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COMPLEX FORMATION BETWEEN UNSATURATED α-AMINOACIDS AND SILVER(I) AND SOME DIVALENT TRANSITION METAL IONS

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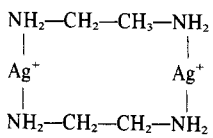
Abstract—A series of aminoacids of general formula $CH_2{:}CH(CH_2)_nCH(NH_2)CO_2H$ has been synthesised and the formation constant of their complexes with H^+, Cu^{2+}, Ni^{2+}, Zn^{2+}, Co^{2+}, Cd^{2+} and Ag^+ measured at 25° and I = 0·10 M (KNO_3). The olefinic bond does not appear to take part in bonding to any of the acceptors with the exception of Ag^+ when it chelates extensively when $n = 1$ and decreasingly when $n = 2$ and 3. The high stability of the resulting "$5\frac{1}{2}$ membered" chelate ring demonstrates the readiness of Ag^+ to accept non-linear co-ordination with soft acceptors.

INTRODUCTION

AS AN acceptor, silver(I) behaves in a markedly different way to first row transition metal ions. As a result silver ions are generally classified as "soft" or class (b) in character. This difference in behaviour is apparent in the preference of silver for co-ordination to the heavier donor atoms of groups VB and VIB and with the olefinic bond. Various explanations have been presented to account for this behaviour. Since silver(I) has a low cationic charge with filled *d* orbitals ($4d^{10}$) and small size it presents orbitals of suitable size and symmetry for back π-bonding and is itself strongly polarizing towards larger polarizable donors. This latter property appears to be the more important factor in the complex chemistry of silver(I). When coordinated to many ligands, especially the "harder" donors such as nitrogen, silver appears to prefer a linear (*sp*) stereochemistry with a co-ordination number of two. However with softer donors a co-ordination number of four (sp^3) or some intermediate value (1 or 3) is often preferred[1].

This contrast shows itself clearly when considering bidentate ligands which tend to force a particular stereochemistry on the metal ion. For example, with 1,2-diaminoethane (en) the first row transition elements from simple stepwise complexes of the type $M(en)_x^{2+}$ with the ligand forming a stable 5-membered puckered chelate ring. With silver, however, polynuclear complex formation takes place giving species such as:



These species allow silver to retain a linear stereochemistry[2, 3]. If now the donor centres in chelating ligands are changed to "soft" centres the stereochemistry readily changes to, presumably, tetrahedral, e.g. with ligands such as:

$$R{\cdot}Se{\cdot}(CH_2)_nCH = CH_2$$

when the Se and olefinic bonds are donor centres[4, 5]. It is found that a maximum stability is found when $n = 2$, to give a "$5\frac{1}{2}$-membered" chelate ring, the stability dropping rapidly when *n* is reduced to 1 and more slowly when increased to 3 or 4.

We wish to report the results of a study of the Ag^+, proton and divalent transition metal ion complexes of a series of α-aminoacids with side chains containing olefinic bonds able to chelate with the metal ions in co-operation with the aminoacid nitrogen atoms. The ligands studied were a series of *C*-substituted glycines of general formula:

$$H_2C = CH{\cdot}(CH_2)_n{\cdot}CH(NH_2)CO_2H$$
(i.e. $R{\cdot}CH(NH_2)CO_2H$)

where $n = 1$, 2, 3. Chelate rings which would be "$5\frac{1}{2}$–$7\frac{1}{2}$-membered" are therefore possible. For comparison ligands containing similar but fully saturated side chains were also prepared and their complexes studied. In addition methionine was studied since this ligand contains a heavy donor atom (sulphur) in place of the olefinic bond.

The only comparable work reported was by Da Silva and Dias[6] who studied some complexes of allylglycine ($n = 1$).

EXPERIMENTAL

Preparation of ligands

The *C*-substituted aminoacids were prepared via the intermediate ethylacetamidocyanoacetates following the procedure described by Albertson[7], given in outline below. The monosodium derivative of ethylacetamidocyanoacetate(I) was refluxed with 10–15% excess of alkenylhalide (*R*Br) to give (II). This was hydrolysed with hot alkali to give the dicarboxylate(III) which decarboxylates spontaneously to IV. Further hydrolysis by refluxing with 10% NaOH for 18 hr removed the acyl group to give the sodium salt of the aminoacid(V). The free aminoacid was

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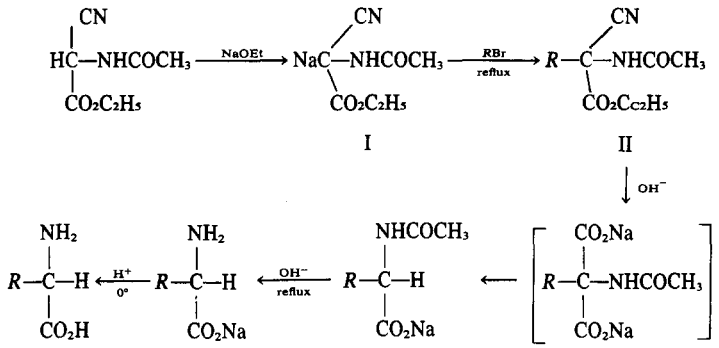

isolated by careful acidification at 0° when the acid precipitated. Products were purified by recrystallization from water/ethanol mixtures. Analyses and melting points are given in Table 1. Complex formation constants for the proton and metals other than Ag^+ were calculated from potentiometric titration curves by the normal methods[3, 8]. The pH meter was calibrated in terms of hydrogen ion concentrations and titrations were carried out at 25° with an ionic strength of 0·1 M (KNO_3). Titrations in the presence of silver ions were followed with a silver/silver chloride indicator electrode in addition to a glass electrode[3]. When the Ag:L ratio was 1:1 a white precipitate often formed which dissolved slowly, suggesting the presence of hydroxy complexes and, possibly, polynuclear species such as Ag_2L_2. As a result the apparent constants calculated from such titration curves often showed definite trends which could not be removed by including more species in the equilibria. With the exception of methionine titrations with an Ag:L ratio of 1:2 did not produce the same problems and generally gave consistent values for β_{AgL} and β_{AgL_2} (β_1 and β_2) over a considerable part of the curve. Experimental values for β_1 and β_2 and β_{Ag_2HL} are given in Table 2 but values for species such as Ag_2L_2 and of methionine are not included since, although there was every indication that such species existed in solution, the precision of the calculated constant was low. As a result of these complications the precision of the constants quoted is less than may be expected.

RESULTS AND DISCUSSION

Calculated proton and metal complex formation constants are given in Tables 2 and 3 respectively, together with those for comparable ligands.

Table 2. Proton complex formation constants for the amino acids $R{\cdot}CH(NH_2)CO_2H$ at 25° and I = 0·10 M. Standard deviations (σ values) in parentheses

Substituent R	log β_{HL}	log β_{H_2L}
H(glycine)	9·582(5)	11·904(7)
$CH_2{:}CHCH_2$	9·275(5)	11·406(8)
	9·25*	11·70*
$CH_2{:}CH(CH_2)_2$	9·434(4)	11·687(8)
$CH_2{:}CH(CH_2)_3$	9·515(4)	11·857(9)
$CH_3(CH_2)_2$(norvaline)	9·640(3)	11·930(6)
$CH_3(CH_2)_3$(norleucine)	9·671(4)	12·011(9)
$CH_3S(CH_2)_2$(methionine)	9·052(2)	11·203(6)
	9·04†	

*Ref. [6].
†Ref. [9].

Proton complex formation constants show the trends expected from the inductive effects of the substituents, expressed quantitatively by their Taft parameters[10]. The olefinic bonds are electron attracting while the methylene and methyl groups are electron repelling. Hence, as the double bond moves further from the donor centres, the proton complexes become more stable. This effect is more noticeable with the protonation of the amine group (log β_{HL}) than the carboxyl group (log K_2) since the amine nitrogen is closer to the substituent. The insertion of a CH_2 group between the double bond and the

Table 1

	M.P. (°C)	C% found	C% reqd.	H% found	H% reqd.	N% found	N% reqd.	overall yield %
Substituted ethyl-acetamidocyanoacetates								
$R = CH_2{:}CHCH_2$	88	56·9	57·1	6·6	6·7	13·1	13·3	80
$Ch_2{:}CH(CH_2)_2$	93	59·2	58·9	7·3	7·2	12·2	12·5	78
$CH_2{:}CH(CH_2)_3$	99	60·7	60·5	7·7	7·6	11·6	11·7	73
$CH_3(CH_2)_2$	118	56·2	56·6	7·4	7·5	13·1	13·2	72
$CH_3(CH_2)_3$	89	58·7	58·4	8·0	8·0	12·2	12·4	80
Substituted aminoacids								
$R = CH_2{:}CHCH_2$	250d	52·0	52·2	8·0	7·8	12·1	12·1	55
$CH_2{:}CH(CH_2)_2$	244d	55·8	55·8	8·6	8·6	10·8	10·8	50
$CH_2{:}CH(CH_2)_3$	238d	58·6	58·6	9·1	9·1	10·0	9·8	37
$CH_3(CH_2)_2$	295d	51·4	51·4	9·5	9·4	11·7	12·0	56
$CH_3(CH_2)_3$	288d	54·7	54·9	10·1	9·9	10·8	10·7	52

Table 3. Metal complex formation constants for the amino acids $R \cdot CH(NH_2)CO_2H$ at 25° and I = 0·10 M. (Standard deviations (σ values) <0·01 unless stated)

Substituent *R*	Cu^{2+}		Ni^{2+}		Zn^{2+}		Co^{2+}		Cd^{2+}		Ag^{+}		
	log β_1	log β_2	log β_1	log β_2	log β_1	log β_2	log β_1	log β_2	log β_1	log β_2	log β_1	log β_2	log β_{AgHL}
H	8·21	15·09	5·75(2)	10·65	4·93	9·26	4·71	8·76	4·26	8·08(2)	3·01	6·22(3)	1·40(5)
$CH_2:CHCH_2$	8·00	14·63	5·31(3)	9·89	4·50(2)	8·51(2)	4·21	7·65	3·77(2)	7·13	4·22	7·38(2)	1·20(3)
$CH_2:CHCH_2$ (ref. [6])	7·82	14·36	5·21	9·67	4·63	8·86	4·03	7·87	3·84	7·57	4·30	7·90	
$CH_2:CH(CH_2)_2$	8·09	14·90	5·38	9·89	4·49	8·60	4·24(2)	7·75	3·76(3)	7·16	3·81	6·74	1·42
$CH_2:CH(CH_2)_3$	8·09	14·91(3)	5·32(2)	9·72	4·45	8·63(2)	4·22(2)	7·68	3·75	7·13	3·34	6·41(3)	1·73
$CH_3(CH_2)_2$(norvaline)	8·12	14·94	5·27(2)	9·65	4·42(2)	8·52(3)	4·15	7·62	3·73	7·03	3·08(2)	6·27(2)	?
$CH_3(CH_2)_3$(norleucine)	8·18	14·88	5·40(2)	10·01	4·59(2)	8·93(3)	8·26	7·79	3·86	7·33	3·21(5)	6·71(3)	?
$(\pm)CH_2S(CH_2)_2$(methionine)	7·85	14·51	5·34	9·90	4·39(2)	8·38	4·16	7·60	3·70(2)	6·97			
$(\pm)CH_3S(CH_2)_2$ (ref. [9])	7·87	14·72	5·19	9·84	4·37	8·33	4·12	7·56	3·67	7·03			

nitrogen atom attenuates the inductive effect of the double bond by a factor of 0·56, close to the value of 0·50 reported by Barlin and Perrin[10]. Methionine protons are the most acidic as a result of the large negative inductive effect of the –SMe group.

With Cu^{2+} all ligands produced dark blue solutions but the solubility of the *bis*-complexes decreased markedly as the saturated alkyl chain increased in length. Complexes with unsaturated ligands were more soluble than those with saturated ones. Assuming solubility was proportional to the degree of formation ($\bar{n}$) at which precipitation commenced for a given concentration the solubility order for the copper complexes was found to be:

glycine > allylglycine > norvaline > but-1-enylglycine > pent-1-enylglycine > norleucine.

With Ni^{2+} equilibrium was reached somewhat slowly, possibly due to the rapid precipitation of $Ni(OH)_2$ followed by slow dissolution. Above $\bar{n} = 1{\cdot}3$ there was some evidence of the formation of *tris*-complexes but, since the maximum M:L ratio used was 1:2, the formation constants calculated were not sufficiently reliable. No reliable evidence was found for MHL^{2+} species in the pH range used.

For metal ions other than Ag^+ the constants calculated fall in the order expected and close to previously reported values for ligands studied elsewhere. There is no indication of bond formation between the metal ions and the olefinic bond. A quantitative comparison of values for $\log \beta_{H_2L} - \log \beta_1$ and $\log \beta_{H_2L} - \log \beta_2$ shows that the affinity of the ligands for protons and divalent metal ions is comparable, whether the ligand contains an olefinic bond or not. Such small differences as there are can be explained in terms of steric factors and the fact that formation of a metal complex involves chelate formation of the –N–M–O– type while the proton complexes involve the formation of separate –N–H and –O–H bonds.

Methionine is a rather different ligand. While the racemic forms of other ligands were used, methionine was available as the optically pure isomers. These were, therefore, titrated separately and the racemic mixture prepared by mixing solutions of the pure isomers in equal quantities. No conclusive evidence of stereoselectivity was found, the differences between $\beta_{M(+L)_2}$, $\beta_{M(-L)_2}$ and $\beta_{M(+L)(-L)}$ being, in all cases, within 3σ. The results shown in Table 3 suggest only limited bonding between the metal ions and the sulphur atom. Comparing results for methionine with those for norleucine, the proton complexes of methionine ($\log \beta_{H_2L}$) are weaker than those of norleucine by 0·81 log units while the metal complexes are only marginally weaker (e.g. $\Delta \log \beta_{CuL} = 0{\cdot}33$). An X-ray diffraction study of $Cu(methionine)_2$ gave no evidence of Cu–S bonding[11] in the crystalline state.

In contrast to the divalent metal ions, Ag^+ gave a definite indication of metal-olefin bonding. Polynuclear complex formation and insolubility prevented reliable constants being calculated for methionine–silver complexes. This, in itself, suggests extensive silver–sulphur bonding.

With nitrogen and oxygen as donor atoms silver(I) shows a marked preference for linear co-ordination. With glycine, crystal structure evidence shows that polymer formation is preferred to chelate formation in the crystal. For instance, silver *mono*glycine contains silver ions bound to the carboxyl group of one glycine and the amino-nitrogen of another with a bond angle of 177° and the hemihydrate contains alternate O–Ag–O and N–Ag–N linkages[12]. Hence the precipitation found in titrations of 1:1 ratios of metal to ligand is readily explained. If the olefinic bond in the ligands studied were able to chelate with the nitrogen donor to the silver ion (as it can with sulphur or selenium) this tendency towards polymerisation should decrease and the formation of *mono* and *bis* complexes should take place in a way similar to that with the divalent metal ions. This was, in fact, found to be the case. The silver complexes were, in general, more stable than the analogous complexes with saturated substituents and precipitation in 1:1 mixtures did not take place. If the results for the unsaturated ligands are compared to those for the fully saturated valine the following figures are obtained:

substituent	$\Delta \log \beta_1$	$\Delta \log \beta_2$
$CH_2{:}CHCH$	1·14	1·11
$CH_2{:}CH(CH_2)_2$	0·73	0·47
$CH_2{:}CH(CH_2)_3$	0·26	0·14

Clearly the most effective chelate formation takes place when the chelate ring is "$5\frac{1}{2}$-membered", decreasing as the ring increases to $6\frac{1}{2}$ and $7\frac{1}{2}$-members, suggesting tetrahedral (or similar) co-ordination. This enhancement of stability on formation of $5\frac{1}{2}$–$7\frac{1}{2}$ membered chelate rings involving olefin co-ordination is very close to that found with analogous ligands containing sulphur and selenium donor atoms[4, 5].

The contrast in behaviour between Ag^+ and the divalent metal ions is clear from a graph in which formation constants of allyl- and butenylglycine complexes are compared to those of norvaline. This contrast is also apparent when the relative magnitude of the stepwise constants, K_1 and K_2 (i.e. β_1 and β_2/β_1) are considered. With the divalent metal ions the ratio K_1/K_2 is always greater than one (i.e. $\log K_1 - \log K_2$ is positive) as a result of statistical and electrostatic considerations. With Ag^+ the reverse is generally the case, i.e. $\log K_1 - \log K_2$ is negative. This is generally explained as resulting from the preference of Ag^+ for linear co-ordination to hard donor centres such as nitrogen. Such a situation is found with the saturated ligands studied here, i.e.

	$\log K_1 - \log K_2$
glycine	−0·20
norvaline	−0·11
norleucine	−0·29
allylglycine	1·06
but-1-enylglycine	0·18
pent-1-enylglycine	0·17

The different behaviour of the ligands able to chelate through the olefinic bond is immediately obvious, particularly with allylglycine where chelation is most extensive. These results suggest that in the *bis*-complexes the silver ion is indeed tetra-coordinated (presumably tetrahedrally) whereas its co-ordination number is only two in the saturated *bis*-complexes (bonding being, presumably, through the nitrogen atoms). An alternative explanation for the fact that $K_1 > K_2$ with unsaturated ligands could be that, for the second ligand to co-ordinate as a mono-dentate ligand, the metal–olefin bond to the first ligand must be broken to give a *bis*-complex with a co-ordination number of two. This is precluded by the fact that the log β_2 value for allylglycine is considerably larger than for norvaline (by 1·1 log units).

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