Crystal and Molecular Structure of 5-Ethoxytrimethylenephosphoric Acid[1]

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5-Ethoxytrimethylenephosphoric acid crystallizes in the monoclinic space group $P2_1/c$ with a = 5.416 (1) Å, b = 18.687 (4) Å, c = 16.677 (3) Å, β = 92.50 (1)°, and Z = 8. The structure was solved by direct methods and refined to an R value of 0.040 for 2276 unique reflections. The cyclic phosphate rings of the two molecules in the asymmetric unit are both in chair conformations, and both ethoxy groups are oriented axially. A comparison of the structure of this monocyclic phosphodiester with the cyclic phosphodiesters found in glycoside cyclic phosphates, including 3',5'-cyclic nucleotides, reveals that the axial orientation of the ethoxy group observed in the present study and the equatorial orientation of the endocyclic glycoside oxygen atoms in the other cyclic esters is the most striking structural difference. This difference is important in the explanation for the unusual thermochemical behavior of the glycoside cyclic phosphates.

The results of a thermochemical investigation of the exothermicity of the hydrolysis of 3',5'-cyclic nucleotides[3] and of theoretical calculations of the conformational energies of these molecules[4] indicate that only about 5 kcal/mol of their 8 kcal/mol excess enthalpy of hydrolysis relative to trimethylene phosphate may be attributed to geometric distortion of the molecules by the trans fusion of the cyclic phosphate and ribofuranoside rings. An explanation for the remaining 3 kcal/mol of excess enthalpy was not apparent from these approaches. However, the results of NMR studies on the solution conformations of a number of substituted trimethylene phosphates[5] led to the suggestion that the excess enthalpy which could not be accounted for by intramolecular strain was the result of solvation effects, which arise because water (and other polar solvents) preferentially solvate the most polar conformation of a solute which can exist in multiple conformations of differing polarity.

In the course of preparing substituted trimethylene phosphates for the NMR study,[5] we found that the crystals of 5-ethoxytrimethylenephosphoric acid we obtained were suitable for X-ray analysis. In previous X-ray studies related to understanding the instability of 3',5'-cyclic nucleotides, Coulter reported the results of structure determinations of tetramethylenephosphoric acid[6] and the cyclohexylammonium salt of methyl α-D-glucopyranoside 4,6-cyclic phosphate[7]. From these structures, Coulter was unable to deduce an explanation for the exothermicity of the hydrolyses of 3',5'-cyclic nucleotides. In this paper, we describe the structure analysis of 5-ethoxytrimethylenephosphoric acid; our results are considerably more successful in contributing to the understanding of the thermochemical properties of the cyclic nucleotides, since in the crystal the ethoxy group is found in an axial orientation, whereas in the cyclic nucleotides the alkoxy substituent of the cyclic phosphate ring is constrained to be in an equatorial position, due to the trans fusion of the cyclic phosphate and ribofuranoside rings. This behavior supports the conclusions of our NMR studies and vividly demonstrates the unusual conformational preferences of polar substituents at the 5-position of six-membered rings containing 1,3-dioxa functionality.[8]

Table I. Experimental Data for the X-ray Diffraction Study of 5-Ethoxytrimethylenephosphoric Acid

(A) Crystal Parameters at 22 °C

space group: $P2_1/c$	V = 1685.5 ± 1.6 Å^3
a = 5.416 (1) Å	Z = 8
b = 18.686 (4) Å	mol wt = 182.11
c = 16.677 (3) Å	ρ_{calcd} = 1.435 g/cm^3
β = 92.50 (1)°	ρ_{obsd} (flotation) = 1.43 g/cm^3

(B) Measurement of Intensity Data

radiation: Mo Kα (λ 0.710 69 Å)
monochromator: graphite
takeoff angle: 2.5°
detector aperture: horizontal, $A + B \tan\theta$ (A = 3.0 mm, B = 1.0 mm); vertical, 4.0 mm
crystal-detector distance: 330 mm
crystal orientation: [010] inclined 50.4° to diffractometer Φ axis
reflections measd: $+h,+k,\pm l$
max 2θ: 52°
scan type: coupled θ(crystal)-2θ(counter)
scan speed: variable; max θ = 10.0°/min, min θ = 1.11°/min
θ scan width: 0.70 + 0.347 tan θ ° on each side of calcd position
background: moving crystal-moving counter; 1/4 additional scan at each end of scan
std reflections: 3 measd after approx each 100 data reflections showed 5% decay
reflections measd: 3750 including absences
data used ($F^2 > 3.0\sigma(F^2)$): 2276 reflections

(C) Treatment of Data

absorption coeff: μ = 3.084 (no correction applied)
ignorance factor: p = 0.03
decay correction: min 0.98, max 1.05

Experimental Procedures

Collection and Refinement of Data. A crystal of 5-ethoxytrimethylenephosphoric acid[5] measuring 0.52 × 0.25 × 0.25 mm was selected and mounted on the end of a thin glass fiber for the diffraction study. Diffraction data were collected at ambient temperature on an Enraf-Nonius CAD-4 automatic diffractometer using graphite monochromated molybdenum Kα radiation. A unit cell was selected through the use of the search, centering, and indexing routines for the CAD-4 system and 25 randomly chosen reflections. The final unit cell parameters were obtained from a least-squares refinement of 25 high-angle reflections ($2\theta > 36°$): a = 5.416 (1) Å, b = 18.687 (4) Å, c = 16.677

(1) According to IUPAC rules, 5-ethoxytrimethylenephosphoric acid is 2-hydroxy-2-oxo-5-ethoxy-1,3,2-dioxaphosphorinane and trimethylenephosphoric acid is 2-hydroxy-2-oxo-1,3,2-dioxaphosphorinane.
(2) NIH Career Development Awardee, CA-00499, 1978-1983.
(3) J. A. Gerlt, N. I. Gutterson, P. Datta, B. Belleau, and C. Penney, *J. Am. Chem. Soc.*, in press.
(4) F. J. Marsh, P. Werner, J. E. Douglas, P. A. Kollman, G. L. Kenyon, and J. A. Gerlt, *J. Am. Chem. Soc.*, in press.
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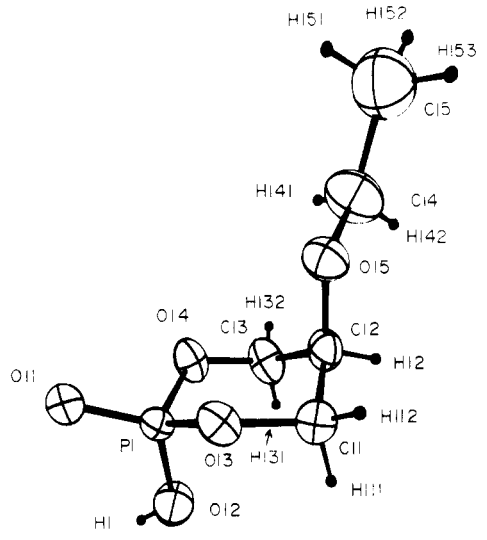

Figure 1. Molecule 1 of the asymmetric unit showing ellipsoids of thermal motion (drawn at 50% probability for nonhydrogen atoms) and the numbering system. An analogous numbering system is used for molecule 2.

(3) Å, β = 92.50 (1)°. The cell dimensions and the observed systematic absences $h0l$ ($l = 2n + 1$) and $0k0$ ($k = 2n + 1$) identified the unique monoclinic space group $P2_1/c$ (No. 14[9]). Crystal data and data collection parameters are listed in Table I.

Three intense standard reflections monitored during data collection showed a slow, small linear decay (5.0%) in their intensities; a linear correction was applied.

Solution and Refinement. All programs used in the solution and refinement of the structure were from the Enraf-Nonius Structure Determination Package.[10] The ORTEP program was modified for use on a Houston Model DP51 XY plotter. All calculations were performed on a PDP 11/45 computer.

The structure was solved by the direct-methods program MULTAN. An E map based on 164 reflections ($E_{min} > 1.70$) provided the coordinates of 20 of the nonhydrogen atoms. The atomic scattering factors for nonhydrogen atoms were taken from Cromer and Waber[11a] and were corrected for both the real and imaginary parts of anomalous dispersion.[11b] The remaining nonhydrogen and hydrogen atoms were located by a series of full-matrix least-squares refinements and difference Fourier syntheses. The least-squares refinement minimized the function $\sum w(|F_o| - |F_c|)^2$, where the weighting factor w is equal to $\sigma(F_o)^{-2}$. The refinement converged to yield the residuals $R = 0.040$, where $R = \sum(||F_o| - |F_c||)/\sum|F_o|$, and $R_w = 0.050$, where $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$. During the final cycle of refinement, no nonhydrogen atom parameter, exclusive of those for atoms C24 and C25, shifted more than 0.07σ; for atoms C24 and C25 the maximum parameter shift was 0.39σ and 0.26σ, respectively. The error of an observation of unit weight, $[\sum w(|F_o| - |F_c|)^2/(NO - NV)]^{1/2}$, where NO = 2276 and NV = 265, was 2.437. A final difference Fourier synthesis yielded no peaks of chemical significance. A final structure factor calculation showed that the calculated structure factors for the rejected reflections were acceptably low.

Ring-Puckering Coordinates and Substituent Orientations. Fortran program RING written by Cremer[12] was obtained from the Quantum Chemistry Program Exchange. Computations were performed on an IBM 370 computer.

Dipole Moment Calculations. The dipole moments of the possible conformations of 5-ethoxytrimethylene phosphate (two with the ethoxy group axial and two with the ethoxy group equatorial) were estimated by summation of vectors whose directions were those of the various polar bonds and whose magnitudes were those of the appropriate bond dipole moments. The atomic coordinates for the axial conformers used in these calculations were generated from the atomic coordinates determined for one of the two molecules in the asymmetric unit by successive 120° rotations about the C2–O5 bond. The atomic coordinates for the equatorial conformers were obtained by rotation of the axial ethoxy group about an axis perpendicular to the plane defined by H2, C2, and O5 so that the C2–O5 bond was in the same direction as the C2–H2 bond and, therefore, in an equatorial position; the ethoxy group was then rotated in 120° increments about the C2–O5 bond. For these calculations a value of 1.1 D was assumed for the C–O bond dipole, 1.2 D for the P–O ester bonds, and 2.2 D for the exocyclic P–O bonds. The computations were performed on an IBM 370 computer.

Table II. Bond Distances and Their Estimated Standard Deviations (Å)

P1-O11	1.462 (1)	P2-O21	1.458 (1)
P1-O12	1.538 (1)	P2-O22	1.534 (1)
P1-O13	1.561 (1)	P2-O23	1.562 (1)
P1-O14	1.571 (1)	P2-O24	1.560 (1)
O13-C11	1.461 (2)	O23-C21	1.448 (3)
O14-C13	1.464 (2)	O24-C23	1.460 (2)
O15-C12	1.422 (2)	O25-C22	1.431 (2)
O15-C14	1.422 (2)	O25-C24	1.401 (3)
C11-C12	1.501 (2)	C21-C22	1.499 (3)
C12-C13	1.520 (3)	C22-C23	1.510 (3)
C14-C15	1.474 (3)	C24-C25	1.448 (4)

Table III. Bond Angles and Their Estimated Standard Deviations (deg)

O11-P1-O12	115.7 (1)	O21-P2-O22	115.8 (1)
O11-P1-O13	112.6 (1)	O21-P2-O23	110.8 (1)
O11-P1-O14	109.4 (1)	O21-P2-O24	110.5 (1)
O12-P1-O13	104.7 (1)	O22-P2-O23	108.1 (1)
O12-P1-O14	109.0 (1)	O22-P2-O24	104.8 (1)
O13-P1-O14	104.9 (1)	O23-P2-O24	106.3 (1)
P1-O13-C11	117.5 (1)	P2-O23-C21	119.1 (1)
P1-O14-C13	117.8 (1)	P2-O24-C23	118.2 (1)
C12-O15-C14	115.1 (2)	C22-O25-C24	115.5 (2)
O13-C11-C12	110.9 (1)	O23-C21-C22	111.2 (2)
O15-C12-C11	107.5 (1)	O25-C22-C21	106.8 (2)
O15-C12-C13	113.5 (2)	O25-C22-C23	112.7 (2)
C11-C12-C13	111.3 (2)	C21-C22-C23	111.1 (2)
O14-C13-C12	110.7 (1)	O24-C23-C22	111.2 (2)
O15-C14-C15	109.7 (2)	O25-C24-C25	111.7 (2)

Results and Discussion

Molecular Structure. The asymmetric unit of crystalline 5-ethoxytrimethylenephosphoric acid contains two molecules. An ORTEP drawing of one molecule in the asymmetric unit is reproduced in Figure 1. As expected, the cyclic phosphate ring of each molecule exists in a chair conformation. The most interesting feature, however, is that in both molecules the ethoxy group had adopted an undistorted axial orientation. The two molecules in the asymmetric unit have similar overall geometries, with the only difference being the relative positions of the acidic hydrogen atom. The two hydrogen atom positions are a requirement of the crystal hydrogen-bonding scheme, which will be described later. The bond lengths and bond angles involving nonhydrogen atoms are listed in Tables II and III, respectively. The carbon–hydrogen bond lengths average 0.935 ± 0.021 Å; both oxygen–hydrogen covalent bonds are 0.811 ± 0.021 Å. The nonhydrogen endocyclic bond lengths and angles are very similar to those reported for trimethylenephosphoric acid.[13] The average endocyclic bond angle at phosphorus is 105.6° (vs. 104.6° for the unsubstituted acid), the ester oxygen bond angles average 118.1° (vs. 118.9° for the unsubstituted

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(10) B. A. Frenz, Structure Determination Package, Molecular Structures, Inc., College Station, Texas, 1976.
(11) "International Tables for X-ray Crystallography", Vol. 4, Kynoch Press, Birmingham, England, 1974: (a) Table 2.2B; (b) Table 2.3.1.
(12) D. Cremer and J. A. Pople, *J. Am. Chem. Soc.*, **97**, 1354 (1975).
(13) Mazhur-ul-Haque, C. N. Caughlan, and W. L. Moat, *J. Org. Chem.*, **35**, 1446 (1970).

Table IV. Dihedral Angles and Displacements of Selected Atoms[a] from Least-Squares Planes for Six-Membered-Ring Phosphodiesters

compd	dihedral angles,[b] deg						displacements,[c] Å		ref
	O_3-P	P-O_1	O_1-C_6	C_6-C_5	C_5-C_4	C_4-O_3	P	C_5	
5-ethoxytrimethylene-phosphoric acid, molecule 1[d]	47.8	−47.2	53.6	−55.4	56.3	−55.5	0.62	0.66	
5-ethoxytrimethylene-phosphoric acid, molecule 2[e]	42.4	−42.4	52.1	−56.5	56.1	−51.8	0.55	0.66	
trimethylenephosphoric acid	46.6	−47.2	54.8	−57.3	56.3	−55.5	0.62	0.67	13
phenyl trimethylene phosphate	42.7	−41.7	52.4	−59.0	59.1	−54.0	0.56	0.69	14
methyl α-D-glucopyranoside 4,6-cyclic phosphate	51.3	−53.2	61.4	−61.8	59.7	−56.9	0.72	0.71	15
3′,5′-cUMP, molecule A	57.4	−56.7	53.6	−61.4	69.1	−66.7	0.72	0.72	16
3′,5′-cUMP, molecule B	49.3	−50.5	60.5	−59.5	67.1	−61.2	0.69	0.71	16
3′,5-cGMP	44.2	−44.3	56.5	−60.5	68.5	−59.8	0.61	0.73	17
ethyl ester of 3′,5′-cAMP	39.6	−40.3	50.9	−59.3	65.9	−54.1	0.52	0.71	18
benzyl ester of 2′-acetyl 3′,5′-cUMP	49.3	−49.1	53.9	−58.9	+67.1	−60.9	0.58	0.57	19

[a] The atoms in these six-membered-ring phosphodiesters are designated by the IUPAC rules. Therefore, for the glycoside cyclic phosphates, the bond common to the two rings is C_4-C_5. [b] Positive angles correspond to clockwise rotation of the ring atom attached to the second atom about the indicated bond. [c] Displacement of the indicated atom from the best least-squares planes defined by atoms C_4, C_6, O_1, and O_3. [d] Equation of the least-squares planes $0.5948x - 0.1670y - 0.7863z + 0.8833 = 0$, where x, y, and z are orthogonalized coordinates derived from the positional parameters in Table II. [e] Equation of the plane: $-0.5987x - 0.5152y - 0.6133z + 7.1730 = 0$.

Table V. Ring-Puckering Coordinates and Substituent Orientations for Six-Membered-Ring Phosphodiesters

compd	ring-puckering coords[a]			orientation,[b] deg				ref
				5-substituent		4-substituent		
	Φ,[c] deg	θ,[d] deg	Q,[e] Å	ax	eq	ax	eq	
5-ethoxytrimethylenephosphoric acid, molecule 1	52.0	174.4	0.52	169.8	63.4	6.4	113.2	
5-ethoxytrimethylenephosphoric acid, molecule 2	63.4	169.2	0.49	177.0	68.6	8.6	114.0	
trimethylenephosphoric acid	59.0	172.4	0.54	*f*	*f*	*f*	*f*	13
phenyl trimethylene phosphate	66.4	167.6	0.52	175.6	70.4	3.3	111.2	14
methyl α-D-glucopyranoside 4,6-cyclic phosphate	29.8	176.3	0.58	177.7	71.7	5.2	109.9	15
3′,5′-cUMP, molecule A	15.3	163.1	0.54	176.9	74.7	1.7	108.8	16
3′,5′-cUMP, molecule B	81.8	173.4	0.58	178.7	83.3	6.5	103.2	16
3′,5′-cGMP	75.9	166.4	0.57	169.8	74.1	5.2	103.5	17
ethyl ester of 3′,5′-cAMP	69.2	163.0	0.53	*f*	70.7	*f*	107.3	18
benzyl ester of 2′-acetyl 3′,5′-cUMP	88.6	170.2	0.58	173.1	72.5	7.3	105.1	19

[a] The numbering for the fused-ring esters starts at $O_{5'}$ in cyclic nucleotides (O_6 in the methyl glucoside cyclic phosphate) and proceeds through the phosphorus atom. [b] The angle of the ring substituent bond with respect to the mean ring plane. Axial substituents have angles between 60 and 120° and equatorial substituents have angles between 0 and 30° or between 150 and 180°. [c] Direction of the calculated distortion from the chair conformation relative to atom 1. [d] Distortion from the chair conformation ($\theta = 0$ or 180° for an ideal chair). [e] Total puckering amplitude. [f] No hydrogen positions were reported.

acid), and all the bonds in the ring are the same length, within error, as those found in trimethylenephosphoric acid. The ring dihedral angles for these compounds (as well as related phosphodiesters to be discussed later) and the deviation of selected ring atoms from the best least-squares planes are listed in Table IV. Within the estimated uncertainty, the values for 5-ethoxytrimethylene-phosphoric acid and trimethylenephosphoric acid are identical. These structural features demonstrate the close similarity in the geometries of these two cyclic esters. In Table V we have tabulated the ring-puckering coordinates calculated for the cyclic phosphate rings of trimethylene-phosphoric acid[13] and its phenyl ester,[14] both molecules of 5-ethoxytrimethylenephosphoric acid, and the glycoside cyclic phosphates for which structural data are available.[15-19] Some of our values are identical with those calculated by Coulter,[15] although some significant differences are apparent. For example, we conclude that molecule A of uridine 3′,5′-cyclic phosphate is more distorted than Coulter described. This can also be seen in its ring dihedral angles when compared with those for the other esters listed in Table IV. We assume that the distortion observed in this cyclic nucleotide is the result of crystal packing forces, suggesting that the trans-fused ring system

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(17) A. K. Chwang and M. Sundaralingam, *Acta Crystallogr., Sect. B*, 30, 1233 (1974).
(18) F. A. Cotton, R. G. Gillen, R. N. Gohil, E. E. Hazen, Jr., C. R. Kirchner, J. Nagyvary, J. P. Rouse, A. G. Stanislowski, J. D. Stevens, and P. W. Tucker, *Proc. Natl. Acad. Sci., U.S.A*, 72, 1335 (1975).
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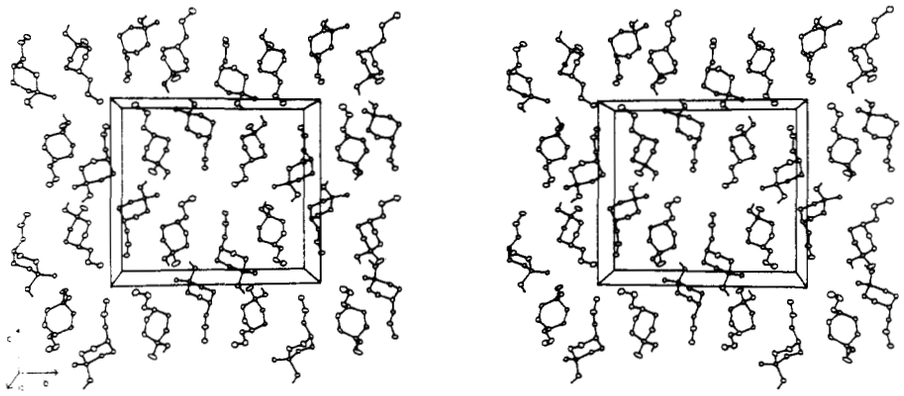

Figure 2. Stereoscopic view of the crystal down the *a* axis. The ellipsoids of thermal motion for the nonhydrogen atoms are drawn at 20% probability. The only hydrogen atoms shown are the acidic hydrogen atoms H1 and H2 which are involved in the hydrogen-bonding scheme.

of 3′,5′-cyclic nucleotides does possess some flexibility. With the exception of that structure and the relatively imprecise structure for the ethyl ester of cAMP,[18] the remaining cyclic phosphate rings are close to the ideal chair conformation, with some flattening of the ring being found in the region of the phosphorus atom. The different orientation of the alkoxy substituent in 5-ethoxytrimethylenephosphoric acid as compared to those in the glycoside cyclic phosphates does not greatly influence the ring geometry. The data in Table IV do indicate, however, that the trans-ring fusion in the 3′,5′-cyclic nucleotides does result in a dihedral angle at the bond common to both the phosphate and riboside rings which is about 10° larger than that found in the other compounds. Presumably this is a subtle indication of the significant geometric destabilization (which amounts to 5 kcal/mol) known to be present in these molecules.[3,4]

Cremer's program for evaluating ring-puckering coordinates also calculates the orientations of ring substituents relative to the mean ring plane. In this way the orientation of substituents can be quantitatively compared. Table V also lists the relative orientations of the substituents at the middle carbon atoms and at an adjacent carbon atom, which in the case of the glycoside cyclic phosphates is the other atom common to both rings. From these data we conclude that the positions of the alkoxy substituents, whether axial as in the monocyclic ester or equatorial as in the glycoside cyclic phosphates, are essentially the same as the hydrogen atoms on the unsubstituted ring of the phenyl ester of trimethylenephosphoric acid (hydrogen atom coordinates were not reported for trimethylenephosphoric acid itself). Thus, the orientations of the alkoxy substituents relative to the ring planes show no evidence for any destabilization. A similar conclusion is reached for the orientations of the carbon atoms in the glycoside ring systems which are bonded to the cyclic phosphate rings.

We are aware of no other crystal structures of conformationally flexible ring systems, e.g., 1,3-dioxanes and cyclohexanes, with a single polar substituent which is found in an axial orientation, although in solution the polar substituents at the 5-position in the dioxanes do have some axial preference.[8]

Relationship to Enthalpies of Hydrolysis of Cyclic Phosphodiesters. Trimethylene phosphate has been shown to have an enthalpy of hydrolysis similar to that found for diethyl phosphate, an acyclic and, therefore, presumably strain-free phosphodiester. The close structural similarity of 5-ethoxytrimethylenephosphoric acid and trimethylenephosphoric acid suggests that the enthalpy of hydrolysis of 5-ethoxytrimethylene phosphate would also show little hydrolytic evidence for strain. Although we have not measured the enthalpy of hydrolysis of this particular alkoxy substituted six-membered ester, we have determined the value for 5-methoxytrimethylene phosphate[3] and have found that it is, in fact, very similar to that reported for trimethylene phosphate.

Table VI. Selected Intermolecular Distances (A)

O11-P2	3.424	O11-C24	3.449
O11-O22	2.566	O14-C23	3.537
O11-C22	3.385	C15-O22	3.545
O11-C23	3.343		

Thermochemical experiments show that the 3′,5′-cyclic nucleotides have an enthalpy of hydrolysis about 5 kcal/mol more exothermic than that found for methyl α-D-glucopyranoside 4,6-cyclic phosphate and about 8 kcal/mol more exothermic than that observed for either trimethylene phosphate or 5-methoxytrimethylene phosphate.[3] The excess enthalpy of hydrolysis of the cyclic nucleotides relative to the methyl glucoside cyclic phosphate is a measure of the geometric distortion in the former compounds relative to their hydrolysis products, since the crystal structure of the methyl glucoside cyclic phosphate revealed no evidence for geometric distortion.[7] The difference between the enthalpies of hydrolysis of the monocyclic esters and the methyl glucoside cyclic phosphate can be explained as arising from solvation effects which result, in part, from the equatorial placement of the analogous oxygen atom in the glucoside cyclic phosphate.[5] We, therefore, consider this structure to be a striking illustration of the explanation for the unexpected exothermicity of hydrolysis of the methyl glucoside cyclic phosphate.[20,21] Since the cyclic nucleotides also have an equatorial oxygen substituent at the central carbon atom of the cyclic phosphate ring, solvation effects presumably are also an important factor in their thermochemical behavior.

Crystal Structure. Inspection of the crystal packing diagram (Figure 2) reveals interesting and relevant intermolecular interactions which can be related to the solution behavior of this molecule.[5] In the figure it is apparent that antiparallel helices of molecules are formed which run parallel to the *b* axis and require four molecules to accomplish a complete turn. The cyclic phosphate rings of adjacent molecules are perpendicular to one another, and adjacent molecules in a helix differ in the relative

(20) J. A. Gerlt, F. H. Westheimer, and J. M. Sturtevant, *J. Biol. Chem.*, **250**, 5059 (1975).

(21) The enthalpy of hydrolysis of the methyl glucoside cyclic phosphate and the geometrically strained five-membered-ring phosphodiester ethylene phosphate are the same within error.[20]

positions of the acidic hydrogen atoms. Selected intermolecular distances are included in Table VI.

The helices are stabilized by three important crystal packing forces: (1) The ethyl groups are organized in hydrophobic cores which run parallel to the *a* axis, thus providing separation of the crystal into hydrophobic and polar regions.

(2) The phosphoric acid groups participate in extensive networks of hydrogen bonds which run parallel to the *a* axis. A molecule with one acidic hydrogen atom relative position participates in a hydrogen bond to each of two molecules with the other acidic hydrogen atom position. One hydrogen bond is 1.688 Å in length and is formed between the H1 and O21 atoms of molecules located in adjacent helices related by a $c/2$ translation and the other is 1.758 Å in length and is formed between the H2 and O12 atoms of molecules located in adjacent helices related by both *a* and $c/2$ translations. This arrangement requires two molecules with differing acidic hydrogen atom positions and leads to a zigzag array of hydrogen-bonded molecules. In this way a given helix of molecules is hydrogen bonded directly to both adjacent antiparallel helices and indirectly through an antiparallel helix to the parallel helices directly above and below.

(3) Most importantly, the axial conformation of the molecule appears to be stabilized by dipolar interactions between adjacent molecules within a helix. Given the expected staggered rotameric conformation about the C2–O5 bond, 5-ethoxytrimethylenephosphoric acid could be found in any of four distinct conformations, two with the ethoxy group axial and two with the ethoxy group equatorial. According to a simple estimate of the dipole moments, these four conformations differ in dipole moment and, therefore, polarity. The two equatorial rotamers have calculated net dipole moments of 2.1 and 2.8 D and the two axial conformers have calculated net dipole moments of 1.9 and 3.6 D. The axial conformer has one rotameric conformation about the C2–O5 bond which is significantly more polar than the other axial and both equatorial conformations. This conformation of highest polarity is that found in the crystal; i.e., the O5–C4 bond is trans to the C2–C1 or, equivalent in polarity, the C2–C3 bond. Within a helix of molecules, the dipoles of adjacent molecules are arranged such that the positive and negative ends of a given molecule's dipole are stabilized by close proximity to the negative and positive ends of the dipole of two adjacent molecules. Therefore, an explanation for the polar axial conformation is that this conformation provides the highest attractive interaction with the polar environment provided by adjacent molecules.

Our NMR data[5] on the solution conformation of 5-ethoxytrimethylene phosphate indicate that in a nonpolar solvent the preferred conformation of the molecule is with the alkoxy group in an equatorial position; in a polar solvent such as deuterium oxide, the preferred conformation is with the alkoxy group in an axial position. Thus, both our solution and crystal studies indicate the importance of solute–solvent interactions in the observed conformations of this conformationally flexible polar molecule.

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Supplementary Material Available: Positional parameters for all atoms in the asymmetric unit, anisotropic thermal parameters for the nonhydrogen atoms, and an ORTEP drawing of the second molecule in the asymmetric unit (4 pages). Ordering information is given on any current masthead page.

Photochemistry of Some Heteroatom-Substituted 5-Acylnorbornenes

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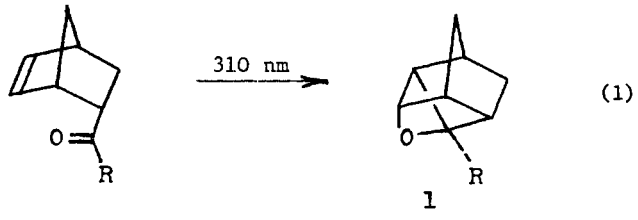
A series of 5-acylnorbornenes with hydroxyl, chloro, benzylthio, and diethylamino as α substituents was prepared as part of a study designed to evaluate the importance of lone-pair interactions in carbonyl photochemistry. Oxetanes were the primary photoproducts formed on irradiation of both the hydroxy ketone and the chloro ketone, but the thioketone and the amino ketone did not lead to detectable amounts of oxetanes. The results are discussed in terms of competitions between the three major competing processes: exciplex formation, intramolecular charge transfer, and bond homolysis.

Extensive studies in these laboratories have revealed the major features of photocyclizations of *endo*-5-acylnorbornenes to form oxetanes (eq 1).[1-4] These reactions are characterized by high chemical and photochemical efficiency even in systems in which side reactions, e.g., type I or type II photoelimination, might have been expected to be competitive with oxetane formation. These results and quenching studies have led us to conclude that the initial interaction, i.e., exciplex formation, between the carbonyl singlet state and the double bond occurs with a rate constant in excess of 10^{11} s^{-1}.[1,5-8] In an effort to define



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