequence S-val < S-leu < S-ileu < S-phen < S-ala is observed. Such a modification arises from differences in the activation parameters over the aminoacidate series. Indeed, for the secondary reactions both enthalpies and entropies of activation follow the order S-phe > S-ileu > S-ala > S-leu > S-val (Table III), which is rather difficult to rationalize in terms of the features of the side chain of the aminoacidate ligands. Notwithstanding, if the S-alaninate system was excluded, the above sequence would correlate with the hydrophobicity scale[22]. The values of enthalpies of activation for the secondary process result to be 3-8 kcal/mol smaller than those of the primary ones (Tables II and III). Again, this fact agrees with the assumption that in the complexes involved in the secondary process the aminoacidate ion behaves as monodentate ligand. From the order previously given for the activation parameters, it might be assumed that the main determining factors for $\Delta H^{\ddagger}$ are both the strength of the nickel-aminoacidate bond and the hydrophobic interactions. The values of activation entropy for the secondary reaction (Table III) turn out to be 6-22 e.u. more negative than those of the primary one. This fact can be explained by the stoichiometry proposed for the secondary reaction, which involves the detachment of both S-aminoacidate and sulfate, i.e. a greater increase in the number of ionic species in comparison to the main process. Further, if the S-alaninate system were excluded, the resulting sequence of $\Delta S^{\ddagger}$ values S-phe > S-ileu > S-leu > S-val would correlate with the hydrophobicity scale[22], i.e. with the degree of disruption of the solvent structure involved in the secondary process. The deviation of the S-alaninate system from the sequences of activation parameters of both primary and secondary process can be explained by assuming that, owing to its smaller size, the S-alaninate ligand should be more involved in hydrogen bonding with the solvent in the transition state.

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