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The Crystal Structures of Two Copper(II) Complexes of the Anti-Tumor Agent 5-(3,3-Dimethyl-1-triazenyl)imidazole-4-carboxamide

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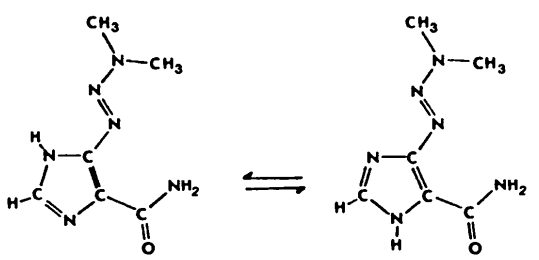
Abstract

The crystal structures of two copper(II) complexes of the anti-tumor agent 5-(3,3-dimethyl-1-triazenyl)-imidazole-4-carboxamide (DTIC) have been determined by X-ray diffraction. Complex (I), $Cu(C_6H_{10}N_6O)Cl_2.2CH_3OH$, crystallizes in the triclinic space group $P\bar{1}$, $a = 8{\cdot}493$ (3), $b = 9{\cdot}054$ (3), $c = 10{\cdot}969$ (2) Å, $\alpha = 90{\cdot}51$ (2), $\beta = 105{\cdot}66$ (2), $\gamma = 104{\cdot}68$ (2)°, $V = 783{\cdot}0$ (5) Å^3, $Z = 2$. Complex (II), $Cu(C_6H_{10}N_6O)Cl_2$, crystallizes in the monoclinic space group $P2_1/c$, $a = 9{\cdot}059$ (1), $b = 13{\cdot}647$ (1), $c = 9{\cdot}538$ (1) Å, $\beta = 92{\cdot}28$ (1)°, $V = 1178{\cdot}3$ (1) Å^3, $Z = 4$. The Cu atoms in both complexes are five-coordinate. The equatorial ligand atoms in each case are the O(amide) and adjacent N(imidazole) of DTIC, and two Cl atoms. In (I) the fifth ligand is an O(methanol) atom. In (II) the axial coordination position is occupied by a Cl atom of an adjacent molecule, resulting in the formation of a dimer. There are significant differences between the coordination geometries in the two complexes. In addition, the triazene group in (I) is rotated by 180° about the C(imidazole)–N(triazene) bond with respect to the conformation which it has both in (II) and in free DTIC.

Introduction

5-(3,3-Dimethyl-1-triazenyl)imidazole-4-carboxamide (NSC-45388, DTIC) is an important chemotherapeutic agent in the treatment of malignant melanoma. The tautomeric forms of DTIC are shown below.



The drug belongs to a general class of substituted triazenylimidazoles. The anti-tumor properties of such compounds have been attributed to decomposition to a purine analogue, 2-azahypoxanthine (Shealy, Montgometry & Laster, 1962). This hypothesis is supported by the observation that DTIC, like many purine analogues, is a xanthine oxidase inhibitor (Iwata, Yamamoto & Muraki, 1969). An alternative explanation of the anti-tumor activity of DTIC is that the drug acts as an alkylating agent (Skibba, Beal, Ramirez & Bryan, 1970).

While the molecular basis of the physiological activity remains uncertain, the interactions between DTIC and metals have recently acquired a potential clinical significance. The observation of elevated serum Cu levels in melanoma patients (Milton & Blomfield, 1970) has raised the question whether DTIC is able to coordinate Cu^{II} under physiological conditions. If coordination does occur then there are three possibilities: the chemotherapeutic effectiveness of the drug may be enhanced, reduced or left unchanged. In tissue-culture experiments the activity of DTIC against one line of melanoma cells has been found to be enhanced significantly by the presence of stoichiometric quantities of Cu^{II} (N. D. Hutchinson, unpublished work). In order to determine the nature and effects of the Cu^{II}–DTIC interactions we have undertaken a crystallographic study of DTIC (Freeman & Hutchinson, 1979) and a number of Cu^{II}–DTIC complexes. We report here the structures of two complexes isolated at low pH.

Experimental

Except where stated otherwise, the DTIC (NSC-45388) was taken from a sample supplied by the Drug Development Branch, National Cancer Institute, Bethesda, Maryland. A methanol solution of $CuCl_2.2H_2O$ (0·06 *M*) and DTIC (0·06 *M*) yielded crystals of a green complex (I) after standing for 12 h. The subsequent structure analysis showed that the crystals had the composition $Cu(DTIC)Cl_2.2CH_3OH$. On exposure to the atmosphere for about 5 min, these green crystals lost methanol to give a non-crystalline yellow product

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(I*b*). Complex (I*b*) was registered as NSC-298183 at the National Cancer Institute for testing against animal tumors. [Calculated for $Cu(DTIC)Cl_2$: C 22·76, N 26·55, H 3·16, Cl 22·39, Cu 20·07%. Found for (I*b*): C 22·86, N 27·34, H 3·36, Cl 22·2, Cu 20·0%.]*

When a saturated methanol solution of equimolar quantities of $CuCl_2.2H_2O$ and DTIC was cooled quickly from 353 K, small dichroic yellow-green crystals (II) were deposited. Larger crystals of (II) were obtained when an aqueous solution prepared from $CuCl_2.2H_2O$ (0·06 *M*) and a clinical sample of DTIC [in citrate (0·12 *M*) and mannitol (0·05 *M*), Dome Laboratories, NDC 0026-8151-20] was allowed to stand for several weeks. The crystals of (II) did not contain methanol. [Calculated for $Cu(DTIC)Cl_2$: as above. Found for (II): C 22·76, N 25·14, H 3·22, Cl 22·0, Cu 19·6 %.]

Infrared mull spectra were recorded in the region 4000–250 cm^{-1} on a Perkin–Elmer 457 grating spectrophotometer.

* Preferred IUPAC notation for the complex: $Cu(dtic)Cl_2$.

Table 1. *Crystal data*

Complex	(I)	(II)
Formula	$Cu(C_6H_{10}N_6O)Cl_2.2CH_3OH$	$Cu(C_6H_{10}N_6O)Cl_2$
M_r	380·7	316·6
Space group	$P\bar{1}$	$P2_1/c$
a (Å)	8·493 (3)	9·059 (1)
b (Å)	9·054 (3)	13·647 (1)
c (Å)	10·969 (2)	9·538 (1)
α (°)	90·51 (2)	–
β (°)	105·66 (2)	92·28 (1)
γ (°)	104·68 (2)	–
V (Å^3)	783·0 (5)	1178·3 (1)
ρ_{meas} (Mg m^{-3})	1·63 (1)	1·75 (1)
ρ_{calc} (Mg m^{-3})	1·615	1·784
Z	2	4
μ (Mo $K\alpha$) (mm^{-1})	1·816	2·361

Table 2. *Data-collection parameters*

Complex	(I)	(II)
Crystal size (mm)	0·55 × 0·28 × 0·10	0·15 × 0·15 × 0·13
Precision required by final scan	$\sigma(I) < 0{\cdot}01(I)$	$\sigma(I) < 0{\cdot}005(I)$
Maximum scan time (s)	60	150
Scan type	ω, θ	ω
Scan width (°)	1·2 + 0·35 tan θ	2·0 + 0·35 tan θ
Horizontal scan aperture (mm)	1·4 + 0·35 tan θ	1·5 + 0·35 tan θ
Range of θ (°)	$1 \le \theta \le 25$	$1 \le \theta \le 27{\cdot}5$
Absorption correction:*		
Number of sampling points	7 × 7 × 6	6 × 6 × 6
Minimum correction	1·187	1·274
Maximum correction	1·660	1·460
Mean correction	1·308	1·349
Number of unique reflections	2739	2708
Number of reflections with $I > 3\sigma(I)$	2377	1904

* Coppens, Leiserowitz & Rabinovich (1965).

X-ray data collection

The unstable crystals of (I) were coated with silicone oil (Dow Corning 702) and sealed in a 0·7 mm capillary tube. All data were recorded on an Enraf–Nonius CAD-4/F automatic diffractometer using graphite-monochromated Mo $K\alpha$ radiation [λ(Mo $K\alpha_1$) = 0·70926, λ(Mo $K\alpha_2$) = 0·71354 Å]. Unit-cell dimensions were fitted by least squares to the 2θ values of 25 automatically centered reflections ($\theta > 19°$). Except where stated otherwise the data-collection procedures were identical with those reported by Freeman & Hutchinson (1979). Crystal data are given in Table 1 and data-collection parameters in Table 2.

Three standard reflections were remeasured at regular intervals of X-ray exposure time. The percentage decrease in the intensities, averaged over the three reflections, was plotted against X-ray exposure time. In the case of (I), the plot of 52 data points was approximately linear and indicated a decomposition of 27% at the end of data collection. No decomposition was observed for (II). The data for (I) were corrected by fitting linear equations to series of six successive points on the plot of decomposition *versus* exposure time, and using each equation to correct the intensities which had been recorded between the third and fourth sets of standard measurements. Application of these corrections to the standard reflections themselves produced values which differed by less than 1% from the mean corrected values.

Data were also corrected for Lorentz, polarization and absorption effects. The variance $\sigma^2(F)$ of each structure amplitude F was recalculated as the sum of the variance from counting statistics plus a component V_s from systematic errors (Freeman & Guss, 1972). For (I), $V_s = l + m|F|$, where $l = 0{\cdot}540$ and $m = -0{\cdot}006$ ($|F| \le 90$) and $l = -2{\cdot}574$ and $m = 0{\cdot}0286$ ($|F| > 90$). In the case of (II), the systematic component was dependent mainly on $\sin\theta/\lambda$ such that $V_s = l + m(\sin\theta/\lambda) + n(\sin\theta/\lambda)^2$ where $l = 3{\cdot}2$, $m = -15$ and $n = 18$.

Structure determination and refinement

The structures were solved using standard Patterson and Fourier syntheses. Full-matrix least-squares refinement was used to minimize the function $\sum w(|F_o| - s|F_c|)^2$ where $w = \sigma^{-2}(F)$ and s was the inverse scale factor. Scattering factors for neutral Cu, Cl, O, N, C and H together with real and imaginary anomalous-dispersion terms for Cu and Cl were taken from *International Tables for X-ray Crystallography* (1974). All H atoms were located in difference Fourier maps. In the final cycles all the non-hydrogen atoms were refined with anisotropic temperature factors. Isotropic temperature factors for the H atoms were refined in the case of (I), but were fixed at $U_{iso} = 0{\cdot}0380$ Å^2 for (II).

Table 3. *Positional parameters* ($\times 10^4$) *with estimated standard deviations in parentheses*

	x	y	z
(I) $Cu(DTIC)Cl_2.2CH_3OH$			
Cu	4351 (1)	3099 (1)	1840 (1)
Cl(1)	3468 (1)	1865 (1)	−97 (1)
Cl(2)	2990 (1)	4904 (1)	1314 (1)
O(1)	4907 (2)	3839 (2)	3704 (1)
O(2)	7107 (3)	4656 (2)	1637 (2)
O(3)	7986 (3)	−2708 (2)	3337 (2)
N(1)	5361 (2)	1500 (2)	2662 (2)
N(2)	6552 (2)	−323 (2)	3323 (2)
N(3)	6110 (3)	3431 (3)	5719 (2)
N(4)	7649 (2)	144 (2)	5533 (2)
N(5)	7773 (2)	1040 (2)	6490 (2)
N(6)	8618 (2)	702 (2)	7577 (2)
C(1)	5712 (3)	264 (3)	2306 (2)
C(2)	6773 (3)	581 (2)	4396 (2)
C(3)	6005 (3)	1733 (2)	3965 (2)
C(4)	5659 (3)	3063 (2)	4494 (2)
C(5)	9386 (4)	−568 (4)	7694 (3)
C(6)	8819 (4)	1684 (4)	8690 (3)
C(7)	8450 (5)	3953 (5)	1754 (4)
C(8)	8731 (5)	−3241 (5)	4478 (4)
H(1)	5475 (24)	−186 (24)	1505 (21)
H(2)	7006 (31)	−1066 (30)	3348 (25)
H(3)	6619 (28)	2819 (29)	6290 (23)
H(4)	5923 (27)	4100 (27)	5988 (23)
H(5)	8550 (37)	−1537 (36)	7337 (30)
H(6)	10049 (37)	−417 (34)	7223 (30)
H(7)	9923 (40)	−490 (37)	8497 (35)
H(8)	10007 (37)	2168 (31)	9089 (27)
H(9)	8328 (37)	1041 (37)	9201 (32)
H(10)	8247 (39)	2460 (39)	8458 (31)
H(11)	6930 (39)	4818 (36)	1133 (26)
H(12)	8863 (41)	3611 (39)	2572 (35)
H(13)	9317 (39)	4464 (35)	1522 (31)
H(14)	8130 (39)	3053 (38)	1252 (34)
H(15)	7649 (39)	−3258 (36)	2853 (30)
H(16)	9712 (47)	−3585 (42)	4366 (35)
H(17)	9271 (43)	−2544 (41)	5008 (34)
H(18)	8050 (44)	−3980 (44)	4683 (35)
(II) $Cu(DTIC)Cl_2$			
Cu	4319 (0·5)	4659 (0·2)	8611 (0·4)
Cl(1)	2692 (1)	3445 (1)	6156 (1)
Cl(2)	3294 (1)	5677 (1)	4998 (1)
O(1)	5449 (3)	5803 (1)	7613 (2)
N(1)	5329 (3)	3909 (2)	8103 (2)
N(2)	6446 (3)	2967 (2)	9655 (3)
N(3)	7132 (4)	6102 (2)	9386 (3)
N(4)	8017 (3)	4168 (2)	10950 (3)
N(5)	8479 (3)	3410 (2)	11658 (3)
N(6)	9487 (3)	3598 (2)	12621 (3)
C(1)	5464 (4)	3009 (2)	8560 (3)
C(2)	6978 (4)	3887 (2)	9928 (3)
C(3)	6274 (3)	4474 (2)	8945 (3)
C(4)	6278 (4)	5511 (2)	8627 (3)
C(5)	10048 (5)	4570 (4)	12902 (5)
C(6)	9976 (6)	2769 (4)	13479 (5)
H(1)	5039 (36)	2489 (23)	8168 (34)
H(2)	6662 (38)	2488 (24)	10009 (36)
H(3)	7530 (40)	5872 (24)	10046 (37)
H(4)	7137 (37)	6666 (26)	9251 (34)
H(5)	9259 (39)	5010 (23)	13151 (34)
H(6)	10275 (37)	4931 (23)	12078 (37)
H(7)	10725 (41)	4510 (24)	13433 (36)
H(8)	9780 (37)	2920 (22)	14430 (37)
H(9)	9544 (39)	2233 (24)	13083 (36)
H(10)	10876 (43)	2760 (25)	13351 (37)

A difference Fourier synthesis after the last refinement cycle showed no peaks larger than 0·22 e Å^{-3} for (I) and 0·54 e Å^{-3} for (II). For (I) the final residuals were $R\ (=\sum||F_o| - s|F_c||/\sum|F_o|) = 0{\cdot}024$ and $R_w = [\sum w(|F_o| - s|F_c|)^2/\sum w|F_o|^2]^{1/2} = 0{\cdot}024$ for the 2377 observed reflections used in the refinement. For (II) the final residuals were $R = 0{\cdot}035$ and $R_w = 0{\cdot}028$ for the 1904 observed reflections used in the refinement. Table 3 gives the final atomic coordinates for the structures.*

Description of the structures

Figs. 1 and 2 together with Table 4 give the molecular dimensions for the two complexes.

* Lists of structure factors, anisotropic thermal parameters, and a table of bond lengths and angles of the DTIC molecules in the present complexes and in DTIC and $HDTIC^+$ have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34439 (45 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

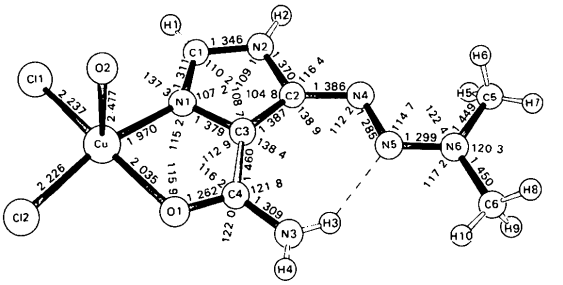

Fig. 1. Molecular geometry and dimensions [bond lengths (Å) and angles (°)] of complex (I). The e.s.d.'s are 0·002 Å for bond distances involving the Cu atom and 0·003 Å for all other bonds, 0·1° for bond angles involving the Cu atom and 0·2° for all other angles. Only the O(2) of the coordinated methanol is shown for clarity. The angle Cu–O(2)–C(7) is 118·9 (2)°. The bond lengths in the coordinated and uncoordinated methanol molecules are, respectively, C(7)–O(2) = 1·418 (4) Å and C(8)–O(3) = 1·392 (4) Å.

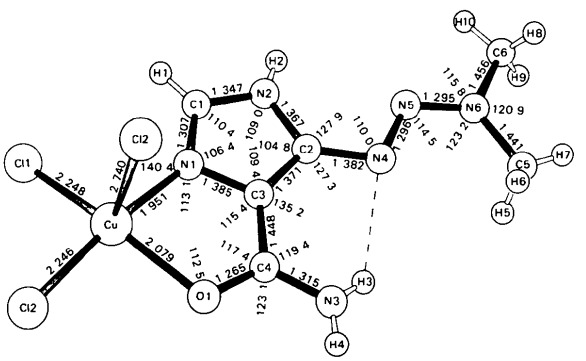

Fig. 2. Molecular geometry and dimensions [bond lengths (Å) and angles (°)] of complex (II). The e.s.d.'s are 0·002 Å for bonds involving the Cu atom and 0·004 Å for all other bonds, 0·1° for bond angles involving the Cu atom and 0·3° for all other angles.

Coordination of the copper atoms

Both complexes contain five-coordinate Cu atoms with square-pyramidal geometries. In each case the equatorial donor atoms are two Cl atoms in *cis* positions, and the O(amide) and adjacent N(imidazole) of a DTIC molecule. In (I) the axial donor is the O atom of a methanol molecule. The second methanol molecule in the formula unit of this compound is not coordinated but is involved in hydrogen bonding. In (II), where the crystals contain no solvent molecules, the complexes form centrosymmetric dimers. The axial coordination position of each Cu is occupied by a Cl(2) atom, which is simultaneously an equatorial donor with respect to the other Cu of the dimer. Thus the Cu atoms of the dimer are linked by double Cl bridges, each Cl being equatorial with respect to one Cu and axial with respect to the other.

There are significant differences between the details of the coordination geometries of the Cu atoms in (I) and (II). Corresponding bond lengths and angles involving the Cu atoms are compared in Table 4. The deviations from a least-squares plane fitted to the four equatorial donor atoms in (I) are Cl(1) 0·00, Cl(2) 0·00, O(1) −0·02, N(1) 0·02, Cu 0·16 Å. The corresponding deviations in (II) are Cl(1) −0·14, Cl(2) 0·13, O(1) −0·17, N(1) 0·17, Cu 0·17 Å. We ascribe the greater displacements from the equatorial plane in (II) to a pair of short non-bonded O(1)···Cl(2) contacts (3·447 Å) in the dimer.*

* A referee has suggested that a more plausible reason for the greater displacements in (II) is the formation of the bond from Cl(2) to the second Cu of the dimer. The formation of the bridging bond causes Cl(2) to be displaced to one side of the equatorial plane, while Cl(1) is displaced to the other side in order to maintain a respectable Cl···Cl separation (3·29 Å). The same referee has pointed out (correctly) that the displacements from the least-squares plane in (I) were calculated with, and those in (II) without, allowance for coordinate errors. The conclusions are not affected by this inconsistency.

Table 4. *Bond distances* (Å) *and angles* (°) *involving the copper atom in* $Cu(DTIC)Cl_2.2CH_3OH$ (I) *and* $Cu(DTIC)Cl_2$ (II)

	(I)	(II)
Cu–N(1)	1·970 (2)	1·951 (2)
Cu–O(1)	2·035 (2)	2·079 (2)
Cu–Cl(1)	2·237 (1)	2·248 (1)
Cu–Cl(2)	2·226 (*1*)	2·246 (*1*)
$Cu–O(2)_{axial}$	2·477 (1)	–
$Cu–Cl(2)_{axial}$	–	2·740 (1)
N(1)–Cu–O(1)	79·4 (1)	81·4 (1)
N(1)–Cu–Cl(1)	94·1 (1)	92·3 (1)
N(1)–Cu–Cl(2)	166·5 (1)	173·3 (1)
N(1)–Cu–O(2)/Cl(2)	94·5 (1)	87·9 (1)
O(1)–Cu–Cl(1)	169·0 (1)	161·7 (1)
O(1)–Cu–Cl(2)	89·3 (1)	91·9 (1)
O(1)–Cu–O(2)/Cl(2)	92·9 (1)	89·9 (1)
Cl(1)–Cu–Cl(2)	95·8 (3)	94·2 (4)
Cl(1)–Cu–O(2)/Cl(2)	96·3 (1)	107·1 (5)
Cl(2)–Cu–O(2)/Cl(2)	95·5 (1)	91·9 (5)

The DTIC ligands

The most important difference between the two complexes is that the triazene groups have different configurations (Figs. 1 and 2). In complex (II) the triazene group has the same orientation as has already been found in the two tautomers of DTIC (Freeman & Hutchinson, 1979) and in $HDTIC^+$ (Edwards, Sherfinski & Marsh, 1974). The sequence N(2)–C(2)–N(4)–N(5) is in the *syn* configuration. There is an intramolecular hydrogen bond between the triazene and carboxamide groups [N(3)–H···N(4) = 3·120 Å]. This hydrogen bond in (II) is weaker than similar bonds in DTIC (2·868, 2·908 Å) and $HDTIC^+$ (2·974 Å). In complex (I) a new configuration is created by a 180° rotation of the triazene group about the C(2)–N(4) bond. The configuration of the sequence N(2)–C(2)–N(4)–N(5) is now *anti*. This makes possible a strong intramolecular hydrogen bond involving atom N(5) instead of N(4) [N(3)–H···N(5) = 2·887 Å].

The bond lengths and angles of the ligands are shown in Figs. 1 and 2. The bond C(3)–C(2) is the only case where corresponding bond lengths in the two complexes [1·387 (3), 1·371 (4) Å] differ by an apparently significant amount [0·016 (5) Å]. A single bond-order difference, not accompanied by changes in bond order elsewhere in the molecules, is unlikely to occur. We conclude that the e.s.d.'s of the atomic positions are larger (possibly by 20%) than the values derived from the least-squares refinements. On the other hand, there are highly significant differences between several pairs of corresponding bond angles in (I) and (II). These include C(3)–C(4)–N(3) in the carboxamide group [121·8 (2), 119·4 (3)°], C(2)–N(4)–N(5) in the triazene group [112·2 (2), 110·0 (3)°], and the external bond angles at the atoms C(2) and C(3) where the side chains are attached to the imidazole ring [C(3)–C(2)–N(4) = 138·9 (2), 127·3 (3)°; N(2)–C(2)–N(4) = 116·4 (2), 127·9 (3)°; N(1)–C(3)–C(4) = 112·9 (2), 115·4 (3)°; C(2)–C(3)–C(4) = 138·4 (2), 135·2 (3)°]. The differences at C(2) can be attributed to a bending of the C(2)–N(4) bond away from the carboxamide group when the triazene group of complex (I) adopts the new configuration. The differences at C(3) are due to a greater movement of the carboxamide group towards the Cu^{II} in (I) than in (II).

A table summarizing the molecular dimensions of DTIC in complexes (I) and (II), in the two tautomers of DTIC itself (Freeman & Hutchinson, 1979), and in $HDTIC^+$ (Edwards *et al.*, 1974) has been deposited (see footnote concerning supplementary material). There is an increase in the amide C=O bond length from 1·23 to 1·26 Å, a decrease in the amide C–N bond length from 1·33 to 1·31 Å, and a decrease in the imidazole bond length C(1)–N(1) from 1·33 to 1·31 Å when Cu^{II} is chelated between atoms O(1) of the amide

group and N(1) of the imidazole group. The formation of the chelate also causes a movement of the carboxamide group towards the Cu^{II} atom, resulting in a decrease of the angle N(1)–C(3)–C(4) and an increase of the angle C(2)–C(3)–C(4). If the values already cited for these angles are compared with the corresponding values in DTIC and $HDTIC^+$, it is found that the movement of the carboxamide is greater for the *anti* configuration of the triazene group in (I) than for the *syn* configuration in (II). Further, the angles between bond C(2)–N(4) and the imidazole ring are relatively unchanged in going from free DTIC to complex (II) but indicate a bending of the C(2)–N(4) bond away from the carboxamide group in complex (I). These movements together with the 'new' triazene configuration in (I) account for the previously mentioned differences between the intramolecular hydrogen-bond lengths in the various molecular species.

The hydrogen-bonded contacts are listed in Table 5 and illustrated in Figs. 3 and 4.

Discussion

The present work shows that the binding of Cu^{II} by DTIC can affect the configuration of the triazene group, and causes significant changes in the orientations of the carboxamide and triazene groups with respect to the imidazole ring. The potential physiological significance of this result is that it provides a rationalization for the modification of the activity of DTIC by Cu^{II} *in vivo*. Even though the detailed mechanism of the action of DTIC is unknown, it is clear that structural changes of the types observed are sufficient to cause changes in the reactivity, stability or transport properties of the molecule.

The weakness of this argument is that complexes (I) and (II), from which our results were obtained, crystallize at pH <7. A different complex, (III), is formed at pH 7. Initially we were able to isolate (III) only as an amorphous powder. Infrared spectra recorded from pure DTIC and from complexes (I*b*), (II) and (III) enable us to draw some conclusions about the nature of (III).

Table 5. *Hydrogen bonds*

(I) $Cu(DTIC)Cl_2.2CH_3OH$

Superscripts refer to the following equivalent positions:

None x, y, z (iii) $x, 1+y, z$
(i) $1-x, 1-y, 1-z$ (iv) $1-x, 1+y, -z$.
(ii) $x, -1+y, z$

X–H···Y	X–Y (Å)	H···Y (Å)	∠X–H···Y (°)
N(2)–H(2)···O(3)	2·733 (3)	1·88 (3)	178 (3)
N(3)–H(3)···N(5)	2·887 (3)	2·07 (3)	145 (2)
O(3)–H(15)···O(2^{ii}) / O(3^{iii})–H(15^{iii})···O(2)	2·828 (3)	2·18 (3)	163 (4)
N(3)–H(4)···O(1^{i}) / N(3^{i})–H(4^{i})···O(1)	2·933 (3)	2·21 (2)	166 (2)
O(2)–H(11)···Cl(2^{iv}) / O(2^{iv})–H(11^{iv})···Cl(2)	3·246 (2)	2·71 (3)	158 (4)

(II) $Cu(DTIC)Cl_2$

Superscripts refer to the following equivalent positions:

None x, y, z (ii) $1-x, -\frac{1}{2}+y, 1\frac{1}{2}-z$.
(i) $1-x, -\frac{1}{2}+y, \frac{1}{2}-z$

X–H···Y	X–Y (Å)	H···Y (Å)	∠X–H···Y (°)
N(3)–H(3)···N(4)	3·120 (4)	2·51 (3)	136 (3)
N(3)–H(4)···Cl(1^{i}) / N(3^{ii})–H(4^{ii})···Cl(1)	3·243 (3)	2·46 (4)	177 (3)
N(2)–H(2)···Cl(2^{iii}) / N(2^{i})–H(2^{i})···Cl(2)	3·150 (3)	2·47 (3)	150 (3)

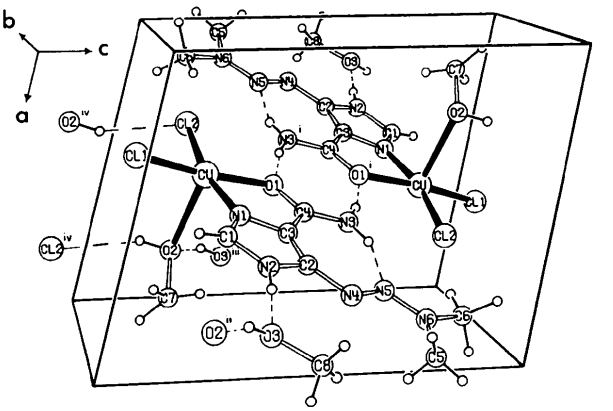

Fig. 3. Packing diagram for the unit cell of complex (I). Hydrogen bonds are shown as dashed lines and the superscripts refer to the equivalent positions of Table 5.

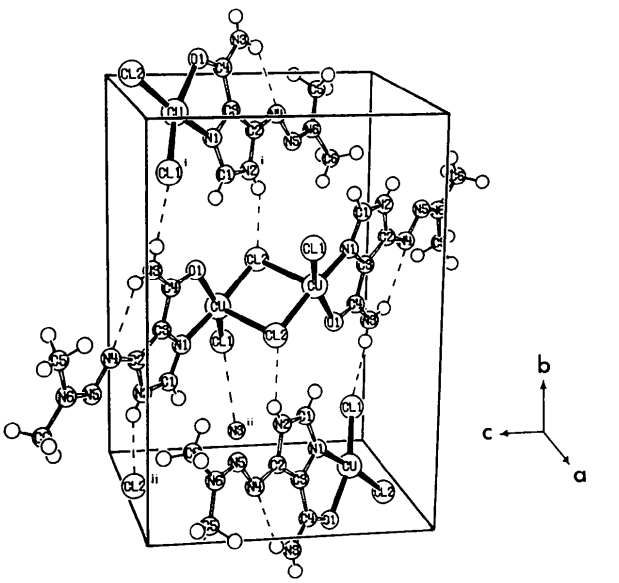

Fig. 4. Packing diagram for the unit cell of complex (II). Hydrogen bonds are shown as dashed lines and the superscripts refer to the equivalent positions of Table 5.

The infrared spectroscopic region of interest is 1660–1580 cm^{-1}. Each of the compounds studied has two bands in this region, due to the C=O(amide) and N=N(triazene) groups. In the spectrum of DTIC the band at higher frequency occurs at 1657 cm^{-1}. This band is assigned to C=O(amide) since it is lowered to 1639 and 1638 cm^{-1} in (I*b*) and (II), respectively, where the O(amide) is known to be coordinated. The lower frequency band of DTIC (1611 cm^{-1}) remains virtually unchanged in (I*b*) (1614 cm^{-1}) and (II) (1615 cm^{-1}). This is consistent with the fact that the triazene group is not coordinated in either of these complexes.

The amorphous complex (III) has infrared bands at 1635 and 1582 cm^{-1}, suggesting that Cu^{II} is bound not only to the amide but also to the triazene group. Recently we have crystallized a Cu–DTIC complex at pH 7 in the presence of glycine. This complex has infrared bands at 1625 and 1590 cm^{-1}, again indicating two binding sites for Cu^{II}. We are currently undertaking the crystal structure analysis of this complex.

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