

In their paper on the structure of sodium tricyanomethanide Andersen, Klewe & Thom (1967) conclude that the tricyanomethanide anion exists in a planar trigonal configuration and that the nonplanar configuration around the central carbon atom in pyrimidinium dicyanomethylide is due to packing effects. The mean carbon-carbon distance of 1.40 Å corresponds closely with the value 1.408 Å found in sodium tricyanomethanide. The mean carbon-nitrogen bond length is 1.16 Å.

The double bond character of the C-S ylid bond, and the planarity of the carbanion of the sulfonium ylid confirms the view of Johnson (1966), that the unshared electrons on the ylid carbanion are delocalized into the 3*d*-orbitals of the sulfur atom as well as into the rest of the carbanion. From dipole moment calculations on fluorenylidenedimethylsulfurane, Johnson (1966) predicted a C-S ylid bond of 1.7 Å, a value that corresponds well with the bond length of 1.72 Å found from the X-ray data.

Considering the uncertainty in the van der Waals radius of the hydrogen atoms as well as the uncertainty in their positions, the packing contacts appear to be normal, see Fig. 3.

The authors are indebted to Dr John Moffatt of the Institute of Molecular Biology, Syntex Research for suggesting the problem.

## References

- ANDERSEN, P., KLEWE, B. & THOM, E. (1967). *Acta Chem. Scand.* **21**, 1530.  
 BUGG, C., DESIDERATO, R. & SASS, R. L. (1964). *J. Amer. Chem. Soc.* **86**, 3157.  
 BUGG, C. & SASS, R. L. (1965). *Acta Cryst.* **18**, 591.  
 COOK, A. F. & MOFFATT, J. G. (1968). *J. Amer. Chem. Soc.* **90**, 740.  
 CRUICKSHANK, D. W. J. (1961). *Acta Cryst.* **14**, 896.  
 ENEMARK, J. H. & HOLM, R. H. (1964). *Inorg. Chem.* **3**, 1516.  
 HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1964). *Acta Cryst.* **17**, 1040.  
 JOHNSON, A. W. (1966). *Ylid Chemistry*, pp. 304, 316, 318. New York and London: Academic Press.  
 KARLE, I. L., ESTLIN, J. A. & BRITTS, K. (1967). *Acta Cryst.* **22**, 273.  
 LEUNG, Y. C. & MARSH, R. E. (1958). *Acta Cryst.* **11**, 17.  
 LOFTHUS, A. (1965). Private communication.  
 PREWITT, C. T. (1964). *GSET4. A Program for Computing Eulerian Orienter Angles*. Wilmington, Delaware: Central Research Department, E. I. Du Pont de Nemours & Co.  
 SHEFTER, E. & MAUTNER, H. (1967). *J. Amer. Chem. Soc.* **89**, 1249.  
 SCHOMAKER, V. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* **24**, 63.  
 TRUTER, M. (1960). *J. Chem. Soc.* p. 997.  
 TRUTER, M. & KUNCHUR, N. R. (1958). *J. Chem. Soc.* p. 2551.

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## The Crystal Structure of 1-(2,6-dichlorobenzyl)-6-hydroxy-1,4,5,6-tetrahydronicotinamide Dihydrate

BY HÅKON HOPE

*Department of Chemistry, University of California, Davis, California 95616 U.S.A.*

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The crystal structure of the 'primary acid modification' product of the DPNH model 1-(2,6-dichlorobenzyl)-1,4-dihydronicotinamide has been determined, identifying the product as 1-(2,6-dichlorobenzyl)-6-hydroxy-1,4,5,6-tetrahydronicotinamide. The compound crystallizes with two molecules of water. The crystals are triclinic plates, cell dimensions:  $a = 8.275$ ,  $b = 8.080$ ,  $c = 13.267$  Å (e.s.d.  $\sim 0.003$  Å);  $\alpha = 92.17$ ,  $\beta = 101.05$ ,  $\gamma = 116.92^\circ$  (e.s.d.  $\sim 0.04^\circ$ ); space group  $P\bar{1}$  with two formula units in the cell. The structure was solved by Patterson and Fourier methods and refined by full-matrix least-squares methods. The final  $R$  is 0.038 for 2044 observed reflections measured with a Picker automatic diffractometer, using Cu  $K\alpha$  radiation. With the exception of C(5) and the hydroxy group, the nicotinamide moiety is planar, with the benzyl C(H<sub>2</sub>) in the same plane. The amide O is *cis* to the ring double bond, and the hydroxy group occupies a pseudo-axial position. Bond distances were corrected for anisotropic thermal motion effects. The N(1)-C(2) bond distance is 1.356 Å, the other two N-C distances are near 1.47 Å. In the benzene ring the distances are: C(CH<sub>2</sub>)-C(Cl), 1.399 Å; C(H)-C(Cl), 1.381 Å; C(H)-C(H), 1.390 Å; C-Cl, 1.748 Å. The internal angle at C(CH<sub>2</sub>) is 115.3°; at C(Cl), 123.4° (average). The estimated standard deviations are  $\sim 0.004$  Å for distances and  $\sim 0.3^\circ$  for angles.

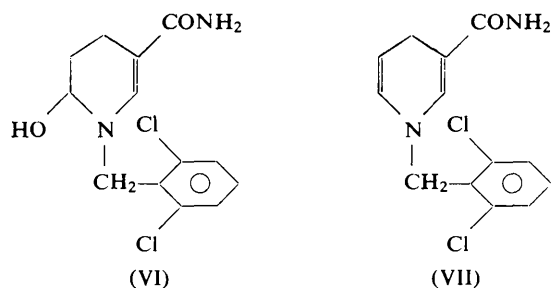
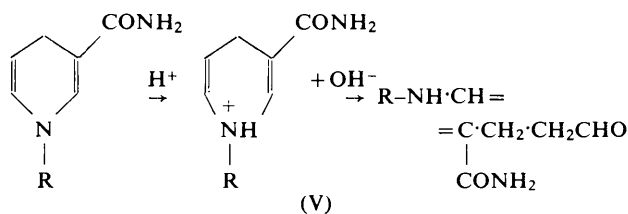
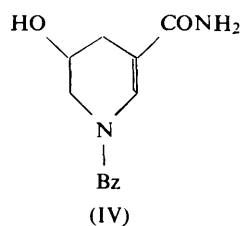
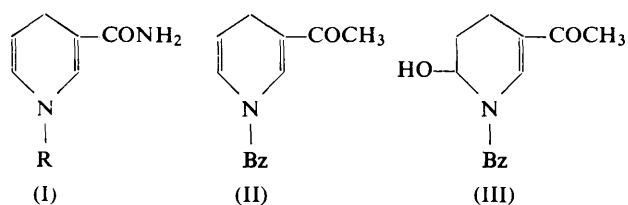
### Introduction

Diphosphopyridine nucleotide participates in a large number of biochemically important red-ox reactions. We can represent its reduced form (DPNH) by formula (1), where R is an adenosine-diphosphate-ribose group.

It has been known for many years (Warburg & Christian, 1934) that DPNH is unstable in acidic solutions, where a reaction known as the 'primary acid modification' will occur. The early studies could only suggest that the reaction took place in the nicotinamide moiety, while no definite conclusions regarding its

nature could be drawn. Over the years, considerable effort has been invested in order to determine the structure of the reaction product. Since the presence of the large and sensitive nucleotide R group complicates the work, numerous investigations were carried out on model compounds where R has been replaced by smaller and more stable groups.

Anderson & Berkelhammer (1958) carried out the primary acid modification on (II) (Bz = benzyl), obtaining a product which they identified as (III), further suggesting that also in the case of the amide the reaction would be an addition of H<sub>2</sub>O to the 5-6 double bond, with the OH group going to C(6). However, other authors questioned the validity of their conclusions on the grounds that replacement of NH<sub>2</sub> by CH<sub>3</sub> might have resulted in a compound which could no longer be considered an adequate model. Segal & Stein (1960) claimed that the reaction resulted in (IV), while Burton & Kaplan (1963) favored the scheme (V). Diekmann, Englert & Wallenfels (1964) prepared a compound (reported m.p. 161-2°) to which they assigned structure (VI), the assignment being based mainly on elemental analysis and chemical considerations.



In all these investigations main obstacles seem to have been low yields and products which were difficult to obtain in a pure form. These difficulties were overcome when Kim & Chaykin (1968) succeeded in synthesizing a primary acid modification product (hydration product) of (VII) in good yield and high purity. (Reported m.p. 180-5°, decomposed).

Since the product could be obtained in the form of good crystals which were perfectly stable in air, the best approach to the structure determination appeared to be an X-ray crystallographic study, the results of which are reported here.

### Experimental

Crystals of the product from the 'primary acid reaction' of 1-(2,6-dichlorobenzyl)-1,4-dihydropyridinamide were grown from a tetrahydrofuran-water mixture (Kim & Chaykin, 1968), and appeared in the form of colorless, diamond-shaped plates. Oscillation and Weissenberg photographs showed triclinic symmetry.

A crystal with dimensions approximately 0.08 × 0.13 × 0.20 mm was mounted with its long direction within about 15° of the  $\phi$  axis on a Picker diffractometer equipped with a full-circle goniostat. Angular coordinates ( $\chi, \phi, 2\theta$ ) for Cu  $K\alpha_{1,2}$  and  $\beta$  reflections for 14 planes (29 coordinate sets) were used in a least-squares calculation of cell dimensions and orientational parameters. The cell dimensions were found to be:

$$a = 8.275, b = 8.080, c = 13.267 \text{ \AA} \text{ (e.s.d. } \sim 0.003 \text{ \AA)}$$

$$\alpha = 92.17, \beta = 101.05, \gamma = 116.92^\circ \text{ (e.s.d. } \sim 0.04^\circ)$$

$$(\lambda \text{ for Cu } K\alpha_1: 1.54051, \alpha_2: 1.54433, \beta: 1.39217 \text{ \AA}).$$

The space group is  $P\bar{1}$  (from the refined structure).

With two molecules of composition C<sub>13</sub>H<sub>14</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>2</sub> in the unit cell, the calculated density is 1.30 g.cm<sup>-3</sup>, while the density observed by flotation was 1.43 g.cm<sup>-3</sup>. With an additional four water molecules in the unit cell the calculated density becomes 1.45 g.cm<sup>-3</sup>. The presence of this amount of water was confirmed during the course of the structure analysis.

The intensities of 2674 unique reflections accessible below  $2\theta = 133^\circ$  were measured with the diffractometer in automatic mode using the  $2\theta$ - $\theta$  scan technique, Ni filtered Cu  $K\alpha$  radiation and a scintillation detector with pulse height analyzer. The scan range was from  $[2\theta(\alpha_1) - 0.75^\circ]$  to  $[2\theta(\alpha_2) + 0.75^\circ]$  with a scan speed of 1°/min; background counts were taken for 20 sec at both ends of the scan range. To prevent serious coincidence losses the attenuator mechanism was set to add an attenuation filter when the count rate exceeded about 10,000 c.p.s. Although the intensity of a low angle check reflection remained constant, a reflection at  $2\theta \sim 70^\circ$  showed a gradual decline in intensity, the decline amounting to about 8% at the end of the data collection, and this was the main reason for limiting the measurements to the  $2\theta$  range below  $133^\circ$ .

Lorentz and polarization corrections were applied in the usual manner. Each recorded number of counts  $N$  was assigned an estimated standard deviation  $s(N) = N^{\frac{1}{2}} + N/200$ , the second term being intended to account for various instabilities. Based on the  $s(N)$  values for scan and background counts, e.s.d.'s for the net intensities were calculated; reflections for which the net intensity was less than four times its e.s.d. were recorded as 'unobserved' with the value  $F(\text{unobs}) = (4\sigma(I_{\text{net}})/Lp)^{\frac{1}{2}}$ . The number of 'observed' reflections was 2044. No absorption correction was applied, and likewise no attempt was made to compensate for the apparent effects of radiation damage.

### Solution and refinement of the structure

A sharpened three-dimensional Patterson function calculated with coefficients  $(F/\Sigma f_i)^2$  displayed a pattern among the largest peaks which strongly suggested the presence of two heavy atom pairs related through a center of symmetry. The structure was solved and refined on the assumption that the space group is  $P\bar{1}$ .

A three-dimensional Fourier synthesis based on the positional parameters for the two Cl atoms derived from the Patterson function revealed the positions of all non-hydrogen atoms, including two water oxygens. After several cycles of full-matrix least-squares refinement of this structure (using anisotropic temperature factors) the  $R$  index was 0.064. A difference Fourier synthesis now clearly indicated positions for all the H atoms except those of the water molecules, which did not appear nearly as convincing as the others and were therefore temporarily left out of the calculations.

Inclusion of the hydrogen atoms placed in 'calculated' positions lowered the  $R$  index to 0.047. The positional parameters of these H atoms were refined through a few least-squares cycles in which their isotropic temperature factors were kept constant at  $4 \text{ \AA}^2$ . At this stage another difference map was calculated in an attempt to account for the water hydrogens. The appearance of this map, together with features of the structure involving hydrogen bonds across centers of symmetry, led to the assumption that at least one hydrogen atom in each water molecule is disordered. Around each water oxygen were then placed one whole H atom and two half H atoms in positions corresponding to maxima in the map; these H atoms were given a temperature factor of  $5 \text{ \AA}^2$ . The water O and H parameters (except hydrogen temperature factors) were adjusted in two least-squares cycles.

The least-squares weighting scheme was then changed from the Hughes (1941) scheme to one where each  $\Delta F^2$  ('observed'  $F$ 's only) was given a weight inversely proportional to  $\sigma^2(F)$ , and a few more cycles of refinement were carried out. Some small changes in positional parameters were observed, none of which exceeded two e.s.d. The final shifts were all less than 1/10 of the corresponding e.s.d. The final positional

parameters are listed in Table 1, and the temperature coefficients in Table 2. The final  $R$  index for all 'observed' reflections is 0.038 for  $F_c$  based on all parameters in Tables 1 and 2, 0.041 if the water H atoms are left out and 0.066 for all reflections and all parameters. A comparison of observed and calculated structure factors, together with the weight given each  $\Delta F$  (the weights on a relative scale only) is given in Table 3.

Table 1. Final positional parameters

E.s.d. (in parentheses) apply to the least significant figures  
No e.s.d. given for water hydrogens.

	<i>x</i>	<i>y</i>	<i>z</i>
N(1)	0.6769 (3)	0.3259 (3)	0.2434 (2)
C(2)	0.8359 (4)	0.3638 (4)	0.2132 (2)
C(3)	0.9286 (4)	0.5140 (4)	0.1665 (2)
C(4)	0.8523 (4)	0.6508 (4)	0.1455 (2)
C(5)	0.7379 (4)	0.6461 (4)	0.2240 (2)
C(6)	0.5907 (4)	0.4475 (4)	0.2257 (2)
C(7)	1.1004 (4)	0.5394 (4)	0.1417 (2)
O(8)	1.1639 (3)	0.4256 (3)	0.1594 (2)
N(9)	1.1972 (3)	0.6925 (4)	0.0998 (2)
O(10)	0.4548 (3)	0.3743 (3)	0.1300 (2)
C(11)	0.5750 (4)	0.1526 (4)	0.2864 (2)
C(12)	0.5694 (4)	0.1961 (4)	0.3977 (2)
C(13)	0.7228 (4)	0.2460 (4)	0.4798 (2)
C(14)	0.7262 (4)	0.2938 (4)	0.5813 (2)
C(15)	0.5684 (5)	0.2923 (5)	0.6029 (2)
C(16)	0.4107 (4)	0.2046 (5)	0.5248 (2)
C(17)	0.4134 (4)	0.1927 (4)	0.4247 (2)
Cl(18)	0.9220 (1)	0.2448 (1)	0.4556 (1)
Cl(19)	0.2091 (1)	0.1237 (1)	0.3298 (1)
O(20)	0.9260 (4)	0.0777 (4)	0.0534 (3)
O(21)	1.5534 (3)	0.8644 (3)	0.0320 (2)
H(021)	0.8842 (42)	0.2643 (41)	0.2241 (23)
H(041)	0.9631 (43)	0.7773 (42)	0.1608 (24)
H(042)	0.7744 (42)	0.6248 (44)	0.0771 (24)
H(051)	0.8360 (43)	0.6947 (43)	0.3044 (24)
H(052)	0.6558 (41)	0.7171 (42)	0.2124 (24)
H(061)	0.5100 (41)	0.4327 (41)	0.2863 (22)
H(091)	1.3211 (41)	0.7124 (41)	0.0842 (23)
H(092)	1.1274 (43)	0.7748 (42)	0.0837 (23)
H(101)	0.3484 (39)	0.3932 (40)	0.1409 (23)
H(111)	0.4341 (41)	0.0966 (43)	0.2408 (24)
H(112)	0.6313 (41)	0.0582 (41)	0.2848 (24)
H(141)	0.8523 (43)	0.3346 (43)	0.6426 (23)
H(151)	0.5770 (42)	0.3481 (42)	0.6844 (23)
H(161)	0.2806 (44)	0.2193 (43)	0.5442 (23)
H(201)	0.9966	0.1742	0.0913
$\frac{1}{2}$ H(202)	1.0053	0.0359	0.0447
$\frac{1}{2}$ H(203)	0.7854	0.0248	0.0672
H(211)	1.5394	0.7977	-0.0257
$\frac{1}{2}$ H(212)	1.5256	0.9376	0.0073
$\frac{1}{2}$ H(213)	1.6498	0.9299	0.0304

### Computing procedures

The calculations were performed on an IBM 7044 computer, using a set of programs listed elsewhere (Hope & Christensen, 1968).

The least-squares program minimizes the value of  $S = \Sigma w(KF_o - G|F_c|)^2$  by a full-matrix routine,  $G$  being one of the adjustable parameters. Since the maximum number of adjustable parameters the program could handle was 163, this number of parameters was adjusted in each cycle, with exchange of 'refined' and

'unrefined' atoms being performed after each cycle. The e.s.d.'s were obtained from the expression  $(a_{ii}S/m)^{\frac{1}{2}}$  where  $a_{ii}$  is the diagonal element in the inverse normal equation matrix and  $m=1800$ . The isotropic temperature factor is of the form  $\exp(-B \sin^2\theta/\lambda^2)$ ; the aniso-

tropic of the form

$$\exp[-(h^2\beta_{11} + k^2\beta_{22} + l^2\beta_{33} + hk\beta_{12} + hl\beta_{13} + kl\beta_{23})].$$

The temperature parameters listed in Table 2 are related to the  $\beta$ 's by  $B_{11}=4a^2\beta_{11}$ ,  $B_{12}=2ab\beta_{12}$  etc. The

Table 2. Final thermal parameters, with e.s.d. in parentheses

The  $B$ 's listed are related to the  $\beta$ 's actually refined by  $B_{11}=4a^2\beta_{11}$ , etc.  $B_{12}=2ab\beta_{12}$  etc.

	$B_{11}$	$B_{22}$	$B_{33}$	$B_{12}$	$B_{13}$	$B_{23}$
N(1)	4.32 (14)	4.71 (15)	4.09 (12)	2.64 (12)	1.95 (10)	1.35 (11)
C(2)	3.98 (16)	4.97 (18)	2.95 (13)	2.42 (14)	0.90 (11)	0.35 (12)
C(3)	3.86 (15)	4.49 (18)	2.83 (12)	2.10 (14)	0.96 (11)	0.49 (12)
C(4)	5.58 (20)	5.45 (20)	4.60 (16)	3.16 (17)	2.06 (14)	1.62 (14)
C(5)	5.64 (19)	4.91 (19)	4.72 (16)	3.01 (16)	2.00 (14)	1.04 (14)
C(6)	4.66 (17)	5.46 (20)	3.68 (14)	3.20 (16)	1.39 (12)	0.77 (13)
C(7)	4.00 (16)	5.48 (20)	2.77 (13)	2.02 (15)	0.57 (11)	0.21 (13)
O(8)	4.73 (12)	6.51 (15)	5.25 (12)	3.43 (12)	1.74 (9)	1.14 (10)
N(9)	4.97 (16)	5.85 (18)	5.36 (15)	2.01 (14)	2.42 (12)	1.60 (13)
O(10)	4.98 (12)	8.40 (16)	4.22 (10)	3.97 (12)	0.64 (9)	0.07 (10)
C(11)	4.75 (18)	4.40 (18)	3.94 (15)	2.05 (15)	1.68 (13)	0.83 (13)
C(12)	4.37 (16)	3.42 (16)	3.78 (14)	1.68 (13)	1.38 (12)	0.80 (12)
C(13)	4.44 (17)	4.27 (18)	4.47 (16)	1.97 (15)	1.31 (13)	1.22 (13)
C(14)	6.04 (21)	5.63 (22)	4.04 (16)	2.38 (18)	0.77 (15)	0.49 (15)
C(15)	8.19 (26)	5.38 (21)	4.00 (16)	3.21 (20)	1.76 (17)	0.34 (15)
C(16)	6.64 (22)	6.21 (22)	4.38 (17)	3.80 (19)	2.45 (16)	1.20 (15)
C(17)	4.43 (17)	4.73 (19)	4.03 (15)	2.22 (15)	1.03 (13)	1.02 (13)
Cl(18)	4.36 (5)	9.13 (7)	5.73 (5)	3.55 (5)	1.69 (4)	2.23 (5)
Cl(19)	4.49 (5)	10.21 (8)	5.03 (5)	3.70 (5)	1.20 (4)	1.35 (5)
O(20)	7.46 (20)	5.91 (18)	14.43 (26)	1.88 (15)	3.06 (18)	-1.30 (17)
O(21)	6.53 (14)	6.56 (15)	6.18 (13)	3.17 (12)	2.44 (11)	0.99 (11)

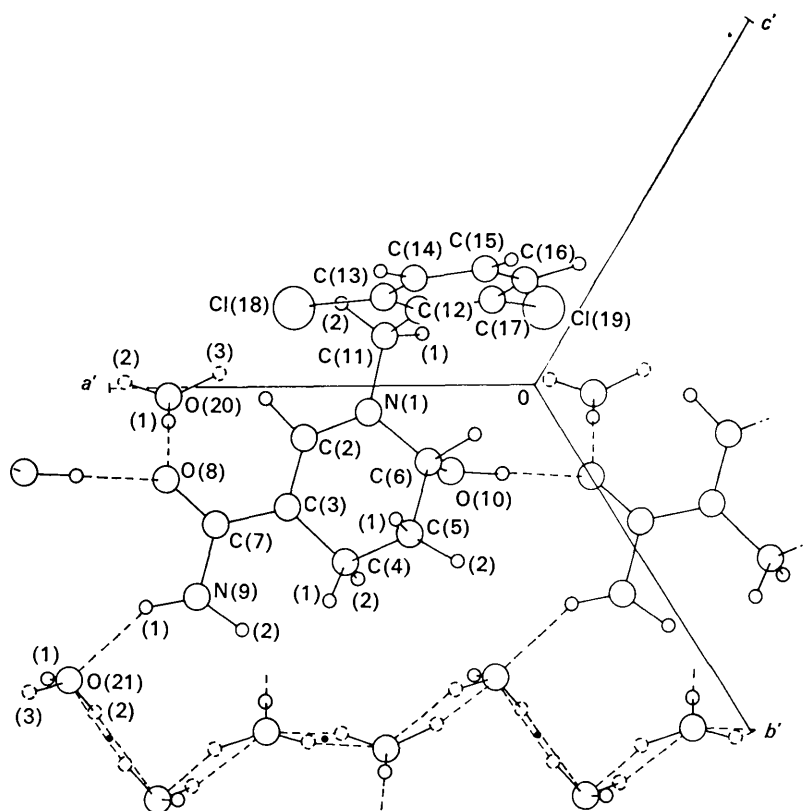


Fig. 1. Projection of the structure on the plane through the planar portion of the tetrahydrocannabinol. Hydrogen bonds are indicated by broken lines. The numbering system adopted is indicated. Broken circles represent 'half' hydrogen atoms.



Table 3 (cont.)

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atomic form factors were those given by Hanson, Herman, Lea & Skillman (1964). The  $R$  index is defined by  $R = \Sigma ||F_o| - |F_c|| / \Sigma |F_o|$ .

### The structure

The main object of this study was the determination of the molecular structure of the 'primary acid modification' product (hydration product) of 1-(2,6-dichlorobenzyl)-1,4-dihydronicotinamide. The representation of the structure in Fig. 1 clearly identifies the product as 1-(2,6-dichlorobenzyl)-6-hydroxy-1,4,5,6-tetrahydronicotinamide.

Initially it was not intended to carry the investigation much beyond the point where the molecular structure had been securely established. However, since the refinement proceeded very smoothly and eventually led to a quite satisfactory agreement between observed and calculated structure factors, and also to reasonably low estimated standard deviations for the structural parameters, it is considered appropriate to describe the results in some detail.

Fig. 2(a) represents a projection of the structure along the  $a$  axis, ('top view') and Fig. 2(b) a projection along a direction in the  $ab$  plane and perpendicular to  $a$  ('front view'). From the positional parameters given in Table 1 the 'uncorrected' distances in Fig. 3(a), the distances given in Table 4, and the angles given in Fig. 3(b) and in Table 5 were calculated. The numbering system used is indicated in Fig. 1. For hydrogen atoms the first two digits designate the 'heavy' atoms to which they are attached.

Table 4. *Interatomic distances (from parameters in Table 1) involving hydrogen atoms, and hydrogen bond distances*

E. s. d.'s are about 0.004 Å for 'heavy atom' distances and 0.03–0.04 Å for distances involving H atoms.

C(2)—H(021)	1.051 Å	C(11)—H(112)	1.059 Å
C(4)—H(041)	0.995	C(14)—H(141)	1.097
C(4)—H(042)	0.960	C(15)—H(151)	1.132
C(5)—H(051)	1.140	C(16)—H(161)	1.094
C(5)—H(052)	1.065	O(20)···O(20')	2.647
C(6)—H(061)	1.116	O(20)···O(21')	2.715
O(8)···O(10')	2.714	O(20)—H(201)	0.805
O(8)···O(20)	2.718	O(20)—H(202)	0.886
N(9)···O(21)	2.971	O(20)—H(203)	0.877
N(9)—H(091)	1.027	O(21)···O(21')	2.813
N(9)—H(092)	1.064	O(21)—H(211)	0.877
O(10)—H(101)	0.994	O(21)—H(212)	0.787
C(11)—H(111)	1.078	O(21)—H(213)	0.735

In an analysis of the thermal motion of the molecule (Schomaker & Trueblood, 1968), the two main parts of the molecule, the tetrahydronicotinamide moiety and the dichlorobenzyl moiety (atoms N(1) through C(11), and C(11) through Cl(19) respectively), were treated as separate rigid bodies. In both groups the translational motion was indicated to be reasonably isotropic. For the nicotinamide group the largest root mean square librational amplitude was 4.7° and the

Table 5. *Bond angles involving H atoms*  
E. s. d.'s are about 1.7–2.0° for one H atom and 2.5–2.8° for angles involving two H atoms.

N(1)—C(2)—H(021)	116.0°
C(3)—C(2)—H(021)	119.3
C(3)—C(4)—H(041)	105.6
C(3)—C(4)—H(042)	113.5
C(5)—C(4)—H(041)	106.3
C(5)—C(4)—H(042)	108.1
H(041)—C(4)—H(042)	113.7
C(4)—C(5)—H(051)	107.6
C(4)—C(5)—H(052)	118.6
C(6)—C(5)—H(051)	106.1
C(6)—C(5)—H(052)	101.3
H(051)—C(5)—H(052)	111.2

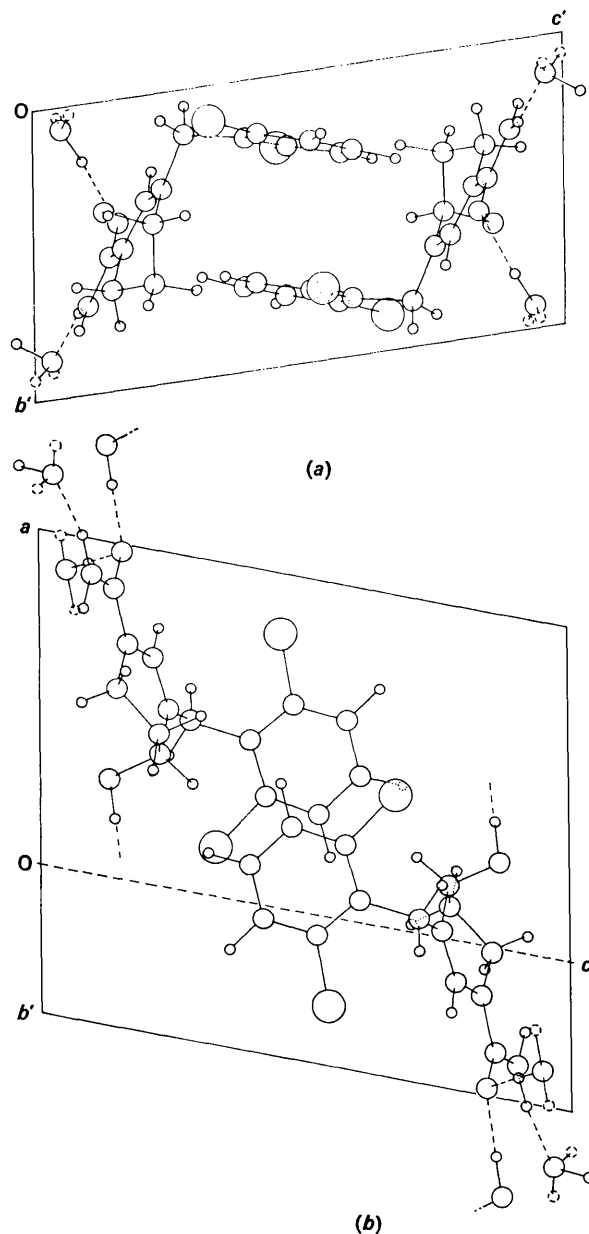


Fig. 2. (a) Projection along the  $a$  axis. (b) Projection along a direction in the  $ab$  plane, normal to  $a$ .

Table 5 (cont.)

N(1)—C(6)—H(061)	107.1
C(5)—C(6)—H(061)	114.8
O(10)—C(6)—H(061)	105.2
C(7)—N(9)—H(091)	118.4
C(7)—N(9)—H(092)	112.8
H(091)—N(9)—H(092)	128.7
C(6)—O(10)—H(101)	105.9
N(1)—C(11)—H(111)	103.4
N(1)—C(11)—H(112)	113.7
C(12)—C(11)—H(111)	106.5
C(12)—C(11)—H(112)	108.1
H(111)—C(11)—H(112)	113.8
C(13)—C(14)—H(141)	120.3
C(15)—C(14)—H(141)	121.3
C(14)—C(15)—H(151)	118.2
C(16)—C(15)—H(151)	120.9
C(15)—C(16)—H(161)	119.9
C(17)—C(16)—H(161)	120.6

smallest  $2.0^\circ$ . The r.m.s. difference between  $U_{ij}$  derived from 'observed' temperature parameters and those calculated from the rigid body model was  $3.5 \cdot 10^{-3} \text{ \AA}^2$ , or about 5–10% of 'observed'  $U_{ii}$ . Corresponding values for the dichlorobenzyl group were  $5.4^\circ$  and  $2.9^\circ$  for the librational amplitudes, and  $2 \cdot 10^{-3} \text{ \AA}^2$  for the r.m.s. deviation. It is thus indicated that the rigid body ap-

proximation is satisfactory for the two parts taken separately. The major librational axis in the benzyl group is roughly parallel to the axis C(12)—C(15), causing rather large amplitudes for the motion of the two Cl atoms in the  $b$  axis direction, in correspondence with the large  $B_{22}$  values found for these atoms.

Based on parameters arrived at in the analysis of the thermal motion, corrected distances were computed (Cruickshank, 1961). The results are given in Fig. 3(a) as 'corrected' distances. Most corrections were in the range between  $0.004 \text{ \AA}$  and  $0.007 \text{ \AA}$ . Corrections to bond angles were quite small and therefore are not listed.

#### The tetrahydronicotinamide group

Fig. 1 represents a projection of the structure on the plane defined by atoms N(1) through C(11), with the exception of C(5) and O(10). The normal form of the equation of this plane is  $1.276x + 2.276y + 10.554z = 4.134 \text{ (\AA)}$ . Individual deviations for the atoms defining the plane are all below  $0.04 \text{ \AA}$ , testifying to the essential planarity of this large group. We note, however, that some of the deviations from the plane are of the order of ten e.s.d.'s. A plane defined by N(1), C(2), C(3), C(4) and C(6) has the equation  $1.351x + 2.385y + 10.359z =$

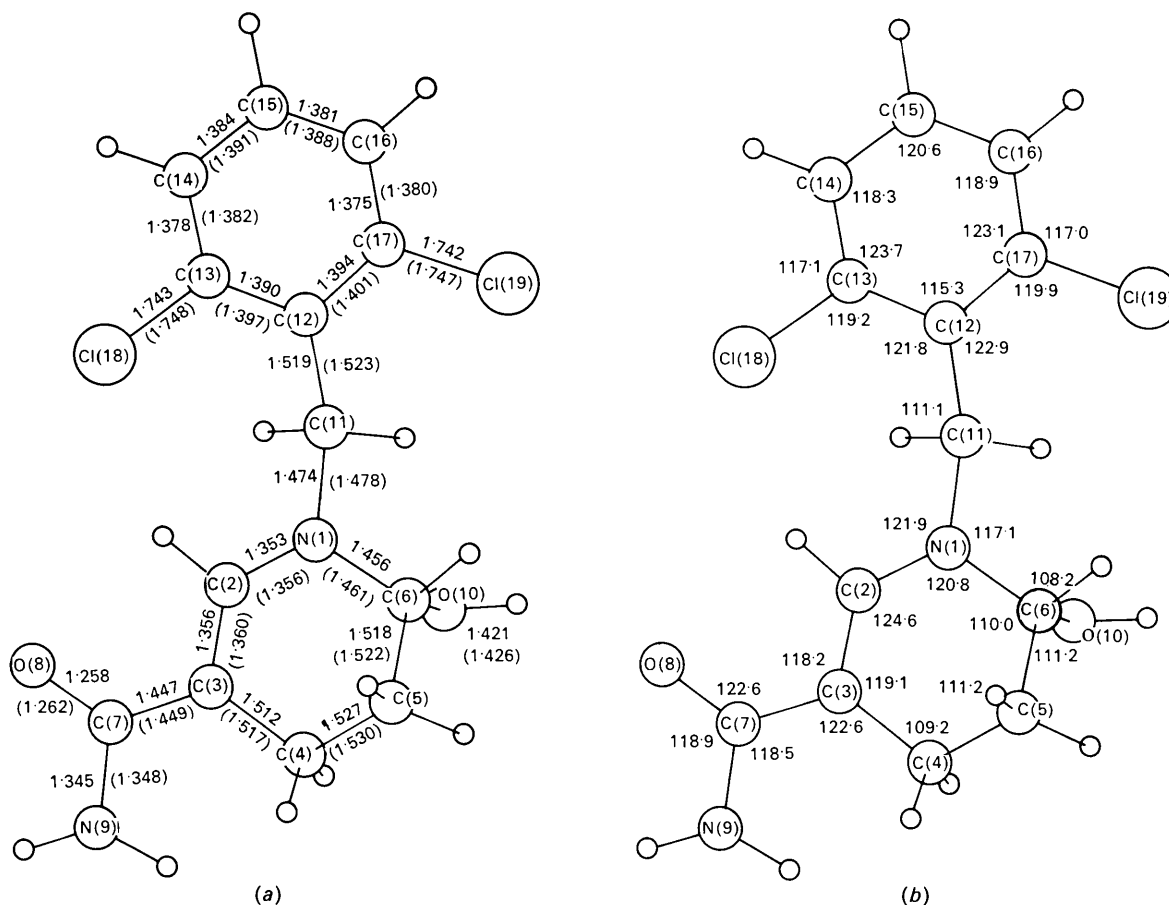


Fig. 3. (a) Interatomic distances (from parameters in Table 1), and (in parentheses) interatomic distances corrected for anisotropic thermal motion effects. E.s.d.'s are about  $0.004 \text{ \AA}$ . (b) Bond angles (uncorrected). E.s.d.'s are about  $0.3^\circ$ .



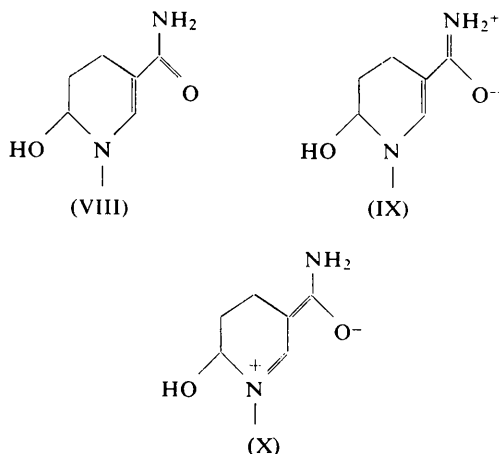
4.208 (Å), with individual deviations 0.006, -0.002, -0.002, 0.003, and -0.004 Å respectively for these atoms. Other deviations are: C(7), 0.033; O(8), 0.031; and N(9), 0.095 Å, indicating that the amide group is bent slightly upwards at the NH<sub>2</sub> end; finally, the distance to C(11) is -0.100 Å.

The only large-scale puckering of the tetrahydronicotinamide ring is the displacement of C(5) by 0.64 Å above the ring plane defined above. The hydroxyl oxygen is in a pseudo-axial position, 1.33 Å below this plane.

Coplanarity of the amide group with the ring is also found in 1-benzyl-1,4-dihydronicotinamide (Karle, 1961), but not in nicotinamide, where the amide group is twisted about 40° out of plane (Wright & King, 1954).

An impression of the orientation of the two rings relative to each other may be obtained from Fig. 1. The torsion angles C(6)-N(1)-C(11)-C(12) and N(1)-C(11)-C(12)-C(17) are 68.5° and 101.5° respectively. We note that this places H(111) near the nicotinamide plane, and H(112) near the benzene ring plane.

It appears that the structure of the tetrahydronicotinamide moiety can be described in terms of the three valence bond structures VIII, IX and X, with VIII as the largest contributor, but with significant contributions also from IX and X. The very nearly planar arrangement around N(1) presumably is caused by a



delocalization of electrons from this atom into a conjugated system extending from N(1) through C(2), C(3) and the amide group. The bonds N(1)-C(6) and N(1)-C(11) are essentially normal C-N single bonds in length, while the distance N(1)-C(2) is considerably shorter (1.356 Å), and the C(2)-C(3) double bond is somewhat longer than the double bond of 1.340 Å in ethylene. The distances within the amide group are in the neighborhood of those found in other amides. (A compilation for a number of amides is given by Bracher & Small, 1967). There are, however, a couple of differences worth noting. The C=O distance is slightly longer than in the previously investigated amides, approaching the value of 1.270 Å ob-

served in urea (Caron & Donohue, 1964). Another, and more marked, difference from other amide structures is found in the N-C-O angle which is nearly 4° smaller than the average of those quoted by Bracher & Small. The contribution from X, which cannot participate in these other structures, is in keeping with this observation. In the same connection we note that the distance C(3)-C(7) is only 1.449 Å, somewhat shorter than the single bond in butadiene (1.467 Å) (Haugen & Trætterberg, 1966). The difference between the two internal angles N(1)-C(2)-C(3) and C(2)-C(3)-C(4) (124.6° and 119.1° respectively) is quite interesting. The cause for this difference is not all clear, although it seems that the short distances from C(2) to both N(1) and C(3) indicate a hybridization for C(2) with somewhat less *p* character than *sp*<sup>2</sup>. The orientation of O and NH<sub>2</sub> in the amide group relative to the ring is the same as in dihydronicotinamide (Karle, 1961) the orientation being dictated by the space requirements of the NH<sub>2</sub> group.

The distance C(6)-O(10) is the same as the average C-O(H) distance in, for example, α-L-sorbose (Kim & Rosenstein, 1967).

The H-N-H angle is observed to be 129°, and even with the e.s.d. in mind an actual value of over 120° seems to be indicated. The mean H-C-H angle observed in the molecule is 113°.

#### The dichlorobenzyl group

The plane defined by the six carbon atoms in the benzene ring has the equation  $0.638x - 7.391y + 3.480z = 0.309$  (Å) with individual deviations C(12), -0.011; C(13), 0.004; C(14), 0.006; C(15), -0.009; C(16), 0.001; C(17), 0.009; C(11) - 0.073; Cl(18), 0.055; and Cl(19), 0.058 Å. The simultaneous displacement of the Cl atoms to one side and the methylene group to the other is interpreted as the result of overcrowding.

The overall shape of the benzene ring is quite interesting. Carter, McPhail & Sim (1966) made the observation that in aromatic nitro compounds the internal angle at the C atom carrying the nitro group is greater than 120°, while in aromatic amino compounds the corresponding angle is less than 120°. They linked the effect to the respective electron withdrawing and electron donating abilities of the substituents. It seems reasonable to assume that the effect is not limited to nitro and amino derivatives, so that the relationship should be expected to hold for any substituent; that is, an electron withdrawing group would cause a widening of the internal angle at the C atom to which it is attached, while an electron donating group would cause a narrowing of the corresponding angle. A striking example illustrating the effect of a strongly electron withdrawing group is found in the benzenediazonium ion, where the internal angle at the C atom carrying the -N<sub>2</sub><sup>+</sup> group is 124.5° (Rømme, 1963). A deviation in the other direction, due to a methinyl group, is seen in 2-phenyl-1,3-dithiane where the angle at the C atom to which the dithiane

ring is attached is  $118.8^\circ$  (Kalf & Romers, 1966), in accordance with the relative electron donating ability of the methinyl group.

In the present structure we find angles of  $123.1^\circ$  and  $123.7^\circ$  at C(13) and C(17) respectively, while the angle at C(12) is  $115.3^\circ$ . The large deviation from the regular  $120^\circ$  angle at C(12) must result from a combination of a narrowing due to the C(11) methylene and from the narrowing which takes place to compensate for the widening at C(13) and C(17). The distances within the benzene ring vary between 1.380 Å and 1.401 Å, but in a quite symmetric way, in that the average C(CH<sub>2</sub>)-C(Cl) distance is 1.399 Å, C(H)-C(H) 1.390 Å and C(Cl)-C(H) 1.381 Å, where each step between the averages given corresponds to about three e.s.d.'s.

The two C-Cl distances are observed to be slightly, and probably insignificantly, longer than the value  $\sim 1.74$  Å found for other C(aromatic)-Cl distances (Sakurai, Sundaralingam & Jeffrey, 1963; Palenik, Donohue & Trueblood, 1968). (It is to be hoped that a value of about 1.74 Å will soon gain access to compilations of bond distances, rather than the remarkably persistent value of 1.71 Å listed for the standard C(arom)-Cl distance; e.g. Sutton, 1965.)

The distance C(11)-C(12) (1.523 Å) is slightly longer than usually found for C(sp<sup>2</sup>)-C(sp<sup>3</sup>) bonds, presumably related to the peculiar internal angle at C(12).

#### Hydrogen bonding

In Fig. 1 the main features of the hydrogen bonding system are indicated, with hydrogen bonds being shown as broken lines. The molecules are linked together in long chains by linear hydrogen bonds (2.71 Å) between O(10) in one molecule and O(8) in the next. The 'water of hydration' molecules are arranged like a ribbon twisting around the *a* axis, with hydrogen bonds O(8)···O(20) (2.72 Å) and N(9)···O(21) (2.97 Å) constituting the linkages between the chain of organic molecules and the 'ribbon' of water molecules.

Half the hydrogen bonds between water molecules go across a center of symmetry, thereby leaving one with a choice between either a symmetric hydrogen bond or a disordered one. A symmetric bond would be rather unusual, and the difference maps calculated gave no indication of this type of bond. The interpretation of the difference maps was not overwhelmingly clear, but with some good will an arrangement with one ordered hydrogen atom and one randomly distributed over two positions, could be imagined for each water molecule. It should be understood, however, that other interpretations of the distribution of H atoms could conceivably fit the present data. The matter is also complicated somewhat by the behavior of O(20), which exhibits a large anisotropy in its temperature factor, probably due to some degree of disorder of that atom.

Although the described type structure seems to be rather uncommon, a few other organic molecules

crystallizing with water of hydration have been found to contain a somewhat similar chain of water molecules hydrogen bonded to the main molecules. Examples are biuret hydrate (Hughes, Yakel & Freeman, 1961), thymine hydrate (Gerdil, 1961) and caffeine hydrate (Gerdil & Marsh, 1960). Common to these structures and to the present one is the observation that the water can be quite easily removed, and that this causes the structure to collapse. There are also indications that in some compounds the amount of water may not be entirely stoichiometric; and although in the crystal investigated here there was no indication of a significant deviation from the assumed water content, it seems reasonable to assume that the structure might tolerate a fair number of missing water molecules.

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#### References

- ANDERSON, A. G. & BERKELHAMMER, G. (1958). *J. Amer. Chem. Soc.* **80**, 992.
- BRACHER, B. H. & SMALL, R. W. H. (1967). *Acta Cryst.* **23**, 410.
- BURTON, R. M. & KAPLAN, N. O. (1963). *Archiv. Biochem. Biophys.* **101**, 139.
- CARON, A. & DONOHUE, J. (1964). *Acta Cryst.* **17**, 544.
- CARTER, O. L., MCPHAIL, A. T. & SIM, G. A. (1966). *J. Chem. Soc. A*, 822.
- CRUICKSHANK, D. W. J. (1961). *Acta Cryst.* **14**, 896.
- DIEKMANN, H., ENGLERT, G. & WALLENFELS, K. (1964). *Tetrahedron*, **20**, 281.
- GERDIL, R. (1961). *Acta Cryst.* **14**, 333.
- GERDIL, R. & MARSH, R. E. (1960). *Acta Cryst.* **13**, 166.
- HANSON, H. P., HERMAN, F., LEA, J. D. & SKILLMAN, S. (1964). *Acta Cryst.* **17**, 1040.
- HAUGEN, W. & TRÆTTEBERG, M. (1966). *Acta Chem. Scand.* **20**, 1726.
- HOPE, H. & CHRISTENSEN, A. T. (1968). *Acta Cryst.* **B24**, 375.
- HUGHES, E. W. (1941). *J. Amer. Chem. Soc.* **63**, 1737.
- HUGHES, E. W., YAKEL, H. L. & FREEMAN, H. C. (1961). *Acta Cryst.* **14**, 345.
- KALFF, H. T. & ROMERS, C. (1966). *Acta Cryst.* **20**, 490.
- KARLE, I. L. (1961). *Acta Cryst.* **14**, 497.
- KIM, C. S. Y. & CHAYKIN, S. (1968). *Biochem.* **7**, 2339.
- KIM, S. H. & ROSENSTEIN, R. D. (1967). *Acta Cryst.* **22**, 648.
- PALENIK, G. J., DONOHUE, J. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* **24**, 1139.
- RØMMING, C. (1963). *Acta Chem. Scand.* **17**, 1444.
- SAKURAI, T., SUNDARALINGAM, M. & JEFFREY, G. A. (1963). *Acta Cryst.* **16**, 354.
- SCHOMAKER, V. & TRUEBLOOD, K. N. (1968). *Acta Cryst.* **B24**, 63.
- SEGAL, R. & STEIN, G. (1960). *J. Chem. Soc.* p. 5254.
- SUTTON, L. E. (1965). *Tables of Interatomic Distances*. London: The Chemical Society.
- WARBURG, O. & CHRISTIAN, W. (1934). *Biochem. Z.* **274**, 112.
- WRIGHT, W. B. & KING, G. S. D. (1954). *Acta Cryst.* **7**, 283.