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Structure of α,α-Dichloro-4′-nitroacetanilide, $C_8H_6Cl_2N_2O_3$

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Abstract. $M_r = 249{\cdot}07$, monoclinic, space group $P2_1/c$, $a = 7{\cdot}966$ (2), $b = 13{\cdot}985$ (10), $c = 9{\cdot}301$ (2) Å, $\beta = 92{\cdot}55$ (2)°, $V = 1035$ (1) Å^3, $Z = 4$, $D_m = 1{\cdot}611$, $D_x = 1{\cdot}598$ Mg m^{-3}, λ(Mo $K\alpha$) = 0·7107 Å, $\mu = 0{\cdot}61$ mm^{-1}, $F(000) = 504$, $T = 297$ K. $R = 0{\cdot}039$ for 1526 'observed' reflections. The structure is compared with those of chloramphenicol and other nitroaromatic hydrocarbons. The acetanilide side chain is in the extended conformation. Intermolecular N(acetanilide)–H(N)···O(keto) hydrogen bonds between the two molecules related by a *c*-glide plane stabilize the structure.

Introduction. Structural studies of the broad-spectrum antibiotic chloramphenicol, D-(−)-*threo*-2,2-dichloro-*N*-[2-hydroxy-1-(hydroxymethyl)-2-(4-nitrophenyl)ethyl]-acetamide, and a number of related compounds have not yet led to any definite conclusion about the correlation between the structure and biological activity of this widely used drug. The efficacy of chloramphenicol appears to be unaffected by the replacement of the *p*-nitro group by other organic radicals, while nitro substitution at the *o* or *m* position results in diminished biological activity (Morris & Smith, 1954; Rebstock, Stratton & Bambas, 1955).

The dichloroacetanilides also exhibit significant antiamœbic and antifungal properties. The dichloroacetamide unit (−NHCOCHCl$_2$) when introduced into heterocyclic carriers has resulted in the synthesis of some reputed antiamœbic agents (Woodruft, Bell & Schofielo, 1956). The present compound, with dichloroacetamido and nitro groups in *p* positions of the benzene nucleus, has been synthesized with the intention of studying it as a structural analogue of chloramphenicol.

Experimental. Needle-shaped crystals from ethanol, initial cell parameters and symmetry from oscillation and Weissenberg photographs, systematic absences $h0l$, $l = 2n + 1$, and $0k0$, $k = 2n + 1$, crystal size: 0·40 × 0·55 × 0·35 mm, cell parameters refined by least-squares fit of 25 reflections ($14 \le \theta \le 18°$); intensity data measured on Enraf–Nonius CAD-4 diffractometer using graphite-monochromatized Mo $K\alpha$ radiation, 1901 unique reflections measured ($2° \le \theta \le 25°$, $-9 \le h \le 9$, $0 \le k \le 16$, $0 \le l \le 11$), 1526 'observed' [$I \ge 3\sigma(I)$], correction for Lp, absorption ignored, intensity variation (<1·5%) corrected for; Cl atoms located from Patterson synthesis, other non-H atoms from a chlorine-phased difference Fourier synthesis, full-matrix least-squares refinement on F (Busing, Martin & Levy, 1962), non-H anisotropic and H (located from ΔF synthesis) isotropic, $R = 0{\cdot}039$* ('observed' reflections), $R_w = 0{\cdot}061$, $w = 1/\sigma^2(|F_o|)$, R(all reflections) = 0·047, maximum shift/error <0·01, peak heights in the range −0·31 to 0·35 e Å^{-3} in final ΔF synthesis, scattering factors for non-H atoms from Cromer & Waber (1965), H from Stewart, Davidson & Simpson (1965), anomalous-dispersion correction for all non-H atoms from *International Tables for X-ray Crystallography* (1974).

Discussion. A view of the molecule together with the atom-numbering scheme is shown in Fig. 1. The final atomic parameters are listed in Table 1, while Table 2 lists the intramolecular bond distances and angles together with some selected torsion angles.

The C(1)—N(1) bond length is shorter than the corresponding bond length, 1·417 (2) Å, in *N*-methyl-2,4,6-trinitroacetanilide (Christoph & Fleischer, 1973). In the present compound the dihedral angle between the

* Lists of structure factors, anisotropic thermal parameters, atomic parameters of H atoms and least-squares planes with deviations of atoms from them have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 39675 (18 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

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amide group and the benzene ring is 31·4° which results in a π overlap of about 73% ($\cos^2 31{\cdot}4°$) of maximum, whereas in *N*-methyl-2,4,6-trinitroacetanilide it is only about 25% of maximum (Christoph & Fleischer, 1973).

The shortening of the N(1)–C(7) single bond, similar to that observed in the peptide linkage (Marsh & Donohue, 1967), is also present in the chloramphenicol molecule (Ravindra Acharya, Sake Gowda & Post, 1979).

The observed dissymmetry in the angles around C(7) may be explained as resulting from the steric repulsion between the oxygen atom, O(1), and the two bulky groups on either side of it. The configuration about the carbon is, however, planar. Such dissymmetry is also observed in chloramphenicol (Ravindra Acharya *et al.*, 1979).

The C(4)–N(2) bond length of 1·466 (4) Å is shorter than the corresponding bond length found in *N*-methyl-2,4,6-trinitroacetanilide (Christoph & Fleischer, 1973) and in a number of other nitroaromatic hydrocarbons (Trotter, 1960). Similar shortening is also present in chloramphenicol (Chatterjee, Dattagupta, Saha, Saenger & Muller, 1979).

The slight widening in the endocyclic angle in the phenyl ring *ipso* to the nitro group is obviously an effect of the electron-withdrawing property of the latter. Such widening is also observed in chloramphenicol (Chatterjee *et al.*, 1979; Ravindra Acharya *et al.*, 1979), and in *N*-methyl-2,4,6-trinitroacetanilide (Christoph & Fleischer, 1973).

The acetanilide side chain is in the extended conformation with C(8) *trans* to C(1) and O(1) *cis* to C(1), which is the usual geometry of the *trans* peptide linkage. The terminal dichloromethyl group assumes the expected staggered conformation with respect to O(1) and N(1). The phenyl ring is essentially planar, with N(1) and N(2) deviating by −0·02 (2) and −0·04 (3) Å, respectively, from the least-squares plane.

The amide nitrogen, N(1), forms a hydrogen bond with the keto oxygen, O(1), of a glide-related molecule [N(1)–H(N) = 0·77 (2), N(1)···O(1) (x, $\frac{1}{2}-y$, $-\frac{1}{2}+z$) = 3·003 (2), H(N)···O(1) (x, $\frac{1}{2}-y$, $-\frac{1}{2}+z$) = 2·23 (2) Å, N(1)–H(N)···O(1) = 171 (1)°]. The molecules are thus seen to form infinite hydrogen-bonded chains extended along the **c** direction. The packing of the molecules viewed down the *b* axis is shown in Fig. 2.

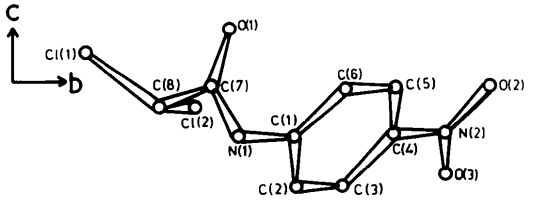

Fig. 1. View of the molecule down the *a* axis.

Table 1. *Fractional atomic coordinates and equivalent isotropic temperature factors (Hamilton, 1959) with e.s.d.'s in parentheses for the non-hydrogen atoms*

	x	y	z	B_{eq}(Å²)
Cl(1)	0·10408 (9)	0·10215 (4)	−0·03466 (8)	5·39
Cl(2)	0·30736 (9)	0·25120 (5)	−0·15053 (12)	7·67
N(1)	−0·1058 (2)	0·3117 (1)	−0·2242 (2)	3·28
N(2)	−0·6008 (3)	0·5963 (2)	−0·2168 (3)	5·76
O(1)	−0·0276 (2)	0·3008 (1)	0·0120 (2)	4·90
O(2)	−0·5900 (3)	0·6572 (1)	−0·1231 (2)	7·07
O(3)	−0·7135 (3)	0·5939 (2)	−0·3061 (4)	10·43
C(1)	−0·2266 (3)	0·3847 (1)	−0·2202 (2)	3·12
C(2)	−0·3577 (3)	0·3839 (2)	−0·3227 (3)	4·15
C(3)	−0·4804 (3)	0·4527 (2)	−0·3215 (3)	4·82
C(4)	−0·4690 (3)	0·5233 (2)	−0·2195 (3)	4·16
C(5)	−0·3373 (3)	0·5276 (2)	−0·1191 (3)	4·21
C(6)	−0·2160 (3)	0·4574 (2)	−0·1188 (2)	3·83
C(7)	−0·0177 (3)	0·2750 (1)	−0·1121 (2)	3·23
C(8)	0·1071 (3)	0·1984 (2)	−0·1540 (2)	3·65

Table 2. *Bond distances* (Å), *bond angles* (°) *and selected torsion angles* (°)

Cl(1)–C(8)	1·746 (3)	O(3)–N(2)	1·196 (4)
Cl(2)–C(8)	1·757 (3)	C(1)–C(2)	1·382 (3)
N(1)–C(1)	1·405 (2)	C(1)–C(6)	1·387 (3)
N(1)–C(7)	1·333 (3)	C(2)–C(3)	1·372 (4)
N(2)–C(4)	1·466 (4)	C(3)–C(4)	1·370 (4)
O(1)–C(7)	1·215 (3)	C(4)–C(5)	1·374 (4)
O(2)–N(2)	1·219 (3)	C(5)–C(6)	1·377 (4)

C(1)–N(1)–C(7)	126·6 (2)	N(2)–C(4)–C(5)	118·9 (2)
O(2)–N(2)–O(3)	122·9 (3)	C(3)–C(4)–C(5)	121·8 (2)
O(2)–N(2)–C(4)	118·1 (2)	C(4)–C(5)–C(6)	119·0 (2)
O(3)–N(2)–C(4)	119·0 (3)	C(1)–C(6)–C(5)	120·0 (2)
N(1)–C(1)–C(2)	118·2 (2)	O(1)–C(7)–N(1)	125·0 (2)
N(1)–C(1)–C(6)	122·0 (2)	O(1)–C(7)–C(8)	121·5 (2)
C(2)–C(1)–C(6)	119·7 (2)	N(1)–C(7)–C(8)	113·4 (2)
C(1)–C(2)–C(3)	120·4 (2)	Cl(1)–C(8)–Cl(2)	110·5 (1)
C(2)–C(3)–C(4)	119·1 (2)	Cl(1)–C(8)–C(7)	110·6 (2)
N(2)–C(4)–C(3)	119·3 (2)	Cl(2)–C(8)–C(7)	107·6 (2)

C(1)–N(1)–C(7)–C(8)	−178·3 (2)
C(1)–N(1)–C(7)–O(1)	−1·1 (3)
N(1)–C(7)–C(8)–Cl(1)	−137·4 (2)
N(1)–C(7)–C(8)–Cl(2)	101·8 (2)
O(1)–C(7)–C(8)–Cl(1)	45·2 (2)
O(1)–C(7)–C(8)–Cl(2)	−75·6 (2)

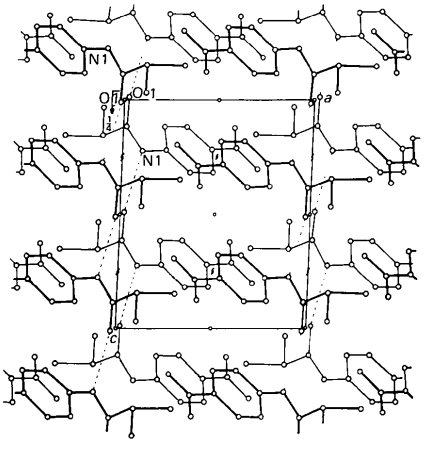

Fig. 2. Projection of the crystal structure down the *b* axis.

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Structure of 4-Hydroxy-3-phenylbutanamide Monohydrate, $C_{10}H_{13}NO_2.H_2O$*

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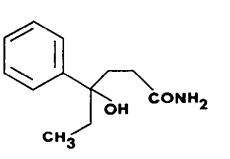
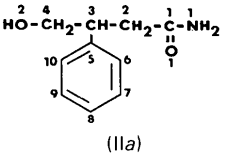
Abstract. $M_r = 197{\cdot}2$, monoclinic, $C2/c$, $a = 16{\cdot}546$ (5), $b = 6{\cdot}445$ (2), $c = 19{\cdot}936$ (5) Å, $\beta = 100{\cdot}77$ (2)°, $V = 2089$ (1) Å^3, $Z = 8$, $D_x = 1{\cdot}25$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, $\mu = 0{\cdot}726$ mm^{-1}, $F(000) = 848$, $T = 293$ K. Final $R = 0{\cdot}039$ for 1313 observed reflections. The X-ray study confirms that in the solid state the structure of the title compound is similar to that inferred from chemical and spectroscopic evidence. Steric hindrance from different chemical groups is minimized by the adoption of a staggered configuration at the central C(2)—C(3) bond. The crystal structure is stabilized by a three-dimensional network of O—H···O and N—H···O hydrogen bonds.

Introduction. Crystal structure studies on a series of derivatives of the anticonvulsant molecule γ-hydroxy-γ-phenylcaproamide (I) (4-hydroxy-4-phenylhexanamide) (Carvajal, Russek, Tapia & Massieu, 1964; Joseph-Nathan, Massieu, Carvajal & Tapia, 1978) have been undertaken in our laboratory to investigate the influence of different substituents on its pharmacological activity.

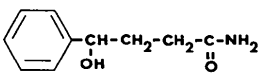
4-Hydroxy-3-phenylbutanamide (II*a*) and 4-hydroxy-4-phenylbutanamide (II*b*) were obtained by condensation of styrene oxide with malonic ester in the presence of sodium ethoxide, followed by successive hydrolysis and decarboxylation of the resulting product and preparation of the amide derivative (Bavin, Hansell & Spickett, 1964).



(I)



(II*a*)



(II*b*)

X-ray analysis of (II*a*) was undertaken to confirm the proposed structure and to obtain details of its molecular conformation.

Experimental. Cube-shaped crystal 0·32 × 0·37 × 0·34 mm, Nicolet *R*3 four-circle diffractometer, graphite-monochromated Cu $K\alpha$, lattice parameters from 15 machine-centered reflections with $10{\cdot}9 < 2\theta < 24{\cdot}6°$; 1610 reflections with $3 < 2\theta < 115°$ for two octants, 1313 independent with $I > 2{\cdot}5\sigma(I)$, index range h ±17, k 0/6, l 0/21, ω-scan mode, variable scan speed, scan width 1·0°(θ), two standard reflections monitored every 50 measurements, Lp correction, absorption ignored; structure solved by direct methods using *SHELXTL* (Sheldrick, 1981); least-squares refinement of all non-H atoms treated anisotropically, H atoms riding on the bonded C, coordinates of H atoms bonded to N and O refined with fixed isotropic temperature factor $U = 0{\cdot}06$ Å^2, function minimized $\sum w(\Delta F)^2$, $w = 1/[\sigma^2(F_o) + 0{\cdot}001 \times (F_o)^2]^{-1}$, $(\Delta/\sigma)_{max.} = 0{\cdot}5$; residual electron

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