

**Cyclophosphazenes as Novel Antitumour Agents: Geometry of the Hexaziridinocyclotriphosphazene,  $N_3P_3Az_6$ , from an X-ray Investigation of the Benzene Clathrate**

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Cyclophosphazenes, Antitumour Agents

Hexaziridinocyclotriphosphazene forms a 2:1 clathrate with benzene. The benzene makes a sandwich between the two phosphazene molecules with the planes of the rings parallel. The geminal aziridinyl groups have a most unusual eclipsed conformation.

The considerable antitumour activity of the aminocyclophosphazenes:  $N_3P_3Az_6$ ,  $N_4P_4Az_8$  and  $N_4P_4Pyr_8$  ( $Az =$  Aziridinyl [ $-N(CH_2)_2$ ],  $Pyr =$  Pyrrolidinyl [ $-N(CH_2)_4$ ]) has been reported recently [1, 2]. This activity is thought [3] to be related to the slow formation of a DNA: aminocyclophosphazene complex, and so the X-ray crystal structures of these symmetric aminocyclophosphazenes are being determined in order to study their complex forming potential.  $N_3P_3Az_6$  is exceedingly soluble [4] in water (101 gm/litre) and so far it has not been successfully recrystallized from this medium. When it is recrystallized from  $CCl_4$  it forms [5] an unstable complex  $N_3P_3Az_6 \cdot 3 CCl_4$ , while from *m*-xylene it forms [6] an orthorhombic, and from  $CS_2$ , a monoclinic unsolvated crystal. The structures of the cyclophosphazene molecule in each of the three crystal samples are very similar [5, 6] and in particular have the axes of the lone pairs of each of the sets of geminal exocyclic nitrogen atoms inclined at an angle of  $\sim 120^\circ$  when viewed along a line joining the two nitrogen atoms. This conformation produces a sterically unhindered molecule and it is the conformation that is expected from simple VSEPR consideration. When, however,  $N_3P_3Az_6$  is recrystallized from benzene it forms a very stable complex 2 ( $N_3P_3Az_6$ )  $\cdot$   $C_6H_6$  with a most unusual conformation (I) at the geminal aziridinyl groups. The structure of this complex is reported here.

*Crystal data* 2 ( $N_3P_3(N(CH_2)_2)_6$ )  $\cdot$   $C_6H_6$ , rhombohedral,  $a = 10.266(1) \text{ \AA}$ ,  $\alpha = 79.21(1)^\circ$ , space group

$R3$ ,  $Z = 1$ ,  $D_c = 1.334 \text{ g cm}^{-3}$ , Mo-K $\alpha$ , (graphite monochromator)  $\lambda = .70926 \text{ \AA}$ . Four circle diffractometry, 2052 unique reflections of which 1448 have  $I > 3\sigma(I)$ . E statistics clearly indicated a non-centro symmetric space group and the structure was solved from a sharpened Patterson function for space group  $R3$ . The structure was refined by full matrix least-squares with anisotropic temperature factors on the heavy atoms, and a single isotropic temperature factor for all the hydrogen atoms. The refinement converged with  $R = 0.028$ ,  $RW = 0.029$  for the 1448 reflections.

The crystal unit cell contains just two unique molecules of  $N_3P_3Az_6$  and one of benzene. The centre of each molecule lies on the three-fold axis, thus the planes of the two  $N_3P_3$  and the  $C_6$  rings are

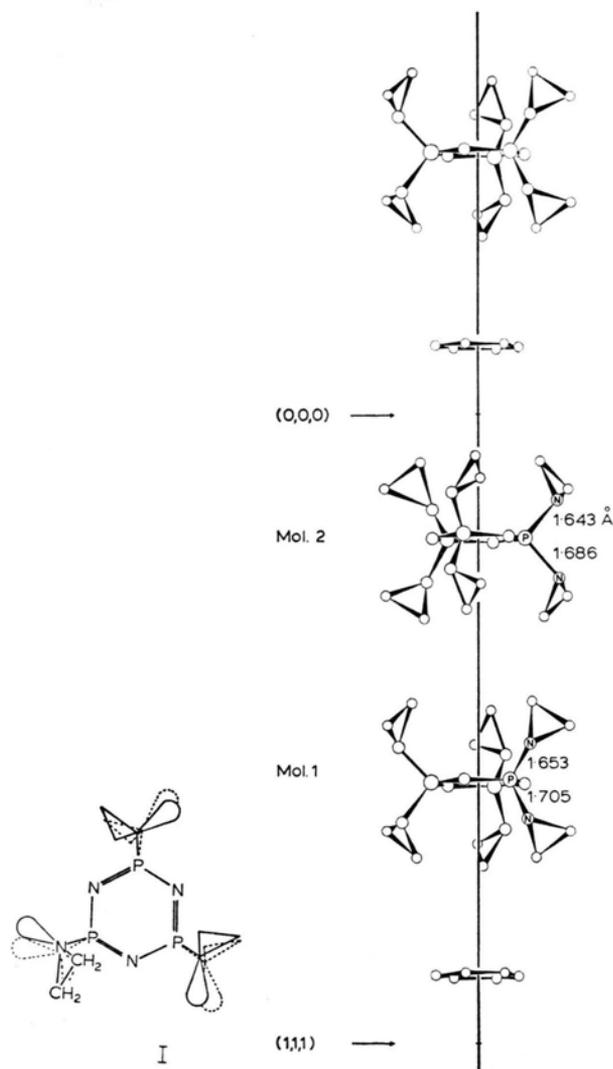


Figure. View of the molecular packing. The three fold axis (111) is inclined at an angle of  $8^\circ$  to the plane of the page.

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all parallel, with a sequence along the three-fold axis of  $N_3P_3Az_6$  (mol. 1),  $N_3P_3Az_6$  (mol. 2),  $C_6H_6$ ,  $N_3P_3Az_6$  (mol. 1) . . . *etc.* (see Figure). There is nearly an inversion centre between the two molecules of the cyclophosphazene but the distance from this inversion centre to the centres of the two benzene rings on either side along the three-fold axis differ by 0.136 Å. This distance, though small, is significant for although the structure is almost in space groups  $R\bar{3}$ , attempts to refine it in that space group produce convergence at  $R=0.12$  with highly elliptical anisotropic temperature factors. The presence of the false inversion centre produces strong correlations within the normal matrix (which were controlled during least-squares refinement by the imposition of Waser [7] constraints) and the dimensions of the molecules must be treated with some caution.

Along the three-fold axis the centres of the two adjacent  $N_3P_3Az_6$  molecules are separated by 8.149(3) Å, and they fit together in a 'cog-like' fashion with three Az groups of one molecule fitting into the space between the three groups of the other. The apparent large space that can be seen in the figure between the two molecules is in fact occupied by the hydrogen atoms of the Az groups. Within the molecule the endocyclic P-N distances are 1.597(3), 1.578(3) (mol. 1), 1.596(3), 1.597(3) Å (mol. 2) which compare with P-N lengths in the range 1.587(3)–1.592(3) Å for  $N_3P_3Az_6 \cdot 3 CCl_4$  [5], and with a value [8] of 1.575(3) Å for each of the three lengths in  $N_3P_3Cl_6$ . The exocyclic nitrogen atoms are highly pyramidal and are 0.68 (mol. 1)

and 0.65 Å (mol. 2) from the plane of the three atoms bonded to them. The corresponding P-N bond lengths are in the range 1.643(9)–1.705(9) Å (see Figure). These are reasonable values [9] but the apparently significant difference among them are not easily explained and could be attributed to the matrix correlation. In the aziridinyl groups there is also some noticeable variation in the N-C and C-C bond lengths, the mean values of 1.46(2) and 1.47(2) Å, however, are unexceptional [5, 6].

The major axes of the lone pair orbitals of the geminal exocyclic nitrogen atom make a mean angle of 91(1)° with a line joining the two nitrogen atoms. The axes of the lone pairs when viewed along this N...N line have torsion angles of 3(1)° (mol. 1) and 10(1)° (mol. 2). Thus the lone pair orbitals of the two geminal nitrogen atoms are practically eclipsed (I). This conformation is unique among aminophosphazenes and must be connected, in some way, with the presence of the benzene. The equivalent torsional angles in the  $CCl_4$  clathrate and unclathrated crystals are [5, 6] in the range 97–134°.

The distance between the centres of the two  $N_3P_3$  rings which have the benzene molecule between them is 12.697(3) Å. It can be seen from (I) and the Figure that there can be no interaction between the nitrogen lone pair electrons and the benzene  $\pi$  system; so the benzene is firmly held within the structure as a simple clathrate.

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