

Structure of Bezafibrate (2-{*p*-[2-(*p*-Chlorobenzamide)ethyl]phenoxy}-2-methylpropanoic Acid)

BY K. DJINOVIĆ

Department of Chemistry and Chemical Technology, Edvard Kardelj University, Ljubljana, PO Box 537, Yugoslavia

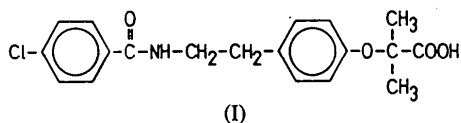
AND M. GLOBOKAR AND P. ZUPET

KRKA – Pharmaceutical and Chemical Works, Novo Mesto, Yugoslavia

(Received 1 July 1988; accepted 9 November 1988)

Abstract. C₁₉H₂₀ClNO₄, *M_r* = 361.83, orthorhombic, *P*2₁2₁2₁, *a* = 10.222 (2), *b* = 17.826 (3), *c* = 19.921 (4) Å, *V* = 3630 (2) Å³, *Z* = 8, *D_m* = 1.30 (4), *D_x* = 1.324 g cm⁻³, Mo *K*α radiation, λ = 0.71069 Å, μ = 2.294 cm⁻¹, *F*(000) = 1520, *T* = 293 (2) K, final *R* = 0.060 and *wR* = 0.066 for 2334 contributing reflections. The conformations of the two molecules in the asymmetric unit resemble each other. The benzene rings in the molecules are inclined towards each other forming angles of 68.3 (11) and 62.1 (14)°. The molecules are connected by O...N and O...O intermolecular hydrogen bonds ranging from 2.557 (9) to 2.926 (7) Å. Distorted bond angles at the benzene C atom bonded to the O(ether) atom, and deviations from the expected C=O and C–OH bond distances have been observed in clofibric acid and related compounds as well as in bezafibrate.

Introduction. Bezafibrate has antihyperlipoproteinemia properties and inhibits gelling of sickle-cell deoxyhemoglobin. The compound can be compared to two molecules of clofibric acid in tandem and boasts roughly twice the physiological activity of clofibric acid (Perutz, Fermi, Abraham, Poyart & Bursaux, 1986; Abraham, Perutz & Phillips, 1983). The stereochemistry of its binding to deoxyhemoglobin has been studied by X-ray structural analysis of the bezafibrate–deoxyhemoglobin complex (Perutz *et al.*, 1986). Here we present the crystal and molecular structure of the title compound (I) and a comparison of its characteristic structural features with those of clofibric acid.



Experimental. Synthesis of bezafibrate in the form of microcrystalline powder was carried out by KRKA –

Pharmaceutical and Chemical Works. Crystals of bezafibrate were prepared by slow evaporation of the ethanol solution. Density by flotation. Crystal size: 0.30 × 0.58 × 0.34 mm. Unit-cell parameters and intensity data obtained using an Enraf–Nonius CAD-4 diffractometer with graphite-monochromated Mo *K*α radiation. Cell dimensions refined by least-squares fitting of 100 centred reflections monitored in the range 10 < θ < 13° using Mo *K*α₁ radiation (wavelength 0.70930 Å). Data-collection parameters: max. scan time 60 s, scan rates varied from 1.177 to 5.493° min⁻¹; ω scan width (°) = 0.8 + 0.3 tgθ; aperture (mm) = 2.4 + 0.9 tgθ. 15 961 reflections collected to (sinθ/λ)_{max} = 0.6390 Å⁻¹, 0 ≤ *h* ≤ 13, -22 ≤ *k* ≤ 22, -25 ≤ *l* ≤ 25. Orientation control monitored after each 400 reflections, standard reflections measured every 15 000 s of scanning time (191, 522, 512) did not show any significant change in intensity (-1.37%). 4405 unique reflections, 1826 observed [*I* > 2.5σ(*I*)], *R_{int}* after merging for space group *P*2₁2₁2₁ 0.097; among 31 systematically absent reflections seven had intensities greater than 2.5σ(*I*), the maximum value being 260.9 counts [= 13.8σ(*I*)] for the 010 reflection. As the considerable number of systematically absent reflections with significant intensity did not support the space group *P*2₁2₁2₁ (No. 19), we tried to determine the structure by direct methods in *P*2₁22 (No. 17) and *P*2₁2₁2 (No. 18) using *MULTAN*87 (Debaerdemaker, Germain, Main, Tate & Woolfson, 1987) and *SHELXS*86 (Sheldrick, 1986), but the *E* maps did not reveal the structure. In spite of the *N*(*Z*) and *E* tests indicating the acentricity of the structure, *Pmmm* (No. 59) was investigated as well but without success. The crystal on which data had been collected was tested for Renninger effects (Renninger, 1937) but the intensities of these reflections did not decrease on changing the orientation of the crystal. Considering the fact that the model of the structure displayed only space group *P*2₁2₁2₁ and that the above mentioned experiments did not yield any solution we decided to refine the

structure in this space group leaving the problem of these significantly non-zero reflections unexplained.

The structure was solved by direct methods using *MULTAN80* (Main, Fiske, Hull, Lessinger, Germain, Declercq & Woolfson, 1980). The correct positions of all non-H atoms were deduced from an *E* map and subsequent Fourier maps and were refined on *F* by block least-squares techniques with the *XRAY76* system of crystallographic programs (Stewart, Machin, Dickinson, Ammon, Heck & Flack, 1976) with anisotropic displacement parameters. Hydrogen atoms were generated from the assumed geometries and were included in the refinement as fixed atom contributions with isotropic thermal coefficients. The hand of the structure was checked by refining an imaginary dispersion term of the chlorine atom and was compared to the conformation of bezafibrate bound to deoxy-hemoglobin (Perutz *et al.*, 1986). The agreement confirmed the absolute structure. Empirical weighting function, $w = W_f \times W_s$, where: $W_f(|F_o| < 10.0) = |F_o|/10.00$, $W_f(|F_o| > 17.0) = (17.00/|F_o|)^{0.8}$, $W_f(10.0 \leq |F_o| \leq 17.0) = 1.0$, $W_s(\sin\theta < 0.28) = (\sin\theta/0.28)^{3.0}$, $W_s(\sin\theta > 0.37) = (0.37/\sin\theta)^{1.8}$, $W_s(0.28 \leq \sin\theta \leq 0.37) = 1.0$ applied to keep $\sum w(\Delta F)^2$ uniform over ranges of $\sin\theta/\lambda$ and $|F_o|$. Final agreement values: $R = 0.060$, $wR = 0.065$ for 2345 observed reflections including 'less-thans' for which F_c is greater than F_o . $(\Delta/\sigma)_{\max} = 0.53$, $(\Delta/\sigma)_{\text{av}} = 0.12$, $m = 451$, $m/n = 5.2$, $S = 0.949$; max. and min. heights in final difference Fourier map 0.30 and $-0.39 \text{ e } \text{Å}^{-3}$, respectively.

Atomic scattering factors for H atoms were taken from Stewart, Davidson & Simpson (1965) and for other neutral atoms from Cromer & Mann (1968) and from Cromer & Liberman (1970). All calculations were performed on the DEC-10 computer at RCU, Ljubljana.

Discussion. There are two crystallographically independent bezafibrate molecules in the asymmetric unit. The positional parameters and U_{eq} 's (Hamilton, 1959) along with their standard deviations are listed in Table 1.* The structures of the single molecules *A* and *B* are shown in Fig. 1, while the hydrogen-bonding scheme is presented in Fig. 2. Principal bond distances and angles are listed in Table 2.

The bond distances and angles in the structure are within the ranges of the expected values. The theoretical calculations of the preferred conformation for α -phenoxyisobutyric acid and its *p*-chloro analogue (Zeelen, 1976) indicate that the stable conformation has

* Lists of structure factors, anisotropic thermal parameters, calculated H-atom coordinates, least-squares-plane equations and torsion angles have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 51596 (15 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

Table 1. Atom coordinates ($\times 10^4$) and equivalent isotropic temperature factors ($\text{Å}^2 \times 10^3$) (Hamilton, 1959) with their e.s.d.'s in parentheses

	x	y	z	U_{eq}
Cl(1)	-6256 (2)	1258 (1)	2849 (1)	68 (1)
O(1)	234 (4)	978 (3)	2914 (2)	61 (3)
O(2)	6689 (5)	1693 (3)	5699 (3)	72 (3)
O(3)	8375 (5)	625 (3)	5220 (3)	77 (3)
O(4)	8297 (7)	39 (4)	6179 (3)	95 (4)
N(1)	-83 (5)	994 (3)	4028 (3)	53 (3)
C(1)	-4580 (6)	1213 (3)	3011 (3)	50 (3)
C(2)	-4150 (6)	1362 (4)	3652 (3)	51 (3)
C(3)	-2822 (6)	1297 (3)	3787 (3)	47 (3)
C(4)	-1956 (6)	1082 (3)	3283 (3)	43 (3)
C(5)	-2438 (7)	951 (4)	2644 (3)	53 (3)
C(6)	-3752 (7)	1020 (4)	2506 (3)	56 (3)
C(7)	-521 (6)	1010 (3)	3394 (3)	47 (3)
C(8)	1307 (6)	1041 (4)	4175 (3)	60 (4)
C(9)	1526 (6)	949 (4)	4915 (4)	63 (4)
C(10)	2921 (6)	1115 (4)	5108 (3)	51 (3)
C(11)	3860 (7)	571 (4)	5178 (4)	66 (4)
C(12)	5093 (7)	712 (4)	5367 (5)	67 (4)
C(13)	5461 (6)	1461 (3)	5515 (3)	51 (3)
C(14)	4552 (7)	2013 (4)	5433 (4)	65 (4)
C(15)	3313 (7)	1868 (4)	5228 (4)	66 (4)
C(16)	7461 (7)	1272 (4)	6170 (4)	66 (4)
C(17)	6700 (10)	1021 (7)	6780 (4)	96 (6)
C(18)	8570 (10)	1794 (6)	6370 (6)	107 (7)
C(19)	8086 (6)	603 (4)	5802 (3)	54 (3)
Cl(2)	-1106 (2)	1616 (2)	902 (1)	102 (2)
O(5)	5306 (5)	1060 (3)	772 (2)	70 (3)
O(6)	11889 (5)	1819 (3)	-1865 (3)	81 (3)
O(7)	13497 (6)	679 (3)	-1494 (3)	82 (3)
O(8)	13511 (6)	222 (3)	-2511 (3)	79 (3)
N(2)	5002 (6)	1163 (4)	-328 (3)	67 (3)
C(21)	545 (7)	1475 (4)	717 (4)	64 (4)
C(22)	1332 (8)	1166 (4)	1189 (3)	62 (4)
C(23)	2641 (7)	1054 (4)	1034 (3)	61 (4)
C(24)	3141 (6)	1251 (3)	419 (3)	51 (3)
C(25)	2309 (8)	1555 (4)	-68 (4)	66 (4)
C(26)	981 (7)	1670 (5)	92 (4)	69 (5)
C(27)	4552 (7)	1149 (3)	302 (3)	56 (3)
C(28)	6400 (8)	1158 (5)	-484 (4)	77 (5)
C(29)	6640 (7)	1203 (5)	-1219 (4)	73 (4)
C(30)	8041 (8)	1327 (4)	-1386 (3)	62 (4)
C(31)	8957 (9)	735 (4)	-1425 (5)	82 (5)
C(32)	10223 (8)	872 (4)	-1598 (6)	85 (6)
C(33)	10636 (7)	1609 (4)	-1720 (4)	64 (4)
C(34)	9753 (9)	2179 (4)	-1656 (5)	75 (5)
C(35)	8500 (9)	2046 (4)	-1494 (5)	76 (5)
C(36)	12619 (8)	1425 (4)	-2390 (4)	70 (5)
C(37)	13735 (11)	1993 (6)	-2529 (7)	111 (7)
C(38)	11815 (10)	1247 (7)	-3002 (5)	103 (7)
C(39)	13251 (7)	731 (4)	-2087 (3)	57 (3)

the plane of the benzene ring perpendicular to the plane defined by the ether-O atom, the α -C atom and one methyl-C atom. In our compound the dihedral angles between these planes are 73.4 (11) and 75.7 (14) $^\circ$.

The conformation of the carboxyl group can be synplanar-synplanar or synplanar-antiplanar, according to Leiserowitz (1976) and Kennard, Smith & White (1982) (Figs. 3*a* and 3*b*). In clofibric acid the carboxyl group adopts the *syn-anti* conformation while in our compound the arrangement is *syn-syn* in both molecules. The non-bonding O(ether)-O(carbonyl) distances, 2.716 (8) and 2.739 (7) Å , are similar to the analogous distance in clofibric acid, 2.711 Å (Kennard *et al.*, 1982).

Two structural characteristics have been observed in clofibric acid and related compounds as well as in bezafibrate. (*a*) Distorted bond angles at the benzene C atom bonded to the O(ether) atom, the angles on the

Table 2. Bond lengths (Å) and bond angles (°) with their *e.s.d.*'s in parentheses

Molecule A		Molecule B	
Cl(1)—C(1)	1.745 (6)	Cl(2)—C(21)	1.746 (8)
O(1)—C(7)	1.229 (8)	O(5)—C(27)	1.224 (8)
O(2)—C(13)	1.372 (8)	O(6)—C(33)	1.365 (9)
O(2)—C(16)	1.438 (9)	O(6)—C(36)	1.464 (10)
O(3)—C(19)	1.195 (8)	O(7)—C(39)	1.213 (9)
O(4)—C(19)	1.273 (9)	O(8)—C(39)	1.268 (8)
N(1)—C(7)	1.341 (8)	N(2)—C(27)	1.337 (8)
N(1)—C(8)	1.454 (8)	N(2)—C(28)	1.462 (10)
C(1)—C(2)	1.377 (9)	C(21)—C(22)	1.355 (10)
C(1)—C(6)	1.360 (9)	C(21)—C(26)	1.366 (11)
C(2)—C(3)	1.388 (9)	C(22)—C(23)	1.387 (11)
C(3)—C(4)	1.393 (8)	C(23)—C(24)	1.374 (9)
C(4)—C(5)	1.383 (8)	C(24)—C(25)	1.399 (10)
C(4)—C(7)	1.489 (9)	C(24)—C(27)	1.472 (9)
C(5)—C(6)	1.377 (10)	C(25)—C(26)	1.410 (11)
C(8)—C(9)	1.501 (10)	C(28)—C(29)	1.487 (11)
C(9)—C(10)	1.507 (9)	C(29)—C(30)	1.486 (11)
C(10)—C(11)	1.371 (10)	C(30)—C(31)	1.413 (11)
C(10)—C(15)	1.422 (10)	C(30)—C(35)	1.383 (10)
C(11)—C(12)	1.339 (10)	C(31)—C(32)	1.361 (12)
C(12)—C(13)	1.418 (9)	C(32)—C(33)	1.402 (11)
C(13)—C(14)	1.364 (9)	C(33)—C(34)	1.364 (11)
C(14)—C(15)	1.355 (11)	C(34)—C(35)	1.342 (12)
C(16)—C(17)	1.510 (12)	C(36)—C(37)	1.550 (14)
C(16)—C(18)	1.520 (13)	C(36)—C(38)	1.504 (13)
C(16)—C(19)	1.538 (10)	C(36)—C(39)	1.519 (10)
C(2)—C(1)—Cl(1)	118.4 (5)	C(6)—C(1)—Cl(1)	119.1 (5)
N(1)—C(7)—O(1)	121.5 (6)	C(4)—C(7)—O(1)	120.4 (5)
C(16)—O(2)—C(13)	121.3 (5)	C(12)—C(13)—O(2)	125.6 (6)
C(14)—C(13)—O(2)	116.0 (6)	C(17)—C(16)—O(2)	113.4 (6)
C(18)—C(16)—O(2)	105.1 (7)	C(19)—C(16)—O(2)	108.7 (6)
O(4)—C(19)—O(3)	123.7 (7)	C(16)—C(19)—O(3)	122.7 (6)
C(16)—C(19)—O(4)	113.6 (6)	C(8)—N(1)—C(7)	121.0 (5)
C(4)—C(7)—N(1)	118.0 (5)	C(9)—C(8)—N(1)	109.7 (5)
C(6)—C(1)—C(2)	122.5 (6)	C(3)—C(2)—C(1)	118.4 (6)
C(5)—C(6)—C(1)	118.8 (6)	C(4)—C(3)—C(2)	120.4 (5)
C(5)—C(4)—C(3)	118.9 (6)	C(7)—C(4)—C(3)	122.9 (5)
C(7)—C(4)—C(5)	118.2 (5)	C(6)—C(5)—C(4)	121.1 (6)
C(10)—C(9)—C(8)	111.7 (5)	C(11)—C(10)—C(9)	123.3 (6)
C(15)—C(10)—C(9)	119.7 (6)	C(15)—C(10)—C(11)	117.0 (6)
C(12)—C(11)—C(10)	123.7 (6)	C(14)—C(15)—C(10)	119.6 (6)
C(13)—C(12)—C(11)	119.0 (6)	C(14)—C(15)—C(12)	118.3 (6)
C(15)—C(14)—C(13)	122.3 (6)	C(18)—C(16)—C(17)	110.7 (8)
C(19)—C(16)—C(17)	111.7 (7)	C(19)—C(16)—C(18)	106.8 (6)
C(22)—C(21)—Cl(2)	119.1 (6)	C(26)—C(21)—Cl(2)	118.1 (6)
N(2)—C(27)—O(5)	120.3 (6)	C(24)—C(27)—O(5)	120.8 (6)
C(36)—O(6)—C(33)	119.9 (6)	C(32)—C(33)—O(6)	125.1 (7)
C(34)—C(33)—O(6)	115.9 (7)	C(37)—C(36)—O(6)	100.9 (7)
C(38)—C(36)—O(6)	113.7 (7)	C(39)—C(36)—O(6)	108.9 (6)
O(8)—C(39)—O(7)	123.3 (7)	C(36)—C(39)—O(7)	122.6 (6)
C(36)—C(39)—O(8)	114.1 (6)	C(28)—N(2)—C(27)	122.4 (6)
C(24)—C(27)—N(2)	118.9 (6)	C(29)—C(28)—N(2)	111.7 (6)
C(26)—C(21)—C(22)	122.8 (7)	C(23)—C(22)—C(21)	118.5 (6)
C(25)—C(26)—C(21)	118.9 (7)	C(24)—C(23)—C(22)	121.3 (6)
C(25)—C(24)—C(23)	119.5 (6)	C(27)—C(24)—C(23)	118.3 (6)
C(27)—C(24)—C(25)	122.2 (6)	C(26)—C(25)—C(24)	119.0 (7)
C(30)—C(29)—C(28)	112.8 (6)	C(31)—C(30)—C(29)	122.7 (7)
C(35)—C(30)—C(29)	120.0 (7)	C(35)—C(30)—C(31)	117.3 (7)
C(32)—C(31)—C(30)	120.7 (7)	C(34)—C(35)—C(30)	121.7 (7)
C(33)—C(32)—C(31)	119.9 (7)	C(34)—C(33)—C(32)	118.8 (7)
C(35)—C(34)—C(33)	121.5 (7)	C(38)—C(36)—C(37)	113.3 (8)
C(39)—C(36)—C(37)	106.8 (7)	C(39)—C(36)—C(38)	112.5 (7)

atom being 116.0 (6), 125.6 (6), 118.3 (6)° in the first molecule and 115.9 (7), 125.1 (7), 118.8 (7)° in the second molecule. This conformation for substituted benzoic acids can be explained by steric hindrance from the oxopropanoic side chain. (b) Deviations of bond distances (and angles) within the carboxylic group from the expected C=O and C—OH bond distances (1.214 and 1.308 Å) (Allen, Kennard, Watson, Brammer, Orpen & Taylor, 1987). The corresponding observed values in the bezafibrate molecules are 1.195 (8), 1.273 (9) Å and 1.213 (9), 1.268 (9) Å.

The two benzene rings in each molecule are close to being perpendicular to each other, forming dihedral angles of 68.3 (11) and 62.1 (14)°. The atoms of the peptide bonds are planar within limits of experimental error. The angles between the least-squares planes of the peptide group and the benzene rings are 14.0 (11) and 82.2 (11)° in the first, and 21.6 (14) and 83.3 (14)° in the second crystallographically independent molecules.

The O...O and O...N hydrogen bonds of 2.557 (8), 2.634 (7) and 2.926 (7), 2.916 (8) Å connect the molecules in chains parallel to the [100] direction.

The financial support of KRKA – Pharmaceutical and Chemical Works is gratefully acknowledged.

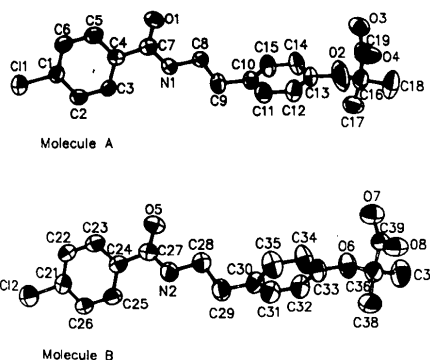


Fig. 1. ORTEP plots (Johnson, 1965) of the two independent molecules in the asymmetric unit. Anisotropic ellipsoids enclose 50% probability.

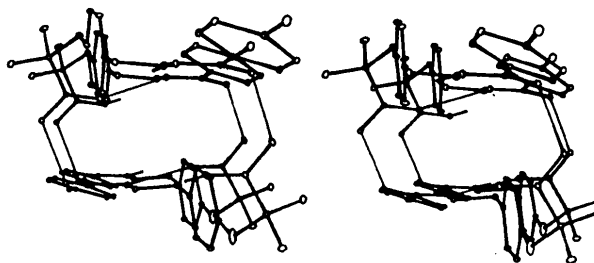


Fig. 2. View along the *x* axis to show the system of hydrogen-bond connections. The units of four bezafibrate molecules are hydrogen bonded forming an infinite chain along the *x* axis, giving the crystal a fibrous structure.

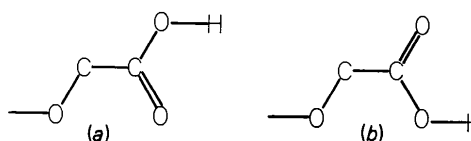


Fig. 3. Conformations of the carboxyl group: (a) synplanar-synplanar and (b) synplanar-antiplanar.

References

- ABRAHAM, D. J., PERUTZ, M. F. & PHILLIPS, S. E. V. (1983). *Proc. Natl Acad. Sci. USA*, **80**, 324–328.
- ALLEN, F. H., KENNARD, O., WATSON, D. G., BRAMMER, L., ORPEN, A. G. & TAYLOR, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–S19.
- CROMER, D. T. & LIBERMAN, D. (1970). *J. Chem. Phys.* **53**, 1891–1898.
- CROMER, D. T. & MANN, J. B. (1968). *Acta Cryst.* **A24**, 321–324.
- DEBAERDEMAKER, T., GERMAIN, G., MAIN, P., TATE, C. & WOOLFSON, M. M. (1987). *MULTAN87. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- HAMILTON, W. C. (1959). *Acta Cryst.* **12**, 664–665.
- JOHNSON, C. K. (1965). *ORTEP*. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA.
- KENNARD, C. H. L., SMITH, G. & WHITE, A. H. (1982). *Acta Cryst.* **B28**, 868–875.
- LEISEROWITZ, L. (1976). *Acta Cryst.* **B32**, 775–802.
- MAIN, P., FISKE, S. J., HULL, S. E., LESSINGER, L., GERMAIN, G., DECLERCQ, J.-P. & WOOLFSON, M. M. (1980). *MULTAN80. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*. Univs. of York, England, and Louvain, Belgium.
- PERUTZ, M. F., FERMI, G., ABRAHAM, D. J., POYART, C. & BURSAUX, E. (1986). *J. Am. Chem. Soc.* **108**, 1064–1078.
- RENNINGER, M. (1937). *Z. Phys.* **106**, 141–176.
- SHELDRIK, G. M. (1986). *SHELXS86. Program for the Solution of Crystal Structures*. Univ. of Göttingen, Federal Republic of Germany.
- STEWART, J. M., MACHIN, P. A., DICKINSON, C. W., AMMON, H. L., HECK, H. & FLACK, H. (1976). The *XRAY76* system. Tech. Rep. TR-446. Computer Science Center, Univ. of Maryland, College Park, Maryland.
- STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.
- ZEELEN, F. J. (1976). *Quantitative Structure-Activity Relationships*, edited by M. TICHY, pp. 161–164. Basel: Springer.

Acta Cryst. (1989). **C45**, 775–777

1,3,2λ⁵-Diazaphosphorinan – ein cyclisches Diamid der Thiophosphorsäure

VON UDO ENGELHARDT UND BARBARA SCHEFFLER

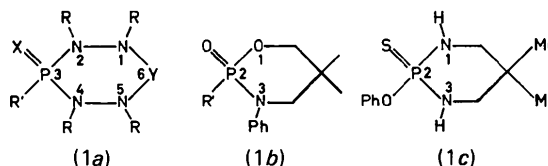
Institut für Anorganische und Analytische Chemie der Freien Universität Berlin, Fabeckstraße 34–36, D-1000 Berlin 33, Bundesrepublik Deutschland

(Eingegangen am 21. Juni 1988; angenommen am 18. November 1988)

Abstract. 5,5-Dimethyl-2-phenoxy-1,3,2λ⁵-diazaphosphorinane 2-sulfide, C₁₁H₁₇N₂OPS, *M_r* = 256·306, monoclinic, *P*2₁/*n*, *a* = 12·239 (2), *b* = 9·621 (2), *c* = 12·030 (2) Å, β = 106·45 (20)°, *V* = 1359 (2) Å³, *Z* = 4, *D_x* = 1·253 Mg m⁻³, λ(Cu Kα) = 1·54179 Å, μ = 3·01 mm⁻¹, *F*(000) = 544, *T* = 293 K, *R* = 0·038 for 2033 unique contributing reflections. The compound has been prepared in our laboratory from phenoxythiophosphoryl dichloride and 2,2-dimethyl-1,3-propanediamine in the presence of excess triethylamine for a comparison of its ring conformation with those of 1,2,4,5,3λ⁵,6λ⁵-tetraazadiphosphorinanes. The saturated six-membered ring adopts a slightly distorted chair conformation, torsion angles: PNCC ± 46·2 (4), NCCC ± 58·2 (4) and CNPN ± 28·4 (2)°. Bond distances: P–S 1·919 (1), P–N 1·629 (3), P–O 1·620 (2), N–C 1·468 (4) Å. Weak hydrogen bridges between NH groups and O at P–O–Ph groups are found in the crystal.

Einleitung. Im Zusammenhang mit unseren Strukturuntersuchungen an offenkettigen und cyclischen Phosphorsäure- und Thiophosphorsäuredihydraziden (Engelhardt & Giersdorf, 1986; Engelhardt & Franzmann, 1987; und die dort zitierte Literatur) interessieren zum Vergleich auch entsprechende

Diamide der Phosphorsäure insbesondere das konformative Verhalten von cyclischen Diamiden der Phosphorsäure, bei denen sowohl der Phosphor als auch die beiden Amid-N-Atome Glieder eines gesättigten Sechsrings sind. In den cyclischen Dihydraziden vom Typ (1a) findet man in vielen Fällen eine Twist-Konformation des Ringes, während in für die Antikrebs-therapie wichtigen 1,3,2-Oxazaphosphorinanen (1b) beim Fehlen besonderer Substituenten überwiegend 'normale' Sessel-Konformationen angetroffen werden [man vergleiche z.B. Bentrude, Setzer, Sopchik, Bajwa, Burright & Hutchinson (1986) oder Nelson (1978) und die dort zitierte Literatur]. Wir haben jetzt das cyclische Diamid (1c) in unserem Laboratorium synthetisiert und seine Struktur untersucht.



R = H, Me, -(CH₂)-
R' = MeO-, EtO-, PhO-, Me₂N-
X = O, S
Y = >P(=X)-*R'*, >SiMe₂, >SiPh₂

0108-2701/89/050775-03\$03.00

© 1989 International Union of Crystallography