The Stereochemical Basis of Anticonvulsant Drug Action. I. The Crystal and Molecular Structure of Diphenylhydantoin, a Noncentrosymmetric Structure Solved by Centric Symbolic Addition

By Arthur Camerman*

Department of Biological Structure, University of Washington, School of Medicine, Seattle, Washington, U.S.A.

AND NORMAN CAMERMAN

Department of Biochemistry, University of Toronto, Toronto, Canada

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To investigate relationships between the molecular shape and biological activity of anticonvulsant drugs we have determined the molecular structure of diphenylhydantoin. The compound crystallizes in the orthorhombic system with cell dimensions a=6.230, b=13.581, c=15.532 Å, space group $Pn2_{1a}$. A total of 1210 independent reflections to $2\theta = 50^{\circ}$ for Mo K α radiation was measured on a fourcircle diffractometer. The structure was solved by centrosymmetric phasing techniques, utilizing Sayre's equation for direct sign determination in space group Pnma. This technique proved successful because the 7-atom hydantoin group lies in a plane only 2.40° from (010) with the two phenyl rings on each side of the plane. Thus, the structure approximates the situation that would exist for special position (c) of Pnma, and many reflections have phases close to 0 or π . The plane of the hydantoin ring forms angles of 113 and 114° with the planes through the two phenyl rings. The phenyl-phenyl angle is 90°. Final R index is 0.052.

Introduction

Various barbiturates and hydantoins exhibit markedly different hypnotic and anticonvulsant properties, depending on the nature of the substituents at the C(5) position of the heterocyclic ring. Compounds with aliphatic side groups at this position are commonly used as sedatives, whereas phenyl substitution is necessary to obtain effective activity against grand mal epilepsy. These facts indicate to us a possible steric mode of behavior for this type of drug – the spatial properties of the C(5) substituent relative to the rest of the molecule may be an important factor in determining the drug's pharmacological site of action.

Accordingly, in order to investigate relationships between the molecular shape and biological activity, we have studied the molecular structures of a number of chemically different compounds that are used as anticonvulsants in treating *grand mal* epilepsy. The first of these is diphenylhydantoin.

Since its introduction into medicine (Merritt & Putnam, 1938), diphenylhydantoin (DPH) has been an extremely effective and widely used drug for treating *grand mal* and psychomotor epilepsies. Unlike barbiturates, which are also used in seizure therapy, DPH is not a sedative, thus proving that antiepileptics need not impair consciousness.

Experimental

DPH was obtained as the sodium salt, and colorless lath-shaped crystals of the free acid were grown from

aqueous solution adjusted to pH 11.0 with NaOH. The crystals are orthorhombic and systematic absences indicated space groups Pnma or $Pn2_1a$. Unit-cell dimensions were determined by least-squares minimization of the difference between calculated and observed θ values for 12 reflections measured at both $+2\theta$ and -2θ with Mo K α radiation ($\lambda = 0.71069$ Å) on a four-circle diffractometer. The crystal density was measured by flotation in a mixture of methylene chloride and methyl alcohol. The crystallographic data are:

Diphenylhydantoin, $C_{15}H_{12}N_2O_2$

a	$= 6.230 \pm 0.001 \text{ Å}$	F(000) = 528
b	$= 13.581 \pm 0.001$	μ (Mo K α) = 0.9 cm ⁻¹
с	$=15.532 \pm 0.002$	Systematic absences:
Ζ	=4	$0kl \rightarrow k+l$ odd
D_m	$= 1.29 \text{ g.cm}^{-3}$	$hk0 \rightarrow h \text{ odd}$
D_x	=1.28	Space group: $Pnma$ or $Pn2_1a$;
M.W	., 252·3	$Pn2_1a$ indicated by struc-
		ture analysis.

Intensities were measured to $2\theta = 50^{\circ}$, corresponding to an interplanar spacing of 0.84 Å; the crystal used had dimensions $0.3 \times 0.2 \times 0.1$ mm along *a*, *b*, and *c* respectively, and was mounted with *a* parallel to the φ axis of the diffractometer. The ω -2 θ scan technique with Nb-filtered Mo K α radiation was employed, with a scan rate of 2°/min and stationary background counts for half the scan time on each side of the reflection. A total of 1210 independent reflections was measured, of which 876 had intensities greater than $2\sigma_c$, where $\sigma_c = (N_{B1} + N_{PK} + N_{B2})^{\frac{1}{2}}$; N_{B1} and B_{B2} are stationary background counts on each side of the peak over a total time equal to the scan time, and N_{PK} is the scan count. Reflections with intensities less than $2\sigma_c$ were

^{*} Present address: Department of Neurology, University of Washington School of Medicine, Seattle, Wash., U.S.A.

		Centrosymmetric space group	Noncentric space group	Diphenylhydantoin
Average	$E \\ E^2 - 1$	0·798	0·886	0·814
Average		0·968	0·736	0·858
Fraction	E > 1	0·3173	0·3679	0·2946
	E > 2	0·0455	0·0183	0·0432
	E > 3	0·0027	0·0001	0·0043

Table 1. Intensity statistics

classified as unobserved and were not used in the structure refinement. Frequently measured standard reflections indicated the diffractometer reliability to be $\pm 1\%$; hence, the estimated error in the intensity of each reflection was taken to be $\sigma_I = [\sigma_c^2 + (0.01\sigma_c^2)^2]^4$. Structure amplitudes were obtained from the intensities in the usual fashion and weights were taken as $\sqrt[3]{w=1/\sigma_F}$. No absorption corrections were applied. The linear absorption coefficient for Mo $K\alpha$ is 0.9 cm⁻¹.

Solution of the structure

Systematic extinctions indicated the space group to be $Pn2_1a$ or Pnma. Since density measurements show Z=4, Pnma would restrict the hydantoin ring to lie in a mirror plane at $y=\frac{1}{4}$ and the two phenyl groups to be related through the mirror. Statistical analysis of the normalized structure amplitudes (Table 1) suggested the centrosymmetric space group to be more appropriate; accordingly, the reiterative application of Sayre's equation (Sayre, 1952) was used to determine the phases of 142 reflections having E > 1.5. A computer program written by Long (1965) was employed in the phase determination. The features of this program are: (1) the origin-determining reflections may be chosen arbitrarily or they may be specified automatically by the program based on the magnitude of $\sum \times E_h$, where \sum is the sum in Sayre's equation, $\sum_{k} (E_h E_{h-k})$; (2) two methods of iteration

are possible: (a) newly predicted signs may be used immediately in determining signs of reflections that are still unknown, or (b) newly determined signs are not used to predict additional signs until the next cycle; (3) once the origin-determining reflections are specified, n other reflections are alternately assigned phases of 0 or π to yield 2^n different solutions.

In the first attempt at structure solution, the reflections that were to have phases assigned were allowed to be specified by the program routine; 32 solutions were obtained by using both iteration procedures. None of these solutions was satisfactory, however, as all solutions predicted some signs of the seven specified input reflections to be different from those which were originally assigned to these reflections. One criterion for the acceptability of any solution is that the signs finally predicted for the input reflections are the same as those initially assigned.

For a second attempt at solving the structure, three origin-determining reflections and four other reflec-

tions whose phases were allowed to assume the values of 0 and π were arbitrarily chosen based on high *E* values only; this time a number of solutions satisfied the criterion discussed above. Table 2 lists the reflections used in both trials. *E* maps were computed for two acceptable sets of signs, one from each iterative procedure, the sets having the highest consistency index in their respective groups. The map obtained from the set of signs derived by procedure 2(b) was not interpretable, but that from the signs obtained by method 2(a) showed the 7 atoms of the hydantoin group in the mirror at $y = \frac{1}{4}$. No phenyl ring atoms could be located.

Table 2. Reflections to which phases were assigned to implement Sayre's equation.

First three reflections were used to specify the origin. Final phases are in millicycles.

	-				
	Trial 1			Trial 2	
hkl	E Fin	al phase	hkl	E Fin	al phase
22	2.26	954	511	2.69	980
1 15	3.53	984	1 4 14	3.66	904
23	1.52	142	469	2.15	878
1 1	1.93	966	377	2.59	839
62	2.31	841	122	2.26	954
215	2.01	990	215	2.01	990
57	2.23	869	1 1 15	3.53	984



Fig. 1. Distribution of normalized intensities for diphenylhydantoin. N(z) is the fraction of the reciprocal lattice points where the normalized intensity is less than z.

These 7 atom positions were used to calculate structure factors (R=0.50) and a three-dimensional Fourier map which showed the positions of the 6 phenyl ring atoms. However, a cycle of full-matrix least-squares refinement of the 13 atomic positions and isotropic temperature parameters dropped R only to 0.33. Clearly, something was wrong with the structure.

At this point, it was decided to change to the acentric space group $Pn2_1a$. The 13 atomic positions were left unchanged, the multiplicities of the 7 hydantoin atoms were adjusted, and a cycle of full-matrix leastsquares refinement was performed in $Pn2_1a$ (R=0.30). It is emphasized here that meaningful refinement can be performed in space group $Pn2_1a$ by leaving the atoms positions derived in space group Pnma unchanged. The starting structure is, of course, different in the two space groups: the action of the mirror plane in *Pnma* requires only one phenyl ring to be located, the mirror symmetry automatically fixing the second ring. In $Pn2_1a$ the two phenyl rings are independent of each other and, hence, 6 additional atoms must be located in addition to the 13 which completely specified the structure in *Pnma*. A difference Fourier map was then calculated and it yielded the positions of the atoms in the second phenyl ring. Two cycles of fullmatrix isotropic least-squares refinement followed by two cycles of anisotropic refinement dropped R to 0.081. All hydrogen atoms were located in a difference Fourier map. Further refinement of all atoms reduced R to 0.052. In all least-squares refinements the quantity minimized was $\sum w(F_o - F_c)^2$. The average shift/error ratio in the last least-squares cycle was 0.23; the final goodness-of-fit parameter was 1.23.

Inspection of the E values used in the two attempts at structure solution (Table 2) suggests that the more important criterion in selecting origin-determining reflections is the magnitude of E. Choosing the 123 plane with E of only 1.52 as an origin-determining reflection may have been one of the causes of failure in the first attempt to solve the structure.

Another possible reason for the failure of the first set of starting reflections to yield a solution and the

Table 3. Fractional coordinates and anisotropic temperature parameters $(Å^2)$ for the nonhydrogen atoms.

Estimated standard deviations are given in parentheses. The anisotropic thermal parameters are in the form $\exp \left[-0.25(h^2 B_{11}a^{*2} + \ldots + 2k l B_{23}b^*c^*)\right].$

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	x	У	Z	B_{11}	B_{22}	B ₃₃	B_{12}	B ₁₃	B ₂₃
N(1)	0.4027 (9)	0.2424 (7)	0.4425 (4)	1.5 (2)	5.6 (4)	2.8 (2)	-0.0(3)	0.2 (2)	0.6 (3)
C(2)	0.3271 (10)	0.2479 (8)	0.3623 (4)	3.1 (3)	3.4 (3)	2.3 (2)	-0.5(6)	0.4 (2)	0.1 (3)
N(3)	0.1043 (9)	0.2502 (9)	0.3689 (4)	3.0 (2)	5.1 (4)	2.1 (2)	0.4 (4)	-0·9 (2)	0.2 (3)
C(4)	0.0365 (10)	0.2538 (10)	0.4509 (4)	2.3(2)	3.5 (3)	2.6(3)	-0.5(5)	-0.5(2)	0.2 (4)
C(5)	0.2381 (9)	0.2500	0.5091 (3)	1.5 (2)	4.3 (3)	2.3 (2)	-0.1(4)	0.1(2)	0.6 (5)
O(6)	0.4267 (9)	0.2498 (9)	0.2956 (3)	4.8 (3)	8.0 (4)	2.5 (2)	0.2(4)	1.2 (2)	0.2 (3)
O(7)	-0·1494 (7)	0.2548 (9)	0.4761 (3)	1.8 (2)	6.7 (3)	4.3 (2)	-0.2(4)	-0.1(2)	0.2 (3)
C(8)	0.2246 (13)	0.1560 (9)	0.5619 (4)	3.5 (3)	4.1 (4)	2.2 (3)	-0.3(3)	-1.1(3)	0.2 (3)
C(9)	0.0696 (41)	0.1457 (19)	0.6263(13)	5.0 (7)	11.7 (1.4)	6.4 (7)	-0.1(9)	1.5 (5)	5.1 (9)
C(10)	0.0532 (36)	0.0642 (20)	0.6764 (11)	9.3 (1.0)	13.7 (1.5)	7.9 (8)	-4.2(9)	0.7 (7)	6.5 (9)
C (11)	0.1901 (45)	-0·0185 (16)	0.6604 (11)	15.5 (1.6)	7.4 (1.0)	5.9 (7)	<i>−</i> 6·7 (9)	- 5.3 (9)	3.1 (7)
C(12)	0.3356 (38)	-0·0113 (13)	0.6016 (10)	16.7 (1.4)	4.5 (6)	5.9 (6)	− 0·1 (8)	- 4·2 (9)	0.3 (6)
C(13)	0.3543 (25)	0.0773 (12)	0.5503 (7)	9.2 (8)	5.0 (6)	3.4 (4)	0.2 (6)	-0.3(5)	0.1 (4)
C(14)	0.2657 (12)	0.3412 (10)	0.5649 (4)	2.6 (3)	5.5 (5)	2.4 (3)	-1.0(3)	0.3 (3)	-0.5(3)
C(15)	0.1299 (22)	0.4183 (10)	0.5613 (6)	7.9 (6)	4.0 (5)	4.8 (4)	0.8 (5)	-0.4(5)	0.3 (4)
C(16)	0.1774 (62)	0.5010 (18)	0.6101 (11)	14.8 (1.7)	4.3 (6)	5.5 (6)	0.6 (8)	-0.3(8)	0.1 (5)
C(17)	0.3548 (29)	0.5029 (13)	0.6640 (7)	9.9 (9)	6.3 (7)	4.8 (5)	-2.6(7)	1.9 (6)	-2.5(5)
C(18)	0.4840 (27)	0.4272 (20)	0.6645 (9)	5.8 (7)	14.8 (1.6)	7.4 (8)	-2.9(8)	0.2 (6)	-6.8(9)
C(19)	0.4424 (19)	0.3395 (15)	0.6172 (7)	4.0 (4)	10.6 (9)	5.9 (5)	-0·7 (6)	-0.8(4)	-4.3 (6)

Table 4. Fractional coordinates, isotropic temperature parameters $(Å^2)$, and bond distances (Å) for the hydrogen atoms.

Estimated standard deviations are given in parentheses.

	x	У	Z	В	H-C (or N)
H(1)	0.548 (13)	0.246 (9)	0.456 (5)	4.2 (1.9)	0.93 (8)
H(3)	0.043(10)	0.250 (8)	0.323 (4)	2.7 (1.5)	0.80 (7)
H(9)	0.037 (30)	0.176 (11)	0.627 (9)	8.7 (3.4)	0.46 (16)
H(10)	-0.117(42)	0.069 (23)	0.714 (16)	15.5 (8.7)	1.22 (26)
H(11)	0.110 (36)	-0.059 (17)	0.701 (11)	12.9 (5.7)	0.97 (21)
H(12)	0.477 (40)	-0.076(23)	0.585 (14)	13.6 (8.3)	1.28 (28)
H(13)	0.458 (18)	0.089 (11)	0.512 (7)	6.6 (3.1)	0.89(12)
H(15)	-0.029(24)	0.417(12)	0.522 (8)	9.3 (3.7)	1.17 (15)
H(16)	0.102 (58)	0.526 (27)	0.622(21)	23.2 (10.0)	0.61 (36)
H(17)	0.321(18)	0.588 (12)	0.693 (7)	6.4 (2.9)	1.26 (15)
H(18)	0.582 (24)	0.426 (14)	0.706 (9)	11.1 (4.3)	0.89 (15)
H(19)	0.559 (20)	0.300(10)	0.618(8)	9.3 (3.3)	0.91(13)

success of the second set may lie in the fact that the reflections in the first set are, in total, less centric than those in the second set. Inspection of the final phases of each of the reflections (Table 2) reveals that in trial 1, 3 of the 7 reflections assigned centric phases have phase angles differing from 0 or 180° by 45° or more; whereas in trial 2, only one reflection is that different in phase from centricity. Programs used in the structure determination and refinement were from the X-ray 67 system (Stewart et al., 1967). Scattering factors used were the following: O, N and C (Berghuis, Haanappel, Potters, Loopstra, MacGillavry & Vee-

nendaal, 1955) and H (Stewart, Davidson & Simpson, 1965).

Results and discussion

Fractional coordinates and temperature parameters for the non-hydrogen atoms are listed in Table 3. As can be seen from the y coordinates, the seven atoms comprising the hydantoin group lie in a plane which is almost perpendicular to **b**. When the y coordinate of C(5) is set at 0.25 to fix the origin in the space group, the maximum deviation of any of the other 6 atoms from the plane at $y = \frac{1}{4}$ is 0.1 Å and the average

Table 5. Comparison of observed and calculated structure amplitudes for diphenylhydantoin

The data are listed in groups of constant h and k. The four columns within each group are l, $10|F_o|$, $10|F_o|$ and phase (millicycles). The sign in front of $10|F_o|$ is that of the A part of the structure factor. Reflections whose measured intensities were less than $2\sigma_c$ are indicated with an asterisk and were treated as unobserved reflections and left out of the refinement procedure.

0+0+L	14 115 109 219	15 109 -103 918	9 3032 872	13 294 12 92	2.9.L	10 60 -66 846	9 62 -62 198	5 100 -96 145	9 349 37 422	5+5+L	613.L
2 849 895 8 4 707 -730 500 6 226 235 8	0+11+L 1 43 42 955	17 32* 24 14 1+4+L	11 31* -14 873 12 31* 15 865 13 31* 10 74	15 64 -66 953 16 324 13 984 17 37 26 167	0 97 -104 202 1 36 -34 865 2 32 -31 92	12 102 -108 933 13 119 -128 963 14 61 -56 89	10 45 30 434 11 46 47 851 12 48 53 184 13 329 -11 775	5 33 29 867 7 299 -20 222 8 77 80 970 9 162 159 997	10 67 58 862 11 33* 22 982	1 52 49 967 2 31 -19 145 3 98 101 898	0 108 105 817 1 310 -28 854 2 118 118 895
10 245 -242 500 12 208 -217 500 14 109 110	5 31 -40 861 7 28* 10 877 9 61 59 866	1 163 166 247 2 147 155 923	14 34 28 810 1+11+L	2+3+L	3 28 -31 923 4 93 93 914 5 128 -128 802.	15 50 38 961 16 50 -38 125	14 75 -65 833 3.9.L	10 41 -53 905 11 65 59 147 12 76 -84 966	0 40 -40 837 1 33 24 834	4 62 61 939 5 178 186 887 6 138 135 881	3 32* 25 186 4 91 91 949 5 32* -24 810
16 169 166 0 18 93 88 0	11 65 74 752 13 34 45 244	4 171 166 896 5 153 -164 196 6 119 124 812	1 226 224 220 2 52 -56 954 3 44 -39 184	1 363 352 940 2 214 -201 135 3 31 27 852	7 106 -103 788 8 59 -57 846 9 53 -47 239	3+2+L 1 138 -144 138 2 389 -362 966	1 280 -23 99 2 300 -43 235 3 105 -110 211	13 32° 15 123 14 32° 30 931 15 33° -25 156	2 47 -50 795 3 60 65 837 4 44 30 236 5 318 31 23	7 43 35 862 8 33° -26 950 9 40 30 937	6 38 45 214 7 56 41 948 8 49 -42 851
0+1+L 1 273 -255 075	0+12+L 0 421 -417 215	7 217 -210 926 8 90 -87 933 9 43 43 184	4 115 -118 923 5 44 -48 225 6 31 -23 169	4 194 -213 831 5 31 -37 114 6 226 224 184	10 30• -20 177 11 30• -18 116 12 31• 21 69	3 173 -176 858 4 103 -95 850 5 138 -143 976	4 62 72 963 5 53 55 229 6 31 20 143	4,3,L 0 61 52 955	6 31° 12 878 7 31° 11 13 8 34° 46 823	10 64 -67 896 11 64 67 896 12 37 -20 945	10 33• -21 910
5 75 -74 185 7 216 -214 16 9 171 -175 994	4 52 40 124 6 299 9 988 8 52 49 167	11 94 -92 195 12 247 -256 923 13 40 42 836	8 45 31 179 9 54 -56 224 10 47 -41 835	7 180 178 948 8 171 172 815 9 54 -51 859	13 32° 23 842 14 33° -21 177	6 258 -268 948 7 66 -60 33 8 31 -19 176 9 94 -09 903	7 29* 8 115 8 52 -65 47 9 32* -11 105	1 108 -101 965 2 114 116 26 3 145 -146 943	9 42 48 767 10 324 25 974	5+6+L 1 30* 17 860	0 31+ 3 845 1 31+ 12 802
11 174 -172 2 13 133 132 988 15 309 -29 883	10 44 62 212 12 51 52 248	14 229 -232 904 15 88 84 9 16 41 30 932	11 67 -61 244 12 31* 17 114 13 43 38 202	11 55 53 870 12 73 83 126 13 29• 22 868	0 27• 35 4 1 38 47 208	10 43 50 924 11 83 -80 939 12 61 65 949	10 31 -64 768 12 49 -45 757 13 51 -50 778	5 85 -89 867 6 59 68 759 7 32 -30 919	4+11+L 0 44 31 785 1 51 48 239	2 82 -72 860 3 91 94 867 4 132 -137 882 5 55 61 941	2 39 24 20 3 63 -56 5 4 42 -46 852 5 95 -104 917
0+2+L	0+13+L 1 75 99 172 3 78 72 176	17 34 -34 850 1+5iL	1+12+L	14 47 -50 962 15 40 -34 817 16 41 -33 230	2 65 67 781 3 67 71 23 4 77 -69 224	13 31• 37 125 14 97 103 949 15 32• 34 90	3+10+L	8 135 1.9 817 9 113 -112 943 10 82 -83 950	2 31* 23 866 3 55 53 228 4 35 31 179	6 112 -120 889 7 78 -80 882 8 31* 7 243	6 31• -7 886 7 51 -53 866 8 33• 15 926
0 656 -664 973 2 676 -691 963 4 554 -545 929	5 30* -45 101 7 30* -23 895 9 54 51 236	1 230 22 775 2 86 92 133 3 87 -102 941	2 62 54 176 3 41 -48 845 4 87 93 240	214 14 157	5 80 75 98 6 31 26 826 7 57 -63 781 8 30* 16 15	3+3+L	1 29* 18 10 2 101 -106 787 3 44 36 243 4 78 -82 764	11 68 -64 922 12 34 -34 782 13 56 51 988 14 339 -21 761	5 32* 7 117 6 31* -20 140 7 32* 16 249 8 31* -28 219	9 330 -27 6 10 330 11 176 11 340 18 7	9 330 4 233 4151L
8 100 -98 964 10 66 59 869 12 297 302 925	0.14.L 0 55 -49 787	4 161 157 22 5 124 124 883 6 134 -126 789 7 100 88 925	5 30° -11 228 6 57 70 245 7 31° 30 29 8 30° -5 41	6 59 -60 042 1 150 143 779 2 25° 20 792	9 33 -18 18 10 300 -9 979 11 310 -11 61	1 244 32 217 2 254 -22 821 3 146 151 895	5 32 -41 812 6 109 111 248 7 31* -24 10	15 41 -39 996 4.4.L	9 33+ -32 771 4+12+L	5+7+L 1 6961 868	0 70 -62 887 1 46 51 850 2 103 -96 885
14 188 -195 960 16 132 -142 937 18 63 61 965	2 32* -22 766 4 31* 29 154 6 61 52 177	8 227 232 990 9 68 66 929 10 90 92 882	• 30• 11 885 10 36 -37 187 11 32• 18 821	4 116 122 886 5 218 230 815 6 211 -221 910	15 33+ -26 23 2+11+L	5 66 75 931 6 42 40 20 7 207 197 958	9 32* -32 868 10 35 -28 168 11 39 -48 400	0 238 -241 909 1 40 -43 791 2 279 24 227	0 32* 34 156 1 32* 23 222 2 32* 21 284	2 30* 17 784 3 101 -112 653 4 61 -61 753 5 112 -111 649	3 37 52 849 4 73 -76 925 5 32• 33 831
0.3.L 1 1109 1120 931	8 57 46 181 0+15+L	11 36 -36 964 12 112 -104 114 13 34 -32 77	15 33• 58 530 1+13+F	7 155 159 883 8 351 -342 902 9 280 -30 189	0 69 -64 845 1 59 -57 237	8 53 -62 202 9 68 69 875 10 290 13 912	12 67 58 767 3+11+L	3 107 -110 909 4 74 81 902 5 57 63 993	3 49 -46 782 4 45 -41 226 5 33* -25 91	4 102 -106 800 7 320 -25 150 8 320 -31 245	7 33° -23 975 8 34 25 973 9 51 -54 888
3 720 733 926 5 389 365 906 7 487 476 941	1 53 -51 193 3 66 -73 177 5 66 -57 141	15 55 56 869 16 31* -28 873 17 32* -10 797	1 43 -46 198 2 31* 11 878 3 31* -30 24	12 102 105 14 12 94 -100 935 13 103 100 165	3 84 -67 258 4 30* 21 239 5 109 109 761	12 74 82 890 13 70 66 6 14 49 61 887	1 30° 18 950 2 30° 44 168 3 55 59 750	5 56 -61 238 7 64 67 176 8 69 70 858 9 154 -161 963	6 32* -10 938 7 33* -6 765	9 44 -35 819 10 43 44 757 11 41 -49 764	6,6,L
11 26• 12 70 13 256 -264 949 15 120 -124 941	0+16+L 0 76 -77 123	1+6+L	4 31* -28 20 5 30* -13 29 6 31* 5 22	14 31* 36 814 15 35 38 20 16 44 47 935	6 42 48 994 7 56 45 778 8 31* -15 987	15 75 -75 899 16 43 43 19	4 40 34 47 5 33 -23 212 6 310 6 750	10 64 63 935 11 57 -65 118 12 40 39 942	0 330 35 246 1 320 -21 162	5+8+L 1 45 -41 830	1 320 -7 8 2 320 -26 14 3 50 42 816
17 32+ 9 905 0+4+L	2 320 -11 210 1.0.L	2 540 -523 841 3 145 139 958 4 65 63 917	8 34 36 816 9 31* 8 925 19 32* -15 136	21 330 -7 76 2151L	9 31 25 102 10 329 -28 965 11 36 28 217 12 43 26 868	1 125 -118 184	8 32 -20 923 9 314 -11 35 10 324 18 884	13 31* 3 59 14 40 -22 799	2 33° -18 844 3 33° -22 118 4 33° -25 132	2 32* 37 930 3 71 -70 915 4 37 14 165 5 47 -43 764	4 44 33 819 5 92 88 851 6 36* 6 121
0 1358 1331 905 2 122 124 948 4 134 -153 798	1 104 -106 500 2 859 -906 500 3 222 -237 500	5 87 -85 938 6 234 230 860 7 99 105 783 8 65 66 965	1+14+L	0 270 268 976 1 240 15 24 2 86 94 957	2.12.L	3 103 102 941 4 26* 28 105 5 124 128 882	11 46 - 45 215 3+12+L	0 102 -96 961 1 63 50 831	5+0+L" 1 41 -44 500	6 67 61 823 7 83 78 881 8 33* 26 805	8 330 17 44 6.7.L
6 415 403 917 8 182 183 924 10 44 48 181	4 564 -550 500 5 78 73 8 6 247 -258 500	9 36 33 24 10 52 52 894 11 294 -19 184	2 87 95 150 3 38 29 793 4 32* 23 13*	4 178 183 936 5 82 -82 933 6 127 132 81	1 39 -27 113 2 56 49 214 3 309 -13 156	7 93 180 38 8 34 -34 978 9 169 173 71	1 30° 12 25 2 46 -46 203 3 31° 23'797	2 82 -83 931 3 28* -15 820 4 70 70 827 5 88 -99 849	2 72 -16 500 3 134 -140 500 4 30* 15 0 5 66 -71 500	9 43 37 800 10 33* -19 842	8 58 67 865 1 39 -31 853 2 79 80 7
14 67 69 759 16 41 -36 891	7 251 -247 500 8 170 -165 500 9 240 -9 500 10 113 104 0	12 151 148 859 13 46 -43 23 14 99 97 878 15 35 -37 817	5 31° 6 822 6 32° -14 192 7 32° -10 125 8 32° -2 61	7 38 41 788 8 129 -126 31 9 28- 7 95	4 32° -3 32 5 36 37 835 6 30° -3 15	10 136 144 894 11 60 57 960 12 30* 17 807	4 49 -48 205 5 32* -16 118 6 40 -35 239	6 29* -18 863 7 30* -23 103 8 79 -63 752	6 168 167 0 7 141 142 0 8 32 24 0	1 125 124 R03 2 49 -36 940	3 32° 12 189 4 63 52 648 5 33° 20 181
0.5.L	11 48 46 0 12 58 -61 500 13 28 20 0	16 31+ 12 84 1+7+L	1+15+L	11 175 -184 868 12 61 -57 811 13 30° -13 20	8 41 -33 762 9 31° -6 918 18 32° -14 801	14 102 -96 883 15 31* -14 990 16 43 30 22	6 31• 2 118 9 40 34 813	10 64 70 936 11 81 93 914 12 32* 27 779	41 39 0 10 34* -1 500 11 33* -20 500 12 51 58 0	3 86 99 820 4 38 -43 124 5 46 42 867 6 75 45 776	6 33° -26 63 7 34° 12 84
5 119 -112 928 7 240 -45 98 9 128 -127 851	15 31• 19 0 16 55 59 0 17 36 -37 500	1 149 -167 797 2 40 37 72 3 146 148 843	1 32° 20 15 2 39 -26 816 3 56 -44 131	14 50 41 986 15 46 43 860 16 31° -19 873	11 33+ 19 443 2+13+L	3+5+L	3+13+L 1 31+ -10 171	13 33• 32 949 14 34• 21 881	13 31+ -0 500 5+1+L	7 33* -35 776 8 33* 14 140	0 49 46 211 1 33• 22 952
11 71 -70 795 13 266 274 871 15 60 61 804	18 55 -56 500 1+1+L	4 99 100 233 5 40 25 38 6 40 43 832	5 33° -6 771 6 32° -9 824	2+6+L 0 321 -294 853	8 44 -41 45 1 310 -9 30 2 44 -41 927	2 103 -98 229 3 116 -123 951 4 38 40 152	3 43 36 185 4 32+ 33 874 5 32+ 18 228	0 153 160 837 1 280 25 160	1 261 270 980 2 29+ 25 217 3 128 135 3	5+10+L 1 33* 36 416 2 44 -52 246	2 40 30 211 3 52 40 154 4 33° -18 787 5 65 47 803
0.6.L	1 881 909 966 2 354 363 228 3 142 -141 969	8 105 -110 822 8 105 -111 825 9 56 -58 837 10 32 -27 766	2+0+L 0 94 90 0 1 244 292 0	1 115 -124 855 2 250 19 845 3 37 -32 993 4 53 57 862	3 31• 19 211 4 32• 14 806 5 61 62 185	5 47 37 241 6 124 -123 50 7 251 -263 860	6 32* 11 119 7 33* 2* 236 8 32* -10 57	2 112 107 865 3 72 70 875 4 30* -32 791	4 55 60 37 5 110 107 960 6 150 160 10	3 67 61 764 4 33* -10 967 5 34* 26 780	6+9+L
8 602 -606 899 2 252 -264 876 4 421 -468 846	4 629 631 779 5 173 -179 33 6 198 -203 61	11 54 54 834 12 35 -32 30 13 31+ -21 958	2 448 -422 500 3 36 20 0 4 154 -145 500	5 125 -137 884 6 121 121 862 7 99 -184 834	7 31+ 24-235 8 32+ 18 44 9 32+ -12 146	9 226 -233 872 19 84 90 170 11 125 -121 901	3+14+L 1 32+ -18 133	6 130 -135 870 7 75 72 106 8 47 -54 832	8 33 -30 890 9 31* 8 71 10 83 -73 76	6 55 -48 783 7 74 -63 780 5-11-1	0 67 -65 915 1 330 -14 846 2 70 -70 843
8 116 118 774 10 73 75 860 12 165 163 888	8 240 244 74 9 108 -107 942 10 124 124 902	15 44 -53 871 16 33• 31 814	5 220 235 0 6 55 62 0 7 202 201 0 8 77 -84 500	8 298 291 854 9 49 54 783 10 94 88 865 11 62 -45 979	2+14+L	12 93 -91 814 13 31* -33 45 14 32* -32 947	2 45 44 136 33• 19 64 • 34 14 0	9 131 126 878 10 80 -96 815 11 65 -50 125	11 32° 15 21 12 33 -37 153 13 43 -36 985	1 49 -77 779 2 33+ 23 868	7+0+L
14 62 -60 872 16 39 -43 838	11 158 -161 952 12 49 54 37 13 49 55 15	1+8+L 1 204 -284 9	9 20 -33 500 10 46 52 0 11 57 61 0	12 35 35 976 13 30° -10 833 14 31° 20 818	1 31• 7 131 2 31• -13 796 3 32• 9 843	. 3.6.L	5 34 -27 763 4181L	12 105 -104 851 13 32• 2 750	5+2+L	3 48 -56 779 4 33* 23 183 5 34 -38 787	1 33* -34 500 2 32* -0 500 3 37 -33 500
1 320 340 844	15 209 215 984 16 65 -66 5 17 79 86 986	2 36 44 698 3 92 -87 908 4 28 -39 64 5 108 102 98)	12 122 -126 500 13 40 -39 500 14 122 -115 500	15 39 -46 873 16 32* -29 901	4 31° -6 8° 5 32° 5 186 6 34° -46 206	1 53 -48 88 2 133 -128 862 3 59 -63 828	0 125 -118 500 1 25• 9 0 2 26• 27 0	0 71 73 846 1 67 -62 844	2 29* 29 28 3 112 105 921 4 29* -16 774	6.0.L 0 116 -113 500	5 34 -24 500 6 34+ 37 6
5 73 67 842 7 125 118 881 9 111 112 862	18 33° 26 99 1+2+L	6 43 -49 197 7 116 -119 794 8 28* -23 94	16 35 -29 500 17 32 42 0	0 242 243 203 1 91 108 824	2+15+L	5 95 -99 889 6 44 51 845 7 64 -65 985	4 48 58 0 5 27+ 35 0 6 27+ -1 500	3 30 26 99 4 74 -74 899 5 47 55 929	5 70 76 982 6 120 -130 965 7 137 -141 881 8 300 -17 54	1 30° 3 0 2 40 -39 500 3 67 -65 500	7+1+L 1 67 -73 981
11 59 57 94 13 202 -206 817 15 41 -53 947	1 239 236 832 2 918 -932 954 3 972 585 142	9 289 25 225 10 31 -19 831 11 88 89 941 12 153 -150 800	2+1+L 0 334 322 1	2 70 82 197 3 27 36 756 4 103 -104 901	8 33* 26 209 1 32* -12 51 2 37 -19 834	8 29+ -19 28 9 55 -62 755 10 114 -116 854	7 33 22 0 8 59 -44 500 9 154 -160 500	6 31+ -31 121 7 31+ -33 933 8 105 103 978	9 67 -72 815 10 31 -10 85 31 32* 16 871	5 106 -110 500 6 66 59 0 7 40 -45 500	3 62 -62 999 4 34 37 818 5 344 -23 962
0.8.L 0 620 623 813	4 257 287 989 5 120 -123 811 6 278 273 933	13 32• 36 867 14 109 -117 815 15 40 -32 163	2 361 388 786 3 167 -174 955 4 282 303 925	6 270 -20 863 7 34 44 893 8 100 -99 185	4 32+ -3 247 3+0+L	12 39+ -30 940 13 47 -42 33 14 36 39 800	10 34 37 0 11 300 -6 500 12 86 90 8 13 300 -17 500	9 85 -78 906 10 55 68 234 11 62 -64 896 12 54 -58 953	12 42 -48 970 13 33• -26 192 5.34	8 32* 36 0 9 31* -4 580 10 32* -12 580	7+2+L
2 129 138 850 4 89 88 239 6 90 89 879 8 120 112 413	8 49 44 830 9 91 -93 130 10 39 46 863	1+9+L 2 68 55 799	5 504 -505 990 6 303 296 209 7 240 -221 957 8 115 -110 945	9 67 68 799. 10 120 -120 88 11 41 51 889	1 100 90 0	15 34 22'794 3+7+L	14 36 8 0 15 32+ -5 500	13 33+ -24 963 4+8+L	1 147 -158 966 2 42 40 868	6.1.L 0 105 -101 860	2 33• 6 750 3 33• 12 994 4 33• 19 778
10 47 -61 216 12 85 -89 825 14 314 13 911	11 63 -70 89 12 127 123 955 13 61 27 159	2 27* -36 16 3 58 -55 918 4 61 61 813	9 132 128 27 10 42 34 908 11 64 66 915	13 30* 14 185 14 35 37 187 15 32* -13 50	4 201 100 0 5 115 121 0 6 280 261 0	1 94 -95 814 2 71 -69 27 3 279 14 783	0 116 -113 848 1 179 175 986	0 84 -87 828 1 33 33 229 2 52 41 825	4 82 -88 20 5 141 -136 917 4 161 -158 986	1 32° 14 235 2 106 -123 949 3 69 -61 7 4 105 -106 16	5 46 47 834 7+3+L
0+9+L	15 71 -70 937 16 51 51 21 17 31* 15 805	5 2/0 7 63 6 82 85 48 7 40 32 865 8 55 50 907	12 87 -91 838 13 119 111 972 14 309 9 963 15 48 41 981	2+8+L	7 77 75 0	4 36 15 73 5 74 79 892 6 90 -88 162	2 44 -94 6 3 185 163 977 4 112 113 856	3 78 -76 871 4 85 92 837 5 106 -99 92	7 31* 20 955 8 54 49 12 9 31* -7 892	5 34 -31 174 6 31• 25 773 7 43 -29 943	1 43 47 942 2 59 46 227 3 34 32 941
1 283 -292 776 3 185 -196 794 5 47 -41 888	18 67 63 988 1+3+L	9 44 -44 236 10 304 -27 123 11 314 -33 866	14 41 -39 17 17 31+ -25 102	1 84 79 971 2 28 -22 986 3 116 116 32	11 87 91 0 12 130 -135 509 13 30- 10 0	8 93 -101 67 9 73 80 820 10 97 95 37	5 80 81 978 6 58 -60 990 7 67 67 985 8 119 -118 904	7 :30 -35 992 8 32* -28 922 9 85 84 239	10 64 64 52 11 320 -8 48 12 320 13 8 13 360 27 843	9 83 -82 956 10 33* 29 891	4 37 -43 798 7,4,L
9 90 -86 790 31 30* -41 134 13 115 113 780	1 75 -70 864 2 307 -313 147 3 402 393 937	12 J1* 19 765 13 32* -20 193 14 33* -3 155 15 90 AA 74*	2+2+L 8 168 -166 3 1 193 -194 844	47 -51 242 5 98 96 917 6 132 -134 791	14 116 -122 500 15 38* -4 500 16 54 53 0	11 76 88 844 12 87 95 980 13 67 57 798	9 81 75 967 10 101 105 36 11 33 24 37	10 15 41 784 11 324 18 42 12 334 -27 225	5+4+L	6+2+L 0 90 101 442	1 51 -48 39 2 33° -21 872 3 33° -19 842
15 33+ -28 750 0+104L	4 379 -377 81 5 25 -14 895 6 214 214 63	1+10+L	2 160 163 946 3 65 -68 889 4 222 211 956	8 143 -142 829 9 29• 39 844 10 37 -32 939	3+1+L 1 141 148 964	324 27 838 3+8+L	12 40 51 837 13 35 -48 938 14 42 45 800 15 37 34 944	4.9.L 0 310 -47 804	1 56 -60 862 2 98 107 893 3 86 -85 864 4 75 -84 893	1 40 46 214 2 31* 19 29 3 81 90 96	7+5+L
0 309 -312 704 2 156 -160 785 4 55 -64 851	7 195 -199 908 A 187 -189 785 9 148 -139 935 10 147 -139 Am	1 47 46 792 2 122 123 227 3 55 -50 135 4 82 89 787	5 323 -312 60 6 160 162 960 7 234 -249 39 8 105 05 050	11 56 50 812 12 81 -83 792 13 38 -33 900	2 185 176 12, 3 402 -390 976 4 117 110 202	1 75 75 62 2 134 134 785 3 62 75 895	4+2+L	1 49 -51 239 2 30* 23 197 3 97 100 771	5 72 -72 647 6 126 123 923 7 111 114 833	5 00 107 1 6 40 -32 86 7 41 53 958	2 33- 21- 854
6 39 -47 905 8 28 12 116 10 93 99 764 12 95 98 795	11 46 45 836 12 47 -43 41 13 63 -62 952 14 66 71 269	5 32 27 8 6 112 111 611 7 73 70 876 8 31 32 917	9 269 -7 94 10 289 25 28 11 56 -59 851 12 160 160 6	15 32+ -22 169	6 74 -76 43 7 78 -73 916 8 46 -49 147	5 66 66 829 6 84 81 829 7 64 -67 115	2 51 -45 91 3 145 140 991	5 81 80 795 6 60 -61 952 7 37 22 762	6 48 30 174 9 32• 45 855 10 32• -21 803 11 33• -20 833	8 41 -33 982 9 329 -18 242 10 339 11 32	

deviation is 0.044 Å. The dihedral angle between the best plane through the 7 hydantoin atoms and (010) is 2.40°. Thus, it is readily apparent why the centro-symmetric symbolic addition procedure yielded the atomic positions of the hydantoin group even though the true space group for diphenylhydantoin is non-centrosymmetric; the proximity of the hydantoin-group plane to (010) results in all of the phases, calculated from the positions of those atoms only, to be very close to 0 or π .

Analysis of the distribution of normalized intensities by the zero moment, N(Z), test is shown in Fig. 1. For normalized intensities from 0 to 0.5 the distribution for diphenylhydantoin follows that of an acentric structure, but for normalized intensities of 0.6 or greater the distribution is that of a centric space group. It may be that whenever such a mixed distribution of intensities occurs, a sufficiently large part of a structure in a non-centrosymmetric space group approximates a centrosymmetric arrangement in the unit cell, and use of centric sign-determining methods may provide a partial structure as a starting point in the crystallographic determination.

Table 4 lists the hydrogen-atom coordinates, tem-



Fig. 2. Perspective drawing of the diphenylhydantoin molecule, illustrating relative thermal motions of the atoms.

perature parameters, and bond lengths. Observed and calculated structure amplitudes are listed in Table 5.

Fig. 2 shows the conformation of the molecule and the magnitudes and shapes of the atomic thermal ellipsoids. The two phenyl rings are planar (maximum deviation of the ring atoms from the best plane through each ring is 0.02 Å), as is the 5-atom hydantoin ring (maximum deviation of a ring atom from the plane is 0.03 Å with O(6) and O(7) situated -0.09 and +0.05 Å respectively from the plane through the five ring atoms). The obtuse angles between the normals to the respective planes are: hydantoin-phenyl [C(8)-C(13)], 114°; hydantoin-phenyl [C(14)-C(19)], 113°; phenylphenyl, 90°.

Bond lengths for the non-hydrogen atoms are illustrated in Fig. 3, and bond angles are listed in Table 6. Large standard deviations and fairly large differences between chemically equivalent bonds in the phenyl rings are primarily due to the large, extremely anisotropic thermal motion of these groups (Fig. 2). Analysis of the individual atomic thermal ellipsoids in terms of rigid-body tensors was performed using the method of Schomaker & Trueblood (1968). Calculations were carried out for a molecule consisting of three connected rigid bodies: (a) hydantoin group plus C(8) and C(14); (b) C(8)–C(13) + C(5); and (c) C(14)– C(19) + C(5). The differences between the U(I,J)derived from the input B(I,J) and those calculated from the rigid-body parameters indicate that the rigid-body treatment of the thermal motion is acceptable. Root-mean-square $\Delta U(I,J)$'s for the three rigid bodies, (a), (b) and (c) are 0.0048, 0.0049 and 0.0066 $Å^2$ respectively. Table 7 lists the r.m.s. amplitudes of libration and translation along the principal axes of the libration and translation tensors and the direction cosines of the respective axes referred to the cell axes a, b and c. Rotational corrections derived from the rigid-body analyses were applied to the molecule. These corrected bond lengths are shown in parentheses in Figure 3. Before thermal correction the averaged bond lengths for the two phenyl groups were 1.370 and 1.379 Å, and after correction they were

122.4(1.3)

Table 6. Bond angles (°)	ın	diphe	enyi	nya	ant	oin
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Estimated standard deviations in parentheses.

C(2) - N(1) - C(5)	114.2(5)	C(5) - C(14) - C(15)	122.5 (0.8)
N(1)-C(5)-C(4)	99·1 (4)	C(5) - C(14) - C(19)	114.6 (1.1)
N(1) - C(5) - C(8)	111.2 (9)	C(15) - C(14) - C(19)	122.9 (1.3)
N(1) - C(5) - C(14)	112.4(8)	C(14) - C(15) - C(16)	118.2 (1.7)
C(4) - C(5) - C(8)	107.4 (8)	C(15) - C(16) - C(17)	121.0 (2.3)
C(4) - C(5) - C(14)	113.4 (9)	C(16) - C(17) - C(18)	118.7 (1.7)
C(8) - C(5) - C(14)	112.5 (6)	C(17) - C(18) - C(19)	123.0 (1.5)
C(5) - C(4) - N(3)	107.3 (5)	C(18) - C(19) - C(14)	116.0 (1.5)
C(5) - C(4) - O(7)	125.6 (5)	C(5) - C(8) - C(13)	124.0 (0.8)
N(3) - C(4) - O(7)	127.0 (6)	C(5) - C(8) - C(9)	120.5 (1.3)
C(4) - N(3) - C(2)	112.6 (5)	C(9) - C(8) - C(13)	115.4 (1.3)
N(3)-C(2)-N(1)	106.6 (5)	C(8) - C(9) - C(10)	123.0 (2.1)
N(3) - C(2) - O(6)	125.0 (6)	C(9) - C(10) - C(11)	119.7 (1.9)
N(1)-C(2)-O(6)	128.4(6)	C(10) - C(11) - C(12)	118.8 (1.9)
		C(11) - C(12) - C(13)	120.6 (1.9)

C(12)-C(13)-C(8)

	Rigi	d body (a):	tatoms 1-8	+14
L and	5∙70°	0.013	-0·147	- 0.989
direction	3.93	0.514	0.849	-0.120
cosines	3.41	0.828	-0.507	0.087
T and	0·218 Å	0.088	-0.981	-0.173
direction	0.163	0.388	0.193	-0.901
cosines	0.145	0.918	0.012	0.398
	Rigic	1 body (c):	atoms 5+14	-19
L and	13·32°	0.047	0.649	0.759
direction	3.42	0.188	-0.752	0.632
cosines	2.55	0.981	0.113	−0 ·157
T and	0·304 Å	-0.606	0 ·741	-0.291
direction	0.212	-0.507	-0.641	-0.576
cosines	0.181	-0.613	-0.505	0.764

Table 7. Principal-axis r.m.s. amplitudes of libration L and translation T and direction cosines referred to cell axes a, b and c

1.396 and 1.407 Å. Bond lengths for the hydantoin group are all normal and compare well with those found for the hydantoin atoms in allantoin (Mootz, 1965).

A second model which could also adequately describe the apparent phenyl anisotropy is one featuring disorder. If we were to choose two orientations for each phenyl ring with atom positions at the extremes of the thermal ellipsoids (Fig. 2), we might obtain more acceptable individual bond lengths for the aromatic bonds. However, the two orientations for each ring would be so close to one another that analytical refinement of the atom positions would not be rewarding. As the anisotropic thermal model is also satisfactory (the relationship between dynamic and static disorder in this case is one too close to distinguish without re-examining the structure at low temperature), it was unnecessary to investigate a disordered model more closely.

Whichever is the correct model, the effect upon the hydrogen-atom positions is unfortunate. As shown in Table 4, the estimated standard deviations in the hydrogen-atom positions and thermal parameters are extremely large and some of the bond lengths involving hydrogen are peculiar to say the least. It appears that the errors introduced by the dynamic or static disorder of the phenyl rings are large enough to make the hydrogen parameters unreliable.

The question of whether or not certain conformational features are necessary for antiepileptic efficacy can best be answered by further structural studies on other useful anticonvulsants and comparison with diphenylhydantoin. Such studies are in progress in these laboratories, and preliminary results (Camerman & Camerman, 1970) indicate that structural features of this molecule which may be pertinent to its anticonvulsant properties are the two phenyl rings at C(5)and the two carbonyl oxygen atoms. Distances between the centroids of the phenyl rings and the oxygen positions have been calculated and are shown in Table 8.

Table 8. Distances (Å) between phenyl-ring centroids and
oxygen atoms

Rigid body (b): atoms 5+8-13

0.709

0.625

0.327

0.771

-0.042

-0.636

-0.703

0.588

0.400

-0.362

-0.250

0.898

-0.058

-0.514

-0.856

0.682

0.586

0.437

13·42° 6·20

0.331 Å

0.207

0.167

2.53

C(8) - C(13) - C(14) - C(19)	4.835
C(8) - C(13) - O(6)	5.677
C(8) - C(13) - O(7)	3.968
C(14)-C(19)-O(6)	5.514
C(14)-C(19)-O(7)	4.227
O(6)–O(7)	4.555

Intermolecular distances

The molecules are laced together through hydrogen bonds between hydrogens bonded to the nitrogen atoms and the two carbonyl oxygen atoms. Distances and angles between the atoms involved are listed in Table 9.



Fig. 3. Bond lengths with e.s.d.'s in parentheses. The bond lengths in parentheses are the thermally corrected ones. Estimated standard deviations are the same as for the uncorrected distances.

Table 9. Intermolecular hydrogen bonding scheme

O(6') is at symmetry position $\left[-\frac{1}{2}+x, y, \frac{1}{2}+z\right]$.							
O(7') is at symmetry position $[1+x, y, z]$.							
$H(1) \cdots O(7')$	1·92 Å	H(3)···O(6')	1·98 Å				
$N(1) \cdots O(7')$	2.84	$N(3) \cdots O(6')$	2.78				
N(1)-H(1)-O(7')	176·3°	N(3)-H(3)-O(6')	173·3°				

Undoubtedly, it is this hydrogen-bonding scheme that restrains the hydantoin atoms from exhibiting the large thermal motion exhibited by the unfettered phenyl groups.

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Crystal and Molecular Structure of Nitratobis-(2,2'-dipyridyl)cobalt(III) Hydroxide Nitrate Tetrahydrate, [Co(C₁₀H₈N₂)₂(NO₃)](NO₃)(OH).4H₂O

BY C.W. REIMANN, M. ZOCCHI*, A.D. MIGHELL AND A. SANTORO

Institute for Materials Research, National Bureau of Standards, Washington, D. C. 20234, U.S.A.

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The structure of nitratobis-(2,2'-dipyridyl)-cobalt(III) hydroxide nitrate tetrahydrate, [Co(C₁₀H₈N₂)₂(NO₃)](NO₃) (OH).4H₂O, has been determined by single-crystal X-ray diffraction techniques. Crystals of this complex are monoclinic with a = 10.923(2), b = 15.998(4), c = 14.442(2) Å, $\beta = 101.93(2)^{\circ}$, space group C2/c, $\rho_c = 1.57$ g.cm⁻³, $\rho_o = 1.54$ g.cm⁻³, and Z = 4. The structure was solved by Patterson and Fourier methods. The cobalt atom is octahedrally coordinated by two molecules of 2,2'-dipyridyl and by a bidentate nitrate group. Water molecules, nitrate groups, and the hydroxide ions are involved in hydrogen bonds which extend continuously in the **a** and **c** directions. The final refinement of the structure by full-matrix anisotropic least-squares analysis resulted in an *R* value of 6.2%, based on 2995 observed reflections.

Introduction

Most of the information on the stereochemistry of first-row transition metal ion complexes that contain coordinated nitrate groups and nitrogen donor ligands is derived from spectroscopic data (Addison & Sutton, 1967). From the analysis of the spectroscopic data it is inferred that the nitrate groups may act as monodentate, bidentate, or bridging ligands. But very few crystal-structure data are available to confirm the spectroscopic interpretations and to provide accurate bond distances and angles for coordinated nitrate groups.

As part of a series of studies of amine complexes of

transition metal nitrates, a crystalline hydrate containing two molecules of 2,2'-dipyridyl, two nitrate groups, and one hydroxide ion per cobalt(III) ion was selected for an X-ray diffraction analysis. In this complex the 2,2'-dipyridyl molecules may assume either a cis or trans configuration, each permitting several possibilities for the overall coordination, including coordination by one or both of the nitrate groups. The presence of water molecules and hydroxide ions, moreover, indicates that hydrogen bonding would occur in the structure. Therefore, determination of the structure was undertaken, to determine the role of the nitrate groups in the structure, to provide accurate values of the bond distances and angles for the nitrate groups and the 2,2'-dipyridyl molecule, and to obtain information on the hydrogen-bonding network.

^{*} Present address: Istituto Politecnico di Milano, Milano, Italy.