Stereochemical Analysis of Cobalt(III) Complexes with Tridentate Imino- and Amino-Oxime Ligands

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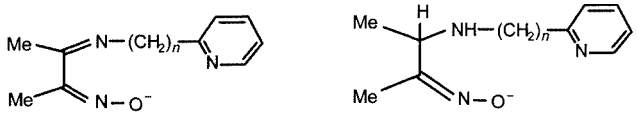
The stereochemistry of a new class of models of the vitamin B_{12} system, containing tridentate pyridyl-imino-oxime [$C_6H_5N(CH_2)_nNC(CH_3)C(CH_3)NO^-$; n = 1, L^1; n = 2, L^2] and pyridyl-amino-oxime [$C_6H_5N(CH_2)_nNHCH(CH_3)$-$C(CH_3)NO^-$; n = 1, L^3; n = 2, L^4] ligands, has been investigated through molecular mechanics calculations based on a specific force field. It is shown that, among all the possible diastereomers of the imino complexes $[Co(L^{1,2})_2]^+$, the minimum strain energy is exhibited in a *mer* configuration. For the amino complexes $[Co(L^{3,4})(HL^{3,4})]^{2+}$, the minimum is exhibited in a *fac* configuration, with the amino nitrogen atoms all having the same chirality, opposite to that of the adjacent carbon atoms. Furthermore, comparison of the effect of five- (L^1, L^3) or six-membered (L^2, L^4) chelate rings on the complexes indicates that the strain energy decreases upon passing from L^1 to L^2 complexes, while it increases upon passing from L^3 to L^4 complexes. The effect of rotation around the axial pyridyl Co–N bond on the coordination geometry has also been studied through a conformational analysis of the methyl (R = Me) and adamantyl (R = Adam) organocobalt derivatives $[RCo(L^4)(HL^4)]^+$. The most important result is that the rotation is rather hindered in the case of the bulky Adam group, while in the Me case the pyridyl group can rotate across a wide angular range. In both cases, the rotation causes a significant change in the Co–N bond length, while the Co–C distance is almost unaffected. It is also shown that the aromatic base is oriented with respect to the equatorial ligand in a fashion quite different from other B_{12} models.

Introduction

In recent years,[1−3] tridentate imino- and amino-oxime ligands, obtained by condensation of biacetyl monoxime with 2-(aminomethyl)pyridine and 2-(2-aminoethyl)pyridine (see Scheme 1), have been used to prepare stable alkylcobalt complexes, which differ in a number of respects from the widely studied tetradentate ligand derivatives.[4] Thus, it has recently been shown[3] that organocobalt(III) complexes of formula $[RCo(L^4)(HL^4)]^+$ (Figure 1, a), containing the tridentate 3-[2-(2-pyridyl)ethylamino]butane-2-one-oximato ligand (L^4) and its protonated form (HL^4), constitute a new type of model of alkylcobalamins (vitamin B_{12} system).[5] Their geometry is reminiscent of the lariat-type complexes (Figure 1, b),[6] which combine the corrin-like features of iminocobaloximes with an appended axial base, but differs by having a more crowded equatorial moiety. Structural evidence[3] indicates that their properties are closer to those of alkylcobalamins (particularly for the C−Co−N axial fragment) than that of any of the other previously reported models,[7] such as the well documented alkylcobaloximes, $RCo(DH)_2L$ (DH = monoanion of dimethylglyoxime). This has been attributed to the more crowded nature of the equatorial moiety (planar in cobaloximes), which would cause stronger steric interactions with the axial ligands.[2,3] Therefore, these compounds offer the opportunity to study the influence of the electronic and steric factors on the axial Co−C and Co−N bonds, thereby extending the previous molecular mechanics (MM) investigation on alkylcobaloximes.[8]

Structural investigations of lariat-type complexes[6] and alkylcobaloximes[7,8] have shown that the Co−N axial bond length is significantly affected by the relative orientation of the N and equatorial ligands. This feature becomes relevant in light of the evidence of substitution in some B_{12} enzymes of the Co-bound benzimidazole residue with a histidine group of the protein chain.[9] Therefore, the study of the nature of the Co−N bond in simple models,[6a,10] and particularly of the influence of the orientation of the nitrogen base with respect to the equatorial ligand, is of special interest.[8,11]



n = 1, L1 n = 2, L2 n = 1, L3 n = 2, L4

Scheme 1

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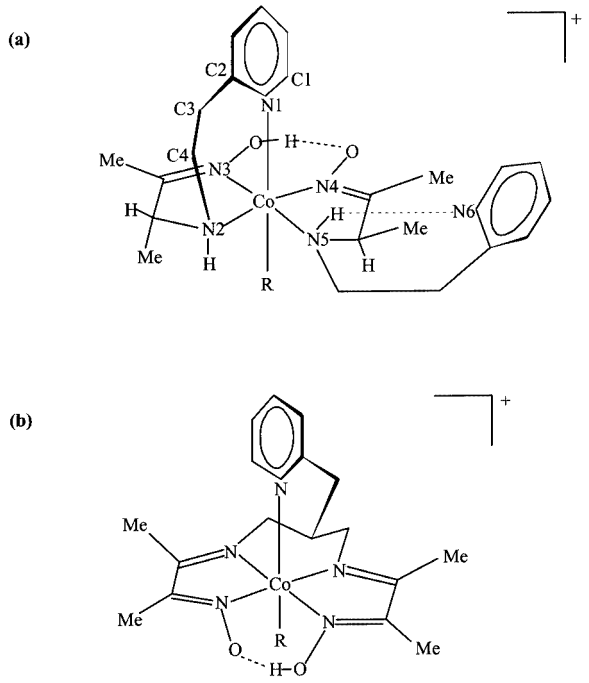

Figure 1. (a) Sketch of the structure of $[RCo(L^4)(HL^4)]^{2+}$ with a numbering scheme for the relevant atoms. (b) Sketch of the structure of a lariat type complex

$[RCo(L^4)(HL^4)]^+$ species may be obtained from $[Co(L^4)(HL^4)]^{2+}$ by reduction and successive oxidative alkylation.[3] In turn, the latter complex may be obtained by hydrogenation of the imino-oxime derivative $[Co(L^2)_2]^+$ (Figure 2).[2] Interestingly, starting from the 2-(aminomethyl)pyridine complex $[Co(L^1)_2]^+$ and under the same conditions, the metal reduction and alkylation reactions do not occur and only the hydrogenation product $[Co(L^3)(HL^3)]^{2+}$ is obtained.[2] This difference has been attributed to a more strained coordination in the L^1 complex with respect to that in the L^2 derivative.[2]

In order to provide some insight into the different strain energies of the $[Co(L^1)_2]^+ - [Co(L^2)_2]^+$ and $[Co(L^3)(HL^3)]^{2+} - [Co(L^4)(HL^4)]^{2+}$ complexes, a stereochemical investigation has been carried out through MM calculations, by implementation of the previously derived cobaloxime force field.[8] Furthermore, the present investigation includes an analysis of all the possible diastereomers of these complexes, denoted as $[Co(A\hat{}B\hat{}C)_2]$, where A^B^C represents the tridentate ligand with its three different nitrogen donors, A, B, and C (Figure 3). In the cases of the L^3 and L^4 complexes, ligand chirality, arising from the presence of stereogenic nitrogen and carbon centres in the equatorial ligand (N2, N5, and their adjacent C atoms, see Figure 2, b), has also been taken into account. This appears to be of some interest for an investigation of the possible species present in solution, considering that the $[Co(L^1)_2]^+$ [12] and $[Co(L^2)_2]^+$ complexes have been found in the solid state in a *mer* configuration, while the $[Co(L^3)(HL^3)]^{2+}$ and $[Co(L^4)(HL^4)]^{2+}$ complexes have been isolated in the *fac* configuration with *trans* pyridyl groups and *cis* amino and oxime nitrogen atoms.[2]

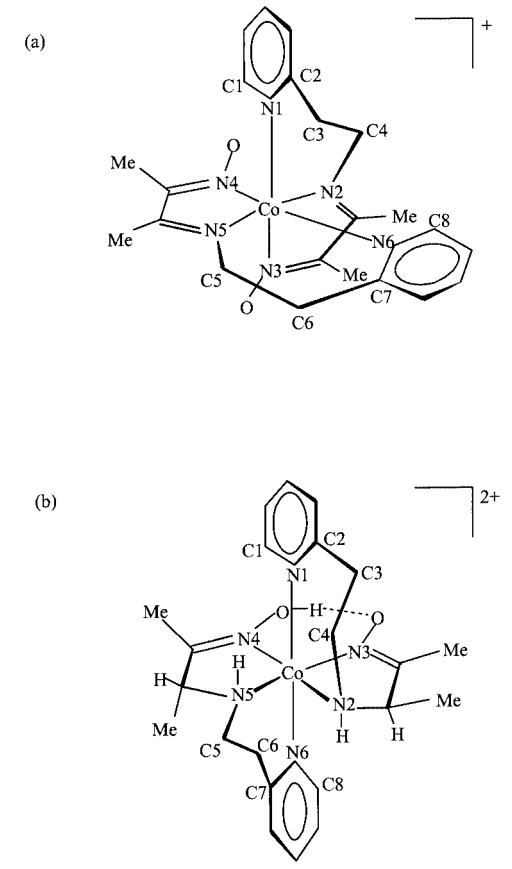

Figure 2. Sketch of the structure of $[Co(L^2)_2]^+$ (a) and $[Co(L^4)(HL^4)_2]^{2+}$ (b), with a numbering scheme for the relevant atoms. Hydrogen atoms are shown for H bonds and the chiral C and N atoms

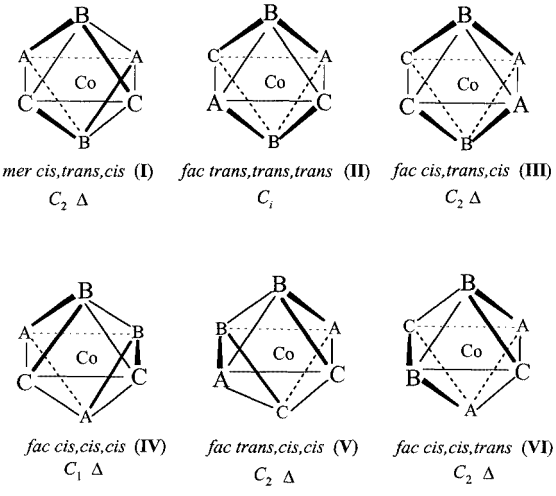

Figure 3. Schematic depiction of the six possible diastereomers for octahedral cobalt complexes containing two tridentate ligands A^B^C. Point symmetry and complex chirality are also shown. Larger letters define the octahedron upper triangular face. Thick lines represent the ligand bites

After validation of the force field, the effect of rotation around the axial Co−N bond on the metal coordination geometry has been investigated for the $[MeCo(L^4)(HL^4)]^+$

complex. The study has also been extended to the much bulkier adamantyl (Adam) derivative, even if not thus far isolated, in order to address the effects of the alkyl bulkiness. The results of the conformational analysis are also useful for a comparison between sterically different equatorial ligands, such as $(L^4)(HL^4)$ and $(DH)_2$.[4,5]

Results

Methods

Energy calculations have been performed with a Pentium III PC, using the HyperChem 6.01 molecular modelling system.[13] The Polak−Ribiere version of the conjugate gradient method was used in all energy minimisation calculations with a convergence criterion of 0.001 kcal·mol^{-1}·Å^{-1}.

The AMBER force field,[14] already implemented for the stereochemical investigation of cobaloximes,[8] has been used after further addition of the new atom types, NP_R, NI_R, NH_R, NE_R, and NO_R (R = X, Y, Z) for the pyridyl (py), imino (im), amino (am), protonated and nonprotonated oximato (ox) nitrogen atoms, respectively. The relative stretching and bending force field constants (Table 1) have been derived by the methods and optimisation procedure previously described,[8,15] which are based on the crystal structure atom parameters of the Co−L^{1-4} complexes.[3] The minimised function is GOF = $[\Sigma_i w_i \Delta_i^2/(n_{obsd.} - n_p)]^{1/2}$, where $n_{obsd.}$ is the number of observables (388 in the present case) with weights $w_i = 1/\sigma_i^2$, n_p is the number of variable parameters (11), the summation being extended to all the differences, Δ_i, between each observed and calculated value. In order to simulate crystal packing effects that can affect the torsion angles and yield to strained geometries, the pyridyl endocycle N−Co−N−C and N−C−C−C torsion angles were restrained to the observed values by force constants of 20 kcal·mol^{-1}. In order to estimate the electrostatic contribution to the total strain energy, E, the dielectric constant D = 7.8 has been used, as for cobaloximes.[8]

Table 1. Optimised force field stretching [k^d (kcal·mol^{-1}·Å^{-2}), d^o (Å)] and bending [k^θ (kcal·mol^{-1}·rad^{-2}), θ^o (°)] constants

[a]	k^d	d^o
CO3−NE_R	104.03	1.9712
CO3−NP_R	123.30	1.9255
CO3−NI_R	108.37	1.9600
CO3−NH_R	101.69	1.9776
CO3−NO_R	108.27	1.9602
NO_R−O1	647.61	1.2713
	k^θ	θ^o
CO3−NH_R−CT	61.89	110.40
CO3−NI_R−CDH	53.22	120.10
CO3−NI_R−CT	48.36	125.50
CO3−NO_R−CDH	51.15	122.50
CO3−NO_R−O1	65.57	121.10

[a] R = X, Y, Z.

Atomic charges for each molecule have been calculated by the semi-empirical ZINDO/1 method, using restricted Hartree Fock functions,[13] and then averaged over chemically equivalent atoms. At convergence GOF was 4.786, with a difference between the lowest and highest GOF values of less than 0.0001.

In order to explore, as thoroughly as possible, the conformational space of the complexes of type $[Co(L)_2]^+$ and $[Co(L)(HL)]^{2+}$ (L = L^3, L^4), all possible stereoisomers have been built using HyperChem, considering all combinations of nitrogen and carbon chiralities. The strain energies of all these diastereomers have been calculated by molecular energy minimisation, without any torsion restraint and with $D = r_{ij}$, in order to simulate solvent effects.[14]

Because of the uncertainty in the location of the oxime bridge hydrogen atoms, it has been assumed, as in the case of cobaloximes,[8] that the hydrogen atom (atom type HDH) lies on the median of the O···O segment (atom types ODH). The energy of the H-bonding interaction is given by electrostatic interactions and by the stretching of the ODH−HDH bond (d^o = 1.269, k^d = 198.9 kcal·mol^{-1}·Å^{-2}). Where it has been assumed that this H bond is not present (L^o ligands), one ODH−HDH bond has been substituted by an ODH−HO bond (d^o = 0.96 Å, k^d = 553.0 kcal·mol^{-1}·Å^{-2}) and the other oxygen atom treated as type O1. In this case, when properly oriented, the O1 atom can give rise to a hydrogen bond interaction with HO only through electrostatic interactions.

For the conformational analysis of the alkyl derivatives $[RCo(L^4)(HL^4)]^+$, with R = Me and Adam, the strain energy has been minimised (D = 7.8) by rotating about the Co−N(py) bond (torsion angle φ_1 = N2−Co−N1−C2, see Figure 1) in steps of 5°, with a restraint constant of 1000 kcal·mol^{-1}. For these complexes, the force field constants derived for the axial ligands of the relative alkyl/pyridine cobaloxime have been adopted.[8] The Δ isomer with S and R configurations for the nitrogen and carbon atoms, respectively, has been used in the calculations, maintaining the intramolecular N5···N6 hydrogen bond (Figure 1, a) present in the solid state.

In all calculations, the same improper torsion parameters have been assigned to trigonal carbon atoms (atom type CA) and trigonal nitrogen atoms, taking the parameters of CA given in AMBER.[14] As in previous calculations,[8] torsion barriers around the coordination bonds have not been considered.

A local program[16] has been used for all the geometrical calculations, including the ring puckering parameter Q,[17] and the conformation discriminator Δ_c.[18]

Validation of the Force Field

As shown in Table 2, the agreement between observed and calculated bond lengths and angles for the Co−L^{1-4} complexes is quite satisfactory, on the basis of the values of the average differences $<\Delta>$ and the root-mean-square deviations, rms = $[(\Sigma_i \Delta_i^2)/n]^{1/2}$.

Moreover, the consistency of the force field is well illustrated (Table 3) by its ability to reproduce the observed vari-

Table 2. Average differences, <Δ>, between observed and calculated bond lengths [Å] and angles [°], together with rms values (Å) and number of observations, *n*; X, Y, and Z represent generic non-metal atoms

Distances	<Δ>	rms	n
Co−X	−0.006	0.019	24
X−Y	−0.015	0.022	116
Angles			
X−Co−Y	−0.2	1.6	60
Co−X−Y	−0.4	1.5	48
X−Y−Z	0.3	1.4	140

Table 3. Selected average observed and calculated bond lengths [Å] and angles [°] for $[Co(L)_2]^+$ (L = L^1, L^2), and $[Co(L)(HL)]^{2+}$ (L = L^3, L^4)

	L^1 obsd.	L^2 obsd.	L^1 calcd.	L^2 calcd.
Co−N(py)	1.953	2.038	1.926	2.018
N(py)−Co−N(im)	83.8	93.8	85.2	94.1
	99.5	94.6	96.6	93.1
N(py)−Co−N(ox)	166.1	174.9	168.2	174.6
Co−N(py)−C_α[a]	125.7	119.0	127.3	121.3
Co−N(py)−C_β[a]	113.9	123.8	112.9	121.7
Co−N(im)−C [b]	118.1	123.2	118.6	125.3
	116.2	114.0	116.0	114.1
	L^3 obsd.	L^4 obsd.	L^3 calcd.	L^4 calcd.
Co−N(py)	1.916	2.026	1.921	2.042
N(py)−Co−N(am)	83.5	88.3	84.7	89.1
	92.1	89.7	93.3	88.5
N(py)−Co−N(ox)	89.9	84.8	87.4	86.3
	94.7	93.0	94.6	92.2
Co−N(py)−C_α[a]	126.0	116.8	126.8	119.1
Co−N(py)−C_β[a]	114.3	126.5	113.8	124.8
Co−N(am)−C [c]	106.9	114.9	107.7	115.0
	111.1	111.5	109.5	110.5

[a] C_α and C_β represent, respectively, the pyridyl carbon atoms like C1, C2 and C8, C7 in Figure 2. [b] The first line refers to the pyridyl bridge, the second one to the oxime ring. [c] The first line refers to the pyridyl bridge, the second one to the equatorial ring.

ations[2] of both bond lengths and angles on passing from $[Co(L^1)_2]^+$ to $[Co(L^2)_2]^+$, as well as from $[Co(L^3)(HL^3)]^{2+}$ to $[Co(L^3)(HL^3)]^{2+}$, that is on passing from complexes with ligands L^1, L^3 [$-(CH_2)-$ bridges] to complexes with ligands L^2, L^4 [$-(CH_2)_2-$ bridges]. The conformational parameters of the calculated structures are also in good agreement with those observed (Table 4).

In the case of the methyl derivative, $[MeCo(L^4)(HL^4)]^+$, the agreement between observed and calculated coordination bond lengths (Table 5) is not as good (rms = 0.033 Å) as that found in the Co−L^{1-4} complexes (rms = 0.019 Å). This indicates that the force field is not completely transferable to the organometallic derivatives. However, for the limited scope of this work, it is sufficient that the trend in the Co−N bond lengths, Co−N(ox) < Co−N(am) < Co−N(py), as well as the deviations from 90° of the coordination bond angles involving the coordinated pyridyl ligand (Table 5), are well reproduced. Furthermore, it is to be stressed that the perchlorate anion and the methyl group in the crystal structure are affected by thermal motion, reducing the accuracy of the crystal structure determination.[3] Correction of the experimental distances for this effect (riding model) reduces the rms deviation of the Co−X distances to 0.022 (Table 5).

Table 4. Conformational parameters of the two pyridyl chelate rings for $[Co(L)_2]^+$ (L = L^1, L^2) and $[Co(L)(HL)]^{2+}$ (L = L^3, L^4). The two rings are defined by the bites N1−N2 and N5−N6, respectively

	L^1 obsd.	L^1 calcd.	L^2 obsd.	L^2 calcd.
Conformation	planar	planar	half-chair[a]	half-chair[a]
	planar	planar	half-chair [b]	half-chair[b]
Helicity			δ	δ
			δ	δ
Discriminator (Δ_c)	5.4	1.6	10.9	12.5
	5.7	1.6	11.4	12.5
Puckering (Q)	0.073	0.025	0.62	0.63
	0.081	0.025	0.63	0.63
	L^3 obsd.	L^3 calcd.	L^4 obsd.	L^4 calcd.
Conformation	envelope[c]	envelope[c]	sofa[c]	sofa[c]
	envelope[d]	envelope[d]	half-chair[e]	half-chair[e]
Helicity	λ	λ	λ	λ
	λ	λ	λ	λ
Discriminator (Δ_c)	2.2	3.7	4.0	1.4
	2.9	3.7	1.8	6.9
Puckering (Q)	0.35	0.32	0.52	0.51
	0.39	0.32	0.53	0.53

[a] Flag: Co,N1−C3,C4. [b] Flag: Co,N6−C6,C7. [c] Flag: C3. [d] Flag: N5. [e] Flag: N5,C5−N6,C7.

Table 5. Selected bond lengths [Å] and angles [°] for $[MeCo(L^4)(HL^4)]^+$. Torsion (φ, °), and bending angles (α, °) and Co out-of-plane displacement (*d*, Å) are also reported

Distances	calcd.	obsd.[a]
Co−C	2.013	1.960(7), 1.982[b]
Co−N(ox)	1.924	1.888(6), 1.900[b]
Co−N(am)	2.016	1.996(5), 2.003[b]
	2.034	2.017(5), 2.018[b]
Co−N(py)	2.117	2.134(5), 2.137[b]
Angles		
N(py)−Co−N(am)	93.0 89.0	92.2(2) 88.7(2)
N(py)−Co−N(ox)	92.0 89.3	92.1(2) 89.2(2)
N(py)−Co−C	177.3	177.3(3)
Co−N(py)−C1	119.0	117.0(4)
Co−N(py)−C2	124.4	126.4(5)
φ	−37.0	−38.3
α	6.5	9.1
d	0.029	0.018

[a] Molecule A; esd in parentheses. [b] The second value refers to the bond length corrected for thermal motion using the riding model.

Table 6. Scaled minimum strain energies (kJ·mol^{-1}) for the possible diastereomers of the [Co(A^B^C)$_2$] type complexes: [Co(L)$_2$]$^+$, (L = L^1, L^2), and [Co(L)(HL)]$^{2+}$, (L = L^3, L^4, L^{3o} and L^{4o}). L^{3o} and L^{4o} represent the L^3 and L^4 ligands without the oxime intramolecular hydrogen bond (O···H···O). For the L^3−L^4 type ligands, the chirality of the stereogenic centres (in the order: N2, N5, and their adjacent C atoms, see Figure 2, b) are also reported, for the minimum energy structures

Isomer	Configuration[a]	L^1	L^2	L^3	L^4	L^{3o}	L^{4o}
I	Δ *mer cis,trans,cis*	0	0	3292 *RSSR*	119.3 *SSRR*	3182 *RSSR*	57.8 *SSRR*
II	*fac trans,trans,trans*	117.3	63.3	1249 *RRRR*	249.4 *RSSR*	251.7 *RRRR*	95.4 *SSRR*
III	Δ *fac cis,trans,cis*	129.8	49.3	146.7 *RSSR*	90.2 *SSRR*	14.6 *SSRR*	14.1 *SSRR*
IV	Δ *fac cis,cis,cis*	144.1	61.2	72.7 *SSRR*	125.3 *RSSR*	253.5 *RSRR*	26.7 *RSRR*
V	Δ *fac trans,cis,cis*	146.4	100.7	0 *SSRR*	0 *SSRR*	0 *SSRR*	0 *SSRR*
VI	Δ *fac cis,cis,trans*	134.9	57.4	910 *SSRR*	1008 *SSRR*	31.7 *SSRR*	27.2 *SSRR*

[a] The *cis*/*trans* descriptors refer, in the order, to the pairs of the nitrogen atoms of the tridentate ligands, N(py), N(am)/N(im), and N(ox), labelled, respectively, A, B, and C in Figure 3.

Diastereomers of Complexes Co−L$^{1-4}$

The relative minimum energies for the six possible diastereomers of the [Co(L)$_2$]$^+$ (L = L^1, L^2) and [Co(L)(HL)]$^{2+}$ (L = L^3, L^4) complexes are reported in Table 6. Structures **I**−**VI** refer to those depicted in Figure 3, that is, the bis-tridentate ligand octahedral complexes [Co(A^B^C)$_2$], where A = N(pyridyl), B = N(imine), and C = N(nonprotonated oxime) for L^1 and L^2, and A = N(pyridyl), B = N(amine), and C = N(protonated oxime) for L^3 and L^4.

It is evident that the L^1 and L^2 complexes are stable only in the *mer cis,trans,cis* configuration (**I**), the *cis*/*trans* descriptors referring, respectively, to the pairs of A, B, and C nitrogen atoms of the tridentate ligands in [Co(A$_2$B$_2$C$_2$)]. On the other hand, the L^3 and L^4 complexes have a minimum strain energy in the *fac trans,cis,cis* configuration (**V**). In order to address the possibility of the opening of the O···H···O oxime hydrogen bond, especially in the highly strained configurations with *trans* NE atoms, Table 6 also lists the relative strain energies for the [Co(HL^{3o})$_2$]$^{2+}$ and [Co(HL^{4o})$_2$]$^{2+}$ complexes, where HL^{3o} and HL^{4o} represent the HL^3 and HL^4 ligands without the symmetric oxime intramolecular hydrogen bond.

It should be noted that the high values of the strain energies of some diastereomers (Table 6) are merely indicative of highly distorted improbable structures, having been calculated by the harmonic force field functionals of AMBER.[14]

Δ/Λ descriptors can be applied to designate the chirality of the complexes, on the basis of the 'skew lines' convention.[19] In this work, because of the different nature of the three donor atoms and the different number of skew lines, the descriptor is defined by the orientation of the two lines AB, or, when they are parallel as in **VI**, by the skew lines AB and BC. This convention is applied to the descriptors given in Figure 3.

Conformational Analysis of [RCo(L^4)(HL^4)]$^+$

Figure 4 shows the variation of the total strain energy E for the methyl and adamantyl derivatives as a function of the rotation angle φ = C1−N1−Co−N*, where N* represents the midpoint between the oxime nitrogen atoms (N3, N4 in Figure 1, a). Moreover, according to the usual convention, the sign of φ, as well as of all torsion angles, is positive for anticlockwise rotations and negative for clockwise rotations. According to the definition of the two torsion angles, (φ_1 − φ) is approximately 50°, that is, half the N3−Co−N4 bond angle (Figure 1, a).

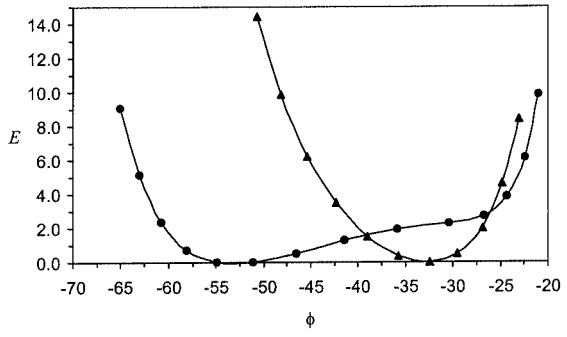

Figure 4. Plot of the scaled strain energy (E, kJ·mol^{-1}) as a function of the rotation angle φ around the axial Co−N bond for [RCo(L^4)(HL^4)]$^+$ with R = Me (circles) and Adam (triangles)

The E/φ plot of the methyl derivative is characterised by a broad asymmetric minimum (E < 2.5 kJ·mol^{-1}), in the range −60° < φ < −25°, with E = 0 at φ = −53°. For the adamantyl derivative, the energy plot is nearly symmetric, with a narrower minimum (−42° < φ < −26°, for E < 2.5 kJ mol^{-1}) centred at φ = −32°.

Figure 5 shows the variation of the axial Co−C and Co−N bond lengths as a function of the rotation angle φ. Figure 6 (see a) reports the α/φ plot, where α is the dihedral angle between the two moieties of the equatorial ligand (Figure 1, a), while Figure 6 (see b) shows the trend of the cobalt out-of plane displacement (d) from the least-squares plane defined by the four equatorial nitrogen atoms. The plots refer to the φ range corresponding to low energy regions of the methyl and adamantyl derivatives.

Tables S1 and S2 in the Supplementary Information (see also footnote on the first page of this article), report for R = Me and R = Adam, respectively, the scaled total strain

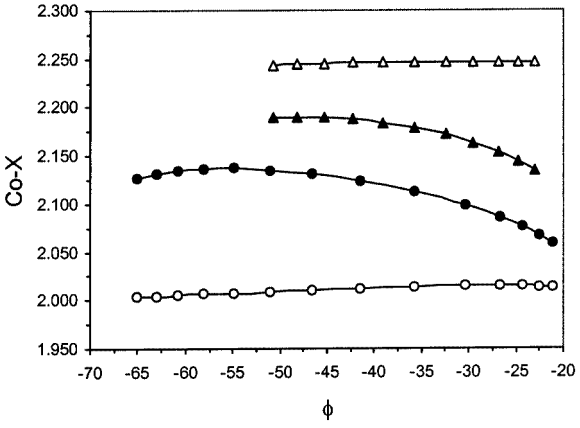

Figure 5. Plot of the axial Co−X distances [Å] as a function of the rotation angle φ [°] for $[RCo(L^4)(HL^4)]^+$. Circles refer to R = Me, with open circles for X = C, and full circles for X = N. Triangles refer to R = Adam, open for X = C, full for X = N

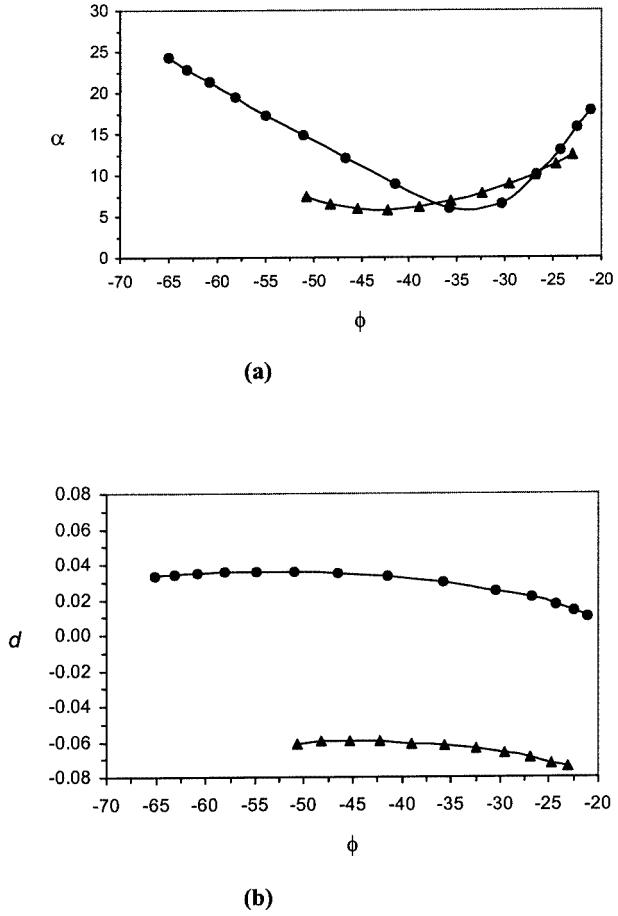

Figure 6. Plot of the dihedral angle α [°] (a), and of the cobalt out-of-plane displacement *d* [Å] (b), as a function of the rotation angle φ (°) for $[RCo(L^4)(HL^4)]^+$. Circles refer to R = Me, triangles to R = Adam

energy (*E*) calculated as a function of the torsion angle φ_1 (C2−N1−Co−N2), together with the rotation angle φ, the ethylene bridge torsion angle φ_2 (C2−C3−C4−N2), the cobalt out-of-plane displacement (*d*), the dihedral angle α, and the axial Co−C and Co−N bond lengths.

Discussion

Stereochemical Features of the Bis(tridentate ligand)cobalt Complexes

Octahedral metal complexes with bis-tridentate ligands of the type $[M(A\hat{}B\hat{}C)_2]$, where A, B, and C represent three different coordinating atoms, can in principle[19b,20] give rise to the six diastereomers illustrated in Figure 3 for M = Co, where A = N(py), B = N(im, or am), and C = N(ox). Of these, only the facial isomer **II**, with its C_i point symmetry, is achiral (ignoring the possible inherent ligand chirality), while all the others are chiral and exist as Δ/Λ enantiomeric pairs (Table 6).[19b,20]

The different stability of the six isomers depends on the nature of the donor atoms and on the length of the chelate bridge. Thus, in the case of $[Co(L^1)_2]^+$ it is evident from molecular models that all the *fac* isomers (**II**−**VI**) can be built only with great difficulty because of the trigonal nature of the imino nitrogen atoms (B) and the short A−(CH_2)−B bridge. In fact, MM calculations show (Table 6) that the *mer cis,trans,cis* arrangement (**I**) has the lowest strain energy, with the closest *fac* arrangement *trans,trans,trans* (**II**) at a significantly higher energy (117.3 kJ·mol^{-1} higher), thereby corresponding to an unrealistic structure. Owing to the longer bridge A−$(CH_2)_2$−B, the $[Co(L^2)_2]^+$ complex is more flexible and the energy difference between the minimum energy isomer (**I**) and the closest *fac* isomer *cis,trans,cis* (**III**) is reduced to 49.3 kJ·mol^{-1}, although this difference is still rather high. These results are in perfect agreement with the observation that, both in the solid state and in solution, only isomer **I** has been detected.[2]

Isomer stability is more complicated in the case of the L^3 and L^4 derivatives, $[Co(L^3)(HL^3)]^{2+}$ and $[Co(L^4)(HL^4)]^{2+}$, because of the presence of tetrahedral amino nitrogen atoms at B. Moreover, in this case, chiral centres are present at the positions of the amine nitrogen atoms (N2, N5) and of their adjacent carbon atoms in the equatorial five-membered rings (Figure 2, b), which gives rise to further possible diastereomers. On the other hand, molecular model inspection suggests that the nitrogen atom chirality is a crucial factor for the ring closure, so that a limited number of reasonable diastereomers is to be expected. Further restriction arises from formation of intramolecular hydrogen bonds involving the oxime nitrogen atoms (atom type NE, atom C in Figure 3). If these are to be maintained, all structures with *trans* NE atoms would be highly strained with respect to those with *cis* NE atoms.

The results of the present MM calculations show that both $[Co(L^3)(HL^3)]^{2+}$ and $[Co(L^4)(HL^4)]^{2+}$ complexes exhibit minimum strain energy in the configuration *fac trans,cis,cis* (isomer **V**), with *S* and *R* configurations for the nitrogen and carbon atoms, respectively (see Table 6). All other diastereomers have markedly higher energies. As expected, isomers **II** and **VI**, with *trans* oxime nitrogen atoms have exceedingly high energies, indicating that they cannot exist. When the constraint on the oxime hydrogen bond is re-

moved, the energy values decrease on passing from $L^{3,4}$ to $L^{3o,4o}$ ligands, but again isomers of type **V** have the lowest energy.

Data in Table 6 show that in the minimum energy structures of the $[Co(L^3)(HL^3)]^{2+}$ and $[Co(L^4)(HL^4)]^{2+}$-complexes the chirality of the nitrogen and carbon atoms depends on the isomer type. Nevertheless, any change from the *SSRR* chirality to the other configurations does not significantly lower the energy of the nonminimum energy isomers.

Further elements of chirality could derive from the helicity of the chelate rings. However, the oxime five-membered rings are essentially planar and the helicity of the metallacycles formed by the pyridyl ligands, as defined by the IUPAC rules,[19] is rather small (pseudo-torsion angles, defined by the N···N and C···C skew lines, of 10°−12°). Therefore, it seems likely that in solution the helicity can be easily reversed, so this factor can be neglected.

Another important conformational feature is defined by the torsion angle (φ_2) around the C−C bonds of the six-membered rings in the L^2 and L^4 complexes. MM calculations show that for $[Co(L^2)_2]^+$ inverting the sign of both the torsion angles increases the strain energy by only 1.0 kJ·mol^{-1}, while a significant increase (28.7 kJ·mol^{-1}) occurs by changing the sign of one only. On the contrary, for $[Co(L^4)(HL^4)]^{2+}$ all changes in the torsion angles cause a significant increase in the strain energy.

As experimentally observed and confirmed by the present MM calculations (Table 3), passage from N(py)−(CH_2)−N(am,im) to N(py)−$(CH_2)_2$−N(am,im) bridges (that is, on meeting the ring closure condition by passing from five- to six-membered chelate rings) causes a lengthening of about 0.10 Å of the Co−N(py) bond lengths together with significant angular changes in the pyridyl metallacycles. The largest effect, observed in both the L^1, L^2 and L^3, L^4 pairs, is the narrowing of the pyridyl exo-cycle bond angles (av. calcd. Co−N(py)−C_α, from 127.0(3)° to 120(1)°], which is paralleled by a widening of the endo-cycle angles (av. calcd. Co−N(py)−C_β, from 113.4(5)° to 123(2)°]. These observations are in very good agreement with the experimental X-ray data (see Table 3, where C_α and C_β represent, respectively, the pyridyl carbon atoms like C1, C2 and C8, C7 in Figure 2)

However, the total strain energy of $[Co(L^1)_2]^+$ is 19.1 kJ·mol^{-1} higher than that of $[Co(L^2)_2]^+$, while in $[Co(L^3)(HL^3)]^{2+}$ it is 67.9 kJ·mol^{-1} lower than in $[Co(L^4)(HL^4)]^{2+}$, paralleling the ring strain energies (sum of only stretching and bending contributions). These results suggest that the pyridyl ring closure introduces a severe strain in the $[Co(L^1)_2]^+$ (five-membered rings) and $[Co(L^4)(HL^4)]^{2+}$ (six-membered rings) complexes with respect to their L^2 and L^3 analogues.

Stereochemical Features of the Organometallic Complexes $[RCo(L^4)(HL^4)]^+$

The results of the conformational analysis of the organocobalt methyl derivative $[MeCo(L^4)(HL^4)]^+$ (see Figure 4 and Table S1 show that the pyridyl group can rotate around the axial Co−N bond across a rather wide range ($-60° < \varphi \leq -25°$) while maintaining the total strain energy within a limit of 2.5 kJ·mol^{-1}. This is in agreement with the observation that in the solid state two crystallographically independent molecules are present, with φ values of −38° and −48°, and that similar values were also found for the ethyl and trifluoroethyl derivatives, with φ = −36° and −44°, respectively.[3] This corresponds to the pyridyl ring being more or less parallel to the N2−Co−N4 axis ($-15° < \varphi_1 < 24°$).

In the case of the adamantyl group, the minimum strain energy is also observed at a similar torsion angle ($\varphi \approx -32°$), but the MM calculations show that, in the case of this much bulkier alkyl group, the pyridyl rotation is rather restricted ($\Delta\varphi \approx \pm 8°$ with $\Delta E < 2.5$ kJ·mol^{-1}) (Figure 4, Table S2).

Thus, the present results confirm the observation that in complexes with tridentate amino-oxime ligands the orientation of the planar nitrogen base is quite different from that commonly found in cobaloximes and lariat-type complexes ($\varphi \approx 0°$),[6] and in iminocobaloximes ($\varphi \approx 90°$).[3]

Interestingly, the variation of φ is accompanied by significant changes in the geometry of the pyridyl metallacycle, such as the variation of the torsion angle φ_2. Of particular interest is the significant increase of the Co−N(py) bond length with decrease (more negative values) of the rotation angle φ (Figure 5). This confirms the appreciable effect of steric factors in determining the *trans* influence of an alkyl group.[3]

On the contrary, the Co−C bond length of both the Me and Adam derivatives show negligible variations (Figure 5), in agreement with FT-Raman studies which do no detect any change in the Co−C force constants even in base-on and base-off cobalamins.[10a]

In order to maintain the total strain energy around its minimum, the variation of φ also causes distortions in the equatorial ligand, as shown by the variation of the dihedral angle α between its two moieties. This is the combination of bending and twisting deformations of the two equatorial five-membered rings. Inspection of molecular diagrams shows that when α is less than 7° ($-36° < \varphi < -30°$ for R = Me; $-46° < \varphi < -35°$ for R = Adam) the two rings are essentially twisted without significant bending, while for higher values the latter component becomes more appreciable. The calculations indicate that this effect is stronger in the methyl derivative (see Figure 6, a), in which the equatorial ligand is bent away from the axial alkyl group when φ increases from −30°. This trend is in good agreement with that experimentally observed.[3] The opposite bending occurs when φ is less than −36°. The variation of α with φ (in the low strain energy region) is much lower in the adamantyl derivative (Figure 6, a) because the bending towards the alkyl group is hindered by the alkyl bulkiness.

Finally, it is interesting to observe that while in the Me derivative the cobalt atom is displaced towards the pyridyl nitrogen atom, in the Adam derivative the displacement is nearly doubled and reversed, the Co atom moving towards the carbon atom (Figure 6, b).

Acknowledgments

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