

- CROMER, D. T. & WABER, J. T. (1974). *International Tables for X-ray Crystallography*, Vol. IV, edited by J. A. IBERS & W. C. HAMILTON, Table 2.2B, pp. 99–101. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)
- DAVIES, K. (1983). *CHEMGRAF* suite, program *SNOOPI*. Chemical Design Ltd, Oxford, England.
- FRENCH, S. & WILSON, K. (1978). *Acta Cryst.* A34, 517–525.
- HOWARD-LOCK, H. E., LOCK, C. J. L., MARTINS, M. L., FAGGIANI, R. & DUARTE, M. (1987). *Can. J. Chem.* 65, 878–883.
- HOWARD-LOCK, H. E., LOCK, C. J. L., MEWA, A. & KEAN, W. F. (1986). *Semin. Arthritis Rheum.* 15, 261–281.
- HOWARD-LOCK, H. E., LOCK, C. J. L. & SMALLEY, P. S. (1985). *Can. J. Chem.* 63, 2411–2419.
- MAROV, K. (1965). *Acta Chem. Scand.* 19, 1509.
- MAZZI, F. & TADINI, C. (1963). *Z. Kristallogr.* 118, 378–392.
- MERRIL, C. R., SHAW, C. F., SPADARO, J. A. & ETRIS, S. F. (1987). In *Proceedings of the First International Conference on Gold and Silver in Medicine*. Washington, DC: The Gold Institute/The Silver Institute.
- PAULING, L. (1960). *The Nature of the Chemical Bond*, 3rd ed., pp. 224, 228. Ithaca, NY: Cornell Univ. Press.
- SHELDRIK, G. M. (1976). *SHELX76*. Program for crystal structure determination. Univ. of Cambridge, England.
- SLOT, H. J. B., KRON, J., BROUWER, A. C. & BOS, H. J. T. (1981). *Acta Cryst.* B37, 1871–1873.
- STEWART, J. M. & HALL, S. R. (1983). The *XTAL* system. Tech. Rep. TR-1364. Computer Science Center, Univ. of Maryland, College Park, Maryland, USA.

Acta Cryst. (1989). C45, 1031–1034

Structure of a Propynyl Adduct of an Oxa-Bridged Octalin*

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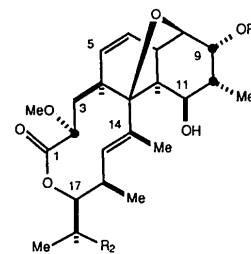
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(Received 17 May 1988; accepted 3 January 1989)

Abstract. C₂₀H₃₀O₆, *M_r* = 366.45, monoclinic, *P*2₁/*n*, *a* = 10.411 (2), *b* = 16.084 (3), *c* = 11.991 (1) Å, β = 100.98 (2)°, *V* = 1971 (6) Å³, *Z* = 4, *D_x* = 1.23 Mg m⁻³, *Mo Kα*, λ = 0.71069 Å, μ = 0.097 mm⁻¹, *F*(000) = 792, *T* = 296 K, *R* = 0.050, *wR* = 0.065 for 3430 observed unique reflections. The structure of a key synthetic intermediate for use in a total synthesis of the nargenicin antibiotics has been established by X-ray single-crystal methods. Its structure is characterized by an essentially strain-free tricyclic oxa-bridged octalin nucleus, low-energy methoxymethyl ether side-chain conformations and an intramolecular hydrogen bond between the hydroxyl group hydrogen atom and a methoxymethyl ether oxygen atom. Intermolecular packing contacts less than the sum of van der Waals radii consist of weak C–H...O interactions.

Introduction. The nargenicins [(1)–(3), Scheme 1] constitute a new structural class of macrolide antibiotics which exhibit significant activity against drug-resistant microorganisms. First isolated by groups at Pfizer (Celmer, Chmurny, Moppett, Ware, Watts & Whipple, 1980) and Upjohn (Whaley, Chidester, Misak & Wnuk, 1980; Magerlein & Reid, 1982), the nargenicins are characterized by the presence of a highly

functionalized decanolid system fused to an 11-oxatricyclo[4.4.1.0^{2,7}]undecene nucleus. Studies in our laboratories have focused on the development of an efficient, stereo-controlled route to the nargenicins (Kallmerten, 1984; Kallmerten & Plata, 1987) and have recently culminated in the total synthesis of 18-deoxynargenicin A₁, (3) (Plata & Kallmerten, 1988). While our convergent approach to (3) rapidly assembles the key structural elements of the nargenicin macrolide system, it ultimately fails to control stereochemistry at C₁₆ and C₁₇ (Scheme 1). Consequently, we are investigating an alternative strategy in which the remote stereochemical elements of the macrolide system will be introduced *via* the stereoselective sigmatropic homologation of a tertiary allylic ether.



- (1) R₁ = 2-carboxypyrrrole, R₂ = OH, nargenicin A₁
 (2) R₁ = H, R₂ = OH, nodusmicin
 (3) R₁ = 2-carboxypyrrrole, R₂ = H, 18-deoxynargenicin A₁

Scheme 1

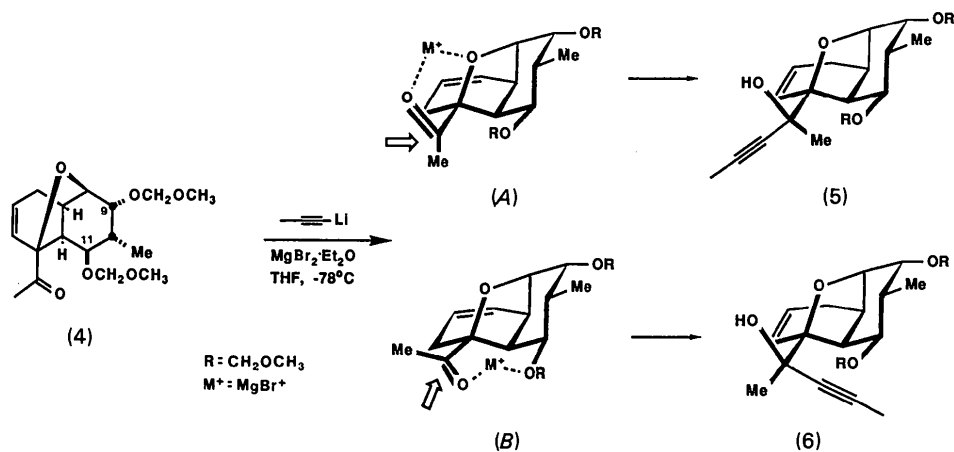
* IUPAC name: (2*R**)-2-[(1*R**,5*S**,6*S**,7*S**,8*S**,9*S**,10*R**)-7,9-bis(methoxymethoxy)-8-methyl-11-oxatricyclo[4.4.1.0^{2,7}]undec-2-en-3-yl]-3-pentyn-2-ol.

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A pivotal step in our revised synthetic plan was the addition of a propynyl nucleophile to ketone (4) (Scheme 2). At the outset of our studies, the diastereofacial preference for nucleophilic attack on this substrate was unclear. An analysis of models suggests that two modes of chelation-controlled addition to (4) can take place; addition to an α -chelate (A) involving the oxygen of the ether bridge, affording (5), or addition to a seven-membered chelate (B) involving the C₁₁[(4), Scheme 2] methoxymethyl group to give (6). In the event, addition of propynyl Grignard reagent to (4) was highly stereoselective, yielding a single product. Since assignment of the relative configuration at the newly formed chiral center was crucial to our synthetic strategy, we resorted to X-ray crystallography to determine the structure of our adduct. Herein we report the structure of this adduct to be (5), suggesting that nucleophilic addition to (4) occurs *via* the α -chelate.

of all 26 non-hydrogen atoms with isotropic refinement of all 30 hydrogen atoms (354 variables plus scale factor, 3430 observed reflections) converged at $R = 0.050$, $wR = 0.065$, $S = 1.60$. The maximum shift in the final cycle $(\Delta/\sigma)_{\max} = 0.04$. Largest peaks in final difference map, $+0.21$ and $-0.19 \text{ e } \text{\AA}^{-3}$. A MicroVAXII-based *TEXRAY* (1985) system, which includes the *TEXSAN* crystallographic software package, was used for diffractometer control and all calculations. Atomic scattering factors from *International Tables for X-ray Crystallography* (1974). Hydrogen scattering factors are those of Stewart, Davidson & Simpson (1965).

Discussion. The final positional parameters, along with their estimated standard deviations and equivalent isotropic temperature factors for non-hydrogen atoms,



Scheme 2

Experimental. Colorless, transparent crystals were grown from ether at 253 K. Crystal size $0.5 \times 0.4 \times 0.5 \text{ mm}$. Rigaku AFC-5S four-circle diffractometer, graphite-monochromated Mo $K\alpha$ radiation. All data obtained at 296 K. Unit-cell dimensions from 20 reflections ($20^\circ < 2\theta < 23^\circ$). Intensities measured in ω - 2θ mode, 2θ maximum 60.1° (h 0 to 14, k 0 to 22, l -16 to 16), scan speed $16^\circ \text{ min}^{-1}$ in ω . 5981 independent reflections collected, 3430 observed [$|F_o| > 3\sigma(|F_o|)$]. Weights were assigned as $w = 1/\sigma^2(F_o)$, where σ is the standard deviation of observed amplitudes based on counting statistics. No systematic changes in $\bar{2}06$, $\bar{4}62$, $\bar{1}16$ measured every 100 reflections. Range of ψ -scan transmission factor (averaged) 0.944 to 1.000. ψ correction applied. Structure solved by *MITHRIL* (Gilmore, 1983). All 26 non-hydrogen atoms were located from the initial E map; all hydrogen atoms were located from a difference Fourier synthesis after three cycles of isotropic least-squares refinement. Anisotropic full-matrix least-squares refinement (on F)

are given in Table 1.* Fig. 1 is an *ORTEP* (Johnson, 1976) drawing of an isolated molecule which illustrates the molecular configuration as well as the atomic numbering scheme used. Table 2 lists the intramolecular bond distances and angles for the non-hydrogen atoms. Estimated standard deviations are seen to be small, this being the result of the availability of a well ordered, good quality, crystal which made possible the gathering of an extensive high-quality data set. The high internal correspondence to within one estimated standard deviation of the structural results for

* Lists of structure factors, anisotropic thermal parameters, positional parameters for H atoms, intramolecular bond lengths and bond angles involving H atoms, and intermolecular contacts involving the H atoms have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51703 (48 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Positional and equivalent isotropic thermal parameters for the non-hydrogen atoms and their *e.s.d.*'s at 296 K

$$B_{eq} = (8\pi^2/3)(U_{11} + U_{22} + U_{33} + 2U_{12}\cos\gamma + 2U_{13}\cos\beta + 2U_{23}\cos\alpha).$$

	x	y	z	$B_{eq}(\text{\AA}^2)$
O(1)	0.1144 (1)	0.09785 (9)	0.1112 (1)	3.17 (5)
O(2)	0.3979 (1)	0.14569 (8)	0.3671 (1)	3.26 (5)
O(3)	0.4974 (1)	0.1081 (1)	0.5510 (1)	4.14 (6)
O(4)	-0.0071 (1)	0.0562 (1)	0.3709 (1)	4.64 (7)
O(5)	-0.2335 (2)	0.0677 (1)	0.3140 (1)	4.55 (7)
O(6)	0.3298 (1)	0.21703 (8)	0.1593 (1)	3.37 (5)
C(1)	0.2496 (2)	0.0717 (1)	0.1219 (1)	2.70 (7)
C(2)	0.2807 (2)	0.0352 (1)	0.2439 (1)	2.70 (7)
C(3)	0.2831 (2)	0.0938 (1)	0.3455 (1)	2.83 (7)
C(4)	0.1641 (2)	0.1514 (1)	0.3342 (2)	3.37 (8)
C(5)	0.0367 (2)	0.1062 (1)	0.2856 (2)	3.63 (8)
C(6)	0.0567 (2)	0.0487 (1)	0.1902 (2)	3.39 (8)
C(7)	0.1570 (2)	-0.0181 (1)	0.2358 (2)	3.31 (8)
C(8)	0.1550 (3)	-0.0940 (1)	0.1588 (2)	4.4 (1)
C(9)	0.2102 (3)	-0.0739 (1)	0.0558 (2)	4.4 (1)
C(10)	0.2538 (2)	0.0007 (1)	0.0388 (2)	3.50 (8)
C(11)	0.3321 (2)	0.1452 (1)	0.0902 (1)	2.83 (7)
C(12)	0.2763 (2)	0.1729 (1)	-0.0269 (2)	3.21 (7)
C(13)	0.2361 (2)	0.1960 (1)	-0.1203 (2)	3.68 (8)
C(14)	0.1842 (4)	0.2263 (2)	-0.2352 (2)	5.4 (1)
C(15)	0.1574 (3)	0.1957 (2)	0.4451 (2)	5.2 (1)
C(16)	0.4740 (2)	0.1174 (2)	0.0968 (2)	3.75 (9)
C(17)	0.5081 (2)	0.1093 (2)	0.4371 (2)	3.58 (9)
C(18)	0.5222 (4)	0.1863 (2)	0.6056 (3)	6.1 (1)
C(19)	-0.1260 (3)	0.0824 (2)	0.3998 (2)	4.7 (1)
C(20)	-0.2606 (4)	-0.0180 (2)	0.2944 (3)	5.6 (1)

Table 2. Bond distances (\AA), bond angles ($^\circ$), and *e.s.d.*'s for the non-hydrogen atoms

O(1)–C(6)	1.449 (2)	C(2)–C(7)	1.535 (3)
O(1)–C(1)	1.451 (2)	C(2)–C(3)	1.537 (3)
O(2)–C(17)	1.414 (2)	C(3)–C(4)	1.532 (3)
O(2)–C(3)	1.441 (2)	C(4)–C(15)	1.522 (3)
O(3)–C(17)	1.391 (2)	C(4)–C(5)	1.527 (3)
O(3)–C(18)	1.419 (3)	C(5)–C(6)	1.516 (3)
O(4)–C(19)	1.412 (3)	C(6)–C(7)	1.525 (3)
O(4)–C(5)	1.442 (2)	C(7)–C(8)	1.528 (3)
O(5)–C(19)	1.388 (3)	C(8)–C(9)	1.493 (4)
O(5)–C(20)	1.416 (3)	C(9)–C(10)	1.312 (3)
O(6)–C(11)	1.424 (2)	C(11)–C(12)	1.482 (3)
C(1)–C(10)	1.522 (3)	C(11)–C(16)	1.531 (3)
C(1)–C(11)	1.551 (3)	C(12)–C(13)	1.178 (3)
C(1)–C(2)	1.552 (2)	C(13)–C(14)	1.465 (3)
C(6)–O(1)–C(1)	107.5 (1)	O(4)–C(5)–C(4)	111.3 (2)
C(17)–O(2)–C(3)	114.7 (2)	C(6)–C(5)–C(4)	110.2 (2)
C(17)–O(3)–C(18)	113.5 (2)	O(1)–C(6)–C(5)	107.0 (2)
C(19)–O(4)–C(5)	114.8 (2)	O(1)–C(6)–C(7)	106.1 (2)
C(19)–O(5)–C(20)	113.3 (2)	C(5)–C(6)–C(7)	110.0 (2)
O(1)–C(1)–C(10)	107.9 (1)	C(6)–C(7)–C(8)	114.6 (2)
O(1)–C(1)–C(11)	109.3 (1)	C(6)–C(7)–C(2)	98.0 (2)
O(1)–C(1)–C(2)	102.6 (1)	C(8)–C(7)–C(2)	113.5 (2)
C(10)–C(1)–C(11)	108.9 (1)	C(9)–C(8)–C(7)	111.4 (2)
C(10)–C(1)–C(2)	107.9 (2)	C(10)–C(9)–C(8)	121.7 (2)
C(11)–C(1)–C(2)	119.6 (1)	C(9)–C(10)–C(1)	122.0 (2)
C(7)–C(2)–C(3)	106.2 (2)	O(6)–C(11)–C(12)	105.2 (1)
C(7)–C(2)–C(1)	97.4 (1)	O(6)–C(11)–C(16)	109.2 (2)
C(3)–C(2)–C(1)	118.9 (2)	O(6)–C(11)–C(1)	113.8 (1)
O(2)–C(3)–C(4)	107.1 (2)	C(12)–C(11)–C(16)	109.7 (2)
O(2)–C(3)–C(2)	112.6 (1)	C(12)–C(11)–C(1)	109.0 (1)
C(4)–C(3)–C(2)	114.2 (1)	C(16)–C(11)–C(1)	109.8 (2)
C(15)–C(4)–C(5)	112.1 (2)	C(13)–C(12)–C(11)	177.6 (2)
C(15)–C(4)–C(3)	112.1 (2)	C(12)–C(13)–C(14)	178.5 (2)
C(5)–C(4)–C(3)	112.0 (2)	O(3)–C(17)–O(2)	112.4 (2)
O(4)–C(5)–C(6)	107.6 (2)	O(5)–C(19)–O(4)	112.8 (2)

the two identical methoxymethyl ether (MOM) side chains also supports this view: C(3)–O(2) = 1.441 (2) *vs* C(5)–O(4) = 1.442 (2); O(2)–C(17) = 1.414 (2) *vs* O(4)–C(19) = 1.412 (3); C(17)–O(3) = 1.391 (2) *vs* C(19)–O(5) = 1.388 (3); O(3)–C(18) = 1.419 (3) *vs* O(5)–C(20) = 1.416 (3) \AA . Although the average value for a C–O single bond has been reported as 1.426 \pm 0.005 \AA (Sutton, 1965), it has recently been demonstrated that this bond can show considerable variability (Allen & Kirby, 1984, and references therein). This is also evident in the relatively few structures containing MOM groups which have been reported to date (Jones, Kennard, Kirby & Osborne, 1978; Jones, Kennard, Kirby, Osborne & Abdul Malik, 1978; Jones, Sheldrick, Glenn & Kirby, 1983; Egert, Cruse & Kennard, 1983; Jones, Sheldrick, Kirby & Briggs, 1984, 1985). It is interesting to note that the two most stable (symmetry-related) conformations found in the *ab initio* molecular-orbital calculations of Jeffrey, Pople, Binkley & Vishveshwara (1978) for dimethoxymethane are, to a first approximation, those found for the two MOM groups in this structure, one being +*sc*, +*sc*, $\theta = +77.2^\circ$, $\varphi = +75.4^\circ$ and the other being –*sc*, –*sc*, $\theta = -67.2^\circ$, $\varphi = -70.9^\circ$, which may be compared to the ideal torsion angles of $\theta = \varphi = +60$ or -60° for the lowest-energy conformations.

No unexpected or unusual bond distances or angles were found in the oxa-bridged octalin core which is indicative of relatively low strain, an observation suggested earlier by model building (Kallmerten, 1984). Likewise, the five-membered oxygen-atom-containing ring in the tricyclic core is seen to possess the lower-energy twist form which is the conformation of free tetrahydrofuran (Luger & Buschmann, 1983).

Calculated intramolecular contacts revealed the existence of an intramolecular hydrogen bond from the hydroxyl group hydrogen atom to a methoxymethyl ether group oxygen atom, O(6)–HO(6)···O(2) (see Fig. 1), which has the following structural parameters: HO(6)···O(2) distance = 1.87 (3) \AA ; O(6)–HO(6)···O(2) angle = 157 (2) $^\circ$; O(6)···O(2) distance = 2.711 (2) \AA ; O(6)–HO(6) distance = 0.89 (3) \AA ; C(11)–O(6)–HO(6) angle = 105 (2) $^\circ$. It is note-

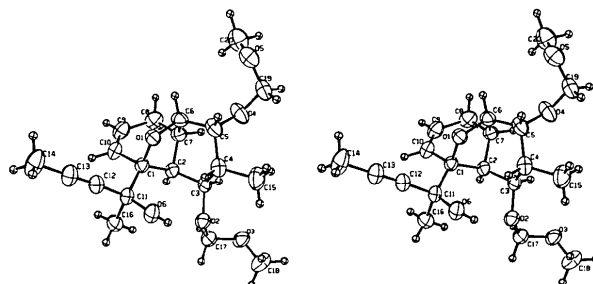


Fig. 1. Molecular structure and numbering scheme. Non-hydrogen thermal ellipsoids are drawn at 50% probability. Molecule shown is the enantiomer of the molecule whose coordinates are given in Table 1.

worthy that all calculated intermolecular packing contacts which were approximately equal to or less than the sum of the van der Waals radii for the atoms involved consisted of what may be described as weak C—H...O interactions. O(6)...H(18C) (ADC = 45404) distance = 2.54 (4) Å; O(5)...H(14A) (ADC = 45504) distance = 2.61 (4) Å; O(3)...H(17A) (ADC = 65603) distance = 2.61 (4) Å.* According to the criteria set forth by Taylor & Kennard (1982), it is clear that none of these interactions can be considered to be a C—H...O hydrogen bond; however, it is likely that these interactions may play a role in determining the molecular packing of this compound. Berkovitch-Yellin & Leiserowitz (1984) in their atom-atom potential-energy calculation approach to the question of Coulomb and van der Waals energy contributions to C(sp³)—H...O, C(sp²)—H...O, and C(sp)—H...O interactions in a variety of crystal structures concluded that Coulombic contributions are dominant and are thus important even for long H...O distances.

The support of this work by the National Institutes of Health (AI-19632) is gratefully acknowledged. We wish to acknowledge NSF award CHE-85-1486 to the Department of Chemistry of Syracuse University for the purchase of a single-crystal X-ray diffractometer.

* The ADC (atom designator code) specifies the positions of the target atom in a crystal. The five-digit number is a composite of three one-digit numbers and one two-digit number: TA (1st digit) + TB(2nd digit) + TC (3rd digit) + SN (4th and 5th digits), where TA, TB, and TC are the crystal lattice translation digits along cell edges *a*, *b*, and *c* with a value of 5 indicating the origin unit cell and SN refers to the number of the symmetry operator used to generate the coordinates of the target atom.

References

- ALLEN, F. H. & KIRBY, A. J. (1984). *J. Am. Chem. Soc.* **106**, 6197–6200.
- BERKOVITCH-YELLIN, Z. & LEISEROWITZ, L. (1984). *Acta Cryst.* **B40**, 159–165.
- CELMER, W. D., CHMURNY, G. N., MOPPETT, C. E., WARE, R. S., WATTS, P. C. & WHIPPLE, E. B. (1980). *J. Am. Chem. Soc.* **102**, 4203–4209.
- EGERT, E., CRUSE, W. B. T. & KENNARD, O. (1983). *Acta Cryst.* **C39**, 95–99.
- GILMORE, C. J. (1983). *MITHRIL*. A computer program for the automatic solution of crystal structures from X-ray data. Univ. of Glasgow, Scotland.
- International Tables for X-ray Crystallography* (1974). Vol. IV. Birmingham: Kynoch Press. (Present distributor Kluwer Academic Publishers, Dordrecht.)
- JEFFREY, G. A., POPLE, J. A., BINKLEY, J. S. & VISHVESHWARA, S. (1978). *J. Am. Chem. Soc.* **100**, 373–379.
- JOHNSON, C. K. (1976). *ORTEPII*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- JONES, P. G., KENNARD, O., KIRBY, A. J. & OSBORNE, R. (1978). *Acta Cryst.* **B34**, 2923–2924.
- JONES, P. G., KENNARD, O., KIRBY, A. J., OSBORNE, R. & ABDUL MALIK, K. M. (1978). *Acta Cryst.* **B34**, 2925–2927.
- JONES, P. G., SHELDRIK, G. M., GLENN, R. & KIRBY, A. J. (1983). *Z. Kristallogr.* **163**, 85–91.
- JONES, P. G., SHELDRIK, G. M., KIRBY, A. J. & BRIGGS, A. J. (1984). *Acta Cryst.* **C40**, 545–547.
- JONES, P. G., SHELDRIK, G. M., KIRBY, A. J. & BRIGGS, A. J. (1985). *Acta Cryst.* **C41**, 1377–1379.
- KALLMERTEN, J. (1984). *Tetrahedron Lett.* **25**, 2843–2846.
- KALLMERTEN, J. & PLATA, D. J. (1987). *Heterocycles*, **25**, 145–149.
- LUGER, P. & BUSCHMANN, J. (1983). *Angew. Chem. Int. Ed. Engl.* **22**, 410.
- MAGERLEIN, B. J. & REID, R. J. (1982). *J. Antibiot.* pp. 254–255.
- PLATA, D. J. & KALLMERTEN, J. (1988). *J. Am. Chem. Soc.* **110**, 4041–4042.
- STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
- SUTTON, L. E. (1965). *Tables of Interatomic Distances and Configuration in Molecules and Ions*. Chemical Society Special Publication No. 18. London: The Chemical Society.
- TAYLOR, T. & KENNARD, O. (1982). *J. Am. Chem. Soc.* **104**, 5063–5070.
- TEXRAY* (1985). Registered trademark of The Molecular Structure Corporation, The Woodlands, Texas 77381, USA.
- WHALEY, H. A., CHIDESTER, C. G., MIZSAK, S. A. & WNUK, R. J. (1980). *Tetrahedron Lett.* **21**, 3659–3662.

Acta Cryst. (1989). **C45**, 1034–1039

Structure of Antischistosome Compounds. V. 1,6-Hexanediylbis(triphenylphosphonium) Dibromide

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(Received 6 September 1988; accepted 23 November 1988)

Abstract. C₄₂H₄₂P₂²⁺·2Br⁻, *M_r* = 768.6, triclinic, *P* $\bar{1}$, *a* = 13.328 (2), *b* = 23.110 (3), *c* = 9.417 (1) Å, α = 90.75 (1), β = 109.62 (1), γ = 91.23 (1)°, *V* =

2730.86 Å³, *Z* = 3, *D_x* = 1.402 g cm⁻³, graphite-monochromatized Cu K α radiation, λ = 1.5418 Å, μ = 52.0 cm⁻¹, *F*(000) = 1182, *T* = 292 K. Final *R* =

0108-2701/89/071034-06\$03.00

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