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COMPLEXES OF BIOLOGICALLY IMPORTANT LIGANDS: THERMAL PROPERTIES OF COORDINATION COMPOUNDS OBTAINED BY REACTION OF SOME DIVALENT METAL IONS WITH 2-METHYL- AND 4-METHYLIMIDAZOLE

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ABSTRACT

The role of the imidazole group of the histidyl residue in proteins is very important in the understanding of the reactivity and the mechanisms of interaction between proteins and several metallic ions. The ligand power of the imidazole and its derivatives is correlated with the basicity of the molecule, the π- and σ-electron-acceptor ability, the hydrogen bonding ability and the steric hindrance of the molecules.

The thermal characteristics of coordination compounds obtained by reaction of Co^{II}, Ni^{II} and Cu^{II} with 2-methyl- and 4-methylimidazole are studied here by means of thermoanalytical techniques, and IR and reflectance spectroscopy and compared with those of the coordination compounds obtained by reaction of the same ions with imidazole and *N*-methylimidazole previously published.

The compounds prepared were $Me(HL)_x(NO_3)_2$, ($Me \equiv Co^{II}$, Ni^{II} or Cu^{II}; $HL \equiv$ 2-methylimidazole (2mIm) or 4-methylimidazole (4mIm); $x = 4$ or 6). Two different forms of $Co(2mIm)_4(NO_3)_2$ and $Ni(2mIm)_4(NO_3)_2$ showing different thermal and spectroscopic characteristics were obtained.

INTRODUCTION

The role of the imidazole group of the histidyl residue in proteins is very important in the understanding of the reactivity and the mechanisms of interaction between proteins and several metallic ions.

Imidazole and its derivatives are amphoteric and can act as moderately strong organic bases able to accept protons at the N-3 nitrogen, as well as very weak acids capable of losing a proton from the N-1 nitrogen [1,2]. The coordination ability of these ligands is strictly correlated with the aromatic nature of the imidazolic ring and hence with its σ-acceptor capability, which is moderate, and with its π-acceptor capability which is weak. The ab initio calculations on imidazole [3] indicate that all the hydrogen atoms are

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σ-donors as, to a lesser extent, is the C-2. Carbon atoms 4 and 5 of the imidazole ring are σ-acceptors. All the carbon atoms are weak π-acceptors, but polarisation of the σ-electrons dominates the overall charge distribution. The N-1 nitrogen does not act as a ligand site for proton or metal ions because the π-electrons at N-1 are part of the aromatic sextet, so that bonding protons or metal ions would compromise the aromaticity of the ring. Therefore, the only energetically favorable coordinating site in the neutral molecule of imidazole is the N-3 nitrogen. The ligand power of the imidazole and its derivatives is correlated with the basicity of the molecule, the π-electron acceptor ability, the hydrogen bonding ability and the steric hindrance of the molecules. The importance of the π-acceptor capabilities in the bonding of imidazole to metal ions is supported by noting that 4-methylimidazole, substituted in the same position as the imidazole ring in the histidyl residue in peptide chains, is nearly four times stronger a base than imidazole, yet it binds Cu^{II} and Zn^{II} less strongly [4,5].

The aim of this paper is to study the influence of these parameters on the thermal characteristics of coordination compounds obtained by reaction of Co^{II}, Ni^{II} and Cu^{II} with 2-methyl- and 4-methylimidazole and to discuss them in comparison with those of the coordination compounds of the same cations with imidazole and *N*-methylimidazole previously published [1], in order to obtain a homogeneous and sequential change in the ligand structure; the methyl group and its position in the ring are the variables in the system.

The compounds studied are $Me(HL)_x(NO_3)_2$ ($Me \equiv Co^{II}$, Ni^{II} or Cu^{II}; $HL \equiv$ 2-methylimidazole (2mIm) or 4-methylimidazole (4mIm); $x = 4$ or 6). Nitrate was selected as counter-ion because of its very low coordination ability and because it shows characteristic absorption bands in its IR spectrum.

EXPERIMENTAL

Instrumentation

A Perkin–Elmer thermobalance (model TGS-2) and differential scanning calorimeter (model DSC-2 B), both equipped with a data station, were used. The heating rate ranged between 2.5 and 10 °C min^{-1} and the atmosphere was air or very pure nitrogen (99.99%) at flow rates of 50–100 ml min^{-1}. The IR spectra were recorded using a Nicolett 510 instrument. The reflectance spectra were recorded using a Beckman DK2-A spectroreflectometer.

Synthesis of the compounds

2-Methylimidazole and 4-methylimidazole were obtained from Aldrich Chemical Co.; other chemicals employed were of reagent grade. The

2-methylimidazole and 4-methylimidazole, and the Co^{II}, Ni^{II} and Cu^{II} nitrate salts were dissolved in absolute ethanol.

To obtain coordination compounds of general formula $Me(LH)_6(NO_3)_2$, a warm solution of the metal salt was added to a warm solution of the ligand to yield a final metal : ligand ratio of 1 : n, where n was between 12 and 50.

To prepare coordination compounds of general formula $Me(HL)_4(NO_3)_2$, a warm solution of the ligand was added to a warm solution of the metal salt to obtain a final metal : ligand ratio of 1 : n, where n ranged between 0.5 and 4.

The mixtures obtained were cooled and left at room temperature for some days until a precipitate was obtained. The precipitates were washed with a mixture of absolute ethanol and ether (1 : 1 v/v), then with ether and dried in a vacuum.

In this way the following compounds were obtained: $Co(2mIm)_4(NO_3)_2$ (pink, form A); $Ni(2mIm)_4(NO_3)_2$ (pale blue, form A); $Cu(2mIm)_4(NO_3)_2$; $Co(4mIm)_6(NO_3)_2$; $Ni(4mIm)_6(NO_3)_2$; $Cu(4mIm)_6(NO_3)_2$ and $Cu(4mIm)_4(NO_3)_2$.

When ethyl ether was added to the room-temperature solutions of the 2-methylimidazole complexes of Co^{II} and Ni^{II} with a final metal–ligand ratio of 1 : 4, an oil was obtained: purple in the case of Co^{II} and blue in the case of Ni^{II}. The oils were treated twice with successive portions of ethyl ether and then stored at 0 ° C until the crystals corresponding to the formula $Co(2mIm)_4(NO_3)_2$, form B, and $Ni(2mIm)_4(NO_3)_2$, form B, were obtained. It was impossible to apply the same process to the Cu^{II} solutions because the precipitate is obtained almost immediately after mixing the ligand and metal solutions. The preparation, especially in the case of Ni^{II}, is difficult to reproduce.

The purity of the compounds was checked by elemental analysis and by thermogravimetric techniques; the analytical results for all the compounds were good.

RESULTS

The TG curves in air and in nitrogen show that the tetrakis complexes of cobalt(II) and nickel(II) with 2-methylimidazole, $Co(2mIm)_4(NO_3)_2$ and $Ni(2mIm)_4(NO_3)_2$, start to decompose by losing 0.5 molecules of ethanol and then 3 molecules of ligand, see Figs. 1 and 2. The residual compound decomposes in air by an exothermic process involving decomposition of the nitrate group, loss and oxidation of 2-methylimidazole and formation of the metal oxide; in nitrogen the reaction is smooth and does not reach a constant weight in the operational temperature field. The DTG and DSC curves, see Fig. 3, show that the first three molecules of the ligand are not isoenergetically bound and are lost by two different overlapping steps.

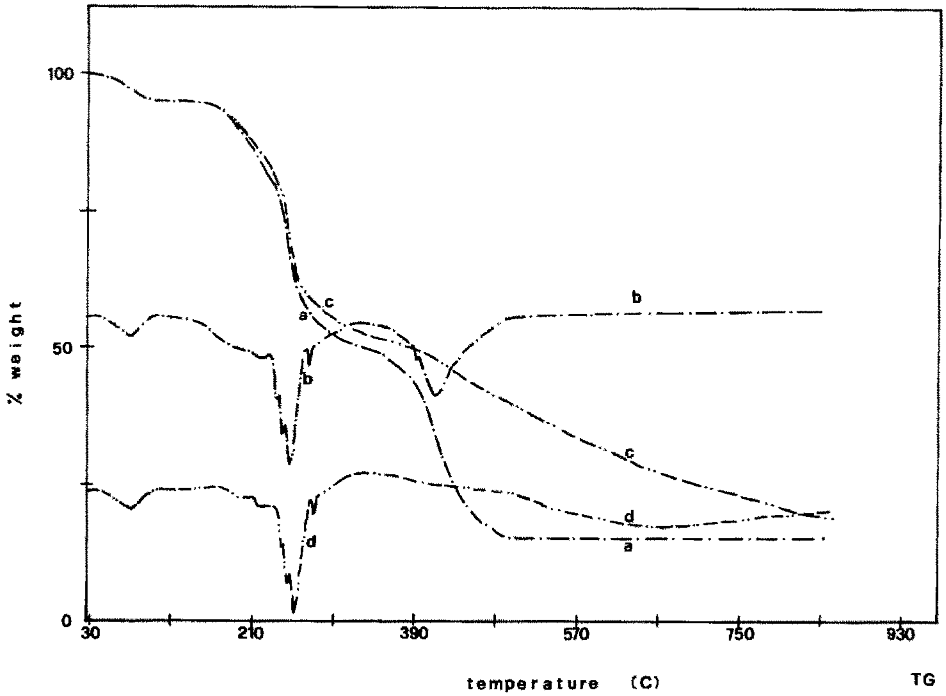

Fig. 1. TG and DTG curves of $Co(2mIm)_4(NO_3)_2$, form A: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10°C min^{-1}.

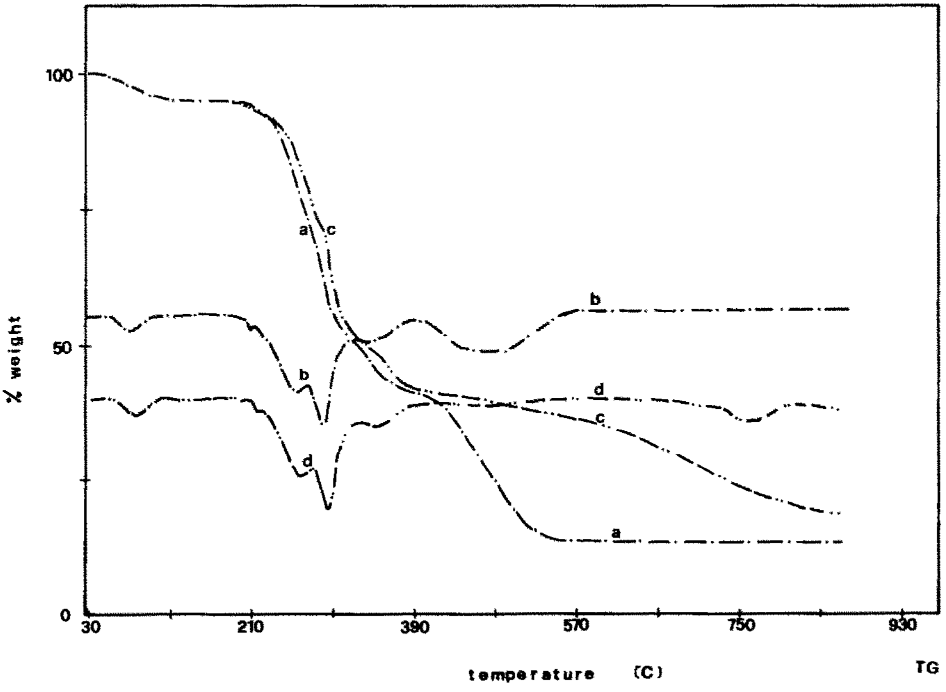

Fig. 2. TG and DTG curves of $Ni(2mIm)_4(NO_3)_2$, form A: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10°C min^{-1}.

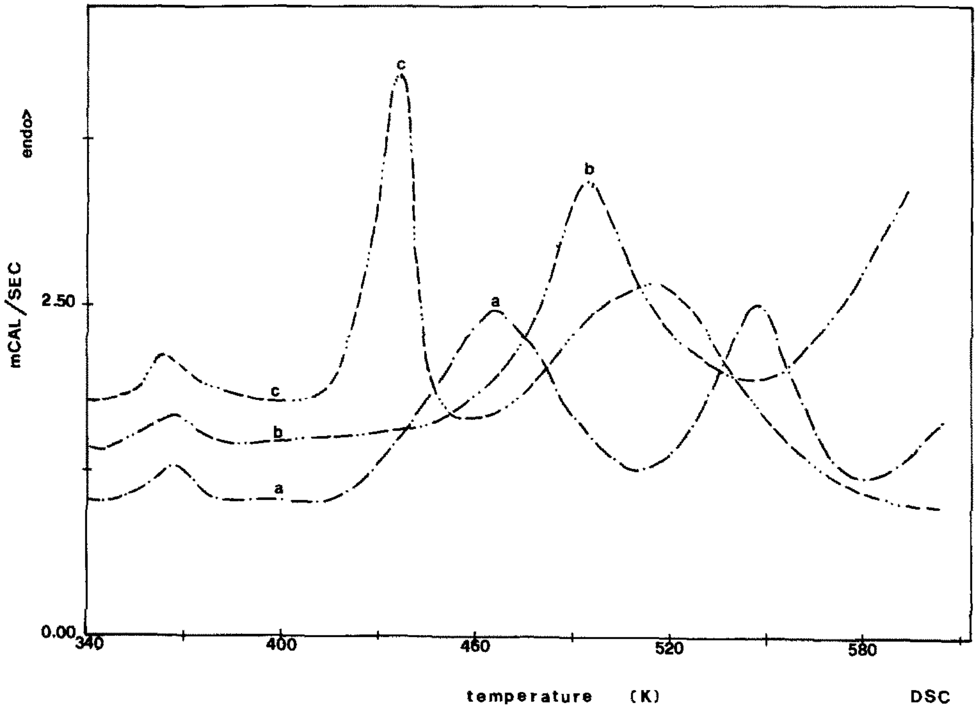

Fig. 3. DSC curves of: a, Co(2mIm)$_4$(NO$_3$)$_2$; b, Ni(2mIm)$_4$(NO$_3$)$_2$; c, Cu(2mIm)$_4$(NO$_3$)$_2$. Nitrogen atmosphere; heating rate 10 °C min^{-1}.

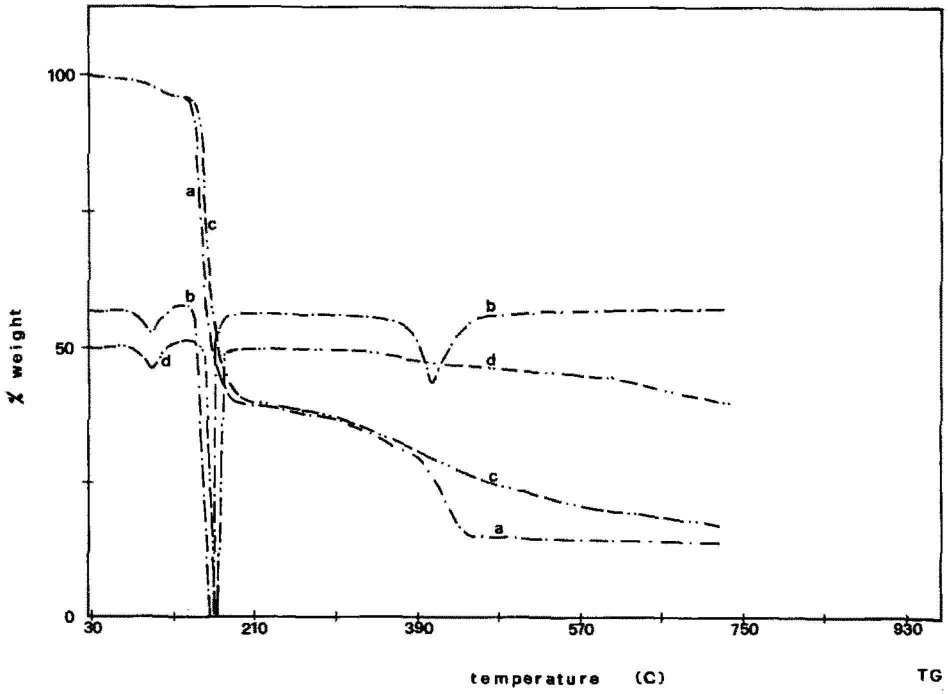

Fig. 4. TG and DTG curves of Cu(2mIm)$_4$(NO$_3$)$_2$: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10 °C min^{-1}.

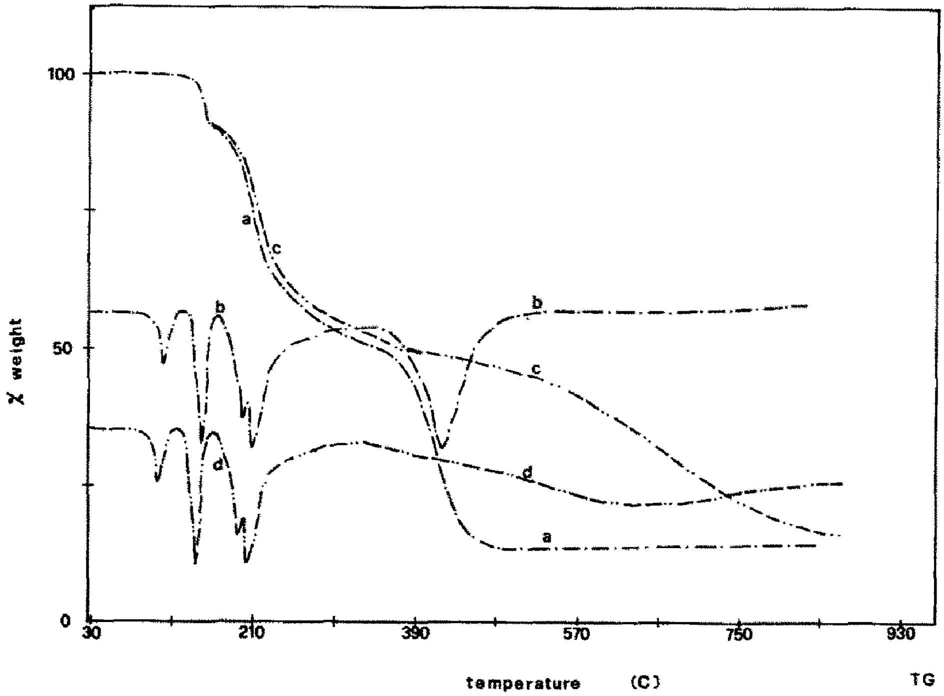

Fig. 5. TG and DTG curves of $Co(2mIm)_4(NO_3)_2$, form B: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10 °C min^{-1}.

The $Cu(2mIm)_4(NO_3)_2$, see Figs. 3 and 4, loses 0.5 molecules of ethanol, then 3 ligand molecules; the residue decomposes in a smooth reaction but does not reach a constant weight in the operational temperature field. In air, the decomposition, after the loss of the ethanol, occurs with a first sharp step that does not yield a stoichiometrically defined residue, and this decomposes to the metal oxide in one more step.

The $Co(2mIm)_4(NO_3)_2$ and $Ni(2mIm)_4(NO_3)_2$ compounds, form B, see Figs. 5 and 6, first lose ethanol (1 molecule for the Co^{II} complex and 0.5 molecules for the Ni^{II} complex), then the residuals decompose, starting at temperatures lower than the corresponding A compounds, through two main steps, the first overlapping with many unresolved thermal processes, to give the oxides. The DTG curve in nitrogen first shows a small endothermic peak corresponding to the loss of the ethanol, followed by another peak corresponding to the convolution of many overlapping unresolved processes.

The hexakis complexes of 4-methylimidazole of general formula $Me(4mIm)_6(NO_3)_2$, where $Me \equiv Co^{II}$, Ni^{II} or Cu^{II}, see Figs. 7–9, start to decompose in air and in nitrogen atmosphere by losing 5 ligand molecules, in accordance with the following reaction

$$Me(4mIm)_6(NO_3)_2(s) \rightarrow Me(4mIm)(NO_3)_2(s) + 5(4mIm)(g)$$

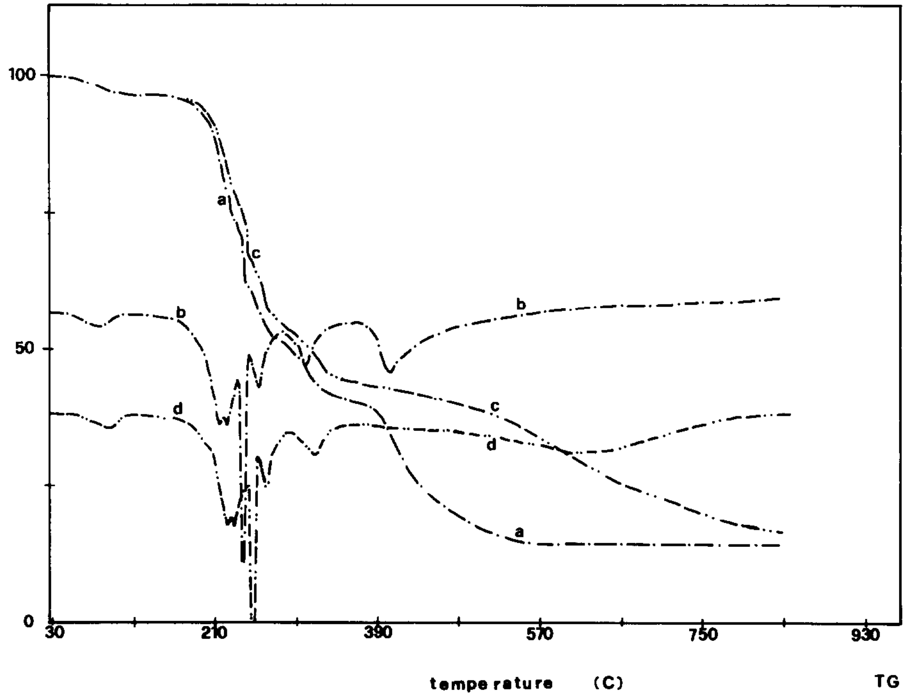

Fig. 6. TG and DTG curves of $Ni(2mIm)_4(NO_3)_2$, form B: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10 °C min^{-1}.

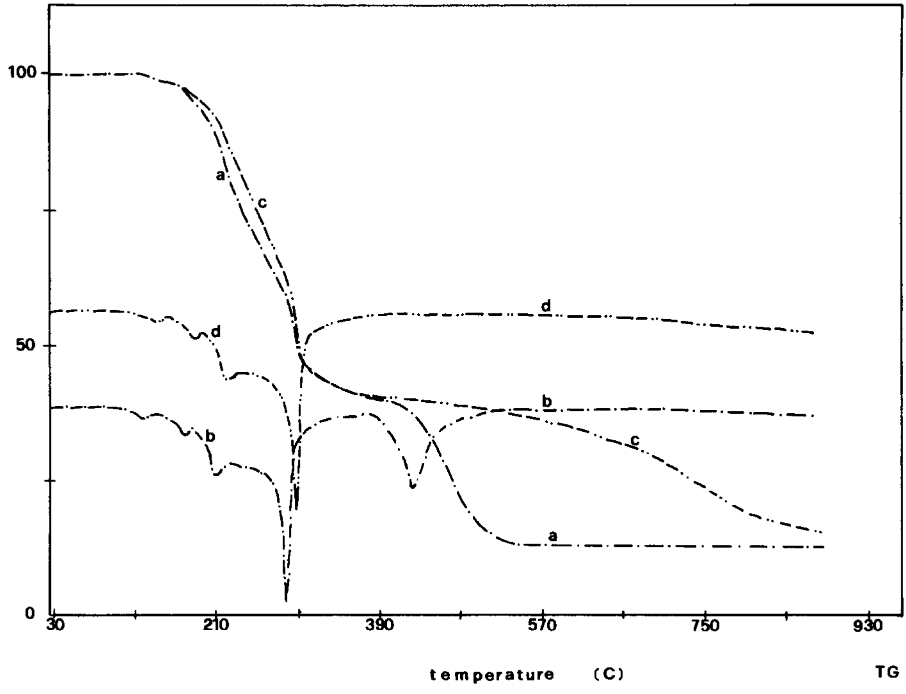

Fig. 7. TG and DTG curves of $Co(4mIm)_6(NO_3)_2$: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10 °C min^{-1}.

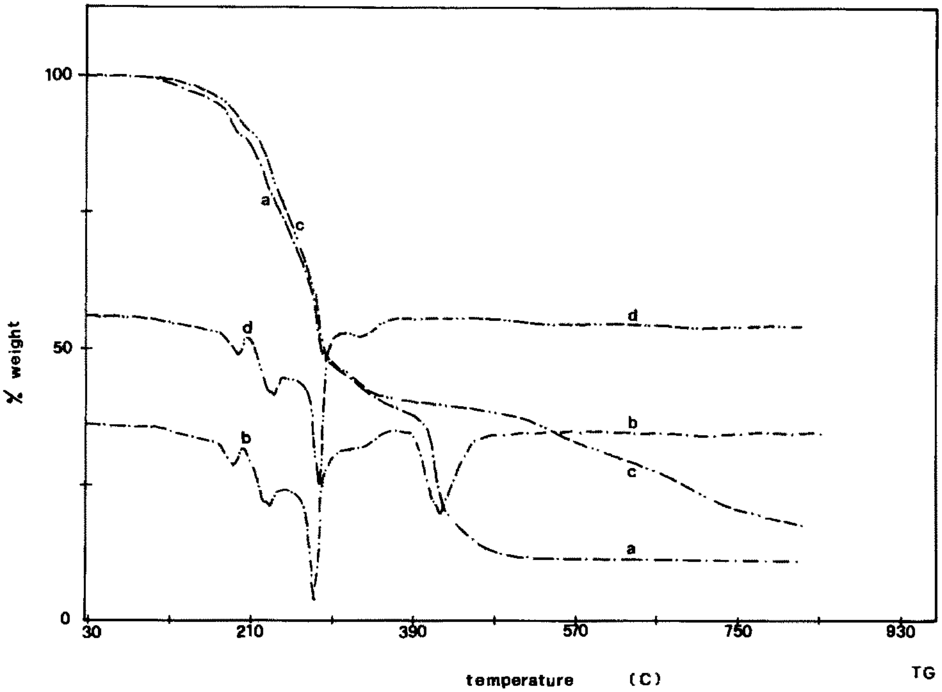

Fig. 8. TG and DTG curves of Ni(4mIm)$_6$(NO$_3$)$_2$: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10 °C min^{-1}.

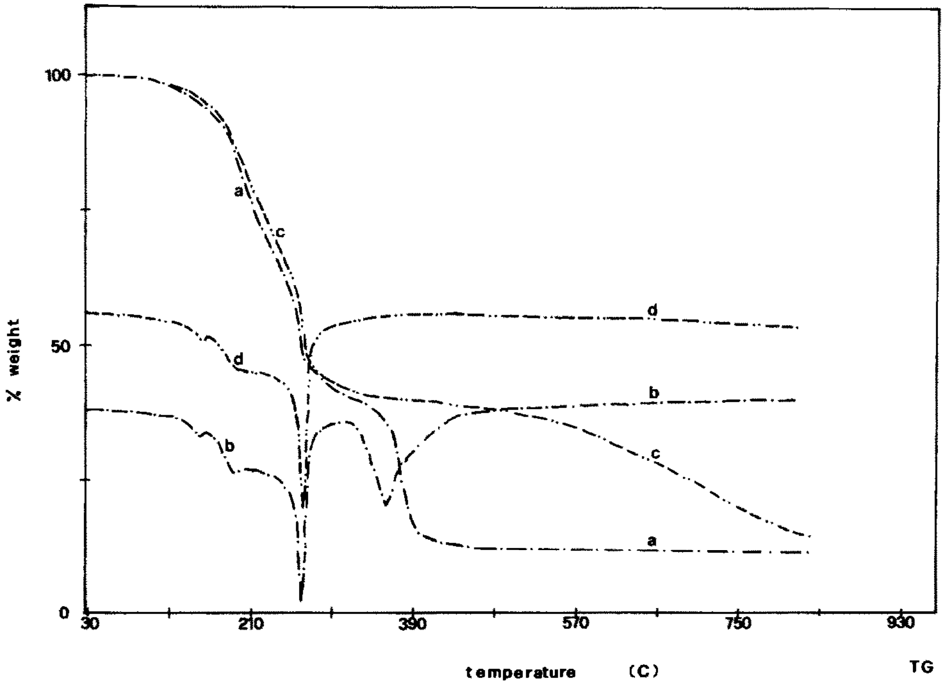

Fig. 9. TG and DTG curves of Cu(4mIm)$_6$(NO$_3$)$_2$: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10 °C min^{-1}.

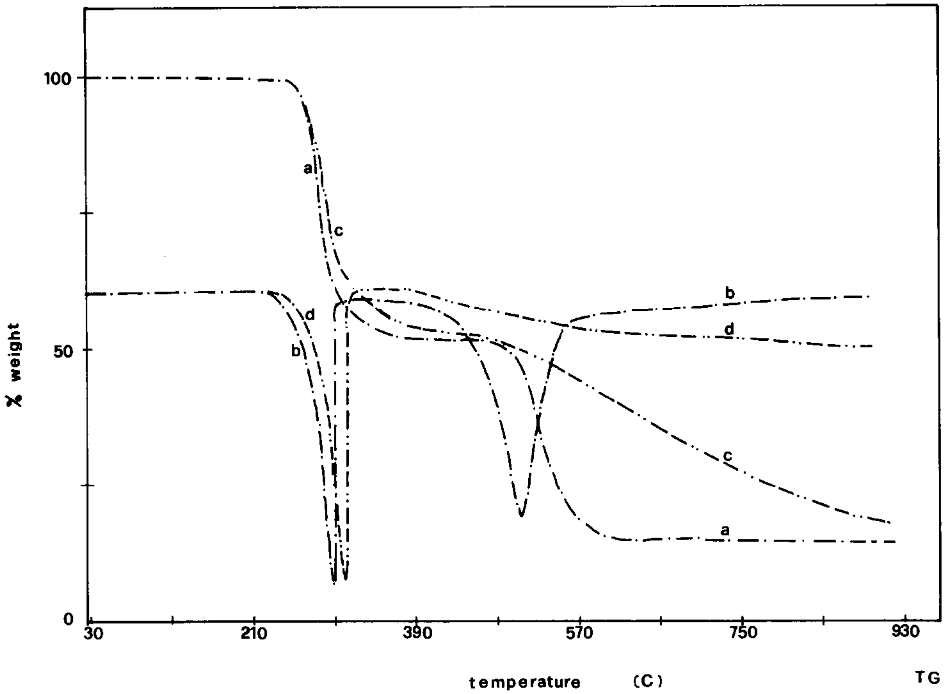

Fig. 10. TG and DTG curves of $Cu(4mIm)_4(NO_3)_2$: a and b, air atmosphere; c and d, nitrogen atmosphere. Heating rate 10 °C min^{-1}.

The residual $Me(4mIm)(NO_3)_2$ then decomposes in air in one step involving decomposition of the nitrate group, and loss and oxidation of the 4-methylimidazole to yield, finally, the metal oxides. In nitrogen, the decomposition of the $Me(4mIm)(NO_3)_2$ occurs in a very smooth step corresponding to some moderately overlapping processes which do not yield a constant weight in the operational temperature field.

The $Cu(4mIm)_4(NO_3)_2$ appears to be much more stable than the corresponding hexakis compound, see Fig. 10. There are two steps corresponding to the thermal decomposition: the first is the loss of three ligand molecules, followed by the second, involving the nitrate anions and the remaining ligand molecule, that yields copper oxide CuO in air, while the process does not reach a constant weight in nitrogen.

DISCUSSION

The only 2-methylimidazole coordination compounds obtained by reaction with Co^{II}, Ni^{II} and Cu^{II} are tetrakis complexes of general formula $Me(2mIm)_4(NO_3)_2$; all attempts to obtain hexakis complexes failed.

The cobalt(II) and nickel(II) compounds were obtained in two different forms: A and B. The two different cobalt(II) tetrakis compounds formed by reaction with 2-methylimidazole were already known [6,7]. The two different nickel tetrakis compounds have not been synthesized before.

It is interesting to note that half a molecule of ethanol (one for the $Co(2mIm)_4(NO_3)_2$, form B), is present in the solid coordination compounds of this ligand and that the ethanol is weakly bound; in fact the ethanol is lost at low temperatures. This is in accordance with the structural study of Akhtar et al. [7] who said that the $Co(2mIm)_4(NO_3)_2$, form A, contains some (a half molecule) disordered ethanol in the lattice. The thermal stability of the two forms is different, form A being more stable than form B. The different structures of the two forms explain this behaviour.

The reflectance spectra of form A are typical of a distorted octahedral configuration for the Co^{II} compound, and of an essentially octahedral geometry for the Ni^{II} compound. The B forms have electronic spectra from which it is not easy to interpret the coordination geometry, but which suggest that the B form could, according to Goodgame et al. [6], either contain five-coordinated metal ions or have one anion only weakly coordinated.

The IR spectra confirm this hypothesis, although some of the 2-methylimidazole bands are interfering. The A forms show a strong band at 1048 cm^{-1} and two other bands at 1345 and 1405 cm^{-1} typical of the coordinated nitrate anion, while the B forms show either the described band, but comparatively less strong, or else relatively unresolved bands at 710 and 828 cm^{-1} and a sharp band at 1377 cm^{-1}. These bands are not very strong but suggest the presence of an uncoordinated nitrate in the molecule, supporting the theory of a five-coordinated cation in the molecule.

The thermal stability of each series was determined as $Ni(2mIm)_4(NO_3)_2$ (A form) > $Co(2mIm)_4(NO_3)_2$ (A form) > $Cu(2mIm)_4(NO_3)_2$; and $Ni(2mIm)_4(NO_3)_2$ (B form) > $Co(2mIm)_4(NO_3)_2$ (B form).

The 4-methylimidazole coordination compounds are hexakis complexes for Co^{II}, Ni^{II} and Cu^{II} and it was possible to obtain the tetrakis compound for Cu^{II} only; all attempts to obtain the tetrakis Co^{II} or Ni^{II} complexes failed.

The spectral studies suggest an octahedral geometry for the hexakis complexes of Co^{II} and Ni^{II} and a distorted octahedral geometry for the Cu^{II} complex, with the nitrate ions uncoordinated; this was demonstrated by the IR band characteristic of uncoordinated nitrate. Analysis of the spectra corresponding to the $Cu(4mIm)_4(NO_3)_2$ complex suggests an octahedral distorted structure with the nitrate ions coordinated to the Cu^{II} as shown by the IR spectra. In fact, the nitrate ion bands at 1050, 1347 and 1404 cm^{-1} are typical of coordinated nitrate.

Comparing the series with respect to their thermal stabilities and considering the Cu^{II} tetrakis compounds of imidazole [1], *N*-methylimidazole [1],

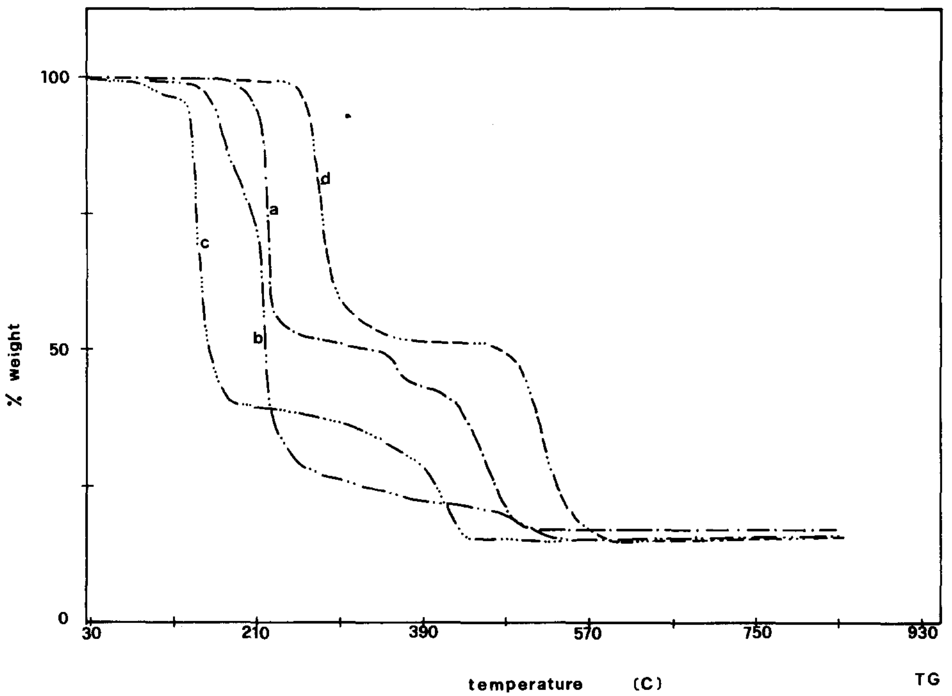

Fig. 11. TG curves of: a, Cu(imidazole)$_4$(NO$_3$)$_2$; b, Cu(N-methylimidazole)$_4$(NO$_3$)$_2$; c, Cu(2-methylimidazole)$_4$(NO$_3$)$_2$; d, Cu(4-methylimidazole)$_4$(NO$_3$)$_2$. Air atmosphere; heating rate 10 °C min^{-1}.

2-methylimidazole and 4-methylimidazole in order to obtain a homogeneous series, it is possible to see that the thermal stability scale, Fig. 11, is: 4-methylimidazole > imidazole > N-methylimidazole > 2-methylimidazole.

Looking at the parameters involved in the metal–ligand bonding, it can be seen that the stability constants found show that the trend of the decreasing affinity for the copper ion is the same as that of the increasing affinity for the hydrogen ion [4]. The absence of a parallel trend between affinity for the Cu^{II} ion and the basicity of the imidazole derivatives implies that other factors play an essential role in the metal–ligand bonding. If the σ-bonding ability was the only factor determining the stability constant, the values for NH$_3$ [8] should not be very similar, as reported, but would be appreciably higher than those for imidazole. The increased ability of imidazole to bind copper(II) ions could also be ascribed to its greater π-acceptor capability which allows this ligand to accept electronic charge from the d-orbitals of the metal ion. This hypothesis, concerning the strengthening of the bonding of the imidazole to the metal ion due to its π-acceptor qualities, is supported by considering that 4-methylimidazole is about four times stronger a base than imidazole, but 4-methylimidazole, a less strong base, binds Cu^{II}. This phenomenon could be ascribed to the hyperconjugative effect of the methyl group in position 4 which reduces the π-acceptor capability of the imidazole ring. *N*-Methylimidazole and imidazole, according to the position of the methyl group on the imidazole ring, exhibit nearly identical pK_a and stability constant values. The 2-methylimidazole shows the higher pK_a. There is no information available concerning its value for the Cu^{II} complex, but considering the position of the methyl group on the imidazole ring, the π-acceptor capability could be lower than that of 4-methylimidazole. Considering that the thermal stability scale shows that the 4-methylimidazole is the most stable compound and 2-methylimidazole is the least stable, the data discussed are not sufficient to justify this trend.

The other parameters that must be considered are the steric hindrance of the substituent and the presence of hydrogen bonding. In the solid state, the imidazole compounds show the presence of hydrogen bonding involving the pyrrolic hydrogen [9], which is impossible in the case of *N*-methylimidazole, and this parameter, the basicity of the two ligands and the known stability constants being the same [10,11], plays an essential role in the thermal stability [1]. In 4-methylimidazole, the methyl group is fairly far removed from the pyrrolic nitrogen and should not interfere with the hydrogen-bonding capability of the hydrogen at the N-1 site; while in 2-methylimidazole, the presence of the methyl group near the N-1 site could hinder the possible formation of hydrogen bonds. The study by Akhtar et al. on the crystal structure of tetrakis(2-methylimidazole)cobalt(II) nitrate · 0.5 ethanol [7] does not show any evidence suggesting the possibility of hydrogen bonding in this compound. Finally, the steric hindrance of the substituent is a powerful factor in the formation of the complexes, but strongly depends on the position of the substituent on the imidazolic ring. The study of Cowgill and Clark [12] shows that the coordination appeared to be strongly inhibited in those derivatives in which, as for 2-methylimidazole, both nitrogen atoms are adjacent to the carbon atom that carries the substituent. The same trend in the thermal stability scale, considering the ligand as the variable, is found in any possible homogeneous series available among the studied compounds of these four ligands with Co^{II}, Ni^{II} or Cu^{II}.

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