

Table 2. Main interatomic distances (Å), bond angles (°) and hydrogen-bond scheme (Å, °) in Na₂[(CH₂)₂-(NH₃)₂][HPO₄]₂·6H₂O

PO ₄ tetrahedron				
P	O(1)	O(2)	O(3)	O(4)
O(1)	1.518 (1)	2.480 (2)	2.501 (2)	2.504 (2)
O(2)	106.21 (9)	1.583 (1)	2.501 (2)	2.501 (2)
O(3)	110.96 (9)	107.53 (8)	1.517 (1)	2.513 (2)
O(4)	111.61 (8)	107.95 (9)	112.25 (9)	1.509 (1)
P-P		4.320 (2)		
NaO ₆ octahedron				
Na-O(4)	2.439 (2)	Na-O(W2)	2.416 (2)	
Na-O(W1)	2.346 (2)	Na-O(W2)	2.456 (2)	
Na-O(W1)	2.461 (2)	Na-O(W3)	2.511 (2)	
NH ₃ -(CH ₂) ₂ -NH ₃ group				
N-C	1.475 (3)	N-C-C	110.5 (2)	
C-C	1.509 (4)			
Hydrogen bonds				
	O-H		O-O	O-H...O
	N-H	H...O	N-O	N-H...O
O(2)-H...O(3)	0.82 (3)	1.71 (3)	2.529 (2)	174 (3)
N-H(1N)...O(4)	0.90 (3)	1.83 (2)	2.732 (2)	176 (3)
N-H(2N)...O(1)	0.91 (3)	2.00 (3)	2.901 (2)	174 (3)
N-H(3N)...O(3)	0.85 (3)	1.87 (3)	2.707 (2)	168 (3)
O(W1)-H(1W1)...O(1)	0.83 (3)	1.99 (3)	2.806 (2)	168 (3)
O(W1)-H(2W1)...O(W3)	0.77 (4)	2.10 (4)	2.859 (2)	170 (4)
O(W2)-H(1W2)...O(2)	0.80 (3)	2.08 (3)	2.839 (2)	158 (3)
O(W2)-H(2W2)...O(1)	0.84 (3)	1.94 (3)	2.773 (2)	172 (3)
O(W3)-H(1W3)...O(4)	0.82 (3)	1.97 (3)	2.787 (2)	172 (3)
O(W3)-H(2W3)...O(1)	0.80 (4)	2.20 (4)	2.922 (2)	152 (4)
H(1W1)-O(W1)-H(2W1)	107 (3)	H(1W3)-O(W3)-H(2W3)	102 (3)	
H(1W2)-O(W2)-H(2W2)	101 (3)			

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Monopotassium Phosphoenolpyruvate: New Diffractometer Data

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Abstract. Potassium 2-(phosphonoxy)propenoate, C₃H₄O₆P⁻·K⁺, *M_r* = 206.14, orthorhombic, *Pbca*, *a* = 14.534 (8), *b* = 13.863 (6), *c* = 6.883 (3) Å, *V* = 1387 Å³, *Z* = 8, *D_m* = 1.96, *D_x* = 1.97 Mg m⁻³, Mo *K*α, λ = 0.71069 Å, μ = 0.97 mm⁻¹, *F*(000) = 832, *T* = 294 (2) K, final *R* = 0.042 for 1821 non-zero reflexions. The value of *b* differs significantly from that reported by Hosur & Viswamitra [*Acta Cryst.* (1981), B37, 839-843]. The length of the P-O(ester) bond is 1.622 (2) Å, the P-O(H) bond is 1.545 (2) Å.

Introduction. During statistical analysis of the geometry of the monophosphate group in organic esters (Starynowicz & Lis, 1985; Starynowicz, Lis &

The HPO₄ and organic groups alternate in planes perpendicular to the *a* axis. The HPO₄ groups are associated in pairs forming centrosymmetric finite clusters [H₂P₂O₈]⁴⁻, the two tetrahedra being linked by hydrogen bonds, not drawn in Fig. 1 but reported in Table 2. In such a group the P-P distance is relatively short (4.320 Å). In these same planes ethylenediamine is present as the zwitterion, (CH₂)₂(NH₃)₂²⁺. This group is centrosymmetrical.

Between these planes and separated by a distance of 11.70 Å are located the Na atoms and the six water molecules. Na atoms have a sixfold coordination formed by five water molecules and one O atom.

Main interatomic distances, bond angles and hydrogen bonds are reported in Table 2. The potassium salt is isotopic with the following unit-cell dimensions: *a* = 11.77, *b* = 10.62, *c* = 6.93 Å, β = 102.68°.

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Weichsel, 1986; Starynowicz, 1986) it was found that in monopotassium phosphoenolpyruvate (Hosur & Viswamitra, 1981) the P-O(H) distance does not differ from other P-O(terminal) distances. Since this is unexpected it was decided to reinvestigate this structure.

Experimental. Crystals of monopotassium phosphoenolpyruvate were obtained from an aqueous solution at room temperature of the commercially available compound (Boehringer). An almost parallelepipedal fragment 0.2 × 0.5 × 0.4 mm was cut from a large crystal; preliminary examination by rotation and Weissenberg photographs. Syntex P₂₁ diffractometer

and Mo $K\alpha$ radiation were used for lattice parameters (13 reflexions in the range $21 < 2\theta < 25^\circ$) and intensity measurements. The value obtained for b [13.863 (3) Å] differs significantly from the value of $b = 13.364$ (5) Å reported by Hosur & Viswamitra (1981). Since the unit-cell volume reported by Hosur & Viswamitra is similar to that obtained in the present paper, it seems that the value of b quoted in their previous paper was probably a misprint. 4647 reflexions were measured below $2\theta = 65^\circ$ (h 0→20, k 0→20, l -10→10) operating in the ω - 2θ scan mode. After each group of 50 reflexions two standards were measured; variation $\pm 10\%$. D_m measured pycnometrically in $\text{CH}_2\text{Br}_2/\text{CCl}_4$. Most calculations performed on a NOVA 1200 computer with locally modified *XTL/XTLE* (Syntex, 1976) programs. Scattering factors for K^+ , P, O, C and H were from *International Tables for X-ray Crystallography* (1974); real and imaginary dispersion corrections included for all non-H atoms. The refinement was started with the published coordinates of Hosur & Viswamitra (1981). An absorption correction following the *DIFABS* procedure (Walker & Stuart, 1983) was applied on isotropically refined data; min. and max. absorption corrections 0.899 and 1.168. The symmetry-related reflexions were averaged after *DIFABS* to give 1821 data with $I > 3\sigma(I)$; $R_{\text{int}}(wF^2) = 0.028$. Full-matrix refinement (K, O, P, C anisotropic, H isotropic) with $w = 1/\sigma^2(F_o)$ gave final $R = 0.042$ and $wR = 0.045$; max. $\Delta/\sigma = 0.04$. Residual electron density in final difference Fourier map within -0.53 and 0.40 e \AA^{-3} . The final atomic parameters (with the same numbering scheme as in the data of Hosur & Viswamitra) are given in Table 1.*

Discussion. The structure of monopotassium phosphoenolpyruvate has been discussed previously (Hosur & Viswamitra, 1981) and the new atomic coordinates do not differ significantly from the previous refinements, though the new e.s.d.'s are considerably lower. The principal interatomic distances and angles are given in Table 2. The orientation of the phosphate group with respect to the quite planar enolpyruvate system is depicted in Fig. 1. The present result for the P—O(H) bond length [1.545 (2) Å] differs significantly from the previously reported value [1.494 (6) Å] and may be accepted as the normal P—O(H) bond length in a monoionized monoesterified phosphate group (Starynowicz, 1986). The other differences in bond lengths and angles compared with the previously reported data are smaller.

* Lists of structure factors, anisotropic thermal parameters and least-squares-planes data have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 44101 (13 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Final atomic parameters for monopotassium phosphoenolpyruvate

$$B_{\text{eq}} = \frac{1}{3}(B_{11} + B_{22} + B_{33}).$$

	x	y	z	$B_{\text{eq}}/B_{100}(\text{\AA}^2)$
K	0.35692 (4)	0.47584 (5)	0.39097 (8)	2.06 (4)
P	0.32985 (5)	0.14984 (5)	0.43498 (9)	1.34 (3)
O(11)	0.3437 (2)	0.2601 (2)	0.4494 (3)	2.07 (14)
O(12)	0.2552 (2)	0.1096 (2)	0.5593 (3)	2.15 (14)
O(13)	0.4205 (2)	0.1017 (2)	0.5325 (3)	1.82 (13)
O(14)	0.3257 (2)	0.1234 (2)	0.2249 (3)	2.26 (14)
O(21)	0.6551 (2)	0.1364 (2)	0.6450 (4)	2.88 (18)
O(22)	0.5385 (2)	0.0776 (2)	0.8210 (3)	2.27 (15)
C(1)	0.5104 (2)	0.1286 (2)	0.4960 (4)	1.55 (17)
C(2)	0.5688 (2)	0.1110 (2)	0.6716 (5)	1.67 (18)
C(3)	0.5426 (3)	0.1638 (3)	0.3316 (5)	2.43 (23)
H(11)	0.335 (3)	0.289 (3)	0.542 (6)	3.6 (10)
H(32)	0.618 (3)	0.181 (3)	0.332 (6)	3.7 (9)
H(31)	0.504 (3)	0.177 (3)	0.224 (5)	2.5 (8)
H(21)	0.683 (4)	0.134 (4)	0.766 (7)	5.6 (12)

Table 2. Bond lengths (Å), bond angles ($^\circ$), torsion angles ($^\circ$), potassium coordination distances (Å) and H-bonding data in monopotassium phosphoenolpyruvate

P—O(11)	1.545 (2)	P—O(12)	1.490 (2)
P—O(13)	1.622 (2)	P—O(14)	1.493 (2)
C(1)—O(13)	1.382 (3)	C(1)—C(2)	1.497 (4)
C(2)—O(21)	1.314 (3)	C(2)—O(22)	1.211 (3)
C(1)—C(3)	1.318 (4)		
O(13)—P—O(11)	105.9 (2)	O(13)—P—O(12)	101.5 (2)
O(13)—P—O(14)	109.5 (2)	O(11)—P—O(12)	115.4 (2)
O(11)—P—O(14)	108.1 (2)	O(12)—P—O(14)	115.8 (2)
P—O(13)—C(1)	125.6 (2)	O(13)—C(1)—C(2)	110.2 (3)
O(13)—C(1)—C(3)	126.3 (3)	C(2)—C(1)—C(3)	123.5 (3)
C(1)—C(2)—O(21)	112.6 (3)	C(1)—C(2)—O(22)	122.8 (3)
O(21)—C(2)—O(22)	124.6 (3)	P—O(11)—H(11)	124 (3)
O(11)—P—O(13)—C(1)	-46.6 (3)	O(12)—P—O(13)—C(1)	-167.4 (3)
O(14)—P—O(13)—C(1)	69.7 (3)	P—O(13)—C(1)—C(3)	-30.7 (5)
K—O(11)	3.023 (2)	K—O(12)	2.727 (2)
O(12 ⁱⁱ)	2.966 (2)	O(13 ⁱⁱ)	2.845 (2)
O(14 ⁱⁱⁱ)	2.717 (2)	O(22 ^{iv})	2.783 (2)
O(22 ^{iv})	2.869 (2)		

Symmetry code: (i) $0.5-x, 0.5+y, z$; (ii) $x, 0.5-y, z-0.5$; (iii) $x, 0.5-y, 0.5+z$; (iv) $1-x, 0.5+y, 1.5-z$.

H-bond distances (Å) and angles ($^\circ$)

O—H...O	O...O	O—H	H...O	\angle O—H...O
O(11)—H(11)...O(14 ⁱ)	2.504 (3)	0.77 (4)	1.75 (4)	168 (5)
O(21)—H(21)...O(12 ⁱⁱ)	2.530 (3)	0.92 (5)	1.64 (5)	162 (5)

Symmetry code: (i) $x, 0.5-y, 0.5+z$; (ii) $0.5+x, y, 1.5-z$.

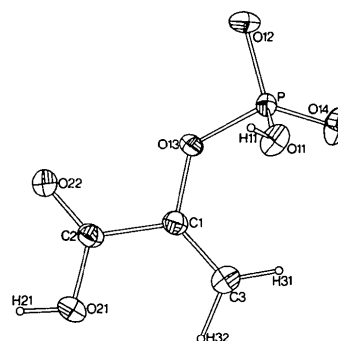


Fig. 1. View of phosphoenolpyruvate monoanion perpendicular to the pyruvate group. (Thermal ellipsoids for non-H atoms are at the 50% probability level.)

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Structure of Nedocromil Sodium: a Novel Anti-asthmatic Agent

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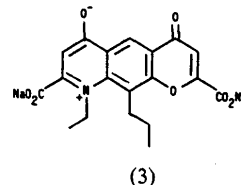
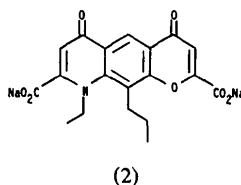
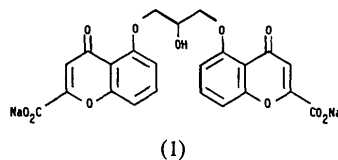
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Abstract. Disodium 9-ethyl-4,6-dioxo-10-propyl-4*H*,6*H*-pyrano[3,2-*g*]quinoline-2,8-dicarboxylate trihydrate, C₁₉H₁₅NO₇²⁻·2Na⁺·3H₂O, *M_r* = 469·4, monoclinic, *P*2₁/*n*, *a* = 21·550 (1), *b* = 14·506 (1), *c* = 27·332 (3) Å, β = 111·40 (1)°, *V* = 7955·2 Å³, *Z* = 16, *D_x* = 1·57 g cm⁻³, λ(Cu Kα) = 1·5418 Å, μ = 14·12 cm⁻¹, *F*(000) = 3904, *T* = 291 K, final *R* = 0·069 for 7317 unique observed reflections. The four tricyclic units are, within experimental error, identical, with side-chain groups on N(9) and C(10) extended away from the ring system. The carboxylate group on C(2) lies almost in the same plane as the pyranoquinoline ring, whereas the group on C(8) is almost perpendicular to this ring system. Within the crystal lattice the four tricyclic rings are pseudosymmetrically related and are stacked one on top of each other up the *b* axis. Sodium ions and water molecules lie in discrete channels and do not encroach into the tricyclic ring domain.

Introduction. It is now more than 17 years since the introduction of sodium cromoglycate (cromolyn sodium) (1) (Beach *et al.*, 1970) into clinical practice for the prophylactic treatment of allergic diseases, especially asthma. Much effort has been expended by more than 50 pharmaceutical companies (Sheard & Suschitzky, 1984) in an attempt to find related drugs with improved potency and efficacy. Until last year these attempts had been without success. However, workers at Fisons Pharmaceuticals have undertaken the

synthesis and biological evaluation of new pyrano[3,2-*g*]quinoline-2,8-dicarboxylic acids with potential for the topical treatment of asthma (Cairns, Cox, Gould, Ingall & Suschitzky, 1985). The most promising member of the series was identified as nedocromil sodium (2), now marketed in the United Kingdom as Tilade®. It was therefore expedient to determine the crystal structure of (2) to ascertain the geometry of the carboxylic-acid groups and the packing mode of the sodium ions and water molecules.



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Experimental. Slow cooling of a hot solution of nedocromil sodium (1 part) in isopropyl alcohol (9 parts) and water (3 parts by volume) afforded a colourless cube-shaped crystal *ca* 0·6 × 0·5 × 0·3 mm which was used in data collection, CAD-4 diffractometer. Preliminary, and subsequently detailed, Weissenberg photographs indicated crystals to be