Stereochemistry and Tautomeric Equilibria of Zinc(II) Complexes of the Condensation Products between (1*R*)-3-Hydroxymethylenebornan-2-one and L-Amino Acids †

Luigi Casella * and Michele Gullotti
Dipartimento di Chimica Inorganica e Metallorganica dell'Università, Centro C.N.R., Via Venezian 21, 20133 Milano, Italy
Antal Rockenbauer
Central Research Institute for Chemistry of the Hungarian Academy of Sciences, Pusztaszeri út 59-67, H-1025 Budapest, Hungary

The zinc(II) complexes derived from the condensation of (1*R*)-3-hydroxymethylenebornan-2-one and a series of L-amino acids, [ZnL], undergo tautomeric equilibria in solution between enolimine and ketoenamine species. While the enolimine forms exhibit the expected behaviour for metal complexes of amino acid Schiff bases, the ketoenamine forms appear structurally similar to the complex derived from the cyclic amino acid L-proline, containing a chiral tetrahedral nitrogen donor. The presence of this tetrahedral nitrogen atom and the possibility for the metal atom itself to become a chiral centre can originate up to four diastereomeric ketoenamine forms of the [ZnL] complexes, while only two can be formed for the derivative of L-proline, where the nitrogen atom co-ordinates stereospecifically to the metal. The diastereomeric ketoenamine forms of the [ZnL] complexes can be interconverted through the planar enolimine form, and this tautomerization process can be followed by n.m.r. measurements, since the signals of the various isomers approach the fast exchange limit near 100 °C. For the derivative of L-proline this possibility is no longer available and the proton signals of the two diastereomeric ketoenamines are not averaged by heating the sample up to *ca.* 130 °C.

We have recently undertaken a systematic investigation of the stereochemical properties of metal complexes of the Schiff bases derived from amino acids and a variety of carbonyl compounds including pyridoxal [3-hydroxy-5-(hydroxymethyl)-2-methylisonicotinaldehyde], salicylaldehyde, pyruvic acid, 2-formylpyridine, and (1*R*)-3-hydroxymethylenebornan-2-one (hmb).[1-7] These studies have provided a basis for the understanding of stereochemical features of the enzymic reactions of amino acids catalyzed by pyridoxal 5′-phosphate,[8] or pyruvate,[9] and may explain the observed stereoselectivity in synthetic reactions occurring at the amino acid residues.[10] Of special interest are the chelates derived from histidine, since the mode of co-ordination of this amino acid appears to be controlled by the chelate ring type of the carbonyl residue conjugated to it. In this paper we report an investigation of the zinc(II) complexes derived from the condensation of hmb and a series of L-amino acids, including histidine, since only the corresponding copper(II) complexes have been reported previously.[4-6] A main aim of the present study is to clarify the structures of the species that may be present in the tautomeric equilibrium in solution, as exemplified by (I) and (II).

Experimental

All reagents were of the highest grade commercially available and were used as received. (1*R*)-3-Hydroxymethylenebornan-2-one was prepared according to a literature method;[11] the u.v.,[12] c.d.,[12] i.r.,[13] and ^{1}H n.m.r.[13] spectra of the product were identical with those reported in the literature. ‡ Elemental analyses were from the microanalytical laboratory of the University of Milan. Electronic and circular dichroism spectra were recorded on a Beckman DK-2A and a Jobin-Yvonne Mark III instrument, respectively. I.r. spectra were obtained on a Nicolet MX-1E FT-IR instrument. Solution conductivities were measured on a Philips conductimeter PR 9 500. Proton n.m.r. spectra were obtained with a Bruker WP-80 spectrometer operating at 80 MHz, and ^{13}C n.m.r. spectra were obtained with a Varian XL-200A spectrometer operating at 25.2 MHz and using a Fourier transform technique.

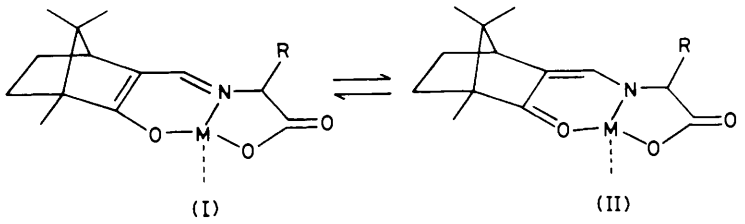
Preparation of the Zinc(II) Complexes.—The complexes [ZnL^1], [ZnL^2], [ZnL^3], and [Zn(HL^4)][O$_2$CMe] were prepared according to the following procedure.‡ A mixture of hmb (5 mmol), the amino acid (5 mmol), ethanol (50 cm^3), and water (5 cm^3) was refluxed for 2—3 h. Then zinc(II) acetate dihydrate (5 mmol) was added under stirring to the light yellow, clear solution. After approximately 2 h the solution was evaporated to dryness under vacuum in order to remove the acetic acid formed in the reaction. The solid residue was dissolved in the minimum amount of ethanol and the complex was precipitated by the addition of diethyl ether. The product was collected by filtration, washed with small amounts of methanol–water (1 : 1), and dried under vacuum. The complex [ZnL^5] was obtained by refluxing a solution of hmb (5 mmol) and L-histidine (5 mmol) in methanol (50 cm^3) for 1 h, and then adding zinc(II) acetate dihydrate to the solution. A light yellow solid precipitated almost immediately. This was filtered off, washed with methanol–water (1 : 1), and dried under vacuum.

To obtain [Zn(HL^6)][O$_2$CMe], L-histidine methyl ester was freed from its dihydrochloride salt (5 mmol) by treatment with the appropriate amount of methanolic sodium hydroxide (*ca.* 1 mol dm^{-3}) and chloroform (100 cm^3) with stirring. After filtering off of the precipitate of sodium chloride, evaporation to dryness under vacuum of the solution gave a light

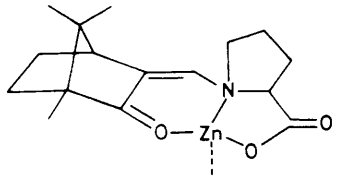
† Taken as Part 7 in the series ' Coordination Modes of Histidine.' For part 6, see ref. 3.

‡ For a discussion of the tautomeric equilibria originated by hmb see ref. 13.

‡ H_2L = general neutral condensation product of hmb with an L-amino acid. Specific abbreviations: condensation product of hmb with L-alanine = H_2L^1, with L-valine = H_2L^2, with L-phenylalanine = H_2L^3, with L-proline = H_2L^4, with L-histidine = H_2L^5, and with L-histidine methyl ester = H_2L^6.



(I) (II)



(III)

Table 1. Elemental analyses (%) for the zinc(II) complexes, with calculated values in parentheses

Compound	C	H	N
$[ZnL^1]\cdot H_2O$	51.00	6.65	3.80
	(50.55)	(6.35)	(4.20)
$[ZnL^2]\cdot 2H_2O$	50.50	6.80	3.30
	(50.75)	(7.20)	(3.70)
$[ZnL^3]\cdot 1.5H_2O$	57.50	6.50	3.05
	(57.50)	(6.25)	(3.35)
$[ZnL^5]\cdot 2H_2O$	48.90	5.70	10.15
	(49.00)	(6.05)	(10.10)
$[Zn(HL^6)][O_2CMe]\cdot H_2O$	51.00	5.90	8.40
	(50.80)	(6.15)	(8.90)
$[Zn(HL^6)][NO_3]\cdot H_2O$	45.25	5.10	11.75
	(45.45)	(5.50)	(11.80)
$[Zn(HL^4)][O_2CMe]\cdot H_2O$	51.40	6.55	3.10
	(51.60)	(6.50)	(3.35)

yellow oil. This was dissolved in methanol (50 cm^3) and hmb (5 mmol) was added. The solution was refluxed for 1 h and then zinc(II) acetate dihydrate (5 mmol) was added. After stirring for approximately 1 h the solution was evaporated to dryness under vacuum. The residue was dissolved in the minimum amount of ethanol and the product precipitated upon addition of diethyl ether. The product was filtered off, washed with a small amount of diethyl ether, and dried under vacuum. A similar procedure was followed for the preparation of $[Zn(HL^6)][NO_3]$, using zinc(II) nitrate hexahydrate instead of the acetate salt. The light yellow product precipitated from the reaction solution, since its solubility is very low. This was filtered off, washed with methanol–water, and dried under vacuum. The elemental analyses of the zinc(II) complexes are reported in Table 1.

The preparation of $K[HL^3]$ and of the copper(II) complexes derived from hmb and amino acids has been reported elsewhere.[4a,5]

Decomposition of $[Zn(HL^4)][O_2CMe]$.—In order to ascertain whether some extent of racemization of the L-amino acid had occurred during the preparation of the complexes the derivative of L-proline was decomposed, and the amino acid recovered, according to the following procedure. Approximately 20 mmol of $[Zn(HL^4)][O_2CMe]$ were dissolved in 250 cm^3 of a 1% aqueous solution of hydrochloric acid. The solution was extracted with diethyl ether (3 × 50 cm^3) in order to remove hmb and the pH was brought to *ca.* 4 with concentrated ammonia. The aqueous solution was treated with gaseous hydrogen sulphide for *ca.* 2 h, and the precipitate of zinc sulphide was removed by filtration. The filtrate was boiled to remove excess H_2S, filtered through Celite, and poured onto a column (23 × 3.8 cm) of Amberlite IR 120 (H^+ form). The column was then washed with water (2 l) and eluted with aqueous ammonia (1 mol dm^{-3}) until the eluate became alkaline. The eluate was evaporated to dryness under reduced pressure and the residue was treated with ethanol. The amino acid was collected by filtration and dried *in vacuo*. Recovery of the amino acid was >85%, α(1 g dl^{-1} in H_2O, 293 K, 589.3 nm) = −80.0°; for L-proline, α(1 g dl^{-1} in H_2O, 293 K, 589.2 nm) = −80.9°.

Results and Discussion

The present series of zinc(II) chelates was obtained by metal template condensation of hmb and the amino acid in aqueous alcoholic solution. The i.r. spectra of the chelates show that condensation between the carbonyl compound and the amino acid has occurred, since the strong C=O stretch at 1 711 cm^{-1} of hmb [13] is replaced by bands in the range 1 650—1 680 cm^{-1}, indicative of the presence of metal co-ordinated enolimine (I) or ketoenamine (II) (M = Zn) structures (Table 2). For the compound $[Zn(HL^4)][O_2CMe]$, for which the ketoenamine form (III) is the only structure available, the i.r. data should be compared appropriately with those of β-ketovinyl quaternary ammonium salts ($R'-CO-CH=CH-\overset{+}{N}R_3\tilde{X}$),[14] where the ν(C=O) and ν(C=C) bands occur near 1 700 and 1 650 cm^{-1}, respectively. The imine bands of the complexes are flanked by broad bands centred near 1 600 cm^{-1} comprising absorptions of the asymmetric carboxylate stretch of the amino acid residue, ν_{asym}(COO), and the ν(C=C) modes. The position of the symmetric carboxylate stretch, ν_{sym}(COO), is uncertain, since several bands are generally observed in the range 1 300—1 400 cm^{-1}, where ν_{sym}(COO) usually occurs.[15] By comparing the i.r. spectra of $[Zn(HL^6)][O_2CMe]$ and $[Zn(HL^6)][NO_3]$ it is possible to locate the bands of the anions. Thus the acetate ν_{asym}(COO) and ν_{sym}(COO) frequencies occur at 1 588 and 1 411 cm^{-1}, respectively, while the nitrate absorptions occur at 1 315 and near 1 610 cm^{-1}. The acetate bands are observed nearly at the same positions in the i.r. spectrum of $[Zn(HL^4)][O_2CMe]$. The positions of the i.r. absorptions for both these acetate [16] and nitrate [15,17] groups are rather typical for co-ordinated anions, though the mode of co-ordination of these anions is not easily inferred from the i.r. data. Skeletal i.r. bands that can be considered typical for the hmb residue are observed near 1 218, 1 105, 1 073, and 950 cm^{-1}. Additional bands near 3 300 cm^{-1} in the i.r. spectra of all the zinc(II) chelates are attributable to ν(OH) or ν(NH) absorptions, since these undergo the expected shift to lower energy upon deuteriation.

A useful comparison can be made between the i.r. spectra of the [ZnL] chelates and their copper(II) analogues,[4,5] for which an *X*-ray crystal structure determination is available.[6] The i.r. data of the [CuL] complexes were not reported before; therefore representative examples are collected in Table 2. In the

Table 2. Electrical conductivity and i.r. data for the zinc(II) and copper(II) complexes

Compound	Λ_M [a]/ S cm^2 mol^{-1}	ν [b]/cm^{-1}
$[ZnL^1]\cdot H_2O$	20	3 300br, 3 170w, 1 660m, 1 587s br, 1 505w, 1 418m, 1 294m, 1 218w, 1 191w, 1 182w, 1 149m, 1 106m, 1 073m, 1 026m, 953w
$[ZnL^2]\cdot 2H_2O$	25	3 300br, 3 160w, 1 674m, 1 606s br, 1 498w, 1 420 (sh), 1 344w, 1 286w, 1 261w, 1 218w, 1 182w, 1 161w, 1 148w, 1 105m, 1 073m, 1 027m, 947w, 805m, 732m
$[ZnL^3]\cdot 1.5H_2O$	15	3 300br, 3 160w, 3 083w, 3 058w, 3 022vw, 1 675m, 1 605s br, 1 496m, 1 423m, 1 345w, 1 312w, 1 288w, 1 218w, 1 197w, 1 155m, 1 105m, 1 075m, 1 034m, 950w, 755m, 700m
$[ZnL^5]\cdot 2H_2O$	5	3 250br, 3 141m, 1 674m, 1 591s br, 1 500m, 1 404w, 1 339w, 1 313w, 1 278w, 1 217w, 1 192w, 1 166m, 1 107m, 1 074m, 1 033w, 968w, 950w
$[Zn(HL^6)][O_2CMe]\cdot H_2O$	30	3 260br, 3 139m, 1 742s, 1 685s, 1 588s br, 1 505w, 1 411m, 1 336m, 1 289m, 1 254m, 1 217w, 1 198w, 1 163m, 1 106m, 1 074m, 1 026m, 970w, 950m
$[Zn(HL^6)][NO_3]\cdot H_2O$	*c*	3 270br, 3 138w, 1 739m, 1 674s, 1 608s br, 1 496m, 1 333m, 1 315m, 1 240w, 1 217w, 1 166w, 1 110m, 1 075m, 1 046w, 978w, 951w
$[Zn(HL^4)][O_2CMe]\cdot H_2O$	33	3 250br, 1 652m, 1 587s br, 1 414m, 1 324m, 1 287m, 1 244w, 1 218w, 1 185w, 1 163w, 1 151w, 1 142w, 1 122w, 1 105m, 1 074m, 1 040w, 1 014w, 958m
$K[HL^3]\cdot 1.5H_2O$	68 [d]	3 350s br, 1 671s, 1 612s br, 1 573s br, 1 494s, 1 452s, 1 398m, 1 364m, 1 272w, 1 229w, 1 193w, 1 178w, 1 155w, 1 106m, 1 072m, 1 033m, 996w, 955m, 911m, 808m
$[CuL^2]$	2	1 616s, 1 599s, 1 562s, 1 496s, 1 441s, 1 344s, 1 309s, 1 289w, 1 276w, 1 262w, 1 223w, 1 203w, 1 184w, 1 164w, 1 147w, 1 112m, 1 081m, 1 027m, 1 000w, 970m, 934w, 844w, 793m, 752m, 695m
$[CuL^3]$	4	3 062w, 3 024w, 1 612s, 1 594s, 1 563s, 1 492s, 1 444s, 1 384m, 1 342s, 1 309s, 1 290w, 1 275w, 1 240w, 1 220w, 1 203w, 1 182w, 1 111m, 1 096w, 1 078m, 1 044w, 975w, 911w, 777m, 755m, 697m
$[CuL^5]\cdot H_2O$	0	3 140w, 1 609s br, 1 582s br, 1 494s, 1 342m, 1 310m, 1 287w, 1 276w, 1 224w, 1 168w, 1 110m, 1 079m, 1 022w, 975w
$[Cu(HL^4)][O_2CMe]$	32	3 087m, 1 673s, 1 635s, 1 620 (sh), 1 513s, 1 351s, 1 296s, 1 222m, 1 194m, 1 185w, 1 159m, 1 108m, 1 078s, 1 051m, 978s, 941m, 915w, 845w, 802m, 751m, 730m

[a] Measured in methanol solution (10^{-3} mol dm^{-3}). [b] Recorded as Nujol mulls. [c] Too insoluble. [d] Ref. 4*a*.

range 1 500—1 700 cm^{-1} the spectra invariably show only bands at wavenumbers lower than 1 620 cm^{-1}. The only exception is represented by the ionic derivative of L-proline, $[Cu(HL^4)][O_2CMe]$ which has a band at 1 673 cm^{-1}. The different location of the i.r. bands in the region 1 500—1 700 cm^{-1} indicates structural differences between the neutral zinc(II) and copper(II) chelates of the type [ML], since the position of these bands is related to the bond order of the functional groups of the ligand involved. According to the results of the *X*-ray structural determination of $[CuL^3]$,[6] the six-membered chelate ring is planar and the bond distances are in agreement with extended π-delocalization involving also the ligand to copper bonds. The structure of the neutral [CuL] chelates, therefore, is better represented by (IV), although in order to simplify the notation we will assimilate the delocalized structure (IV) to the enolimine structure (I) (M = Cu). One reason for this is that the Cu–O(enolate) bond distance in $[CuL^3]$ is actually the shortest of the whole co-ordination set and falls within the range found for the Cu–O(phenolate) bond lengths in the structures of several copper(II) complexes of amino acid Schiff bases derived from pyridoxal or salicylaldehyde,[18] while we would expect a somewhat weaker Cu–O interaction for the corresponding ketoenamine tautomer. Secondly, while the i.r. absorption in the range 1 650—1 680

cm^{-1} exhibited by the neutral [ZnL] chelates may be related to the ketoenamine tautomer (II) (M = Zn), the solution behaviour of these complexes is better explained in terms of the existence of a tautomeric equilibrium between the enolimine (V) and a ketoenamine form containing a protonated, tetrahedral nitrogen donor, (VI). This latter structure provides a ligand environment equivalent to that of the L-proline complexes of type (III) and obviously accounts for the presence of i.r. bands in the range 1 650—1 680 cm^{-1}, since these are typical for the ketoenamine complexes [Zn(HL⁴)][O_2CMe] and [Cu(HL⁴)][O_2CMe], and are also exhibited by the i.r. spectrum of K[HL³], for which the presence of the nitrogen-protonated form of the ketoenamine anion was firmly established in solution.[4a]

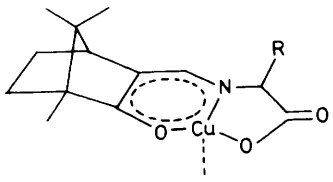
The need to introduce ionic ketoenamine species of type (VI) results mainly from the attempt to rationalise the electronic and c.d. spectra and the electrolytic behaviour of the [ZnL] chelates. These exhibit molar conductivities in methanol solution (10^{-3} mol dm^{-3}) almost comparable with those of [Zn(HL⁴)][O_2CMe], [Zn(HL⁶)][O_2CMe], and [Cu(HL⁴)][O_2CMe], while the neutral [CuL] chelates are essentially non-electrolytes (Table 2). In lower donating solvents such as acetonitrile the conductivity of the [ZnL] complexes is lower; this may reflect a higher amount of the neutral enolimine form (V) at the equilibrium or simply a lower degree of dissociation of the ketoenamine complexes (VI). The electronic spectra of the [ZnL] complexes in methanol solution are characterized by the presence of two bands of comparable intensity near 325 and 350 nm, that we assign to $\pi \rightarrow \pi^*$ transitions of the ketoenamine (VI) and enolimine form (V), respectively (Table 3). This assignment is dictated by the observation of a single u.v. band at 323 nm in the spectrum of [Zn(HL⁴)][O_2CMe] that is approximately twice as intense as the corresponding absorptions of the neutral [ZnL] complexes. The bathochromic shift of the u.v. band of the enolimine form (V), compared to the position of the corresponding band of the ketoenamine (VI), is attributed to the increase of conjugation provided by the planar nitrogen atom. Note that a ketoenamine form containing a planar nitrogen atom, such as (II), would be expected to absorb at wavelengths bathochromically shifted with respect to the corresponding enolimine form (I). This trend is well established in the chemistry of pyridoxal [7,19] and salicylaldehyde [20] Schiff bases of amino acids. Thus the u.v. spectra of the zinc(II) complexes clearly show the structural similarity between the ketoenamine form of [Zn(HL⁴)][O_2CMe] and those of the [ZnL] complexes. Comparisons of this kind were hampered in the case of the copper(II) complexes [4,5] by the occurrence of intense charge-transfer bands in the region of the ligand $\pi \rightarrow \pi^*$ transitions. Interestingly, in acetonitrile solution the enolimine band dominates the u.v. spectrum of the zinc(II) complexes, as shown in Figure 1 for [ZnL¹], but unfortunately the very low solubility of the derivatives of L-histidine precluded a complete investigation in this solvent.

The c.d. spectra of the [ZnL] complexes in methanol solution are summarised in Table 3. In general, the spectra show well resolved enolimine c.d. bands near 350 nm, while, except for [Zn(HL⁴)][O_2CMe], the ketoenamine c.d. bands are apparently much weaker and occur as poorly defined shoulders between the enolimine bands and the positive c.d. absorption at higher energy, which is typical for the hmb residue.[12] C.d. spectra recorded in acetonitrile solution confirm the larger amount of enolimine tautomer in this solvent than in methanol solution; for [ZnL¹] this difference is remarkable (Figure 1). Possibly the spectra in acetonitrile reflect the tautomeric composition of the solid as it is obtained in the preparation, while methanol may promote the formation of the ketoenamine tautomer (VI) by stabilizing it through hydrogen bonding. The sign of the c.d. band of the enolimine tautomer (V) correlates with the preferred conformation of the amino acid chelate ring, since the chelate ring of the hmb residue can be considered planar. As for the other complexes of tridentate Schiff bases of amino acids this preferred conformation involves a pseudo-axial side chain.[1-7] The c.d. features exhibited by [ZnL⁵] are the same as those of the complexes derived from non-polar L-amino acids, while for [Zn(HL⁶)][O_2CMe] the Cotton effects within the enolimine c.d. band are of opposite sign (Figure 2). Therefore, we conclude that the six-membered chelate ring of the hmb residue imposes a glycine-like co-ordination mode to the histidine residue of [ZnL⁵], (VII), while the histamine-like mode (VIII) is the only available in [Zn(HL⁶)][O_2CMe]. The preferred conformations for these two modes have opposite chirality

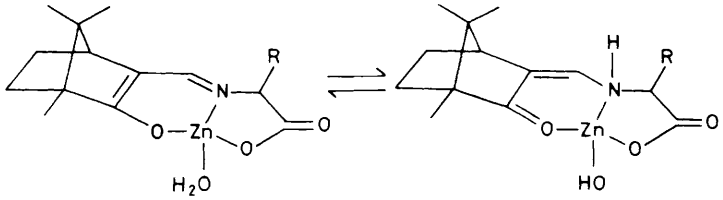
Table 3. Electronic and c.d. spectral data of the zinc(II) complexes in methanol solution

Compound	$\lambda_{max.}$/nm (ε/dm^3 mol^{-1} cm^{-1})	$\lambda_{max.}$/nm ($\varepsilon_l - \varepsilon_r$) *
[ZnL¹]·H_2O	325 (8 200)	298 (+3.37)
	349 (7 700)	357 (−0.15)
[ZnL²]·2H_2O	326 (9 500)	298 (+3.23)
	349 (sh) (8 300)	353 (−1.07)
[ZnL³]·1.5H_2O	328 (8 600)	298 (+2.23)
	350 (8 700)	350 (−6.29)
[ZnL⁵]·2H_2O	325 (11 200)	298 (+1.16)
	350 (9 700)	362 (−5.40)
[Zn(HL⁶)][O_2CMe]·H_2O	316 (10 200)	295 (+4.39)
	345 (9 500)	348 (+3.24)
		372 (−0.74)
[Zn(HL⁴)][O_2CMe]·H_2O	323 (22 300)	300 (+8.28)
		332 (−2.48)

* $\varepsilon_l - \varepsilon_r = \Delta\varepsilon$/$dm^3$ mol^{-1} cm^{-1}.



(IV)



(V) (VI)

for histidine residues of the same absolute configuration and determine the opposite trend observed in the c.d. spectra.

In considering the ketoenamine structures of type (VI) these simple conformational arguments are no longer applicable, since the tetrahedral nitrogen donor and probably also the metal atom become chiral centres. It is obviously very difficult to infer the co-ordination geometry of metal ions, such as zinc(II), which are diamagnetic and with poor optical properties. However, it can be shown by molecular models that the co-ordination environment of (VI), containing a tetrahedral nitrogen donor, can be fitted with less strain in a structure containing significant distortion of the metal geometry from planar toward tetrahedral. If a chiral, pseudo-tetrahedral geometry at the metal centre is allowed, diastereoisomeric ketoenamines of type (VI) will result. Definite evidence for the presence of various isomers of the complexes in solution is found in their n.m.r. spectra, to be discussed later. We only wish to summarise here the various possibilities of diastereoisomerism in the ketoenamine complexes, starting from the L-proline derivative [Zn(HL⁴)][O₂CMe], which is the simplest system. The nitrogen-donor atom of the L-proline residue of (III) co-ordinates stereospecifically to the metal with the *S*-configuration; however, assuming a *T*-4 symmetry site at the metal,[21,22] two diastereoisomeric complexes with absolute configurations *R* (IX) and *S* (X) can be formed [the fourth donor atom in the co-ordination set of (IX) and (X) can represent either the acetate ion or a water molecule without affecting the priority ranking of the ligands]. If we consider now the ketoenamine form (VI) of the [ZnL] complexes, the configuration at the nitrogen donor is no longer stereospecifically imposed, since it can be thought that protonation of nitrogen in (V) can occur from both sides of the co-

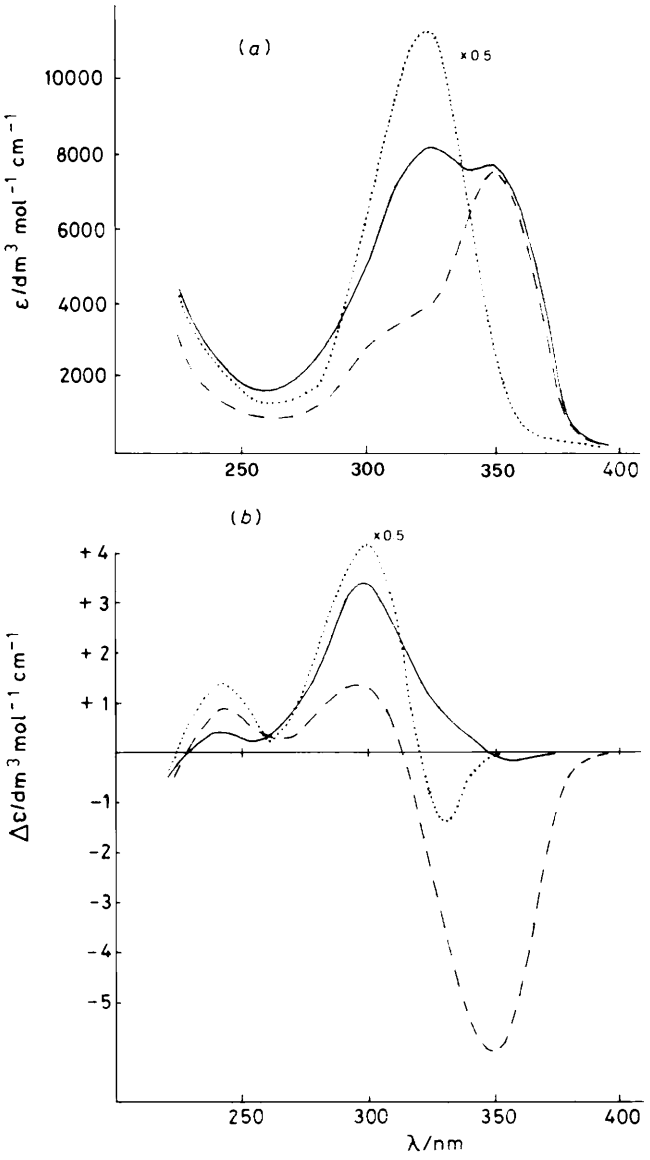


Figure 1. (*a*) Electronic and (*b*) c.d. spectra of [ZnL¹]: in methanol (——) and acetonitrile (— — —) solution, and of [Zn(HL⁴)][O₂CMe] in methanol solution (· · · ·)

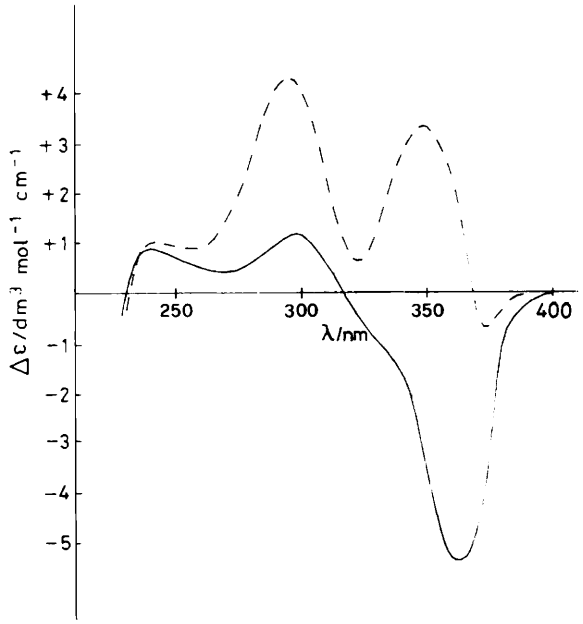
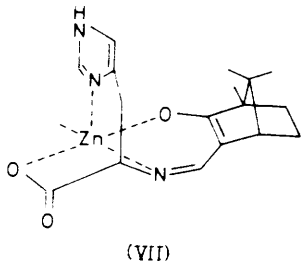
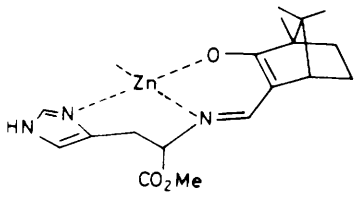


Figure 2. Circular dichroism spectra of [ZnL⁵] (——), and [Zn(HL⁶)][O₂CMe] (— — —) in methanol solution



(VII)



(VIII)

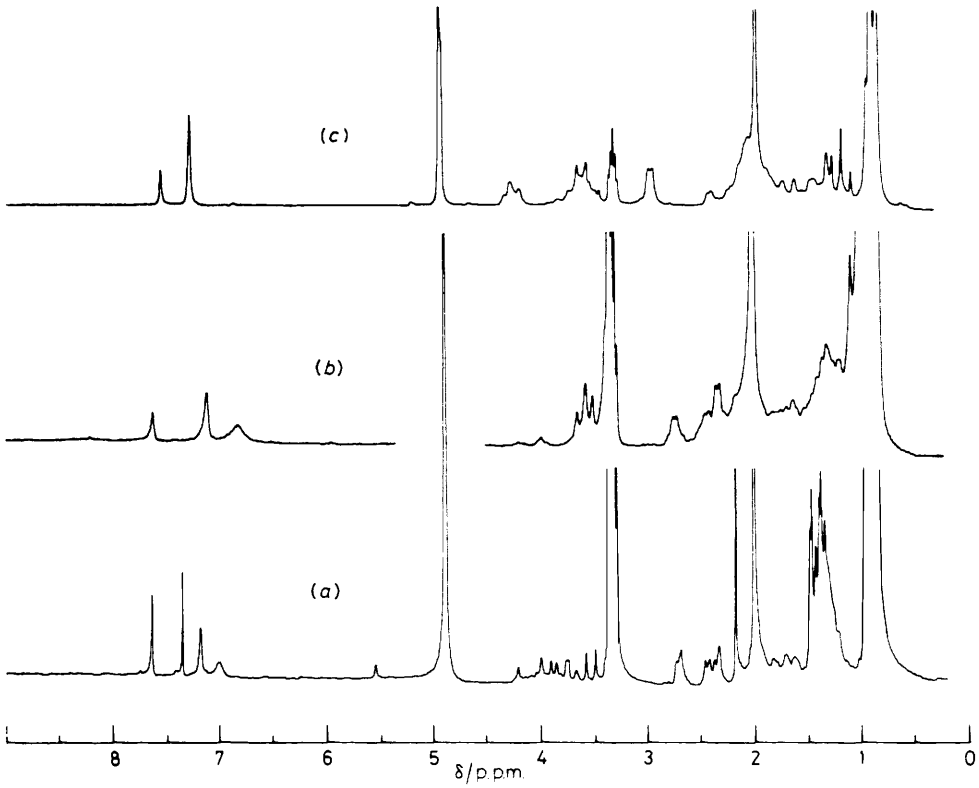
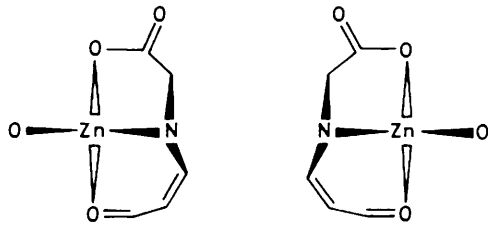


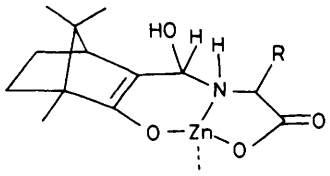
Figure 3. Hydrogen-1 n.m.r. spectra in CD_3OD of: (*a*) [ZnL^1], (*b*) [ZnL^2], and (*c*) [$Zn(HL^4)][O_2CMe$]



R (IX) *S* (X)

ordination plane. Although some degree of stereoselectivity is to be expected, up to four diastereoisomeric ketoenamine complexes of type (VI) can theoretically be formed. The interconversion of these can in principle occur through the planar enolimine tautomer (V), provided the activation energy for the tautomerization process is not too high. However, the presence of diastereoisomeric ketoenamines accounts for the almost negligible c.d. activity associated with the bands near 325 nm in the spectra of the [ZnL] complexes.

For solubility reasons the proton and carbon-13 n.m.r. spectra of the zinc(II) complexes were routinely recorded in CD_3OD solution, although in a few instances the spectra could also be obtained in lower donating solvents such as CD_3CN or $CDCl_3$. In general the spectra are complicated by the presence of several species; these are clearly evidenced by the proton signals in the range δ *ca.* 7—8, where the resonances of the imine and olefinic protons occur, and at δ *ca.* 3.5—4.5, where the absorptions of the amino acid α-CH groups occur. Representative examples of the proton n.m.r. spectra are given in Figure 3. The simplest spectra are those of [$Zn(HL^4)][O_2CMe$], consisting of two diastereoisomeric ketoenamines of type (III). These are characterized in the proton n.m.r. spectra by two olefinic (δ *ca.* 7.5 and *ca.* 7 in CD_3OD, intensity ratio 1 : 3) and α-CH signals (δ *ca.* 4.3 and *ca.* 3.8, ratio 3 : 1, the latter partially obscured by other absorptions), whose position, but not relative intensity, is slightly solvent dependent. In the ^{13}C n.m.r. spectra these ketoenamine forms are clearly indicated by two carbon resonances of different intensity at fields as low as *ca.* 210 p.p.m. (downfield from $SiMe_4$), that can originate only from C=O groups of the hmb residue, since the amino acid or acetate carboxyl groups absorb in the range 170—185 p.p.m.[23] The proton n.m.r. spectra of the other [ZnL] complexes show more than two signals in the range δ *ca.* 7—8, and correspondingly complex patterns of signals at higher fields (Figure 3). For instance, the spectrum of [ZnL^1] in CD_3OD shows four resolved singlets at low fields and four overlapping quartets of α-CH groups in the range δ *ca.* 3.5—4, giving rise to a complicated pattern of doublets for the methyl groups of the amino acid residue (near δ 1.5). Unfortunately the solubility of [ZnL^1] in CD_3CN, where the amount of enolimine form is higher, is too low to obtain reliable spectra, while in $CDCl_3$ solution several signals are observed at δ *ca.* 5.5—8. Some of these are broad and are apparently associated with OH or NH groups, since they disappear upon addition of D_2O, leaving four sharper peaks in the range δ 6.5—7.5 that resemble the low-field pattern observed in CD_3OD. Similar arguments apply to the ^1H n.m.r. spectra of [ZnL^2], for which three signals in the range δ 7—8 are observed in CD_3OD (Figure 3). The ^1H spectra of the derivatives of L-phenylalanine and L-histidine exhibit rather complex patterns of signals at low fields, since the aromatic or imidazole protons also absorb in the range δ *ca.* 7—8. Interestingly, for [ZnL^3] an additional proton signal at δ 5.5 in CD_3OD probably arises from a species such as (XI).[24] The presence of several isomers of the



(XI)

[ZnL] complexes complicates the assignments of the individual signals also in the ^{13}C n.m.r. spectra; however, we note that all these spectra exhibit carbon resonances near δ 210 p.p.m. that are to be assigned to the C=O groups of the ketoenamine species.

As mentioned earlier, the configurational interconversion at the metal of the ketoenamine forms (VI) of the [ZnL] complexes can occur through the planar enolimine tautomer (V) provided the tautomerization rate becomes sufficiently fast. This can be accomplished by heating the solution of the complex in a sufficiently high-boiling solvent such as dimethyl sulphoxide (dmso). Figure 4 shows the changes observed in the low-field region of the ^1H n.m.r. spectrum of [ZnL^1] in [$^2H_6$]dmso on heating the sample up to 100 °C. At this temperature the fast exchange condition is approached and a single broad signal results. The signals of the α-CH groups at δ 3—4 undergo similar changes, although this observation is somewhat disturbed by the HDO signal near δ 3.3 that increases considerably the broadening of the featureless signal near the fast exchange limit. On slow cooling of the sample the reverse spectral changes occur and the initial spectrum is again obtained. A similar behaviour is exhibited by [ZnL^2] and we expect that this behaviour is common to the other [ZnL] complexes. It can be anticipated, however, that the tautomerization pathway should be inhibited for [$Zn(HL^4)$][O_2CMe], and indeed heating a solution of this compound in [$^2H_6$]dmso up to 130 °C produces only a slight broadening of the lowest field proton resonance, with no change in position or relative intensity of any signal in the spectrum. The possibility that these isomers of [$Zn(HL^4)$][O_2CMe] originated from a partial racemization of the amino acid during preparation of the complex, although unlikely, since all the complexes were prepared in slightly acidic media, was ruled out by isolating the amino acid after decomposition of the complex with hydrogen sulphide. Thus the need to invoke the metal as a centre of chirality to differentiate the ketoenamine forms of [$Zn(HL^4)$][O_2CMe] becomes apparent, even though the assumption of four-co-ordination for the metal centre is clearly only tentative. The interconversion of the ketoenamine forms of [$Zn(HL^4)$][O_2CMe] can possibly occur at higher temperature, through rearrangement pathways involving high energy barriers.[25]

In conclusion, this investigation has shown that the zinc(II) complexes derived from hmb and a series of L-amino acids consist of tautomeric mixtures of the enolimine form (V) and of ketoenamine forms of type (VI), containing a tetrahedral nitrogen donor, that appear structurally similar to the complex of structure (III) derived from the cyclic amino acid L-proline. The distinction between enolimine and ketoenamine forms is probably not significant in the case of the corresponding copper(II) complexes since their structure is best represented by tautomeric equilibria of the type (I) ⇌ (II), involving atoms with the same hybridization and an almost aromatic chelate ring. We note that these [ZnL] complexes appear to be the first metal systems derived from amino acid Schiff bases that exhibit keto–enol equilibria not involved in transamination processes.[3,26] Such keto–enol equilibria are usually observed only in metal-free systems,[7,19,20,27] while the

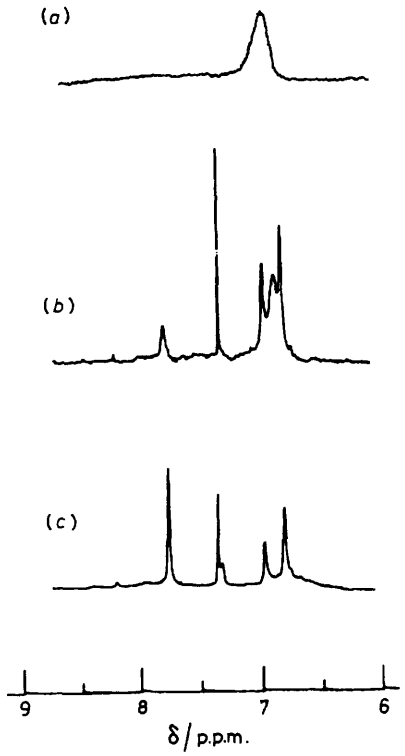


Figure 4. Variable-temperature ^1H n.m.r. spectra of [ZnL^1] in [$^2H_6$]dmso solution: (*a*) 100, (*b*) 70, and (*c*) 30 °C

corresponding metal complexes, including zinc(II),[1,7] exist exclusively in the aldimine forms.[26] The preference for these aldimine forms is probably related to the planarity of the chelate ring of the carbonyl residue, which is imposed by the phenolic aldehydes (pyridoxal or salicylaldehyde) usually employed for the synthesis of the complexes. In the systems derived from hmb there is more flexibility. Thus the planarity of the chelate ring fused to the norbornane skeleton can be maintained by metal ions, such as copper(II), which exhibit a strong preference for planar co-ordination, while the preference for a pseudo-tetrahedral environment by zinc(II) is partially met by the ligand undergoing the tautomerization process of the type (V) ⇌ (VI).

Acknowledgements

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