

## The Crystal Structure of Acetanilide

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The structure of crystalline acetanilide has been determined from its X-ray diffraction pattern. The crystals are orthorhombic with  $a = 19.640$ ,  $b = 9.483$ , and  $c = 7.979$  Å, and space group  $Pbca$ . The trial structure was deduced from the packing and was checked by the use of polarized infra-red radiation. The approximate atomic co-ordinates were refined by standard three-dimensional Fourier syntheses, utilizing finally 1,513 experimental structure amplitudes. Corrections were made for termination of series errors by computing an  $F_c$  synthesis. Molecules of acetanilide are linked together in chains by N-H-O hydrogen bonds of length 2.969 Å. A single molecule lies approximately in two planes, one containing the aniline portion, and the other the acetyl group, inclined to each other at  $37^\circ 54'$ . Slight distortions occur owing to steric hindrance. Hydrogen atoms, including that in the hydrogen bond, have been located by difference syntheses, and the geometry of the molecule has been examined in some detail.

### Introduction

During the course of some work on polarized infra-red radiation by Crooks (1947) in these laboratories, it was found that acetanilide crystals were very suitable for examination; they could readily be crystallized from the melt in a parallel growth as thin sheets between rocksalt plates, and they exhibited dichroism in several absorption bands. These phenomena could not be correlated with the bonds in the molecules as the structure was then unknown. For this reason, an X-ray examination was carried out, and the trial structure derived from a limited amount of X-ray diffraction data confirmed the molecular disposition suggested by the infra-red dichroism. This trial structure was partially refined and a short note describing it has already been published (Brown & Corbridge, 1948).

The structure presented a number of points of interest, such as the acetyl group which might be expected to bear some resemblance to the peptide portion of amino acids and proteins, and whether the molecules in the crystal exist in the amido or imidol form. To elucidate these, a full three-dimensional determination of the structure was undertaken.

### Morphology and optical properties

Crystals of acetanilide with slightly different habit were grown from a variety of solvents. From water, very thin {100} plates were formed, with bounding faces {010}, {001} and {011}. From xylene bipyramids {111} separated, truncated by {100} faces, while from ethanol all forms could be obtained by varying the conditions. From the melt, crystals grew elongated

along [b] with {100} tabular; this form was used in the infra-red work. The crystals used in the X-ray work were grown from aqueous ethanol as fairly large {100} plates about 0.5 mm. thick, and suitable sections were cut as required.

The cleavage was perfect parallel to the tabular {100} faces, and fairly good parallel to {001}.

Optical data given by Winchell (1943) are

$$\alpha = 1.51, \beta = 1.62, \gamma = 1.73, 2V = 88^\circ.$$

The indices were re-determined roughly and found to be in agreement. The  $\gamma$  vibration direction is parallel to [a], and the plane of the optic axes is {010}.

### Unit cell and space group

The unit-cell dimensions, obtained by the method described by Farquhar & Lipson (1946), using the van Arkel film mounting, were

$$a = 19.640, b = 9.483, \text{ and } c = 7.979 \text{ \AA}.$$

These give axial ratios

$$a:b:c = 2.071:1:0.841,$$

in agreement with Winchell's (1943) value

$$2.067:1:0.842.$$

The experimental specific gravity, determined by flotation, was 1.206, while that calculated, assuming eight molecules per unit cell, is 1.207. Observed extinctions were {0kl} for  $k$  odd, {h0l} for  $l$  odd and {hk0} for  $h$  odd, whence the space group is unambiguously  $Pbca-D_{2h}^{15}$ .

### Experimental

X-ray intensity data were obtained in the first place from [c] oscillation photographs, and later from Weis-

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senberg moving-film photographs about the three principal axes. Multiple films were used, and the intensities of the reflexions were estimated visually by comparison with a time-exposure calibrated film strip. The  $[c]$  zero-layer photograph was also measured on a modified version of the scan microdensitometer described by Robertson & Dawton (1941). The various batches of films and layers were related and corrected for geometrical and polarization factors in the usual way. The structure amplitudes were placed on the absolute scale by comparison with the calculated values in the later stages of the analysis. In all, reflexions from 1,513 planes were observed. A few reflexions observable with  $\text{Cu } K\alpha$  radiation were missed owing to the geometrical limitations of the Weissenberg camera, but allowance was made for these in the final refinement by the termination-of-series corrections.

### Determination of the trial structure

The trial structure was deduced mainly from considerations of packing and cleavage, and the optical properties. The molecule was expected to be roughly planar, and a model was constructed taking all the known data into account. The longest direction was placed parallel to the direction of highest refractive index, the two cleavage planes were kept free from interlocking groups, and, as it was known that organic crystals often grow most rapidly parallel to their hydrogen bonds, these were placed along  $[b]$ . This model was found to be identical with that suggested by the infra-red work of Crooks (1947), who, by considering the dichroism of the absorption bands, was able to relate the plane of the benzene ring and the direction of the  $\text{N-H}$ ,  $\text{C=O}$ ,  $\text{N-C}_6\text{H}_5$  and  $\text{C-CH}_3$  bonds to the crystal axes.

As a result of this confirmation of the molecular orientation, trial structure amplitude calculations were made for the  $\{hk0\}$  terms. The outstanding intensity of this zone was  $F(16,0,0)$ , which had a unitary structure factor  $U = 0.71$ ; and as the spacing of this plane was  $1.22 \text{ \AA}$ , it was necessary to ensure that all the atoms in the model were almost in phase. The use of an inequality  $S(16,0,0) = S(810) \cdot S(8\bar{1}0)$  indicated the phase of this structure amplitude to be negative, and it was not long before the phases of about 40 others were determined with moderate certainty. At a later stage, the method of Zachariasen (1952) was tried on this projection, and 37 out of the first 43 signs were given correctly by his probability procedure, at least sufficient to enable a start to be made in the refinement process.

### Refinement of the atomic co-ordinates

The  $x$  and  $y$  co-ordinates were refined first, using two-dimensional Fourier syntheses; it was not possible to carry this process to the limit owing to two atoms,  $\text{C}_5$  and  $\text{O}$ , overlapping with their mirror images in

projection, and a number of phases were indeterminate. Approximate  $z$  co-ordinates were obtained by geometry, assuming a planar molecule, and a sufficient number of  $F(hkl)$  were calculated to refine these values of  $z$ . It was at this stage that a preliminary note describing the structure was published (Brown & Corbridge, 1948). It was found after this that further refinement of  $z$  was impossible, and this was due to all values of  $x$  being  $0.25$  in error, a wrong origin having been chosen. When this was corrected, refinement proceeded without difficulty until the phases of all  $F(hkl)$  with  $l = 1, 2$  and  $3$  were known. These terms were then used in two bounded projections (Booth, 1948) in order to improve the  $x$  and  $y$  co-ordinates, particularly of the overlapping atoms.

Finally, all  $F(hkl)$  were calculated from the best  $x$ ,  $y$  and  $z$  obtained from the three-dimensional line syntheses and the bounded projections. The phases were used with all experimental values of the structure amplitudes, and three-dimensional lines and sections were computed for each atom separately. The result of this, in the form of a composite electron-density map, is shown in Fig. 1. The same three-dimensional

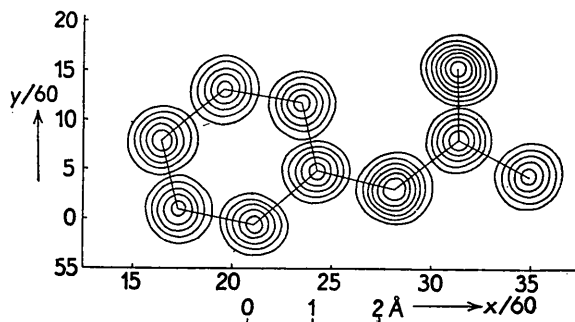


Fig. 1. Composite three-dimensional electron-density map of acetanilide. The lowest contour is  $2 \text{ e.}\text{\AA}^{-3}$  and subsequent contours are at intervals of  $1 \text{ e.}\text{\AA}^{-3}$ .

lines and sections were then re-calculated with the same phases but with calculated structure amplitudes to allow for possible errors due to the artificial termination of the Fourier series and a few omitted terms. These corrections were only slight: in two cases  $0.003$ , in two cases  $0.002$ , in thirteen cases  $0.001$ , and the remaining thirteen co-ordinates were unchanged. The corrected atomic co-ordinates are listed in Table 1. All the Fourier calculations were carried out manually

Table 1. *Final atomic co-ordinates*

	$x$	$y$	$z$
$\text{C}_1$	0.407	0.077	0.130
$\text{C}_2$	0.357	1.983	0.171
$\text{C}_3$	0.290	0.005	0.112
$\text{C}_4$	0.276	0.118	0.011
$\text{C}_5$	0.328	0.213	1.969
$\text{C}_6$	0.394	0.190	0.025
$\text{C}_7$	0.526	0.134	0.214
$\text{C}_8$	0.586	0.080	0.305
$\text{N}$	0.473	0.048	0.196
$\text{O}$	0.524	0.257	0.167

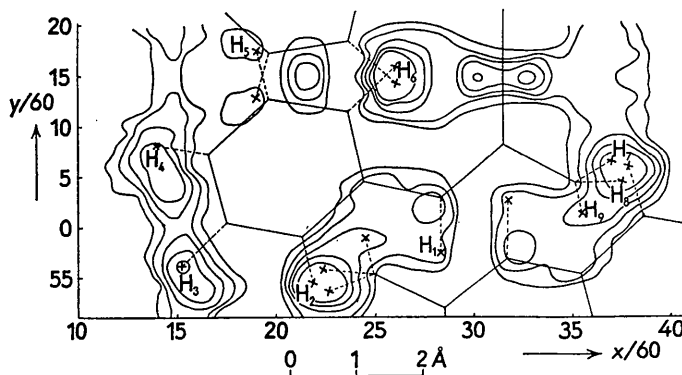


Fig. 2. Difference projection along  $[c]$  showing electron density associated with hydrogen atoms. The contours are at intervals of  $0.2 \text{ e.}\text{\AA}^{-2}$ .

using Beavers-Lipson strips, the summations being computed at intervals of  $1/120$ th of the cell edges.

### Location of hydrogen atoms

A difference projection, using as coefficients  $F(hk0)_o - F(hk0)_c$ , was computed, resulting in the electron-density contour map shown in Fig. 2. There is positive density in the neighbourhood of the places where hydrogen atoms are expected, but the peaks are not of sufficiently good resolution to enable their centres to be marked precisely. Therefore, theoretical co-ordinates were assigned to the hydrogen atoms, assuming C-H and N-H distances to be  $1.06 \text{ \AA}$ . These values are given in Table 2.

Table 2. Co-ordinates of hydrogen atoms (calculated)

	$x$	$y$	$z$
H <sub>1</sub> (attached to N)	0.474	$\bar{1}.941$	0.242
H <sub>2</sub> (attached to C <sub>2</sub> )	0.368	$\bar{1}.895$	0.248
H <sub>3</sub> (attached to C <sub>3</sub> )	0.250	$\bar{1}.934$	0.141
H <sub>4</sub> (attached to C <sub>4</sub> )	0.226	0.134	$\bar{1}.965$
H <sub>5</sub> (attached to C <sub>5</sub> )	0.317	0.301	$\bar{1}.892$
H <sub>6</sub> (attached to C <sub>6</sub> )	0.434	0.261	$\bar{1}.996$
H <sub>7</sub> (attached to C <sub>7</sub> )	0.611	0.121	0.430
H <sub>8</sub> (attached to C <sub>8</sub> )	0.611	0.121	0.210
H <sub>9</sub> (attached to C <sub>9</sub> )	0.587	$\bar{1}.974$	0.320

In order to confirm the position of the hydrogen atom attached to the nitrogen atom, a three-dimensional section, using all the  $F(hkl)$  terms, was computed at  $x = 0.525$ , which is the plane almost exactly parallel

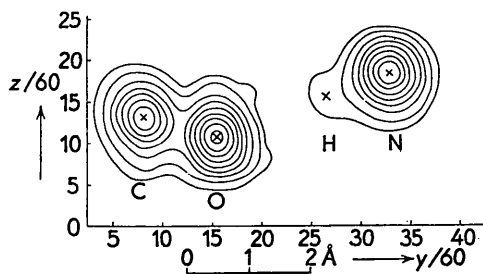


Fig. 3. Three-dimensional section at  $x = 0.525$ , in the plane of the hydrogen bond.

to the hydrogen bond ( $x$  for C<sub>7</sub> =  $0.526$ , for O =  $0.524$ , and for N' =  $0.527$ ). The section is shown in Fig. 3, and the position of the hydrogen atom is clearly discernible, indicating that crystalline acetanilide

exists in the amido  $-\text{N}-\overset{\text{O}}{\parallel}{\text{C}}-$  and not the imidol  $-\text{N}=\overset{\text{OH}}{\text{C}}-$  form.

### Structure-amplitude calculations

The structure amplitudes were calculated in the usual way from the final set of atomic co-ordinates, allowing nitrogen to have  $7/6$  and oxygen  $4/3$  times the scattering power of carbon. The ratio of the experimental structure amplitudes to the geometrical structure factors was plotted against  $\sin \theta/\lambda$  for each plane in order to determine an experimental scattering-factor curve. There was evidence of slight anisotropy, but as no very useful purpose appeared to be served by investigating this more fully, a mean temperature factor was chosen with  $B = 5.0 \text{ \AA}^2$ . The values of  $f_C$  and  $f_H$  used are given in Table 3.

Table 3. Atomic scattering factors

$\sin \theta/\lambda$	0	0.1	0.2	0.3	0.4	0.5	0.6	0.7
$\frac{\partial f_C}{\partial f_H}$	48.0	38.3	25.2	13.3	6.9	3.9	2.3	1.4
$\frac{\partial f_H}{\partial f_C}$	8.0	6.1	3.1	1.2	0.4	—	—	—

Hydrogen atoms were included in the calculations for all planes with spacing greater than  $1.25 \text{ \AA}$ . Below this limit their contribution to the structure amplitudes was negligible. The usual residual  $R$ , summed over all the 1,513 planes, omitting those where  $F_o = 0$ , amounts to  $11.2\%$ . Tables of structure amplitude agreement are omitted from this paper for reasons of economy, but are available for inspection on application to the authors.

Certain of the strongest planes, viz: (111), (021), (121), (221), (102), (202), (112), (212), (022) and (122), were found to be affected by extinction, the experimental  $F$ 's being appreciably lower than the calculated in each case. As it was considered that any mathe-

matical correction for this extinction would, in any case, be somewhat empirical,  $F_c$  was substituted for  $F_o$  for these terms in the final Fourier synthesis. The good agreement amongst all the other structure amplitudes appeared to be adequate justification for this procedure.

### Description of the structure

The crystal structure of acetanilide consists of discrete molecules linked together in chains by single hydrogen bonds. Adjoining hydrogen-bonded molecules are related by screw axes parallel to  $[b]$ . The whole unit cell contains eight molecules related by the space-group symmetry  $Pbca$ , thereby requiring no symmetry in the molecule. The bond lengths and inter-bond angles derived from the final atomic co-ordinates are shown in Fig. 4. The length of the hydrogen bond

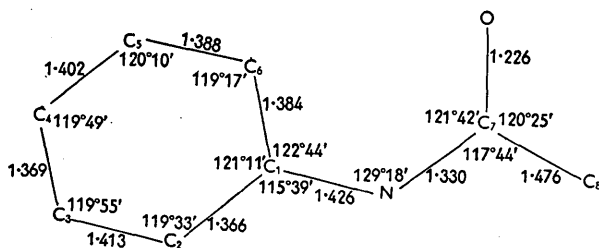


Fig. 4. Diagrammatic representation of the molecule of acetanilide, showing bond lengths and inter-bond angles.

$N-H-O$  is 2.969 Å. The angles which this bond makes with adjacent covalent bonds are  $C_7-O-N = 141^\circ$  and  $O-N-C_7 = 126^\circ$ .

The planarity of the benzene ring was tested by evaluating the mean plane through the six carbon atoms by least squares. This was found to be

$$x - 2.658y - 3.897z = 2.086,$$

from which the atoms were displaced by the following amounts:

$$C_1 - 0.017; C_2 + 0.008; C_3 - 0.002; C_4 + 0.002; \\ C_5 - 0.011 \text{ and } C_6 + 0.016 \text{ \AA.}$$

The nitrogen atom is  $-0.023$  Å out of this plane, which, being in the same sense as the displacement of  $C_1$ , indicates that the ring may be slightly distorted from strict planarity. If this were so, it would seem from consideration of the magnitude of the displacements that the disturbance occurs mostly at  $C_6$  and may possibly be due to the proximity of the oxygen atom of the same molecule, which is only 2.85 Å away. This idea was tested by evaluating the mean plane through atoms  $C_1, C_2, C_3, C_4, C_5$  and  $N$  by least squares. This was

$$x - 2.542y - 3.769z = 2.246,$$

from which the displacements were:

$$C_1 - 0.002; C_2 + 0.009; C_3 - 0.005; C_4 + 0.006; \\ C_5 + 0.005; C_6 + 0.039 \text{ and } N - 0.002 \text{ \AA.}$$

The system  $C_1C_2C_3C_4C_5N$  is thus much more planar than the system  $C_1C_2C_3C_4C_5C_6$ , the sum of the squares being only  $175 \times 10^{-6}$  compared with  $738 \times 10^{-6}$ .

The displacement of  $C_6$  from the mean plane is therefore real, and is due to the steric interaction between  $H_6$  and  $O$  in the same molecule. It would appear that there are restoring forces tending to keep the whole molecule planar, arising from resonance or  $\pi$ -electron orbitals, but if it were planar, atoms  $H_6$  and  $O$  would be impossibly close. The situation is relieved in three ways: (a) the depression of  $C_6$  and  $H_6$  out of the plane of the benzene ring; (b) the increase in the angles at  $C_1, N$  and  $C_7$  from  $120^\circ$  each to  $122^\circ 44', 129^\circ 18'$  and  $121^\circ 42'$  respectively; and (c) the rotation of the acetyl group about the  $C_1-N$  bond.

The equation of the mean plane through the acetyl group was evaluated by least squares through  $N, C_7, O$  and  $C_8$  to be

$$x - 0.771y - 2.278z = 5.514,$$

from which the atomic displacements are

$$N - 0.004; C_7 + 0.029; O - 0.005 \text{ and } C_8 - 0.002 \text{ \AA.}$$

This shows that the planarity of the acetyl group is only approximate, the central carbon atom being very slightly pyramidal. This distortion is almost certainly connected with the steric hindrance between  $H_6$  and  $O$ , whereby the oxygen atom is displaced slightly from the natural plane of the acetyl group. The plane through  $N, C_7, O$  and  $C_8$  and the plane through  $C_1, C_2, C_3, C_4, C_5$  and  $N$  intersect at an angle of  $37^\circ 54'$ .

The bond lengths within the molecule call for some comment. At first sight the bonds in the benzene ring were thought to be highly irregular, ranging in length from 1.366 to 1.413 Å. There is some evidence that the benzene ring, which was until recently always regarded as a plane regular hexagon, and has in the last year or two been shown to be not necessarily planar (e.g. Brown, 1953*a, b*; McIntosh, Robertson & Vand, 1952) may not necessarily be regular either. In the structure of salicylic acid, for example, (Cochran, 1953) the lengths vary from 1.369 to 1.414 Å, and the accuracy of the structure determination has been carried so far as to leave no doubt that the variations are real. It may well be that in finer analyses such occurrences will be common, and it is hoped that when sufficient experimental data are available, adequate theoretical treatment will be given.

The  $C_1-N$  bond (1.426 Å) is shorter than the sum of the covalent atomic radii, but this shortening always occurs when a nitrogen atom is attached to a benzene ring; a summary of corresponding lengths in other compounds has already been given (Brown, 1949). Similarly, the  $N-C_7$  bond (1.330 Å) is short, but it is in good agreement with determinations of similar 'peptide' linkages in numerous other compounds. A list of this and other dimensions of the amide group in peptides and related compounds has recently been given (Smits & Wiebenga, 1953), and Pauling, Corey

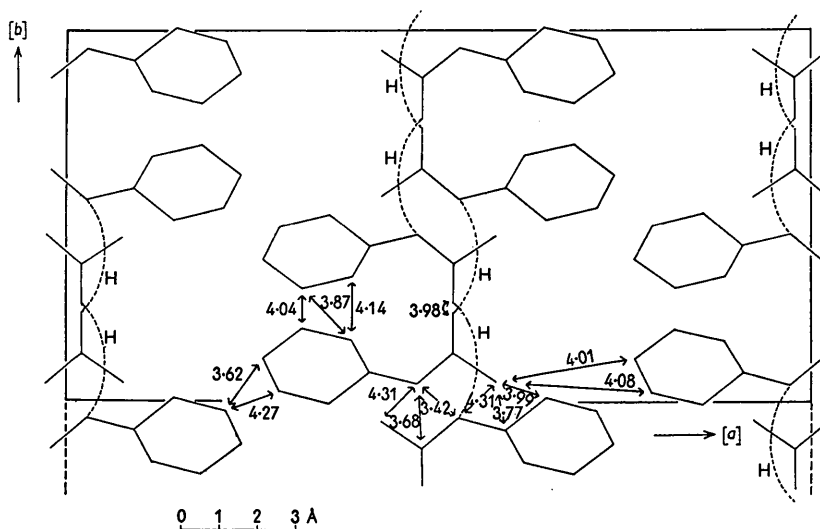


Fig. 5. Projection of unit cell of acetanilide, showing packing and intermolecular contacts.

& Branson (1951) have assumed 1.32 Å as standard for this bond in their exploratory work on proteins.

The C=O bond is normal, but the C<sub>7</sub>-C<sub>8</sub> bond length (1.476 Å) is rather surprisingly low. It would seem that hyperconjugation is the only likely explanation of this shortening. A rapid calculation of this effect (by G. R. Lester) shows that a standard C-C bond of length 1.54 Å is reduced by approximately 0.03 Å when adjacent to a carbonyl group; e.g. in acetyl-glycine (Carpenter & Donohue, 1950) the experimental value is 1.50 Å. No value entirely comparable with that found in acetanilide is available, but it is not unreasonable to expect that the additional resonating system of a benzene ring would reduce the length still further.

Intermolecular contacts are of the usual order. The closest approach is between nitrogen atoms related by a centre of symmetry (3.42 Å), and there are several others from 3.62 Å upwards which are shown in Fig. 5. The terminal methyl group is 4.01 Å from the end of the benzene ring of the adjacent molecule along [a].

#### The accuracy of the determination

An assessment of the accuracy was made by applying the treatment described by Cruickshank (1949). The standard deviation of the atomic co-ordinates, derived by the equation

$$\sigma(x) = \frac{2\pi\sqrt{\{\sum h^2(F_o - F_c)^2\}}}{aVC(x)},$$

is  $\sigma(x) = \sigma(y) = \sigma(z) = 0.0039$  Å for the carbon atoms and 0.0029 Å for the oxygen. This compares very favourably with other recent determinations where the lowest values reported are 0.0050 Å for carbon and 0.0044 Å for oxygen. Lists of values of standard deviations have been given by Jeffrey & Cruickshank (1953).

The standard deviation of a bond is  $\sqrt{2}(\sigma_x) = 0.0056$  Å and hence the Gaussian probable error is  $\pm 0.004$  Å. Whether these figures have any significance in relation to the absolute accuracy of the structure is not certain, particularly as the atomic coordinates are not determined to as many places of decimals. But they are quoted here as a matter of interest to indicate the order of accuracy attained, which is believed to be the best in the absence of electronic computing.

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