

Table 4. Selected geometric parameters (Å, °) for (2)

P—C1	1.860 (3)	P—C4	1.872 (3)
P—C7	1.856 (3)	C1—C2	1.529 (5)
C1—C3	1.522 (4)	C4—C5	1.531 (4)
C4—C6	1.527 (5)	C7—C8	1.534 (5)
C7—C9	1.533 (4)		
C7—P—C4	102.0 (1)	C7—P—C1	102.9 (1)
C4—P—C1	104.7 (1)	C3—C1—C2	109.9 (2)
C3—C1—P	110.5 (2)	C2—C1—P	108.6 (2)
C6—C4—C5	110.5 (3)	C6—C4—P	109.5 (2)
C5—C4—P	117.5 (2)	C9—C7—C8	111.1 (3)
C9—C7—P	109.0 (2)	C8—C7—P	117.4 (2)

The crystal decay of compound (2) during data collection is caused by mechanical stress in the capillary as described elsewhere (Bruckmann Krüger & Lutz, 1995). In the present case, the deterioration of the crystal is even more apparent because of the method of sample preparation (Bruckmann, 1995).

For both compounds, data collection: *CAD-4 Software* (Enraf–Nonius, 1989); cell refinement: *CAD-4 Software*; data reduction: *DATAP* (Coppens, Leiserowitz & Rabinovich, 1965); program(s) used to solve structures: *SHELX86* (Sheldrick, 1990); program(s) used to refine structures: *SHELX93* (Sheldrick, 1993); *GFMLX* (Flack, 1983; Busing, Martin & Levy, 1962); molecular graphics: *ORTEPII* (Johnson, 1976); *XANADU* (Roberts & Sheldrick, 1976); *SYBYL* (Tripos Associates Inc., 1994); software used to prepare material for publication: *DAESD* (Davis & Harris, 1970); *DISCOVER94.0* (Biosym Technologies Inc., 1994).

Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: JZ1100). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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O-Phospho-DL-threonine and O-Phospho-L-threonine Compared with their Serine Analogs

WALDEMAR MANIUKIEWICZ,†† WITOLD KWIATKOWSKI†‡§
AND ROBERT H. BLESSING*

Hauptman-Woodward Institute, 73 High Street, Buffalo, New York 14203, USA

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Abstract

In crystals of *O*-phospho-DL-threonine and *O*-phospho-L-threonine, the molecules are zwitterions HO₃⁻POCH₂(CH₃)CH(NH₃⁺)CO₂H linked by three-dimensional networks of strong P—O—H...O=P, C—O—H...O=P, N—H...O=P and N—H...O=C hydrogen bonds with (O...O) = 2.55 (3) Å and (N...O) = 2.84 (4) Å. Both the molecular conformations and the nearest-neighbor hydrogen-bonded surroundings are very similar in the racemic and enantiomeric crystals of the threonine compounds, but earlier studies of crystals of the analogous serine compounds have shown that the serine zwitterions HO₃⁻POCH₂CH(NH₃⁺)CO₂H have different conformations about the C_β—O_γ—P phosphate ester bonds and different hydrogen-bonded surroundings.

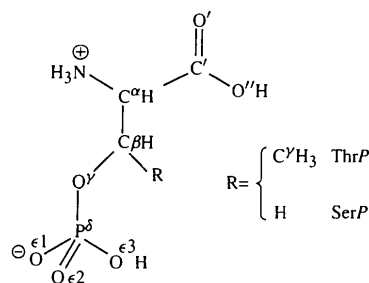
Comment

The phosphate esters, *O*_γ-phosphoserine, *O*_γ-phosphothreonine, *O*_ζ-phosphotyrosine, and the phosphoramidate, N δ 1- or N ϵ 2-phosphohistidine, correspond to the residues involved in the reversible protein phosphorylations that regulate many cellular processes. Crystal structure determinations have been reported for both DL and L forms of the phosphate esters (see scheme below) of both serine (Putkey & Sundaralingam, 1970; Sundaralingam & Putkey, 1970) and threonine (Cole, 1968; Slone & Cole, 1971) but no atomic coordinates or structural details were published for the threonine compounds. We have recently carried out charge-density analyses of the serine compounds (Kwiatkowski, Maniukiewicz & Blessing, 1994) and, preliminary to corresponding analyses of the threonine compounds, we have redetermined their crystal structures.

† Permanent address: Technical University of Łódź, 90-924 Łódź, Poland.

‡ Present address: Institut de Ciencia de Materials, Campus de la UAB, 08193 Bellaterra, Barcelona, Spain.

§ Present address: Department of Chemistry, University of Missouri at St Louis, 8001 Natural Bridge Road, St Louis, Missouri 63121-4499, USA.



As expected, the valence geometry (Table 2) is much the same in both the DL and L crystals of both *O*-phosphothreonine and *O*-phosphoserine. The molecular conformations (Table 3 and Fig. 1) are also very similar in the two threonine structures, but the serine structures manifest the conformational flexibility of the $C\beta-O\gamma-P$ ester linkage: relative to the phosphothreonine conformations, the phosphate group in *O*-phospho-DL-serine is rotated by $\Delta\chi^3 \simeq -25^\circ$ about the $O\gamma-P$ bond, and in *O*-phospho-L-serine the phosphate group is further rotated by $\Delta\chi^2 \simeq -20^\circ$ about the $C\beta-O\gamma$ bond. These conformational differences seem to be due to intermolecular crystal forces rather than intramolecular steric forces and the conformational

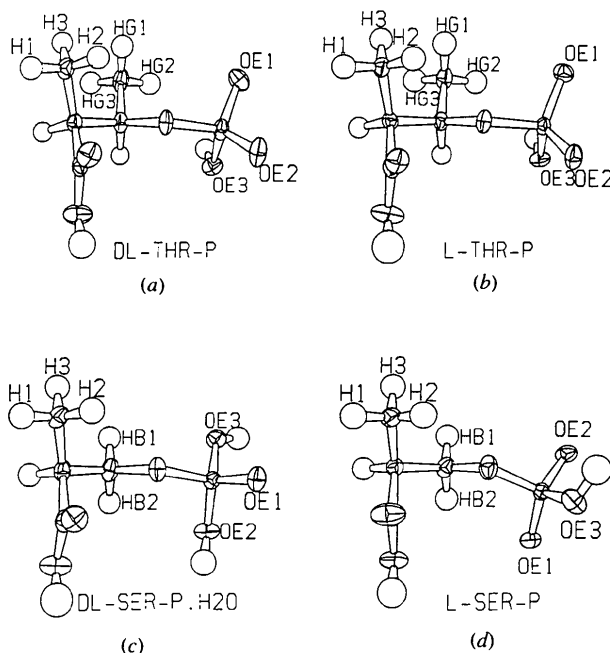
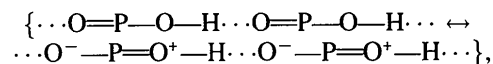


Fig. 1. Perspective illustrations of the L-molecular structures projected onto planes perpendicular to their $C\alpha-C\beta-C\gamma$ planes and parallel to their $C\alpha-O\gamma$ directions: (a) *O*-phospho-DL-threonine, (b) *O*-phospho-L-threonine, (c) *O*-phospho-DL-serine, and (d) *O*-phospho-L-serine. The (295 K) displacement ellipsoids are plotted at 50% probability levels. The two phosphate H atoms in (c) are disordered 'half-atoms' (see footnote to Table 2).

similarity in the two threonine crystals does not imply that the γ -methyl group imparts conformational rigidity. A conformation folded about $C\beta-O\gamma$, as in the L-phosphoserine crystals [Fig. 1(d)], would surely also be favorable for phosphothreonine.

Uniquely among the four structures, *O*-phospho-DL-serine crystallizes as a monohydrate and its zwitterionic structure is unique in that its phosphate proton is disordered between two sites. The groups that bear the disordered proton, $P-O\epsilon 2-H_{0.5}$ and $P-O\epsilon 3-H_{0.5}$, each form hydrogen bonds to symmetrically equivalent groups; the $\epsilon 2$ groups bond across inversion centers and the $\epsilon 3$ groups bond across diad axes. These disordered $P-O-H \cdots O=P \rightleftharpoons P=O \cdots H-O-P$ hydrogen bonds are very short with $O \cdots O = 2.49 \text{ \AA}$, and presumably they involve proton tunnelling in double-well potentials with low central barriers (Jeffrey & Saenger, 1991). In low-temperature diffraction experiments with *O*-phospho-DL-serine monohydrate, we have found no evidence of a disordered-to-ordered phase transition down to 125 K.

Although the packing arrangements (Fig. 2) in the four crystal structures are quite different, the hydrogen-bond networks have a number of features in common, including rather similar hydrogen-bond dimensions (Table 4). The four hydrogen-bond networks are intricately connected in three dimensions; there is no segregation into discrete molecular complexes or chains or layers. In the two threonine structures, the non-polar γ -methyl groups occupy more-or-less isolated interstices in the polar hydrogen-bond networks. In all four structures, the $P-O-H \cdots O=P$ bonds, even though they link pairs of like-charged anionic phosphate groups, are very strong, with $\langle O \cdots O \rangle = 2.52(3) \text{ \AA}$ and $\langle H \cdots O \rangle = 1.62(9) \text{ \AA}$. The salt-bridge $N-H \cdots O=P$ bonds, on the other hand, even though they link oppositely charged ammonium and phosphate groups, are somewhat weaker, with $\langle N \cdots O \rangle = 2.83(4) \text{ \AA}$ and $\langle H \cdots O \rangle = 1.88(3) \text{ \AA}$. In the $P2_1/c$ DL-threonine structure, the phosphate groups form hydrogen-bonded cyclic dimers around the inversion centres at $0,0,0$ and $0,1/2,1/2$; in the $C2/c$ DL-serine structure, the disordered, short hydrogen bonds link the phosphates into zigzag chains along $[0,0,z]$ and $[1/2,1/2,z]$ with alternating inversion symmetry and diad symmetry at successive links; in the $P2_12_12_1$ L-threonine and L-serine structures, the phosphates form hydrogen-bonded chains along the screw axes parallel to $[100]$ and to $[010]$, respectively. In both the rings and chains of phosphate groups, the hydrogen bonds are cooperatively strengthened by mutual polarization,



that increases the contribution of the charge-separated canonical forms to the resonance-hybrid structures.

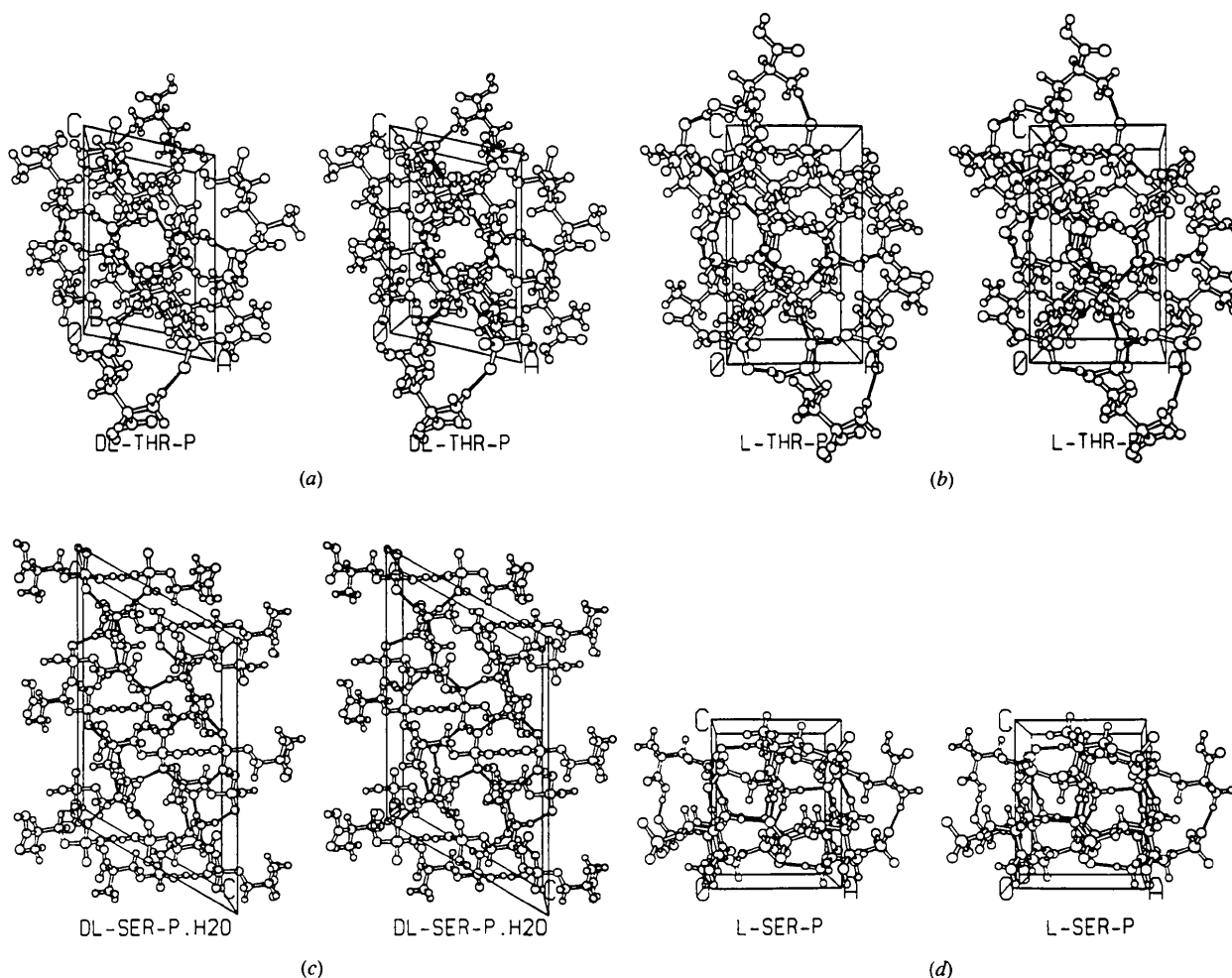
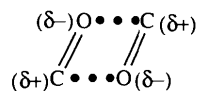


Fig. 2. Stereoscopic diagrams of the unit-cell packing for: (a) *O*-phospho-DL-threonine, (b) *O*-phospho-L-threonine, (c) *O*-phospho-DL-serine monohydrate, and (d) *O*-phospho-L-serine. Parts (a) and (b) this work; part (c) Putkey & Sundaralingam (1970), *C*2/*c*, $a = 18.402$, $b = 8.298$, $c = 12.276$ Å, $\beta = 120.63^\circ$, $Z = 8$; and part (d) Sundaralingam & Putkey (1970), *P*2₁2₁2₁, $a = 7.741$, $b = 9.060$, $c = 10.159$ Å, $Z = 4$. The phosphate H atoms in (c) are disordered 'half-atoms' (see footnote to Table 2).

All of the phosphohydroxyl P—OH groups and carboxyl C—OH groups are single donors in hydrogen bonds to phosphoryl P=O groups; none of the P—OH groups, and only one of the C—OH groups, namely that in the *L*-serine structure, accepts a hydrogen bond. The water molecule in the *DL*-serine structure accepts from two N—H donors and donates to two P=O acceptors. All but two of the P=O groups are double acceptors; the exceptions occur in the *DL*-serine structure in which O ϵ 1 is a triple acceptor and O ϵ 3 is a single acceptor. The O γ atoms of the phosphate ester linkages do not accept intermolecular hydrogen bonds, but they do form relatively short intramolecular contacts with the N—H₂ H atoms of the α -ammonium groups, with $\langle \text{N} \cdots \text{O} \rangle = 2.88$ (7), $\langle \text{H} \cdots \text{O} \rangle = 2.53$ (9) Å, and $\langle \text{N—H} \cdots \text{O} \rangle = 101$ (2) $^\circ$. Whereas the P=O groups are strong, multiple acceptors, the C'=O' groups are relatively weak, single acceptors; the N \cdots O and H \cdots O

distances are 0.03–0.2 Å longer in the N—H \cdots O'=C' than in the N—H \cdots O=P hydrogen bonds. In general, the stronger donors tend to bind strong acceptors, and the weaker donors tend to bind the weaker acceptors. In the two *DL*-structures the C'=O' groups interact in centrosymmetric, antiparallel dipole pairs,



with O \cdots C = 2.982 (2) and 3.224 (2) Å, and C=O \cdots C = 101.1 (2) and 100.9 (2) $^\circ$, in the serine and threonine structures, respectively.

A referee pointed out that the intricate hydrogen-bonding schemes in these crystals might profitably be analysed by the graph-set method (Etter, MacDonald & Bernstein, 1990); we intend to do this along with our

work in progress on analyses of the thermal vibrations and charge-density distributions in the crystals. In addition, the editor pointed out that the two ThrP structures are somewhat unusual in that, in violation of Wallach's rule (Wallach, 1895; as cited by Brock, Schweizer & Dunitz, 1991), the racemic crystals are more dense than the enantiomeric crystals. The difference in mass densities is 0.5%, which is possibly significant in terms of the uncertainty in the difference in unit-cell volumes. It also turns out that in the nominally more dense L crystals $\langle U_{\text{iso}} \rangle_{\text{non-H}} = 0.025$ (6) Å² while in the nominally less dense DL-crystals $\langle U_{\text{iso}} \rangle_{\text{non-H}} = 0.027$ (5) Å²; this also hints that there might be slightly more free volume in the racemic crystals.

Experimental

Crystals of *O*-phospho-DL-threonine, *O*-phospho-L-threonine, *O*-phospho-DL-serine monohydrate, and *O*-phospho-L-serine were grown from aqueous solutions of commercially available microcrystalline materials (Sigma Chemical Co.) by vapor diffusion of acetone. Our diffraction analyses of the threonine structures are summarized below. Our analyses of the serine structures were similar, and confirmed the results reported by Putkey & Sundaralingam (1970) and Sundaralingam & Putkey (1970); details are included with the archived supplementary materials.

O-Phospho-DL-threonine

Crystal data

C₄H₁₀NO₆P

M_r = 199.10

Monoclinic

*P*2₁/*c*

a = 7.249 (2) Å

b = 9.893 (2) Å

c = 11.247 (3) Å

β = 102.86 (2)°

V = 786.3 (3) Å³

Z = 4

D_x = 1.682 Mg m⁻³

D_m not measured

F(000) = 416 e

Data collection

Siemens *P*3 diffractometer

ω/2θ scan profiles

Absorption correction:

none

2073 measured reflections

1031 unique reflections

917 unique reflections with

$[|F|^2 \geq 3\sigma(|F|^2)]$

R_{int}($|F|^2$) = 0.012

Refinement

Full matrix on $|F|^2$

R($|F|$) = 0.028

Mo *K*α radiation

λ = 0.71069 Å

Cell parameters from 25

reflections

θ = 10–20°

μ = 0.344 mm⁻¹

T = 295 K

Needle

0.4 × 0.2 × 0.15 mm

Colourless

θ_{max} = 25°

(sinθ_{max})/λ = 0.595 Å⁻¹

h = 0 → 7

k = -10 → 10

l = -12 → 12

2 standard reflections

frequency: 60 min

intensity variation: <2%

Extinction correction: $|F_c|' =$

$|F_c|(1+g\lambda^3|F_c|^2/\sin 2\theta)^{-1/4}$

$wR(|F|^2) = 0.075$

S = 3.08

917 reflections

110 parameters

w = 1/σ²($|F_o|^2$)

Final cycle

$|\delta|/\sigma \leq 0.004$

$-0.32 \leq \Delta\rho \leq 0.20$ e Å⁻³

O-Phospho-L-threonine

Crystal data

C₄H₁₀NO₆P

M_r = 199.10

Orthorhombic

*P*2₁2₁2₁

a = 6.709 (1) Å

b = 9.854 (1) Å

c = 11.766 (2) Å

V = 777.9 (2) Å³

Z = 4

D_x = 1.700 Mg m⁻³

D_m not measured

F(000) = 416 e

Data collection

Siemens *P*3 diffractometer

ω/2θ scan profiles

Absorption correction:

none

2410 measured reflections

821 unique reflections

762 unique reflections with

$[|F|^2 \geq 3\sigma(|F|^2)]$

R_{int}($|F|^2$) = 0.014

Refinement

Full matrix on $|F|^2$

R($|F|$) = 0.026

$wR(|F|^2) = 0.065$

S = 2.38

762 reflections

110 parameters

w = 1/σ²($|F_o|^2$)

Final cycle

$|\delta|/\rho \leq 0.06$

$-0.20 \leq \Delta\rho \leq 0.21$ e Å⁻³

Extinction coefficient:

g = 1.12 (27) × 10⁻⁵

Atomic scattering factors

from Cromer & Waber

(1974) and Stewart,

Davidson & Simpson

(1965) (H)

Mo *K*α radiation

λ = 0.71069 Å

Cell parameters from 25

reflections

θ = 10–20°

μ = 0.348 mm⁻¹

T = 295 K

Needle

0.35 × 0.15 × 0.15 mm

Colourless

θ_{max} = 25°

(sinθ_{max})/λ = 0.595 Å⁻¹

h = 0 → 7

k = -11 → 11

l = -13 → 13

2 standard reflections

frequency: 60 min

intensity variation: <3%

Extinction correction: $|F_c|' =$

$|F_c|(1+g\lambda^3|F_c|^2/\sin 2\theta)^{-1/4}$

Extinction coefficient:

g = 3.88 (4) × 10⁻⁵

Atomic scattering factors

from Cromer & Waber

(1974) and Stewart,

Davidson & Simpson

(1965) (H)

Table 1. Fractional atomic coordinates and equivalent isotropic mean-square displacement parameters (Å²)

	<i>x</i>	<i>y</i>	<i>z</i>	<i>U_{iso}</i>
<i>O</i> -Phospho-DL-threonine				
P	0.19361 (9)	0.11575 (7)	-0.07310 (6)	0.0215 (3)
Oe1	0.2372 (3)	0.05417 (20)	0.05325 (15)	0.0307 (5)
Oe2	0.2748 (3)	0.25441 (19)	-0.07862 (17)	0.0346 (5)
Oe3	-0.02078 (25)	0.11244 (18)	-0.12768 (16)	0.0285 (5)
Oγ	0.29014 (24)	0.02803 (17)	-0.16134 (15)	0.0249 (5)
O'	0.5195 (3)	0.04781 (18)	-0.36067 (17)	0.0301 (5)
O''	0.2149 (3)	0.03444 (20)	-0.45690 (18)	0.0368 (6)
N	0.5158 (3)	-0.18718 (21)	-0.24594 (19)	0.0242 (5)
C'	0.3660 (4)	-0.0068 (3)	-0.38022 (23)	0.0225 (6)

C α	0.3300 (4)	-0.13146 (25)	-0.31021 (22)	0.0210 (6)
C β	0.2056 (4)	-0.09412 (25)	-0.22121 (22)	0.0222 (6)
C γ	0.1917 (4)	-0.2055 (3)	-0.13155 (25)	0.0308 (7)

O-Phospho-L-threonine

P	0.12560 (13)	0.12779 (8)	0.06989 (6)	0.0178 (3)
O ϵ 1	0.1546 (4)	0.19011 (24)	-0.04481 (18)	0.0257 (6)
O ϵ 2	0.2042 (4)	-0.01321 (23)	0.08430 (19)	0.0277 (6)
O ϵ 3	-0.0982 (3)	0.13046 (23)	0.10616 (18)	0.0252 (6)
O γ	0.2415 (3)	0.21409 (22)	0.16278 (18)	0.0230 (6)
O'	0.5415 (4)	0.18037 (23)	0.35573 (21)	0.0279 (6)
O''	0.2450 (4)	0.2019 (3)	0.44187 (21)	0.0407 (8)
N	0.5071 (5)	0.4211 (3)	0.24966 (25)	0.0216 (6)
C'	0.3857 (6)	0.2391 (3)	0.3725 (3)	0.0226 (7)
C α	0.3272 (5)	0.3664 (3)	0.30744 (25)	0.0195 (7)
C β	0.1638 (5)	0.3310 (3)	0.2228 (3)	0.0194 (7)
C γ	0.1107 (6)	0.4467 (3)	0.1429 (3)	0.0282 (8)

For the non-H atoms,

$$U_{\text{iso}} = (1/3) \sum_{i=1}^3 \sum_{j=1}^3 U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j,$$

where the U_{ij} are from atomic Debye-Waller factors $W = \exp(-2\pi^2 \sum_{i=1}^3 \sum_{j=1}^3 h_i h_j a_i^* a_j^* U_{ij})$.

Table 2. Bond lengths (Å) and valence angles (°) in DL- and L-crystals of O-phosphothreonine and O-phosphoserine

	DL-ThrP	L-ThrP	DL-SerP.H ₂ O*	L-SerP*
N—C α	1.485 (3)	1.487 (4)	1.479 (3)	1.489 (3)
C α —C'	1.517 (3)	1.521 (4)	1.513 (3)	1.529 (3)
C'—O'	1.212 (3)	1.211 (4)	1.205 (3)	1.201 (3)
C'—O''	1.300 (3)	1.301 (4)	1.309 (3)	1.308 (3)
C α —C β	1.534 (3)	1.522 (4)	1.514 (4)	1.519 (3)
C β —C γ	1.512 (4)	1.520 (4)	—	—
C β —O γ	1.451 (3)	1.448 (4)	1.447 (3)	1.436 (3)
O γ —P	1.593 (2)	1.588 (2)	1.585 (2)	1.592 (2)
P—O ϵ 1	1.513 (2)	1.495 (2)	1.498 (2)	1.497 (2)
P—O ϵ 2	1.499 (2)	1.496 (3)	1.523 (2)	1.498 (2)
P—O ϵ 3(H)	1.539 (2)	1.561 (2)	1.518 (2)	1.548 (2)
N—C α —C'	108.2 (2)	108.6 (3)	110.2 (2)	107.2 (2)
N—C α —C β	111.9 (2)	111.7 (3)	110.5 (2)	110.1 (2)
C α —C'—O'	121.7 (2)	122.3 (3)	123.4 (2)	122.3 (2)
C α —C'—O''	112.5 (2)	111.1 (3)	110.4 (2)	112.3 (2)
O'—C'—O''	125.8 (2)	126.5 (3)	126.2 (3)	125.4 (2)
C'—C α —C β	109.7 (2)	109.0 (3)	109.7 (2)	109.9 (2)
C α —C β —C γ	113.3 (2)	113.6 (3)	—	—
C α —C β —O γ	104.7 (2)	104.0 (3)	106.5 (2)	105.5 (2)
C γ —C β —O γ	112.4 (2)	112.3 (3)	—	—
C β —O γ —P	123.0 (1)	125.8 (2)	120.7 (2)	121.1 (2)
O γ —P—O ϵ 1	109.7 (1)	109.7 (1)	103.7 (1)	109.2 (1)
O γ —P—O ϵ 2	104.0 (1)	104.3 (1)	108.2 (1)	108.9 (1)
O γ —P—O ϵ 3	106.5 (1)	105.9 (1)	106.4 (1)	101.2 (1)
O ϵ 1—P—O ϵ 2	113.9 (1)	116.0 (1)	114.3 (1)	114.5 (1)
O ϵ 1—P—O ϵ 3	110.3 (1)	111.4 (1)	115.0 (1)	110.0 (1)
O ϵ 2—P—O ϵ 3	111.9 (1)	108.9 (1)	108.8 (1)	112.2 (1)

* Results for the DL-SerP.H₂O and L-SerP structures are from room temperature Mo X-ray data that we measured just prior to low-temperature measurements for charge-density analyses (Kwiatkowski, Maniukiewicz & Blessing, 1994). Our room-temperature results confirm those of Putkey & Sundaralingam (1970) and Sundaralingam & Putkey (1970) from Cu X-ray data, but we have relabeled the atoms to conform to IUPAC-IUB conventional nomenclature, and we were able to resolve the symmetrically disordered 'half-H atoms' of the phosphate group in DL-SerP.H₂O. The disordered H atoms were refined with restrained O—H = 0.95 ± 0.005 Å and constrained $U_{\text{iso}}(\text{H}) = 1.5U_{\text{iso}/\text{eq}}(\text{O})$, and with their populations constrained to sum to unity. This gave P—O ϵ 2—H_{0.56(3)} with a slightly longer P—O bond and P—O ϵ 3—H_{0.44(3)} with a slightly shorter P—O bond, and normal anisotropic displacement ellipsoids (Fig. 1) for O ϵ 2 and O ϵ 3. Details of our re-analyses of the two SerP structures are included in the archived supplementary materials.

Table 3. Conformation angles (°) in DL- and L-crystals of O-phosphothreonine and O-phosphoserine

	DL-ThrP	L-ThrP	DL-SerP.H ₂ O*	L-SerP*
$\psi = \text{N—C}\alpha\text{—C}'\text{=O}'$	-14.4 (3)	-15.1 (4)	-15.7 (3)	-1.9 (3)
$\chi_{1,1}^{1,1} = \text{N—C}\alpha\text{—C}\beta\text{—O}\gamma$	73.5 (2)	69.5 (3)	66.4 (2)	61.2 (2)
$\chi_{1,2}^{1,2} = \text{N—C}\alpha\text{—C}\beta\text{—C}\gamma$	-49.4 (3)	-53.0 (4)	—	—
$\chi_{1,3}^{1,3} = \text{C}\alpha\text{—C}\beta\text{—O}\gamma\text{—P}$	171.7 (2)	175.4 (2)	168.2 (1)	152.8 (2)
$\chi_{2,1}^{2,1} = \text{C}\beta\text{—O}\gamma\text{—P=O}\epsilon$ 1	82.4 (2)	87.2 (3)	-178.4 (2)	-45.9 (2)
$\chi_{2,2}^{2,2} = \text{C}\beta\text{—O}\gamma\text{—P=O}\epsilon$ 2	-155.4 (2)	-148.0 (2)	-56.8 (2)	79.8 (2)
$\chi_{2,3}^{2,3} = \text{C}\beta\text{—O}\gamma\text{—P=O}\epsilon$ 3(H)	-37.0 (2)	-33.1 (3)	59.9 (3)	-161.9 (2)

* See footnote to Table 2.

Table 4. Hydrogen-bond distances (Å) and angles (°) in DL and L crystals of O-phosphothreonine and O-phosphoserine*

D'—D—H...A—A'	H...A	D...A	D—H...A
DL-ThrP			
P—O ϵ 3—H ϵ 3...O ϵ 1 ¹ =P	1.63	2.542 (3)	160
C'—O''—H''...O ϵ 2 ¹ =P	1.64	2.587 (3)	174
N—H2...O ϵ 1 ¹ =P	1.87	2.812 (3)	156
N—H1...O ϵ 2 ¹ =P	1.81	2.805 (3)	177
N—H3...O' ¹ =C'	1.94	2.918 (3)	166
L-ThrP			
P—O ϵ 3—H ϵ 3...O ϵ 1 ¹ =P	1.63	2.529 (3)	157
C'—O''—H''...O ϵ 2 ¹ =P	1.62	2.526 (3)	158
N—H2...O ϵ 1 ¹ =P	1.93	2.827 (4)	148
N—H1...O ϵ 2 ¹ =P	1.83	2.826 (4)	179
N—H3...O' ¹ =C'	1.88	2.858 (4)	166
DL-SerP.H ₂ O			
P—O ϵ 2...H...O ϵ 2 ¹ =P	1.56	2.494 (3)	168†
P—O ϵ 3...H...O ϵ 3 ¹ =P	1.55	2.493 (3)	172†
C'—O''—H''...O ϵ 1 ¹ =P	1.64	2.593 (2)	178
N—H1...O ϵ 1 ¹ =P	1.96	2.886 (3)	153
N—H2...OW	1.82	2.793 (2)	164
N—H3...OW ^A	1.99	2.868 (2)	145‡
N—H3...O' ¹ =C'	2.45	3.107 (3)	123‡
OW—HW1...O ϵ 1 ¹ =P	1.92	2.850 (2)	170
OW—HW2...O ϵ 2 ¹ =P	1.83	2.770 (3)	170
L-SerP			
P—O ϵ 3—H ϵ 3...O ϵ 1 ¹ =P	1.63	2.547 (2)	162
C'—O''—H''...O ϵ 2 ¹ =P	1.53	2.477 (2)	177
N—H1...O ϵ 2 ¹ =P	1.80	2.780 (3)	165
N—H3...O ϵ 1 ¹ =P	1.84	2.786 (3)	156
N—H2...O' ¹ =C'	1.98	2.953 (4)	163

Symmetry codes: (i) $-x, -y, -z$; (ii) $x, \frac{1}{2}-y, -\frac{1}{2}+z$; (iii) $1-x, -y, -z$; (iv) $1-x, -\frac{1}{2}+y, -\frac{1}{2}-z$; (v) $-\frac{1}{2}+x, \frac{1}{2}-y, -z$; (vi) $\frac{1}{2}-x, -y, \frac{1}{2}+z$; (vii) $\frac{1}{2}+x, \frac{1}{2}-y, -z$; (viii) $1-x, \frac{1}{2}+y, \frac{1}{2}-z$; (ix) $-x, y, -\frac{1}{2}-z$; (x) $x, -y, \frac{1}{2}+z$; (xi) $\frac{1}{2}-x, \frac{1}{2}+y, \frac{1}{2}-z$; (xii) $\frac{1}{2}-x, \frac{1}{2}-y, -z$; (xiii) $\frac{1}{2}+x, \frac{1}{2}-y, \frac{1}{2}+z$; (xiv) $-x, -\frac{1}{2}+y, -\frac{1}{2}-z$; (xv) $-\frac{1}{2}-x, -y, -\frac{1}{2}+z$; (xvi) $-1+x, y, z$; (xvii) $-\frac{1}{2}-x, -y, \frac{1}{2}+z$; (xviii) $-1-x, -\frac{1}{2}+y, -\frac{1}{2}-z$.

* H atoms were found in difference electron density maps and refined with O—H and N—H bond lengths restrained to 0.95 and 1.00 ± 0.005 Å, respectively. † These two P—O—H...O=P = P=O...H—O—P hydrogen bonds each involve a pair of symmetrically disordered 'half-hydrogen atoms' (see footnote to Table 2). ‡ These are two branches of a three-center N—H(...O)₂ hydrogen bond.

Non-H atoms were refined anisotropically. H atoms were located in difference electron-density maps and refined isotropically with C—H, N—H and O—H bond lengths restrained to 1.05, 1.00 and 0.95 ± 0.005 Å, respectively, and $U_{\text{iso}}(\text{H}) = 1.5U_{\text{iso}/\text{eq}}(\text{C}, \text{N}, \text{or O})$. Atomic scattering factors were as given by Cromer & Waber (1974), including the spherically

contracted H-atom scattering factor from Stewart, Davidson & Simpson (1965).

Unit-cell dimensions and intensity data: Siemens diffractometer software (Siemens, 1990). Diffraction data reduction and error analysis: local programs (Blessing, 1989). Structure determination: *DIRDIF* (Beurskens *et al.*, 1992) as implemented in *TEXSAN* (Molecular Structure Corporation, 1992). Least-squares refinement: *SHELXL93* (Sheldrick, 1993). Structure drawings: *ORTEPII* (Johnson, 1976); *PLUTO* (Motherwell, 1979) as implemented in *TEXSAN* and *PLATON* (Spek, 1990).

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Lists of structure factors, anisotropic displacement parameters, H-atom coordinates and complete geometry have been deposited with the IUCr (Reference: BK1167). Copies may be obtained through The Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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3-Isopropylamino-4-methyl-4H-pyrido-[4,3-e][1,2,4]thiadiazine 1,1-Dioxide

LÉON DUPONT,^a BERNARD PIROTTE,^b PASCAL DE TULLIO^b
AND JACQUES DELARGE^b

^aUnité de Cristallographie, Institut de Physique B5, Université de Liège au Sart Tilman, B-4000 Liège, Belgium, and ^bLaboratoire de Chimie Pharmaceutique, Institut de Pharmacie F1, Université de Liège, Rue Fusch 5, B-4000 Liège, Belgium. E-mail: u210406@vm1.ulg.ac.be

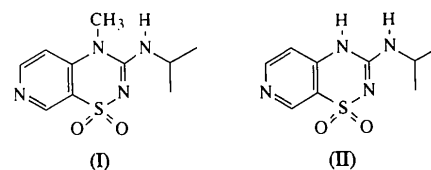
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Abstract

The title compound, C₁₀H₁₄N₄O₂S, is the 4-methyl analogue of an original potassium channel opener molecule related to diazoxide. The crystal structure determination of a compound with a methyl substituent in the 4-position provides geometric reference data which may be useful for analysing the preferential 2*H*- or 4*H*-tautomeric form adopted in unsubstituted derivatives of this class of compounds in the solid state.

Comment

The title compound, (I), is the methyl analogue of (II), a potassium channel opener structurally related to diazoxide [7-chloro-3-methyl-2*H*(or 4*H*)-1,2,4-benzothiadiazine 1,1-dioxide] (Bandoli & Nicolini, 1977; Pirotte *et al.*, 1993; de Tullio *et al.*, 1996).



The present crystallographic investigation of (I) will help our knowledge of the conformational behaviour of 4-methyl-substituted derivatives compared with unsubstituted derivatives of this class of heterocyclic compounds. Indeed, the presence of a methyl substituent in the 4-position of the thiadiazine ring imposes the adoption of a 4*H*-tautomeric form for (I). Thus, comparison of the N2—C3 [1.326 (4) in (I) and 1.315 (4) Å in (II)] and C3—N4 [1.381 (4) in (I) and 1.366 (4) Å in (II)] bond lengths of the two compounds may allow prediction of the preferential tautomeric form adopted by compound (II) and other unsubstituted derivatives of this class of compounds in the solid state. The cohesion of the crystal is the result of van der Waals interactions and of one intermolecular N11—H11···O1ⁱ hydrogen bond; N11···O1ⁱ 2.882 (3), H11···O1ⁱ 2.10 Å and N11—H11···O1ⁱ 152° [symmetry code: (i) 1 - x, -½ + y, ½ - z].