Structure of Methylguanidinium Dihydrogenorthophosphate. A Model Compound for Arginine–Phosphate Hydrogen Bonding[1]

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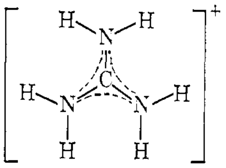
Abstract: The crystal structure of methylguanidinium orthophosphate, $CH_3NHC(NH_2)_2PO_2(OH)_2$, has been determined. Crystal data: space group, $P2_1/c$; unit cell dimensions $a = 7.557$ (3) Å, $b = 14.346$ (7) Å, $c = 6.897$ (3) Å, $\beta = 101.78°$; D(obsd) = 1.545 g cm^{-3}, D(calcd) = 1.552 for $Z = 4$. Using Zr-filtered Mo Kα radiation 3451 independent reflections having $\lambda^{-1} \sin\theta \leqslant 0.817$ were collected with an automated diffractometer. The 2840 reflections with $I > \sigma(I)$ were used to solve and refine the structure including all hydrogen atoms by Patterson, difference Fourier, and least-squares procedures to final unit weighted and weighted residuals of 0.048 and 0.056, respectively. The methylguanidinium ions are planar except for the hydrogen atoms. Some important bond lengths are H_3C–N, 1.446 Å; C–NH_2 (mean), 1.323 Å; P–OH, 1.565, 1.565 Å; P–O, 1.512, 1.492 Å. All guanidinium hydrogen atoms are engaged in H bonding to phosphate ions. In one case hydrogen atoms on adjacent nitrogen atoms each form a bond to a different oxygen atom of a phosphate ion, thus providing a model of the system observed in inhibitory binding in micrococcal nuclease. The effects of protonation and strong hydrogen bonding on P–O bond lengths and the highly precise dimensions now available for the guanidinium ion are also discussed.

The guanidinium ion, **1**, has a singular structure, which equips it to engage in patterns of hydrogen bonding which are rare, if not indeed unique. These properties may well account for the evolutionary selection of arginine as one of the small group of about 20 amino acids commonly found in proteins. A specific need for its particular structural capabilities may well be indicated by the consistent occurrence of two invariant arginine residues in cytochrome *c* over a wide range of species.[3]



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Our own attention was drawn to the detailed structural nature of the guanidyl group as a result of our observations on the interactions which play a prominent role in the binding of deoxythymidine 3′,5′-diphosphate (pdTp) to staphylococcal nuclease in the nuclease–Ca^{2+}–pdTp ternary complex. The high-resolution structure of this complex has recently been reported.[4] The binding appears to depend critically upon the interaction of the guanidyl side chains of certain arginine residues with the 5′-phosphate group. Fortunately, the electron density maps in this region of the molecule are particularly clear. The way in which the oxygen atoms of the 5′-phosphate group become involved in hydrogen bonds to the guanidyl nitrogen atoms of two arginine residues, 35 and 87, is shown in the ORTEP drawing in Figure 1. For each guanidyl group, a pair of hydrogen bonds is formed between two guanidyl nitrogen atoms and two phosphate oxygen atoms; the two three-atom chains, O–P–O and N–C–N are connected by O· · H–N hydrogen bonds to give an elongated hexagon.

Naturally, even in a relatively well defined region of the electron density map of a protein such structural features are not entirely distinct. It is possible, though unlikely, that in the present case there is some qualitative error in our fitting of models to the electron density. Given, however, that the broad features of the phosphate–arginine interactions have been correctly inferred, there is then considerable interest in evaluating the local dimensions of such an arrangement accurately. The preparation and crystallographic study of a compound which models the phosphate–guanidyl interaction was thus motivated initially by two objectives: (1) to confirm the plausibility of the overall arginine–phosphate interactions in the nuclease–pdTp–Ca^{2+} complex, and (2) to obtain accurate structure parameters which could assist in final fitting of models to the electron density maps.

In addition, it was thought that the type of interaction under study might have more general importance since the binding of phosphate-containing molecules (DNA, RNA, ATP, various enzyme cofactors) to proteins and enzymes is a pervasive feature of the chemistry of living systems. This aspect will be discussed further in a future publication.

Experimental Section

An aqueous solution containing equimolar quantities of methylguanidinium sulfate (Eastman Organic Chemicals) and $Ba(OH)_2$ was stirred overnight to precipitate $BaSO_4$ which was then filtered off. A 1:1 equivalent amount of phosphoric acid was added to the filtrate to form an aqueous solution of methylguanidinium dihydrogenphosphate (pH ~4.0). After evaporating this solution to near dryness, ethanol was added until the solution became turbid. Large single crystals of methylguanidinium dihydrogenphosphate grew overnight. *Anal.* Calcd for $[(NH_2)_2CNHCH_3](H_2PO_4)$: C,

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(1) (a) This study was supported by Grant GM13300 from the National Institute of General Medical Sciences, National Institutes of Health. (b) This structure has been briefly described in a preliminary note: F. A. Cotton, E. E. Hazen, Jr., V. W. Day, S. Larsen, J. G. Norman, Jr., S. T. K. Wong, and K. H. Johnson, *J. Amer. Chem. Soc.*, **95**, 2367 (1973).

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(3) R. E. Dickerson, *J. Mol. Biol.*, 57, 1 (1971).

(4) A. Arnone, C. J. Bier, F. A. Cotton, V. W. Day, E. E. Hazen, Jr., D. C. Richardson, J. S. Richardson, and A. Yonath, *J. Biol. Chem.*, **246**, 2302 (1971).

14.04; N, 24.56; H, 5.89. Found: C, 13.91; N, 24.39; H, 5.84.

A nearly cube-shaped specimen 0.45 mm on an edge was cut out of a larger crystal under a microscope and glued to the end of a glass fiber with a tip diameter of 0.05 mm.

Precession photographs, used to determine a preliminary set of lattice constants, indicated monoclinic, $2/m$, symmetry. The systematically absent reflections were those uniquely required by the centrosymmetric space group, $P2_1/c\text{-}C^5_{2h}$. This choice was fully supported by the results of sensitive tests for piezoelectricity and by the subsequent structure determination. The crystal was accurately centered on a General Electric quarter-circle goniometer and a total of 21 reflections, chosen to give a good sampling of reciprocal space and diffractometer settings, were used to align the crystal and calculate angular settings for each reflection. A least-squares refinement of the diffraction geometry for these 21 reflections, recorded at the ambient laboratory temperature of 21 ± 1° with Mo Kα radiation (λ (Mo Kα_1) 0.70926 Å) gave the lattice constants $a = 7.557 \pm 0.003$ Å, $b = 14.346 \pm 0.007$ Å, $c = 6.897 \pm 0.003$ Å, and $\cos \beta = -0.20413 \pm 0.00026$ ($\beta = 101.78°$). A unit cell content of four methylguanidinium dihydrogenphosphate molecules gives a calculated density of 1.552 g/cm^3, in good agreement with the observed density of 1.545 g/cm^3, measured by flotation in a mixture of bromobenzene and iodobenzene.

Intensity measurements utilized Zr-filtered Mo Kα radiation and the θ–2θ scanning technique with a 2° takeoff angle and a standard-focus X-ray tube on a Datex controlled G. E. XRD-6 diffractometer. A scanning rate of 2°/min was employed for the scan between 2θ settings 1.0° above and below the calculated Kα doublet values (λ (Kα_1) 0.70926 and λ (Kα_2) 0.71354 Å) of each reflection. Background counts of 20 sec each were taken at both ends of the scan range. A total of 3451 independent reflections having $(\sin \theta/\lambda) \leqslant 0.817$ (twice the number of data in the limiting Cu Kα sphere) were measured in concentric shells of increasing 2θ containing approximately 600 reflections each. The four standard reflections, measured every 75 reflections as a monitor for possible disalignment and/or deterioration of the crystal, gave no indication of either.

The linear absorption coefficient of the crystal for Mo Kα radiation is 0.35 mm^{-1}, yielding μR of 0.10 for a spherical crystal having the same volume as the cube-shaped specimen used for intensity measurements. The absorption of X-rays by a spherical crystal having $\mu R = 0.10$ is essentially independent of scattering angle, and deviations from this absorption occasioned by the use of a cube-shaped specimen are negligible. Therefore no absorption correction was made, and the intensities were reduced to relative squared amplitudes, $|F_o|^2$, by means of standard Lorentz and polarization corrections.

Of the 3451 reflections examined, 611 were rejected as objectively unobserved by applying the rejection criterion, $I < \sigma(I)$, where $\sigma(I)$ is the standard deviation in intensity computed from

$$\sigma^2(I) = (C_t + k^2B) + (0.01I)^2$$

C_t being the total count from scanning, k the ratio of scanning time to total background time, and B the total background count. The remaining 2840 observed intensities were used in the determination and refinement of the structure.

Structure determination was achieved through a combination of the heavy-atom technique, difference Fourier syntheses, and least-squares refinement.

Anisotropic full-matrix refinement[5] using unit weighting for the ten nonhydrogen atoms gave $R_1 = 0.064$, for 1136 reflections. All of the 2840 reflections were then included in a fully anisotropic least-squares minimization of the function $\Sigma w(|F_o| - k|F_c|)^2$ to give, with unit weighting (*i.e.*, all $w = 1$), $R_1 = 0.063$. This and all subsequent refinement cycles employed an anomalous dispersion correction[6] to the scattering factor of the phosphorus atom and a least-squares refineable extinction correction[7] of the form $1/(1 + gIc)^{1/2}$, where the extinction coefficient, g, refined to a final value of 5.77×10^{-4}. A Fourier difference synthesis based on the refined parameters afforded direct evidence for the placement of all ten hydrogen atoms. Further unit-weighted full-matrix least-squares cycles were used to refine hydrogen atoms isotropically and all other atoms anisotropically to give $R_1 = 0.047$ and a conventional weighted residual, $R_2 = \{\Sigma w(|F_o| - |F_c|)^2/\Sigma w|F_o|^2\}^{1/2}$, of 0.046.

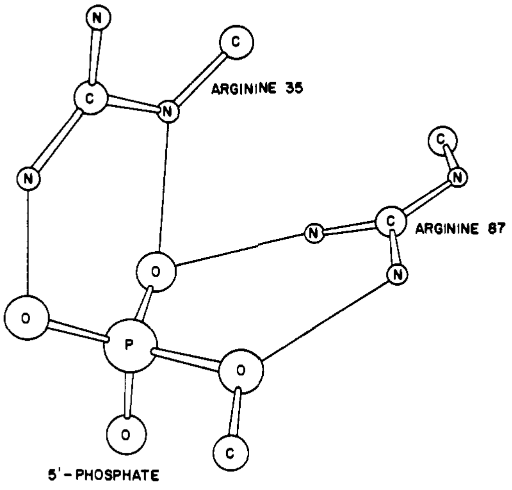

Figure 1. Perspective drawing of the hydrogen bonding interaction of the guanidinium ions of arginine-35 and -87 with the 5′-phosphate of thymidine 3′,5′-diphosphate as seen in the ternary complex of the staphylococcal nuclease, thymidine 3′,5′-diphosphate and calcium ion.

Empirical weights ($w = 1/\sigma^2$) were then calculated from

$$\sigma = \sum_0^3 a_n|F_o|^n = 0.37 - 0.11 \times 10^{-1}F + 0.65 \times 10^{-3}F^2 - 0.21 \times 10^{-5}F^3$$

the a_n being coefficients derived from the least-squares fitting of the curve

$$||F_o| - |F_c|| = \sum_0^3 a_n|F_o|^n$$

The F_c values were calculated from the fully refined model using unit weighting. The final cycles of least-squares refinement utilized these weights and anomalous dispersion corrections for the phosphorus atom to refine hydrogen atoms isotropically and all other atoms anisotropically together with the scale factor and extinction coefficient to give final values of 0.048 and 0.056 for R_1 and R_2, respectively. During this last cycle of refinement no parameter shifted by more than 0.08σ, with the average shift being 0.02. No significant differences were observed for the final parameters from least-squares refinement cycles utilizing these empirical weights, units weights, or those derived from counting statistics.

The following computer programs were employed in this work: DIFDAR, data reduction program written by A. S. Parkes; FORDAP, Fourier and Patterson synthesis program, a modified version of A. Zalkin's original program; ORFLSE, full-matrix least-squares structure refinement program, a highly modified version of Busing, Martin, and Levy's original ORFLS; ORFFE, bond lengths and angles with standard deviations by Busing, Martin, and Levy; PICK2, crystal orientation matrix and lattice constant determination, a highly modified version of J. A. Ibers version of W. C. Hamilton's original MODEL program; ORTEP, thermal ellipsoid plotting program by C. K. Johnson; MPLANE, least-squares mean plane calculation program from L. Dahl's group.

Results

The final coordinates and anisotropic thermal parameters for all atoms except hydrogen atoms are listed in Tables I and II, respectively; the refined positions and isotropic thermal parameters of the hydrogen atoms are listed in Table III.[8] The rule used in the atom number-

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[5] Scattering factors were taken from D. T. Cromer and J. B. Mann, *Acta Crystallogr., Sect. A*, **24**, 321 (1968).

[6] D. T. Cromer, *Acta Crystallogr.*, **18**, 17 (1965).

[7] W. H. Zachariasen, *Acta Crystallogr.*, **23**, 558 (1967).

(8) A structure factor table will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N. W., Washington, D. C. 20036, by referring to code number JACS-73-4834. Remit check or money order for $4.00 for photocopy or $2.00 for microfiche.

Table I. Atomic Coordinates in Crystalline Methylguanidinium Dihydrogenphosphate[a]

Atom type	Coordinates 10^4x	10^4y	10^4z
O_1	−5636 (2)	1900 (1)	−5343 (2)
O_2	−3064 (1)	776 (1)	−4313 (2)
O_3	−6054 (2)	563 (1)	−3277 (2)
O_4	−3848 (2)	1833 (1)	−1811 (2)
N_1	−388 (2)	1378 (1)	575 (2)
N_2	2617 (2)	1024 (1)	709 (2)
N_3	623 (2)	1066 (1)	−2260 (2)
C_1	−200 (3)	1447 (2)	2698 (3)
C_2	947 (2)	1159 (1)	−308 (2)
	10^5x	10^5y	10^5z
P	−46,592 (5)	12,718 (3)	−35,933 (5)

[a] Figures in parentheses are the estimated standard deviations.

Table II. Anisotropic Thermal Parameters in Crystalline Methylguanidinium Dihydrogenphosphate[a]

Atom type	Anisotropic parameters, Å² B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}	B,[b] Å²
P	1.79 (1)	2.57 (1)	1.95 (1)	−0.05 (1)	0.31 (1)	−0.26 (1)	2.08
O_1	2.51 (4)	3.65 (6)	3.06 (5)	−0.36 (4)	−0.47 (4)	0.76 (4)	2.99
O_2	1.81 (3)	3.80 (5)	3.09 (5)	−0.19 (3)	0.76 (3)	−0.86 (4)	2.65
O_3	2.75 (4)	3.10 (5)	3.45 (5)	−0.30 (4)	1.70 (4)	−0.41 (4)	2.76
O_4	3.09 (5)	3.99 (6)	2.66 (4)	0.58 (4)	−0.48 (4)	−1.21 (4)	3.05
N_1	2.17 (4)	4.47 (7)	2.24 (4)	0.37 (5)	0.48 (4)	0.04 (5)	2.77
N_2	1.98 (4)	5.00 (8)	2.89 (6)	0.28 (5)	0.01 (4)	−0.06 (5)	3.09
N_3	2.27 (5)	5.94 (9)	2.22 (5)	0.40 (5)	0.41 (4)	−0.59 (5)	3.06
C_1	3.95 (8)	4.74 (10)	2.48 (6)	0.08 (7)	1.13 (6)	−0.15 (6)	3.48
C_2	1.98 (4)	2.96 (6)	2.24 (5)	−0.03 (4)	0.30 (4)	0.12 (4)	2.37

[a] The number in parentheses that follows each B_{ij} value is the estimated standard deviation in the last significant figure. The B_{ij}'s in Å² are related to the dimensionless β_{ij} employed during refinement as $B_{ij} = 4\beta_{ij}/a_i^*a_j^*$. [b] Isotropic thermal parameter calculated from $B = 4[V^2 \det(\beta_{ij})]^{1/3}$.

Table III. Refined Parameters for Hydrogen Atoms in Crystalline Methylguanidinium Dihydrogenphosphate[a]

Atom[b] type	Fractional coordinates 10^3x	10^3y	10^3z	Isotropic thermal parameter B, Å²
H_{O1}	−509 (4)	217 (2)	−559 (5)	2.7 (8)
H_{O2}	−337 (4)	30 (2)	−515 (4)	2.1 (6)
H_{N1}	−139 (4)	151 (2)	−12 (4)	1.0 (5)
H_{N21}	287 (4)	126 (2)	186 (4)	2.0 (6)
H_{N22}	347 (4)	89 (2)	15 (4)	1.9 (6)
H_{N31}	141 (4)	94 (2)	−275 (4)	2.1 (6)
H_{N32}	−52 (4)	105 (2)	−292 (4)	1.7 (6)
H_{C11}	−130 (4)	161 (2)	297 (4)	2.0 (6)
H_{C12}	17 (4)	88 (2)	325 (5)	3.4 (8)
H_{C13}	63 (4)	186 (2)	324 (5)	3.2 (7)

[a] Figures in parentheses are the estimated standard deviations. [b] Each symbol for a hydrogen atom carries a literal and numerical subscript which indicates the atom to which it is attached. A second numerical subscript is used to distinguish among hydrogens attached to the same atom.

ing scheme for methylguanidinium dihydrogenphosphate is as follows. A numerical subscript is used to differentiate atoms of the same nonhydrogen element. For each hydrogen atom the subscript letter and first subscript number indicate the atom to which it is covalently bonded, while the second numerical subscript distinguishes among hydrogen atoms attached to the same atom.

A projection of one asymmetric unit is presented in Figure 2; each atom is numbered in conformity with Tables I–VIII and is represented by an ellipsoid having shape, orientation, and relative size consistent with the thermal parameters listed in Tables II and III. Bond lengths and angles in the molecular skeleton are presented in Figure 3 and are listed along with their estimated standard deviations in Tables IV and V; the dimensions of various interionic hydrogen bonds are listed in Table VI. The equations of the mean planes that partially characterize important subgroupings of atoms within the asymmetric unit specified by the coordinates of Tables I and III are given in Table VII, and the displacements from these planes of the atoms constituting the asymmetric unit are listed in Table VIII. Figure 4 is an ORTEP stereo drawing of the contents of one unit cell showing some of the types of hydrogen bonds which stabilize this particular crystalline arrangement.

Discussion

Comparison with L-Arginine Phosphate Monohydrate. Shortly after this investigation began two structures of L-arginine phosphate monohydrate were reported.[9,10] As we had anticipated, this compound, though seemingly more similar to the protein systems of interest, has a very complex structure and interpretation of specific binding properties of the guanidyl group toward the discrete phosphate ion is thus rendered difficult. It therefore appeared justifiable and desirable to proceed with the work we are now reporting.

Insofar as the two structures can be compared, there are no important differences in the structural units (*i.e.*, guanidyl groups, phosphate ions) which they have in common. The guanidyl portions of arginine seems to be faithfully modeled by the methylguanidinium cation we have used. The arginine residue in L-arginine phosphate monohydrate is, in turn, closely comparable to arginine residues found in several other arginine–acid complexes, as shown by Aoki, Nagano, and Iitaka[9] and Saenger and Wagner.[10] Detailed comparison of the phosphate groups and the hydrogen bonding network in the two substances is not useful since they differ in many ways.

The Methylguanidinium Cation. The main structural features are: (1) there are three virtually equal guanidyl C–N bonds, with an average length of 1.323 (2)

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(9) K. Aoki, J. Nagano, and Y. Iitaka, *Acta Crystallogr., Sect. B*, **27**, 11 (1971).

(10) W. Saenger and K. G. Wagner, *Acta Crystallogr., Sect. B*, **28**, 2237 (1972).

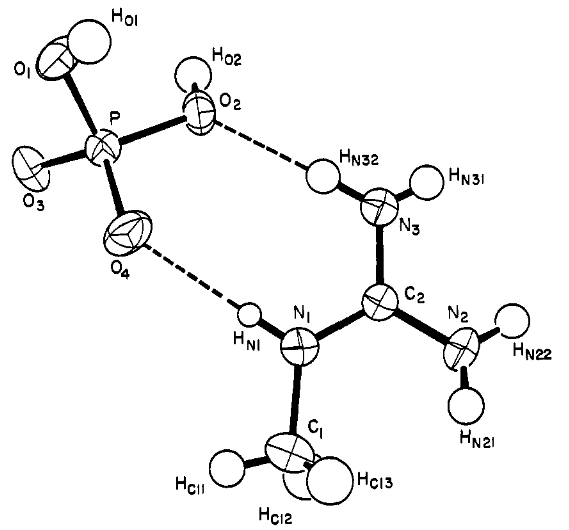

Figure 2. A perspective view of one asymmetric unit. The atom numbering scheme is explained in the text.

Table IV. Bond Lengths in Methylguanidinium Dihydrogenphosphate[a]

Type[b]	Bond length, Å	Av	Type[b]	Bond length, Å	Av
P–O$_1$	1.565 (1)		O$_1$–H$_{O1}$	0.62 (3)	
	(1.580[c])				
		1.565			0.76
P–O$_2$	1.565 (1)		O$_2$–H$_{O2}$	0.90 (3)	
	(1.577[c])				
P–O$_3$	1.512 (1)		C$_1$–H$_{C11}$	0.92 (3)	
	(1.524[c])				
		1.502			
P–O$_4$	1.492 (1)		C$_1$–H$_{C12}$	0.92 (3)	0.90
	(1.504[c])		C$_1$–H$_{C13}$	0.89 (3)	
C$_1$–N$_1$	1.446 (2)		N$_1$–H$_{N1}$	0.83 (3)	
			N$_2$–H$_{N21}$	0.85 (3)	
C$_2$–N$_1$	1.319 (2)				
C$_2$–N$_2$	1.326 (2)	1.323	N$_2$–H$_{N22}$	0.84 (3)	0.84
C$_2$–N$_3$	1.325 (2)		N$_3$–H$_{N31}$	0.77 (3)	
			N$_3$–H$_{N32}$	0.89 (3)	

[a] The figure in parentheses following each individual distance is the estimated standard deviation. [b] Atoms numbered to agree with Figures 2 and 3 and Tables I, II, and III. [c] Bond length corrected for liberation of $H_2PO_4^-$ group as a rigid body according to method of Schomaker and Trueblood.[d] The authors would like to thank Referee III for performing this calculation. [d] V. Schomaker and K. N. Trueblood, *Acta Crystallogr., Sect. B*, **24**, 63 (1968).

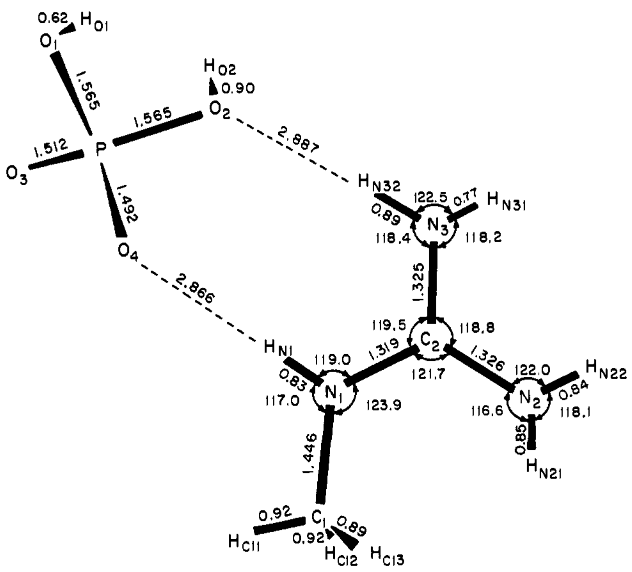

Figure 3. Bond lengths and angles for the asymmetric unit as seen in Figure 2. A complete set of values and standard deviations are listed in Tables IV, V, and VI.

Table V. Bond Angles in Methylguanidinium Dihydrogenphosphate[a]

Type[b]	Angle, deg	Av	Type[b]	Angle, deg	Av
O$_1$–P–O$_2$	106.8 (1)		H$_{O1}$–O$_1$–P	110 (3)	
					113
			H$_{O2}$–O$_2$–P	116 (2)	
O$_1$–P–O$_3$	105.4 (1)				
O$_1$–P–O$_4$	112.0 (1)		H$_{C11}$–C$_1$–N$_1$	108 (2)	
		108.6			
O$_2$–P–O$_3$	110.1 (1)		H$_{C12}$–C$_1$–N$_1$	108 (4)	
O$_2$–P–O$_4$	107.0 (1)		H$_{C13}$–C$_1$–N$_1$	113 (2)	109.50
			H$_{C11}$–C$_1$–H$_{C12}$	111 (3)	
O$_3$–P–O$_4$	115.2 (1)				
			H$_{C11}$–C$_1$–H$_{C13}$	109 (3)	
N$_1$–C$_2$–N$_2$	121.7 (2)		H$_{C12}$–C$_1$–H$_{C13}$	107 (3)	
N$_1$–C$_2$–N$_3$	119.5 (1)	120.0			
			H$_{N21}$–N$_2$–H$_{N22}$	118 (3)	
N$_2$–C$_2$–N$_3$	118.8 (2)				
			H$_{N21}$–N$_2$–C$_2$	117 (2)	
C$_1$–N$_1$–C$_2$	123.9 (2)		H$_{N22}$–N$_2$–C$_2$	122 (2)	119.3
			H$_{N31}$–N$_3$–C$_2$	118 (2)	
H$_{N1}$–N$_1$–C$_1$	117 (2)				
		118.0	H$_{N32}$–N$_3$–C$_2$	118 (2)	
H$_{N1}$–N$_1$–C$_2$	119 (2)		H$_{N31}$–N$_3$–H$_{N32}$	122 (3)	

[a] Figures in parentheses are the estimated standard deviations. [b] Atoms numbered to agree with Figures 2 and 3.

Å; (2) the single bond from the methyl carbon atom to one guanidyl nitrogen atom is relatively short, 1.446 (2) Å, and the methyl carbon atom is slightly displaced (0.070 Å) from the mean plane of the guanidyl group; (3) the three nitrogen atoms and central carbon atom of the guanidyl group are not significantly displaced from their mean plane; the guanidyl group is strictly planar within the experimental uncertainties.

Guanidine is an extremely strong base (pK_a = 13.6), closely approaching the hydroxide ion in this property. This has been attributed to the resonance or delocalization energy in the π system of the cation.[11] The C to N distances within the guanidinium ion strongly support this view, since the observed average value, 1.323 Å, is much closer to the expected value[12] for a C=N bond, 1.29 Å, than to that for a C—N bond, 1.41 Å, estimated from the sum of single bond radii for sp^2 hybridized C(0.743 Å[13]) and N(0.67[14]) atoms.

As noted, the N–CH$_3$ bond has a length of 1.446 (2) Å, which might, on first consideration, seem short. A bond of essentially this same length was found in L-arginine phosphate monohydrate[9,10] and the authors commented on its seemingly anomalous shortness. In fact, this is just the length to be expected for a C(sp^3)–N(sp^2) single bond, since the sum of the appropriate radii is 0.77 + 0.67 = 1.44 Å.

The Dihydrogenphosphate Anion. The $PO_2(OH)_2$

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(11) *Cf.* P. Gund, *J. Chem. Educ.*, **49**, 100 (1972), for a review with leading references.

(12) L. Pauling, "The Nature of the Chemical Bond," 3rd ed, Cornell University Press, Ithaca, N. Y., 1960, p 228.

(13) D. R. Lide, Jr., *Tetrahedron*, **17**, 125 (1962).

(14) J. R. Knox and C. K. Prout, *Acta Crystallogr., Sect. B*, **25**, 1952 (1969).

Table VI. Interionic Hydrogen Bonds in Methylguanidinium Dihydrogenphosphate

Donor[a] atom (D)	Acceptor atom (A)	Distance,[b] Å D···A	Distance,[b] Å H···A	Angle,[b] deg H–D···A	Asymmetric unit of (A)
			Intracomplex Bonds[c]		
N_1–H_{N1}	O_4	2.866 (2)	2.04 (3)	0 (5)	x, y, z
N_3–H_{N32}	O_2	2.887 (2)	2.00 (3)	7 (2)	x, y, z
			Intercomplex Bonds[c]		
O_1–H_{O1}	O_4	2.591 (2)	1.99 (3)	11 (3)	$x, \frac{1}{2} - y, z - \frac{1}{2}$
O_2–H_{O2}	O_3	2.538 (2)	1.64 (3)	1 (2)	$-1 - x, \bar{y}, -1 - z$
N_3–H_{N31}	O_3	2.835 (2)	2.09 (3)	12 (2)	$1 + x, y, z$
N_2–H_{N21}	O_1	3.044 (2)	2.23 (3)	13 (2)	$1 + x, y, 1 + z$
N_2–H_{N22}	O_3	3.183 (2)	2.51 (3)	32 (2)	$1 + x, y, z$

[a] The hydrogen atom actually involved in the bond is also indicated. [b] Figures in parentheses are the estimated standard deviations of the last significant digit. [c] The complex is considered to be the asymmetric unit of Tables I and III and of Figures 2 and 3.

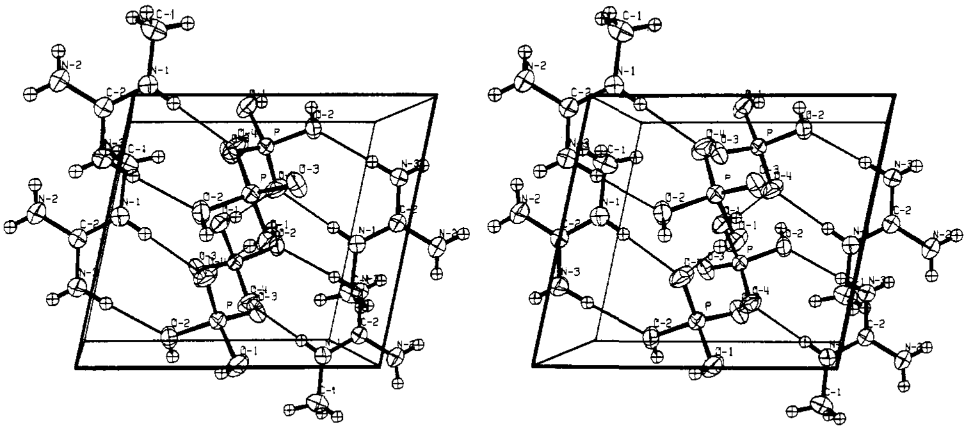

Figure 4. An ORTEP stereo drawing of a full unit cell as viewed down b^*. The positive a axis is directed from right to left across the page while the positive c axis is directed from top to bottom down the page.

Table VII. The Mean Planes of Some Characteristic Groupings of Atoms

No.	Atomic groupings	Equation of mean plane[a,b]
I	Guanidyl group[c]	$0.2222x + 0.9707y - 0.0915z = 1.800$
II	Methylguanidyl group[c]	$0.2128x + 0.9741y - 0.0761z = 1.790$
III	N_1 sp^2 system[c]	$0.2657x + 0.9637y - 0.0279z = 1.806$
IV	N_2 sp^2 system[c]	$0.2492x + 0.9265y - 0.2820z = 1.770$
V	N_3 sp^2 system[c]	$0.1183x + 0.9843y - 0.1308z = 1.762$

[a] x, y, and z are orthogonal coordinates measured (in Å) along a, b, and the normal to (001), respectively. [b] Angles (deg) between the normals to selected pairs of planes are I–II, 1.1°; I–III, 4.4°; I–IV, 11.3°; I–V, 6.4°. [c] The atoms comprised in each grouping are N_1, N_2, N_3, and C_2 in I; N_1, N_2, N_3, C_1, and C_2 in II; N_1, C_1, C_2, and H_{N1} in III; N_2, C_2, H_{N21}, and H_{N22} in IV; and N_3, C_2, H_{N31}, and H_{N32} in V.

Table VIII. Atomic Displacements from Mean Planes of Table VII

Atom	Displacements (å) from mean plane[a] of— I Guanidyl group	II Methyl-guanidyl group	III N_1 sp^2 system	IV N_2 sp^2 system	V N_3 sp^2 system
P	0.477	0.470	0.781	0.147	0.005
O_1	−0.396	0.393	0.011	−0.899	−0.978
O_2	0.833	0.848	1.106	0.343	0.487
O_3	1.728	1.711	2.059	1.423	1.164
O_4	−0.274	−0.299	−0.057	−0.350	−0.673
N_1	0.000*	−0.026*	0.012*	0.141	−0.089
N_2	0.000*	−0.004*	−0.096	0.075*	0.156
N_3	0.000*	0.016*	0.080	−0.274	−0.037*
C_1	0.070	0.020*	−0.003*	0.492	0.019
C_2	−0.001*	−0.006*	−0.003*	−0.018*	0.008*
H_{O1}	−0.891	−0.882	−0.490	−1.420	−1.438
H_{O2}	1.474	1.499	1.783	0.849	1.104
H_{N1}	−0.076	−0.102	−0.005*	0.002	−0.255
H_{N21}	−0.264	−0.282	−0.409	−0.028*	−0.080
H_{N22}	−0.005	0.004	−0.110	−0.030*	0.214
H_{N31}	−0.006	0.022	0.064	−0.370	0.015*
H_{N32}	0.148	0.164	0.289	−0.191	0.013*
H_{C11}	0.048	−0.014	0.003	0.539	−0.089
H_{C12}	0.848	0.797	0.737	1.300	0.844
H_{C13}	−0.592	−0.645	−0.708	−0.089	−0.579

[a] Starred displacements are those of the atoms used in determining the least-squares mean plane.

group is essentially tetrahedral as shown by the O–P–O angles listed in Table V. The two P–OH bond lengths are essentially equal, with a mean of 1.565 (1) Å, and are significantly longer than the P–O bond lengths. The latter, which have lengths of 1.492 (1) and 1.512 (1) Å differ by an amount which is slight but almost certainly significant ($\Delta/\sigma = 10$).

From the results of a host of recent, accurate, structure determinations of phosphate compounds[15,16] it is clear that P–O bond lengths fall broadly into two ranges. For P–OH groups (with the H atom participating in a

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(15) Representative recent papers where many references to earlier work may be found are: A. D. Mighell, J. P. Smith, and W. E. Brown, *Acta Crystallogr., Sect. B*, **25**, 776 (1969); A. A. Khan, J. P. Roux, and W. J. James, *ibid.*, **28**, 2065 (1972); E. C. Kostansek and W. R. Busing, *ibid.*, **28**, 2454 (1972); D. Mootz and K.-R. Albrand, *ibid.*, **28**, 2459 (1972).

(16) R. H. Blessing and E. L. McMcGandy, *J. Amer. Chem. Soc.*, **94** 4034 (1972).

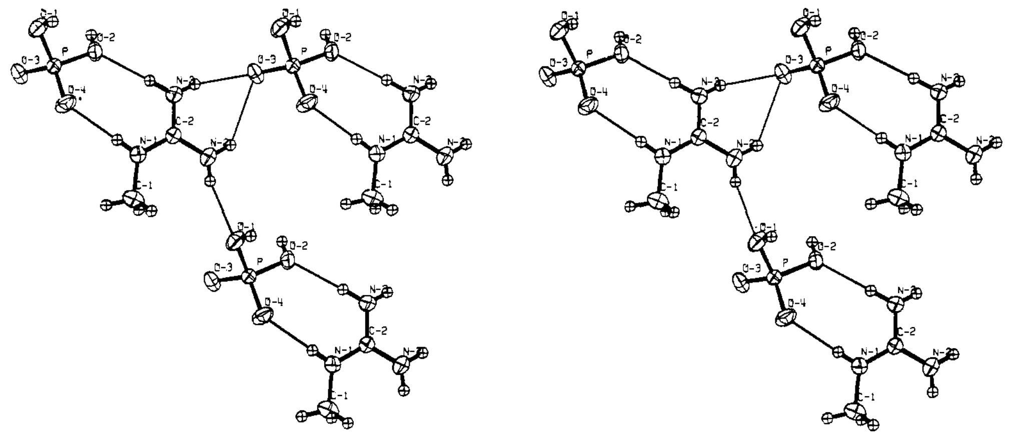

Figure 5. An ORTEP stereo drawing showing the hydrogen bonding pattern for the methylguanidinium ions.

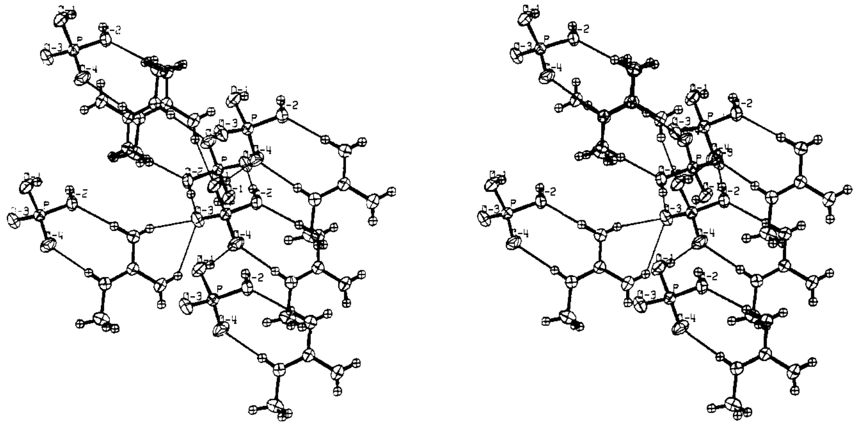

Figure 6. An ORTEP stereo drawing showing the hydrogen bonding around the phosphates and the stacking of the methylguanidinium ions.

hydrogen bond to another atom) the P–O distances are in the range 1.55–1.59 Å. For P–O groups (which are themselves interacting with protons attached primarily to other atoms) the P–O distances are in the range 1.51–1.53 Å. O–P–O angles generally deviate little from the ideal tetrahedral value, ranging from 106 to 112°. The present results, which have generally lower esd's than for any previously reported phosphate structure, conform well with these ranges, although there are two values slightly outside of them. The P–O_4 distance, 1.492 (1) Å, is slightly shorter than any previously reported P–O distance in a comparable structure. The O_3–P–O_4 angle, 115.2 (1)°, is a few degrees greater than any previously reported value for such an angle.

Hydrogen Bonding. This is extensive, but the pattern is simple and easily comprehended. First, each of the five N–H groups of the guanidinium ion forms one hydrogen bond to a phosphate oxygen atom. This is most clearly seen in Figure 5, which shows all of the hydrogen bonds formed by one guanidinium ion. Three of the N–H···O bonds are of normal strength, with N–O distances of 2.84–2.89 Å, while two are quite weak, with N–O distances of 3.04 and 3.18 Å. Indeed, the latter, which also has its H atom markedly displaced from the N···O line, may be of negligible energetic importance.

Each of the phosphate hydrogen atoms participates in bonding to an oxygen atom of a neighboring phosphate ion. This is most clearly seen in Figure 6, which shows how chains of hydrogen bonded phosphate groups run through the crystal. These O–H···O bonds are evidently quite strong, with O···O separations of only 2.54 and 2.59 Å. These separations are quite similar to those found in other structures containing $O_3POH\cdots OPO_3$ hydrogen bonds.

Overall Structure. This is best appreciated by examination of Figure 6. It consists of chains of PO_4 tetrahedra connected alternately by single POH···OP hydrogen bonds and double, cyclic hydrogen bond systems. Between these chains and tying them together into the three-dimensional structure are the methylguanidinium ions.

Note should also be taken in Figure 6 that there is stacking of guanidinium ions. While the 3.58 Å separation between the mean planes of the two methylguanidinium ions (related to each other by a crystallographic inversion center) is close to or perhaps slightly smaller than the sum of their van der Waals thickness and therefore indicative of at least a weak interaction between these ions, it is considerably larger than the 3.19 and 3.40 Å interplanar separations observed for similar groups in the crystal structures of methylglyoxal bisguanylhydrazone dichloride monohydrate[17] and dimethylglyoxal bisguanylhydrazone dichloride dihydrate,[18] respectively.

Comparison with 5′-PO_4 Binding in Staphylococcal Nuclease. The pair of hydrogen bonds shown in

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(17) W. C. Hamilton and S. J. La Placa, *Acta Crystallogr., Sect. B*, **24**, 1147 (1968).

(18) J. W. Edmonds and W. C. Hamilton, *Acta Crystallogr., Sect. B*, **28**, 1362 (1972).

Figures 2 and 3 between the guanidyl and phosphate groups within the asymmetric unit resembles very closely the hydrogen bonding interaction between the guanidyl moiety of arginine-35 and the 5′-phosphate group of the deoxythymidine 3′,5′-diphosphate (pdTp) inhibitor observed in the high-resolution structure of staphylococcal nuclease and shown in Figure 1. Additionally, in the enzyme the third guanidyl nitrogen atom of this arginine forms bridging hydrogen bonds to backbone carbonyl oxygen atoms. In methylguanidinium dihydrogenphosphate, the third nitrogen atom, N_2, hydrogen bonds weakly through its two hydrogen atoms (H_{n21} and H_{n22}) to oxygen atoms of phosphate groups in two other asymmetric units. The remaining guanidinium hydrogen atom, H_{n31}, also hydrogen bonds to a phosphate oxygen in another asymmetric unit.

Organometallic Chalcogen Complexes. XXVII. Structure and Bonding of a Metal Carbonyl Tetramer, $Co_4(CO)_4(\mu_2\text{-}SC_2H_5)_8$, Containing a Planar Tetrametal Cluster System. A Direct Stereochemical Appraisement of Strong Metal–Metal Interactions in a Ligand-Bridged Complex[1,2]

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Contribution from the Biology Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830, the Department of Organic Chemistry of the University of Chemical Engineering, Veszprém, Hungary, Laboratory of the Chemistry and Technology of the Radioelements of the CNR, 35100-Padova, Italy, and the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received January 22, 1973*

Abstract: A structural characterization of $Co_4(CO)_4(\mu_2\text{-}SC_2H_5)_8$ has not only revealed a new kind of organometallic cluster system of general formula $M_4L_4(\mu_2\text{-}X)_8$ containing a planar array of four metal atoms but also has afforded from the determined molecular parameters a *direct* assessment of the effect of localized metal–metal interactions upon the molecular geometry of a ligand-bridged complex. The four cobalt atoms are situated at the corners of a rectangle with each pair of cobalt atoms connected by two bridging mercapto sulfur atoms. Each chemically equivalent cobalt atom has a distorted (tetragonal-pyramidal)-like environment of four bridging sulfur atoms in the basal plane and the carbonyl ligand at the apex. An electron-pair metal–metal bond may be assumed to complete an octahedral-like coordination about each cobalt atom. The basic $Co_4(CO)_4(\mu_2\text{-}S)_8$ framework of the molecule ideally conforms to D_{2h} symmetry which is lowered by inclusion of the sulfur-attached ethyl groups to the crystallographically required C_i symmetry. The *severe* orthorhombic D_{2h} distortion of the Co_4S_8 core from a tetragonal D_{4h} model is ascribed to the energy stabilization of the tetramer by the formation of two localized electron-pair cobalt–cobalt bonds such that each Co(II) attains a closed-shell electronic configuration. The considerable bond strength of these localized metal–metal bonds is directly gauged in this molecule *per se* through (1) the resulting short Co–Co bonding distance of 2.498 (5) Å for one opposite pair of cobalt atoms in the tetracobalt rectangle *vs.* a normal nonbonding Co · · · Co distance of 3.312 (9) Å for the other opposite pair, and (2) the sharply acute Co–S–Co bond angles of 67.8° (av) for the two (metal–metal)-bonded Co_2S_2 fragments compared to the normally obtuse Co–S–Co bond angles of 94.0° (av) for the other two Co_2S_2 fragments without the cobalt–cobalt bonds. The architecture of the $Co_4(CO)_4(\mu_2\text{-}SC_2H_5)_8$ molecule is compared with those of the structurally related $Fe_2(CO)_6(\mu_2\text{-}SC_2H_5)_2$-type dimer and of the structurally analogous $Ru_4(NO)_4(\mu_2\text{-}Cl)_4(\mu_2\text{-}P(C_6H_5)_2)_4$ tetramer, and its metal–metal bonding is discussed relative to that for a hypothetical tetragonal D_{4h} model. One salient feature is that, whereas the two S–CH_2 bonds in each (cobalt–cobalt)-bonded $Co_2(SC_2H_5)_2$ fragment are "equatorial–axial" anti, the two S–CH_2 bonds in each $Co_2(SC_2H_5)_2$ fragment without the Co–Co bond are "bisequatorial" syn (relative to the tetracobalt plane); the fact that this latter arrangement is unprecedented in the dinuclear $Fe_2(CO)_6(\mu_2\text{-}SR)_2$ molecules is rationalized from stereochemical considerations. $Co_4(CO)_4(\mu_2\text{-}SC_2H_5)_8$: triclinic; $P\bar{1}$; $a = 9.22$ (2), $b = 10.55$ (2), $c = 10.84$ (2) Å; $\alpha = 61° 21 (10)'$, $\beta = 79° 10 (10)'$, $\gamma = 66° 12 (10)'$; $\rho_{obsd} = 1.63$ *vs.* $\rho_{calcd} = 1.69$ g cm^{-3} for $Z = 1$. Least-squares refinement gave $R_1(F) = 8.3\%$ and $R_2(F) = 7.4\%$ for 1575 independent photographically collected data.

During the last 10 years considerable effort has been directed toward preparative and structural studies of organometallic sulfur clusters in order to elucidate the detailed nature of metal–metal interactions in these complexes and especially to systematize the influence of

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(2) Previous paper in this series: G. L. Simon and L. F. Dahl, *J. Amer. Chem. Soc.*, **95**, 2164 (1973).

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