Stereoselectivity in Bis(α-amino-acid)copper(II) Complexes: Stability Constants from Circular Dichroism and Electronic Spectra

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The circular-dichroism spectra of aqueous solutions containing cupric ions, *N*-benzyl-L-proline, and either L- or D-valine or L- or D-proline, have been measured and used to calculate the formation constants for the mixed complexes [Cu(*N*-benzyl-L-proline)(D-valine)], [Cu(*N*-benzyl-L-proline)(L-proline)], and [Cu(*N*-benzyl-L-proline)(D-proline)]. The results indicate that considerable stereoselectivity occurs in the formation of these complexes, and this is confirmed by measurements of electronic absorption spectra. Careful measurements of the electronic absorption spectrum of [Cu(valine)$_2$] and [Cu(proline)$_2$] indicate that some stereoselectivity occurs even with these complexes, resulting in differences between the spectra of optically active and *meso*-complexes.

X-RAY structural determinations show that five-membered chelate rings in complexes of α-amino-acids are nearly planar. Thus unlike the complexes of 1,2-diamines in which the non-planar chelate ring causes considerable stereoselectivity [1] especially in octahedral tris-complexes, with α-amino-acids there is no interaction between the two chelate rings in the square-planar bis(amino-acid) complexes. The α-alkyl groups of α-amino-acids in these bis-complexes are too far removed from each other to be able to interact. Therefore there should be no stereoselectivity ‡ in complexes of this type, *i.e.* the properties of [Cu(L-α)(L-α)], [Cu(L-α)(D-α)], and [Cu(D-α)(D-α)] should be identical.

In good agreement with these predictions the electronic spectra and the stability constants of the copper(II) bis-complexes with bifunctional α-amino-acids such as alanine,[2-4] valine,[3] proline,[3] phenylalanine,[4] and those with trifunctional amino acids [5] such as asparagine, aspartic acid, glutamine, and glutamine acid have been found to be independent of the steric configuration of the ligands. The difference between the formation constants observed [6] for the mixed copper(II) complexes of L-proline with L- and D-valine (log $\beta = 16{\cdot}86 \pm 0{\cdot}09$ and $17{\cdot}00 \pm 0{\cdot}20$ respectively) does not exceed the error of the experiment.

Although the original theory [1] predicts a much higher stereoselectivity for bis-complexes of 1,2-diamines than for bis(amino-acid) complexes, more recent calculations [7] predicted that owing to the flexibility of the conformations of the chelate rings no stereoselectivity should occur in square-planar bis-(1,2-diamine) complexes. This has been confirmed by experiment.[8]

On the other hand, using ligand chromatography as a novel method for investigation of the mixed complexes,[9] we could easily observe stereoselectivity in a large number of kinetically labile complexes. For instance an optically active ion-exchange resin, prepared by the reaction of L-proline with chloromethylated polystyrene, displays in the presence of Cu^{II} ions a considerably higher affinity for D-amino-acids as compared with the L-enantiomers.[9]

The observed stereoselectivity in the chromatographic experiments could arise from one of several causes. (*a*) The influence of the polystyrene support. (*b*) The effect of the *N*-benzyl group on the proline causing it to behave in a manner different to the other amino-acid systems. (*c*) The enhancement, by the ligand chromatographic method, of a stereoselectivity which though present in normal Cu(amino-acid)$_2$ complexes, is too small to be detected by normal spectroscopic techniques.

To investigate these possibilities it is necessary to study mixed copper(II) bis-(amino-acid) complexes with *N*-benzyl-L-proline as one of the ligands.

By potentiometric titration we have shown [10] that the Cu(L-BzPro)(D-BzPro) complex is more stable than the Cu(L-BzPro)$_2$ complex (log β $13{\cdot}53 \pm 0{\cdot}07$ and $12{\cdot}39 \pm 0{\cdot}10$ respectively). As this is in contrast with previous results with copper(II) complexes of other α-amino-acids, in the present work we report results obtained by spectroscopic and circular-dichroism measurements on Cu-complexes containing *N*-benzylproline, valine, and proline.

EXPERIMENTAL

Circular-dichroism spectra were recorded on a Roussel–Jouan ' Dichrograph ' model B. As the wavelength range of particular importance in this work was near the photomultiplier changeover at 600 nm, the region between 600 and 550 nm was usually recorded using each photomultiplier. Electronic absorption spectra were recorded on a

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‡ By the term ' stereoselectivity ' we mean the difference in the interaction of two molecules which are optical enantiomers with some third chiral molecule. This difference can be of kinetic origin—*i.e.* result in the difference in the rate of interaction of this chiral molecule with the two enantiomers—or of thermodynamic origin as well, *i.e.* result in the difference in the stability or other properties (including spectroscopic properties) of the two labile diastereoisomeric pairs formed.

[1] E. J. Corey and J. C. Bailar, *J. Amer. Chem. Soc.*, 1959, **81**, 2620.

[2] R. D. Gillard, H. M. Irving, R. Parkins, N. C. Payne, and L. D. Pettit, *Chem. Comm.*, 1965, 81.

[3] R. D. Gillard, H. M. Irving, R. Parkins, N. C. Payne, and L. D. Pettit, *J. Chem. Soc.* (*A*), 1966, 1159.

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[5] J. H. Ritsma, G. A. Wiegers, and F. Jellinek, *Rec. Trav. chim.*, 1965, **84**, 1577.

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[7] J. R. Gollogly and C. J. Hawkins, *Inorg. Chem.*, 1969, **8**, 1168; 1970, **9**, 576.

[8] A. T. Advani, D. S. Barnes, and L. D. Pettit, *J. Chem. Soc.* (*A*), 1970, 2691.

[9] V. A. Davankov and S. V. Rogozhin, *Doklady Akad. Nauk S.S.S.R.*, 1970, **193**, 94; *J. Chromatog.*, 1971, **60**, 280.

[10] V. A. Davankov, S. V. Rogozhin, and A. A. Kurganov, *Izvest. Acad. Nauk S.S.S.R. Ser. khim.*, 1971, 204.

Hitachi–Perkin-Elmer model 124 spectrophotometer in a 1-cm cell.

All measurements were made at 25°. The importance of a good thermostat for both the circular-dichroism and absorption spectral measurements was demonstrated by separate experiments in which the circular-dichroism spectra and absorption spectra were measured as a function of temperature.

The total copper concentration in all the solutions investigated was 0·02M. The total ligand concentration of 0·10M provides a 2·5-fold excess in all the systems. The presence of an excess of free ligand is necessary to suppress the dissociation of the bis-complexes and the formation of the monoamino-acid-bis-aquo-complexes, which unlike the free ligands, have some absorption and circular-dichroism bands in the visible region which was studied. Due to the partial dissociation the solutions prepared by dissolving the solid complexes in water may have extinction coefficients differing by up to 20% from the true values, depending on the concentration of the solution and the stability of the complex.

The pH of the solution requires special attention as well. At low pH, depending on the p*K* of the amino-acid, the concentration of the anionic form of the ligand may be insufficient for complete formation of the bis(amino-acid)-copper(II) complex. At high pH, depending on the stability of the bis(amino-acid) complex, mixed hydroxy-complexes may also be formed. The pH value of 9·5 used in all the solutions studied here was determined by the least stable of the complexes, [Cu(L-BzPro)$_2$]. Its solutions display maximal and constant ε and $\Delta\varepsilon$ values only in the region of pH 9·1—9·9. Therefore all the starting ligand solutions contained a certain amount of NaOH, so that on addition of 0·5 ml of a 0·1M-Cu(NO$_3$)$_2$ solution to 2 ml of the 0·125M-ligand solution the pH of the resulting 0·02M-complex solution was *ca.* 9·6—9·9. The final solutions were adjusted to pH 9·5 by addition of 4M-HNO$_3$ by means of a Radiometer automatic titrator, model 11. The dilution never exceeded 0·4% and was not taken into account in calculations.

A series of mixtures containing 0·5 ml of 0·1M-Cu(NO$_3$)$_2$, $(2{\cdot}0 - x)$ ml 0·125M-L-BzPro (B), and x ml of 0·125M-amino-acid (A) solutions were prepared. At pH 9·5 the equilibrium mixture consists of [CuB$_2$], [CuBA], and [CuA$_2$] species in different proportions but with a constant total concentration of 0·02M. Circular-dichroism and electronic spectra of each mixture were measured at 25°. In several cases the results allowed calculation of the equilibrium composition ($[\mathrm{MB_2}] + [\mathrm{MAB}] + [\mathrm{MA_2}] = 0{\cdot}02$) of the mixture and thence the stability constants of the mixed [CuBA] species. The Table lists the data obtained in the system containing *N*-benzyl-L-proline and D-valine as ligands (B and A). Due to the favourable shape of circular-dichroism spectra of all the three species the calculations in this particular system were more accurate than in other systems.

RESULTS AND DISCUSSION

In a solution containing metal ions M^{2+} and a sufficient excess of anions of two different amino-acids (A$^-$ and B$^-$) there exists an equilibrium between three different bis-amino-acid complexes:

$$\mathrm{MA_2} + \mathrm{MB_2} \rightleftharpoons 2\mathrm{MAB} \qquad K = \frac{[\mathrm{MAB}]^2}{[\mathrm{MA_2}][\mathrm{MB_2}]} \qquad (1)$$

The equilibrium constant *K* may be expressed *via* the formation constants of the three species (the charges are omitted):

$$\mathrm{M} + 2\mathrm{A} \rightleftharpoons \mathrm{MA_2} \qquad \beta_{\mathrm{MA_2}} = \frac{[\mathrm{MA_2}]}{[\mathrm{M}][\mathrm{A}]^2}$$

$$\mathrm{M} + 2\mathrm{B} \rightleftharpoons \mathrm{MB_2} \qquad \beta_{\mathrm{MB_2}} = \frac{[\mathrm{MB_2}]}{[\mathrm{M}][\mathrm{B}]^2}$$

$$\mathrm{M} + \mathrm{A} + \mathrm{B} \rightleftharpoons \mathrm{MAB} \qquad \beta_{\mathrm{MAB}} = \frac{[\mathrm{MAB}]}{[\mathrm{M}][\mathrm{A}][\mathrm{B}]}$$

$$K = \frac{(\beta_{\mathrm{MAB}})^2}{\beta_{\mathrm{MA_2}} \cdot \beta_{\mathrm{MB_2}}}$$

When the position of the disproportionation equilibrium (1) and the formation constants $\beta_{\mathrm{MA_2}}$ and $\beta_{\mathrm{MB_2}}$ of symmetric species are known, the formation constant of the mixed [MAB] complex can be calculated:

$$\beta_{\mathrm{MAB}} = \sqrt{K} \cdot \beta_{\mathrm{MA_2}} \cdot \beta_{\mathrm{MB_2}} \qquad (2)$$

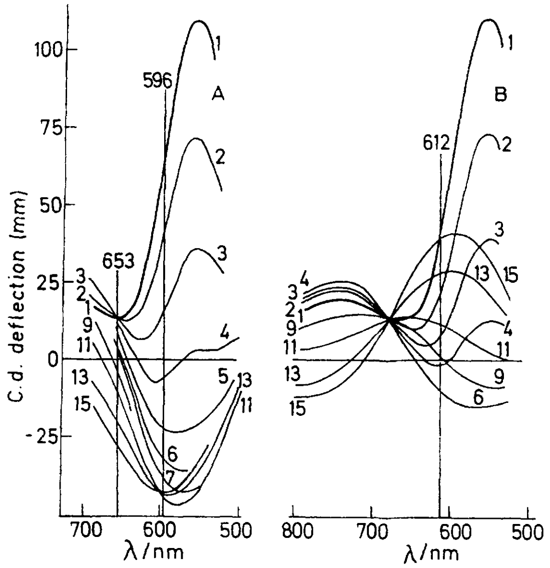

FIGURE 1 Circular-dichroism curves of copper(II) bis-complexes. A, with L-benzylproline (1), D-valine (15), and mixtures of them (2)—(13); B, with L-benzylproline (1), L-valine (15), and mixtures of them (2)—(13)

The N-*Benzyl-*L-*proline–valine System*.—To study the equilibrium (1) we have used circular-dichroism measurements. A series of solutions was investigated, where the mol fraction of the ligand A gradually increases from 0 to 1. Figure 1A represents the change of circular dichroism in a system containing cupric ions, *N*-benzyl-L-proline (ligand B) and D-valine (ligand A). The set of curves displays two crossover-points at 653 and 596 nm. This means that the mixed MAB complex has at 653 nm the same molar circular-dichroic extinction coefficient ($\Delta\varepsilon$) as the MB$_2$ complex, and at 596 nm the same value of $\Delta\varepsilon$ as the MA$_2$ complex. More accurate measurements of circular dichroism of solutions at 653 and 596 nm make it possible to calculate the equilibrium composition of all the mixtures. All the data obtained are presented in the Table. Due to the favourable shape of c.d. spectra of all the three species (relatively high values of $\Delta\varepsilon$ at 653 and 596 nm) the equilibrium constant $K = 29{\cdot}6 \pm 2{\cdot}2$ in this particular system can be calculated more accurately than in the other systems studied in this work. In the absence of any stereoselectivity, statistical effects would give a value of $K = 4$. Thus considerable stereoselectivity is present in this system. Figure 2 shows the quantities of the [Cu(L-BzPro)$_2$], [Cu(L-BzPro)(D-Val)], and [Cu(D-Val)$_2$] species present in the system as the ratio of the starting concentrations of L-BzPro to D-Val decreases.

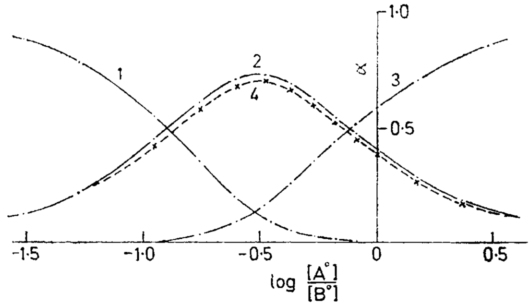

FIGURE 2 Mole-fraction composition of the mixtures of complexes at equilibrium as a function of the initial concentration of L-benzylproline, [B°] and valine [A°]. (1) [Cu(L-BzPro)$_2$]; (2) [Cu(L-BzPro)(D-Val)]; (3) [Cu(D-Val)$_2$]; (4) [Cu(L-BzPro)(L-Val)]

Circular-dichroism measurements in a system containing L-benzylproline, D-valine, and Cu^{2+} pH 9·5, 25°

Soln. no.	0·125M-L-BzPro (ml) B°	0·1M-Cu(NO$_3$)$_2$ (ml)	0·125M-D-Val (ml) A°	log $\frac{[A^\circ]}{[B^\circ]}$	C.d. deflection 654 nm (mm)	C.d. deflection 594 nm (mm)	$\alpha_{\mathrm{CuA_2}}$	$\alpha_{\mathrm{CuB_2}}$	α_{CuBA}	K	
(1)	2·0	0·5	0·0	−∞	−14·5	−67·5	0	1	0		
(2)	1·9	0·5	0·1	−1·279	−14·5	−43·0	0	0·778	0·222		
(3)	1·8	0·5	0·2	−0·954	−14·5	−17·8	0	0·550	0·450		
(4)	1·7	0·5	0·3	−0·753	−13·0	4·0	0·037	0·353	0·610	28·1	29·6 ± 2·2
(5)	1·6	0·5	0·4	−0·602	−10·8	20·7	0·092	0·202	0·706	26·6	
(6)	1·5	0·5	0·5	−0·477	−8·0	30·5	0·163	0·113	0·724	28·6	
(7)	1·4	0·5	0·6	−0·368	−4·0	37·0	0·262	0·054	0·684	33·0	
(8)	1·3	0·5	0·7	−0·269	0·0	39·5	0·363	0·032	0·605	31·6	
(9)	1·2	0·5	0·8	−0·176	3·0	41·0	0·437	0·018	0·545	37·6	
(10)	1·1	0·5	0·9	−0·087	6·0	41·5	0·513	0·014	0·473	31·2	
(11)	1·0	0·5	1·0	0	9·0	42·0	0·588	0·009	0·403	30·8	
(12)	0·8	0·5	1·2	0·176	14·0	42·5	0·712	0·005	0·283	25·0	
(13)	0·5	0·5	1·5	0·477	19·8	43·0	0·857	0	0·143		
(14)	0·2	0·5	1·8	0·955	23·0	43·0	0·938	0	0·062		
(15)	0·0	0·5	2·0	∞	25·5	43·0	1	0	0		

Using published values of the formation constants of bis(L-benzylprolinato)copper,[10] log $\beta_{\mathrm{MB}_2} = 12{\cdot}39 \pm 0{\cdot}10$, and of bis(D-valinato)copper,[3] log $\beta_{\mathrm{MA}_2} = 15{\cdot}18$, and the measured values of the equilibrium constant $K = 29{\cdot}6 \pm 2{\cdot}2$, we can calculate from equation (2) the formation constant * of the mixed [Cu(L-BzPro)(D-Val)] complex, log $\beta_{\mathrm{MAB}} = 14{\cdot}52 \pm 0{\cdot}20$.

In the system containing cupric ions, *N*-benzyl-L-proline, and L-valine the shapes of the c.d. curves are much less favourable. As shown in Figure 1B there is only one crossover-point in the c.d. curves of all three species, in the region of 680 nm. This does not permit accurate calculations of the equilibrium constant *K*. Nevertheless using the fact that the values of $\Delta\varepsilon$ of [Cu(L-BzPro)$_2$] and of [Cu(L-Val)$_2$] at 612 nm are equal (Figure 1B, curves 1 and 15), we can compare this system with the similar one containing D-valine instead of L-valine. Let us assume that the mole fraction of [Cu(L-BzPro)(L-Val)] in the solution with a ratio of *N*-benzyl-L-proline to L-valine of 1·9 : 0·1 (*cf.* solution 2 in the Table for D-valine) equals that of [Cu(L-BzPro)(D-Val)] (0·222) in the analogous solution. This allows us to calculate from the curves 1, 2, and 15 in Figure 1B the value of $\Delta\varepsilon$ for [Cu(L-BzPro)(L-Val)] at 612 nm as 0·216. Using this value and measuring more accurate values for $\Delta\varepsilon$ of all the mixtures (the initial compositions of them being equal to those shown for D-valine in the the Table) at 612 nm we can calculate the mole fraction α_{MAB} of [Cu(L-BzPro)(L-Val)] in all the mixtures (Figure 2). The mole fraction of [Cu(L-BzPro)(L-Val)] is always lower than the mole fraction of [Cu(L-BzPro)(D-Val)] in corresponding mixtures. This means that the assumed mole fraction $\alpha_{\mathrm{MAB}} = 0{\cdot}222$ of [Cu(L-BzPro)(L-Val)] in the mixture 2 is too high and the calculated value of $\Delta\varepsilon = 0{\cdot}216$ is too low. Therefore the curve 4 in Figure 2 should be considered as the highest possible mole fraction of [Cu(L-BzPro)(L-Val)] in the mixtures. As the stabilities of [Cu(L-Val)$_2$] and of [Cu(D-Val)$_2$] are equal and the mole fraction of [Cu(L-BzPro)(L-Val)] is lower than that of [Cu(L-BzPro)(D-Val)] in corresponding mixtures, we can state that [Cu(L-BzPro)(D-Val)] is more stable than [Cu(L-BzPro)(L-Val)]. This shows the presence of stereoselectivity in this system.

Knowing the exact composition of complex species in the L-BzPro + D-Val system (and the less accurate values for the L-BzPro + L-Val system) from the c.d. and the electronic spectra of the mixtures the c.d. and the electronic spectra of the [Cu(L-BzPro)(D-Val)] and the [Cu(L-BzPro)(L-Val)] species can be easily calculated

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* Unfortunately the formation constants for [Cu(L-Val)$_2$] and the values used below for [Cu(L-Pro)$_2$] have been measured at 20°, whereas all our measurements were carried out at 25°. This may give rise to an error in log β of $\pm 0{\cdot}20$, ref. 11.

[11] N. C. Li, J. M. White, and R. L. Yoest, *J. Amer. Chem. Soc.*, 1956, **78**, 5218.

(Figures 3 and 4). The curves obtained for the last complex are less accurate and are drawn with dotted lines. It is remarkable that both the spectra of the species considered are not superposable. Therefore the isosbestic points of [Cu(L-BzPro)$_2$] with [Cu(L-BzPro)(L-Val)] and with [Cu(L-BzPro)(D-Val)] lie at different wavelengths (645 and 670—700 nm respectively). These isosbestic points are clearly seen in the series of the electronic absorption spectral curves obtained in the *N*-benzyl-L-proline + L-valine and *N*-benzyl-L-proline + D-valine systems.

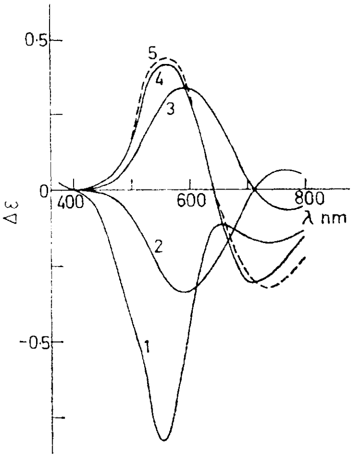

FIGURE 3 Molar circular-dichroism spectra of (1) [Cu(L-BzPro)$_2$]; (2) [Cu(L-Val)$_2$]; (3) [Cu(D-Val)$_2$]; (4) [Cu(L-BzPro)(D-Val)]; (5) [Cu(L-BzPro)(L-Val)]

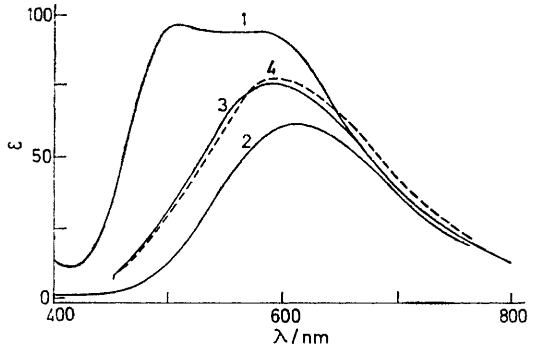

FIGURE 4 Electronic absorption spectra of (1) [Cu(L-BzPro)$_2$]; (2) [Cu(D-Val)$_2$]; (3) [Cu(L-BzPro)(D-Val)]; (4) [Cu(L-BzPro)(L-Val)]

The N-*Benzyl*-L-*Proline–Proline Systems*.—The methods of investigation of these systems are similar to those described for the valine-containing systems. Figure 5 shows the circular-dichroism curves of mixtures containing increasing amounts of D- and L-proline (the compositions of the mixtures were exactly the same as those shown in the Table: L- or D-proline being used instead of D-valine). It can be seen from Figure 5A that the value of $\Delta\varepsilon$ of [Cu(L-BzPro)(D-Pro)] is equal to that of [Cu(L-BzPro)$_2$] at 624 nm and to that of [Cu(D-Pro)$_2$] at 636 nm. The accuracy of calculations of the compositions of the mixtures from the measurements of $\Delta\varepsilon$ at 624 and 636 nm can be considerably improved by measurements at 561 nm, where $\Delta\varepsilon = 0$ for [Cu(D-Pro)$_2$] and $\Delta\varepsilon$ is maximal for [Cu(L-BzPro)$_2$]. Measurements at the same wavelength (561 nm) in combination with the values of $\Delta\varepsilon$ at 641 nm in the *N*-benzyl-L-proline, L-proline system (see Figure 5B) can be successfully used for the calculation of the compositions of the mixtures in this case as well.

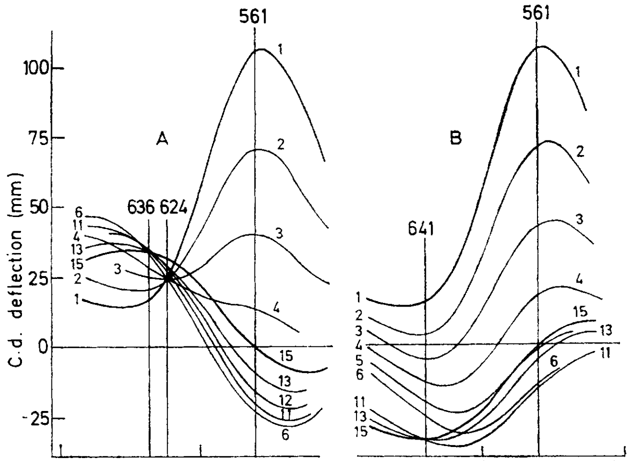

FIGURE 5 Circular-dichroism curves of copper(II) bis-complexes A, with L-benzylproline (1), D-proline (15), and mixtures of them (2)—(13); B, with L-benzylproline (1), L-proline (15), and mixture of them (2)—(13)

The results obtained are presented in Figure 6. It is evident that [Cu(L-BzPro)(D-Pro)] is much more stable than [Cu(L-BzPro)(L-Pro)]. While the equilibrium constant $K = 8{\cdot}0 \pm 0{\cdot}7$ for the latter can be calculated easily, the determination of $K = 165 \pm 50$ in the *N*-benzyl-L-proline + D-proline system is less accurate. This is due to the fact that, as the formation constants of [Cu(L-BzPro)$_2$] and [Cu(D-Pro)$_2$] are considerably different (the values of log β are 12·39 and 16·58 respectively), the region of simultaneous existence of all three species MB_2, MAB, and MA_2 is too small and the estimation of the very low concentrations of MB_2 and MA_2 in this region becomes rather difficult.

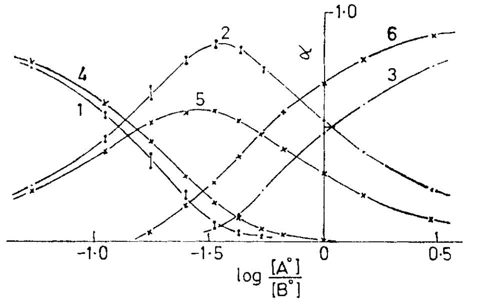

FIGURE 6 Mole fraction composition of the mixtures of complexes at equilibrium as a function of the initial concentration of L-benzylproline [B°] and proline [A°]. (1) [Cu(L-BzPro)$_2$]; (2) [Cu(L-BzPro)(D-Pro)]; (3) [Cu(D-Pro)$_2$]; (4) [Cu(L-BzPro)$_2$]; (5) [Cu(L-BzPro)(L-Pro)]; (6) [Cu(L-Pro)$_2$]

Using the published value of the formation constant of [Cu(L-Pro)$_2$] and [Cu(D-Pro)$_2$], log β_{MA_2} = 16·58, we obtain formation constants

$$\log \beta = 14{\cdot}93 \pm 0{\cdot}20 \text{ for } [\mathrm{Cu(L\text{-}BzPro)(L\text{-}Pro)}]$$

and

$$\log \beta = 15{\cdot}60 \pm 0{\cdot}30 \text{ for } [\mathrm{Cu(L\text{-}BzPro)(D\text{-}Pro)}]$$

The calculated circular-dichroism spectra of both complexes are shown in Figure 7, and the calculated electronic spectra in Figure 8. The dramatic difference in the electronic spectra of both components reflects the exceptionally high stereoselectivity in this system. The isosbestic points of [Cu(L-BzPro)(D-Pro)] with [Cu(D-Pro)$_2$] at 584 nm and with [Cu(L-BzPro)$_2$] at 653 nm are easily seen in the series of electronic spectra of the mixtures. [Cu(L-BzPro)(L-Pro)] has only one isosbestic point, with [Cu(L-BzPro)$_2$] at 578 nm.

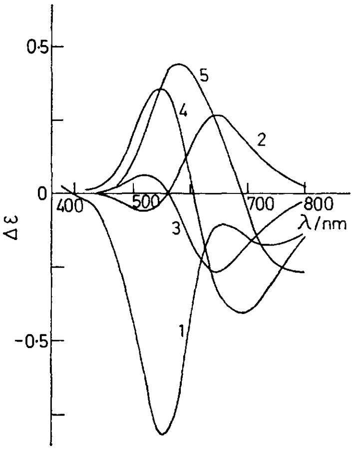

FIGURE 7 Molar circular dichroism of (1) [Cu(L-BzPro)$_2$]; (2) [Cu(L-Pro)$_2$]; (3) [Cu(D-Pro)$_2$]; (4) [Cu(L-BzPro)(D-Pro)]; (5) [Cu(L-BzPro)(L-Pro)]

The Proline and Valine Systems.—The two systems considered above show that changes in electronic spectra can be sufficiently sensitive to allow detection of the effects of stereoselectivity in copper amino-acid complexes. Therefore we prepared solutions of [Cu(L-Val)$_2$] and [Cu(D-Val)$_2$] of equal concentrations, containing an excess of the amino-acid to suppress dissociation, checked that their absorption spectra were exactly superimposable and mixed equal quantities of the solutions. The optical density of the mixture at the maximum (615 nm) is 2·0 ± 0·2% higher than that of the individual enantiomers. On mixing [Cu(L-Pro)$_2$] and [Cu(D-Pro)$_2$] solutions in the same manner, the extinction decreases by 1·3 ± 0·2%. Moreover with the copper–proline complexes there is a shift of the absorption maximum from 610 to 603 nm. This very simple experiment gives evidence for the presence of stereoselectivity with both bis-valine and bis-proline complexes. An alternative explanation for the observed spectral changes is that the visible spectrum of the mixed complex is considerably different from that of the individual optically active complexes. Although previous workers [2,3] have assumed that if the spectra of the racemic and optically active complexes are not identical, stereoselectivity is present, this need not be the case. Indeed large differences are observed between the visible spectra of the diastereoisomeric complexes [Cu(L-Bz-Pro)(D-Val)] and [Cu(L-Bz-Pro)(L-Val)]. It is interesting that no stereoselectivity was found [2] by a similar method for [Cu(L-Ala)(D-Ala)], although an earlier report,[12] states that the absorption spectra of bis(amino-acid)copper(II) complexes of L- and DL-alanine and of L- and DL-phenylalanine are slightly different. The earlier result could be due to the different hydration of the optically active and *meso*-complexes.[13] Very early experiments by Cotton [14] clearly demonstrate the large stereoselectivity present in the more complicated polynuclear copper(II) tartrate system, by a similar method, although this probably involves polynuclear species.[15]

Conclusion.—Circular dichroism proves to be a very useful method of investigation of optically active kinetically labile complexes. We have succeeded in determining the stability constants of mixed copper complexes of *N*-benzyl-L-proline with D- and L-valine and with D- and L-proline, using circular-dichroism measurements. The high stereoselectivity found in this system is in good agreement with the results obtained by the ligand chromatographic method from which one would predict that the mixed complexes of *N*-benzyl-L-proline with D-amino-acids must be more stable than those with the L-enantiomers. This means that the ligand chromatographic method gives valid information about the situation in labile mixed complexes and that this situation is not changed by the polymer support.

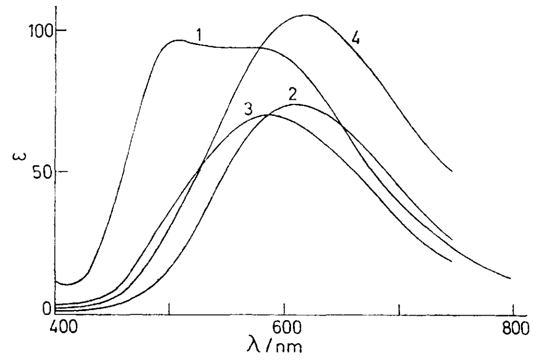

FIGURE 8 Electronic absorption spectra of (1) [Cu(L-BzPro)$_2$]; (2) [Cu(D-Pro)$_2$]; (3) [Cu(L-BzPro)(D-Pro)]; (4) [Cu(L-BzPro)(L-Pro)]

Another result of this work is the demonstration that the stereoselectivity is not an uncommon feature in the square-planar copper amino-acid complexes. This is valid not only for the *N*-substituted (*N*-benzyl-L-proline)

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[12] N. C. Li and E. Doody, *J. Amer. Chem. Soc.*, 1954, **76**, 221.

[13] C. Dijkgraaf, *Spectrochim. Acta*, 1964, **20**, 1227.

[14] A. Cotton, *Trans. Faraday Soc.*, 1930, **26**, 377.

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and cyclic amino-acids (proline) but for the unsubstituted open-chain amino-acids (valine) as well. Electronic absorption spectroscopy is probably the simplest method to make at least qualitative conclusions about the stereoselectivity in similar systems. However, it is worth mentioning that in the [Cu(Ala)$_2$] complexes no stereoselectivity was found[2] even by spectroscopic methods.

The presence of stereoselectivity demonstrates the existence of an interaction between the two chelate amino-acid rings in square-planar complexes. The origin of this interaction will be considered in more detail in a later publication.

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