J. Am. Chem. Soc. **1987**, *109*, 380-386

An Unusual Copper–Uridine Octamer: Existence in Solution and Structural Study in Its Auto-Built Zeolitic Network in the Solid State

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Abstract: The structure of a copper(II)–uridine complex has been determined from a single-crystal X-ray structure determination. The compound $Cu_8(urid)_8Na_8{\cdot}5NaClO_4{\cdot}48H_2O$ (urid = uridine(3−)) crystallizes in a cubic cell of dimensions $a = 23.716$ Å with $Z = 3$ and space group $P432$. The complex forms an octamer of formula $[Cu_8(urid)_8Na(H_2O)_6]^{7-}$; this molecular species exhibits a toric structure. The uridine ligand is three-coordinated toward three copper atoms by N(3), O(3′), and O(2′), this last oxygen atom bridging two copper atoms. The conformation about the glycosidic bond is anti, the puckering of the ribose ring is C(2′) endo, and the conformation about C(4′)–C(5′) is gauche–gauche. The sodium atoms form a three-dimensional network quite similar to the framework of the synthetic Linde A zeolite. Two kinds of cavities are thus defined: chambers, occupied by water molecules and sodium cations, and tunnels, occupied by perchlorate groups and the octamer copper–uridine complex. In aqueous solutions, the existence of either the same octamer or a similar complex has been demonstrated by both potentiometric titrations and small-angle X-ray scattering measurements.

The biological roles of nucleic acids and nucleotides are dependent on metal ions; some examples are the use of certain transition-metal complexes (particularly platinum compounds) in the chemotherapy of some tumors and the involvement of metal cations in biological processes which distinguish between ribo- and deoxyribonucleotides.[2] Many studies have been made of the interactions between metal ions, nucleosides, and nucleotides in order to understand the much more complicated nucleic acid–metal systems. The building blocks of nucleic acids contain a large number of oxygen and nitrogen donor sites of varying basicity and, hence, of varying donor properties. An increasing number of crystallographic studies are progressively bringing out information of the general bonding types of different metal ions in complexes of nucleic acid constituents.[3,4] There are also a number of studies made in solution, mainly by NMR technique and conventional potentiometry.[5]

Nevertheless, the information about nucleoside complexes is scarce, due to the lack of both precise structural and solution chemical data. This is in part due to the weak stability of the complexes formed,[5] which makes it difficult both to interpret solution chemical data and to obtain suitable single crystals.

We have selected the copper(II)–uridine system in order to obtain data on the structure and bonding in a metal nucleoside system both in the solid state and in solution.

Literature studies on the complex formation between Cu(II) and uridine in aqueous solutions are scarce and contradictory. Fiskin and Beer[6] determined the equilibrium constant for the 1:1 complex by measuring proton displacement in acid ($\approx$pH 5) solutions. On the other hand, Reinert and Weiss[7] found no complex formation at <pH 6, but above $\approx$pH 8 they found a soluble 1:1 green–blue complex. Chao and Kearns[8] studied water–Me_2SO solutions of the Cu(II)–uridine system with ESR spectroscopy, establishing the existence of a diamagnetic (or antiferromagnetic[9]) complex between pH 8.2 and 10. Berger and Eichhorn[10] found, with the NMR technique, that uridine binds Cu^{2+} both at N(3) and at the ribose hydroxyls. However, the dependence of complex formation on pH has not always been investigated;[10-12] in some cases the pH values are not even reported, which makes it impossible to assess the composition of the complexes.

This experimental study consists of three parts: (1) a study of the stoichiometry and equilibrium constants of the complexes formed in aqueous solution between Cu^{2+} and uridine, (2) the preparation of single crystals of a copper–uridine complex and the determination of its structure by means of X-ray diffraction, and (3) a correlation of the solution chemical data and the structure data by using small-angle X-ray scattering data (SAXS) from solutions of Cu^{2+} and uridine.

Experimental Section

Chemicals. A stock solution of sodium perchlorate was prepared from sodium carbonate (Merck) and perchloric acid (Merck). Its salt content was determined by weighing samples dried at 110 °C. The copper(II) perchlorate stock solution was prepared from copper(II) oxide (Merck) and perchloric acid (Merck). The solution was analyzed for copper by electrodeposition. The H^+ excess of these perchlorate stock solutions was determined potentiometrically by means of Gran[13] plots. Sodium hydroxide solutions were prepared by diluting 50% NaOH (EKA) with boiled bidistilled water. Uridine (Serva) was dried to 110 °C.

The solid copper–uridine compound used for the single-crystal diffraction measurements was prepared as described previously.[14] Anal. Calcd for $Cu(urid)(ClO_4)_{0.625}Na_{1.625}(H_2O)_6$: C, 20.98; H, 4.69; N, 5.44; Cu, 12.33; Cl, 4.30; Na, 7.25. Found: C, 20.51; H, 4.39; N, 5.72; Cu, 12.22; Cl, 4.55; Na, 7.30.

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† This work is part of the Ph.D. thesis of I.P. at the Royal Institute of Technology.

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Table I. Crystallographic Data and Conditions for Data Collection and Refinement

Physical and Crystallographic Data

formula: $Cu_8(urid)_8Na_8 \cdot 5NaClO_4 \cdot 48H_2O$
molecular weight: 4098.7
crystal system: cubic
space group: $P432$
a = 23.716 (5) Å
V = 13 339 Å^3
ρ_{exp} = 1.55 g cm^{-3}
ρ_{calcd} = 1.53 g cm^{-3}
absorption factor: $\mu_{(\lambda Cu\ K\alpha)}$ = 30.5 cm^{-1}
$\mu R \approx 0.8$
morphology: cube 0.25 × 0.25 × 0.25 mm

Data Collection

temperature: 22 °C
radiation: copper
λCu Kα = 1.540 51 Å
monochromator: oriented graphite crystal
crystal-detector distance: 208 mm
detector window: height[a] = 4 mm; width[a] = 4.00 + 0.35 tan θ
take-off angle: 5°
scan mode: θ–2θ
maximum Bragg angle: 30°
scan angle: $\Delta\theta = \Delta\theta_0 + B \tan\theta$; $\Delta\theta_0$[a] = 1.6°; B[a] = 0.14
values determining the scan speed:
SIGPRE[a] = 0.30; SIGMA[a] = 0.01; VPRE[a] = 10° mm^{-1} in θ; TMAX[a] = 200 s
controls: intensity
reflections: 800; 033; 303
periodicity: 7200 s

Conditions for Refinement

reflections for refinement of cell dimensions: 25
recorded reflections: 2167
independent reflections: 2009
utilized reflections: 1007 with $I \geq 1.5\sigma(I)$
reliability factors:
$R = \sum |k|F_o| - |F_c|| / \sum k|F_o|$
$R_w = [\sum w^2(k|F_o| - |F_c|)^2 / \sum w^2k^2F_o^2]^{1/2}$

[a] These parameters have been described in ref 3.

Single-Crystal X-ray Data Collection and Structure Determination. The data were collected at 22 °C on a CAD4 Enraf-Nonius automatic single-crystal diffractometer, by means of the θ–2θ scan technique, using Cu Kα radiation monochromatized with graphite, following the scheme in Table I and as described elsewhere.[3] During the course of the data collection, three standard reflections (Table I) were measured every 2 h, and the deviations of these reflections from their averages were all within counting statistics.

Examination of a single crystal of the copper–uridine complex by means of precession technique showed that this compound belongs to the cubic system. The cubic crystalline system is very unusual with this class of compounds, and a rather complicated structure was expected. The observed Laue symmetry group $m3m$ and the absence of systematic extinctions led to three possible space groups: $P432$, $P\bar{4}3m$, and $Pm3m$. Cell constants and corresponding standard deviations, listed in Table I, were derived from least-squares refinement of the settings of 25 automatically centered reflections.

Based on a unit-cell volume of 13 339 Å^3, the calculated density (1.53 g cm^{-3}) is in good agreement with the density of 1.55 g cm^{-3} measured by flotation in a carbon tetrachloride and 1,1,2,2-tetrabromoethane medium.

The shape of the selected crystal was a cube with bounding faces (100), (010), and (001). The dimensions were 0.25 mm for the three edges. Among the 2009 unique reflections, 1007 have intensities $I \geq 1.5\sigma(I)$, and only these reflections were included in subsequent refinements.

The structure was solved by Patterson and Fourier methods and refined by full-matrix least-squares techniques.[15] The minimized quantity is $\sum w(|F_o| - |F_c|)^2$, where $|F_o|$ and $|F_c|$ are the observed and calculated structure amplitudes and where the weights, w, are taken as $4F_o^2/\sigma^2(F_o^2)$. The agreement indexes are defined in Table I. Values of the atomic scattering factors and the anomalous terms for the copper, sodium, and chlorine atoms were taken from Cromer and Waber's tables.[16]

The statistical tests, performed on normalized structure factors, indicate that the space group is probably noncentrosymmetric.

From the Patterson function, it was possible to deduce the copper atom position. The chosen space group is $P432$. From subsequent Fourier series, the ligand uridine and an octahedral $Na(H_2O)_6$ group were localized. Refinement of this partial solution gives reliability indexes R = 0.22 and R_w = 0.30.

At this point of the structural solution, two facts have to be pointed out: (a) the copper–uridine complex forms an octamer and the molecular species has the formula $Cu_8(urid)_8Na(H_2O)_6$ and (b) in the huge cubic cell, these entities occupy the oxygen positions of a well-known simple solid-state structural type, the perovskite ABO_3.

This last remark allowed us to obtain the final structural solution by dividing the structure in two spatial volumes: B, an octahedron having $Cu_8(urid)_8Na(H_2O)_6$ at its corners, and A, a cuboctahedron containing perchlorate anions, sodium cations, and water molecules.

Partial Fourier synthesis was carried out on both the A and B volumes. In this way, we found one perchlorate anion in the B volume. The other atoms (Na atoms, water molecules, and perchlorate anions) are disordered in the A volume. We have not been able to refine all their positions. The disorder accounts for the poor quality of our diffraction data.

Refinement of the positional parameters led to the final reliability index R = 0.13. We kept isotropic temperature factors because of the small number of reflections.

Atomic parameters are listed in Table II. The main interatomic distances and angles are given in Table III.

emf Titrations. Copper–uridine solutions with $[H^+] \approx 10^{-11}$ were titrated with perchloric acid to $[H^+] \approx 10^{-9.5}$. In order to test the equilibrium condition of the measurements, one experiment was performed by starting from a copper–uridine solution with $[H^+] \approx 10^{-8}$ which was titrated with sodium hydroxide. Variations of activity coefficients and liquid junction potentials were minimized by keeping a constant ionic medium $[ClO_4^-]$ = 3 M through the titrations. The emf of both a glass electrode (Metrohm EA107T) and a copper(II) ion-selective electrode (Orion 94-29A) was measured against a double-junction Ag/AgCl reference electrode by using a digital voltmeter (Fluke 8810A) and an operational amplifier (Analog Devices 309K) in a minicomputer-controlled measuring system,[17] which also performed the additions from an automatic buret (Metrohm Dosimat). The titration vessel and reference electrode were immersed in a thermostated oil bath at 25.00 ± 0.03 °C. The titrated solution was stirred with a magnetic bar, and nitrogen was used to prevent CO_2 gas contamination. The concentration range studied was 0.004–0.050 M for uridine and 0.0002–0.045 M for Cu^{2+}. Both electrodes were calibrated by Gran[13] plots, which also gave a check on the value of initial total proton excess.

Unfortunately, the copper-selective electrode used did not function well in the pH region studied. This was true both for the commercial electrodes used and for the copper amalgam electrodes tested. The precision achieved in the emf measurements was 3 mV, corresponding to log $[Cu^{2+}]$ = 0.1. We do not know the reason for this low precision, as at lower pH one can easily attain a precision of 0.2 mV. One reason for the observed behavior might be adsorption of ligand at the electrode surface. Phenomena of this type are known to affect the behavior of the electrodes.[18]

Small-Angle X-ray Scattering Measurements. The SAXS data were recorded with the monitor type camera developed by Kratky et al.,[19] which was set up in a room thermostated at 21 °C. The sample container was a thin-walled Deybe–Sherrer glass capillary with an inner diameter of 0.96 mm. Monochromatization of the copper radiation was made with a nickel filter and a pulse-height discriminator together with a proportional counter. The absolute intensity was obtained by using the Lupolen method.[20]

The composition of the solutions used in the SAXS study are given in Table VI. For each sample, the background scattering of a solution containing a uridine concentration equal to $[H_3urid]_{tot} - [Cu^{2+}]_{tot}$, and the same ionic composition, was measured and substracted from the scattering data.

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(15) In addition to local programs for the CII IRIS 80 computer, local modifications of the following programs were employed: Zalkin's Fourier program, Ibers and Doedens' NUCLS program, Busing, Martin, and Levy's ORFFE program, and Johnson's ORTEP program.

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Table II. Final Atomic Parameters with esd's Enclosed in Parentheses[a]

			atom	*x*	*y*	*z*	*B*
24	k	1	Cu	0.1403 (3)	0.4512 (3)	0.1954 (3)	2.8 (1)
24	k	1	O(2)	0.0255 (13)	0.4244 (12)	0.1574.(14)	3.1 (1)
24	k	1	O(4)	0.1264 (14)	0.4556 (12)	0.3227 (14)	3.0 (1)
24	k	1	O(1′)	−0.0842 (9)	0.3330 (10)	0.2397 (9)	2.7 (1)
24	k	1	O(2′)	−0.1341 (8)	0.4616 (8)	0.1935 (9)	2.9 (2)
24	k	1	O(3′)	−0.1855 (9)	0.3700 (9)	0.1634 (9)	3.2 (1)
24	k	1	O(5′)	−0.1268 (16)	0.2402 (15)	0.2896 (21)	4.9 (2)
24	k	1	N(1)	−0.0229 (13)	0.4139 (10)	0.2423 (15)	2.9 (1)
24	k	1	N(3)	0.0717 (9)	0.4378 (7)	0.2427 (10)	2.4 (1)
24	k	1	C(2)	0.0231 (10)	0.4211 (9)	0.2111 (11)	3.0 (1)
24	k	1	C(4)	0.0791 (11)	0.4363 (9)	0.3015 (12)	3.1 (2)
24	k	1	C(5)	0.0271 (11)	0.4325 (10)	0.3327 (13)	2.9 (1)
24	k	1	C(6)	−0.0186 (10)	0.4170 (10)	0.3017 (12)	2.5 (1)
24	k	1	C(1′)	−0.0719 (9)	0.3868 (9)	0.2182 (10)	2.7 (2)
24	k	1	C(2′)	−0.1217 (11)	0.4202 (10)	0.2372 (13)	3.0 (1)
24	k	1	C(3′)	−0.1703 (10)	0.3778 (9)	0.2221 (12)	3.1 (1)
24	k	1	C(4′)	−0.1426 (12)	0.3207 (9)	0.2314 (13)	3.2 (1)
24	k	1	C(5′)	−0.1557 (14)	0.2881 (12)	0.2813 (15)	3.8 (2)
6[b]	e	4	Na(1)	0.4741 (8)	0	0	7.1 (1)
12	j	2	W(1)	$^1/_2$	0.0686 (10)	0.0686 (12)	10.7 (3)
6	e	4	W(2)	0.3731 (11)	0	0	10.7 (3)
24	k	1	Na(2)	0.4351 (5)	0.1404 (5)	0.3951 (6)	6.3 (1)
6	f	4	W(3)	$^1/_2$	0.1402 (9)	$^1/_2$	8.5 (2)
24	k	1	W(4)	0.4021 (13)	0.2017 (11)	0.3199 (15)	9.1 (4)
24	k	1	W(5)	0.4451 (12)	0.2411 (10)	0.4152 (15)	9.0 (4)
3	c	42	Cl(1)	$^1/_2$	0	$^1/_2$	5.1 (1)
24[b]	k	1	O(11)	0.4654 (35)	0.0351 (22)	0.4673 (29)	10.1 (4)
12	i	2	Cl(2)	0.1708 (6)	0	0.1708 (6)	5.8 (1)
24	k	1	O(21)	0.1798 (15)	−0.0012 (4)	0.1115 (18)	11.2 (3)
24	k	1	O(22)	0.1949 (14)	0.0511 (14)	0.1950 (18)	11.0 (3)

[a] The first column indicates the number of positions, the Wyckoff notation, and the point symmetry. The positions of Na(3), W(6), W(7), and W(8) have not been refined. The sodium ion (position i) and two water molecules, W(6) and W(7) (position k), are located in the A zeolitic cage (cf. Figure 5). The W(8) water molecule (position k) is situated in the tunnel *B*. [b] 50% occupancy.

The analysis of the SAXS data followed conventional procedures involving correction for drift in the primary intensity and desmearing,[21] as well as model calculations using a weighted least-squares method.[22] The radius of gyration, R_g, and forward scattering, $I(0)$, were obtained from Guinier plots.

Results

A. Description of the Crystal Structure. The structure has two interesting aspects: (1) molecular entities Cu_8urid_8, containing $Na(H_2O)_6$ ions, surrounded by perchlorate anions and (2) a three-dimensional framework based on sodium atoms, giving rise to the formation of tunnels where the copper complexes are allocated, and cages containing perchlorate anions, sodium cations, and water molecules.

I. Molecular Species Cu_8urid_8. The uridine ligand is three-coordinated toward three copper atoms: by the nitrogen atom N(3) of the pyrimidine base and by the oxygen atoms O(3′) and O(2′) of the ribose, this last oxygen atom bridging two copper atoms (Figure 1).

The metal atoms are in a square-planar configuration and associated in dinuclear units in the Cu_8urid_8 octamer species. The Cu–Cu distance within the dinuclear units is rather short (2.96 Å).

The coordination of the nucleoside through the N(3) atom of the base has now been properly established in several structures of complexes containing transition metals and pyrimidine bases. However, to our knowledge, the double coordination of the ribose in the crystalline state is extremely unusual, although there is an example in an osmium bispyridine ester of adenosine.[23] Such a coordination for the copper–uridine system has been suggested[8] from a ESR study in Me_2SO solutions. However, in this study, a structure was proposed where the pyrimidine base does not participate in the coordination.

The coordination of the pyrimidine base found in our study leads to distortions in the ligand geometry. The precision of the structure refinement does not allow a precise comparison of bond lengths and angles; nevertheless, it appears interesting to discuss the values of the torsion angles (Table IV).

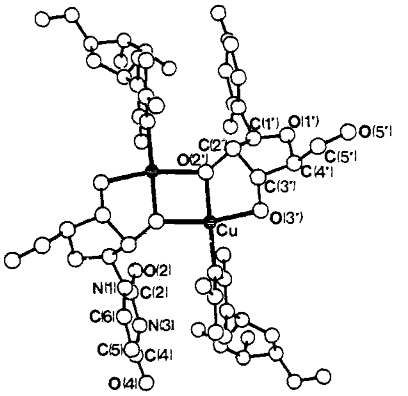

Figure 1. Coordination around the copper atom.

The deviations from planarity (Table V) of the pyrimidine ring are larger than those in the free ligand[24] but smaller than in dihydrouridine,[25] for example.

The nucleoside conformation about the glycosidic bond N(1)–C(1′) is anti, as in the free ligand and all the uridine analogues except 4-thiouridine.[26] The value of the corresponding torsion angle χ_{CN} is in the 0–72° interval defined by Sundaralingam for the pyrimidine nucleosides.[27]

The puckering of the ribose ring is C(2′) endo, as shown by both the θ angles (Table IV) and the positions of C(2′) and C(5′)

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Table III. Main Interatomic Distances and Angles[a]

	Distances (Å)		
Cu–O(2′)	1.94	C(3′)–C(2′)	1.57
Cu–N(3)	2.00	C(2′)–O(2′)	1.46
Cu–O(3′)	2.01	C(2′)–C(1′)	1.49
Cu–O(3′)	2.07	C(4′)–C(5′)	1.45
		C(5′)–O(5′)	1.34
N(1)–C(2)	1.33	Na(1)–W(1)	2.38
C(2)–N(3)	1.43	Na(1)–W(2)	2.40
N(3)–C(4)	1.41	Na(2)–W(4)	2.43
C(4)–O(4)	1.31	Na(2)–W(5)	2.45
C(4)–C(5)	1.44	Na(2)–W(3)	2.92
C(5)–C(6)	1.36	Na(2)–O(4)	3.04
C(6)–N(1)	1.41	Na(2)–O(4)	3.13
		Na(2)–O(11)	3.11
N(1)–C(1′)	1.45		
C(1′)–O(1′)	1.41	Cl(1)–O(11)	1.40
O(1′)–C(4′)	1.43	Cl(2)–O(21)	1.42
C(4′)–C(3′)	1.52	Cl(2)–O(22)	1.45
C(3′)–O(3′)	1.45		
	Angles (deg)		
O(2′)–Cu–O(3′)	81.8	N(1)–C(2)–O(2)	127
O(2′)–Cu–O(2′)	84.5	N(1)–C(2)–N(3)	114
N(3)–Cu–O(3′)	97.7	C(2)–N(3)–C(4)	128
N(3)–Cu–O(2′)	96.5	N(3)–C(4)–O(4)	119
		N(3)–C(4)–C(5)	114
O(11)–Cl(1)–O(11)	108	C(4)–C(5)–C(6)	115
O(11)–Cl(1)–O(11)	107	C(5)–C(6)–N(1)	127
O(11)–Cl(1)–O(11)	113	C(6)–N(1)–C(2)	119
O(21)–Cl(2)–O(21)	107	C(6)–N(1)–C(1′)	118
O(21)–Cl(2)–O(22)	110	N(1)–C(1′)–C(2′)	106
O(21)–Cl(2)–O(22)	108	C(1′)–C(2′)–O(2′)	108
O(21)–Cl(2)–O(22)	112	C(1′)–C(2′)–C(3′)	100
		C(2′)–C(3′)–O(3′)	119
W(1)–Na(1)–W(1)	86	C(2′)–C(3′)–C(4′)	103
W(1)–Na(1)–W(2)	105	C(3′)–C(4′)–C(5′)	120
W(4)–Na(2)–W(5)	67	C(3′)–C(4′)–O(1′)	105
W(4)–Na(2)–O(4)	97	C(4′)–O(1′)–C(1′)	110
W(4)–Na(2)–O(4)	86	O(1′)–C(1′)–C(2′)	102
W(5)–Na(2)–W(3)	78	C(4′)–C(5′)–O(5′)	118
W(5)–Na(2)–O(4)	96		
W(5)–Na(2)–O(4)	97		
W(3)–Na(2)–O(4)	93		

[a] Average esd's are 0.02 Å for Cu–O and Cu–N bonds, 0.10 Å for other bonds, 0.6° for A–Cu–B angles, and 1.5° for other bond angles.

Table IV. Torsion Angles (deg)[a]

		Cu complex	uridine
χ_{CN}	C(6)–N(1)–C(1′)–O(1′)	51	21.3
ϕ_{OO}	O(5′)–C(5′)–C(4′)–O(1′)	60	-75.3
ϕ_{OC}	O(5′)–C(5′)–C(4′)–C(3′)	175	42.7
θ_1	C(4′)–O(1′)–C(1′)–C(2′)	-42	7.0
θ_2	O(1′)–C(1′)–C(2′)–C(3′)	44.5	-29.6
θ_3	C(1′)–C(2′)–C(3′)–C(4′)	-33	40.0
θ_4	C(2′)–C(3′)–C(4′)–O(1′)	10	-37.0
θ_0	C(3′)–C(4′)–O(1′)–C(1′)	19.5	19.0

[a] The values of torsion angles for the free uridine are the average values.

Table V. Least-Square Planes[a]

	Δ(1)		Δ(2)
N(1)	-0.001	C(1′)	0.058
C(2)	0.063	O(1′)	-0.099
O(2)	-0.047	C(4′)	0.110
N(3)	-0.018	C(3′)	-0.073
C(4)	0.111	C(2′)	-0.643
O(4)	-0.047	C(5′)	-0.830
C(5)	-0.065		
C(6)	0.006		

[a] Plane 1: N(1), C(2), O(2), N(3), C(4), O(4), C(5), C(6); $0.237X - 0.971Y + 0.389Z + 9.433 = 0$. Plane 2: C(1′), O(1′), C(4′), C(3′), $0.043X - 0.252Y - 0.961Z + 7.597 = 0$.

Table VI. Composition of the Aqueous Solutions Used for the SAXS Measurements (mol/L)

	sample			
	1	2	3	4
$[Cu^{2+}]_{tot}$	0.0307	0.0511	0.0730	0.051
$[H_3urid]_{tot}$	0.100	0.100	0.100	0.100
$[ClO_4^-]$	0.20	0.20	0.22	0.0
$[Na^+]$	0.30	0.30	0.32	0.10
$-\log [H^+]$	≈11.1	≈11.2	≈11.6	≈11.3

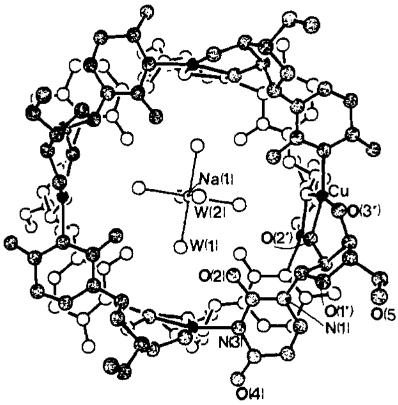

Figure 2. The molecular species $[Cu_8(urid)_8Na(H_2O)_6]^{7-}$.

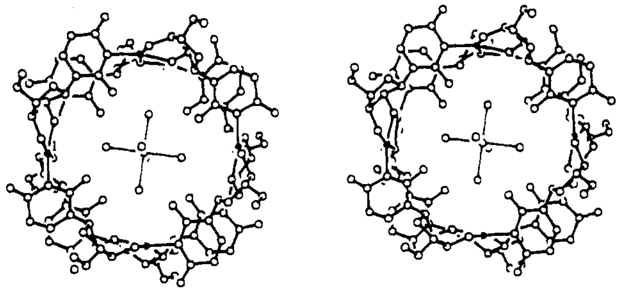

Figure 3. Stereoscopic view of a $Cu_8(urid)_8Na(H_2O)_6$ entity.

vs. the best mean plane of the ribose (Table V). Moreover, the two torsion angles $\phi_{O\text{-}O}$ and $\phi_{O\text{-}C}$ show a gauche–trans conformation about the C(4′)–C(5′) bond. Thus, the ribose conformation in the present complex is drastically different from the one observed in the free ligand[24] (where the puckering of the ribose ring is C(3′) endo and the conformation about the C(4′)–C(5′) bond is gauche–gauche) but very similar to the conformation of dihydrouridine.[25]

In the Cu_8urid_8 octamer, the eight metal atoms occupy the summits of a distorted Archimedian square antiprism (diagonal of the square fan: 11.4 Å). The eight interconnected uridine ligands form a kind of toric structure (Figure 2 and 3). The external and internal diameters of the torus, calculated with the O(4) and O(2) oxygen atoms of the pyrimidine rings, are 16.4 and 7.6 Å, respectively.

There is an extensive overlap of the pyrimidine rings; the angle between two rings is about 6°, and the mean distance is 3.67 Å, the shortest one being 3.45 Å (C(5)–C(5)). This overlap is much greater than the usual one defined by Bugg's study.[28]

II. Molecular Species $Na(H_2O)_6$. This octahedron of water molecules around a sodium atom occupies the center of the octamer Cu_8urid_8 (Figure 2). The O(2)–W(1) distance (2.95 Å) indicates the existence of hydrogen bonds O–H···O and that this $Na(H_2O)_6$ entity is thus locked by the O(2) atoms of the pyrimidine rings in the center of the Cu_8urid_8 toric structure.

There are two positions, within this octahedron, statistically occupied at 50% by the Na(1) cation. The coordination around the Na(1) atom is best described as a square pyramid, with the Na atom being displaced along the 4-fold axis from the square base toward the apex by 0.61 Å. The sixth water molecule is then very weakly coordinated to the sodium cation. Such a coordination polyhedron for a sodium atom is not very common, although it

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(28) Bugg, C. E.; Thomas, J. M.; Sundaralingam, M.; Rao, S. T. *Biopolymers* **1971**, *10*, 175.

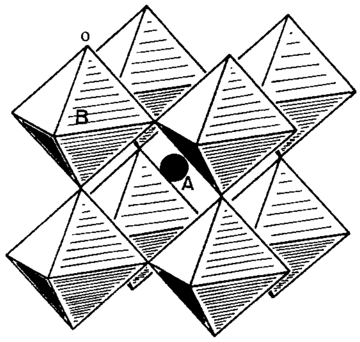

Figure 4. The ABO_3 perovskite structure.

is found in synthetic or natural sodium silicates.[29]

III. Three-Dimensional Framework. The environment of the Cl(1) atom of the $ClO_4(1)$ group is a cube of oxygen atoms, the eight summits being half occupied. The $ClO_4(1)$ group is thus statistically distributed between two positions and is centered on the faces of the cubic perovskite cell. The $ClO_4(2)$ groups occupy the summits of a cuboctahedron, centered on the cell origin (B cage of ABO_3).

The Na(2) atoms are at the center of a distorted square pyramid formed by O(4) oxygen atoms of the pyrimidine bases and water molecules. A sixth oxygen atom, which belongs to the $ClO_4(1)$ group, completes this polyhedron to give a distorted octahedron.

We have used structure elements from two mineral structures, the ABO_3 pervoskite and the zeolites, to describe the structure.

In the perovskite model (Figure 4), which has been of great help to solve the structure, the oxygen sites are occupied by the $Cu_8(urid)_8Na(H_2O)_6$ molecular species and the B sites by the formal association of 12 ClO_4 groups and one water molecule (W(8)). The A sites are filled by a very intricate sodium–water network. The Na(2) atoms also occupy the summits of a distorted polyhedron called snub-cube. Inside this polyhedron, we have a third Na^+ and two water molecules (W(6) and W(7)). These atoms are distributed on two succesive snub-cubes and a cuboctahedron, reminiscent of a nest of Russian dolls. However, the disorder makes it impossible to refine the positions, and we are not able to give a full description of the filling of the A sites. Nevertheless, this description requires a drastic idealization of the structure, especially for the A sites.

The description in terms of the zeolite model is more satisfactory. The Na(2) snub-cubes are connected to each other in a zeolitic framework, quite similar to the framework of the synthetic Linde A zeolite (Figure 5). The network of truncated octahedra connected by cubes (Linde A) is replaced by a network of snub-cubes connected by distorted Archimedian antiprisms in the present structure.

Two kinds of cavities are thus defined: cages A, inside the snub-cubes, and tunnels B, parallel to the 4-fold axis. The mean diameter of these tunnels (about 16 Å) is much larger than those observed in synthetic or natural zeolites (for example, 11.8 Å[30] in faujasite), which have similar cell dimensions (a = 24.6 Å).

The connections between the snub-cubes, across the Archimedian antiprisms, are made by the $ClO_4(1)$ groups. In the tunnels B, the $Cu_8(urid)_8Na(H_2O)_6$ molecular species alternate with the $ClO_4(2)$ cuboctahedra. Thus, each molecular entity is surrounded by four $ClO_4(1)$ groups at the corners of the equatorial plane of an octahedron, the apices of which are the $ClO_4(2)$ cuboctahedra. The position of the copper–uridine octamer, in the tunnel, is shown in Figure 6.

This very intricate architecture, with a high symmetry, reminds one of the unusual copper(I)–copper(II) complex of D-penicillamine.[31] This coordination compound crystallizes in the cubic system, and the structure consists of mixed valence clusters $Cu_{14}L_{12}$ with a chloride ion locked at the center. These $Cu^I{}_8Cu^{II}{}_6L_{12}Cl^{5-}$ molecular species are surrounded by an extremely complicated network of thallium ions and water molecules (5 Tl^+ and 55 H_2O per cluster unit). This thallium–water network is completely disordered as in our case.

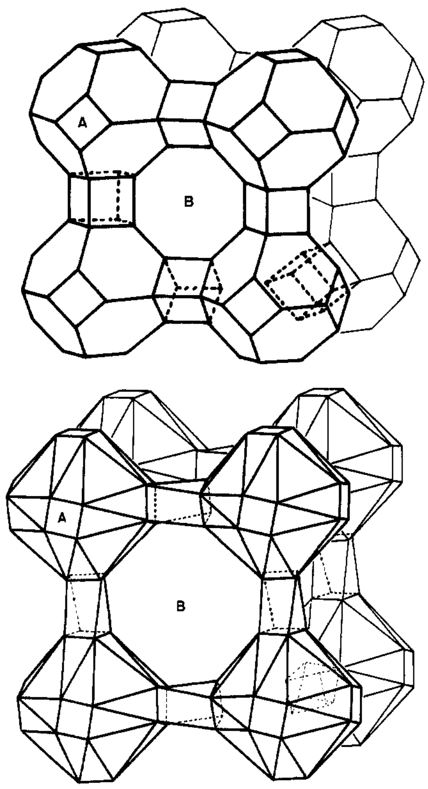

Figure 5. Comparison between the sodium network and the Linde A zeolite structure.

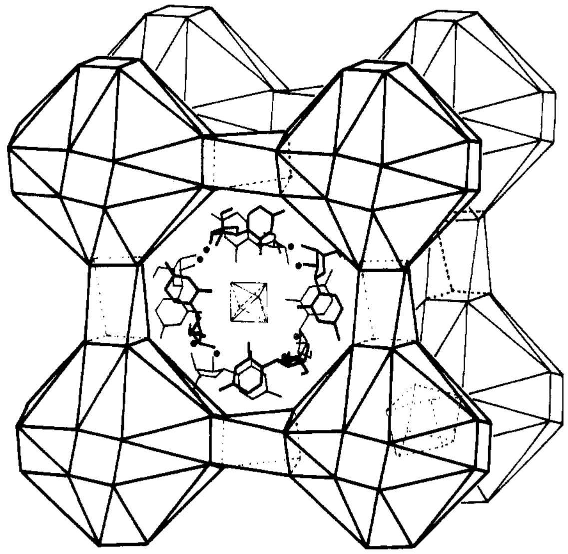

Figure 6. Position of the copper–uridine complex in the tunnels.

B. Complex Formation in Aqueous Solutions. Two different experimental methods have been used, small-angle X-ray scattering (SAXS) and potentiometric titrations. The equilibria will be described according to the expression

$$qCu^{2+} + sH_3urid \rightleftharpoons H_{3s-p}Cu_q urid_s{}^{2q-p} + pH^+$$

where H_3urid stands for uridine. The equilibrium constants are

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(29) (a) Jost, K.-H.; Hilmer, W. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1966**, *21*, 583. (b) Perrault, G.; Boncher, C.; Vicat, J.; Cannillo, E.; Rossi, G. *Acta Crystallogr., Sect. B: Struct. Crystallogr. Cryst. Chem.* **1973**, *B29*, 1432.

(30) Barrer, R. M. *Molecular Sieves*; Meier, W. M., Uytterhoeven, J. B., Eds.; Advances in Chemistry 121; American Chemical Society: Washington, DC, 1973; pp 1–28.

(31) Birker, P. J. M. W. L.; Freeman, H. C. *J. Chem. Soc., Chem. Commun.* **1976**, 312.

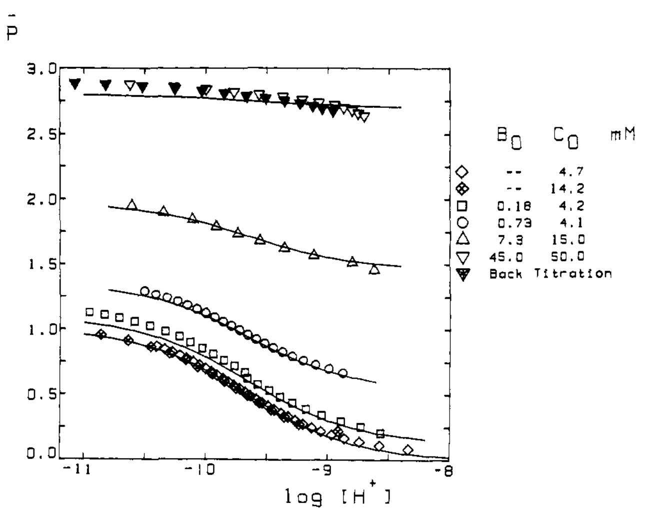

Figure 7. Average H^+ released per uridine molecule vs. log [H^+] for titrations with different initial copper(II) and uridine concentrations (B_0 and C_0, respectively).

then log β_{pqs} = log [$H_{3s-p}Cu_q urid_s^{2q-p}$] + p log [H^+] − q log [Cu^{2+}] − s log [H_3urid].

In preliminary experiments we found that a solid (possibly copper hydroxide) is formed when the acidity of solutions of copper and uridine is decreased below [H^+] $\lesssim 10^{-5}$. At least some of the solid redissolves, and a dark-blue solution is formed, if the acidity is further decreased below [H^+] $\lesssim 10^{-8}$. In order to redissolve all the solid, the total concentration of copper must be less than the total concentration of uridine, suggesting that the complexes in the aqueous solution have $q \leq s$. When the amount of alkali that is added to decrease the acidity, and redissolve the solid, is measured, it is found that $[OH^-]_{tot} \geq 2[Cu^{2+}]_{tot} + [H_3urid]_{tot}$. This suggests that the complexes in the aqueous solution have $p \geq 2q + s$. In the solid phase discussed in the previous section, one has $q = s$ and $p = 2q + s$, and therefore, from the global composition of the aqueous solutions, one cannot exclude the possibility that the same octanuclear complex is present in solution.

Aqueous solutions of the dark-blue complex frozen at about 80 K gave no ESR signal, as is the case for Me_2SO solutions.[8,9] This indicates that antiferromagnetic complexes with $q > 1$ predominate in the solutions. The absorption spectra of the dark-blue solutions, which show a band with a maximum near 670 nm, do not change either with [H^+] or with the concentration ratio of Cu(II) to uridine, suggesting that only one copper complex dominates in the solutions.

I. emf Titrations. The acidity constant of uridine, which is needed in later calculations, had to be determined first in copper-free solutions and was found to be log β_{101} = log [H_2urid^-] + log [H^+] − log [H_3urid] = −9.66 ± 0.01 (at 25 °C, [ClO_4^-] = 3 M).

The results of the glass electrode measurements are shown in Figure 7, in the form $\bar{p} = ([H^+] - [OH^-] - [H^+]_{tot})/[H_3urid]_{tot}$, i.e., average p value per uridine vs. log [H^+]. The continuous curves were calculated assuming only one complex in the solutions with $s = q$ and $p/q = 3$, i.e., the values found in the solid phase $Cu_8(urid)_8Na_8{\cdot}5NaClO_4{\cdot}48H_2O$. From the glass electrode measurements it is not possible to ascertain the value of q for the aqueous complex. Data of this type may be obtained from measurements of the free Cu^{2+} concentration, but the precision of our ion-selective electrode measurements is not enough to establish a unique chemical model for the Cu^{2+}–uridine system. However, from the precise log [H^+] data we know that the reaction taking place is

$$qCu^{2+} + qH_3urid \rightleftharpoons Cu_q urid_q^{q-} + 3qH^+$$

From the equilibrium condition, we obtain log [Cu^{2+}] − 3 log [H^+] + log [H_3urid] = $(1/q)$ log [$Cu_q urid_q^{q-}$] − $(1/q)$ log β_{pqs}, and from the mass balance condition for copper, we obtain $[Cu^{2+}]_{tot} = [Cu^{2+}] + q[Cu_q urid_q^{q-}] \approx q[Cu_q urid_q^{q-}]$. Thus, we have plotted in Figure 8 the function −log [Cu^{2+}] − 3 log [H^+] + log [H_3urid] vs. log $[Cu^{2+}]_{tot}$, and these data can be used to test different models. q values between 4 and 8 give a satisfactory fit of the experimental data. The corresponding equilibrium constants are log $\beta_{12,4,4}$ = −68.4 and log $\beta_{24,8,8}$ = −133.8.

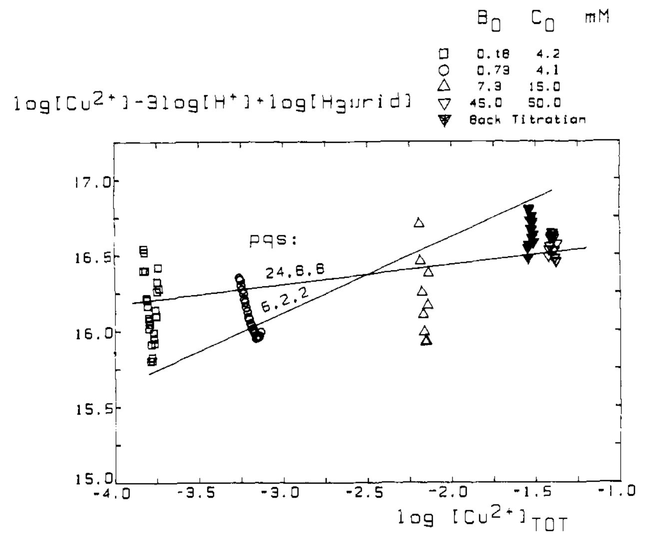

Figure 8. Results from the copper(II) ion-selective electrode measurements for titrations with different initial copper(II) and uridine concentrations (B_0 and C_0, respectively).

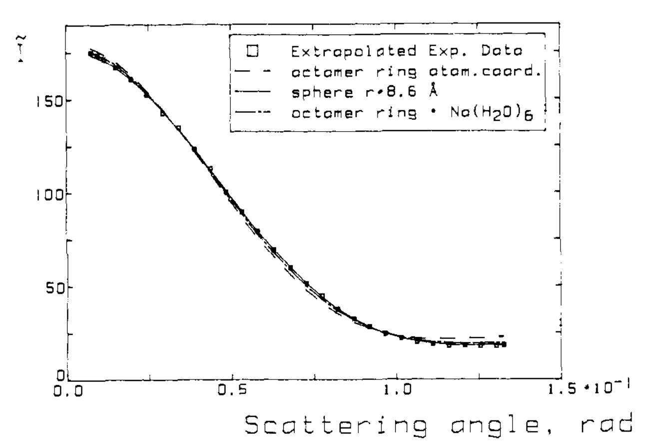

Figure 9. Comparison of the experimental X-ray scattering curve extrapolated to $[Cu^{2+}]_{tot} = 0$, with the three theoretical curves described in the text. For clarity, only half of the experimental points are plotted.

II. SAXS Measurements. Table VI presents the chemical composition of the samples studied; an inert ionic medium of [ClO_4^-] ≈ 0.2 mol/L was selected. The effect of the ionic medium was checked by studying one sample (No. 4, Table VI) without perchlorate, which was found to have a higher interparticle scattering effect than the rest of the samples. The effect of the interparticle scattering was eliminated by extrapolating the $\tilde{I}(m)/[Cu^{2+}]_{tot}$ values for samples 1, 2, and 3 to $[Cu^{2+}]_{tot} = 0$.

After desmearing[21] the extrapolated curve, we obtain a radius of gyration equal to 6.95 Å. From the forward scattering $I(0)$, we calculate a molecular weight equal to 3.1×10^3 using the equation given by Kratky[32] and a partial specific volume equal to 0.537 cm^3/g.

The extrapolated scattering curve is presented in Figure 9, where a comparison with some theoretical models is also given. Three different theoretical models were tested: model a, a homogeneous spherical particle; model b, the atomic coordinates for the Cu-uridine octamer ring found in the single crystal; and model c, the atomic coordinates for the Cu-uridine octamer with the $Na(H_2O)_6$ molecular unit in its center.

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(32) Kratky, O. *Prog. Biophys. Mol. Biol.* **1963**, *13*, 107.

A weighted least-squares method[22] was used to fit the models to the extrapolated scattering curve. Theoretical scattering curves for models b and c were calculated by using the Debye formula.[33]

A small, constant background was also fitted to the experimental data to compensate for the difference in ionic medium of the scattering curve compared with the background curve. Of the three models, the sphere model a gave the best fit, with a fitting index U (cf. eq 5 in ref 18) equal to 0.71% and a sphere radius equal to 8.63 Å. The U values obtained for models b and c were 3.57% and 1.40%, respectively. Thus we can conclude that the best fit with scattering data is obtained for a single sphere model, but an acceptable fit is also obtained for the octamer ring, with the $\mathrm{Na(H_2O)_6}$ unit in the center. A sphere of radius equal to 8.63 Å corresponds to a radius of gyration equal to 6.68 Å, which is in agreement with the value, 6.95 Å, obtained from Guinier plots after desmearing. From the forward scattering $I(0)$ obtained with the sphere model a, a molecular weight of 3.0×10^3 is calculated, which is also in good agreement with the value 3.1×10^3 obtained from Guinier plots after desmearing. It may seem surprising that such a good fit is obtained from such a simplified model. However, similar observations have been made before.[34]

C. Discussion. The structures of the copper(II)–uridine complex and its surrounding zeolitic framework are highly unusual. From the single-crystal structure determination it was not clear if the geometry of the complex is due to the unusual three-dimensional framework or if it is the geometry of the complex that determines the existence of the zeolitic framework. However, it seems chemically reasonable to expect such a structure for the copper(II)–uridine complex. In fact, the coordination of metal ions by the 2′ and 3′ hydroxy oxygens of the ribose group has been proposed several times,[7,8,12,23] and stacking of nucleosides in aqueous solutions is a well-known phenomena[28,35] that favors the overlap of pyrimidine rings. Furthermore, several examples may be found of complexes with head-to-tail arrangements of purine or pyrimidine type ligands.[4b,36]

The results from the emf titrations show unequivocally that the following complex formation reactions take place in aqueous solutions:

$$n\mathrm{Cu}^{2+} + n\mathrm{H}_3\mathrm{urid} \rightleftharpoons \mathrm{Cu}_n\mathrm{urid}_n{}^{n-} + 3n\mathrm{H}^+$$

Furthermore, the SAXS data can be adequately explained both with a sphere of radius 8.63 Å and with the molecular species $[\mathrm{Cu_8(urid)_8Na(H_2O)_6}]^{7-}$, whose molecular weight, 2569, agrees fairly well with the value, 3.1×10^3, obtained from the SAXS data for the particles in solution. It is also interesting that the introduction of the $\mathrm{Na(H_2O)_6}$ unit into the center of the octamer ring gives a more than 6-fold decrease in the error square sum, U. The slightly better fit for the solid sphere of radius 8.63 Å, as compared with the octamer ring, and the small difference in molecular weights might reflect either a certain degree of flexibility in the ring structure or, rather, the association of further $\mathrm{Na^+}$ ions to compensate for the charge of the complex.

Thus, it should be concluded that the dominating Cu(II)–uridine complex in solution has either the same structure as the octamer ring found in the single crystal or a similar one and that, therefore, the peculiar zeolitic framework found in the crystal is due to the geometric properties of the complex.

This type of large polynuclear metal–nucleoside complex has not been reported previously, possibly due to the fact that they are difficult to detect in aqueous solution unless SAXS experiments are performed. Furthermore, single-crystal structure determinations of this kind of highly symmetrical and disordered solids are not a routine procedure.

Although the situation in the tunnels can be regarded as a model of zeolitic sorption because of the relatively large "windows", in fact, it results from a clathration process, since the liberation of the molecular species would induce a host-lattice breakdown. A related phenomena is the template synthesis of some zeolites with quaternary alkylammonium cations.[37]

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Some Aspects of the Reactivity of the First Stable Germaphosphene

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Abstract: Germaphosphene **1**, the first stable compound with a germanium–phosphorus double bond, is very reactive toward compounds with active hydrogens producing secondary phosphines with a high regiospecificity and toward halogens to give adducts **11** and halogermylphosphines **12**. Reaction with carbon tetrachloride allows, after addition followed by β-elimination, the quantitative synthesis of phosphaalkene **16**. **1** reacts easily with nucleophilic compounds such as lithio compounds and Grignard reagents and probably via a radical process with dimethyl disulfide. The germanium–phosphorus double bond of **1** is reduced by lithium aluminum hydride and by the complex $\mathrm{BH_3{\cdot}SMe_2}$ with formation of the germylphosphine **22**; in the last case, a competitive addition of borane to the double bond was also observed.

Compounds of groups 14 and 15 in low coordination state are of particular interest at the present time.[1] Until recently metallaphosphenes (>M=P—, M = Si, Ge, Sn) were postulated only as reactive intermediates and characterized by trapping reactions.

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