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Preparation and characterisation of new oxovanadium(IV) Schiff base complexes derived from salicylaldehyde and simple dipeptides

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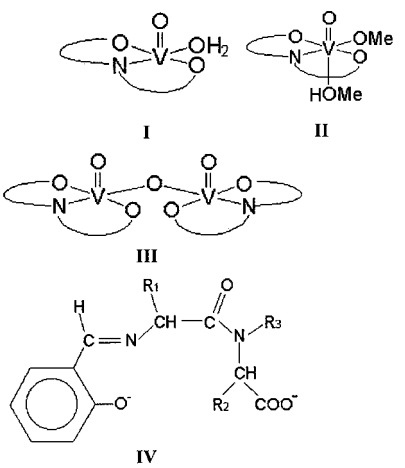
Abstract

A range of mostly new oxovanadium(IV) complexes is described. They contain coordinated Schiff bases, made from simple dipeptides (glycylglycine, glycylsarcosine, L-alanylglycine, L-alanyl-L-alanine, D,L-alanyl-D,L-alanine and L-serylglycine), and salicylaldehyde. The compounds are characterised and the nature of their coordination spheres shown by analysis, TLC, by appropriate spectroscopy (EPR, IR, electronic and circular dichroism of solution and solids) and by magnetic susceptibility measurements. Serylglycine and threonylglycine are formed by reaction of VO(salGlyGly) with formaldehyde and acetaldehyde, respectively. © 2000 Elsevier Science S.A. All rights reserved.

Keywords: Vanadium complexes; Schiff base complexes; Dipeptide complexes

1. Introduction

While complexes of *N*-salicylideneamino acids have been the subject of extensive research, typified by their vanadium compounds [1–19], little attention has been given to Schiff bases derived from simple peptides. *N*-Salicylideneamino acid vanadium(IV) and (V) complexes often have coordination geometries such as those in **I** or **II** [3–5,11,12]. In a few cases, dimeric oxo-bridged V^{IV}–O–V^{V} or V^{V}–O–V^{V} compounds **III** have been obtained [4,5,11,13,15]. The present paper deals with the preparation of several complexes containing **IV**, a Schiff base ligand resulting from the condensation of a dipeptide with salicylaldehyde. The dipeptides are glycylglycine (GlyGly), glycylsarcosine (GlySar), L-alanylsarcosine (AlaSar), L-alanylglycine (AlaGly), L-alanyl-L-alanine (AlaAla), D,L-alanyl-D,L-alanine (D,L-Ala-D,L-Ala) and L-serylglycine (SerGly). The complexes were characterised by elemental analysis, IR, EPR, electronic and circular dichroism spectroscopy. In some cases, magnetic moments were measured in the range 5–296 K. Solids were also similarly obtained with glycyl-L-alanine (GlyAla), glycyl-L-aspartic acid (GlyAsp) and L-serylglycine (SerGly), but their elemental analyses do not fit the formulations very closely.



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To our knowledge, of the compounds we describe, only the vanadium complex VO(Sal-GlyGly)$(H_2O)_n$ (**1**) with $n = 1.5–3.0$, containing ligand **IV** ($R_1 = R_2 = R_3 = H$) is known [16]. Its formulation was based on the elemental analysis (C, H, N, S, V, Na), IR, TLC, TG-DSC, and magnetic susceptibility measurements, where $\mu_{eff} \approx 1.75$ BM in the range: 25–300 K. It is only very slightly soluble in common solvents and practically insoluble in water. In attempts to obtain crystals of this compound, $(NH_4)_4(Na)_2[V_{10}O_{28}]\cdot 10H_2O$ in fact precipitated: this was characterised by X-ray diffraction. In this system with GlyGly, metal ion oxidation and decomposition/deamination of the amino acid yielded NH_4^+, identified as a counter ion of the decavanadate.

The enhanced roles of metal ions in non-enzymatic pyridoxal-mediated reactions in model systems (e.g. transaminations, racemisations, decarboxylations, eliminations) have been extensively studied (e.g. [20–23]); an intermediate Schiff-base is expected to form, and a metal ion is required in model studies as a template and/or to stabilise the resulting product. With vanadium in the presence of salicylaldehyde, racemisations (for the L-serine, L-asparagine and L-histidine systems), and decomposition/deaminations producing $(NH_4)_4(Na)_2[V_{10}O_{28}]\cdot 10H_2O$ have been reported for the GlyGly [16] and Thr [19] systems, and is also reported here for the GlyAla and AlaGly systems. Oxovanadium(IV/V) is also one of the most active metal ions in β-eliminations [24,25]; examples of the reverse type of reactions are also reported here, particularly that of VO(salGlyGly)$(H_2O)_n$ with formaldehyde or acetaldehyde in basic medium to produce the VO(salSerGly) or VO(salThrGly) complexes which after hydrolysis with acid yield SerGly or ThrGly, respectively.

2. Experimental

2.1. Synthesis of Schiff base complexes

The Schiff base complexes were obtained as described previously [3,5,17,19] for similar *N*-salicylideneamino acidato compounds. Elemental analyses are in Table 1. For **1**–**5** these are in the expected range. However those for VO(salAlaGly) (**6**), VO(salGlyAla) (**7**), VO(salGlyAsp) (**8**) and VO(salGlySer) (**9**) are not satisfactory. While for GlyGly, GlySar, AlaSar, AlaAla, GlyAsp, precipitation occurred during, or shortly after, the addition of the $V^{IV}O^{2+}$ solution to the mixture containing salicylaldehyde and dipeptide, it took 1 h for GlySer, and AlaGly, 1 day for GlyAla, and 2 days for SerGly. For the GlyAla and AlaGly systems, after separation of the solids by filtration, the mother liquor was left in the refrigerator. Two (GlyAla) or four (AlaGly) weeks later, orange–brown crystals were collected and characterised by X-ray diffraction as $(NH_4)_4(Na)_2[V_{10}O_{28}]\cdot 10H_2O$.

2.2. HPLC experiments

These were performed using Jasco HPLC system including a Jasco 870-UV (absorbance) and 821-FP (fluorescence) detectors. A Rheodine 7125 injection valve (20 μl loop) and a reverse phase column (LiChrosorb C_{18}-5 μm particules, 250 × 4 mm) were used. The eluent (9% methanol, 5.2% THF, 4.2% acetonitrile and 0.1 M sodium acetate aqueous solution at pH 6.8) was always filtered before use (45 μm filters), degassed and its flow was 1.0 ml min^{-1}. The dipeptides were analysed using the precolumn derivatisation *o*-phthaldi-

Table 1
Elemental analyses, formulation and corresponding expected analytical data of some Schiff base complexes [a,b]

Compound		%C	%H	%N	%V; %Na
1	Found	39.2	4.0	8.0	15.8 ± 1; <0.2
$VO(sal\text{-}GlyGly)(H_2O)_2$	$C_{11}H_{14}N_2O_7V$	39.18	4.19	8.31	15.1; 0
2	Found	44.2	3.9	8.3	15.7 ± 1; <0.1
$VO(salGlySar)(H_2O)_{0.5}$	$C_{12}H_{13}N_2O_{5.5}V$	44.46	4.04	8.64	15.73; 0
$V_2O_3(salGlySar)_2$	$C_{24}H_{24}N_4O_{11}V_2$	44.60	3.74	8.67	15.76; 0
3	Found	43.9	4.7	7.5	12.8 ± 1.5; <0.1
$VO(sal\text{-}DL\text{-}Ala\text{-}DL\text{-}Ala)(H_2O)_{1.5}$	$C_{13}H_{17}N_2O_{6.5}V$	43.83	4.81	7.86	14.30; 0
$V_2O_3(sal\text{-}DL\text{-}Ala\text{-}DL\text{-}Ala)_2(H_2O)_2$	$C_{26}H_{32}N_4O_{13}V_2$	43.96	4.54	7.89	14.34; 0
4	Found	42.4	4.6	7.7	13.1 ± 1.5; <0.3
$VO(salAlaAla)(H_2O)_2$	$C_{13}H_{18}N_2O_7V$	42.75	4.97	7.67	13.95; 0
$V_2O_3(salAlaAla)_2(H_2O)_3$	$C_{26}H_{34}N_4O_{14}V_2$	42.87	4.70	7.69	13.99; 0
5	Found	40.8	3.8	7.6	43.9 ± 1; <0.2
$VO(salSerGly)(H_2O)_{1.5}$	$C_{12}H_{15}N_2O_{7.5}V$	40.24	4.22	7.82	14.22; 0
$V_2O_3(salSerGly)_2(H_2O)_2$	$C_{24}H_{28}N_4O_{15}V_2$	40.35	3.95	7.84	14.26; 0

[a] For VO(sal-AlaSar) (**10**) the amount of solid available was not enough for elemental analysis. As solids **6**–**9** have non-satisfactory elemental analysis they are not included in the table.

[b] Values of vanadium analysis within ± (1–1.5) may be considered acceptable, depending on the amount of solid used in each determination.

aldehyde/mercaptoethanol procedure for aminoacid analysis [26]. The presence of products in samples was confirmed by comparing their retention times with the dipeptide standards.

2.3. TLC experiments

Those preparations both where formulations do not agree with the elemental analysis, and for **1** were monitored by TLC, on Merck TLC plates (Art. 5626, 10 × 20 cm). Samples of 2 μl of the reaction mixture, and of similar samples after hydrolysis with HNO_3 were applied to the plates 20 mm from the bottom. Elutions were carried out in Camag twin chambers with walls covered with filter paper impregnated with the eluent. Eluents used were: (**A**) 7:3 ethanol/water, (**B**) 10:10:2:5 *n*-butanol/ethanol/propionic acid/water. When the eluents reached ~120 mm from the bottom, the plates were removed and dried. The chromatogram was developed with a ninhydrin–collidine–copper solution prepared according to Moffat and Lytle [27], followed by iodine vapour.

For preparative TLC we used Merck TLC plates (Art. 105745, 20 × 20 cm, 2 mm thickness). The acidified samples (1.0 ml) were applied as a streak using a syringe. Eluent B was used and a 1 × 20 cm part of the plate was developed with iodine vapour to localise the components. Due to a greater band broadening there is a much greater superposition of bands than for the analytical TLC plates. Those parts of the SerGly and ThrGly bands that appeared not to be contaminated were scraped with a spatula and the dipeptides extracted with water. After filtration and evaporation of the filtrate around 10 mg of each dipeptide were obtained (three plates for each reaction mixture).

2.4. Synthesis of SerGly and ThrGly

2.4.1. Procedure 1 (under N_2)

To 10 ml of an aqueous solution of GlyGly (0.66 g, 5 mmol), an ethanolic solution of salicylaldehyde (2.0 ml, 1.0 mmol) and $VOSO_4 \cdot 5H_2O$ (0.228 g, 0.90 mmol) in 5 ml of water were added. Na_2CO_3 was added until pH 8. Formaldehyde (0.5 ml) or acetaldehyde (0.5 ml) were also added. New 0.5 ml portions of these aldehydes were added every 15 min. Up to a total of 2.0 ml (27 mmol) or 2.5 ml (44 mmol), respectively.

2.4.2. Procedure 2 (under N_2)

To 10 ml of methanol, GlyGly (0.142 g, 1.07 mmol) and salicylaldehyde (0.11 ml, 0.86 mmol) were added. After stirring for ~5 min., $VOSO_4 \cdot 5H_2O$ (0.217 g, 0.857 mmol) was added. After ~5 min, 15 ml of methanol containing sodium methoxide (0.74 g, ~13 mmol) were added. Formaldehyde (0.5 ml) or acetaldehyde (0.5 ml) was then added. New 0.5 ml portions of the aldehydes were added every 15 min. Up to a total of 2.0 ml (27 mmol) and 2.5 ml (44 mmol), respectively.

The reactions described in procedures 1 and 2 were monitored by TLC using eluent **B** for ~3 h, using also standards of GlySer ($R_f = 0.11$), SerGly ($R_f = 0.18$) and GlyThr ($R_f = 0.18$) in the same TLC plates. During elution the complexes hydrolyse extensively and the formation of either SerGly or ThrGly is confirmed by the presence of spots at $R_f = 0.18$ (SerGly) or $R_f = 0.29$ (ThrGly). Acid was added to samples to hydrolyse the vanadium complexes present in the reaction mixture and the acidified samples (pH ≈ 1) were frozen and later analysed by HPLC. The presence of peaks at 17.0–17.2 min (SerGly), or 20.3–20.5 min (GlyThr) and 21.4–21.7 (ThrGly), confirmed the formation of either the serine- or threonine-containing dipeptides. In the same conditions, the GlyGly peak shows up at 19.0–19.2 min.

Reaction yields may be estimated from the HPLC band areas based on the mmol of GlyGly initially present: SerGly-20% (proc. 1) or 40% (proc. 2), and ThrGly-40% (proc. 1) or 70% (proc. 2). These agree with the dimension/intensity of the corresponding TLC spots. Due to overlapping bands (resulting in lower recovery for a better purity) the global yields of the products isolated by preparative TLC are much lower and may be grossly estimated as 5% for procedure 2.

2.5. Magnetic measurements

The magnetic susceptibilities of complexes **2** (20.06 mg) and **3** (18.5 mg) were measured in the range 5–296 K using a 7-Tesla Faraday Oxford Instruments system coupled to a Sartorius S3D-V microbalance, at 1 Tesla and with a 5 T/m gradient.

2.6. Spectroscopic measurements

The circular dichroism spectra were run on a Jasco 720 spectropolarimeter with the red sensitive (400–1000 nm) photomultiplier, isotropic absorption spectra with a Perkin–Elmer λ9 spectrophotometer, Electron Spin Resonance spectra on a Bruker ER 200d (connected to a Brucker B-MN C5) spectrometer and IR either with a Perkin–Elmer 683 or a BioRad FTS 3000 MX FT-IR spectrometer.

2.7. CD spectra of solid complexes

Samples of compounds **1**, **3**–**9** and of VO(salAlaSar) **10** were prepared as described previously [3], either dispersed in Nujol mulls or in KBr disks, and placed between two microscope slides. One to three of such paired microscope slides were placed in the sample compartment. Each final spectrum is the average of 4–6 spectra in all, recorded as described in Ref. [3].

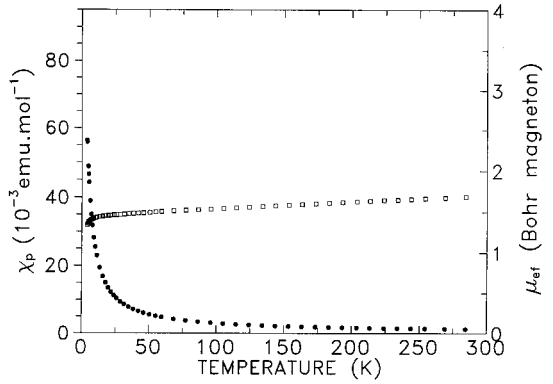


Fig. 1. Temperature dependence of the magnetic susceptibility and μ_{eff} of [VO(salGlySar)(H_2O)] between 5 and 296 K. The data were corrected for the diamagnetic contribution ($\chi_d^M = -1.45 \times 10^{-4}$ emu mol^{-1}).

3. Results and discussion

3.1. TLC experiments

Distinct and clear spots (S) corresponding to the Schiff base complexes are normally detected for the reaction mixture. Distinct spots with characteristic colours (PP) are also detected at the R_f of the free peptides and the spots S each tailed down towards the spot PP. This tailing is more significant with eluent **B**, and is due to hydrolysis of the Schiff base during elution. R_f values are higher with eluent **A** than with **B**.

3.2. VO(salGlyGly), VO(salGlySar), VO(sal-D,L-Ala-D,L-Ala), VO(salAlaAla), VO(SalSerGly)

The formation of the Schiff base complex is clearly seen after the addition of $V^{IV}O^{2+}$. The solids isolated from the reaction mixtures give satisfactory analysis.

3.3. VO(salGlyAla) (*7*)

Although the solid, which precipitated only about a day after mixing the reagents, had satisfactory N and V analysis, the formation of the Schiff base complex is clearly seen shortly after addition of VO^{2+}: spots S at $R_f = 0.72$ and 0.60, for **A** and **B**, respectively, each tailing down towards the spots PP ($R_f = 0.33$ and 0.16, for **A** and **B**, respectively). A product with $R_f = 0.63$ and 0.48, for **A** and **B**, respectively, is also detected, possibly corresponding to a non-coordinated Schiff base. However, no decomposition of the dipeptide into its amino acid fragments is detected by TLC; for the samples hydrolysed with HNO_3 only the spots PP appear. On ageing the mother liquor, orange–brown crystals of $(NH_4)_4(Na)_2[V_{10}O_{28}]$ were obtained and characterised by X-ray diffraction and IR spectroscopy. The formation of a compound of vanadium(V) may be explained by the oxidation of oxovanadium(IV) by atmospheric oxygen. The NH_4^+ cations presumably form by deamination of the GlyAla present in solution. The compound is identical to those obtained from similar solutions containing not GlyAla or AlaGly, but either GlyGly [16] or L-Thr [19].

3.4. VO(salGlySer) (*9*)

Although a solid with unsatisfactory analysis precipitated about 1 h after mixing the reagents, the formation of the Schiff base complex is clearly seen a few minutes after addition of VO^{2+}: spots S at $R_f = 0.72$ and 0.56, for **A** and **B**, respectively, each tailing down towards the spots (PP) for the free dipeptide ($R_f = 0.32$ and 0.18, for **A** and **B**, respectively). A product with $R_f = 0.55$ and 0.58, for **A** and **B**, respectively, possibly a non-coordinated Schiff base, is also detected with ninhydrin even before the addition of $V^{IV}O^{2+}$. Two other weak spots are detected with iodine vapours.

3.5. VO(Sal-GlyAsp) (*8*)

Although a solid precipitated shortly after mixture of the reagents, its elemental analysis is incompatible with any simple formulation. The formation of the Schiff base complex is clearly seen with eluent **A** (spot S at $R_f = 0.62$), while with eluent **B** most of the Schiff base decomposes during elution ($R_f \approx 0.50$). The dipeptide is clearly detected (spots PP at $R_f = 0.32$ and 0.16, for **A** and **B**, respectively). After about 1 h of VO^{2+} mixing the reagents, the additional spots that were detected with $R_f = 0.43$ and 0.35 (eluent **A**) could correspond to aspartic acid and glycine, respectively. With eluent **B** the severe tailing of spot S is also compatible with partial decomposition of GlyAsp.

Attempts to produce the oxovanadium(IV) Schiff base complex of pyridoxal with GlyGly failed. The degree of formation of its complex in solution appears to be much lower than for the corresponding complex with salicylaldehyde, as no spot S was detected by TLC. The $\pi \rightarrow \pi^*$ transition at 380 nm, originating mainly in the azomethine chromophore, is clearly seen only if a 5–10-fold excess of GlyGly is used.

3.6. Magnetic moments

The magnetic susceptibilities of **2** and **3** were measured by the Faraday method between 5 and 296 K. For **2** the results (e.g. Fig. 1), particularly the μ_{eff} values, are very similar to those obtained for **1** (see above). This is consistent with a compound with spin 1/2 per formula unit, suggesting that **2** is monomeric. For all complexes the plot of $1/\chi_P$ versus T show slight deviations from linearity that can be accounted for

assuming a Curie–Weiss law and a temperature-independent paramagnetism (TIP) term: 2.3×10^{-4} for **2** and 7.8×10^{-4} for **3**. The Weiss constant θ is close to zero in both cases.

At room temperature the μ_{eff} values per V atom, obtained from the χ_P-TIP values, are 1.70 for **2** and 1.60 for **3**. For **3** this is slightly below the normal range (1.68–1.78) for oxovanadium(IV) complexes [28], but in the absence of further proof we assume a monomeric formulation for this compound.

3.7. Infrared spectra

The IR of **1**–**6** and **10** show narrow bands, but are quite complex. All compounds present a broad band in the 3000–3500 cm^{-1} region, which may be ascribed to hydrogen-bonded ν(O–H) and/or ν(N–H), and may also include ν(C–H). Except for **2** and **10**, corresponding to GlySar and AlaSar, respectively, relatively sharp bands emerge from this broad band at 3578 cm^{-1} (for **1**), possibly due to ν(O–H), and at 3230–3245 and 3090–3120 cm^{-1} (for **1**, **3**–**9**), possibly amide N–H absorption [29,30].

A medium/strong band at 1530–1560 cm^{-1}, always present, may originate from the vibration of the (Ph–)C—C(=N) bond [31] and typifies complexes derived from salicylaldehyde [3,5,31,32]. All complexes present very strong and broad bands centred around 1630–1670 cm^{-1}; these may correspond to ν(C=N) and ν_{as}(COO), but either ν(C=O_{amide}; O_{amide} coordinated) {or ν(–CON–; N_{amide} coordinated)} may also be present [33]. The bands are probably also broadened because of an overlap with aromatic ring-carbon stretching. In some cases, peaks at $\sim$1620–1660 cm^{-1} and 1585–1605 cm^{-1} emerge from the broad background. Bands at 1400–1420 cm^{-1} may be ascribed to ν_s(COO). The ν(V=O) band appears in the range 950–995 cm^{-1}.

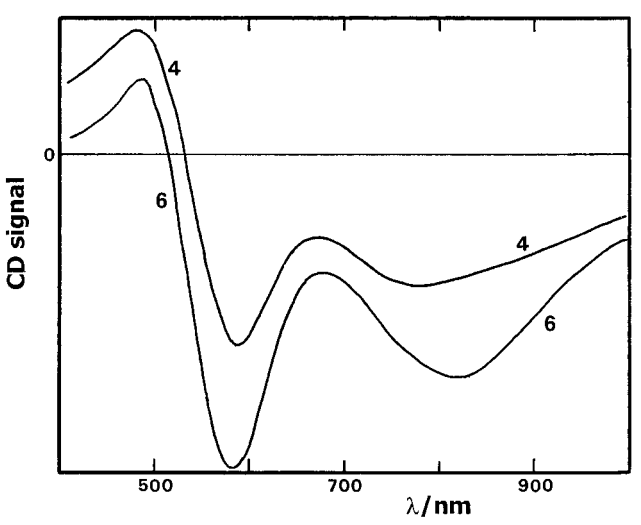


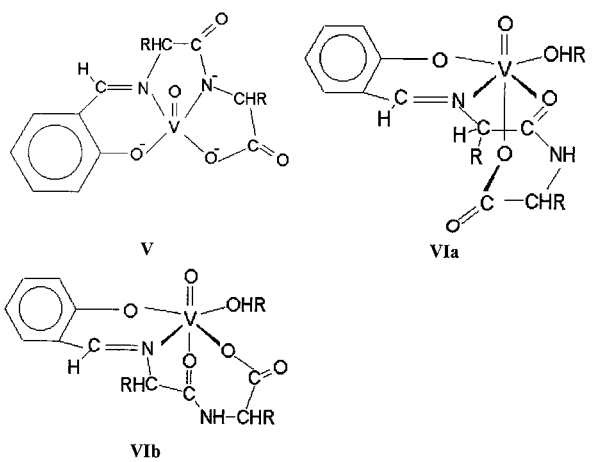
Fig. 2. Circular dichroism spectra of complexes **4** and **6** (solids dispersed in KBr disk).

The spectra of complexes **7**–**9** show some relatively broad bands; this again suggests that the compounds may be impure, or are a mixture of complexes, or are of polymeric nature.

3.8. ESR spectra

The ESR spectra may help to elucidate which groups coordinate in equatorial position in solution. However, the present Schiff base complexes are only very slightly soluble in methanol and the species present in solution may differ from the solid state. The ESR of **1** was discussed previously [16]. Two species were detected and designated by **A** and **B** ($A_{\|}$(**A**) < $A_{\|}$(**B**)), which could be consistent with structures **V** and **VI**, respectively.

The X-band ESR spectrum of a powdered frozen sample of **2** gave a broad signal with $g = 1.977$, within the range normally found for VO^{2+} compounds [34]. No signal was detected at $g \approx 4$. In the spectrum of a frozen dilute methanolic solution of **2**, only one species was detected and it could be simulated using the program EPRPOW [35] yielding: $A_{\|}$, $A_{\perp} = 172$, 62.8×10^{-4} cm^{-1} and $g_{\|}$, $g_{\perp} = 1.949$, 1.979. These results are as expected [3,5,36,37] for structures such as **VIa** or **VIb**.



3.9. Circular dichroism

Solids containing the dipeptides Gly-L-Ala, Gly-L-Asp, Gly-L-Ser, L-SerGly, D,L-Ala-D,L-Ala and GlyGly show little optical activity in the range 450–1000 nm: the signal is very low and noisy, with an apparent pattern of −, +, −. As the same type of spectrum was also obtained for **1** and **3** dispersed either in Nujol or in KBr disk, all these CD spectra nearly coincide with the base line. The CD spectrum of VO(sal-L-AlaSar) in KBr disk shows a pattern +, −, − for bands II, Ib and Ia, respectively [38], and the signal is

stronger. The CD of **4** and **6** (Fig. 2), containing L-Ala-L-Ala and L-AlaGly, is significantly stronger showing bands at ≈ 480 ($\Delta\varepsilon > 0$), ≈ 580 and ≈ 780 (**4**) or 820 nm (**6**) (both with $\Delta\varepsilon < 0$). Although such CD spectra give no reliable quantitative information, their overall intensity for these sal-aa-aa complexes is lower than that for VO(sal-L-Ala)(H_2O) [3].

In the solid-state coordination, geometries such as **V** must be ruled out as the negative charge for **V** is not compatible with the Na^+ analyses (see above). This is also not in agreement with the CD spectra: for **V**, a relatively strong signal, would be expected for ligands sal-Gly-aa (aa = L-Ala, L-Ser, L-Asp), and this is not the case. The coordination geometry of the present Schiff base complexes therefore differs from that suggested for the Cu(II) complexes Na[Cu(sal-GlyGly)]·$6H_2O$ [39,40], where N_{amide} is expected to coordinate.

The results for **2**–**10** discussed here and for **1** [16], particularly the μ_{eff} values for **1** and **2**, are in agreement with a monomeric formulation for these Schiff base complexes. For steric reasons one of these four donor atoms must be coordinated axially, but it is not clear if this is O_{amide} or $O_{carboxylate}$. Assuming the vicinal effect [41] is the determining factor for the CD signal, one would expect that equatorial coordination of COO^- in these VO(sal-Gly-L-aa) complexes would correspond to a relatively strong CD signal. This is not the case here (however, one should note that compounds **6**–**9** were not properly characterised). For coordination geometry such as **VIb**, which assumes equatorial coordination of COO^-, one would expect a relatively strong CD signal for **4** and **7**. In fact, **7** shows no optical activity and the pattern and intensity of the CD signal is similar for **4** and **6**, indicating that the N-terminal residue is the relevant one in determining the CD signal. This suggests O_{amide} coordinates equatorially, **VIa** being the relevant structure for this set of Schiff base complexes.

Compound **5**, containing SerGly, shows no optical activity in the visible range. As it took 2 days to precipitate, the L-Ser residue may have racemised, as observed with L-serine [19] and asparagine [42] in similar conditions. Racemisation at the N-terminal residue is a known process in, e.g. Cu^{II}(sal-aa-aa) complexes as well as specific activation in the N-terminal residue of GlyGly and aldol-type condensations with formaldehyde and acetaldehyde to yield SerGly and ThrGly, respectively [40,42].

We describe here the formation of seryl- and threonylglycine by reaction of VO(salGlyGly) with HCHO and CH_3CHO, respectively. The Schiff base complexes with Co(III), Ni(II), [43] and Cu(II) [40] show activation in the N-terminal residue. The presence of the metal ion contributes to the formation of the Schiff base and may lead to selective bond cleavage/formation and at least in the experimental conditions described above (procedures 1 and 2) the reaction does not proceed in the absence of the metal ion. The mechanism presumably involves intermediate oxazolidine-type complexes [44–47]. In fact, in a few cases such complexes have been isolated and characterised by X-ray diffraction. In our systems no characterisable solids were obtained from the reaction mixtures that could correspond to the product peptide Schiff base complexes.

In the present VO(sal-dipeptide) complexes the N_{amide} is not coordinated, as expected for the Schiff base-dipeptide complexes of Co(III), Cu(II) and Ni(II), but the selective activation in the N-terminal residue of GlyGly again indicates that the coordination geometry corresponds to **VIa** and not to **VIb**. In fact, it has been proposed for reactions catalysed both in enzymes [48–50] and in *N*-pyridoxylideneamino acidato complexes that the bond to be broken should be the one that achieves maximal orbital overlap with the π system of the ligand, i.e. it should be perpendicular to the plane of the extended conjugated system of the ligand. In the present vanadium Schiff base complexes, the fastest reactions appear to be racemisations and aldol-type condensations, and the requisite geometry is available only in the case of **VIa**.

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