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# The hydrated and anhydrous gold(III) tetrachloride salts of L-ecgonine, an important forensic toxicology marker for cocaine

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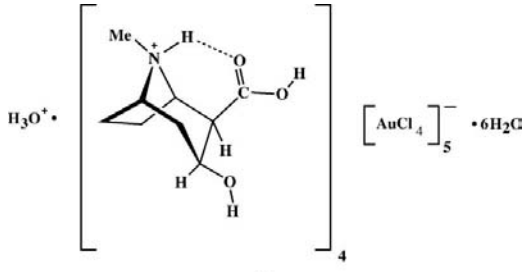
The structure of the hydrated gold(III) tetrachloride salt of L-ecgonine {hydronium tetrakis[(1*R*,2*R*,3*S*,5*S*,8*S*)-3-hydroxy-8-methyl-8-azoniabicyclo[3.2.1]octane-2-carboxylate pentakis[tetrachloridoaurate(III)] hexahydrate}, $(C_9H_{16}NO_3)_4(H_3O)[AuCl_4]_5\cdot 6H_2O$, demonstrates an unprecedented stoichiometric relationship between the cations and anions in the unit cell. The previous tropane alkaloid structures, including the related hydrochloride salts, all have a cation–anion ratio of 1:1, as does the anhydrous salt described here, namely (1*R*,2*R*,3*S*,5*S*,8*S*)-3-hydroxy-8-methyl-8-azoniabicyclo[3.2.1]-octane-2-carboxylate tetrachloridoaurate(III), $(C_9H_{16}NO_3)[AuCl_4]$. The hydrated salt, however, consists of four monopositive N-protonated units of the alkaloid and five $[AuCl_4]^-$ counter-ions, plus seven solvent water molecules. The H atom required for change balance has been assigned to a water molecule. In addition, the hydrate has a novel arrangement, with all seven of the water molecules and all of the O atoms in the cations participating in an alternating arrangement of interleaved sheets of the anionic species. Both the hydrate and the anhydrous salt of the same toxicologically important marker for cocaine show that the cation and anion are in close proximity to each other, as was found in the gold(III) tetrachloride salt of L-cocaine.

## Comment

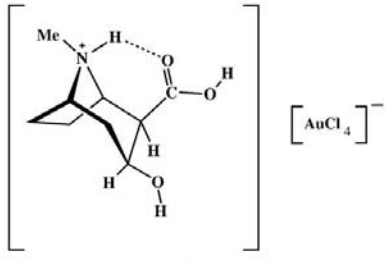
L-Ecgonine and L-cocaine are among 22 naturally occurring alkaloids found in the leaves of the coca plant, *i.e. Erythroxylum coca* (Ensing & Hummelen, 1991). L-Ecgonine ($C_9H_{15}NO_3$), a nitrogen-bridged bicyclo[3.2.1]octane, is both a precursor and a human metabolite of L-cocaine. It is the hydroxy acid obtained by complete acidic, alkaline or enzymatic hydrolysis of both ester functions in L-cocaine, and can crystallize as the hydrochloride salt (Wood *et al.*, 2008). During *in vitro* storage of blood, cocaine can undergo selective monohydrolysis *via* two mechanisms, *viz.* partial saponification under alkaline conditions to yield benzoyl ecgonine or enzymatic hydrolysis catalyzed by pseudocholinesterase to yield methyl ecgonine (ecgonine methyl ester) (Isenschmid *et al.*, 1989). Both of these breakdown products can degrade further to a common stable product, L-ecgonine (Klingmann *et al.*, 2001), which is consistently observed in *post mortem* blood specimens and whole-blood specimens of cocaine addicts, thus demonstrating the utility of L-ecgonine as a stable marker for recent cocaine use (Logan, 2001). Because time, temperature, drug concentration and the presence of preservative agents can all affect the stability of cocaine in blood and plasma (Baselt, 1983), L-ecgonine, the fully hydrolyzed degradation product, is a much better marker for cocaine use than either benzoyl ecgonine or ecgonine methyl ester.

The use of the gold(III) chloride microcrystal test in the identification and differentiation of L-cocaine from its seven stereoisomers (Allen *et al.*, 1981) and similar related structures, *i.e.* L-ecgonine (Amelink, 1938), has been described by the current authors in a previous paper (Wood *et al.*, 2007).

In studying the three-dimensional structures of several cocaine derivatives, the authors have previously reported those of the gold(III) tetrachloride salt of L-cocaine (Wood *et al.*, 2007) and of the hydrochloride salt of L-ecgonine (Wood *et al.*, 2008). We report here the structures of the gold(III) tetrachloride salt of L-ecgonine, which exists as both the hydrate form, $(C_9H_{16}NO_3)_4(H_3O)[AuCl_4]_5\cdot 6H_2O$, (I), and the anhydrous form, $(C_9H_{16}NO_3)[AuCl_4]$, (II).




(I)




(II)

The asymmetric unit of (I) contains four monopositive N-protonated L-ecgonine cations surrounded by five $[AuCl_4]^-$ anions. For charge balance, one of the seven water molecules has to be a hydronium ion or one of the hydroxy groups of the cations has to be diprotonated. However, the additional proton was not found and we have no evidence as to whether

† Deceased.

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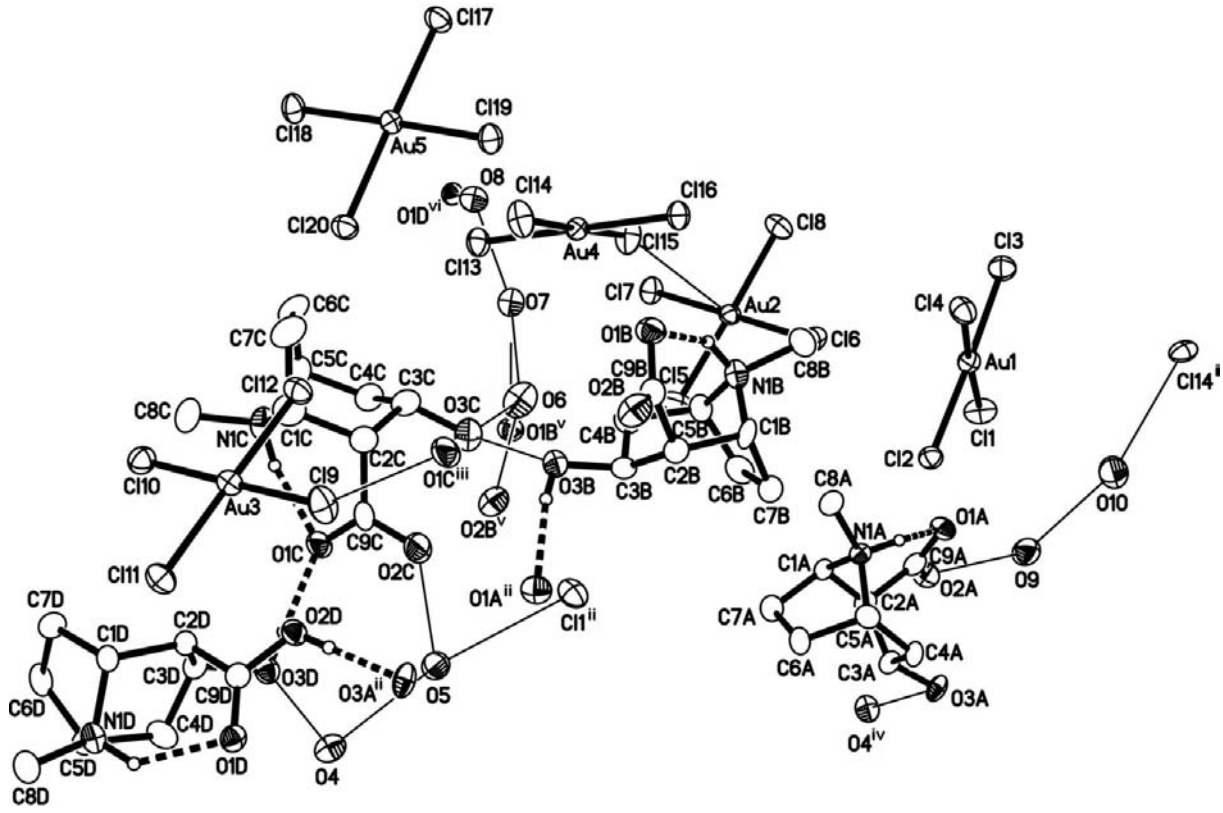


**Figure 1**
The asymmetric unit of (I), showing the atom-numbering scheme and including nine symmetry-related atoms to show the hydrogen bonding or close contacts. Displacement ellipsoids are drawn at the 40% probability level. All C-bound H atoms have been omitted for clarity. The four monopositive N-protonated L-ecgonine cations are surrounded by five $[AuCl_4]^-$ counter-ions plus seven water molecules, one of which (not identified) could exist as a hydronium ion, for charge balance. Heavy dashed lines indicate the intramolecular hydrogen bond in each cation and the locations of the known hydrogen bonds in the structure. Thin solid lines show the intermolecular close contacts. [Symmetry codes: (i) $-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$; (ii) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$; (iii) $x+1, y, z$; (iv) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$; (v) $x-1, y, z$; (vi) $x-1, y+1, z$.]

it is consistently positioned in the structure. Each of the four L-ecgonine cations has its quaternary N-bound H atom intramolecularly hydrogen bonded to its carboxyl C═O group (Table 2, entries 1–4), as was found in (−)-norcocaine [N···O = 2.306 (2) Å; Zhu *et al.*, 1994], in the tetrachloridoaurate(III) salt of L-cocaine [N···O = 2.756 (6) Å; Wood *et al.*, 2007], and in the hydrochloride salt of L-ecgonine [N···O = 2.7608 (17) Å; Wood *et al.*, 2008]. All of the L-ecgonine cations in (I) have ordered carboxyl groups, except for molecule *B* where C9*B*—O1*B* = 1.261 (13) Å and C9*B*—O2*B* = 1.280 (15) Å. As a result of this disorder, the acid H atom of this cation could not be found.

Four of the five $[AuCl_4]^-$ anions of (I) exhibit square-planar geometry, with mean deviations from the five-atom plane ranging from 0.006 (3) (for the Au3 anion) to 0.013 (2) Å (for the Au4 anion). The fifth anion (containing Au1) has a mean deviation from the plane of 0.048 (3) Å, with the $Au^{III}$ center 0.0069 (11) Å above the best plane. In this anion, one *trans* pair of Cl atoms is above the best plane by 0.051 (2) Å and the other pair below the plane by 0.054 (2) Å. In a search of the Cambridge Structural Database (CSD, Version 5.29, update of 2008; Allen, 2002), 106 structures containing the gold(III) tetrachloride anion were found, several containing multiple $[AuCl_4]^-$ species, for a total of 136 different anions. Of these, 71 are essentially flat, and the rest have varying degrees of bowing of the square-planar arrangement of the $[AuCl_4]^-$ moiety. Only three show flexing larger than that found in (I), namely tetra(methylthio)tetrathiafulvalene bis(tetrachloroaurate) (refcode GEHSOB01; Jones, 1989), the gold(III) tetrachloride salt of L-cocaine (refcode SETLOT; Wood *et al.*, 2007) and *N*-benzyl-*N*,*N*-bis(pyridinium-2-ylmethyl)amine chloride tetrachloroaurate(III) (refcode NIBWEB; Cao *et al.*, 2007).

Within the asymmetric unit of (I) there are three short Cl···O distances (Table 1), two of which involve water molecules and are 0.05–0.06 Å shorter than the relevant van der Waals sum of 3.27 Å (Bondi, 1964), while the third is proximal to the acid carbonyl of an L-ecgonine cation and is shorter than the van der Waals sum by 0.12 Å. Additionally, a single close contact exists between atom Cl15 of the Au4 anion and Au2 (Table 1), which is slightly longer than the shortest reported Au—Cl···Au contact of 3.281 Å found in the CSD (refcode VIMFUS; Dvorkin *et al.*, 1990). Since this Au4 anion uniquely resides in a cavity surrounded predominantly by O atoms, we speculate that this close contact is a result of its location.

Intermolecular hydroxy-to-carbonyl hydrogen bonds (Table 2, entries 5 and 6) and the one acid-to-hydroxy

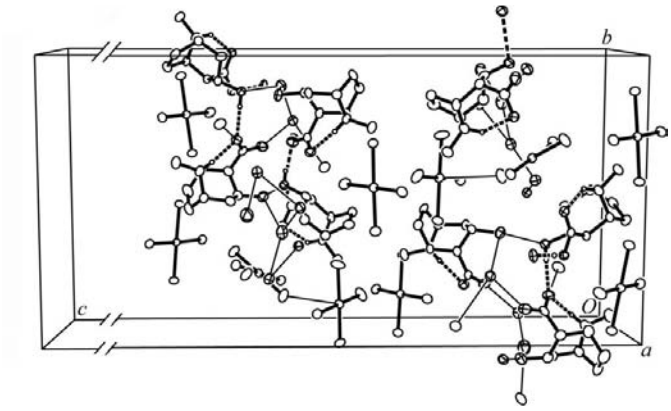


**Figure 2**
A partial packing diagram for (I), showing two asymmetric units. For the sake of simplicity, only half of the unit cell along the *c* direction is shown; the other half of the cell is generated by the screw axis. The N—H···O hydrogen bonding within each of the four organic cations and that between molecules is shown by dashed lines. Thin solid lines show the intermolecular close contacts. The bands of O atoms (shown as full ellipsoids with shaded octants) are clearly seen, and repeat every quarter of the cell length along *c*. For clarity, all C-bound H atoms have been omitted. Displacement ellipsoids are drawn at the 40% probability level.

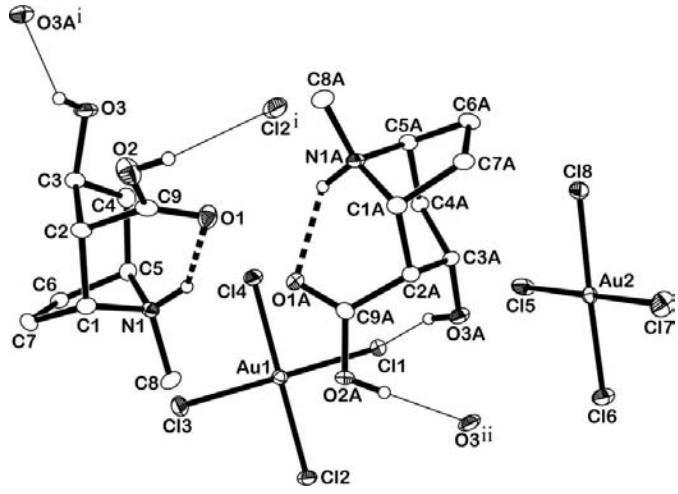


**Figure 3**
The asymmetric unit of (II), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 40% probability level. All C-bound H atoms have been omitted for clarity. The two independent L-ecgonine cations and their tetrachloridoaurate(III) counter-ions are shown. Three symmetry-related atoms are included to show the hydrogen bonding or close contacts. Heavy dashed lines indicate the intramolecular hydrogen bond in each cation and thin solid lines indicate intermolecular hydrogen bonding involving various acceptors. [Symmetry codes: (i) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$; (ii) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$.]

hydrogen bond (entry 7) are the only interactions involving H atoms which could be reliably located.

Within the structure of (I), a network of water molecules was found. It contains close contacts of various types (see Table 1): acid-to-water (entries 9 and 10), hydroxy-to-water (entries 11 and 12), hydroxy-to-hydroxy (entry 13), water-to-acid (entry 14), water-to-carboxyl (entries 15 and 16) and water-to-hydroxy (entry 17). Although the H atoms involved could not be found in difference electron-density maps, the proximity of the donor and acceptor atoms clearly demonstrates that hydrogen bonding exists throughout the structure and forms a network of water molecules which threads its way through the cations and anions.

The cations are all joined into a network by either hydrogen bonds or close contacts, through either their hydroxy or their acid functional groups, to adjacent solvent water molecules. These contacts, plus those between the water molecules, form a two-dimensional layer approximately 3.55 Å thick containing all of the O atoms present in the structure and extending in the *a* and *b* cell directions (Fig. 2). These layers are interleaved with sheets of $[AuCl_4]^-$ anions, recurring every quarter of the cell along *c*. Four of the five anions lie within the alternating parallel sheets of $[AuCl_4]^-$ anions, but the Au4 anion resides within the stratum of O atoms.

The anhydrous salt, (II), of the same toxicologically important marker for cocaine (Fig. 3) shows that the cation and anion are again in close proximity to each other, as was found in (I) and in the gold(III) tetrachloride salt of L-cocaine (Wood *et al.*, 2007). Each of the two unique L-ecgonine cations has its quaternary N-bound H atom intramolecularly hydrogen bonded to its carboxyl C═O group (Table 3).

The two independent $[AuCl_4]^-$ anions of (II) show a bowing of the square-planar arrangement. The Au1 anion has a mean deviation from the plane of 0.0132 (11) Å, with the $Au^{III}$ center 0.0082 (4) Å below the best plane. One *trans* pair of Cl atoms is above the best plane by 0.160 (5) Å and the other below the plane by 0.120 (5) Å. The Au2 anion has a mean deviation from the plane of 0.0174 (13) Å, with the $Au^{III}$ center 0.0117 (5) Å below this plane. One *trans* pair of Cl atoms is above the plane by 0.212 (6) Å and the other below the plane by 0.152 (6) Å.

There are two close hydrogen-bonded contacts involving Cl atoms, one between hydroxy atom O3*A* and atom Cl1, and the other between acid atom O2 and atom Cl2$^{i}$ [Table 3; symmetry code: (i) $x-1, y+\frac{1}{2}, -z+\frac{1}{2}$]. There are also two hydrogen bonds involving the hydroxy O atoms, between atoms O3 and O3*A*$^{i}$, and between atoms O2*A* and O3$^{ii}$ [symmetry code: (ii) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$]. The latter involves the acid H atom in the rare *anti* configuration.

The powder diffraction pattern of the microcrystals [formed as described by Wood *et al.* (2007)] does not uniquely match either the hydrated structure, (I), nor the anhydrous structure, (II), of the ecgonine $Au^{III}$ chloride complex, but has peaks associated with both of them. There are more peaks that are similar to the pure single-crystal generated powder pattern of the anhydrous material, (II), than to that of the hydrate, (I). However, we cannot conclusively say that the microcrystal test material is one or the other, or a combination of the two (possibly because of the humidity or lack thereof in the laboratory preparations), or a completely different form.

## Experimental

For (I), an aqueous solution (200 µl) containing L-ecgonine hydrochloride (100 µg) was combined with a 0.24% gold(III) chloride ($HAuCl_4·3H_2O$) solution in 0.24 *M* HCl (200 µl). Slow evaporation of

this mixture to dryness produced very light-yellow parallelepipeds of (I), which were used directly for X-ray analysis. For (II), the same preparation was repeated at a later date and the resulting crystals were used for X-ray analysis. These proved to be anhydrous, most probably because of the lack of humidity in the laboratory where the crystals were allowed to grow.

## Compound (I)

*Crystal data*

$(C_9H_{16}NO_3)_4(H_3O)[AuCl_4]_5\cdot 6H_2O$
$M_r$ = 2565.86
Orthorhombic, $P2_12_12_1$
$a$ = 9.2153 (16) Å
$b$ = 15.299 (3) Å
$c$ = 51.544 (8) Å
$V$ = 7267 (2) Å$^3$
$Z$ = 4
Cu $K\alpha$ radiation
$\mu$ = 25.82 mm$^{-1}$
$T$ = 100 K
0.35 × 0.11 × 0.10 mm

*Data collection*

Bruker SMART APEXII CCD area-detector diffractometer
Absorption correction: numerical (*SADABS*; Sheldrick, 2001)
$T_{min}$ = 0.040, $T_{max}$ = 0.182
43458 measured reflections
12355 independent reflections
12097 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.057

*Refinement*

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.099
$S$ = 1.08
12355 reflections
761 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 3.15 e Å$^{-3}$
$\Delta\rho_{min}$ = −1.94 e Å$^{-3}$
Absolute structure: Flack (1983), with 5212 Friedel pairs
Flack parameter: 0.031 (10)

## Compound (II)

*Crystal data*

$(C_9H_{16}NO_3)[AuCl_4]$
$M_r$ = 524.99
Orthorhombic, $P2_12_12_1$
$a$ = 10.0276 (1) Å
$b$ = 15.7339 (2) Å
$c$ = 18.6416 (2) Å
$V$ = 2941.15 (6) Å$^3$
$Z$ = 8
Cu $K\alpha$ radiation
$\mu$ = 25.50 mm$^{-1}$
$T$ = 100 K
0.23 × 0.17 × 0.10 mm

*Data collection*

Bruker SMART APEXII CCD area-detector diffractometer
Absorption correction: numerical (*SADABS*; Sheldrick, 2001)
$T_{min}$ = 0.067, $T_{max}$ = 0.185
22091 measured reflections
5121 independent reflections
5053 reflections with $I > 2\sigma(I)$
$R_{int}$ = 0.035

*Refinement*

$R[F^2 > 2\sigma(F^2)]$ = 0.018
$wR(F^2)$ = 0.047
$S$ = 1.08
5121 reflections
332 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.93 e Å$^{-3}$
$\Delta\rho_{min}$ = −0.69 e Å$^{-3}$
Absolute structure: Flack (1983), with 2199 Friedel pairs
Flack parameter: −0.004 (7)

All N- and C-bound H atoms, and two of the four hydroxy H atoms for (I) and both of the hydroxy H atoms for (II), were found in electron-density difference maps. For (I), three of the four carboxylic acid H atoms were found, but the remaining acid H atom was disordered and not found. For (II), both of the acid H atoms were located. The hydroxy and acid H atoms were constrained to idealized positions, with distances fixed at O—H = 0.84 Å and with $U_{iso}$(H) = 1.5$U_{eq}$(O). The methyl H atoms were placed in ideally staggered positions, with C—H = 0.98 Å and $U_{iso}$(H) = 1.5$U_{eq}$(C). The methylene and methine H atoms were placed in geometrically idealized positions and constrained to ride on their parent C atoms, with C—H = 0.99 and 1.00 Å, respectively, and with $U_{iso}$(H) = 1.2$U_{eq}$(C). In (I), because of the small contribution to their total electron density in the cell, no water H atoms were found in difference maps.

For both compounds, data collection: *APEX2* (Bruker, 2006); cell refinement: *APEX2*; data reduction: *SAINT* (Bruker, 2005); program(s) used to solve structure: *SHELXTL* (Sheldrick, 2008); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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**Table 1**
Selected interatomic distances (Å) for (I).

| | | | |
|---|---|---|---|
| O10···Cl14$^{i}$ | 3.217 (11) | O2*C*···O5 | 2.600 (12) |
| O5···Cl1$^{ii}$ | 3.214 (8) | O3*A*···O4$^{iv}$ | 2.773 (11) |
| Cl9···O1*C*$^{iii}$ | 3.150 (8) | O3*D*···O4 | 2.676 (11) |
| Cl15···Au2 | 3.361 (3) | O3*C*···O3*B* | 2.739 (11) |
| O4···O5 | 2.893 (12) | O6···O2*B*$^{v}$ | 2.646 (14) |
| O6···O7 | 3.012 (12) | O8···O1*D*$^{vi}$ | 2.967 (11) |
| O7···O8 | 2.820 (11) | O7···O1*B*$^{v}$ | 2.883 (11) |
| O9···O10 | 2.707 (15) | O6···O3*C* | 2.713 (12) |
| O2*A*···O9 | 2.538 (12) | | |

Symmetry codes: (i) $-x+1, y+\frac{1}{2}, -z+\frac{3}{2}$; (ii) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$; (iii) $x+1, y, z$; (iv) $-x, y+\frac{1}{2}, -z+\frac{3}{2}$; (v) $x-1, y, z$; (vi) $x-1, y+1, z$.

**Table 2**
Hydrogen-bond geometry (Å, °) for (I).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N1*A*—H1*NA*···O1*A* | 0.93 | 2.04 | 2.792 (11) | 137 |
| N1*B*—H1*NB*···O1*B* | 0.93 | 1.99 | 2.757 (11) | 138 |
| N1*C*—H1*NC*···O1*C* | 0.93 | 2.00 | 2.734 (12) | 134 |
| N1*D*—H1*ND*···O1*D* | 0.93 | 2.07 | 2.814 (11) | 136 |
| O3*D*—H3*D*1···O1*C* | 0.84 | 1.90 | 2.743 (10) | 179 |
| O3*B*—H3*B*1···O1*A*$^{ii}$ | 0.84 | 2.02 | 2.852 (10) | 172 |
| O2*D*—H2*D*1···O3*A*$^{ii}$ | 0.84 | 1.81 | 2.645 (10) | 180 |

Symmetry code: (ii) $-x+1, y-\frac{1}{2}, -z+\frac{3}{2}$.

**Table 3**
Hydrogen-bond geometry (Å, °) for (II).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| N1—H1···O1 | 0.93 | 1.99 | 2.768 (4) | 140 |
| N1*A*—H1*A*···O1*A* | 0.93 | 1.97 | 2.721 (5) | 137 |
| O3*A*—H3*A*···Cl1 | 0.84 | 2.43 | 3.219 (3) | 157 |
| O2—H2···Cl2$^{i}$ | 0.84 | 2.32 | 3.159 (3) | 173 |
| O3—H3···O3*A*$^{i}$ | 0.84 | 1.95 | 2.672 (4) | 144 |
| O2*A*—H2*A*···O3$^{ii}$ | 0.84 | 1.82 | 2.624 (4) | 161 |

Symmetry codes: (i) $-x+1, y+\frac{1}{2}, -z+\frac{1}{2}$; (ii) $-x+1, y-\frac{1}{2}, -z+\frac{1}{2}$.

mentor, teacher and friend at Rutgers University–Newark for over 44 years.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SQ3203). Services for accessing these data are described at the back of the journal.

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