Kinetics and Mechanism of Metallacyclization in a Chloromethylcobalt Complex with a Salen-Type Ligand

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Summary: trans-[Co(CH$_2$Cl)(tmsalen)(S)] undergoes metallacyclization in water/methanol, affording the cis β organometallic derivative [Co(tmsalenCH$_2$)(S)$_2$]Cl. The presence of N-donor ligands, L, increases the cyclization rate mainly by electronic effects. The reaction involves the substitution of the solvent by L in a fast preequilibrium step, both [Co(CH$_2$Cl)(tmsalen)(S)] and [Co(CH$_2$Cl)(tmsalen)(L)] undergoing the cyclization reaction. As the cyclization involves the formation of ions from a neutral complex, the large negative activation entropy is attributed to the freezing of the solvent around the incipient ions in the transition state.

Introduction

Metal complexes with tetradentate Schiff base ligands derived from salicylaldehyde and diamines (salen-type ligands) generally adopt a *trans* planar geometry, in which two unidentate ligands occupy the apical positions (Chart 1).[1] In some instances, the quadridentate ligand may assume a folded *cis* configuration, in which the ancillary ligands are *cis* to each other, being either both in the equatorial positions (*cis* α) or one in the equatorial and one in the apical position (*cis β*) (Chart 1).

In the last years, the interest in the *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.[2] Furthermore, as *trans* and *cis β* configurations of metallosalen complexes are interchangeable in appropriate reaction conditions, the possibility that a *trans* metallosalen complex reacts in *cis β* configuration should be considered.[2] Generally, the *cis β* configuration is induced either by a bidentate ligand[3] that occupies two *cis* sites in the coordination sphere or by the bonding nature of the two unidentate ligands, which strongly demand a *cis* coordination.[4] A lengthening of the polymethylenic chain bridging the two imine nitrogen atoms[5] and an increase of the size of the central metal atom[6] may also favor a strained nonplanar configuration.

Chart 1

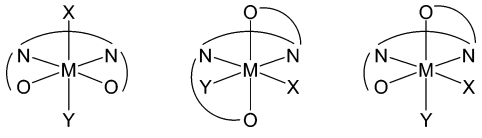
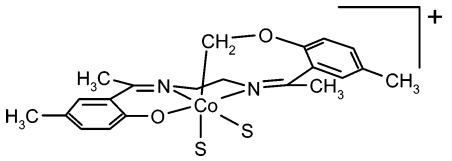


Chart 2. Δ Isomer of [Co(tmsalenCH$_2$)(S)$_2$]$^+$



We have recently reported that *trans* planar [Co(CH$_2$Cl)(tmsalen)(S)], **1**, (tmsalen = 4,4′,7,7′-tetramethylsalen and S = solvent) undergoes a cyclization reaction in coordinating solvents to afford the racemic *cis β* organometallic derivative [Co(tmsalenCH$_2$)(S)$_2$]Cl (Chart 2).[7] The cyclization leads to the formation of a monocationic complex containing a seven-membered ring and to the loss of chloride from the axial chloromethyl group. A qualitative evaluation of the cyclization rate in CD$_3$OD by means of ^{1}H NMR spectroscopy showed that the cyclization was almost complete within about 2 days.[7] The product of the cyclization, which presumably contains two solvent molecules in *cis* position, is not stable in methanolic solution, and further reactions occur after the cyclization is complete. If the reaction occurs in the presence of py, the cyclization is faster and the cyclized complex, which contains an equatorial py and an axial water molecule, is stable in methanolic solution.[7]

Previous examples of intramolecular reactions of XCH$_2$ axial groups (X = Cl, Br, I) with imino−oxime or amino−oxime equatorial ligands have been described.[8,9] In both cases the generation of an equatorial negatively charged nitrogen is required and the reaction occurs only in strongly basic medium. The cyclization of **1**, owing to the presence of negatively charged oxygens in the equatorial ligand, occurs also in neutral medium.[10]

In the present paper we investigate the effect of different nucleophiles on the cyclization rate in order to evaluate the relative importance of the steric and the electronic effects.

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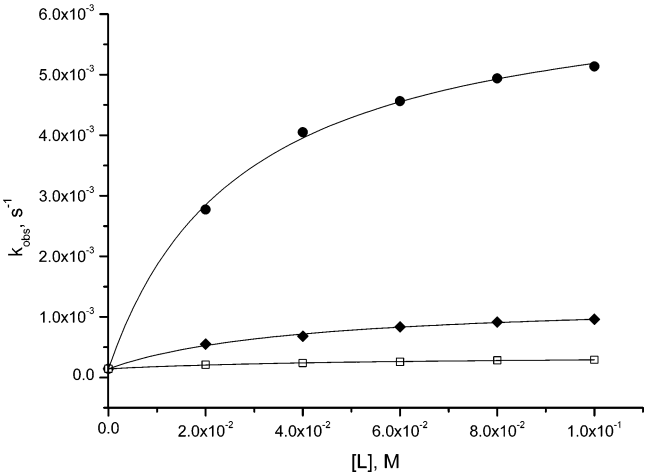
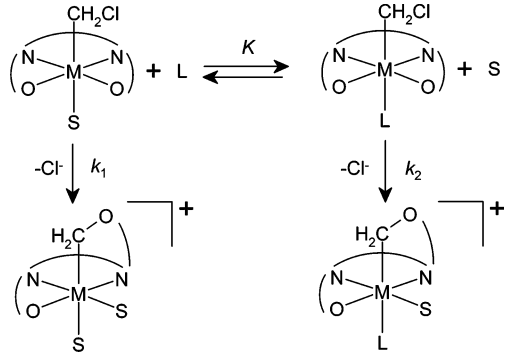


Figure 1. Plots of the pseudo-first-order rate constant, k_{obs}, versus [N-MeIm] (●), [py] (◆), and [4-CNpy] (□) for the cyclization of **1**; for the experimental conditions see the Experimental Section. The solid lines show the fit based on eq 2 of the text with the parameters reported in Table 1.

Scheme 1



Furthermore, a temperature-dependent kinetic study has been carried out for pyridine and *N*-methylimidazole, to gain some insight into the intimate reaction mechanism.

Results and Discussion

The cyclization of **1**, which occurs according to eq 1,

$$[Co(CH_2Cl)(tmsalen)(S)] + L \rightarrow [Co(tmsalenCH_2)(L)(S)]^+ + Cl^- \quad (1)$$

has been carried out in the presence of an excess of L, where L = pyridine (py), 4-CNpyridine (4-CNpy), 4-NH_2pyridine (4-NH_2py), and *N*-methylimidazole (N-MeIm), in 60% methanol/40% water (v/v), I = 0.1 M using $NaClO_4$, at 25 °C. A preliminary experiment showed that the time-resolved UV/vis spectra of **1** in the presence of py in the range 300 to 500 nm exhibit a clean isosbestic point at 313 nm, whereas the largest change in absorbance takes place at 325 nm. Therefore, the reaction progress was monitored by following the changes in absorbance at the latter wavelength. The kinetic traces reveal perfect first-order behavior. The plots of k_{obs} versus [L] show nonzero intercept and significant curvature at high nucleophile concentration (Figure 1 and S1).

The results have be interpreted in terms of the mechanism reported in Scheme 1. This scheme involves the substitution of the solvent by L in a fast preequilibrium step, both [Co(CH_2Cl)(tmsalen)(S)] and [Co(CH_2Cl)(tmsalen)(L)] undergoing the cyclization reaction at different rates. The corresponding rate law is given in eq 2, where K represents the equilibrium constant for the substitution of the solvent by L and k_1 and k_2 are the cyclization rate constants of [Co(CH_2Cl)(tmsalen)(S)] and [Co(CH_2Cl)(tmsalen)(L)], respectively.

$$k_{obs} = \frac{k_1 + k_2K[L]}{1 + K[L]} \quad (2)$$

The value of k_1 has been independently determined carrying out the cyclization reaction in the absence of L (Table 1). It has been previously shown that the cyclization rate is independent of pH in the range 5.6−11,[10] so that the same value applies also to the reaction with 4-NH_2pyridine, carried out in buffer at pH 10 to avoid the protonation of the ligand (Figure S1). Preliminary estimates of k_2 and K have been obtained from the linear plots of $1/(k_{obs} - k_1)$ versus 1/[L]. The final values were calculated from a nonlinear fit of k_{obs} versus [L] and are summarized in Table 1.

The K values relative to the formation of the precursor show relatively large standard errors, as it is often found for the equilibrium constants determined by kinetic methods, which are less precise than conventional methods.[11] Unfortunately, an independent determination of the equilibrium constants for the preequilibrium by spectrophotometric titration is hampered by the relatively fast subsequent cyclization reaction. In the above reaction scheme, the preequilibrium step has been interpreted as the substitution of the axially coordinated solvent by the entering ligand. A further possibility is the nucleophilic attack of L in equatorial position, with the contemporaneous detachment of one of the two oxygens of the chelate. The latter mechanistic picture could explain in a more direct way the fact that the reaction product bears the N-donor ligand in equatorial position, when the cyclization is carried out in the presence of pyridine.[7] A comparison of the K value with the equilibrium constant relative to the axial ligation of py by [Co(tmsalen)(CH_2CF_3)(S)], which can be determined by spectrophotometric titration, because the CF_3CH_2 derivative does not undergo cyclization, may be relevant to this point. Similar values for the axial ligation constants are to be expected because the two R groups have close polar substituent constants (+0.92 for CF_3-CH_2, and +1.05 for CH_2Cl)[12] and comparable *trans* influence in other organocobalt complexes.[13] The value effectively found for [Co(tmsalen)(CH_2CF_3)(S)] (31.6 ± 0.3 M^{-1}) is very close to the K value reported in Table 1 (25.5 ± 4.3 M^{-1}), supporting an axial ligation in the preequilibrium step. In this hypothesis, the presence of py in equatorial position in the structurally characterized reaction product[7] is due to a fast rearrangement following the rate-determining step.

The N-donor ligands increase the cyclization rate to a different extent. Both electronic and steric factors could concur in this effect, but the data of Table 1 suggest that the steric effect is less important. Indeed, for 4-Xpyridines (X = CN, H, NH_2) the steric bulk may be considered constant, but the pK_a values span from 1.7 for 4-CNpy to 9.11 for 4-NH_2-py. The data of Table 1 show that the k_2 values increase remarkably with the pK_a of L. Therefore, the accelerating effect is mainly due to the electron-donor power of the ligand, which increases the electron density on the equatorial chelate and, in particular, makes more nucleophilic the oxygen atoms. The strong ac-

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Table 1. Kinetic and Activation Parameters for the Cyclization of [Co(CH_2Cl)(tmsalen)(S)] in the Presence of Various Ligands in 60% Methanol/40% Water (v/v), I = 0.1 M ($NaClO_4$)

L	T, °C	pK_a	$k_1 \times 10^5$, s^{-1}	$k_2K \times 10^2$, $M^{-1}\,s^{-1}$	K, M^{-1}	$k_2 \times 10^4$, s^{-1}
Py	16.2		5.52 ± 0.01	1.59 ± 0.01	38 ± 5	4.2 ± 0.5
	20.8		9.40 ± 0.01	1.84 ± 0.06	23 ± 1	8.0 ± 0.5
	25.0	5.25[a]	14.31 ± 0.01	3.3 ± 0.4	25 ± 4	13 ± 3
	30.0		26.51 ± 0.02	5.0 ± 0.3	23 ± 2	22 ± 2
	34.5		47.05 ± 0,07	8.0 ± 0.5	26 ± 2	31 ± 3
			$\Delta H_1^* = 83 \pm 3$ kJ mol^{-1}			$\Delta H_2^* = 78 \pm 4$ kJ mol^{-1}
			$\Delta S_1^* = -38 \pm 9$ J $mol^{-1}\,K^{-1}$			$\Delta S_2^* = -39 \pm 14$ J $mol^{-1}\,K^{-1}$
N-MeIm	16.2			10.3 ± 0.6	42 ± 3	24 ± 2
	20.8			15 ± 2	38 ± 6	40 ± 8
	25.0	6.95[a]		24 ± 1	36 ± 3	67 ± 6
	30.0			27 ± 1	29 ± 1	93 ± 5
	34.5			38 ± 5	28 ± 6	136 ± 33
						$\Delta H_2^* = 65 \pm 3$ kJ mol^{-1}
						$\Delta S_2^* = -68 \pm 11$ J $mol^{-1}\,K^{-1}$
4-CNpy	25.0	1.7[b]		0.72 ± 0.1	20 ± 3	3.7 ± 0.7
4-NH_2py	25.0	9.11[a]		17.5 ± 0.5	40 ± 3	44 ± 4

[a] Ref 17. [b] Ref 18.

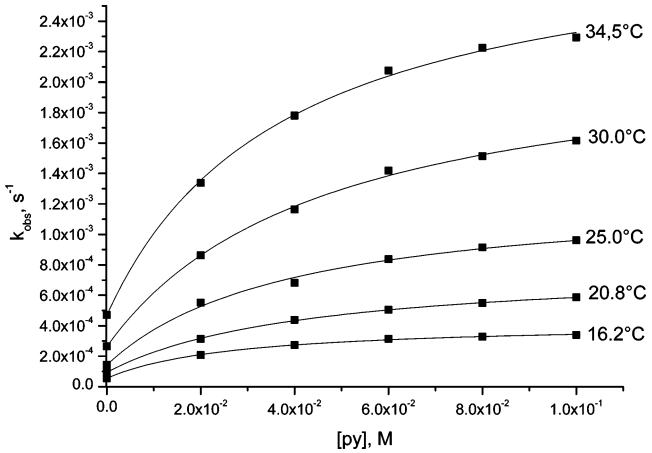

Figure 2. Plots of k_{obs} versus [py] for the cyclization of **1** at various temperatures. For the experimental conditions see the Experimental Section. The solid lines show the fit based on eq 2 of the text with the parameters reported in Table 1.

celerating effect of N-MeIm cannot be entirely ascribed to its electron-donor power, as evaluated on the basis of pK_a (Table 1). However, it is worth noting that Co−N_{ax} distances in [Co(III)(tmsalen)(N-MeIm)$_2$]ClO_4 are significantly shorter than the Co−N_{ax} distances in [Co(III)(tmsalen)(py)$_2$]ClO_4, as expected on the basis of the smaller steric bulk of N-MeIm.[14] The shorter bond may result in a consequent apparent higher electron-donor power of the ligand.

The cyclization of **1** in the presence of py and N-MeIm, under the above-described experimental conditions, has been studied at various temperatures in the range 16.2−34.5 °C (Figure 2 and S2). The corresponding k_1, k_2, and K values and the activation parameters, obtained from the linearized Eyring equation (eq 3 and Figure S3), are reported in Table 1.

$$\ln \frac{k_i}{T} = \ln \frac{\kappa}{h} - \frac{\Delta H_i^*}{RT} + \frac{\Delta S_i^*}{R} \qquad i = 1, 2 \qquad (3)$$

The most relevant feature of these values is the considerably negative activation entropy, which allows some insight into the intimate mechanism of the cyclization. The cyclization reaction proceeds through the internal nucleophilic attack of the "neighbouring group" O^- on the axial chloromethyl group with the detachment of a chloride ion. As the cyclization involves the formation of ions from neutral **1**, the activated complex may be described almost as an ion pair or an exceedingly polar complex approaching an ion pair.[15] The large negative value of the activation entropy, due to the freezing of the solvent around the incipient ions, is in accord with this picture.

A comparison of the reactivity of the chloromethyl derivative **1** with that of the corresponding bromo- and iodo-methyl complexes would be interesting in order to evaluate the degree of bond breaking in the transition state, as the dominant factor that favors bromide over chloride was identified in the bond dissociation energy difference.[16] Unfortunately, several efforts to synthesize these complexes led to the cyclized complex or to mixtures of products. However, this result suggests that the cyclization is faster for bromo- and iodo- than for the chloromethyl derivative.

Finally, it is noteworthy that in the few previously reported examples of intramolecular reaction between the axial XCH_2−Co (X = halogen) group and the equatorial ligand, stable N−Co−C three-membered rings are formed.[8,9] In this case the cyclization leads to the formation of a seven-membered ring. Both these results are compatible with processes involving the participation of a "neighboring group". Indeed, it has been previously pointed out that "a neighboring group may be located at any distance from the center of substitution, provided that in the transition state it can get near enough to the reaction center and can be suitably disposed geometrically to give a transition state approximating that of a S_N2 reaction".[15]

Experimental Section

General Information. All the manipulations were performed in the dark. [Co(III)(CH_2Cl)(tmsalen)]$_2$, **1**, and [Co(III)(CH_2CF_3)(tmsalen)]$_2$ were synthesized as previously described.[14] All the other reagents were analytical grade and used without further purification. NMR spectra were recorded on a JEOL EX-400 (^1H at 400 MHz and ^{13}C at 100.4 MHz). Kinetic runs were recorded using a Uvikon 941 plus (Kontron Instruments). The pH of the solutions was measured using a Radiometer PHM 220 pH meter.

Kinetic Runs. The cyclization kinetics of **1** were followed spectrophotometrically in the mixed solvent 60% methanol/40%

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H_2O (v/v), $I = 0.1$ M using $NaClO_4$. Generally, $(2-4) \times 10^{-4}$ M solutions of complex were used. As the complex did not dissolve completely, the suspension was filtered before the addition of L. The ligand concentration was in large excess (pseudo-first-order conditions). For the reactions with 4-NH_2pyridine, the solution was buffered at pH 10.2 with a borate buffer and the pH checked before any kinetic run. The reactions with 4-CNpyridine and 4-NH_2-pyridine were studied at 25 °C; those with pyridine and N-MeIm, at various temperatures in the range 16.2−34.5 °C. The reaction progress was monitored by following the changes in absorbance at 325 nm. The k_{obs} rate constants were obtained from the linear plots of $\ln(A - A_\infty)$, where A is the absorbance at the time t and A_∞ is the final absorbance, versus time. Kinetic data were analyzed with ORIGIN, version 6.

Equilibrium Study. The value of the equilibrium constant for the ligation of py by [Co(III))(CH_2CF_3)(tmsalen)(S)] was determined by spectrophotometric titration at 325 nm. A 4×10^{-4} M solution of the complex in 60% methanol/40% H_2O (v/v) ($I = 0.1$ M using $NaClO_4$) at 25 °C was titrated with pyridine. As the absorbance of py is not negligible at high concentrations, A_∞, the absorbance at 100% formation of the complex, was calculated from a plot of $(A - A_0)/[L]$ versus A. Subsequently, the data were analyzed by plotting $\log(A - A_0)/(A_\infty - A)$ versus log [py], where A_0 is the absorbance of the starting complex and A is the absorbance at any L concentration. This plot was linear with a slope close to 1, indicating that only one L ligand has been coordinated to the Co atom. The K value was calculated from the intercept of the plot.

Supporting Information Available: Three figures reporting kinetic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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