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## Structure and Superstructure of Dipyridamole, 2,2',2'',2'''-(4,8-Dipiperidinopyrimido[5,4-d]pyrimidine-2,6-diylidinitrilo)tetraethanol, $C_{24}H_{40}N_8O_4$

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**Abstract.**  $M_r = 504.64$ , monoclinic,  $Pa$ ,  $a = 20.746$  (7),  $b = 11.280$  (6),  $c = 11.441$  (5) Å,  $\beta = 105.07$  (2)°,  $V = 2585.3$  Å<sup>3</sup>,  $Z = 4$ ,  $D_m = 1.28$  (1),  $D_x = 1.288$  g cm<sup>-3</sup>,  $Cu K\alpha$ ,  $\lambda = 1.5418$  Å,  $\mu = 7.50$  cm<sup>-1</sup>,  $F(000) = 1088$ ,  $T = 298$  K,  $R = 4.7\%$  for 4019 observed reflections. The two independent molecules are related approximately by an inversion center at (0, 7/8, 0). The main deviation from this symmetry is disorder of one ethanol residue which is observed only in one of the two molecules. Although suggested by the chemical formula, neither of the two molecules is centrosymmetric; however, the centric parts of the molecules form a subcell with half the unit-cell length in the **b** direction, space group  $P2_1/a$ , which was indicated by weak intensities of the  $k = \text{odd}$  reflections.

**Introduction.** The title compound is well known for its pharmacological activity. For many years it has been in use (Persantin®) in the attendance of cardiac diseases. Moreover, in combination with aspirin it is used as Asasantin® for prevention of arterial and venous thromboembolism. Because of this pharmacological importance it seemed useful to obtain detailed information of the molecular geometry for a study of the structure–activity relationship of this compound. Therefore, a single-crystal X-ray investigation of dipyridamole was executed and the results are reported here.

**Experimental.** Yellow prismatic crystals obtained from a solution in ethanol; rotation and Weissenberg photographs with **a** and **b** rotation axes showed Laue

symmetry  $2/m$ ; only the zonal extinction  $h0l$  for  $h = 2n + 1$  observed, indicating  $Pa$  or  $P2_1/a$ ; all layer lines with  $k = \text{odd}$  had remarkably weaker reflection intensities than those with  $k = \text{even}$ , indicating the presence of a superstructure in the  $b$  direction. Crystal  $0.4 \times 0.3 \times 0.15$  mm, lattice constants from 20 high-order reflections, DEC PDP 15/40-controlled Siemens-AED diffractometer, Ni-filtered  $\text{Cu } K\alpha$  radiation,  $\omega$ - $2\theta$  scan, 4318 reflections with  $\theta \leq 64.5^\circ$  in the quadrant  $hkl$  and  $\bar{h}kl$  ( $h$  24–24,  $k$  0–13,  $l$  0–10), 299 reflections unobserved,  $I < 2\sigma$ ; no absorption correction;  $D_m$  by flotation.

The phase problem could not be solved with direct methods (MULTAN, Main, Lessinger, Woolfson, Germain & Declercq, 1977) until molecular scattering factors were calculated in the normalization procedure from the geometry of the two piperidine rings and the pyrimido[5,4-*d*]pyrimidine fragment. After this, the Fourier map based on the phase set with the best combined figure of merit showed two independent molecules in  $Pa$  related approximately by the non-crystallographic symmetry operation  $-x, 7/4 - y, -z$  (Fig. 1). A major deviation from this relation was observed for the hydroxyl group at C(13) which is disordered in molecule (1) but not in molecule (2).

Least-squares refinement with isotropic then with anisotropic temperature factors for non-hydrogen atoms, hydrogens located from difference syntheses isotropic (XRAY76, Stewart, Machin, Ammon, Dickinson, Heck & Flack, 1976);  $\sum w (F_o - F_c)^2$  minimized,  $w = xy$ ,  $x = 1$  for  $\sin \theta > 0.5$ ,  $x = \sin \theta / 0.5$  for  $\sin \theta \leq 0.5$ ,  $y = 1$  if  $|F_o| < 6.0$  and  $y = 6.0 / |F_o|$  otherwise; the parameters for  $w$  were chosen so as to make  $\Delta F$  almost independent of  $|F_o|$  and  $\sin \theta$ ; unobserved reflections included only if  $|F_c| > |F_o|$ ; atomic scattering factors from the standard routine of XRAY76 (Cromer & Mann, 1968; Stewart, Davidson & Simpson, 1965); 152 atoms refined, subdivision of parameters into blocks necessary; for each molecule four chemically reasonable subblocks established, refinement running with eight blocks converged satisfactorily; for the disordered hydroxyl group at C(13) two positions for the OH group [O(14) and O(140)] were found with a population of 60:40 estimated from the peak height; the C(13) thermal parameters of the first anisotropic refinement cycle were assigned to both O(14) and O(140) and these atoms were unrefined. After convergence,  $R = 4.7\%$  ( $R_w = 6.0\%$ ),  $(\Delta/\sigma)_{av} = 0.21$ ,  $\Delta\rho$  excursions  $< 0.28 \text{ e } \text{\AA}^{-3}$  in final difference synthesis. All computer calculations executed on a CDC Cyber 175 computer (Wissenschaftliches Rechenzentrum, WRB, Berlin).\*

\* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 38669 (34 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

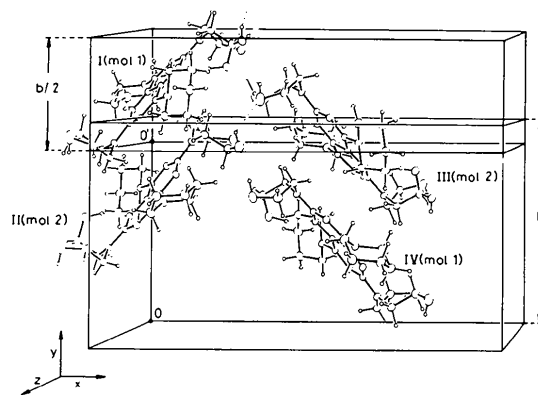


Fig. 1. Unit cell and subcell in space groups  $Pa$  and  $P2_1/a$ . In  $Pa$  the symmetry code is (i)  $x, y, z$ ; (ii)  $-x, \frac{7}{4} - y, -z$ ; (iii)  $\frac{1}{2} + x, 2 - y, z$ ; (iv)  $\frac{1}{2} - x, -\frac{3}{4} + y, -z$ . (ii) and (iv) are only approximations.

**Discussion.** The fractional coordinates and the equivalent isotropic temperature factors (Hamilton, 1959) of the non-hydrogen atoms are given in Table 1.

The molecular structures of the two independent molecules are shown in Fig. 2, which also gives the atom-numbering scheme (atoms of molecule 2 are given primed numbers). With the present choice of the asymmetric unit (see Fig. 1), the molecules are related, to a good approximation, by a center of symmetry at  $0, 7/8, 0$  [except for the disordered group O(14)/O(140)]. It follows that bond lengths (Fig. 3), bond angles and the magnitudes of torsion angles (Tables 2, 3) are generally equal within the standard deviations in those parts of the two molecules not affected by the disorder. Hence, the following discussion is mainly based on the averaged bonding data.

The pyrimido[5,4-*d*]pyrimidine system is planar, as expected. The mean deviation of the atoms C(1)–C(10) from their least-squares plane is  $0.06 \text{ \AA}$  [ $0.05 \text{ \AA}$  for molecule (2)]. Also in this main molecule plane are the piperidine nitrogens N(41) and N(91) and the amine nitrogens N(11) and N(61) with their substituents C(12), C(15) and C(62), C(65), respectively, as is indicated by the torsion angles around the bonds C(1)–N(11) and C(6)–N(61) (Table 3). The bond-length distribution in the pyrimido[5,4-*d*]pyrimidine system agrees well with the corresponding data found in 1-(8-aminopyrimido[5,4-*d*]pyrimidin-4-ylimino)- $\beta$ -D-ribofuranose (Narayanan & Berman, 1975), which is, as we know, the only X-ray investigation of a comparable pyrimido[5,4-*d*]pyrimidine.

In molecule (2), the OH group at C(13) forms an intramolecular hydrogen bond O(14')–H(14')...N(2'). Because of the disorder this hydrogen bond is present for molecule (1) only with a 60% probability. In the second variant the OH group adopts the position O(140)–H(140), which leads to an intermolecular hydrogen bond (Table 4), as holds also for the OH group at C(63).

Table 1. Atomic parameters of dipyridamole, *e.s.d.*'s in parentheses ( $U_{eq}$  and  $U$  in  $\text{\AA}^2 \times 100$ )

$$U_{eq} = \frac{1}{3} \sum_i \sum_j U_{ij} a_i^* a_j^* \mathbf{a}_i \cdot \mathbf{a}_j.$$

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{eq}$ or $U$		<i>x</i>	<i>y</i>	<i>z</i>	$U_{eq}$ or $U$
C(1)	0.0728	1.2906 (3)	-0.0587	3.3 (1)	C(1')	-0.0595 (2)	0.4551 (3)	0.0671 (3)	3.7 (1)
N(2)	-0.0766 (2)	1.2408 (3)	0.0452 (3)	3.6 (1)	N(2')	-0.0663 (2)	0.5080 (3)	-0.0412 (3)	3.7 (1)
C(3)	-0.0293 (2)	1.1545 (3)	0.0475 (3)	3.2 (1)	C(3')	-0.0197 (2)	0.5933 (3)	-0.0446 (3)	3.4 (1)
C(4)	0.0318 (2)	1.0865 (3)	0.1552 (3)	3.3 (1)	C(4')	-0.0237 (2)	0.6608 (3)	-0.1545 (3)	3.5 (1)
N(5)	-0.0092 (2)	0.9956 (3)	0.1507 (3)	3.7 (1)	N(5')	0.0162 (2)	0.7530 (3)	-0.1535 (3)	3.6 (1)
C(6)	-0.0540 (2)	0.9697 (3)	0.0439 (3)	3.5 (1)	C(6')	0.0617 (2)	0.7800 (3)	-0.0470 (3)	3.6 (1)
N(7)	-0.0634 (2)	1.0303 (3)	-0.0589 (3)	3.5 (1)	N(7')	0.0718 (2)	0.7229 (3)	0.0567 (3)	4.0 (1)
C(8)	-0.0200 (2)	1.1226 (3)	-0.0559 (3)	3.4 (1)	C(8')	0.0302 (2)	0.6286 (3)	0.0565 (3)	3.2 (1)
C(9)	-0.0193 (2)	1.1847 (3)	-0.1663 (3)	3.2 (1)	C(9')	0.0306 (2)	0.5677 (3)	0.1697 (3)	3.6 (1)
N(10)	0.0263 (1)	1.2659 (3)	-0.1671 (3)	3.5 (1)	N(10')	-0.0140 (2)	0.4838 (3)	0.1717 (3)	4.0 (1)
N(11)	0.1168 (2)	1.3800 (3)	-0.0659 (3)	3.8 (1)	N(11')	-0.1028 (2)	0.3659 (3)	0.0737 (3)	3.9 (1)
C(12)	0.1610 (2)	1.4250 (4)	0.0466 (4)	4.4 (1)	C(12')	-0.1476 (2)	0.3171 (3)	-0.0378 (4)	3.9 (1)
C(13)	0.2244 (2)	1.3593 (4)	0.0895 (4)	5.5 (1)	C(13')	-0.2123 (2)	0.3843 (4)	-0.0830 (5)	5.2 (1)
O(14)	0.2170	1.2473	0.1388	5.3	O(14')	-0.2035 (2)	0.4944 (3)	-0.1378 (4)	7.3 (1)
O(140)	0.2667	1.3753	0.2069	5.3	C(15')	-0.0970 (2)	0.3070 (4)	0.1909 (4)	4.6 (1)
C(15)	0.1146 (2)	1.4391 (4)	-0.1803 (4)	4.3 (1)	C(16')	-0.1295 (3)	0.3731 (5)	0.2740 (5)	6.4 (2)
C(16)	0.1410 (2)	1.3662 (4)	-0.2699 (4)	4.8 (1)	O(17')	-0.1998 (2)	0.3742 (5)	0.2346 (4)	7.9 (2)
O(17)	0.2088 (2)	1.3314 (3)	-0.2262 (4)	6.6 (1)	N(41')	-0.0719 (2)	0.6374 (3)	-0.2623 (3)	3.7 (1)
N(41)	0.0788 (2)	1.1063 (3)	0.2616 (3)	3.8 (1)	C(42')	-0.0819 (2)	0.5165 (4)	-0.3118 (4)	4.5 (1)
C(42)	0.0919 (2)	1.2262 (4)	0.3135 (4)	4.1 (1)	C(43')	-0.1515 (2)	0.5033 (5)	-0.3979 (5)	5.6 (2)
C(43)	0.1618 (2)	1.2335 (4)	0.3988 (4)	5.5 (1)	C(44')	-0.1632 (3)	0.5955 (5)	-0.4970 (4)	6.1 (2)
C(44)	0.1714 (2)	1.1408 (4)	0.4978 (4)	5.5 (1)	C(45')	-0.1515 (2)	0.7199 (4)	-0.4415 (4)	5.3 (1)
C(45)	0.1563 (2)	1.0193 (4)	0.4401 (4)	4.5 (1)	C(46')	-0.0810 (2)	0.7286 (4)	-0.3558 (4)	4.6 (1)
C(46)	0.0864 (2)	1.0133 (4)	0.3563 (4)	4.6 (1)	N(61')	0.1002 (2)	0.8790 (3)	-0.0521 (3)	4.2 (1)
N(61)	-0.0941 (1)	0.8731 (3)	0.0458 (3)	3.7 (1)	C(62')	0.1489 (2)	0.9171 (4)	0.0584 (4)	5.1 (1)
C(62)	-0.1437 (2)	0.8391 (4)	-0.0658 (4)	3.8 (1)	C(63')	0.2134 (2)	0.8488 (5)	0.0735 (5)	6.2 (2)
C(63)	-0.2083 (2)	0.9103 (4)	-0.0840 (4)	4.7 (1)	O(64')	0.2582 (2)	0.8655 (5)	0.1916 (4)	7.8 (1)
O(64)	-0.2488 (2)	0.8993 (3)	-0.2040 (3)	6.0 (1)	C(65')	0.0899 (2)	0.9477 (4)	-0.1640 (4)	4.7 (1)
C(65)	-0.0884 (2)	0.8069 (4)	0.1573 (4)	4.5 (1)	C(66')	0.1167 (2)	0.8903 (5)	-0.2632 (4)	6.0 (2)
C(66)	-0.1160 (2)	0.8690 (5)	0.2510 (4)	5.8 (2)	O(67')	0.1863 (2)	0.8820 (4)	-0.2372 (4)	7.4 (1)
O(67)	-0.1846 (2)	0.9068 (6)	0.2121 (4)	9.3 (2)	N(91')	0.0729 (2)	0.6012 (3)	0.2778 (3)	4.2 (1)
N(91)	-0.0621 (2)	1.1529 (3)	-0.2768 (3)	3.9 (1)	C(92')	0.0567 (3)	0.5576 (5)	0.3898 (4)	5.3 (1)
C(92)	-0.0449 (2)	1.1897 (4)	-0.3883 (3)	5.0 (1)	C(93')	0.0861 (2)	0.6439 (5)	0.4921 (4)	5.7 (2)
C(93)	-0.0739 (2)	1.1015 (5)	-0.4889 (4)	5.4 (1)	C(94')	0.1616 (2)	0.6535 (5)	0.5137 (4)	5.9 (2)
C(94)	-0.1483 (3)	1.0881 (5)	-0.5091 (4)	6.1 (2)	C(95')	0.1766 (2)	0.6943 (4)	0.3964 (4)	5.4 (1)
C(95)	-0.1650 (2)	1.0548 (5)	-0.3913 (4)	5.5 (1)	C(96')	0.1445 (2)	0.6122 (4)	0.2918 (4)	4.4 (1)
C(96)	-0.1342 (2)	1.1403 (4)	-0.2912 (3)	3.8 (1)					
H(121)	0.137 (3)	1.410 (4)	0.108 (5)	6. (1)	H(121')	-0.123 (2)	0.312 (4)	-0.103 (4)	4. (1)
H(122)	0.169 (2)	1.512 (3)	0.028 (3)	2.8 (8)	H(122')	-0.158 (3)	0.241 (6)	-0.018 (5)	7. (2)
H(13)	0.248	1.363	0.026	3.8	H(131')	-0.234 (3)	0.387 (5)	-0.025 (5)	7. (2)
H(131)	0.256	1.408	0.153	4.0	H(132')	-0.246 (2)	0.359 (3)	-0.173 (3)	1.2 (7)
H(132)	0.213	1.273	0.082	4.0	H(14')	-0.153 (5)	0.516 (8)	-0.118 (8)	14. (3)
H(14)	0.167	1.237	0.118	4.0	H(151')	-0.122 (3)	0.238 (5)	0.182 (4)	6. (1)
H(140)	0.263	1.441	0.188	4.0	H(152')	-0.052 (3)	0.292 (5)	0.231 (5)	8. (2)
H(151)	0.137 (2)	1.523 (4)	-0.158 (4)	5. (1)	H(161')	-0.117 (3)	0.460 (5)	0.274 (5)	7. (2)
H(152)	0.067 (3)	1.462 (5)	-0.218 (5)	6. (1)	H(162')	-0.122 (3)	0.334 (6)	0.355 (6)	8. (2)
H(161)	0.115 (2)	1.286 (5)	-0.282 (4)	6. (1)	H(17')	-0.211 (3)	0.298 (6)	0.216 (6)	7. (2)
H(162)	0.139 (2)	1.412 (4)	-0.349 (5)	6. (1)	H(421')	-0.052 (3)	0.496 (5)	-0.363 (5)	7. (1)
H(17)	0.231 (3)	1.403 (6)	-0.207 (6)	8. (2)	H(422')	-0.076 (2)	0.461 (4)	-0.247 (4)	5. (1)
H(421)	0.055 (2)	1.242 (3)	0.366 (4)	3.5 (9)	H(431')	-0.154 (4)	0.427 (7)	-0.424 (7)	10. (2)
H(422)	0.088 (2)	1.274 (4)	0.256 (4)	4. (1)	H(432')	-0.185 (3)	0.513 (5)	-0.349 (5)	7. (1)
H(431)	0.166 (3)	1.314 (6)	0.447 (6)	8. (2)	H(441')	-0.129 (3)	0.591 (5)	-0.548 (5)	6. (1)
H(432)	0.196 (3)	1.224 (5)	0.346 (5)	6. (1)	H(442')	-0.210 (3)	0.587 (5)	-0.548 (5)	6. (1)
H(441)	0.219 (3)	1.150 (6)	0.554 (6)	9. (2)	H(451')	-0.156 (3)	0.783 (5)	-0.505 (5)	7. (1)
H(442)	0.140 (3)	1.152 (4)	0.551 (5)	6. (1)	H(452')	-0.192 (4)	0.731 (6)	-0.406 (6)	9. (2)
H(451)	0.162 (2)	0.958 (4)	0.503 (4)	4. (1)	H(461')	-0.075 (2)	0.797 (4)	-0.317 (4)	5. (1)
H(452)	0.186 (2)	0.998 (3)	0.387 (4)	3.1 (9)	H(462')	-0.046 (2)	0.709 (4)	-0.396 (4)	5. (1)
H(461)	0.054 (2)	1.028 (4)	0.402 (4)	4. (1)	H(621')	0.160 (2)	1.010 (4)	0.041 (4)	5. (1)
H(462)	0.070 (2)	0.933 (4)	0.313 (4)	5. (1)	H(622')	0.130 (3)	0.892 (5)	0.138 (6)	8. (2)
H(621)	-0.151 (2)	0.764 (4)	-0.060 (3)	1.9 (8)	H(631')	0.239 (4)	0.877 (6)	0.007 (7)	10. (2)
H(622)	-0.122 (2)	0.851 (4)	-0.128 (4)	4. (1)	H(632')	0.199 (3)	0.760 (6)	0.071 (5)	7. (2)
H(631)	-0.197 (2)	1.002 (4)	-0.083 (4)	5. (1)	H(64')	0.251 (2)	0.933 (4)	0.209 (4)	3. (1)
H(632)	-0.229 (2)	0.883 (4)	-0.026 (4)	4. (1)	H(651')	0.119 (2)	1.026 (4)	-0.148 (4)	5. (1)
H(64)	-0.273 (4)	0.809 (6)	-0.202 (6)	10. (2)	H(652')	0.041 (2)	0.965 (4)	-0.190 (4)	5. (1)
H(651)	-0.037 (2)	0.790 (4)	0.205 (4)	4. (1)	H(661')	0.100 (3)	0.800 (6)	-0.277 (5)	8. (2)
H(652)	-0.106 (2)	0.739 (5)	0.132 (4)	5. (1)	H(662')	0.105 (3)	0.949 (5)	-0.332 (5)	6. (1)
H(661)	-0.102 (3)	0.820 (5)	0.325 (6)	7. (1)	H(67')	0.208 (4)	0.959 (8)	-0.223 (8)	12. (3)
H(662)	-0.092 (2)	0.936 (4)	0.281 (4)	5. (1)	H(921')	0.080 (2)	0.480 (4)	0.406 (4)	4. (1)
H(67)	-0.184 (2)	0.834 (3)	0.228 (3)	0.7 (9)	H(922')	0.009 (3)	0.569 (5)	0.374 (5)	7. (1)
H(921)	0.001 (2)	1.206 (3)	-0.370 (3)	3.4 (9)	H(931')	0.065 (2)	0.723 (5)	0.471 (4)	6. (1)
H(922)	-0.059 (3)	1.271 (5)	-0.418 (5)	6. (1)	H(932')	0.078 (2)	0.612 (4)	0.557 (5)	4. (1)
H(931)	-0.052 (2)	1.024 (5)	-0.458 (4)	6. (1)	H(941')	0.176 (2)	0.699 (4)	0.567 (5)	5. (1)
H(932)	-0.061 (4)	1.137 (6)	-0.569 (7)	10. (2)	H(942')	0.183 (3)	0.565 (5)	0.550 (5)	7. (2)
H(941)	-0.170 (3)	1.166 (6)	-0.538 (6)	9. (2)	H(951')	0.225 (3)	0.706 (5)	0.403 (5)	6. (1)
H(942)	-0.165 (3)	1.023 (6)	-0.575 (6)	10. (2)	H(952')	0.151 (3)	0.769 (6)	0.364 (6)	9. (2)
H(951)	-0.156 (2)	0.972 (4)	-0.362 (4)	5. (1)	H(961')	0.170 (2)	0.529 (4)	0.324 (4)	4. (1)
H(952)	-0.217 (2)	1.067 (4)	-0.398 (4)	5. (1)	H(962')	0.149 (2)	0.635 (3)	0.218 (4)	4. (1)
H(961)	-0.140 (2)	1.105 (4)	-0.217 (5)	5. (1)					
H(962)	-0.155 (3)	1.217 (6)	-0.304 (6)	9. (2)					

Table 2. Bond angles ( $^{\circ}$ , *e.s.d.*'s in parentheses) for molecules (1) and (2)

	(1)	(2)		(1)	(2)		(1)	(2)
N(2)–C(1)–N(10)	126.5 (3)	126.0 (3)	C(8)–C(9)–N(10)	120.8 (3)	120.4 (3)	C(44)–C(45)–C(46)	111.7 (4)	110.1 (4)
N(2)–C(1)–N(11)	119.2 (2)	117.7 (3)	C(8)–C(9)–N(91)	121.3 (3)	121.6 (3)	N(41)–C(46)–C(45)	109.4 (3)	110.1 (4)
N(10)–C(1)–N(11)	114.2 (2)	116.4 (3)	N(10)–C(9)–N(91)	117.6 (3)	117.8 (3)	C(6)–N(61)–C(62)	119.0 (3)	118.5 (3)
C(1)–N(2)–C(3)	116.5 (3)	115.5 (3)	C(1)–N(10)–C(9)	117.8 (2)	118.9 (3)	C(6)–N(61)–C(65)	120.6 (3)	120.6 (3)
N(2)–C(3)–C(4)	121.4 (3)	120.7 (3)	C(1)–N(11)–C(12)	118.3 (3)	120.2 (3)	C(62)–N(61)–C(65)	120.4 (3)	120.8 (3)
N(2)–C(3)–C(8)	122.1 (3)	123.6 (3)	C(1)–N(11)–C(15)	121.5 (2)	119.0 (3)	N(61)–C(62)–C(63)	111.9 (3)	109.9 (4)
C(4)–C(3)–C(8)	116.3 (3)	115.5 (3)	C(12)–N(11)–C(15)	119.8 (3)	120.2 (3)	C(62)–C(63)–O(64)	111.4 (4)	112.1 (4)
C(3)–C(4)–N(5)	119.9 (3)	120.5 (3)	N(11)–C(12)–C(13)	114.7 (4)	114.3 (3)	N(61)–C(65)–C(66)	115.1 (4)	115.1 (4)
C(3)–C(4)–N(41)	122.2 (3)	122.1 (3)	C(12)–C(13)–O(14)	113.7	112.6 (4)	C(65)–C(66)–O(67)	116.3 (4)	115.2 (4)
N(5)–C(4)–N(41)	117.7 (3)	117.3 (3)	C(12)–C(13)–O(140)	122.0		C(9)–N(91)–C(92)	118.3 (3)	116.8 (3)
C(4)–N(5)–C(6)	118.9 (3)	117.8 (3)	N(11)–C(15)–C(16)	115.1 (3)	114.1 (4)	C(9)–N(91)–C(96)	121.2 (3)	121.2 (3)
N(5)–C(6)–N(7)	126.3 (3)	127.2 (3)	C(15)–C(16)–O(17)	114.2 (3)	113.5 (4)	C(92)–N(91)–C(96)	113.6 (3)	112.7 (3)
N(5)–C(6)–N(61)	115.5 (3)	114.5 (3)	C(4)–N(41)–C(42)	121.6 (3)	120.9 (3)	N(91)–C(92)–C(93)	109.5 (4)	108.4 (4)
N(7)–C(6)–N(61)	118.1 (3)	118.3 (3)	C(4)–N(41)–C(46)	116.7 (3)	116.1 (3)	C(92)–C(93)–C(94)	111.6 (4)	111.1 (4)
C(6)–N(7)–C(8)	115.1 (3)	115.2 (3)	C(42)–N(41)–C(46)	112.3 (3)	113.1 (3)	C(93)–C(94)–C(95)	110.4 (4)	108.4 (4)
C(3)–C(8)–N(7)	123.3 (3)	123.7 (3)	N(41)–C(42)–C(43)	110.7 (3)	110.8 (3)	C(94)–C(95)–C(96)	111.5 (4)	111.1 (4)
C(3)–C(8)–C(9)	116.3 (3)	115.6 (3)	C(42)–C(43)–C(44)	111.1 (4)	110.9 (4)	N(91)–C(96)–C(95)	111.4 (4)	111.3 (4)
N(7)–C(8)–C(9)	120.0 (3)	120.3 (3)	C(43)–C(44)–C(45)	109.0 (4)	110.0 (4)			

Table 3. Some chosen relevant torsion angles ( $^{\circ}$ , *e.s.d.*'s in parentheses) for molecules (1) and (2)

	(1)	(2)
N(2)–C(1)–N(11)–C(12)	–7.3 (4)	9.8 (5)
N(10)–C(1)–N(11)–C(15)	–1.9 (4)	–0.7 (5)
N(5)–C(6)–N(61)–C(65)	1.3 (5)	1.5 (5)
N(7)–C(6)–N(61)–C(62)	1.8 (5)	–1.6 (5)
N(11)–C(12)–C(13)–O(14)	–73.6	74.4 (5)
N(11)–C(12)–C(13)–O(140)	–167.5	–
N(11)–C(15)–C(16)–O(17)	–60.0 (5)	69.7 (5)
N(61)–C(62)–C(63)–O(64)	165.2 (3)	–168.6 (4)
N(61)–C(65)–C(66)–O(67)	55.6 (6)	–67.7 (5)
C(3)–C(4)–N(41)–C(42)	50.2 (6)	–51.2 (5)
C(8)–C(9)–N(91)–C(96)	51.1 (5)	–52.4 (5)
C(8)–C(9)–N(91)–C(92)	–159.9 (4)	163.4 (4)

Table 4. Hydrogen bonding

X–H...Y	X...Y (Å)	X–H (Å)	H...Y (Å)	Symmetry operation for Y
O(14)–H(14)...N(2)	2.829	1.01	1.85	$x, y, z$
O(140)–H(140)...O(17')	2.908	0.77	2.24	$\frac{1}{2} + x, 2 - y, z$
O(17)–H(17)...O(14')	2.690 (5)	0.93 (7)	1.81 (6)	$\frac{1}{2} + x, 2 - y, z$
O(64)–H(64)...O(17)	2.738 (5)	1.14 (7)	1.63 (7)	$-\frac{1}{2} + x, 2 - y, z$
O(67)–H(67)...O(14)	2.647	0.84 (4)	2.25	$-\frac{1}{2} + x, 2 - y, z$
O(14')–H(14')...N(2')	2.778 (4)	1.04 (9)	1.79 (9)	$x, y, z$
O(17')–H(17')...O(64')	2.844 (7)	0.90 (7)	1.95 (7)	$-\frac{1}{2} + x, 1 - y, z$
O(64')–H(64')...O(67)	2.814 (8)	0.82 (5)	2.24 (5)	$\frac{1}{2} + x, 2 - y, z$
O(67')–H(67')...O(64)	2.788 (5)	0.97 (9)	1.82 (9)	$\frac{1}{2} + x, 2 - y, z$

Obviously, this situation influences the C–N-bond lengths C(1)–N(2) and C(1)–N(10) which are the major examples where the average bond length differs by more than  $3\sigma$  from the contributing data of the two molecules. In molecule (1), with the intramolecular hydrogen bond only partially present, these two bonds differ significantly just as the corresponding bonds C(6)–N(5) and C(6)–N(7) do. In molecule (2), with this hydrogen bond present without exception, both bond lengths approach similar values [1.349 (5) and 1.357 (4) Å].

The geometry of the piperidine chairs is as expected and needs no detailed discussion.

For the eight independent ethanol residues having in fact nine independent arrangements [owing to the

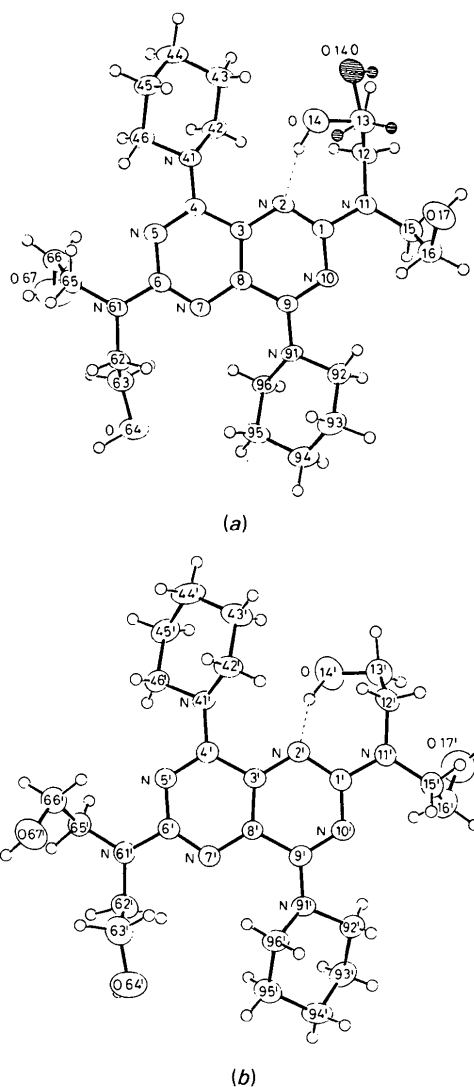


Fig. 2. Molecular models and atom-numbering schemes for the two independent molecules of dipyrindimole. (a) Molecule (1), (b) molecule (2).

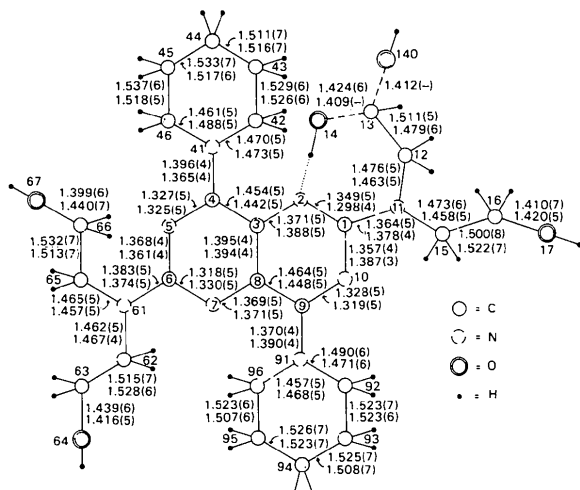


Fig. 3. Bond lengths (Å, e.s.d.'s in parentheses) for dipyridamole, upper values for molecule (2).

disordered group O(14)/O(140)], two types of conformers can be observed. In three cases the hydroxyl oxygen is *trans* to the corresponding amine nitrogen (torsion angle O—C—C—N close to 180°, see Table 3). In six cases a *gauche* conformation is present (magnitude of the O—C—C—N torsion angle close to 60°). In all three cases of *trans* conformation [for O(140), O(64) and O(64')] this arrangement prevents the formation of an intramolecular hydrogen bond in favor of an intermolecular hydrogen bond (Table 4).

Although the chemical formula suggests a centrosymmetric molecule this analysis shows that neither molecule (1) nor molecule (2) is centrosymmetric. The presence of one intramolecular hydrogen bond in molecule (2) and in molecule (1) [for the O(14) variant] is a deviation from that symmetry. Also, the two piperidine rings of each molecule are not arranged centrosymmetrically with respect to the molecule center on the middle of the bond C(3)—C(8). For example, in Fig. 2, C(42) and C(96) are both lying below the paper plane, C(42') and C(96') are both above the paper plane. This cannot hold for a centric arrangement. Nevertheless, major parts of the molecule are centric; these are the pyrimido[5,4-*d*]pyrimidine system and all hydroxyethylamino substituents which are not involved in intramolecular hydrogen bonds.

A summary of the hydrogen bonding is given in Table 4. Besides the already mentioned intramolecular O—H...N bonds seven intermolecular O—H...O hydrogen bonds between the OH groups of the terminal ethanol residues are present. O(140) and O(67') act

only as donors whereas all other OH groups are involved twice in hydrogen bonds, once as donors and once as acceptors. As Fig. 1 shows the hydrogen bonds (dotted lines) are gathered in a puckered layer near the planes  $x = \frac{1}{4}, \frac{3}{4}, \text{etc.}$

### Superstructure

From the observation of weaker reflection intensities for the layer lines with  $k = \text{odd}$  the presence of a subcell with half length in the **b** direction can be concluded. This subcell can easily be deduced from Fig. 1.

It has already been mentioned that large parts of the molecule are centric with respect to the molecular center C(3)/C(8). Now, if we shift the origin to  $O' = (0, 7/8, 0)$ , these centric parts of the molecule form a subcell having  $b/2$  as unit-cell length in the **b** direction. With this new origin the *a*-glide plane is at  $y = \frac{1}{4}$  and a twofold screw axis is at  $x, z = \frac{1}{4}, 0$ , which means that this subcell belongs to space group  $P2_1/a$ . This finding was also supported by the fact that on the  $0k0$  series only reflections with  $k = 4n$  had intensities remarkably over the background. Two molecules are in the subcell, hence one half of the centric fragment is in its asymmetric unit. It has, however, to be noted that it is not only the non-centricity of the molecule which proves the supercell to be the correct unit cell: the refinement has also shown that the molecule centers do not differ exactly by 0.5 in the *y* direction. The actual difference between (1) and (2) is 0.53, so that each molecule, which is neighbored in *y* by two molecules of the opposite type, has one distance larger and one smaller than 0.5 to its neighbors. This is a further deviation from the lattice of the subcell.

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