Crystal Structure of 1,3-Bis(*p*-methylphenyl)-2-fluoro-1,3,2-diazaphospholidine-2-oxide

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Diazaphospholidines have the ability to bind with metals and to inhibit cholinesterase (ChE), an enzyme that has a vital role in nerve impulse transition. The crystal structure of 1,3-bis(*p*-methylphenyl)-2-fluoro-1,3,2-diazaphospholidine-2-oxide (**1**) was determined using single-crystal X-ray diffraction. The five-membered ring containing phosphorus, nitrogen and carbon atoms is slightly puckered. The coordination environment around the phosphorus atom in this compound is approximately tetrahedral.

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The synthesis and biological studies of cyclophosphamides and structurally related analogs are of both practical relevance and academic interest. These compounds are studied in different areas of chemistry: cholinesterase and urease inhibitors, insecticides and pesticides, efficient ligands in coordination chemistry, ashless antioxidants, antirust and antiwear additives for lubricating oil, synthetic purposes, and structural study.¹⁻⁴ Although cyclophosphamides have been the subject of intensive studies for more than a century, considerably less attention has been devoted to diazaphospholidine derivatives.⁵ A thorough knowledge of the crystal properties of these compounds should be beneficial to a detailed understanding of the effect of structure on pharmacological effects. The crystal structure of novel diazaphospholidines (**1**), is reported here.

Fig. 1 Chemical structure of title compound.

Fig. 2 Crystallographically determined molecular structure for **1** drawn with 50% probability ellipsoids and with hydrogen atoms shown as circles of arbitrary radii.

Single crystal of **1** was obtained from a solution of chloroform and heptane (with ratio 6/1). The solution upon keeping in a CaCl₂ desiccator for a few days yielded shiny colorless crystal of **1** suitable for X-ray analysis. The molecular structure of **1** along with the atom numbering scheme is presented in Fig. 2.

Data collection and refinement parameters are listed in Table 1. The structure was solved by direct methods. The positions of the hydrogen bonds were obtained from a difference Fourier map. The atomic coordinates for non-hydrogen atoms are listed in Table 2, and selected inter atomic parameters are collected in Table 3.

Table 1 Crystal data and structure refinement for **1**

Empirical formula: C ₁₆ H ₁₈ FN ₂ OP	
Formula weight = 304.29	
Crystal structure: triclinic	
Space group: <i>P</i> 2 ₁ / <i>c</i>	<i>Z</i> = 4
<i>a</i> = 7.702(10) Å	α = 90°
<i>b</i> = 11.545(7) Å	β = 102.25(5)°
<i>c</i> = 16.730(18) Å	γ = 90°
<i>V</i> = 1454(3) Å ³	
Calculated density = 1.390 Mg/m ³	
Absorption coefficient/mm ⁻¹ = 0.200	
<i>F</i> (0 0 0) = 640	
Crystal size = 0.3 × 0.2 × 0.2 mm	
No. of reflection used = 13129	
No. of parameters = 190	
$\theta_{\max}$ = 27.10° with Mo <i>K</i> α	
<i>R</i> 1 = 0.0457 [<i>I</i> ≥ 2σ(<i>I</i>)]	
<i>wR</i> 2 = 0.0961	
Goodness-of-fit on <i>F</i> ² = 1.012	
(Δ/σ) = 0.000	
(Δρ) = 0.336 e Å ⁻³	
(Δρ) = -0.234 e Å ⁻³	
Measurement: Bruker SMART 1000 CCD	
Program system: SADABS	
Structure determination: SHELXTL	
Refinement: full-matrix least-squares on <i>F</i> ²	

CCDC 245760 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.uk/data_request/cif.

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Table 2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) of non-hydrogen atoms

Atom	x	y	z	U(eq)
P(1)	3363(1)	3730(1)	1259(1)	31(1)
F(1)	4981(2)	2980(1)	1159(1)	40(1)
O(1)	2023(2)	2966(1)	1464(1)	36(1)
N(1)	2892(2)	4520(1)	422(1)	31(1)
N(2)	4130(2)	4795(1)	1877(1)	31(1)
C(1)	-1277(3)	2945(3)	-2642(2)	47(1)
C(2)	-177(3)	3359(2)	-1844(1)	37(1)
C(3)	506(3)	2587(2)	-1215(1)	38(1)
C(4)	1503(2)	2959(2)	-474(1)	35(1)
C(5)	1847(3)	4135(2)	-331(1)	30(1)
C(6)	1171(3)	4922(2)	-954(1)	35(1)
C(7)	193(3)	4519(2)	-1694(1)	36(1)
C(8)	3240(3)	5751(2)	585(1)	32(1)
C(9)	4472(3)	5831(2)	1427(1)	33(1)
C(10)	4975(3)	4641(2)	2714(1)	30(1)
C(11)	4340(3)	3824(2)	3190(1)	33(1)
C(12)	5178(3)	3679(2)	4001(1)	34(1)
C(13)	6651(3)	4333(2)	4363(1)	34(1)
C(14)	7221(3)	5163(2)	3887(1)	37(1)
C(15)	6417(3)	5325(2)	3071(1)	35(1)
C(16)	7544(4)	4130(2)	52429(2)	44(1)

The crystal structure of **1** consists of a five-membered ring containing phosphorus, nitrogen and carbon atoms in a PNCCN fashion. This ring is slightly puckered. Such puckering may lead to an unsymmetrical ring formation. The least-squares planes for the P(1), N(1) and N(2) atoms in **1** is $-7.4995x - 1.9105y - 6.0210z = 1.0512$. According to the distance of atoms from this plane, the phosphorus and two nitrogen atoms are coplanar, while two carbon atoms are displaced to opposite sides of the plane (C(8) and C(9) by 0.3297 and 0.723 Å respectively). The fluorine atom is 1.4175 Å above the PN(2) plane, defined by N(1)-P(1)-N(2), while O(1) is 1.1032 Å below.

The coordination environment around the phosphorus atom in this compound is approximately tetrahedral, since the average angle involving P is 109.21° . However, the coordination is clearly distorted, arising from the presence of phosphorus in a five-membered ring. The angles O(1)-P(1)-N(2) and C(2)-P(1)-N(1) have values of $119.15(10)$ and $96.14(11)^\circ$, respectively. A similar geometry has been observed in similar cyclophosphamides.⁵

The data collected in Table 3 indicated that the distances between the phosphorus and amine nitrogen atoms are shorter than the value expected for a P-N single bond.⁵ In **1** the P-N bond lengths are 1.634(2) and 1.645(2) Å. In this structure the amine group is nearly planar, as measured by the sum of the three bond angles of N. The sums are 358.07 and 356.27° . The trigonal-planar bond angles observed in these compounds

Table 3 Selected interatomic distances (Å) and angles between interatomic vectors ($^\circ$) for **1** with the standard uncertainties in parentheses

Bond distances			
P(1)-O(1)	1.4529(18)	N(2)-C(9)	1.476(3)
P(1)-F(1)	1.5557(18)	C(1)-C(2)	1.499(3)
P(1)-N(2)	1.634(2)	C(2)-C(7)	1.381(3)
P(1)-N(1)	1.645(2)	C(2)-C(3)	1.393(3)
N(1)-C(5)	1.415(3)	C(10)-C(11)	1.389(3)
N(2)-C(10)	1.422(3)	C(5)-C(6)	1.397(3)
Bond angles			
O(1)-P(1)-F(1)	108.26(11)	C(10)-N(2)-C(9)	120.86(16)
O(1)-P(1)-N(2)	119.15(10)	C(10)-N(2)-P(1)	123.82(14)
F(1)-P(1)-N(2)	107.22(10)	C(9)-N(2)-P(1)	111.59(15)
O(1)-P(1)-N(1)	119.84(10)	C(4)-C(5)-N(1)	120.66(18)
F(1)-P(1)-N(1)	104.68(9)	C(6)-C(5)-N(1)	120.7(2)
C(2)-P(1)-N(1)	96.14(11)	C(11)-C(10)-N(2)	120.40(18)
C(5)-N(1)-C(8)	121.23(16)	C(15)-C(10)-N(2)	120.51(18)
C(5)-N(1)-P(1)	124.41(15)	C(7)-C(2)-C(3)	116.9(2)
C(8)-N(1)-P(1)	112.43(14)	C(4)-C(3)-C(2)	121.9(2)

are in accordance with the short P-N bond lengths (Table 3).

Despite the fact that the nitrogen atoms in this compound are nearly sp^2 hybridized, the phosphorus heterocyclic ring is significantly puckered and some strain in this ring is suggested by the deviation from the 120° angle about the nitrogen, C(8)-N(1)-P(1) ($112.43(14)^\circ$) and C(5)-N(1)-P(1) ($124.41(15)^\circ$) in N(1) and C(9)-N(2)-P(1) ($111.59(15)^\circ$) and C(10)-N(2)-P(1) ($123.82(14)^\circ$) in N(2).

The remaining stereochemistry around phosphorus center appears to be normal. The P=O bonds lengths is typical for cyclophosphamides (1.4592(2) Å).

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