

analyses. Scattering factors were inlaid (Sheldrick, 1976). Atom coordinates and equivalent isotropic thermal parameters are given in Table 1 while selected molecular-geometry parameters appear in Table 2.* The atom-numbering scheme for the cation is shown in Fig. 1, which was generated using *ORTEP* (Mallinson & Muir, 1985). The centrosymmetric, hydrogen-bonded species comprising one macrocyclic dication and two picrate monoanions is shown in Fig. 2; selected hydrogen-bonding parameters are listed in Table 3. Molecular-geometry calculations were performed using *CALC* (Gould & Taylor, 1985).

Related literature. The unmethylated, neutral molecule 1,4,10,13-tetrathia-7,16-diazacyclooctadecane (Ammon, Chandrasekhar, Bhattacharjee, Shinkai & Honda, 1984) likewise lies across an inversion centre. However, it does not participate in significant hydrogen bonding, and has a different ring conformation

* Lists of structure factors, anisotropic thermal parameters and H-atom coordinates have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51900 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 3. Selected hydrogen-bonding parameters for N—H...O—C

Distances (Å)			
H(7N)...O(1')	1.848 (12)	H(16N)...O(1'')	1.684 (12)
Angles (°)			
N(7)—H(7N)...O(1')	150.5 (9)	N(16)—H(16N)...O(1'')	152.2 (9)
H(7N)...O(1')—C(1')	140.1 (8)	H(16N)...O(1'')—C(1'')	144.5 (9)

with no exdentate S atoms. Four *anti* C—N and eight *gauche* C—S bond conformations are observed for this species. In contrast, the title compound shows two C—N bonds *anti* and two *gauche*, with six *gauche* and two *anti* C—S bond conformations.

References

- AMMON, H. L., CHANDRASEKHAR, K., BHATTACHARJEE, S. K., SHINKAI, S. & HONDA, Y. (1984). *Acta Cryst.* **C40**, 2061–2064.
 GOULD, R. O. & TAYLOR, P. (1985). *CALC*. Program for molecular geometry calculations, Fortran77 version. Univ. of Edinburgh, Scotland.
 MALLINSON, P. D. & MUIR, K. W. (1985). *ORTEPII*, interactive version, *J. Appl. Cryst.* **18**, 51–53.
 SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
 SHELDRIK, G. M. (1986). *SHELX86*. Program for crystal structure solution. Univ. of Göttingen, Federal Republic of Germany.

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Structure of *S*-Phenyl *O*-3'-ThymidinyI Methylphosphonothioate*

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Abstract. *S*-Phenyl *O*-3'-thymidinyI methylphosphonothioate-tetrahydrofuran (1/1), C₁₇H₂₁N₂O₆PS.C₄H₈O, *M_r* = 484.51, monoclinic, *P*2₁, *a* = 10.7577 (17), *b* = 9.0981 (16), *c* = 12.4311 (28) Å, β = 100.425 (16)°, *V* = 1196.5 (4) Å³, *Z* = 2, *D_x* = 1.34 g cm⁻³, λ(Mo *K*α) = 0.71073 Å, μ = 1.99 cm⁻¹, *F*(000) = 512, *T* = 296 K, *R* = 0.039, *wR* = 0.048 for 3156 unique observed reflections. *S*-Phenyl *O*-3'-thymidinyI methylphosphonothioate has been obtained in crystalline form as its monotetrahydrofuranate. In the crystal, each molecule is linked by two intermolecular hydrogen bonds to two different adjacent molecules. Acceptor for both types of hydrogen bonds is the phosphoryl group of the

phosphonothioate moiety. The 5'-hydroxyl H atom (O...H 2.01; O...O 2.839 Å) and the N³ hydrogen of the thymidine residue (O...N 2.952 Å) function as donors. The title compound is one of a series of nucleotide synthons directed towards introducing chiral internucleotidic linkages into DNA. DNA modified in this manner may have several applications in biology and medicine. Phosphonothioate-containing mononucleotides can easily be *P*-diastereomerically resolved which is a significant improvement over previous synthons of this type.

Experimental. The title compound was obtained as its tetrahydrofuran (THF) adduct from the high *R_f* *P*-diastereomer of *S*-phenyl *O*-(5'-*O*-tritylthymidine-3'-yl) methylphosphonothioate (0.5 mmol) (Brill & Caruthers, 1988) by treatment with 20% TFA in

* Nucleotide Chemistry. Part XXVII. Part XXVI: Grandas, Marshall, Nielsen & Caruthers (1989).

Table 1. Atomic fractional coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$)

Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U_{eq}
P(1)	-4504 (1)	-2589	6986 (1)	49 (1)
S(1)	-5391 (1)	-750 (2)	7478 (1)	70 (1)
N(1)	33 (3)	-1644 (3)	5039 (2)	45 (1)
C(2)	1203 (3)	-2117 (4)	5582 (3)	45 (1)
O(2)	1377 (2)	-2713 (4)	6466 (2)	68 (1)
N(3)	2170 (3)	-1862 (4)	5013 (3)	50 (1)
C(4)	2081 (3)	-1234 (4)	3995 (3)	52 (1)
O(4)	3037 (3)	-1108 (4)	3584 (3)	79 (1)
C(5)	832 (3)	-759 (5)	3489 (3)	48 (1)
C(6)	-118 (3)	-999 (4)	4025 (3)	45 (1)
C(7)	647 (4)	-59 (5)	2381 (3)	68 (2)
C(1')	-1081 (3)	-2011 (4)	5508 (3)	46 (1)
O(1')	-1889 (2)	-2902 (3)	4751 (2)	49 (1)
C(2')	-1877 (3)	-704 (5)	5723 (3)	47 (1)
O(3')	-3219 (2)	-2106 (3)	6652 (2)	52 (1)
C(3')	-3174 (3)	-1371 (4)	5620 (3)	44 (1)
C(4')	-3190 (3)	-2507 (4)	4720 (3)	47 (1)
C(5')	-3791 (4)	-1964 (5)	3586 (3)	55 (1)
O(5')	-3206 (3)	-674 (4)	3271 (2)	60 (1)
O(6)	-5443 (2)	-3240 (3)	6093 (2)	56 (1)
C(8)	-3955 (4)	-3749 (5)	8109 (3)	60 (2)
C(11)	-4285 (4)	-5 (6)	8581 (3)	66 (2)
C(12)	-3589 (5)	1222 (7)	8429 (5)	87 (2)
C(13)	-2849 (6)	1868 (9)	9311 (6)	122 (3)
C(14)	-2764 (7)	1306 (11)	10335 (6)	124 (4)
C(15)	-3427 (7)	84 (10)	10508 (5)	106 (3)
C(16)	-4225 (5)	-559 (7)	9628 (4)	86 (2)

Table 2. Bond lengths (\AA) and bond angles ($^\circ$)

P(1)—S(1)	2.072 (1)	P(1)—O(3')	1.576 (2)
P(1)—O(6)	1.482 (3)	P(1)—C(8)	1.765 (4)
S(1)—C(11)	1.778 (5)	N(1)—C(2)	1.384 (4)
N(1)—C(6)	1.373 (4)	N(1)—C(1')	1.463 (4)
C(2)—O(2)	1.209 (4)	C(2)—N(3)	1.379 (4)
N(3)—C(4)	1.376 (5)	C(4)—O(4)	1.234 (4)
C(4)—C(5)	1.443 (5)	C(5)—C(6)	1.335 (4)
C(5)—C(7)	1.498 (5)	C(1')—O(1')	1.415 (4)
C(1')—C(2')	1.516 (5)	O(1')—C(4')	1.439 (4)
C(2')—C(3')	1.505 (5)	O(3')—C(3')	1.455 (4)
C(3')—C(4')	1.521 (5)	C(4')—C(5')	1.523 (5)
C(5')—O(5')	1.420 (5)	C(11)—C(12)	1.377 (7)
C(11)—C(16)	1.386 (6)	C(12)—C(13)	1.366 (8)
C(13)—C(14)	1.359 (9)	C(14)—C(15)	1.358 (10)
C(15)—C(16)	1.391 (8)		
O(3')—P(1)—S(1)	109.0 (1)	O(6)—P(1)—S(1)	104.8 (1)
O(6)—P(1)—O(3')	115.2 (1)	C(8)—P(1)—S(1)	110.8 (1)
C(8)—P(1)—O(6)	101.0 (2)	C(8)—P(1)—O(6)	116.0 (2)
C(11)—S(1)—P(1)	104.8 (1)	C(6)—N(1)—C(2)	121.8 (3)
C(1')—N(1)—C(2)	118.2 (3)	C(1')—N(1)—C(6)	119.6 (3)
O(2)—C(2)—N(1)	124.0 (3)	N(3)—C(2)—N(1)	113.7 (3)
N(3)—C(2)—O(2)	122.3 (3)	C(4)—N(3)—C(2)	127.4 (3)
O(4)—C(4)—N(3)	119.7 (4)	C(5)—C(4)—N(3)	115.5 (3)
C(5)—C(4)—O(4)	124.8 (4)	C(6)—C(5)—C(4)	118.0 (3)
C(7)—C(5)—C(4)	119.1 (3)	C(7)—C(5)—C(6)	122.8 (3)
C(5)—C(6)—N(1)	123.6 (3)	O(1')—C(1')—N(1)	108.3 (3)
C(2')—C(1')—N(1)	114.9 (3)	C(2')—C(1')—O(1')	105.5 (3)
C(4')—O(1')—C(1')	110.6 (3)	C(3')—C(2')—C(1')	102.3 (3)
C(3')—O(3')—P(1)	122.1 (2)	C(3')—C(3')—C(2')	106.8 (3)
C(4')—C(3')—C(2')	102.9 (3)	C(4')—C(3')—O(3')	109.8 (3)
C(3')—C(4')—O(1')	105.6 (3)	C(5')—C(4')—O(1')	110.7 (3)
C(5')—C(4')—C(3')	114.0 (3)	O(5')—C(5')—C(4')	112.9 (3)
C(12)—C(11)—S(1)	120.5 (4)	C(16)—C(11)—S(1)	119.8 (4)
C(16)—C(11)—C(12)	119.3 (5)	C(13)—C(12)—C(11)	119.4 (5)
C(14)—C(13)—C(12)	121.3 (7)	C(15)—C(14)—C(13)	120.5 (7)
C(16)—C(15)—C(14)	119.1 (6)	C(15)—C(16)—C(11)	120.2 (6)

dichloromethane (5 ml) for one minute at 298 K. After quenching and extraction with saturated aqueous sodium bicarbonate, the organic layer was dried over MgSO_4 and evaporated to dryness. Dissolution of the colorless gum in THF/toluene, 1:4 (2 M), gave a clear solution from which X-ray quality crystals were obtained after slow evaporation for 8 h at 298 K. Longer evaporation leads to unsuitable crystalline material. The low R_f P-diastereomer of *S*-phenyl *O*-(5'-*O*-tritylthymidin-3'-yl) methylphosphonothioate did not yield crystalline material after similar treatment. Intensities were measured with a Nicolet *P3/F* diffractometer equipped with a graphite incident-beam monochromator. The sample, a crystal of dimensions $0.1 \times 0.2 \times 0.55$ mm, was mounted on a glass fiber with epoxy resin. Cell parameters were determined and refined using the setting angles of 25 reflections in the range 26.0 to 28.1° . A total of 5689 reflections were measured using θ - 2θ scans ($3.0 \leq 2\theta \leq 50.0^\circ$) in the range $-12 \leq h \leq 3$, $-11 \leq k \leq 11$, $-15 \leq l \leq 15$, and averaged to 4227 unique reflections ($R_{av} = 0.0023$), of which 3156 were observed [$F > 6.00\sigma(F)$]. Four standard reflections (111, 323, 346, 541) monitored after every 100 reflections showed only statistically random variations. There was no correction for absorption. The structure was solved using direct methods (Sheldrick, 1987). H atoms were located in difference maps and, except for the 5'-hydroxyl hydrogen, H(13), were included in constrained idealized positions with a single overall thermal parameter for all H atoms. The methyl H atoms on C(7) are disordered. The hydroxyl hydrogen, H(13), was refined with an isotropic thermal parameter. The THF solute is significantly disordered. Atoms describing the solute were included as C atoms using partial occupancies with isotropic thermal parameters. All other non-H atoms were refined anisotropically. The

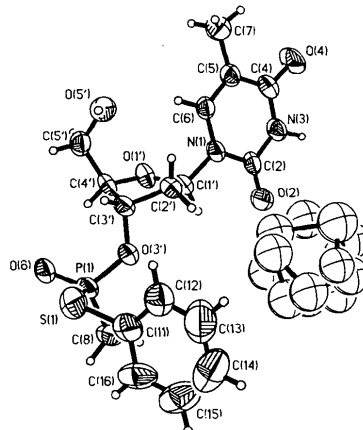


Fig. 1. View of *S*-phenyl *O*-3'-thymidinyl methylphosphonothioate showing the numbering scheme adopted. Thermal ellipsoids are shown at the 50% probability level. Labels for the disordered tetrahydrofuran molecule are omitted for clarity.

function minimized in the full-matrix least-squares calculations was $\sum w(|F_o| - |F_c|)^2$ where $w = 1.0/[\sigma^2(F) + 0.006F^2]$. 307 variables were refined. The ratio of observations to parameters is 10:1. At convergence $R = 0.039$, $wR = 0.048$, $S = 1.29$, $\Delta/\sigma_{av} = 0.003$ while $\Delta/\sigma_{max} = 0.059$ for a positional coordinate of an atom in the disordered THF. Final difference electron density excursions are -0.22 and $+0.28 \text{ \AA}^3$. The absolute configuration of the methylphosphonothioate enantiomer was determined from the known configuration of the thymidiny moiety. Atomic scattering factors for neutral atoms are from *International Tables for X-ray Crystallography* (1974). Atomic fractional coordinates and equivalent isotropic displacement parameters are given in Table 1 for the title compound.* Selected bond

* Tables of parameters for the disordered THF atoms and for the H atoms, anisotropic thermal parameters and structure factors have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51966 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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Structure of a Protected C(1)–C(10) Subunit* of C(2)-*epi*-Erythronolides A and B

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Abstract. 1-[5-(2-Hydroxy-1,3-dimethyl-4-pentenyl)-2,2,4-trimethyl-1,3-dioxolan-4-yl]-2-methyl-3-pentanone, $C_{19}H_{34}O_4$, $M_r = 326.48$, monocline, $P2_1$, $a = 11.409$ (3), $b = 7.889$ (2), $c = 11.690$ (3) \AA , $\beta = 109.24$ (2) $^\circ$, $V = 993.4$ (4) \AA^3 , $Z = 2$, $D_x = 1.09 \text{ g cm}^{-3}$, $\text{Mo K}\alpha$, $\lambda = 0.71069 \text{ \AA}$, $\mu = 0.6963 \text{ cm}^{-1}$, $F(000) = 360$, $T = 194 \text{ K}$, $R = 0.0595$ for 1496 reflections [$F_o \geq 4\sigma(F_o)$]. Molecules stack into columns parallel to the screw axis. Molecules are hydrogen bonded within each column. A hydrogen bond involving the hydroxyl group of one molecule and the carbonyl O of a second molecule (related by $-x, -\frac{1}{2} + y, -z$) with an O...O distance of 2.859 (7) \AA , an H...O distance of 2.01 (7) \AA and an O—H...O angle of 164 (6) $^\circ$ is observed.

Experimental. (1) corresponds to the C(1)–C(10) portion of the 2-*epi*-erythromycins and was synthe-

* [4*R*-(4 α ,5 β)]-5-[(1*S**,2*R**,3*R**)-2-Hydroxy-1,3-dimethyl-4-pentenyl]-2,2,4-trimethyl-4-[(2*R**)-2-methyl-3-oxopentyl]-1,3-dioxolane.

distances and angles are given in Table 2. Fig. 1 shows the atom-numbering scheme.

Related literature. Methylphosphonothioates of nucleosides have not been reported. This structure was solved as part of an effort to introduce, with defined stereochemistry, chiral internucleotidic linkages into oligodeoxyribonucleotides. Continuing work will be published elsewhere.

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References

- BRILL, W. K.-D. & CARUTHERS, M. H. (1988). *Tetrahedron Lett.* **29**, 1227–1230.
 GRANDAS, A., MARSHALL, W. S., NIELSEN, J. & CARUTHERS, M. H. (1989). *Tetrahedron Lett.* **30**, 543–546.
International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)
 SHELDRICK, G. M. (1987). *SHELXL-PLUS*. Program for crystal structure determination. Version 2.1. Nicolet Analytical Instruments, Madison, Wisconsin, USA.

sized by Lewis acid-mediated crotylstannane addition to an aldehyde (Keck & Abbott, 1984). The optical purity was established by an asymmetric aldol condensation (Evans, Bartroli & Shih, 1981) using a (1*S*,2*R*)-(+)-norephedrine hydrochloride derived reagent. Full synthetic details will be described elsewhere (Martin & Pacofsky, 1989). Crystals of (1) were obtained by slow evaporation from hexanes. The data crystal was a colorless needle and had dimensions 0.08 × 0.12 × 0.80 mm. The data were collected on a Nicolet R3 diffractometer, using a graphite monochromator, and equipped with a Nicolet LT-2 low-temperature delivery system (194 K). The lattice parameters were obtained from the least-squares refinement of 42 reflections with

