

Crystal and Molecular Structure of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4 \cdot 8\text{H}_2\text{O}$. Correlations with ^{113}Cd NMR Spectra of the Solid and Implications for Cadmium-Thiolate Ligation in Proteins

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^{113}Cd NMR chemical shifts in the solid state are reported for $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$ and $[\text{Cd}_{10}(\text{SCH}_2\text{C}(\text{H}_2\text{OH})_{16})(\text{ClO}_4)_4 \cdot 8\text{H}_2\text{O}$. The crystal structure of the latter salt has also been solved and is reported here in greater detail than was previously available for the sulfate salt. The perchlorate octahydrate crystals are monoclinic, space group $C2/c$, with $a = 32.074$ (6) Å, $b = 13.1417$ (6) Å, $c = 25.162$ (4) Å, $\beta = 126.12$ (1)°, and $Z = 4$. The combination of crystallographic and NMR data provides structural confirmation of previously assigned resonances to CdS_4 , CdS_4O , and CdS_3O_3 coordination sites, correlations of the spectra with the site symmetry in the crystalline compounds, and structural insights into the mechanism proposed for CdS_4 - CdS_4O site exchange observed by NMR in solution. previously unrecognized adamantane-like tetranuclear Cd-S fragments of the cation resemble those proposed for CdS_4 sites in metallothionein. Three of the four resonances we assign to CdS_4 sites in the cations (667, 650, and 623 ppm) fall within the range of 670–604 ppm observed for ^{113}Cd -labeled metallothionein. The remaining resonance (705 ppm) falls downfield of this range but well upfield of that assigned to a CdS_4 site in horse liver alcohol dehydrogenase (750 ppm). Our results have the following implications for CdS_4 sites in proteins: (i) Differences in bond distances and angles of ≤ 0.03 Å and $\leq 10^\circ$ are sufficient to induce ^{113}Cd chemical shift differences of up to 82 ppm, a range larger than that observed for metallothionein. (ii) Differences in numbers of bridging vs. nonbridging thiolates need not be invoked to explain the range of resonances observed for metallothionein. Our data also suggest that CdS_4 sites with an average Cd-S distance less than 2.52 Å will have a ^{113}Cd chemical shift downfield of 685 ± 10 ppm. The resonance assigned to the structural site of horse liver alcohol dehydrogenase falls into this category.

Introduction

NMR of the ^{113}Cd nucleus ($I = 1/2$, 12.3% natural isotopic abundance), has been used frequently in recent years to distinguish coordination environments of metal sites in proteins.¹ From solution NMR data on several compounds, a ^{113}Cd chemical shift scale was constructed that spans a range of more than 880 ppm.² Even for a single type of ligand, namely aliphatic thiolate, a chemical shift range of more than 100 ppm has been observed in solution.³ These ranges reflect an extraordinary sensitivity to variations in the Cd^{2+} coordination sphere. High-resolution ^{113}Cd NMR of solids has proven to be a useful adjunct to the solution studies because it removes the complication of chemical exchange averaging and because the spectra can in many cases be correlated with the crystal structure of the solid.⁴⁻⁷ Our previous NMR study of solid $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4$ illustrates these advantages.⁶ The resonance observed at 652 ppm on the δ scale in the ^{113}Cd NMR spectrum of this solid was assigned to the distorted-tetrahedral CdS_4 coordination sites in the cation. This value falls within the range of 600–670 ppm observed in spectra of the cadmium binding protein metallothionein, in which exclusive $\text{Cd}(\text{S-Cys})_4$ ligation has been proposed.^{1f,g} This same coordination sphere presumably occurs when Cd^{2+} is substituted for Zn^{2+} in the structural site of horse liver alcohol dehydrogenase (HLAD), yet its ^{113}Cd NMR resonance occurs at ~ 750 ppm.^{1c}

We have now obtained high-resolution solid-state ^{113}Cd NMR spectra of two different salts of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}]^{4+}$. In order to provide more detailed structural data than those published for the sulfate salt of this cation,⁸⁻¹¹ we have in addition determined the structure of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4 \cdot 8\text{H}_2\text{O}$ by X-ray diffraction techniques. These studies were undertaken in an attempt to provide a structural explanation for the range of resonances observed in metallothionein and for the large deviation from this range of the corresponding resonance for HLAD.

Experimental Section

Preparation of Compounds. $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4$, $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}$, and $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{O}(\text{H}))_{16}](\text{NO}_3)_4$ were prepared by published methods.⁹ The sulfate salt gave an elemental analysis consistent with its formulation as a tetrahydrate. We were never able to obtain satisfactory elemental analyses of the nitrate salt, even after recrystallization. Therefore, although the spectra closely resembled those of the perchlorate salt, NMR data for the nitrate salt are not reported. A consistent analysis for the perchlorate salt, which indicated the anhydrous formulation of Haberkorn et al.,² was obtained after storage for several weeks in a desiccator over CaSO_4 . Since the originally published formulation for the perchlorate was as a tetrahydrate, freshly prepared undesiccated samples (~ 1 g each) of the sulfate and perchlorate salts were heated in an oven at 80°C for 7–9 h. During this time a weight loss occurred for the sulfate salt consistent with removal of 3.8 mol of water/mol of cation. Two separate determinations for the perchlorate salt gave values of 3.8 and 4.6 mol of water lost/mol of cation. ^{113}Cd NMR spectra of these samples as solids were obtained both before and after heating.

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Table I. Summary of Crystal Data, Intensity Collection, and Structure Refinement for [Cd₁₀(SCH₂CH₂OH)₁₆](ClO₄)₄·8H₂O^a

formula (mol wt)	Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆ (ClO ₄) ₄ ·8H ₂ O (2899.86)
<i>a</i> , Å	32.074 (6)
<i>b</i> , Å	13.1417 (6)
<i>c</i> , Å	25.162 (4)
β, deg	126.12 (1)
cryst syst	monoclinic
<i>V</i> , Å ³	8566.9 (10)
<i>Z</i>	4
<i>d</i> _{calcd} , g/cm ³	2.25
space group	<i>C2/c</i>
radiation	Mo Kα (λ = 0.710 34 Å)
abs coeff, μ, cm ⁻¹	29.11 (no correction made)
% transmission range	60–62
temp, K	143
data collectn range, deg	0 ≤ 2θ ≤ 50
no. of reflexns collected	8988
no. of obsd reflexns	6470
no. of unique data	4911
no. of variables	541
% <i>R</i> (averaging)	4.9
% <i>R</i> (refinement)	7.2
% <i>R</i> _w (refinement)	9.2

^a The unit cell parameters listed in the table were mistakenly attributed to the anhydrous salt in previous work.⁶

Collection of NMR Data. ¹¹³Cd NMR spectra were obtained on solid samples with a homemade cross-polarization spectrometer operating at 12.42 MHz for ¹¹³Cd and 56.02 MHz for ¹H in a 1.3-T field. The spectrometer design has been described elsewhere.⁴ The Hartmann–Hahn condition was obtained with use of rotating *H*₁ fields of 9.3 G for ¹H and 42.1 G for ¹¹³Cd. For each spectrum a contact time of 4 ms, a period of 3 s between accumulations, a dc gain of 50 dB, and an amplifier bandwidth of 20 kHz were used for the acquisition of 30 000 transients. Spectra were obtained at room temperature with magic-angle spinning at 2.5 kHz using ~300 mg of sample in an Andrew–Beams type Delrin rotor. The magic angle was taken as that giving minimum line width (1.5–2 ppm) of the resonance due to solid Cd(NO₃)₂·4H₂O, which also served as the external chemical shift reference. Conversion to the δ scale vs. 0.1 M Cd(ClO₄)₂ was made with use of the published equation.⁶ Spectra are uncorrected for frequency rolloff from the low-pass filter of the Cd signal amplifier, linear phase errors due to time delays in the digitization of the NMR signal, and bulk susceptibilities. All compounds contained the natural isotopic abundance of ¹¹³Cd.

Collection and Reduction of X-ray Data. A colorless single crystal from a recrystallized sample of the perchlorate salt with approximate dimensions of 0.2 mm on a side was selected from the aqueous mother liquor, sealed in a glass Lindemann capillary, and mounted on a goniometer head. On a four-circle diffractometer designed and built at Ames Laboratory equipped with a Dewared cold nitrogen gas delivery system, data were collected at 143 K with use of monochromatic Mo Kα radiation.¹² Nine independent reflections taken from various ω-oscillation photographs at various Φ settings were input into an automatic indexing algorithm.¹³ The resulting reduced cell and reduced cell scalars indicate a centered monoclinic cell. Data were collected from the octants *hkl* and $\bar{h}\bar{k}l$. The intensities of 3 standard near-axial reflections were measured after every 75 reflections during data collection to monitor decay. No appreciable decay was exhibited. The final cell parameters and standard deviations were calculated from the tuned angles for 16 higher angle reflections (25.98° ≤ 2θ ≤ 33.32°). The systematic absences *hkl* (*h* + *k* ≠ 2*n*) and *h0l* (*l* ≠ 2*n*) along with statistical evidence of centricity uniquely define the space group as *C2/c*. All data were corrected for Lp effects and appropriately averaged. All pertinent information relative to the unit cell and data collection is compiled in Table I.

Solution and Refinement of the Structure. All unique cadmium (6), chlorine (2), and sulfur (8) atomic positions were obtained from a Patterson superposition map with use of the program ALCAMPS.¹⁴

Table II. Atomic Coordinates (×10⁴)^a and Average Temperature Factors (Å², ×10³) for [Cd₁₀(SCH₂CH₂OH)₁₆](ClO₄)₄·8H₂O

atom	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> (av) ^b
Cd(1)	40073 (5)	133259 (9)	5126 (7)	48
Cd(2)	50000 (0)	13149 (i)	25000 (0)	52
Cd(3)	37644 (4)	87799 (9)	26157 (5)	35
Cd(4)	47563 (4)	111685 (9)	35943 (6)	39
Cd(5)	50000 (0)	8792 (1)	25000 (0)	32
Cd(6)	37447 (4)	108045 (9)	13070 (5)	35
Cl(1)	3886 (2)	6710 (4)	9578 (3)	71
Cl(2)	2266 (2)	9702 (4)	8727 (2)	54
S(1)	4690 (2)	14314 (3)	1555 (2)	49
S(2)	4486 (1)	11892 (3)	363 (2)	39
S(3)	3363 (1)	12386 (3)	628 (2)	37
S(4)	4356 (1)	11936 (3)	2447 (2)	37
S(5)	4411 (1)	9577 (3)	3742 (2)	37
S(6)	4295 (1)	7709 (3)	2352 (2)	33
S(7)	3260 (1)	10168 (3)	1745 (2)	38
S(8)	4561 (1)	9987 (3)	1513 (2)	33
C(11)	4246 (8)	15133 (15)	1585 (11)	65
C(12)	3863 (9)	15602 (21)	1000 (10)	98
O(11)	3587 (4)	4962 (9)	444 (5)	54
C(21)	4734 (6)	12615 (13)	-32 (7)	45
C(22)	4770 (8)	13715 (15)	100 (12)	87
O(21)	4279 (5)	14110 (9)	-121 (7)	74
C(31)	2950 (6)	11954 (12)	-240 (8)	38
C(32)	2800 (6)	12862 (13)	-694 (8)	47
O(31)	3253 (4)	13316 (11)	-590 (6)	66
C(41)	3857 (7)	12786 (15)	2353 (8)	57
C(42)	3936 (12)	13054 (24)	2962 (14)	147
O(41)	4115 (5)	12352 (10)	3431 (6)	74
C(51)	3944 (7)	9960 (13)	3898 (8)	53
C(52)	3526 (6)	9116 (14)	3686 (8)	54
O(51)	3255 (4)	8963 (9)	3023 (5)	53
C(61)	4623 (6)	6963 (12)	3122 (8)	42
C(62)	4227 (6)	6399 (12)	3168 (7)	37
O(61)	3882 (4)	7115 (8)	3146 (5)	46
C(71)	2695 (6)	9451 (13)	1086 (8)	44
C(72)	2810 (6)	8323 (14)	1098 (8)	50
O(71)	2967 (4)	7926 (9)	1717 (5)	51
C(81)	4256 (7)	9148 (14)	799 (9)	53
C(82)	3756 (8)	9034 (31)	458 (15)	219
O(81)	3399 (4)	9563 (8)	436 (5)	37
O(1)	3882 (5)	7721 (9)	9348 (7)	69
O(2)	3452 (6)	6572 (15)	9586 (10)	130
O(3)	3904 (9)	5983 (13)	9161 (12)	155
O(4)	4343 (5)	6544 (17)	222 (8)	128
O(5)	1820 (5)	9078 (10)	8297 (7)	60
O(6)	2700 (6)	9257 (13)	8795 (9)	98
O(7)	2184 (6)	692 (12)	8458 (7)	79
O(8)	2363 (5)	9731 (13)	9375 (6)	75
O(9)	1883 (9)	1289 (19)	1760 (12)	93
O(10)	7248 (8)	2597 (17)	2007 (13)	127
O(111)	7244 (7)	4459 (18)	2355 (10)	61
O(12)	7689 (12)	5927 (27)	2474 (17)	116

^a ×10⁵ for Cd atoms. ^b Average of *U*₁₁, *U*₂₂, and *U*₃₃.

The remaining non-hydrogen atoms were identified from the resulting electron density map. All positional parameters and thermal parameters were refined with use of a block-diagonal least-squares procedure.¹⁵ Isotropic refinement converged at *R* = 12.4%. All non-hydrogen atoms were refined anisotropically. C(42) and C(82) were refined to relatively large thermal ellipsoids (Table II) with the long axes roughly perpendicular to the mean planes described by atoms Cd(4)–O(41)–C(41)–S(4) and Cd(6)–O(81)–C(81)–S(8), respectively (Figure 5). For these reasons an attempt was made to resolve atoms C(42) and C(82) into two atomic positions each, one above and one below their corresponding mean planes. This model provided no

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(15) Calculations were carried out on a VAX 11/780 computer. Positions of the heavier atoms were obtained from maps created by the program SUPR (C. R. Hubbard, M. W. Babich, and R. A. Jacobson). Structure factor calculations and least-squares refinements were done with use of the block-matrix/full-matrix program ALLS (R. L. Lapp and R. A. Jacobson). Fourier series calculations were done with the program FOUR (D. R. Powell and R. A. Jacobson), and for molecular drawings the program ORTEP (C. K. Johnson) was used.

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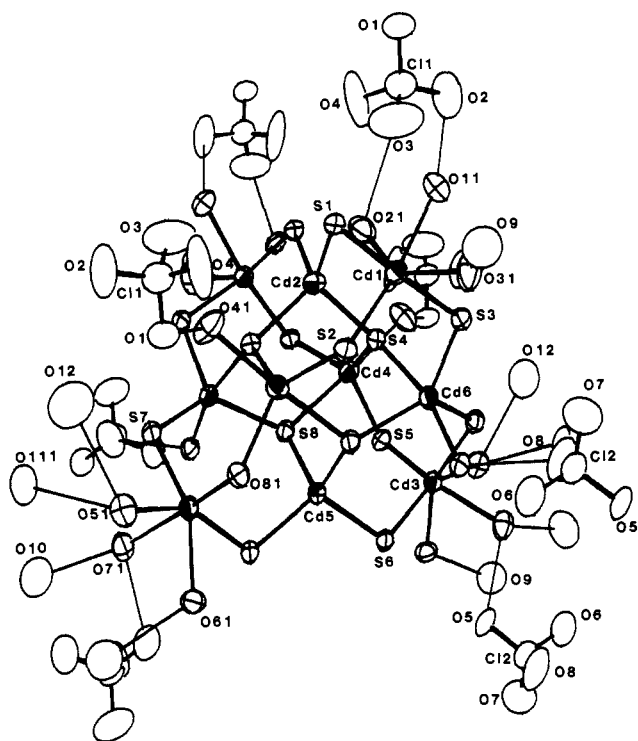


Figure 1. Structure of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}]^{2+}$ (carbon and hydrogen atoms omitted) showing 50% probability ellipsoids, atom-numbering scheme, and hydrogen-bonded perchlorates and oxygens from water. Thinner lines indicate hydrogen bonds. In some cases only one of a pair of identical atoms related by the twofold axis passing through Cd(2) and Cd(5) is labeled. The atom-numbering scheme for β -mercaptoethanols is illustrated in Figure 5.

improvement in the residual agreement factor and did not converge effectively. This attempt was thus abandoned, and C(42) and C(82) were refined as individual atoms. The occupation factor for O(9) was fixed at 0.65, and isotropic refinement was carried on it. For O(10), the occupation factor was set at 0.85 and it was allowed to refine anisotropically. It was necessary to fix these occupancies because of excessive correlation between the occupancy factors and thermal parameters. The occupation factors for O(111) and O(12) were refined along with their anisotropic thermal parameters. These occupancy factors converged to 0.626 and 0.603, respectively. Ethylenic hydrogen atomic positions were calculated but not varied. A final full-matrix refinement of positions and thermal parameters converged at 7.2%. The difference Fourier map was featureless with maxima of less than $1 \text{ e}/\text{\AA}^3$. The atomic scattering factors¹⁶ for cadmium, chlorine, and sulfur were modified for anomalous dispersion.¹⁷

Table I lists unique data used in the refinement of the structure, and Table II lists positional parameters.

Results and Discussion

General Description of the Structure of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{O}-\text{H})_{16}](\text{ClO}_4)_4 \cdot 8\text{H}_2\text{O}$. Figure 1 depicts the structure of the Cd-S framework and hydroxyl oxygens of the cation. The crystallographic C_2 axis that passes through Cd(2) and Cd(5) is oriented vertically. The eight perchlorates and ten oxygens from water which are within hydrogen-bonding distance ($\leq 3.0 \text{ \AA}$) to a cation hydroxyl group are also depicted in Figure 1. Table III lists relevant distances and angles. A stereoview of the unit cell (Figure 2) is included in the supplementary material.

There are two types of perchlorates surrounding each cation. The first type consists of the four perchlorates nearest Cd(2)

Table III. Selected Distances (\AA) and Angles (deg) for $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4 \cdot 8\text{H}_2\text{O}^a$

CdS_3O_3			
Cd(1)-S(1)	2.568 (5)	Cd(3)-S(6)	2.578 (4)
Cd(1)-S(2)	2.595 (4)	Cd(3)-S(7)	2.562 (4)
Cd(1)-S(3)	2.567 (4)	Cd(3)-S(5)	2.549 (4)
Cd(1)-O(11)	2.49 (1)	Cd(3)-O(61)	2.47 (1)
Cd(1)-O(21)	2.45 (1)	Cd(3)-O(71)	2.47 (1)
Cd(1)-O(31)	2.37 (1)	Cd(3)-O(51)	2.40 (1)
S(1)-Cd(1)-S(2)	107.1 (1)	S(6)-Cd(3)-S(7)	110.4 (1)
S(1)-Cd(1)-S(3)	112.8 (2)	S(6)-Cd(3)-S(5)	106.4 (1)
S(2)-Cd(1)-S(3)	104.6 (1)	S(7)-Cd(3)-S(5)	110.4 (1)
O(11)-Cd(1)-O(21)	88.8 (4)	O(61)-Cd(3)-O(71)	80.5 (4)
O(11)-Cd(1)-O(31)	77.6 (4)	O(61)-Cd(3)-O(51)	77.5 (4)
O(21)-Cd(1)-O(31)	75.6 (4)	O(71)-Cd(3)-O(51)	80.5 (4)
S(1)-Cd(1)-O(11)	74.7 (3)	S(6)-Cd(3)-O(61)	75.1 (3)
S(2)-Cd(1)-O(21)	75.1 (3)	S(7)-Cd(3)-O(71)	75.6 (3)
S(3)-Cd(1)-O(31)	78.2 (3)	S(5)-Cd(3)-O(51)	78.3 (3)
CdS_4O			
Cd(4)-S(2)	2.485 (4)	Cd(6)-S(7)	2.520 (4)
Cd(4)-S(4)	2.576 (4)	Cd(6)-S(8)	2.582 (4)
Cd(4)-S(5)	2.496 (4)	Cd(6)-S(3)	2.504 (4)
Cd(4)-S(8)	2.824 (4)	Cd(6)-S(4)	2.767 (4)
Cd(4)-O(41)	2.41 (1)	Cd(6)-O(81)	2.41 (1)
S(2)-Cd(4)-S(4)	124.4 (1)	S(7)-Cd(6)-S(8)	126.0 (1)
S(2)-Cd(4)-S(5)	114.1 (1)	S(7)-Cd(6)-S(3)	113.2 (1)
S(2)-Cd(4)-S(8)	88.9 (1)	S(7)-Cd(6)-S(4)	88.2 (1)
S(2)-Cd(4)-O(41)	97.8 (3)	S(7)-Cd(6)-S(81)	96.0 (3)
S(4)-Cd(4)-S(5)	121.6 (1)	S(8)-Cd(6)-S(3)	120.8 (1)
S(4)-Cd(4)-S(8)	90.7 (1)	S(8)-Cd(6)-S(4)	90.1 (1)
S(4)-Cd(4)-O(41)	75.4 (3)	S(8)-Cd(6)-S(81)	76.5 (2)
S(5)-Cd(4)-S(8)	89.5 (1)	S(3)-Cd(6)-S(4)	91.3 (1)
S(5)-Cd(4)-O(41)	98.9 (3)	S(3)-Cd(6)-O(81)	99.5 (3)
S(8)-Cd(4)-O(41)	166.1 (3)	S(4)-Cd(6)-O(81)	165.8 (3)
CdS_4			
Cd(2)-S(1)	2.491 (5)	Cd(5)-S(6)	2.507 (4)
Cd(2)-S(4)	2.550 (4)	Cd(5)-S(8)	2.548 (4)
S(1)-Cd(2)-S(1)'	104.1 (2)	S(6)-Cd(5)-S(6)'	110.8 (2)
S(1)-Cd(2)-S(4)	118.7 (1)	S(6)-Cd(5)-S(8)	115.3 (1)
S(1)-Cd(2)-S(4)'	106.8 (1)	S(6)-Cd(5)-S(8)'	105.8 (1)
S(4)-Cd(2)-S(4)'	102.7 (2)	S(8)-Cd(5)-S(8)'	104.0 (2)
$\text{Cd}\cdots\text{Cd}$			
Cd(1)-Cd(2)	4.05	Cd(3)-Cd(5)	4.15
Cd(1)-Cd(4)'	4.28	Cd(3)-Cd(4)	4.10
Cd(1)-Cd(6)	4.21	Cd(3)-Cd(6)	4.21
Cd(2)-Cd(4)	4.19	Cd(5)-Cd(4)	4.53
Cd(6)-Cd(4)'	4.70	Cd(6)'-Cd(4)'	4.68
Cd(6)-Cd(2)	4.53	Cd(6)-Cd(5)	4.24

^a Adjacent horizontal listings would be equivalent if the cation had an S_4 axis passing through Cd(2) and Cd(5).

in Figure 1 (perchlorate 1). These are related to each other by translations and rotations of the $C2/c$ space group as are the second type, which consists of those four perchlorates nearest Cd(5) (perchlorate 2). Three of the four oxygens in every perchlorate 1 group are each within hydrogen-bonding distance of a hydroxyl oxygen from adjacent cations. O(4) is not within hydrogen-bonding distance of either a cation hydroxyl group or a water molecule. Two of the oxygens in every perchlorate 2 group are each within hydrogen-bonding distance to a cation hydroxyl while a third oxygen, O(7), is hydrogen bonded to water. O(6) has no hydrogen bonds.

There are 32 water sites per unit cell with $Z = 4$. The calculated site occupancies of the four independent waters, O(9), O(10), O(111), and O(12) (see Experimental Section) lead to a value of 5.5 waters/cation. These values together with the thermal gravimetric data (see Experimental Section) lead to the conclusion that the perchlorate salt is best formulated as an octahydrate with about half the water being rapidly lost at room temperature.

The Cd-S framework closely resembles that of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{SO}_4)_2 \cdot 4\text{H}_2\text{O}^{8,9,11}$ and consists of four dis-

(16) Cromer, D. T.; Waber, J. T. "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. IV, Table 2.2A, pp 71-79.

(17) Templeton, D. H. "International Tables for X-ray Crystallography"; Kynoch Press: Birmingham, England, 1974; Vol. III, Table 3.3.2.c, pp 215-216.

Table IV. Chemical Shift Data in δ (± 5 ppm)^a for ¹¹³Cd NMR Spectra of [Cd₁₀(SCH₂CH₂OH)₁₆]⁴⁺ in Solids

	resonance		
	A (CdS ₃ O ₃)	B (CdS ₄ O)	C (CdS ₄)
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](ClO ₄) ₄ ·8H ₂ O ^b	403	496	650
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](ClO ₄) ₄ ·8H ₂ O ^c	409	503	667
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](ClO ₄) ₄ ·8H ₂ O ^c	404	497	650
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](ClO ₄) ₄ ·8H ₂ O ^c	409	503	667
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](ClO ₄) ₄ ^{b,f}	400	492	673
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](ClO ₄) ₄ ^d	388	481	652
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](SO ₄) ₂ ·4H ₂ O ^e	391	481	623
[Cd ₁₀ (SCH ₂ CH ₂ OH) ₁₆](SO ₄) ₂ ^f	401	507	705
	392	488	625
		504	657
			686

^a Vs. 0.1 M aqueous Cd(ClO₄)₂. ^b Figure 3. ^c From the recrystallized sample used for the X-ray structure. ^d Reference 6. ^e Figure 4. ^f Heated to 80 °C.

torted-octahedral CdS₃O₃ sites (Cd(1) and Cd(3)), four distorted-trigonal-bipyramidal CdS₄O sites (Cd(4) and Cd(6)), and two distorted-tetrahedral CdS₄ sites (Cd(2) and Cd(5)). The positions of the sulfates and water molecules in this latter salt have not been published, which precludes a detailed comparison of hydrogen-bonding patterns in the two salts. Further structural details are discussed below in the context of correlations with ¹¹³Cd NMR spectra.

¹¹³Cd Chemical Shifts. The chemical shifts of various samples of the perchlorate and sulfate salts of the decanuclear cation are listed in Table IV, and representative spectra are shown in Figures 3 and 4. The previously published values⁶ for the chemical shifts of [Cd₁₀(SCH₂CH₂OH)₁₆](ClO₄)₄ are 10–20 ppm upfield of those determined for the anhydrous salt in this work (Table IV). A possible reason for this discrepancy is that the previous data were obtained on a sample that had been stored in a desiccator over CaSO₄ and, unlike those in the present work, had not been heated above room temperature. The chemical shifts are referenced to 0.1 M aqueous Cd(ClO₄)₂ although the actual data were collected with external solid Cd(NO₃)₂·4H₂O as the reference. We have re-measured the chemical shift difference between the two standards and verified that the originally published equation for conversion between the two is correct.⁶ As can be seen from Table IV, our chemical shifts are quite reproducible for two different samples of [Cd₁₀(SCH₂CH₂OH)₁₆](ClO₄)₄·8H₂O. In any case the conclusions from the previous work remain valid. We assign the A resonances to the CdS₃O₃ sites, the B resonances to the CdS₄O sites, and the C resonances to the CdS₄ sites. The chemical shifts assigned to the CdS₃O₃ (A) sites still fall near those observed in the solution NMR spectra of [Cd₁₀(SCH₂CH₂OH)₁₆](ClO₄)₄ (378–409 ppm).² As discussed below, only a single average resonance is seen in solution for the CdS₄O (B) and CdS₄ (C) sites.

Symmetry Aspects. As noted previously,^{2,6} it is convenient to discuss the ¹¹³Cd NMR spectra by first assuming that the cation has S₄ symmetry with the axis passing through Cd(2) and Cd(5), in which case all cadmium sites with the same coordination sphere are equivalent. The actual C₂ symmetry in the crystal splits these sites into nonequivalent pairs. This nonequivalence can be seen both from the dimensions and environment of the cation (Figure 1 and Table III) and from the ¹¹³Cd NMR spectra of the solid hydrates in Figures 3 (top) and 4. The splittings in the NMR spectra are *not* due to two different cation sites in the crystal. From Figure 3 and Table IV it can also be seen that dehydration of the perchlorate (but not the sulfate) causes the cation to more closely approximate S₄ symmetry. The first three sets of data in Table IV show that dehydration achieved by heating of the perchlorate salt results in a spectrum whose A, B, and C resonances match

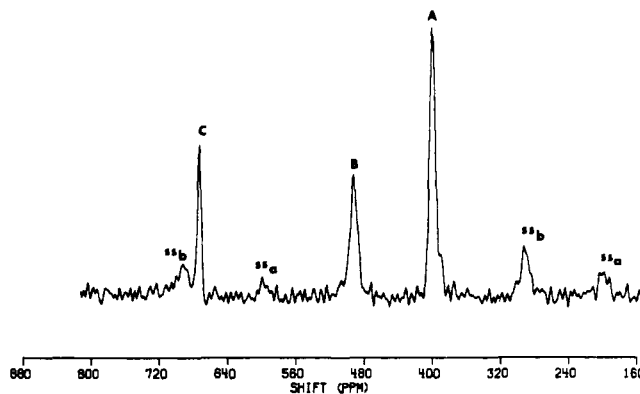
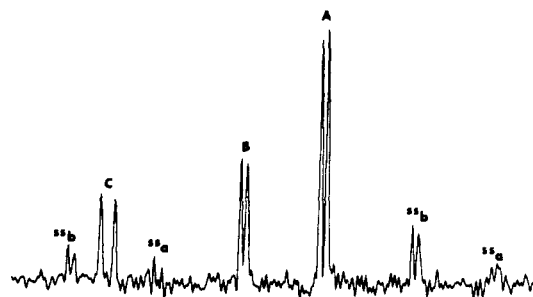


Figure 3. ¹¹³Cd NMR spectra of solid [Cd₁₀(SCH₂CH₂OH)₁₆](ClO₄)₄·8H₂O (top) and the same sample dehydrated by heating at 80 °C (bottom). The chemical shift scale is in δ relative to aqueous 0.1 M Cd(ClO₄)₂. Resonances assigned to the CdS₃O₃ (A), CdS₄O (B), and CdS₄ (C) sites are labeled. Spinning satellites are indicated by SS with the subscript referring to the parent peak.

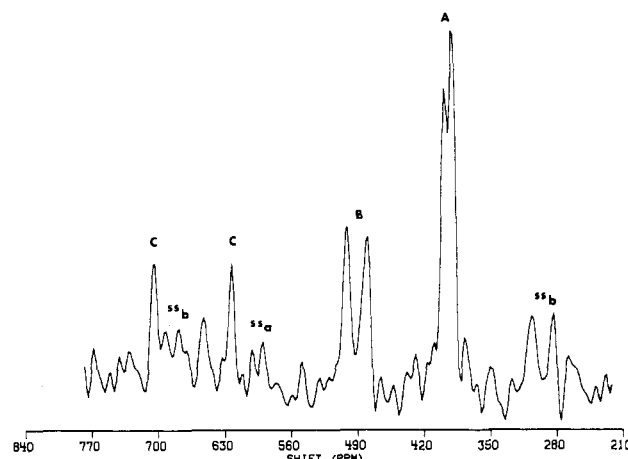


Figure 4. ¹¹³Cd NMR spectrum of solid [Cd₁₀(SCH₂CH₂OH)₁₆](SO₄)₂·4H₂O. The scale and labeling are those listed in the legend to Figure 3.

closely with one component of the corresponding doublet in the spectra of the hydrates. The top half of the cation as depicted in Figure 1 is less highly hydrated than the bottom half. On this basis it is tempting to assign the matching components in the spectra of the hydrate to Cd(1) (403–404 ppm), Cd(4) (496–497 ppm), and Cd(2) (650 ppm). However, we were unable to obtain crystals of the anhydrous perchlorate suitable for determination of an X-ray structure. Therefore, we could not elucidate the structural changes that lead to the higher symmetry observed by NMR. One structural change that could accompany dehydration may be achieved by rotation

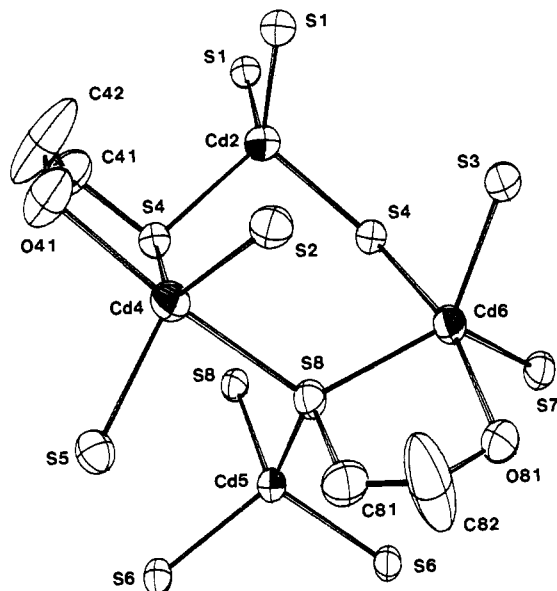


Figure 5. Structure of the CdS_4O and CdS_4 sites in $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4 \cdot 8\text{H}_2\text{O}$ including the carbon atoms of the β -mercaptoethanols proposed to be involved in the site exchange (see text). Fifty percent probability ellipsoids are shown.

of the perchlorates depicted at the bottom of Figure 1 around the $\text{O}(71)\cdots\text{O}(5)$ hydrogen bonds such that a second hydrogen bond forms between a remaining perchlorate oxygen and $\text{O}(61)$. With loss of water this hydrogen-bonding pattern would then more closely resemble that depicted at the top of Figure 1, where $\text{O}(11)\cdots\text{O}(2)$ and $\text{O}(21)\cdots\text{O}(3)$ hydrogen bonds occur. This change could be either the cause or the effect of other structural changes in and around the cation that together result in a closer approximation to at least local S_4 symmetry.

The relative intensities, I , of the first-order spinning satellites in each of the spectra of Figures 3 and 4 vary in the order $I_B > I_A > I_C$. This order reflects the relative magnitudes of the chemical shift anisotropies and indicates the range of bonding distances at the CdS_4O (B), CdS_3O_3 (A), and CdS_4 (C) sites.⁶

CdS_4 - CdS_4O Site Exchange. Above -40°C in dimethylformamide solution a single exchange-averaged resonance is seen for the CdS_4O and CdS_4 sites in the ^{113}Cd NMR spectrum of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4$,² whereas the well-separated resonances B and C, respectively, are seen for these sites in the spectrum of the solid (Figure 3 and Table IV). From the separation between these resonances in the spectrum of the solid a rate of $1.3 \times 10^4 \text{ s}^{-1}$ was estimated for CdS_4 - CdS_4O site exchange in solution above -40°C .⁶ Support for and further insight into a mechanism proposed by Haberkorn et al.² can be gleaned from an examination of Figure 5. The mechanism for site exchange between $\text{Cd}(2)$ and $\text{Cd}(4)$ consists of breakage of the $\text{Cd}(4)\text{-O}(41)$ bond and formation of a bond between $\text{Cd}(2)$ and $\text{O}(41)$. Similarly, site exchange between $\text{Cd}(5)$ and $\text{Cd}(6)$ occurs via $\text{O}(81)$. Note that $\text{Cd}(4)$ and $\text{Cd}(6)$ each consist of a symmetry-related pair in the solid. The thermal ellipsoids for $\text{C}(42)$ and $\text{C}(82)$ are significantly larger than for any other carbon atom in the molecule (Table II). Furthermore, as can be seen in Figure 5, the long axes of these ellipsoids point in a direction approximately perpendicular to the mean planes of the five-membered rings containing $\text{C}(42)$ and $\text{C}(82)$. For each of the eight independent β -mercaptoethanols in the molecule one can define a torsional angle between the $\text{O}(N1)\text{-C}(N2)$ line and the plane defined by $\text{S}(N)$, $\text{C}(N1)$, and $\text{C}(N2)$. The average value for $N = 1-7$ is $60.4 (1.8)^\circ$. The value for $N = 4$ is 38.4° and for $N = 8$ is 16.7° , deviations of 12σ and 24σ , respectively, from the above average value. These deviations may reflect a strain

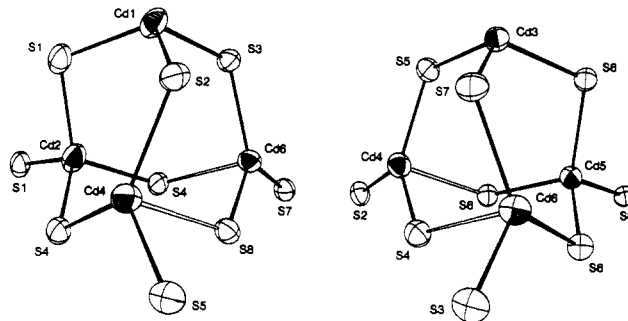


Figure 6. The two adamantane-like tetranuclear fragments within $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}](\text{ClO}_4)_4 \cdot 8\text{H}_2\text{O}$ oriented so that the single CdS_3O_3 site per fragment is on top. Only Cd and S atoms as 50% probability ellipsoids are shown. The S atoms depicted as terminal actually bridge other Cd atoms outside these fragments. Open lines represent long ($\sim 2.8 \text{ \AA}$) Cd-S bonds.

in the five-membered rings depicted in Figure 5 that is relieved by predominately perpendicular movements of $\text{C}(42)$ and $\text{C}(82)$ in the solid and by breakage of the Cd-O bonds in solution. $\text{S}(1)\text{-Cd}(2)\text{-S}(4)$ at 118.7° and $\text{S}(6)\text{-Cd}(5)\text{-S}(8)$ at 115.3° are the two largest angles within the CdS_4 sites. In the crystal these angles might allow the greater movement of $\text{C}(42)$ and $\text{C}(82)$, respectively. These angles also face likely pathways of attack by the exchanging $\text{O}(41)$ and $\text{O}(81)$, respectively. The long ($\sim 2.8 \text{ \AA}$) axial Cd-S bonds of the CdS_4O sites and the connectivities in the molecule suggest that the site exchange may be cooperative. For example, formation of a $\text{Cd}(2)\text{-O}(41)$ bond would presumably lengthen the trans $\text{Cd}(2)\text{-S}(4)$ bond,¹⁰ which in turn might render $\text{S}(4)$ more nucleophilic toward $\text{Cd}(6)$, thus labilizing the $\text{Cd}(6)\text{-O}(81)$ bond, etc.

Adamantane-like Tetranuclear Fragments. In light of the tri- and tetranuclear clusters of cadmium atoms proposed for the metal binding sites in metallothionein,^{14,8} an ideal model would seem to be a $[\text{Cd}_4(\text{SR})_{10}]^{2-}$ cluster with an adamantane-like Cd-S framework of the type prepared by Hagen et al.¹⁸ However, with $\text{R} = \text{aryl}$, the ^{113}Cd NMR resonance of this cluster is at least 25 ppm upfield of any resonance observed in spectra of ^{113}Cd -enriched metallothionein. Unfortunately, no such cluster with $\text{R} = \text{alkyl}$ has yet been structurally characterized although complexes with a RS^-/Cd ratio of ~ 2.5 probably exist in aqueous solutions of Cd^{2+} and alkanethiolates.^{3,9} We note, however, that adamantane-like tetranuclear clusters exist as fragments of the Cd-S framework of $[\text{Cd}_{10}(\text{SCH}_2\text{CH}_2\text{OH})_{16}]^{4+}$. Figure 6 shows the two such fragments per cation for the perchlorate salt. Although only one cadmium site per fragment ($\text{Cd}(2)$ and $\text{Cd}(5)$) is of the CdS_4 type proposed exclusively for metallothionein, these fragments demonstrate that such sites can exist in adamantane-like clusters with aliphatic thiolate and can exhibit ^{113}Cd NMR resonances (667 and 650 ppm) within the range observed for metallothioneins.

^{113}Cd Chemical Shifts of CdS_4 Sites. Structural Correlations. The fact that a ^{113}Cd chemical shift scale can be set up which correlates reasonably well with type and number of ligands suggests that for an identical ligand set chemical shift differences arise predominately from structural differences within the first coordination shell.^{2,3,5,7} The largest angular difference between the two CdS_4 sites in the hydrated perchlorate salt is 6.7° for the outer S-Cd-S angles that lie on the C_2 axis ($\text{S}(1)\text{-Cd}(2)\text{-S}(1')$ and $\text{S}(6)\text{-Cd}(5)\text{-S}(6)'$ in Table III). The difference between the average Cd-S distances for these two sites is $<0.01 \text{ \AA}$ (2.520 vs. 2.527 \AA). The 17 ppm splitting of the C resonance for this salt could thus be attributed pri-

(18) (a) Hagen, K. S.; Stephan, D. W.; Holm, R. H. *Inorg. Chem.* **1982**, *21*, 3928. (b) Hagen, K. S.; Holm, R. H. *Ibid.* **1983**, *22*, 3171-3174.

marily to angular differences. However, angular differences of about the same magnitude are observed between the two CdS₄ sites in the hydrated sulfate salt,^{11,19} yet a splitting of 82 ppm is observed for the C resonance. We attribute the majority of this latter splitting to a difference of 0.03 Å (2.50 vs. 2.53 Å) between the average Cd–S distances for the two CdS₄ sites.^{11,19} It is important to note that these average distances lie on either side of 2.52 Å, the sum of Cd and S covalent radii.¹⁰ Inspection of Table IV shows that none of the remaining A and B resonances in any of the spectra are split by more than 26 ppm and all of the corresponding differences in average cadmium–ligand distances are <0.02 Å.^{8–11,19} Furthermore, none of these average distances is less than the sum of cadmium plus ligand covalent radii. The structural data on [Cd₁₀(SCH₂CH₂OH)₁₆]⁴⁺ avail us with distances and angles for four different CdS₄ sites and ¹¹³Cd NMR avails us with four chemical shift values: 667 and 650 ppm for the perchlorate octahydrate and 705 and 623 ppm for the sulfate tetrahydrate. We assign the value that shows the largest deviation from the average of these four, namely the 705 ppm resonance, to the CdS₄ site that shows the largest structural deviation, namely that with the 2.50-Å average Cd–S distance. The only other solid-state ¹¹³Cd NMR data we know of for a structurally delineated CdS₄ site that can be considered to have sp³-hybridized sulfurs and tetrahedral geometry is for CdS. The Cd–S distance is 2.52 Å,¹⁰ and the chemical shift is 687 ppm.⁶ From these results we propose the following generalization for CdS₄ sites with sp³-hybridized sulfurs: only those sites with average Cd–S distances below 2.52 Å, i.e. below the sum of Cd and S covalent radii, will exhibit chemical shifts downfield of 685 ± 10 ppm. The range allows for angular and other environmental differences but assumes a tetrahedral or disorted-tetrahedral configuration. We are unaware of previous correlations of this type. However, our proposal is consistent with the 1/*r*³ dependence of the paramagnetic shielding terms, which have been suggested previously to provide the dominant contribution to differences in ¹¹³Cd chemical shifts.^{2,7}

Implications for Cadmium–Thiolate Ligation in Proteins.

Three of the four resonances we assign to CdS₄ sites (667, 650, and 623 ppm) fall within the range of 670–604 ppm observed for ¹¹³Cd-labeled metallothionein.^{1f,8} The remaining resonance (705 ppm) falls downfield of this range but well upfield of that assigned to a CdS₄ site in HLAD (~750 ppm).^{1c} We believe our results have the following implications for CdS₄ sites in proteins: (i) Relatively small differences in bond distances (≤0.03 Å) and angles (≤10°) are sufficient to induce ¹¹³Cd chemical shift differences of up to 82 ppm, a range larger than that observed for ¹¹³Cd-labeled metallothionein. (ii) Differences in numbers of bridging vs. nonbridging thiolates need not be invoked to explain the range of resonances observed for

¹¹³Cd-labeled metallothionein. If our proposed generalization regarding chemical shift vs. Cd and S covalent radii is correct, then two more implications are as follows: (iii) All of the resonances observed in spectra of ¹¹³Cd-labeled metallothionein are due to sites with average Cd–S distances ≥2.52 Å; (iv) The resonance assigned to the structural site in HLAD is highly deshielded because the four nonbridging cysteinate ligands give an average Cd–S distance significantly less than 2.52 Å.

It is not unrealistic to assume that fewer bridges per thiolate should lead to a shorter Cd–S distance. In every CdS₄ site in the perchlorate and sulfate salts of [Cd₁₀(SCH₂CH₂OH)₁₆]⁴⁺, the shorter (outer) Cd–S distance is to a sulfur that bridges two Cd atoms, while the longer (inner) Cd–S distance is to a sulfur that bridges three Cd atoms. These triply bridging sulfurs also participate in CdS₄O coordination, where the same trend is observed. Cd–S distances are longer for triply bridging than for doubly bridging sulfurs (cf. Table III and Figure 1).^{10,11,19} Two compounds of Cd²⁺ with penicillamine have been structurally characterized, neither of which contains a CdS₄ site. Cd[NH₂CH(CO₂)C(CH₃)₂-S]·H₂O contains thiolates that bridge two cadmiums, and the Cd–S distances are 2.563 (7) and 2.567 (7) Å.²⁰ A second compound, [CdBr(SC(CH₃)₂CH(NH₃)COO)H₂O]·2H₂O, contains only a nonbridging thiolate, and the Cd–S distance is 2.444 (2) Å.²¹ This latter distance is to our knowledge the shortest Cd–S distance ever reported, and it occurs in the only structurally characterized example we know of a nonbridging aliphatic thiolate coordinated to Cd²⁺.

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Registry No. [Cd₁₀(SCH₂CH₂OH)₁₆](SO₄)₂, 54800-46-3; [Cd₁₀(SCH₂CH₂OH)₁₆](ClO₄)₄·8H₂O, 88915-68-8; [Cd₁₀(SCH₂CH₂OH)₁₆](NO₃)₄, 54800-43-0; ¹¹³Cd, 14336-66-4.

Supplementary Material Available: Listings of structure factors, anisotropic thermal parameters, calculated H atom coordinates, C–C, C–S, and C–O bond lengths and angles, perchlorate bond distances and angles, and hydrogen-bonding distances and angles and a stereoview of the unit cell (Figure 2) (22 pages). Ordering information is given on any current masthead page.

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(20) Freeman, H. C.; Huo, F.; Stevens, G. N. *J. Chem. Soc., Chem. Commun.* **1976**, 90.

(21) Carty, A. J.; Taylor, N. J. *Inorg. Chem.* **1977**, *16*, 177.