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$[Zn_3(OH)_2(1\text{-MeC-}N3)_5(1\text{-MeC-}O2)_3]^{4+}$ (1-MeC = 1-Methylcytosine): Structural Model for DNA Cross-Linking and DNA Rewinding by Zn(II)?[†]

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Abstract: A trinuclear zinc complex, $[Zn_3(OH)_2(1\text{-MeC})_8](NO_3)_4{\cdot}5H_2O$ (1-MeC = 1-methylcytosine) has been isolated and studied by X-ray crystallography. It is composed of a Zn(OH)Zn(OH)Zn backbone, to which eight 1-MeC nucleobases are bound, five via N(3) and three via O(2). The trinuclear cation can be divided into three parallel Zn(1-MeC-*N3*)(1-MeC-*O2*) "layers" which are connected by two μ-OH-groups and capped by two (1-MeC-*N3*) ligands. Within a layer, the two 1-MeC rings are planar (or close to planar) around tetrahedral Zn ions, which is possible only because one of the two binding sites utilized is an exocyclic one (O(2)). This O(2) oxygen atom is at the same time involved in a H bond to $NH_2(4)$ of the N(3) bound 1-MeC. Crystal data are as follows: monoclinic system, space group *P*2(1)/*m*, *a* = 12.825(3), *b* = 20.193(4), and *c* = 13.076(4) Å, β = 99.68(2), *Z* = 2. The trinuclear complex represents a feasible structural model for metal cross-links which occur in DNA melting in the presence of Zn(II) ions and which probably are responsible for DNA renaturation. Zn-modified guanine, cytosine (G-C) and adenine, thymine (A-T) base pairs are proposed which are formed according to the same principle as ZnC_2 entities: coordination to an unprotonated endocyclic N atom of one base (C–N(3), A–N(1)) and an exocyclic O atom of the second base (G–O(6), T–O(4)) with retention of *one* H bond.

Introduction

The role of Zn(II) in nucleic acid chemistry is in many respects special. (i) Zn(II) ions are integral constituents of zinc finger proteins, which recognize DNA and bind to DNA.[1] (ii) Zn(II) ions are found in many nucleic acid polymerases,[2] where they catalyze the template-directed synthesis of oligonucleotides[3] yet also take part in RNA and DNA hydrolysis.[4] (iii) Zn(II) complexes have been demonstrated to accomplish B → Z transitions of DNA at low concentrations.[5] (iv) Zn(II) ions stabilize pyrimidine–purine–purine triplex structures.[6] (v) Zn(II) ions are unique among metal ions in facilitating the rewinding of melted DNA.[7]

It has been proposed that a fundamental function of Zn(II) in the latter process is to keep the nucleobases "in register" or at least in close proximity, even though this does not necessarily imply the involvement of complementary bases.[7] While Zn(II), like many other metal ions, seems to prefer G-C-rich sequences in double-stranded DNA,[8] as confirmed in NMR studies on synthetic oligonucleotide dodecamers,[9,10] the situation in (partially) melted and/or single-stranded DNA may be different, considering the very much reduced effects of neighboring bases on the electrostatic potential of a particular site, e.g., guanine-N7, and the balanced tendency of Zn(II) to bind to N, O, and S (not relevant here) donor sites.[11] A number of structural models relevant to the question of Zn(II) binding to nucleic acids and their constituents[12,13] and also to related aspects[14] have been reported.

The compound described in this paper, $[Zn_3(OH)_2(1\text{-MeC})_8](NO_3)_4{\cdot}5H_2O$ (1-MeC = 1-methylcytosine), appears to be the first example of a multinuclear nucleobase complex containing an open $M_3(OH)_2$ core. At the same time, it displays several features which bear relevance to the question of DNA rewinding by Zn(II) ions.

Experimental Section

Preparation. The title compound was obtained as colorless cubes from 1-MeC[15] and $Zn(NO_3)_2{\cdot}6H_2O$ upon crystallization from aqueous solution (pH 6, slow evaporation, 39% yield). According to X-ray analysis, the compound contains five molecules of water of crystallization. Elemental

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[†] Dedicated to Prof. F. Huber.

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Table 1. Crystallographic Data and Details of Refinement of the Title Compound for Data Collected at 20 °C Using Mo Kα Radiation (λ = 0.7107 Å)

formula	$Zn_3C_{40}N_{28}O_{27}H_{68}$
fw, g/mol	1569.3
crystal system	monoclinic
space group	$P2(1)/m$
crystal size, mm	0.55 × 0.25 × 0.25
a, Å	12.825(3)
b, Å	20.193(4)
c, Å	13.076(4)
β, deg	99.68(2)
V, Å^3	3338.0(1.4)
Z	2
d_{calc}, g/cm^3	1.562
μ (Mo Kα) cm^{-1}	23.81
F(000)	3240
scan	$2\theta/\omega$
2θ range, deg	2–50
no. of reflcns measd	12 205
no. of reflcns indep	6111 (R(int) = 0.1493)
no. of reflcns obsd	3877 ($I \geq 2\sigma(I)$)
R, %	8.00
R_w,[a] %	23.02
goodness-of-fit	1.033
no. of parameters refined	455

[a] $w = 1/(\sigma^2(F)^2 + 0.1753P)^2 + 0.9001P$, where $P = (F_o^2 + 2F_c^2)/3$.

analysis is consistent with a 4- or 5-hydrate. IR (cm^{-1}): 530 m, 597 s, 637 s, 779 s, 825 m, 1151 s, 1209 s, 1325 vs, 1383 vs, 1511 vs, 1541 vs, 1569 vs, 1661 vs, 3164 vs, 3352 vs. Raman (cm^{-1}): 277(3.7), 296(4.2), 311(3.9), 497(4.9), 500(5.1), 594(3.5), 610(3.7), 647(5.3), 801(10), 809-(5.9), 821(4.3), 1058(8.3), 1161(3.7), 1281(5.1), 1320(3.7). Anal. Calcd for $[Zn_3(OH)_2(C_5H_7N_3O)_8](NO_3)_4{\cdot}4.5H_2O$: C, 30.7; N, 25.2; H, 4.3; Zn, 12.5. Found: C, 30.7; N, 25.2; H, 4.1; Zn, 11.5.

Instruments. IR spectra were recorded on IFS 113v Bruker, and the Raman spectrum was obtained on a ISA TG4000 Instruments S.A. with a Model 3900s Ti:sapphire laser excitation (748.95 nm, from Spectra Physics).

X-ray Analysis. The title compound $[Zn_3(OH)_2(1\text{-MeC})_8](NO_3)_4{\cdot}5H_2O$ was studied by single crystal X-ray crystallography. Unit cell dimensions were determined from 23 centered reflections (7.9 ≤ 2θ ≤ 23.8°). Diffraction data were collected at room temperature using graphite-monochromated Mo Kα radiation (λ = 0.7107 Å) with a Nicolet R3m/V diffractometer. An empirical absorption correction was made (ψ scans). The structure was solved by Patterson and Fourier methods applying the SHELXTL-PLUS[16] program. Full matrix least-squares refinement (on F^2) was performed with anisotropic thermal parameters for non-hydrogen atoms with the exception of the water molecules and nitrate oxygen atoms of N(80) and N(90) using SHELX-93.[17] Crystallographic data and details of the refinement are reported in Table 1. Positional and thermal parameters are listed in Table 2.

Results and Discussion

Description of Structure. The trinuclear cation of the title compound $[Zn_3(OH)_2(1\text{-MeC})_8](NO_3)_4{\cdot}5H_2O$ is shown in Figure 1. Selected interatomic distances and angles are listed in Table 3. The cation consists of a central $Zn_3(OH)_2$ backbone, to which eight 1-MeC ligands are bound, two to the central Zn(II) and three each to the terminal Zn(II) ions. The molecular cation is on a mirror plane that goes through Zn(1) and the two associated nucleobases. For convenience of discussion, the cation may be divided into (i) three parallel Zn(1-MeC-*N3*)(1-MeC-*O2*) layers which are (ii) connected by two bridging hydroxyl groups and (iii) capped by two N(3)-bound cytosines (Chart 1). All three Zn(II) ions display distorted tetrahedral geometries. The central Zn(II) ion has a coordination sphere formed by one N and three O donors, whereas the two other Zn(II) ions have mixed N_2O_2 donor sets. Bond lengths between Zn and the 1-MeC rings are not significantly different, regardless of the coordination site. They compare well with data on other Zn–N(nucleobase) complexes[12–14] and Zn(II) compounds containing neutral O donor groups.[18] In contrast, the Zn–OH bonds of the backbone (1.935-(4) and 1.943(4) Å) are significantly (9–13σ[19]) shorter than bonds between Zn and neutral O ligands and are in the typical range for Zn(OH)Zn entities.[20] The distance between adjacent Zn(II) ions is 3.497(1) Å.

Table 2. Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Coefficients (Å^2 × 10^3) for the Title Compound

	x	y	z	U(eq)
O(3)	3382(3)	6718(2)	1540(3)	59(1)
Zn(1)	2548(1)	7500	1684(1)	66(1)
Zn(2)	3299(1)	5848(1)	2156(1)	48(1)
N(11)	109(4)	5727(3)	2310(4)	64(2)
N(13)	1078(4)	5811(2)	939(4)	55(1)
N(14)	230(5)	5865(3)	–759(5)	72(2)
O(12)	1874(3)	5765(2)	2591(3)	64(1)
C(11)	102(6)	5676(5)	3427(6)	94(3)
C(12)	1050(5)	5771(3)	1940(5)	55(2)
C(14)	153(5)	5826(3)	251(5)	57(2)
C(15)	–836(5)	5809(3)	579(6)	68(2)
C(16)	–830(5)	5752(4)	1607(6)	71(2)
N(21)	3927(4)	4092(3)	743(4)	62(1)
N(23)	3472(3)	5208(2)	1022(3)	47(1)
N(24)	3266(4)	5944(3)	–326(4)	62(1)
O(22)	3668(4)	4458(2)	2332(3)	66(1)
C(21)	4220(9)	3423(4)	1177(7)	102(3)
C(22)	3685(4)	4579(3)	1401(4)	52(2)
C(24)	3464(4)	5337(3)	5(4)	49(1)
C(25)	3672(4)	4829(3)	–675(4)	53(2)
C(26)	3896(5)	4218(3)	–279(5)	60(2)
N(31)	6081(4)	5835(3)	4246(4)	64(2)
N(33)	4245(4)	5831(2)	3563(3)	50(1)
N(34)	3016(5)	5815(3)	4639(4)	76(2)
O(32)	5459(3)	5865(3)	2479(3)	71(1)
C(31)	7165(6)	5869(5)	4053(7)	100(3)
C(32)	5266(5)	5842(3)	3395(4)	54(2)
C(34)	4037(5)	5818(3)	4531(4)	57(2)
C(35)	4866(6)	5824(4)	5407(5)	70(2)
C(36)	5868(6)	5828(4)	5217(5)	72(2)
N(43)	1100(7)	7500	773(7)	69(2)
N(44)	22(10)	7500	2042(9)	113(4)
C(44)	102(11)	7500	1010(10)	86(3)
C(45)	–813(12)	7500	233(13)	105(5)
O(42)	2122(6)	7500	–424(6)	88(2)
C(42)	1224(9)	7500	–229(8)	71(3)
N(41)	355(9)	7500	–1006(8)	88(3)
C(41)	498(12)	7500	–2061(10)	112(5)
C(46)	–665(11)	7500	–769(14)	104(4)
O(52)	2097(8)	7500	3112(6)	103(3)
N(53)	3849(9)	7500	3726(7)	87(3)
N(54)	5661(12)	7500	4354(11)	125(5)
C(52)	2836(12)	7500	3858(9)	86(4)
N(51)	2612(12)	7500	4872(8)	123(4)
C(55)	4371(14)	7500	5634(9)	102(4)
C(56)	3365(15)	7500	5700(10)	112(5)
C(51)	1431(18)	7500	4943(12)	158(7)
C(54)	4667(17)	7500	4526(9)	118(6)
O(4W)	1594(6)	4013(4)	2388(6)	118(2)
O(2W)	9417(7)	8862(4)	5868(7)	141(3)
O(1W)	6513(16)	2500	1834(15)	117(6)
O(3W)	8927(21)	7500	5065(19)	153(9)
N(80)	6090(12)	7500	1597(10)	129(5)
O(81)	5255(11)	7500	1129(11)	153(4)
O(80)	6843(13)	7500	1124(13)	178(5)
O(82)	6430(14)	7500	2487(15)	204(6)
N(70)	2064(5)	5869(3)	–3000(4)	77(2)
O(70)	3015(5)	5914(4)	–2792(5)	119(2)
O(71)	1529(6)	5733(5)	–2342(4)	155(4)
O(72)	1607(5)	5905(5)	–3884(5)	152(4)
N(90)	7147(19)	7500	6693(13)	245(13)
O(91)	7596(23)	7500	7329(25)	314(14)
O(90)	7342(21)	7948(11)	6005(20)	412(14)

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(19) Esd calculated according to $\sigma = (\sigma_1^2 + \sigma_2^2)^{1/2}$, with σ_1 and σ_2 being the errors in bond lengths which are compared.

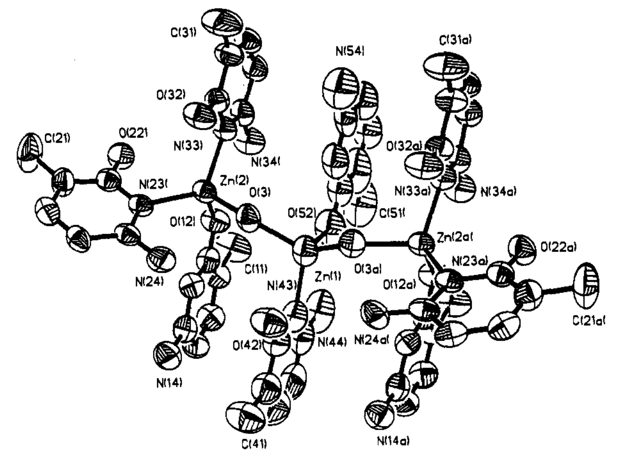


Figure 1. Trinuclear cation $[Zn_3(OH)_2(1\text{-MeC-}N3)_5(1\text{-MeC-}O2)_3]^{4+}$ with atom numbering scheme.

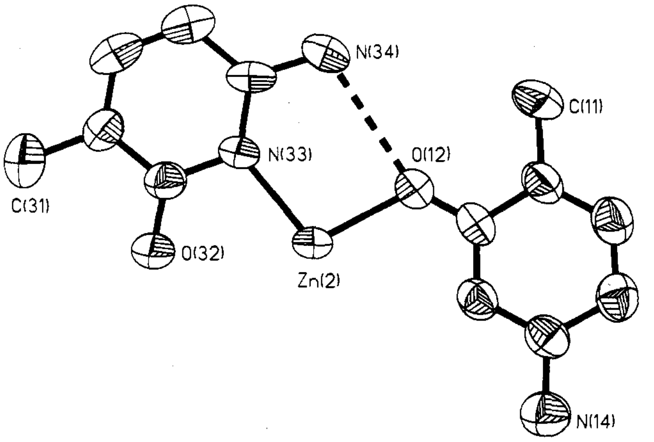


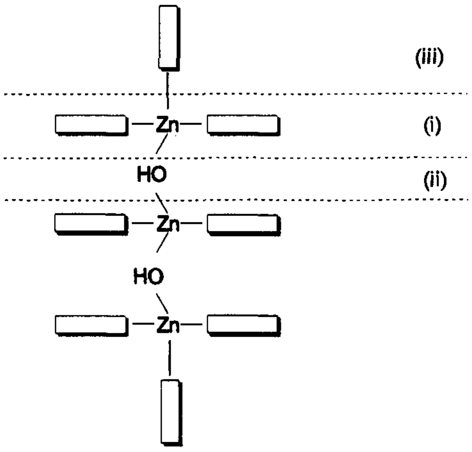
Figure 2. View of Zn-modified C-C base pair with a hydrogen bond (2.828(7) Å) between the two differently bound cytosines. The two other ligands about the Zn (OH, terminal 1-MeC) are omitted for clarity. The central Zn(1) forms a similar base pair, with a H bond of 2.790(15) Å.

Interestingly, each Zn(1-MeC-*N3*)(1-MeC-*O2*) entity (i) is planar (Zn(1)) or nearly planar (Zn(2), Zn(2a), dihedral angle between bases of 3.4(3)°). There is an intrabase hydrogen bond between O(2) of the O-bound 1-MeC and $NH_2(4)$ of the N-bound 1-MeC (e.g., O(52)···N(44), 2.790(15) Å at Zn(1); O(12)···N(34), 2.828(7) Å at Zn(2) and Zn(2a)) which clearly stabilizes the planar arrangement (Figure 2).

The geometries of the 1-MeC rings are not unusual and, as expected, not too much different from the free 1-MeC.[21] Moreover, no significant differences in bond lengths and angles in the linkage isomers can be seen. This even includes the internal ring angles at N(3) atoms, which could have been expected to be smaller in the case of the 1-MeC bonded to the O(2) atom, and the C(2)–O(2) bond lengths.

Six of the eight cytosines within a cation are pairwise parallel, with a typical 3.4-Å separation. The nucleobases stack in a characteristic manner, with exocyclic $NH_2(4)$ groups of both linkage isomers positioned above the π-system of 1-MeC in another layer. Within the crystal, cations are oriented in such a way that the $Zn_3(OH)_2$ backbone runs roughly along the crystallographic *y*-axis, with the central six cytosines of each cation oriented in a parallel fashion along the *x*-axis (supplementary material).

Chart 1



Three of the four nitrate anions have normal geometries. The fourth nitrate anion N(90) displays a disorder for which no satisfactory model could be found. As a result, bond lengths and angles in this anion are unrealistic (supplementary material).

Apart from the three intramolecular H bonds mentioned already, there are two additional ones between the μ-OH groups and the $NH_2(4)$ groups of the capping 1-MeC nucleobases (Table 3). Moreover, there is a series of intermolecular H bonds of less than 3 Å which involve the oxygens of the "normal" nitrates and exocyclic amino groups of the O(2)-bonded 1-methylcytosines, water molecules, and O(2) atoms as well as $NH_2(4)$ sites, water molecules, and nitrate oxygen atoms, and finally water molecules themselves.

Raman Spectrum. The Raman spectrum (solid state) of the title compound has been recorded to find out if the two linkage isomers might be differentiated by this method. However, unlike in linkage isomers of Pt nucleobase complexes,[22] no general doubling of bands is observed, the exception being the split bands at 497 and 500 cm^{-1}. They probably are the equivalents of the 479-cm^{-1} band of the free 1-MeC.

Special Features. There are several features that make the title compound special. (1) OH bridging: The trinuclear complex was obtained from $Zn(NO_3)_2$ and 1-MeC in water. The composition is very much different from that obtained from $ZnCl_2$ and 1-MeC.[12b] There, a mononuclear tetrahedral complex of composition $ZnCl_2(1\text{-MeC-}N3)_2$ is obtained. $CdCl_2$ forms an analogous compound.[23] With $HgCl_2$, a dinuclear compound of $Hg_2Cl_4(1\text{-MeC})_2$ stoichiometry has been structurally characterized.[24] It thus appears that the difference in anions applied accounts for the differences in composition and for formation of a μ-OH compound in the case of the poorly coordinating NO_3^-. To the best of our knowledge, this compound represents the first X-ray structurally characterized metal nucleobase complex containing OH bridges. We have previously postulated[25] and observed[26] (μ-OH)Pt_2 nucleobase complexes but did not isolate such compounds as crystals suitable for X-ray diffraction. (2) $Zn_3(OH)_2$ backbone: The title compound exemplifies a binding pattern that has only rarely been observed in metal nucleobase chemistry, formation of a backbone, here $Zn_3(OH)_2$, to which

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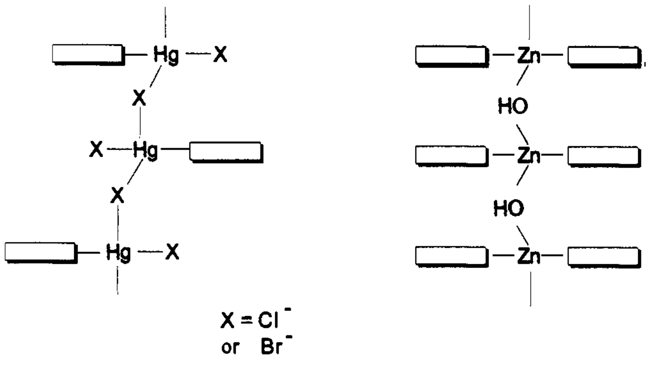
Table 3. Selected Interatomic Distances (Å), Angles (deg), and Hydrogen-Bonding Interaction for the Title Compound

			Distances				
O(3)–Zn(1)	1.935(4)	O(3)–Zn(2)	1.943(4)	N(31)–C(31)	1.456(10)	N(33)–C(34)	1.337(7)
Zn(1)–O(3)^{b}	1.935(4)	Zn(1)–N(43)	2.030(9)	N(33)–C(32)	1.363(8)	N(34)–C(34)	1.341(9)
Zn(1)–O(52)	2.045(8)	Zn(2)–N(23)	2.007(4)	O(32)–C(32)	1.241(7)	C(34)–C(35)	1.425(9)
Zn(2)–O(12)	2.011(4)	Zn(2)–N(33)	2.028(5)	C(35)–C(36)	1.349(11)	N(43)–C(42)	1.347(13)
N(11)–C(12)	1.376(8)	N(11)–C(16)	1.389(9)	N(43)–C(44)	1.37(2)	N(44)–C(44)	1.37(2)
N(11)–C(11)	1.465(9)	N(13)–C(12)	1.318(8)	C(44)–C(45)	1.42(2)	C(45)–C(46)	1.36(2)
N(13)–N(14)	1.363(8)	N(14)–C(14)	1.343(8)	O(42)–C(42)	1.220(13)	C(42)–N(41)	1.376(14)
O(12)–C(12)	1.241(7)	C(14)–C(15)	1.407(10)	N(41)–C(46)	1.39(2)	N(41)–C(41)	1.42(2)
C(15)–C(16)	1.347(10)	N(21)–C(26)	1.354(8)	O(52)–C(52)	1.24(2)	N(53)–C(52)	1.34(2)
N(21)–C(22)	1.375(8)	N(21)–C(21)	1.490(9)	N(53)–C(54)	1.35(2)	N(54)–C(54)	1.33(2)
N(23)–C(24)	1.354(6)	N(23)–C(22)	1.373(7)	C(52)–N(51)	1.403(14)	N(51)–C(56)	1.32(2)
N(24)–C(24)	1.311(8)	O(22)–C(22)	1.246(7)	N(51)–C(51)	1.53(2)	C(55)–C(56)	1.31(2)
C(24)–C(25)	1.412(8)	C(25)–C(26)	1.349(9)	C(55)–C(54)	1.56(2)		
N(31)–C(36)	1.343(9)	N(31)–C(32)	1.393(8)				
			Angles				
Zn(1)–O(3)–Zn(2)	128.9(2)	O(3)–Zn(1)–O(3)^{b}	109.4(3)	C(32)–N(31)–C(31)	118.1(6)	C(34)–N(33)–C(32)	120.2(5)
O(3)–Zn(1)–N(43)	114.1(2)	O(3)^{b}–Zn(1)–N(43)	114.1(2)	C(34)–N(33)–Zn(2)	132.5(4)	C(32)–N(33)–Zn(2)	107.3(3)
O(3)–Zn(1)–O(52)	109.6(2)	O(3)^{b}–Zn(1)–O(52)	109.6(2)	O(32)–C(32)–N(33)	120.2(5)	O(32)–C(32)–N(31)	120.9(6)
N(43)–Zn(1)–O(52)	99.5(4)	O(3)–Zn(2)–N(23)	104.8(2)	N(33)–C(32)–N(31)	118.9(5)	N(33)–C(34)–N(34)	117.0(5)
O(3)–Zn(2)–O(12)	108.0(2)	N(23)–Zn(2)–O(12)	111.9(2)	N(33)–C(34)–C(35)	121.3(6)	N(34)–C(34)–C(35)	121.7(6)
O(3)–Zn(2)–N(33)	109.0(2)	N(23)–Zn(2)–N(33)	122.4(2)	C(36)–C(35)–C(34)	117.2(6)	N(31)–C(36)–C(35)	121.7(6)
O(12)–Zn(2)–N(33)	100.1(2)	C(12)–N(11)–C(16)	118.7(6)	C(42)–N(43)–C(44)	119.3(10)	C(42)–N(43)–Zn(1)	109.0(7)
C(12)–N(11)–C(11)	120.5(6)	C(16)–N(11)–C(11)	120.8(6)	C(44)–N(43)–Zn(1)	131.8(8)	N(43)–C(44)–N(44)	116.8(12)
C(12)–N(13)–C(14)	119.4(5)	C(12)–O(12)–Zn(2)	121.0(4)	N(43)–C(44)–C(45)	122.1(12)	N(44)–C(44)–C(45)	121.1(13)
O(12)–C(12)–N(13)	121.3(5)	O(12)–C(12)–N(11)	117.0(6)	C(46)–C(45)–C(44)	117.4(14)	O(42)–C(42)–N(43)	118.2(10)
N(13)–C(12)–N(11)	121.7(6)	N(14)–C(14)–N(13)	116.7(6)	O(42)–C(42)–N(41)	121.4(11)	N(43)–C(42)–N(41)	120.3(10)
N(14)–C(14)–C(15)	121.4(6)	N(13)–C(14)–C(15)	121.9(6)	C(42)–N(41)–C(46)	120.7(11)	C(42)–N(41)–C(41)	119.7(11)
C(16)–C(15)–C(14)	116.9(6)	C(15)–C(16)–N(11)	121.5(6)	C(46)–N(41)–C(41)	119.6(12)	C(45)–C(46)–N(41)	120.2(13)
C(26)–N(21)–C(22)	120.7(5)	C(26)–N(21)–C(21)	120.7(6)	C(52)–O(52)–Zn(1)	115.0(9)	C(52)–N(53)–C(54)	122.9(12)
C(22)–N(21)–C(21)	118.6(5)	C(24)–N(23)–C(22)	120.0(5)	O(52)–C(52)–N(53)	121.9(10)	O(52)–C(52)–N(51)	119.5(14)
C(24)–N(23)–Zn(2)	128.2(4)	C(22)–N(23)–Zn(2)	111.7(3)	N(53)–C(52)–N(51)	118.6(12)	C(56)–N(51)–C(52)	122.4(14)
O(22)–C(22)–N(23)	119.8(5)	O(22)–C(22)–N(21)	121.0(6)	C(56)–N(51)–C(51)	122.8(11)	C(52)–N(51)–C(51)	114.8(13)
N(23)–C(22)–N(21)	119.2(5)	N(24)–C(24)–N(23)	118.3(5)	C(56)–C(55)–C(54)	117.3(14)	C(55)–C(56)–N(51)	122.5(13)
N(24)–C(24)–C(25)	121.2(5)	N(23)–C(24)–C(25)	120.6(6)	N(54)–C(54)–N(53)	120.6(13)	N(54)–C(54)–C(55)	123.2(14)
C(26)–C(25)–C(24)	118.1(5)	C(25)–C(26)–N(21)	121.4(6)	N(53)–C(54)–C(55)	116(2)		
C(36)–N(31)–C(32)	120.7(6)	C(36)–N(31)–C(31)	121.1(6)				
			Possible Hydrogen Bond Distances < 3 Å				
O(3)–N(24)^{a}	2.878(7)	O(12)–N(34)^{a}	2.828(7)	O(1W)–O(42)^{d}	2.74(2)	O(2W)–N(4W)^{g}	2.815(11)
O(52)–N(44)^{a}	2.790(15)	O(72)–O(2W)^{b}	2.813(11)	O(2W)–O(3W)^{a}	2.972(12)	O(3W)–O(90)^{f}	2.73(4)
O(71)–N(14)^{a}	2.875(9)	O(81)–O(3)^{a}	2.975(12)	O(4W)–N(14)^{e}	2.897(10)	O(4W)–O(22)^{h}	2.826(9)
O(72)–N(34)^{c}	2.860(9)	O(82)–N(54)^{a}	2.79(2)	O(90)–N(54)^{f}	2.90(3)		

^{a} x, y, z. ^{b} x, −y + 1.5, z. ^{c} x, y, z + 1. ^{d} −x + 1, −y + 1, −z. ^{e} −x, −y + 1, −z. ^{f} x, 0.5 − y, z. ^{g} −x + 1, y − 0.5, −z + 1. ^{h} −x, −y, −z.

Chart 2



nucleobases are added in such a way as to stick out into the surroundings. It is feasible that such a backbone can be considerably longer, with a variety of different capping ligands possible. With $HgCl_2$, a similar principle has been observed (Chart 2). A polymeric $[HgX_{2/2}]^+$ backbone (X = Cl or Br) forms, with a single purine base and a terminal X ligand completing the coordination spheres of the tetrahedral Hg ions.[27] (3) O(2) and N(3) binding: The title compound is one of the few cases where coordination to the O(2) atom of cytosine has been established by X-ray crystallography[28] and one of very few metal compounds displaying two different nucleobase binding modes simultaneously.[29] Our findings verify in a sense the interpretation of Marzilli and co-workers[30] who, on the basis of ^{13}C NMR and Raman difference spectroscopy, had proposed the existence of *two types* of complexes of cytidine with $Zn(NO_3)_2$ in DMSO, involving N(3) and O(2) binding. (4) Coplanarity of 1-MeC ligands: Both in $ZnCl_2$(1-MeC-*N3*)$_2$ and in $CdCl_2$(1-MeC-*N3*)$_2$, the cytosine ligands are coordinated through the N(3) atoms in a tetrahedral fashion about the metal. As a consequence, the nucleobases form large dihedral angles. In our compound, pairs of 1-MeC ligands about tetrahedrally coordinated Zn ions are coplanar. This coplanarity is possible only because one of the two nucleobases is coordinated via an exocyclic group (O(2)), a feature that prevents steric interference between exocyclic groups as expected for twofold N(3) coordination and hence avoids

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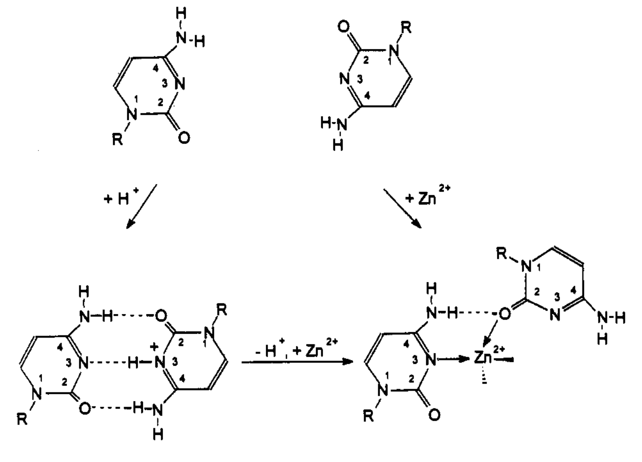

(a) (b)

Figure 3. Schematic representations of C-C base pairs: (a) hemiprotonated, (b) Zn(II)-modified. In both cases, the two bases are practically coplanar.

deviation from planarity.[31] Coplanarity of the two differently bound 1-MeC bases is supported by a H bound between the two bases (cf. Figure 2). We note that intrabase H bonding is also important in other metal bis(nucleobase) complexes containing two nearly planar bases in a distorted trigonal-planar[32] or square-planar *trans* orientation.[33]

Relevance to Hemiprotonated Cytosine. Neutral cytosine ligands and their N(3) protonated forms, when present in a 1:1-ratio, readily form base pairs with three hydrogen bonds.[34] With cytosine-containing oligonucleotides, both parallel duplex structures[35] and recently even a tetraplex structure[36] have been reported. Replacing the acidic proton by a suitable metal ion leads to "metal-modified nucleobase pairs", which we have been studying lately.[32,33] The Zn(II)-modified C-C base pair observed in the title compound allows an analogy to be drawn with CHC^+ (Figure 3). Formally, the Zn(II) analogue is built if (i) two of the H bonds in CHC^+ are opened, (ii) one base slides away, and (iii) the H^+ is replaced by a $[Zn(OH)_{2/2}]^+$ entity. Alternatively, the Zn(II)-modified base pair is formed from two neutral cytosines by insertion of a Zn(II) and simultaneous formation of a H bond.

A point of interest refers to the question of whether oligo-C strands can adopt a regular structure in the presence of Zn(II), similar to the situation in its hemiprotonated form.[34,35] Assuming a $(ZnOH)_n$ backbone and geometries as observed in our compound, it appears that a Zn(II)-modified duplex is not possible for steric reasons (unfavorable orientation of methyl groups at N(1), corresponding to C(1′) of sugar of next neighbors, cf. Figure 4). However, with the CH_3 groups of the first and the third bases being 6.6–7.4 Å apart (e.g., C(31)–C(31a), 6.58 Å; C(11)–C(11a), 7.36 Å), a four-stranded structure with mutually intercalated cytosines might be possible. The overall appearance would then be crescent-shaped, with the $Zn(OH)_n$ backbone accessible to the environment.

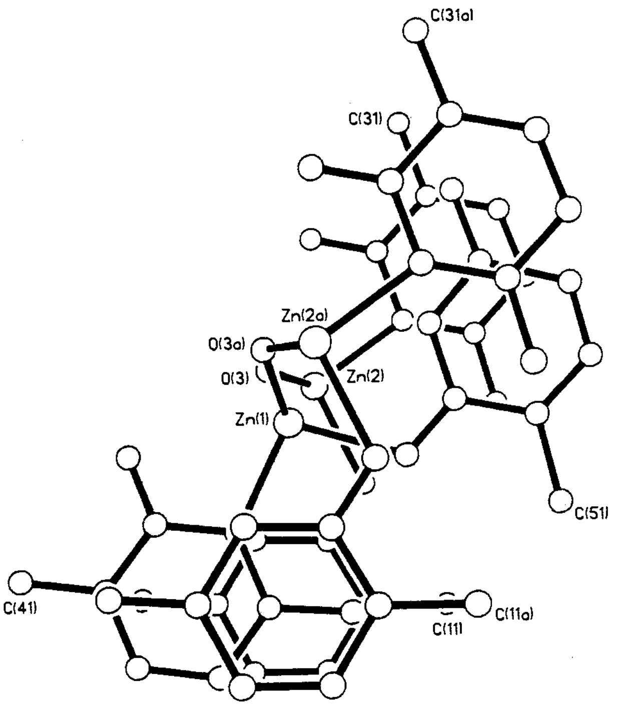

Figure 4. View along the $Zn_3(OH)_2$ axis with capping 1-MeC rings omitted for clarity. Cytosine bases stack at 3.4-Å separations.

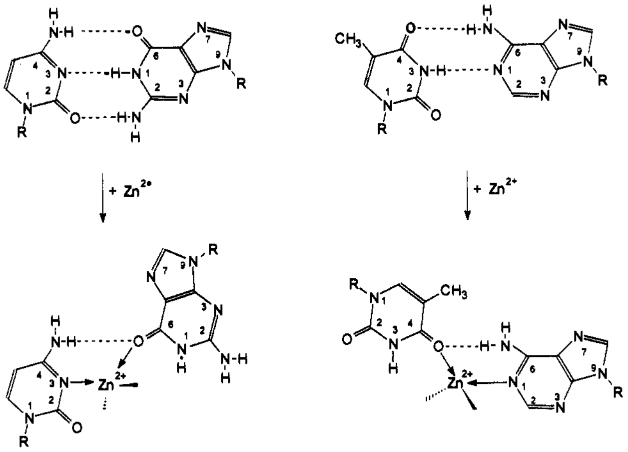

Figure 5. Watson–Crick base pairs between C-G and T-A (top) and proposed Zn(II)-modified base pairs (bottom). The Zn-modified pairs were constructed applying the same principles as seen in ZnC_2 (cf. text).

Possible Relevance to DNA Rewinding. It is generally accepted that metal binding to the phosphate oxygens of an oligonucleotide thermally stabilizes the duplex structure, whereas coordination at the heterocyclic bases leads to destabilization.[37] While a switch of the metal from phosphate to the N(7) atom of the purines in principle might thus be sufficient to induce duplex destabilization and eventually melting, it is more difficult to rationalize why N(7) purine binding should facilitate rewinding by somehow holding base pairs in register. Nevertheless, according to a model proposed by Marzilli et al.,[13e] intrastrand cross-linking of two guanines via the N(7) positions by an octahedrally coordinated Zn(II) should be capable of achieving rewinding. Our title compound provides an alternative model which could explain how, in a partially melted duplex, base pairs could be cross-linked with partial loss of H bonds. Applying the same principle as seen for ZnC_2 to G-C and A-T base pairs (Figure 5), namely loss of two (G-C) or one (A-T) H bond(s) at the expense of *one* Zn–N as well as *one* Zn–O bond, metal-modified base pairs can be constructed in which the bases remain coplanar and are still

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(31) With exclusive binding of exocyclic sites of pyrimidine nucleobases, even a 90° angle between donor–M–donor is possible, see: Fischer, B.; Preut, H.; Lippert, B.; Schöllhorn, H.; Thewalt, U. *Polyhedron* **1990**, *9*, 2199.

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capable of stacking at a 3.4-Å distance. Formally, the base pair modification is achieved by insertion of a Zn(II) ion from the minor groove and by pushing the bases apart. According to this model, there is no need for nucleobase deprotonation, even through Zn(OH) entities have been shown in principle to accomplish thymine deprotonation while binding.[38] Upon duplex renaturation, the progressing base pair formation would simply extrude the Zn(II) while reforming all H bond(s). The relatively low stability constants of Zn nucleobase complexes[30,39] would fit into such a picture.

A major difference of our proposed model from previously published ones is the occurrence of a trinuclear $Zn_3(\mu\text{-OH})_2$ entity. It has been suggested by Shin and Eichhorn[7b] that the Zn(II)-induced rewinding of DNA might require the concerted action of a number of Zn(II) ions. The idea of cationic $Zn_n(OH)_{n-1}$ clusters being involved was not put forward. However, hydroxo-bridged Zn(II) complexes have been known for some time and play important roles both in solid-state inorganic chemistry[18] and in biochemistry.[40] It is even feasible that Zn(II) might form larger aggregates than observed in our case. The capping ligands—here 1-MeC—could certainly be substituted by many other ligands available, including H_2O.

Finally, our findings allow a more general conclusion to be drawn concerning the interactions of tetrahedral metal ions with double-stranded DNA. These metal ions, when forming interstrand cross-links between the heterocyclic rings of the nucleobases, neither automatically disrupt base stacking nor fully prevent H bonding between bases. This holds as long as not more than *one* endocyclic N donor per metal is involved in binding, the other being an exocyclic donor. The major effect on duplex DNA structure to be expected from such a binding mode probably is a distortion of the DNA backbone and a moderate increase in duplex diameter at the site(s) of metal binding.

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Supplementary Material Available: Tables of anisotropic thermal parameters, nitrate geometries, and view of packing (4 pages); tables of observed and calculated structure factors (14 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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