Metal Ion-bridged Intramolecular Stacking Interaction between the Tryptophyl Residue and the Aromatic Heterocyclic Amine within the Ternary Complex (1,10-Phenanthroline)(L-tryptophanato-*O*,*N*)copper(II) Perchlorate–Water (1/2.5): an *X*-Ray Study†

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The crystal and molecular structure of $[Cu(L\text{-}TrpO)(phen)]ClO_4 \cdot 2.5H_2O$ has been determined by *X*-ray diffraction methods. The copper(II) centre is five-co-ordinate. The four equatorial sites are occupied by a bidentate tryptophanato (TrpO) ligand through a carboxylate oxygen [1.93(1) Å] and an amino nitrogen [2.02(1) Å] and a bidentate 1,10-phenanthroline (phen) ligand [average 2.00(1) Å]. The axial position is occupied by another carboxylate oxygen [2.29(1) Å] of a symmetry-related neighbouring tryptophanato molecule. Thus a one-dimensional polymeric structure is formed with an infinite $(-metal-carboxylate-)_n$ spiral from which tryptophyl indole and phen rings project outwards and stack on each other. An indole–phen π–π interaction in the metal ion-bridged stacked folded molecular unit (average spacing 3.51 Å and a tilt angle between the planes of 5°) reflects the significant deviation of the C^{α} atom [0.74(2) Å] from the co-ordination plane and a small angle (18°) between the co-ordination and indole planes. The complex further involves metal–indole ring edge-on close contacts [3.22(2) and 3.24(2) Å]. This is the first crystal structure providing direct evidence for the existence of a metal ion-bridged stacking adduct containing an aromatic amino acid residue.

Due to an excellent π-electron donating property of the indole moiety of tryptophan,[1] in the active centre of enzymes the tryptophyl residue has often been involved in charge-transfer interactions with a variety of substrates such as nucleotides[2] and coenzymes like NAD (or NADP),[3] thiamin pyrophosphate,[4] and FAD,[5] each bearing a heterocyclic aromatic ring(s). Many of these enzymes, additionally, contain tightly bound metal atoms or require metal ions as cofactors for their functions.[6] In this regard, of special interest are solution studies of the ternary metal complexes comprising aromatic amino acids {involving tryptophan (Trp) [2-amino-3-(1*H*-indol-3-yl)propanoic acid], tyrosine, phenylalanine, histidine, or related derivatives} and, as the second ligands, aromatic ring-containing ligands such as adenosine 5′-triphosphate,[7,8] 2,2′-bipyridyl,[9] 1,10-phenanthroline (phen),[10,11] phenyl-containing amines,[12] or aromatic amino acids,[13] where it has been strongly suggested that a metal ion could stabilize aromatic ring stacking by forming a metal ion bridge between the two constituents; otherwise, such charge-transfer interactions would usually be weak.[7a] To our knowledge, however, only a limited number of *X*-ray investigations[10a,14,15c] for the above (or related) ternary metal complex systems are available, where as yet no intramolecular ring–ring stacking has been observed. We report here the crystal and molecular structure of the ternary complex $[Cu^{II}(L\text{-}TrpO)(phen)]ClO_4 \cdot 2.5H_2O$, which provides the first *X*-ray evidence for such a metal ion-bridged stacking adduct containing an aromatic amino acid residue. The complex is also unique in that it additionally involves metal–indole ring close contacts. Furthermore, this is only the fifth[15] crystal structure of a metal–tryptophan compound.

Experimental

Crystals were prepared as described in ref. 11.

Crystal Data.—$C_{23}H_{24}ClCuN_4O_{8.5}$, $M = 591.46$, orthorhombic, $a = 28.430(4)$, $b = 11.085(2)$, $c = 8.162(3)$ Å, $U = 2\,572(1)$ Å^3 (by least-squares refinement on diffractometer angles for 18 automatically centred reflections in the range $19 < 2\theta < 29°$, $\lambda = 0.710\,73$ Å), space group $P2_12_12_1$, $Z = 4$, $D_c = 1.53$ g cm^{-3}, $F(000) = 1\,216$. Dark blue columns. Crystal dimensions: 0.112 × 0.230 × 0.413 mm, μ(Mo-K_α) = 10.1 cm^{-1}.

Data Collection and Processing.[16]—Rigaku diffractometer, ω–2θ mode with ω scan width (°) = 1.2 + 0.5 tanθ, ω scan speed 2.0° min^{-1}, graphite-monochromated Mo-K_α radiation; 1 973 reflections measured ($3 \leqslant 2\theta \leqslant 45°$, $+h, +k, +l$), 1 893 unique, giving 1 310 with $F_o > 3\sigma(F_o)$. No absorption correction [a variation in intensity of less than 3.9% from the mean for an axial 002 reflection ($\chi = 90°$)].

Structure Analysis and Refinement.—Normal heavy-atom procedures. Block-diagonal least-squares refinement with all non-hydrogen atoms anisotropic except for the four disordered perchlorate oxygens and the three water molecules which are isotropic (309 variables); one water is half-weighted. The weighting scheme $w = 1.0$ for $F_o \leqslant 50.0$ and $\sqrt{w} = 50.0/F_o$ for $F_o > 50.0$ gave satisfactory agreement analyses. Final R and R', and the goodness-of-fit values were 0.078, 0.086, and 2.8, respectively. No H atoms located; $(\Delta/\sigma)_{max.} = 0.32$; maximum peak in the final electron density map 0.62 e Å^{-3} near the disordered perchlorate oxygen atom. Programs used and sources of neutral atomic scattering factors with Cu and Cl corrected for anomalous dispersion are given in ref. 16. The final atomic co-ordinates are given in Table 1.

Results and Discussion

Bond lengths and angles are listed in Table 2. Close contacts involving hydrogen bonds are in Table 3.

Description of the Structure.—Figure 1 shows a polymeric structure for the complex cation $[Cu(L\text{-}TrpO)(phen)]^+$, where

† *Supplementary data available:* see Instructions for Authors, *J. Chem. Soc., Dalton Trans.*, 1987, Issue 1, pp. xvii—xx.

Table 1. Final atomic co-ordinates [$\times 10^3$ for O(3)—O(6), O(W1)—O(W3); $\times 10^4$ others] with e.s.d.s in parentheses for [Cu(L-TrpO)(phen)]ClO_4·2.5H_2O

Atom	*x*	*y*	*z*
Cu	1 749(1)	340(2)	2 571(3)
Cl	1 061(3)	6 083(6)	−499(11)
O(1)	2 264(4)	976(11)	1 305(13)
O(2)	2 726(4)	639(11)	−775(14)
N(1)	1 800(5)	−1 081(11)	1 026(15)
N(2)	1 160(6)	2 716(15)	−416(21)
N(3)	1 220(4)	−223(14)	3 978(16)
N(4)	1 569(5)	1 957(13)	3 460(19)
C(1)	2 375(5)	415(17)	83(17)
C(2)	2 047(7)	−621(16)	−486(24)
C(3)	1 683(6)	−194(18)	−1 723(19)
C(4)	1 390(6)	862(16)	−1 096(19)
C(5)	1 507(8)	2 110(17)	−1 205(24)
C(6)	816(8)	2 023(20)	184(27)
C(7)	947(6)	778(14)	−176(18)
C(8)	634(6)	−140(18)	339(25)
C(9)	230(7)	87(22)	1 139(26)
C(10)	117(8)	1 304(27)	1 538(26)
C(11)	407(8)	2 218(23)	1 112(25)
C(12)	1 070(7)	−1 300(20)	4 218(24)
C(13)	666(8)	−1 576(22)	5 294(27)
C(14)	417(7)	−608(25)	5 941(27)
C(15)	591(7)	600(20)	5 693(23)
C(16)	995(6)	741(16)	4 661(19)
C(17)	1 183(7)	1 926(18)	4 403(21)
C(18)	957(6)	2 963(19)	5 009(22)
C(19)	1 188(9)	4 018(20)	4 717(28)
C(20)	1 558(9)	4 132(20)	3 672(30)
C(21)	1 770(9)	3 021(18)	3 078(24)
C(22)	378(7)	1 662(21)	6 305(26)
C(23)	543(7)	2 745(24)	6 074(27)
O(3)	104(1)	689(3)	78(4)
O(4)	149(1)	541(2)	−47(3)
O(5)	109(1)	665(4)	−169(5)
O(6)	69(1)	530(3)	−18(4)
O(W1)	205(1)	689(3)	509(4)
O(W2)	263(1)	350(3)	663(4)
O(W3)*	222(2)	536(5)	767(8)

* O(W3) is half-occupied.

Table 2. Bond lengths (Å) and angles (°) in [Cu(L-TrpO)(phen)]ClO_4·2.5H_2O

(*a*) Co-ordination sphere

Cu–N(1)	2.02(1)	Cu–N(3)	1.99(1)
Cu–O(1)	1.93(1)	Cu–N(4)	2.00(1)
Cu–O(2′)	2.29(1)		
N(1)–Cu–O(1)	84.0(5)	O(1)–Cu–N(4)	93.6(6)
N(1)–Cu–N(3)	99.8(6)	O(1)–Cu–O(2′)	89.7(5)
N(1)–Cu–N(4)	160.4(6)	N(3)–Cu–N(4)	83.0(6)
N(1)–Cu–O(2′)	87.2(5)	N(3)–Cu–O(2′)	90.3(5)
O(1)–Cu–N(3)	176.2(6)	N(4)–Cu–O(2′)	112.3(5)
C(2)–N(1)–Cu	106(1)	C(1)–O(1)–Cu	117(1)
C(12)–N(3)–Cu	129(1)	C(21)–N(4)–Cu	126(1)
C(16)–N(3)–Cu	110(1)	C(17)–N(4)–Cu	113(1)

(*b*) L-Tryptophanato ligand

C(1)–O(1)	1.22(2)	N(2)–C(6)	1.34(3)
C(1)–O(2)	1.24(2)	C(6)–C(7)	1.46(3)
C(1)–C(2)	1.55(3)	C(7)–C(4)	1.47(2)
C(2)–N(1)	1.51(2)	C(7)–C(8)	1.42(2)
C(2)–C(3)	1.52(3)	C(8)–C(9)	1.35(3)
C(3)–C(4)	1.53(3)	C(9)–C(10)	1.42(4)
C(4)–C(5)	1.43(3)	C(10)–C(11)	1.35(4)
C(5)–N(2)	1.36(3)	C(11)–C(6)	1.40(3)
O(1)–C(1)–O(2)	125(2)	N(2)–C(6)–C(7)	106(2)
O(1)–C(1)–C(2)	118(1)	C(6)–C(7)–C(4)	105(1)
O(2)–C(1)–C(2)	117(1)	C(7)–C(4)–C(5)	107(2)
C(1)–C(2)–N(1)	107(1)	C(6)–C(7)–C(8)	117(2)
C(1)–C(2)–C(3)	112(1)	C(7)–C(8)–C(9)	123(2)
N(1)–C(1)–C(2)	109(1)	C(8)–C(9)–C(10)	119(2)
C(2)–C(3)–C(4)	113(1)	C(9)–C(10)–C(11)	121(2)
C(3)–C(4)–C(5)	127(2)	C(10)–C(11)–C(6)	122(2)
C(3)–C(4)–C(7)	126(2)	C(11)–C(6)–C(7)	118(2)
C(4)–C(5)–N(2)	106(2)	C(11)–C(6)–N(2)	136(2)
C(5)–N(2)–C(6)	115(2)	C(8)–C(7)–C(4)	137(2)

(*c*) 1,10-Phenanthroline ligand

N(3)–C(12)	1.28(3)	N(4)–C(21)	1.35(3)
N(3)–C(16)	1.36(2)	N(4)–C(17)	1.34(2)
C(12)–C(13)	1.48(3)	C(17)–C(18)	1.41(3)
C(13)–C(14)	1.39(3)	C(18)–C(19)	1.36(3)
C(14)–C(15)	1.44(3)	C(18)–C(23)	1.48(3)
C(15)–C(16)	1.43(3)	C(19)–C(20)	1.36(4)
C(15)–C(22)	1.42(3)	C(20)–C(21)	1.45(3)
C(16)–C(17)	1.43(3)	C(22)–C(23)	1.30(3)
N(3)–C(12)–C(13)	123(2)	N(4)–C(21)–C(20)	119(2)
C(12)–C(13)–C(14)	117(2)	C(21)–C(20)–C(19)	117(2)
C(13)–C(14)–C(15)	119(2)	C(20)–C(19)–C(18)	124(2)
C(14)–C(15)–C(16)	117(2)	C(19)–C(18)–C(17)	115(2)
C(15)–C(16)–N(3)	122(2)	C(18)–C(17)–N(4)	124(2)
C(16)–N(3)–C(12)	121(1)	C(17)–N(4)–C(21)	120(2)
C(15)–C(16)–C(17)	119(2)	C(16)–C(17)–C(18)	122(2)
C(16)–C(15)–C(22)	117(2)	C(17)–C(18)–C(23)	116(2)
C(15)–C(22)–C(23)	124(2)	C(18)–C(23)–C(22)	121(2)
C(14)–C(15)–C(22)	125(2)	C(19)–C(18)–C(23)	129(2)

(*d*) Perchlorate anion

Cl–O(3)	1.38(3)	Cl–O(5)	1.16(4)
Cl–O(4)	1.42(3)	Cl–O(6)	1.40(3)
O(3)–Cl–O(4)	112(2)	O(4)–Cl–O(5)	104(2)
O(3)–Cl–O(5)	107(2)	O(4)–Cl–O(6)	109(2)
O(3)–Cl–O(6)	103(2)	O(5)–Cl–O(6)	123(2)

the copper atom is co-ordinated in a distorted square-pyramidal geometry by the bidentate phen ligand [Cu–N 2.00(1) and 1.99(1) Å] and by the tryptophanato ligand through the carboxylate oxygen [Cu–O(1) 1.93(1) Å] and amino nitrogen [Cu–N(1) 2.02(1) Å]; the axial position is occupied by the carboxylate oxygen belonging to the symmetrically related neighbouring tryptophanato molecule [Cu–O(2′) 2.29(1) Å]. Thus each carboxylate group of tryptophan links two Cu atoms along a two-fold screw axis (*c* axis), thereby producing an infinite (–Cu–OCO–Cu–OCO–)$_n$ spiral from which tryptophyl indole and phen rings project outwards (but obliquely) and stack on each other, hence the stacking is of the type –T–P–T–P– (T = L-TrpO, P = phen) (average spacings 3.51 and 3.51 Å). Chelation through the amino and the carboxylate groups with the formation of a five-membered ring, a usually observed metal bonding mode for amino acids,[17] also holds for the present and the so far reported metal–tryptophan complexes; aqua(glycyl-L-tryptophanato)copper(II) dihydrate[15a] and dimethyl(DL-tryptophanato)thallium(III) monohydrate;[15b] bis(*N*-acetyl-DL-tryptophanato)diaquabis(pyridine)copper-(II)[15c] and (L-tryptophan)(L-tryptophanium) trichloromercurate(II)[15d] deviate from this rule, *i.e.* monodentate bonding through the carboxylate oxygen in the former and salt-type interaction (neither metal–Trp nor –HTrp$^+$ bonding) in the latter. The conformation of the tryptophyl residue is similar to that found in aqua(glycyl-L-tryptophanato)copper(II)[15a] and the free acids L-tryptophan hydrochloride[18a] and 3-carbamoyl-1-methylpyridinium *N*-acetyl-L-tryptophanate;[18b] the C^γ [C(4)] atom is, with respect to the C^α–C^β bond, *anti* to the α

Table 3. Hydrogen-bonding and other short contacts (Å)[a,b]

(*a*) Hydrogen-bonding contacts

N(1)···O(3^{I})	3.14(3)	O(W1)···O(W2^{IV})	3.00(4)
N(1)···O(W2^{II})	3.18(3)	O(W2)···O(4^{III})	3.28(4)
N(2)^{c}···O(4)	3.13(3)	O(W2)···O(W3)	2.51(7)
N(2)^{c}···O(6)	3.17(3)	O(W3)···O(4^{V})	2.57(6)
O(W1)^{c}···O(1^{III})	3.22(3)	O(W3)···O(W1)	2.75(7)
O(W1)^{c}···O(2^{III})	2.90(3)		

(*b*) Other short contacts

Cu···C(4)	3.22(2)	C(1)···C(5)	3.28(3)
Cu···C(7)	3.24(2)	C(6)···N(4)	3.43(3)
O(1)···C(2^{II})	3.29(2)	C(6)···C(22^{VI})	3.43(3)
O(1)···C(4)	3.17(2)	C(7)···C(22^{VI})	3.44(3)
O(1)···C(5)	3.23(2)	C(8)···N(3)	3.41(2)
N(1)···C(7)	3.33(2)	C(13)···O(5^{V})	3.37(5)
N(2)···C(21)	3.35(3)	C(14)···O(6^{VII})	3.35(4)
N(2)···C(23^{VI})	3.36(3)	C(21)···O(W3^{IV})	3.41(6)
C(1)···O(W1^{IV})	3.41(3)		

[a] Contacts below 3.45 Å. [b] Symmetry operations: I $\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$; II $\frac{1}{2} - x, -y, \frac{1}{2} + z$; III $\frac{1}{2} - x, 1 - y, \frac{1}{2} + z$; IV $\frac{1}{2} - x, 1 - y, z - \frac{1}{2}$; V $x, y, 1 + z$; VI $x, y, z - 1$; VII $-x, y - \frac{1}{2}, \frac{1}{2} - z$. [c] A hydrogen atom attached to this atom may form a bifurcated hydrogen bond.

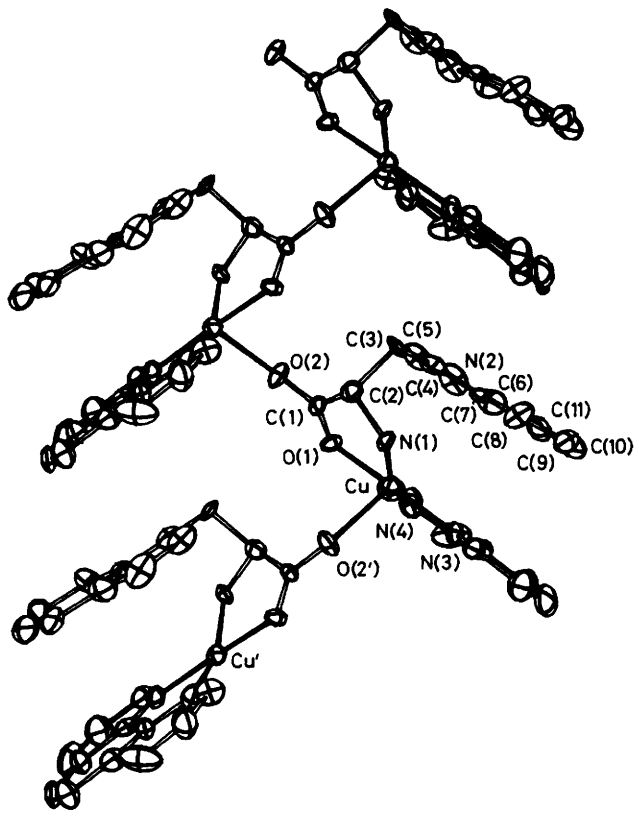

Figure 1. A segment of the polymeric cation [Cu(L-TrpO)(phen)]$^{+}$, showing the stacking arrangement between the tryptophyl residue and the phen rings *via* direct (average spacing 3.51 Å) or indirect (average spacing 3.51 Å) metal-ion bridges, thus the stacking is of the type -T-P-T-P- (T = L-TrpO, P = phen)

hydrogen, thus corresponding to the *h* rotamer,[19] and the C$^{\delta 1}$ [C(5)] atom lies on the same side as the carboxylate group [χ^{1} = N(1)–C(2)–C(3)–C(4) = 63(2)°, $\chi^{2,1}$ = C(2)–C(3)–C(4)–C(5) = 86(2) (see ref. 20 for definition of torsion angles χ), C(1)–C(2)–C(3)–C(4) = −55(2), and O(2)–C(1)–C(2)–N(1) = 155(1)°]. The bond lengths and angles in the

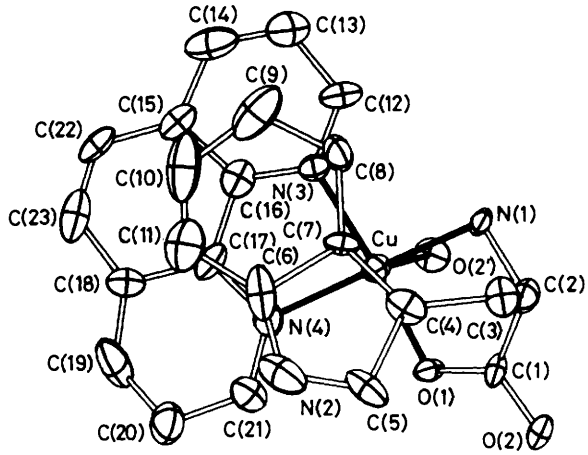

Figure 2. A perspective view showing the mutual orientation of the two aromatic rings within the metal ion-bridged intramolecular stacking structure and also showing the disposition of the Cu atom, *i.e.*, beneath the C(4)–C(7) bond

tryptophanato ligand are mostly as expected[15,18] and those in the phen ligand are also normal[10a] (Table 2).

The most interesting structural feature of the complex is the existence of the metal-ion bridged intramolecular stacking between the tryptophan indole and the aromatic amine rings, as shown in Figure 2. The indole moiety is stacked on the phen ring at an average spacing of 3.51 Å *via* metal–N and –O bridges; the tilt angle between the two planes is 5°. The significant deviation of the C(2) atom [0.74(2) Å] from the co-ordination plane [O(1), N(1), N(3), and N(4)] towards the indole ring, where an angle between the co-ordination and the indole planes is 18°, makes the parallel arrangement of the tryptophyl residue with the phen ligand feasible, while for aqua(glycyl-L-tryptophanato)copper(II)[15a] the C$^{\alpha}$ atom lies essentially on the co-ordination plane and the corresponding angle is 50°. Therefore, the remarkable decrease (32°) in the angle is, in turn, mostly due to the introduction of phen as a second ligand, *i.e.* a result caused by π–π interaction. To our knowledge, there have been no *X*-ray investigations of ternary metal complexes composed of aromatic amino acids (or related derivatives) and aromatic heterocyclic ligands except for a limited number of compounds[10a,14,15c] in which no intramolecular ring–ring stacking occurs; bis(*N*-benzylpyridine-4-carbaldiminato)copper(II)[14c] involves two parallel phenyl groups within the molecule but the interplanar distance of 4.13 Å is too high to indicate any attractive forces, while L-phenylalaninato[*N*-(2-pyridylmethyl)-L-aspartato]cobalt(III)[14d] involves the closest interatomic distance of 3.46 Å between the phenyl and the co-ordinated pyridine rings; [Cu^{II}{(*S*)-bap-(*S*)-Val}][14e] ((*S*)-bap-(*S*)-Val = (*S*)-2-{*o*-[(*N*-benzylprolyl)amino]phenyl}ethylidene-imino-3-methylbutanoate(2−)) and [Ni^{II}{(*S*)-bap-(*S*)-Val}][14e] also have the closest contacts of 3.78 and 3.74 Å between the two phenyl rings within the molecules, respectively, but the dihedral angles between the two planes are 34.5, 32.9, and 31.3° for the Co^{III}, Cu^{II}, and Ni^{II} complexes, respectively. Thus this is the first *X*-ray example providing direct evidence for the existence of a metal ion-bridged stacking adduct for an aromatic amino acid (or its derivative)–metal ion–aromatic amine ternary system, although the metal-ion bridged intramolecular stacked structure itself has so far been exemplified for a nucleotide–metal ion–aromatic amine system in the solid state[21] as well as in solution.[22] An additional noticeable structural feature within the stacked structure is the metal–ring close contact; the Cu atom lies beneath the C(4)–C(7) bond [Cu···C(4) 3.22(2) and Cu···C(7) 3.24(2) Å] (Figure 2). This arrangement is certainly not ideal for a *d*-orbital–π interaction

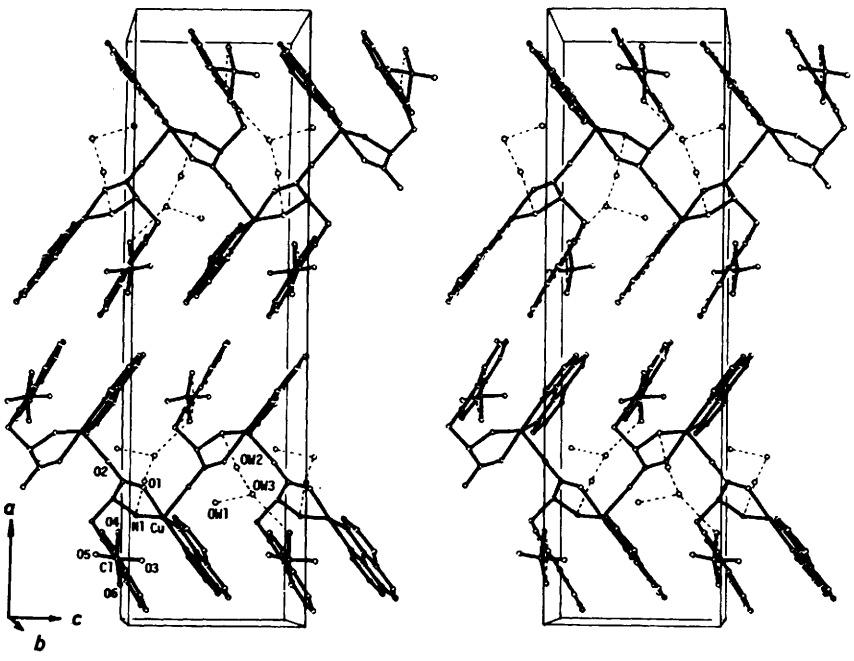

Figure 3. A stereoscopic view of the molecular packing along *b* for [Cu(L-TrpO)(phen)]ClO_4·2.5H_2O. Broken lines show hydrogen bonds

but seems favourable on the basis of the highest electron densities on the C^{γ} and $C^{\delta 2}$ [C(7)] atoms.[1] Similar short contacts between metal ions such as Cu^{II},[15a,23a,b,24a,b] Hg^{II},[23c] or Pd^{II},[23d] and aromatic amino acid residues like tryptophan,[15a] tyrosine,[23] or phenylalanine,[24] have been observed in the solid state.

The crystal packing is largely determined by alternate indole–phen ring–ring stacking interactions, as noted above, and by an extensive network of hydrogen-bonding interactions involving tryptophyl carboxylate oxygens and amino and indole nitrogens, perchlorate anions, and water molecules (Figure 3 and Table 3). A tentative (because hydrogen atoms were not located) hydrogen-bonding scheme is as follows: water molecule O(W1) donates one hydrogen atom to carboxylate oxygens O(1) and O(2) and another to $O(W2^{IV})$ (for symmetry operations, see Table 3), which in turn donates hydrogen atoms to perchlorate oxygen $O(4^{III})$ and O(W3), which further acts as hydrogen donor to O(W1) and $O(4^{V})$; amino nitrogen N(1) donates hydrogen atoms to perchlorate $O(3^{I})$ and $O(W2^{II})$ and indole N(2) forms a bifurcated hydrogen bond with O(4) and O(6) of a perchlorate anion, which further makes a close contact with a neighbouring tryptophyl molcule [closest contact O(3)···C(8) 3.50(4) Å], and thus a perchlorate anion is sandwiched between two indole ring edges.

Factors affecting the Formation and Stability of the Folded Structure.—Most recently, Yamauchi and Odani[11] have demonstrated that aromatic amino acids such as tryptophan, tyrosine, or phenylalanine could form ternary metal complexes with aromatic amines like 1,10-phenanthroline or 2,2′-bipyridyl in solution, where an intramolecular isomeric equilibrium between an 'unstacked-opened' and a 'stacked-folded' form exists. For the L-TrpO–Cu^{II}–phen system, on the basis of its equilibrium constant log $K = 1.39$,[11] the stacked-folded form can be evaluated to exist up to 96% in solution, indicating that the complex is almost fixed in the folded form. It seems of interest to consider from a structural point of view which factors are responsible for this high population. A factor which we should take into account is the conformational preference of the tryptophan molecule itself, if any. The structural change between the two forms is principally responsible for the conformational change about the C^{α}–C^{β} bond of the tryptophyl ligand for the present system, where only the *h* rotamer[19] makes the stacking possible. Theoretical calculations[25] suggest the most probable values for χ^{1} to be 60, 180, and 300° for tryptophan with an equal preference, corresponding to *h*, *g* (C^{γ} is *cis* to the carboxylate group and *trans* to the amino group), and *t* rotamers (C^{γ} is *trans* to the carboxylate group and *cis* to the amino group),[19] respectively, and these rotamers have all been repeatedly observed in crystal structures, the order of reported occurrence being: *t* (nine examples[24a–i]) > *h* (seven examples[15a,b,d,18a,b26j]) > *g* (two examples[15c,26g]). Thus the *h* rotamer itself does not exert its conformational preference compared to the others and hence this cannot explain the observed high population of the folded form. It should be noted here, however, that the conformation about the C^{β}–C^{γ} bond exhibits a pronounced preference, *i.e.* $\chi^{2,1} \sim \pm 90°$ [average $\pm 95(15)°$ and range $\pm(61—117)°$] for 17 examples,[15,18,26] with an exception of $-12.1°$,[15c] and this favours a parallel arrangement of the indole moiety with the co-ordination plane. Therefore, it now becomes clear that the origin of this high population should be from any attractive interactions within the folded structure.

In accordance with the quantitative evaluation of non-covalent interaction energies in dipeptide–aromatic or aliphatic groups containing amine–Pd^{II}–H_2O complexes by Kim and Martin,[12] *i.e.* their decreasing order is phenyl–aromatic > phenyl–propyl (or larger alkyl residue) > ··· > Pd–aromatic ≫ Pd–aliphatic ~ 0, and as originally documented,[11] the ring–ring stacking interaction is a major factor for the formation and the stability of the folded structure. The observed high population is, in turn, good evidence for the considerable stabilizing power of the stacking interaction; this is, however, somewhat surprising, if we assume that the structure in solution is (nearly) the same as that in the solid state, because ring–ring overlapping is incomplete.

Another possible stabilizing factor is a non-covalent metal–ring interaction, which certainly exists in the present crystal

structure, but we must be careful in evaluating its validity, since the indole–phen stacking arrangement inevitably accompanies a close indole–metal contact. There has been no evidence for a metal–ring interaction in solution except for a Pd^{II}–aromatic ring interaction,[12] which is still much weaker than an aromatic–aromatic interaction. Sigel *et al.*[27] have discussed in detail metal–aromatic interactions in solution for binary or ternary phenylalkanecarboxylate complexes (M = Cu^{II} or Zn^{II}), or binary or ternary amino acid complexes (M = Co^{II}, Ni^{II}, Cu^{II}, or Zn^{II}), and concluded that they are of no significance in the structure stabilization. Therefore, at this stage, whether the metal–ring interaction could contribute to the stabilization of the structure is still an open question (at least for Cu^{II}) and further information is needed.

Finally, the following argument, though still tentative, may be attractive in connection with the possible roles of the metal ion in the ternary enzyme–metal ion–substrate interactions. At first, we can expect its template effects, that is, connection of the two reactants concerned and placing and fixing them in appropriate positions. In addition, non-covalent metal–ring interaction, if effective, could be kinetically of significance; *i.e.* placement of the aromatic ring near to the metal ion is favourable for ring–ring stacking, which may in turn strengthen metal–ring interaction. Thus metal–ring and ring–ring interactions work co-operatively. The second role is its electronic effects; that is, a metal atom could activate a substrate with an aromatic ring through an interaction between the metal and the π electrons of the ring with concomitant electron transfer as observed in some copper oxidases.[28]

Conclusions

The significance of the present study is (*i*) to provide the first *X*-ray evidence for metal ion-bridged ring–ring stacking formation in an amino acid-containing ternary complex system, (*ii*) to provide the first *X*-ray example in which metal–ring close contacts are simultaneously involved, and thus (*iii*) to suggest that similar structural features could hold in related ternary metal complex systems, *e.g.* in [Cu(D- or L-HisO)(L-aa)][13a,b] (L-aa = L-TrpO, L-tyrosinate, or L-phenylalaninate; HisO = histidinate) and isolated[11,29] [Cu(L)(L-aa)] (L = phen or 2,2′-bipyridyl; L-aa = L-tyrosinate or L-phenylalaninate) complexes.

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