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Crystal and Molecular Structure of (Nitrato)(1-methylcytosine)silver(I): An Unusual Cross-Linked Polymer Containing a Heavy Metal and a Modified Nucleic Acid Constituent

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A single-crystal X-ray diffraction analysis on the complex (nitrato)(1-methylcytosine)silver(I) is presented. Crystals of the complex are triclinic with the following crystal data: a = 10.474 (3) Å, b = 11.141 (3) Å, c = 3.642 (1) Å, α = 97.33 (2)°, β = 95.82 (2)°, γ = 76.76 (2)°, V = 409.2 Å^3, space group $P\bar{1}$, Z = 2 [for $[Ag(C_5H_7N_3O)(NO_3)]$, mol wt 295.0]. Intensity data were collected in the θ–2θ scan mode on an automated diffractometer. The structure was solved by Patterson and Fourier methods and refined by full-matrix least squares to an R value of 0.033. The packing motif in the crystal is that of a dimeric $[Ag(1\text{-methylcytosine})(NO_3)]_2$ complex with each of the 1-methylcytosine residues doubly cross-linked by two Ag^+ ions through the base binding sites N(3) and O(2). Propagation of this dimeric unit along the crystallographic c axis via a second type of Ag–O(2) bond and base–base overlap yields a two-stranded, cross-linked polymer with the base residues slightly out of register. An attempt is made to relate these observed properties to the binding of Ag(I) to regions of high G–C content in duplex DNA.

Introduction

Many of the important features of the binding of Ag(I) to polynucleotides are well-known. Ag(I), like Hg(II), has one of the highest propensities for binding at base (purine or pyrimidine) sites over phosphate groups.[1,2] Within an assemblage of bases in a polynucleotide, Ag(I) has a marked preference for regions of high G–C[3] content;[2,4] in fact this preference for high G–C regions by Ag(I) has been employed in the separation of DNA molecules of varying base composition.[5] This strong base binding by Ag(I) leads, instead of the unwinding of duplex DNA, to interpolation between the strands and, thus, to a very rigid complex.[1,5]

Solution studies also show that Ag(I) can deprotonate poly rI[N(1)] and poly rU[N(3)] but has no effect on proton ionization in poly rA and poly rC.[6] Tu and Reinosa[7] have accumulated similar evidence that Ag(I) has a pronounced effect on the titration curve for guanosine, and this and other results led them to suggest that Ag–N(7),O(6) and Ag–N(1),O(6) are important chelation modes of binding for guanosine.

While the overall characteristics of the binding of Ag(I) to G–C regions of polynucleotides are at hand, there is surprisingly little known about the details of the binding of Ag(I) to G and C. Until recently, no structural data were known for Ag(I)–C complexes and there remains an absence of data on Ag(I)–G compounds. We[8] have recently reported on the preparation and some of the molecular properties of an interesting complex between $AgNO_3$ and 1-methylcytosine [where the N(1) position on the base is blocked as in cytidine and cytidine 5′-monophosphate]. The very simple empirical formula of this complex belies the complexity of its molecular and structural features. In this report, we present a detailed analysis of the structural properties of this complex and attempt to relate these properties to the binding of Ag(I) to G–C regions of polynucleotides.

Experimental Section

Crystals of the title complex were prepared by the reaction of equal molar quantities of $AgNO_3$ and protonated 1-methylcytosine perchlorate in dilute nitiric acid. The crystals are slightly photosensitive. Pertinent crystal data are collected in Table I. Intensity data were collected on a parallelepiped with the following faces and mean dimensions: (010)–(0$\bar{1}$0) 0.15 mm, (100)–($\bar{1}$00) 0.13 mm, (001)–(00$\bar{1}$) 0.37 mm. The long axis of the crystal was mounted approximately along the ϕ axis of a Syntex $P1$ automated diffractometer. The intensities of 4009 reflections in the full sphere to 2θ = 55° were collected in the θ–2θ scan mode employing graphite-monochromatized Mo Kα radiation. The intensities of three standards were monitored after every 100 reflections and showed no systematic variation over the course of the experiment (the maximum variation of any standard from its mean intensity was about 3%).

Table I. Crystal Data for (Nitrato)(1-methylcytosine)silver(I)

a = 10.474 (3) Å	$[Ag(C_5H_7N_3O)(NO_3)]$
b = 11.141 (3) Å	mol wt 295.0
c = 3.642 (1) Å	space group: $P\bar{1}$
α = 97.33 (2)°	Z = 2
β = 95.82 (2)°	d_{measd} = 2.37 (1) g cm^{-3}
γ = 76.76 (2)°	d_{calcd} = 2.37 g cm^{-3}
V = 409.2 Å^3	λ(Mo K$\bar{\alpha}$) = 0.710 69 Å
	μ(Mo K$\bar{\alpha}$) = 23.8 cm^{-1}

The 4009 measured intensities were assigned observational variances based on the equation $\sigma^2(I) = S + (B_1 + B_2)(T_S/2T_B)^2 + (pI)^2$, where S, B_1, and B_2 are the scan and extremum background counts, T_S and T_B are the scan and individual background counting times ($T_B = T_S/4$), and p was taken to be 0.03 and represents the expected error proportional to the diffracted intensity.[9] The intensities and their standard deviations were corrected for Lorentz and polarization effects and for the effect of absorption (maximum and minimum transmission factors of 0.76 and 0.67, respectively). The data were then averaged to yield 1838 symmetry-independent values with $I_{av} \geq 0.5\sigma(I_{av})$. An approximate absolute scale was determined by the method of Wilson.[10]

All nonhydrogen atom positions were determined from a three-dimensional Patterson synthesis, while the positions of the hydrogen atoms were determined from a difference Fourier map at an intermediate stage in the refinement. Standard full-matrix least squares (nonhydrogen atoms anisotropic and hydrogen atoms isotropic), minimizing the quantity $\sum w(|F_o| - |F_c|)^2$, where $w = 4F_o^2/\sigma^2(F_o^2)$, led to a final R value ($\sum||F_o| - |F_c||/\sum|F_o|$) of 0.033. The final weighted R value $[\{\sum w(|F_o| - |F_c|)^2/\sum wF_o^2\}^{1/2}]$ and goodness of fit $[\{\sum w(|F_o| - |F_c|)^2/(NO - NV)\}^{1/2}$, where NO = 1838 independent observations and NV = 155 variable parameters] were 0.040 and 2.1, respectively. A final difference Fourier map had as its maximum feature a peak of 0.8 e/Å^3 near the Ag atom.

Neutral scattering factors for all atoms were taken from common sources (nonhydrogen atoms;[11] hydrogen atoms[12]). The real part of the scattering curves for the nonhydrogen atoms were corrected for anomalous dispersion effects. Final atomic parameters are collected in Table II. A list of observed and calculated structure factor amplitudes is available as supplementary material.

Discussion

The structure of (nitrato)(1-methylcytosine)silver(I) is dominated by the formation of centrosymmetric dimers in which the 1-methylcytosine ligands are bridged by two Ag^+ ions, Figure 1. Within these dimers, there are two strong metal–ligand bonds, Ag–N(3) = 2.225 (2) Å and Ag–O(2′) = 2.367 (2) Å. The formation of an eight-membered, macrochelate ring as shown in Figure 1 is common[14] to Ag(I)

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Table II. Final Atomic Parameters

atom	x	y	z	B_{11}[d]	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
Ag[a]	−7206 (2)	−12056 (2)	−13519 (7)	613 (3)	569 (3)	9619 (30)	2 (2)	1130 (6)	724 (6)
O(2)[b]	1585 (2)	−247 (2)	−3597 (6)	78 (2)	43 (2)	639 (16)	−10 (1)	65 (5)	43 (4)
O(3)[b]	−1444 (2)	−3222 (3)	1346 (8)	68 (2)	100 (3)	1047 (24)	4 (2)	40 (6)	139 (6)
O(4)[b]	−3478 (3)	−3354 (3)	334 (8)	101 (3)	86 (2)	1165 (26)	−53 (2)	107 (7)	18 (6)
O(5)[b]	−2852 (3)	−1785 (2)	−1200 (7)	90 (3)	59 (2)	1013 (23)	−11 (2)	10 (6)	110 (5)
N(1)[b]	3263 (2)	−1874 (2)	−4913 (6)	48 (2)	55 (2)	460 (16)	−15 (2)	27 (5)	46 (4)
N(3)[b]	1272 (2)	−2171 (2)	−3034 (6)	49 (2)	43 (2)	449 (16)	−10 (2)	19 (4)	38 (4)
N(4)[b]	1011 (3)	−4129 (2)	−2523 (8)	65 (3)	47 (2)	761 (22)	−14 (2)	47 (6)	68 (5)
N(5)[b]	−2601 (3)	−2790 (2)	126 (7)	63 (2)	49 (2)	600 (18)	−12 (2)	65 (5)	34 (5)
C(1)[b]	4062 (3)	−1018 (3)	−5625 (9)	67 (3)	77 (3)	626 (25)	−35 (2)	27 (7)	68 (7)
C(2)[b]	2007 (3)	−1398 (2)	−3832 (7)	50 (2)	45 (2)	343 (16)	−8 (2)	16 (5)	28 (4)
C(4)[b]	1770 (3)	−3405 (2)	−3339 (7)	55 (2)	46 (2)	396 (18)	−13 (2)	−4 (5)	43 (5)
C(5)[b]	3048 (3)	−3916 (3)	−4453 (8)	60 (3)	45 (2)	654 (23)	−4 (2)	34 (6)	46 (6)
C(6)[b]	3768 (3)	−3119 (3)	−5214 (8)	52 (3)	59 (2)	512 (20)	−5 (2)	41 (6)	35 (5)

atom	x	y	z	B, Å²	atom	x	y	z	B, Å²
H(11)[c]	369 (4)	−50 (4)	−799 (13)	4.5 (9)	H(42)[c]	135 (4)	−489 (4)	−221 (11)	3.6 (8)
H(12)[c]	408 (5)	−44 (5)	−329 (14)	5.0 (1.1)	H(50)[c]	339 (4)	−478 (4)	−465 (11)	2.9 (8)
H(13)[c]	488 (6)	−149 (5)	−614 (14)	5.6 (1.2)	H(60)[c]	470 (3)	−333 (2)	−617 (7)	1.5 (4)
H(41)[c]	28 (5)	−382 (5)	−180 (14)	3.8 (1.1)					

[a] Parameters × 10^5. [b] Parameters × 10^4. [c] Parameters × 10^3 and unscaled isotropic thermal parameters. [d] The form of the anisotropic thermal ellipsoid is $\exp[-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + 2B_{12}hk + 2B_{13}hl + 2B_{23}kl)]$.

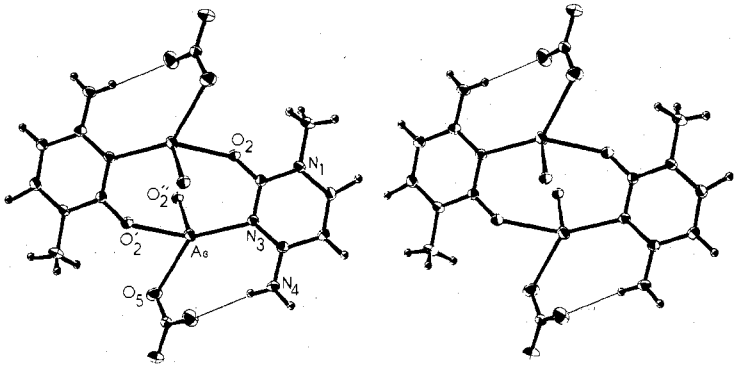


Figure 1. Stereoview of the basic dimeric unit found in (nitrato)(1-methylcytosine)silver(I). Thin lines denote intercomplex hydrogen bonds. The thermal ellipsoids are drawn at the 40% probability level.

chemistry, and we cite the following examples: (1) [(glycylglycine)silver(I)] nitrate,[15] (2) [(glycine)silver(I)] nitrate,[16] and (3) [di-μ-adeninio-disilver(I)] perchlorate.[17] In these three cases, the dimensions in the eight-membered, macrochelate ring are remarkably similar: (a) the Ag–O bond lengths in the glycine and glycylglycine complexes are about 2.2 Å and compare well with the Ag–N(3) = 2.20 (1) Å and Ag–N(9) = 2.16 (1) Å bond lengths in the adeninium complex; (b) the O–Ag–O bond angles for the glycine and the glycylglycine complexes are 163 and 160°, respectively, and the N(3)–Ag–N(9) bond angle is 164.1 (1)° in the adeninium complex; (c) the Ag···Ag distances within the dimers are all [2.88 Å in the glycine complex, 2.92 Å in the glycylglycine complex, and 3.00 Å in the adeninium complex] near to that found in metallic silver, 2.889 Å.[18] While the Ag–N(3) and Ag–O(2′) distances in the 1-methylcytosine complex are similar to those noted above, the Ag···Ag distance at 3.370 (1) Å is nearly 0.4 Å longer than in any of the above examples. In accord with this large Ag···Ag distance, the N(3)–Ag–O(2′) bond angle is very nonlinear at 136.2 (1)°. These striking differences do not appear to be a direct consequence of the geometry of the 1-methylcytosine ligand as the "bite distance" [N(3)···O(2) = 2.28 Å] is essentially equivalent, and even slightly longer than the "bite distance" between the carboxylate oxygen atoms [O···O = 2.22 Å], in glycine. Rather, it would seem that the 1-methylcytosine ligand is less capable than glycine, glycylglycine, or the adeninium cation of delocalizing the positive charge initially located on the Ag^+ ion and the consequently large Coulombic repulsion drives the Ag^+ ions apart and leads

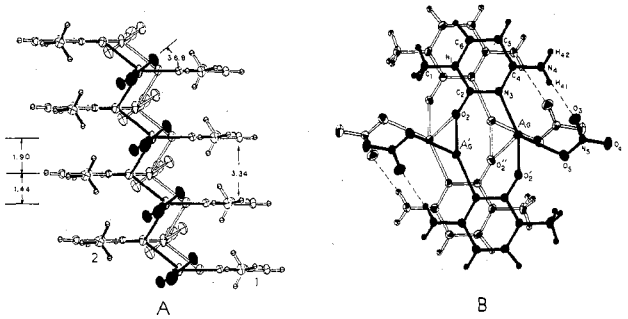


Figure 2. (A) Side view of the columnar, polymeric stacks [molecule 1(x,y,z), molecule 2($\bar{x},\bar{y},\bar{z}$)]. (B) View normal to the plane of the 1-methylcytosine ligands showing the molecular overlap in the base–base stacking.

to the rather sharp bridging angle at the Ag^+.

Another notable difference between the eight-membered, macrochelate rings noted above and that found here is the nonplanarity of the ring system in the 1-methylcytosine complex. In the glycine systems and the adeninium complex, the ring is nominally planar, while a chair conformation, Figures 1 and 2, is found in the 1-methylcytosine complex. In the adopted chair conformation, the mean distance between symmetry-related cytosine rings is substantial at 1.44 Å, Figure 2.

As can be seen in Figure 1, the nitrate anion is also coordinated to the silver ion. One of the nitrate oxygen atoms,

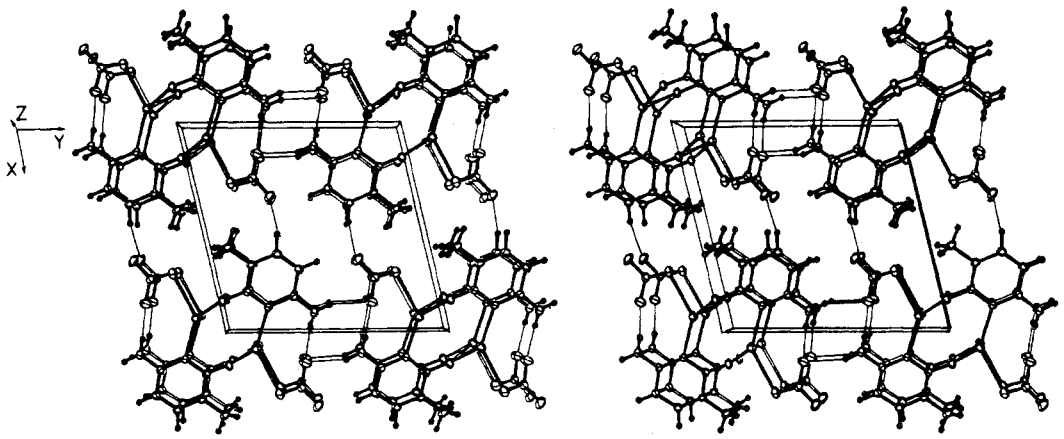


Figure 3. Stereoview of the crystal packing. Thin lines denote intracolumn and intercolumn interactions of the type D–H···A; see Table VI.

Table III. Interatomic Distances (Å) and Angles (deg)

(a) Primary Coordination Sphere about Ag

Bond Lengths

Ag-N(3)	2.225 (2)	Ag-O(5)	2.469 (3)
Ag-O(2′)[a]	2.367 (2)	Ag-O(2″)[a]	2.564 (2)

Bond Angles

N(3)-Ag-O(2′)	136.2 (1)	O(2′)-Ag-O(2″)	95.1 (1)
N(3)-Ag-O(2″)	103.2 (1)	O(2′)-Ag-O(5)	80.8 (1)
N(3)-Ag-O(5)	136.0 (1)	O(2″)-Ag-O(5)	93.6 (1)

(b) 1-Methylcytosine Ligand

Bond Lengths

O(2)-C(2)	1.253 (3)	N(3)-C(4)	1.350 (4)
N(1)-C(1)	1.467 (4)	N(4)-C(4)	1.350 (4)
N(1)-C(2)	1.379 (4)	N(4)-C(4)	1.332 (4)
N(1)-C(6)	1.362 (4)	C(4)-C(5)	1.408 (4)
N(3)-C(2)	1.354 (3)	C(5)-C(6)	1.360 (4)

Bond Angles

Ag′-O(2)-C(2)[b]	131.8 (1)	C(2)-N(3)-C(4)	119.7 (2)
Ag″-O(2)-C(2)[b]	130.8 (1)	O(2)-C(2)-N(1)	118.2 (2)
Ag′-O(2)-Ag″	95.1 (1)	O(2)-C(2)-N(3)	121.9 (2)
C(1)-N(1)-C(2)	119.1 (2)	N(1)-C(2)-N(3)	119.9 (2)
C(1)-N(1)-C(6)	120.5 (2)	N(3)-C(4)-N(4)	117.6 (2)
C(2)-N(1)-C(6)	120.4 (2)	N(3)-C(4)-C(5)	121.6 (2)
Ag-N(3)-C(2)	113.9 (2)	N(4)-C(4)-C(5)	120.9 (3)
Ag-N(3)-C(4)	126.5 (2)	C(4)-C(5)-C(6)	117.6 (3)
		N(1)-C(6)-C(5)	120.8 (3)

(c) Nitrate Group

Bond Lengths

N(5)-O(3)	1.256 (4)	N(5)-O(4)	1.239 (4)
		N(5)-O(5)	1.238 (4)

Bond Angles

Ag-O(5)-N(5)	106.1 (2)	O(3)-N(5)-O(5)	119.0 (3)
O(3)-N(5)-O(4)	120.0 (3)	O(4)-N(5)-O(5)	120.9 (3)

[a] Symmetry transforms for O(2′) and O(2″): O(2′), $-x, -y, -z$; O(2″), $-x, -y, -1-z$. [b] Symmetry transforms for Ag′ and Ag″: Ag′, $-x, -y, -z$; Ag″, $-x, -y, -1-z$.

Table IV. Least-Squares Planes and the Deviation of Individual Atoms from These Planes (Å)[a]

(a) Primary Coordination Sphere

$-0.0679X + 0.6801Y - 0.7300Z = -0.6731$

Ag	0.244	O(2′)[b]	−0.068
N(3)	−0.110	O(5)	−0.065
		O(2″)[c]	−1.455*

(b) Central Eight-Membered Ring of the Dimeric Units

$-0.4445X + 0.6124Y - 0.6537Z = 0.0$

Ag,Ag′	0.0	N(3),N(3′)	∓1.051*
O(2),O(2′)	0.0	C(2),C(2′)	∓0.773*

(c) 1-Methylcytosine Ligand

$-0.2942X + 0.0284Y - 0.9553Z = -0.7214$

N(1)	−0.001	O(2)	0.004*
N(3)	−0.003	N(4)	−0.006*
C(2)	0.003	C(1)	−0.047*
C(4)	0.000	H(41)	−0.038*
C(5)	0.002	H(42)	−0.182*
C(6)	−0.001	H(50)	0.000*
Ag	0.006*	H(60)	0.042*

(d) Nitrate Group

$0.1740X - 0.3931Y - 0.9029Z = 0.5442$

N(5)	0.008	O(4)	−0.003
O(3)	−0.002	O(5)	−0.002
		Ag	0.213*

[a] In each of the equations of the planes, X, Y, and Z are coordinates referred to the orthogonal axes: X along the a axis, Y in the ab plane, and Z along the c^* axis. Atoms designated by an asterisk were given zero weight in calculating the planes; the atoms used to define the planes were given equal weight. [b] Primed atoms are related to unprimed atoms by the transformation $-x, -y, -z$. [c] Doubly primed atoms are related to unprimed atoms by the transformation $-x, -y, 1-z$.

O(5), forms a relatively strong bond to the silver at a distance 2.469 (3) Å, which is similar to several of the shorter Ag–O bonds found in $AgNO_3$ [2.48 Å].[19,20] A second nitrate oxygen atom, O(3), also has a notable Ag–O interaction at 2.842 (3) Å; moreover, this nitrate oxygen atom forms an intracomplex, hydrogen bond to one of the hydrogen atoms of the exocyclic amino group $N(4)H_2$ of the 1-methylcytosine ligand, Figures 1 and 2.

Perhaps the most fascinating aspect of the structure is that the dimeric $[Ag(1\text{-methylcytosine})(NO_3)]_2$ units are formed into columnar stacks along the crystallographic c axis, Figures 2 and 3, via a Ag–O(2″) bond at 2.564 (2) Å. This second Ag–O(2) bond extends the number of ligating atoms about the silver to four, and the best representation of the overall coordination sphere about the Ag^+ is that of a trigonal pyramid, Figure 1 and Tables III and IV. Essential to the formation of both of the dimeric units and the extension to the columnar polymer is the versatility of the cytosine base as a coordinating ligand. Early work by Sundaralingam and Carrabine[21] showed that Cu(II) strongly binds to N(3) of cytosine and that there is a significant interaction between O(2) and the metal center. Such chelation of Cu(II) by N(3) and O(2) of cytosine derivatives has recently been found in a variety of other structures[22] and in a $HgCl_2$ complex of 1-methylcytosine.[23] Aoki[24] has also recently established that O(2) of cytosine 5′-monophosphate can act as a monodentate site in an octahedral complex of Mn(II). Recent Raman and ^{13}C NMR studies further demonstrate that interaction with O(2) is possible in solution.[25] Platinum and palladium,[26-27]

Table V. Intracolumn Stacking Contacts (Å)

(a) Base···Base

H(11)···H(12)[a]	2.03 (7)	C(4)···C(5)[b]	3.440 (3)
N(4)···C(4)[b]	3.397 (3)	N(1)···C(1)[b]	3.467 (4)
N(3)···C(2)[b]	3.407 (3)	N(1)···N(3)[a]	3.467 (3)
C(5)···C(6)[b]	3.422 (3)	N(4)···C(5)[b]	3.468 (3)
N(1)···C(2)[a]	3.438 (3)	C(4)···C(6)[b]	3.471 (3)

(b) Nitrate···Base and Nitrate···Nitrate

O(5)···N(5)[a]	3.230 (4)	O(3)···N(4)[b]	3.292 (4)
O(3)···O(5)[b]	3.276 (4)	O(4)···O(5)[b]	3.425 (4)
		O(3)···N(5)[b]	3.472 (4)

[a] Symmetry transform: $x, y, -1 + z$. [b] Symmetry transform: $x, y, 1 + z$.

Table VI. Inter- and Intracolumn Interactions of the Type A-H···O

A	H	O	A···O, Å	H···O, Å	A-H···O, deg	type
(a) N-H···O Hydrogen Bonds						
N(4)	H(41)	O(3)[a]	2.966 (3)	2.17 (4)	166 (3)	intracolumn
N(4)	H(42)	O(3)[b]	2.961 (3)	2.14 (4)	159 (3)	intercolumn
(b) C-H···O Interactions						
C(6)	H(60)	O(4)[c]	3.393 (4)	2.39 (4)	162 (3)	intercolumn
C(1)	H(11)	O(5)[d]	3.392 (4)	2.54 (4)	134 (4)	intercolumn
C(1)	H(13)	O(4)[c]	3.507 (4)	2.66 (5)	154 (5)	intercolumn

[a] Symmetry transform: x, y, z. [b] Symmetry transform: $-x, -1-y, -z$. [c] Symmetry transform: $1 + x, y, -1 + z$. [d] Symmetry transform: $-x, -y, -1-z$.

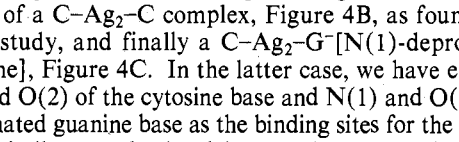
however, bind strongly to N(3) and there is only a suggestion of a metal–O(2) interaction. However, the exocyclic oxygen does bind to Pt in α-pyridone(platinum blue).[28] The multitude of metal–ligand bonds found in the complex described here indicates that cytosine offers an even wider range of ligating power than was previously appreciated. Moreover, while the Ag–N(3) bond lies essentially in the plane of the cytosine ring, Figure 1 and Table IV, the two Ag–O(2) bonds have large out-of-plane components, Figure 2. Thus, the coordination affinity of O(2) of a cytosine base is clearly not limited to the in-plane electron density employed in the Cu(II), Hg(II), and Mn(II) complexes noted above.

A second important feature of the columnar stacking of the $[Ag(1\text{-methylcytosine})(NO_3)]_2$ dimers is the base–base stacking within the columnar arrays. In Figure 2B, we illustrate in a view normal to the cytosine rings, the degree of molecular overlap, and in Table V we present a collection of the short contacts involved in the base stacking. Two features of the base–base stacking are important: (1) the mean-stacking distance at 3.34 Å is small and suggests a significant contribution to the overall stability of the polymeric structure owing to base–base overlap;[29] (2) base stacking is nominally of the ring-over-bond type[30] with the heterobonds N(1)–C(6) and N(3)–C(4) lying almost over the center of the cytosine rings of adjacent bases.

The binding among the columnar stacks is accomplished through interactions of the type D–H···A, Table VI and Figure 3. One of these interactions involves the hydrogen atom on the amino group $N(4)H_2$ which is not involved in the intracomplex hydrogen bonding noted above, and the second strongest interaction involves the hydrogen atom at C(6) of the ring. Each of these interactions utilizes one of the nitrate oxygen atoms as an acceptor site; O(2) of the cytosine ring is normally a good hydrogen bond acceptor,[31] but given its unique role in the binding of the Ag^+ ions, it is not employed here.

Finally, we address the question of the binding of Ag(I) to duplex DNA and the possible extrapolation of the features found in $[Ag(1\text{-methylcytosine})(NO_3)]$ to such binding. Most of the models proposed thus far[4,32,33] have centered on the binding of *one Ag(I) per base pair*. However, as noted above, Ag(I) has a marked tendency to form eight-membered, macrochelate rings where possible; it seems logical, then, that the formation of such a ring system could be important in Ag(I)–DNA complexes and would suggest that models involving *two Ag(I) per base pair* should be considered. In this regard we present in Figure 4, the normal Watson–Crick[34] base-pairing scheme for G–C pairs, Figure 4A, and illustrations of a $C–Ag_2–C$ complex, Figure 4B, as found in the present study, and finally a $C–Ag_2–G^-$[N(1)-deprotonated guanosine], Figure 4C. In the latter case, we have employed N(3) and O(2) of the cytosine base and N(1) and O(6) of the deprotonated guanine base as the binding sites for the two Ag^+ ions. A similar complex involving two deprotonated quanosine residues and two silver ions, $G^-–Ag_2–G^-$, can be formulated and its structure is identical with that given in Figure 4B except that N(1) and O(6) of two deprotonated guanine residues are utilized in binding the two silver ions. Thus, three types of complexes with 2 Ag^+/(G–C) base pair can be invoked, $C–Ag_2–C$, $G^-–Ag_2–C$, and $G^-–Ag_2–G^-$. In the first of these, there would be no proton release per bound Ag(I); in the latter two, proton release is essential and leads to a ratio of released H^+/bound Ag^+ of 0.5 for $G^-–Ag_2–C$ and 1.0 for $G^-–Ag–G^-$.

Moreover, in any $(G–C)_n$ sequence where $n \geq 2$, there are four pathways which can be deduced for the formation of any one of these complexes. We illustrate these four pathways for the case $(G–C)_2$:



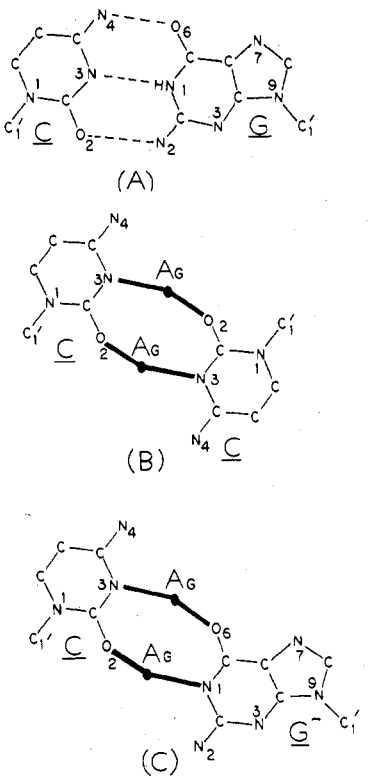


Figure 4. (A) Representation of a G–C hydrogen-bonded base pair. (B) Two cytidine residues linked by Ag^+ ions as found in (nitrato)(1-methylcytosine)silver(I). (C) Possible scheme for the coupling of a cytidine residue and a deprotonated guanosine residue by two Ag^+ ions.

The first two pathways involve the complex formation through the cross-linking of two hydrogen-bonded base pairs, while in the latter two pathways, cross-linking takes place between base residues which are one step out of register. Pathways 1 and 2 may be favored.

Jensen and Davidson[4] and Yamane and Davidson[32] found that three types of silver(I)–polynucleotide complexes can be formed. The first type does not involve proton release, but the second site yields between 0.6 and 1.0 H^+ released/bound Ag^+. This second type, which predominates at higher pH's, may have a structure in which one Ag^+ bridges two bases, with one base deprotonated much of the time. There is also a third type of site where one Ag^+ binds per nucleotide. This third type of site could very likely have the general features of the structure we have found for [Ag(1-methylcytosine)(NO_3)]. In fact, at this juncture, there is no obvious reason to exclude the types of binding we have indicated in Figure 4 for all three sites, with the modification that the type I sites involve bridging of two cytosines as in Figure 4B.

The proposed Ag_2B_2 structures would be more difficult to form between A–T pairs. Both bases must be deprotonated, thymine at N(3) and adenine at the N(6)H_2 amino group. This double-deprotonation requirement may be so unfavorable that it will not take place and, consequently, Ag(I) prefers G–C rich polynucleotides. In this regard it is of interest that fewer protons are released per bound Ag(I) in forming type III complexes in the relatively G–C rich DNA for *Micrococcus lysodeikticus* than in the A–T-rich calf thymus DNA.[4]

Moreover, in the cases where the number of repeating G–C pairs is 2 or greater, there is a distinct possibility that O(2) of cytosine or O(6) of a deprotonated guanine residue will initiate polymer binding parallel to the helix as shown for the present system in Figures 2 and 3. In this regard, the Ag···Ag repeat length along the helix axis in [AgI(1-methylcytosine)(NO_3)] at 3.642 Å (the *c* axis repeat length) is nearly commensurate with the 3.5-Å base–base stacking distance in duplex DNA.[35] Such multiple binding of Ag(I) by O(2) of cytosine or O(6) of deprotonated guanine will markedly enhance the stability of the metal binding.

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Registry No. (Nitrato)(1-methylcytosine)silver(I), 68024-42-0.

Supplementary Material Available: Final observed and calculated structure factor amplitudes (12 pages). Ordering information is given on any current masthead page.

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(3) Abbreviations employed are as follows: G, guanosine; C, cytidine; A, adenosine; T, thymidine; DNA, deoxyribonucleic acid; poly rI, polyriboinosinic acid; poly rA, polyriboadenylic acid; poly rU, polyribouranylic acid; poly rC, polyribocytidylic acid.
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