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Structure of Spiro[1,3-dioxane-2,3′-indolin]-2′-one

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Abstract. $C_{11}H_{11}NO_3$, $M_r = 205{\cdot}21$, monoclinic, $P2_1/a$, $a = 12{\cdot}524\,(1)$, $b = 8{\cdot}576\,(1)$, $c = 9{\cdot}5470\,(4)$ Å, $\beta = 103{\cdot}27\,(2)°$, $V = 998{\cdot}0\,(4)$ Å^3, $Z = 4$, $D_m = 1{\cdot}370$, $D_x = 1{\cdot}366$ Mg m^{-3}, λ(Cu $K\alpha$) = 1·5418 Å, μ = 0·79 mm^{-1}, $F(000) = 432$, $T = 298$ K, $R = 0{\cdot}05$ for 1511 observed reflections. The amide group exhibits delocalization of the π-electrons over the three atoms (N, C and O). The six-membered ring is perfectly planar, whereas the five-membered ring deviates slightly from planarity, and they are inclined at 1·7 (2)° to one another. The dioxane ring is in a chair conformation and is almost perpendicular [88·5 (1)°] to the indolinone group. The bond linking the C(=O) atom to the tetrahedral C atom is a single bond. The crystal structure is stabilized by a three-dimensional network of N(1)—H(N1)···O(1) hydrogen bonds.

Introduction. Anti-epileptic drugs have diverse chemical structures and complex physiological and pharmacological actions. The search for potential anti-epileptic drugs and their mechanism of action has been difficult because of their complexity. There is no single mechanism to explain the action of all anti-epileptic drugs. Some of these drugs have specific modes of action but others have not yet been linked with a specific binding site within the brain. A series of spiro[1,3-dioxane-2,3′-indolin]-2′-ones and structural analogues active against electrically and chemically induced seizures have been studied. These compounds have structural features quite different from the most popular anti-epileptic drugs *viz.* carbamazepine, phenytoin, phenobarbital and diphenylhydantoin. But usually one carbonyl group and a nitrogen heteroatomic system (a cyclic amide) are common in all these structures.

The X-ray analysis of the present compound was undertaken as part of a project to search for common conformational features which may help in understanding the mechanism of action of such compounds at the molecular level.

Experimental. Single crystals of the compound were prepared by slow evaporation of an ethanol solution at room temperature. Prismatic crystals appeared after two weeks. D_m by flotation (tribromoethane–bromoform). Space group and preliminary unit-cell dimensions determined from Weissenberg photographs. A crystal with dimensions 0·44 × 0·32 × 0·26 mm used, Rigaku AFC-5 diffractometer operating at 40 kV and 200 mA, graphite-monochromatized Cu $K\alpha$ radiation. Accurate cell parameters and orientation angles determined by least-squares refinement of 25 reflections with $14 < \theta < 20°$. The intensity data were colleted by $2\theta/\omega$ scan, scan rate 6° min^{-1}, scan range $(1{\cdot}2 + 0{\cdot}15\tan\theta)°$, $2\theta_{\max} = 125°$. 1596 reflections measured with $h = -14$ to 14, $k = 0$ to 9, $l = 0$ to 11. Three reference reflections monitored after every 2 h of X-ray exposure time showed no crystal movement or decay. Intensities corrected for Lorentz and polarization effects, but no absorption correction was applied. 1511 reflections with $|F_o| > 4\sigma(F_o)$ observed.

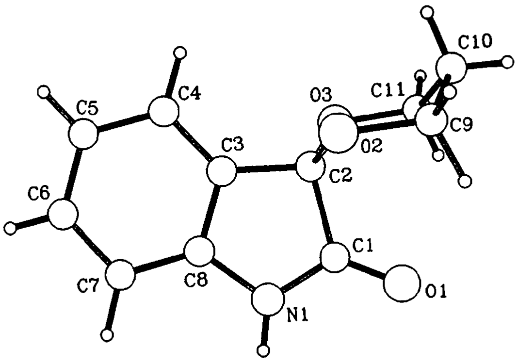

Fig. 1. Perspective view of the molecule showing the atomic labelling scheme.

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The structure was solved by direct methods using *SHELXS*86 (Sheldrick, 1985) and refined on F by the full-matrix least-squares technique (*SHELX*76; Sheldrick, 1976). [Function minimized: $\sum w(F_o - F_c)^2$.] Non-H-atom coordinates were refined with anisotropic thermal parameters; H-atom coordinates were located by ΔF synthesis and refined isotropically. Final $R = 0{\cdot}056$, $wR = 0{\cdot}056$, $S = 0{\cdot}90$ for 1511 observed reflections, $w = 1/(\sigma^2|F_o|)$, 180 parameters refined. Max. Δ/σ in the final refinement cycle is 0·04. Max. and min. peak heights in difference Fourier map were 0·26 and $-0{\cdot}32$ e Å^{-3}. Atomic scattering factors were those incorporated in *SHELX*76. The geometrical parameters of the molecule were computed with program *PLATON* (Spek, 1990).

Discussion. A perspective view of the molecule together with the atom-labelling 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.

It is observed that the lone pair of electrons on the N atom N(1) is involved in conjugation with the carbonyl group. This is indicated by the slight lengthening of the C═O double bond [1·224 (4) Å] and the concomitant shortening of the two N—C(sp^2) single bonds [1·352 (5) and 1·412 (4) Å] (Codding, Lee & Richardson, 1984). The angles subtended at nitrogen are C(1)—N(1)—C(8) = 112·0 (3), C(8)—N(1)—H(N1) = 120 and C(1)—N(1)—H(N1) = 128°. Accordingly, the state of hybridization of the N atom is sp^2 as shown by the sum (360°) of the angles around it and from the perfect planarity of the plane C(1), O(1), N(1), C(8). Similar effects have also been observed in other structures (James & Williams, 1972; De, 1990; De & Kusunoki, 1991; Codding, Lee & Richardson, 1984).

The C—NH—CO—C grouping resembles a *cis* peptide bond. Six atoms of this group are within 0·002 Å from the best least-squares plane defined by the non-H members. The OC—N bond distance [1·352 (5) Å] is not as short as the normal peptide bond (1·325 Å; Dickerson & Geis, 1969) and there is also some distortion in the bond angles. This may be due to the cyclic nature of the system which hinders the favourable overlapping of atomic orbitals.

The indolinone group is nearly planar since the six-membered ring is perfectly planar ($\chi^2 = 4{\cdot}1$) (Stout & Jensen, 1968) and the five-membered ring is quasi-planar ($\chi^2 = 42{\cdot}8$). The five- and six-membered rings are inclined to one another at 1·7 (2)°. The dioxane ring is in the chair conformation and makes an angle of 88·6 (2)° with the six-membered ring and 88·7 (2)° with the five-membered ring. It is almost perpendicular to the indolinone group [88·5 (1)°].

Table 1. *Fractional atomic coordinates and equivalent isotropic thermal parameters* (Å^2) *for the non-*H *atoms with their e.s.d.'s in parentheses*

$$U_{eq} = (1/3)\textstyle\sum_i\sum_j U_{ij}a_i^*a_j^*\mathbf{a}_i.\mathbf{a}_j.$$

	x	y	z	U_{eq}
O(1)	0·4175 (2)	0·4965 (3)	0·3108 (3)	0·0584 (9)
O(2)	0·3307 (2)	0·1763 (3)	0·1907 (2)	0·0387 (7)
O(3)	0·4625 (2)	0·2786 (3)	0·0758 (2)	0·0399 (8)
N(1)	0·5381 (2)	0·3159 (3)	0·4356 (3)	0·0416 (10)
C(1)	0·4612 (3)	0·3680 (4)	0·3218 (4)	0·0406 (11)
C(2)	0·4390 (3)	0·2334 (4)	0·2076 (3)	0·0342 (10)
C(3)	0·5172 (3)	0·1098 (4)	0·2796 (3)	0·0330 (10)
C(4)	0·5368 (3)	−0·0385 (4)	0·2348 (4)	0·0421 (12)
C(5)	0·6117 (3)	−0·1312 (5)	0·3285 (4)	0·0490 (12)
C(6)	0·6642 (3)	−0·0776 (5)	0·4631 (4)	0·0490 (12)
C(7)	0·6455 (3)	0·0720 (4)	0·5090 (4)	0·0444 (11)
C(8)	0·5715 (3)	0·1621 (4)	0·4146 (4)	0·0358 (10)
C(9)	0·2468 (3)	0·2830 (5)	0·1145 (5)	0·0494 (14)
C(10)	0·2692 (3)	0·3219 (5)	−0·0294 (5)	0·0529 (16)
C(11)	0·3842 (3)	0·3873 (5)	−0·0073 (4)	0·0491 (12)

Table 2. *Bond distances* (Å) *and angles* (°) *with their e.s.d.'s in parentheses*

O(1)—C(1)	1·224 (4)	O(2)—C(2)	1·416 (5)
O(2)—C(9)	1·456 (5)	O(3)—C(2)	1·411 (4)
O(3)—C(11)	1·450 (5)	N(1)—C(1)	1·352 (5)
N(1)—C(8)	1·412 (4)	C(1)—C(2)	1·568 (5)
C(2)—C(3)	1·499 (5)	C(3)—C(4)	1·382 (5)
C(3)—C(8)	1·387 (5)	C(4)—C(5)	1·388 (5)
C(5)—C(6)	1·381 (5)	C(6)—C(7)	1·393 (5)
C(7)—C(8)	1·373 (5)	C(9)—C(10)	1·501 (6)
C(10)—C(11)	1·515 (6)		

C(2)—O(2)—C(9)	113·7 (3)	C(2)—O(3)—C(11)	114·3 (3)
C(1)—N(1)—C(8)	112·0 (3)	O(1)—C(1)—N(1)	126·1 (3)
O(1)—C(1)—C(2)	126·8 (3)	N(1)—C(1)—C(2)	107·2 (3)
O(2)—C(2)—O(3)	112·6 (2)	O(2)—C(2)—C(1)	110·2 (3)
O(2)—C(2)—C(3)	108·4 (3)	O(3)—C(2)—C(1)	112·2 (3)
O(3)—C(2)—C(3)	110·8 (3)	C(1)—C(2)—C(3)	102·1 (3)
C(2)—C(3)—C(4)	130·8 (3)	C(2)—C(3)—C(8)	109·1 (3)
C(4)—C(3)—C(8)	120·1 (3)	C(3)—C(4)—C(5)	118·0 (3)
C(4)—C(5)—C(6)	121·1 (4)	C(5)—C(6)—C(7)	121·4 (4)
C(6)—C(7)—C(8)	116·7 (3)	N(1)—C(8)—C(3)	109·6 (3)
N(1)—C(8)—C(7)	127·6 (3)	C(3)—C(8)—C(7)	122·8 (3)
O(2)—C(9)—C(10)	109·4 (3)	C(9)—C(10)—C(11)	109·0 (3)
O(3)—C(11)—C(10)	109·9 (3)		

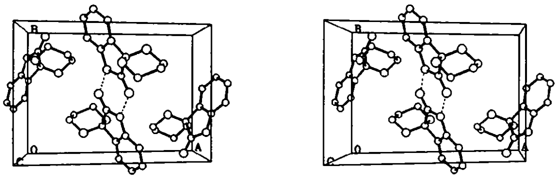

Fig. 2. Stereoview (*PLUTO*; Motherwell & Clegg, 1978) of the packing of the molecule.

The carbonyl C atom to tetrahedral C atom bond distance is typically a single bond. The C(2)—C(3)

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* Lists of structure factors, anisotropic thermal parameters, least-squares planes and H-atom parameters have been deposited with the British Library Document Supply Centre as Supplementary Publication No. SUP 54170 (11 pp.). Copies may be obtained through The Technical Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

bond distance [1·499 (5) Å] appears very short for a C—C single bond value but exactly the same as found in other indolinone nuclei (Itai, Iitaka & Kubo, 1978; De, 1990; Chakraborty & Talapatra, 1985).

A stereoscopic view of the packing of the molecule is shown in Fig. 2. The amide N atom N(1), forms a hydrogen bond with the carbonyl O atom O(1) in the molecule related by the centre of symmetry at the origin [N(1)—H(N1) = 0·87 (4); N(1)···O(1) ($-x$, $-y$, $-z$) = 2·853 (4); H(N1)···O(1) ($-x$, $-y$, $-z$) = 2·01 (4) Å; N(1)—H(N1)···O(1) = 164°]. These bonds link the molecules in pairs around the centres of symmetry.

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Structure of Homovanillic Acid

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Abstract. 4-Hydroxy-3-methoxyphenylacetic acid, $C_9H_{10}O_4$, M_r = 182·18, orthorhombic, *Pbca*, a = 10·571 (5), b = 32·589 (3), c = 4·973 (5) Å, V = 1713 (3) Å^3, Z = 8, D_x = 1·413 Mg m^{-3}, λ(Mo $K\alpha$) = 0·71069 Å, μ = 0·105 mm^{-1}, $F(000)$ = 768, T = 296 K, R = 0·040 for 900 reflections with $I > 3\sigma(I)$. The molecule has the carboxyl side chain oriented perpendicular to the phenyl-ring plane as observed in catecholamines. A hydrogen bond between the carboxyl groups makes a centrosymmetric dimer, as usual.

Introduction. Homovanillic acid (HVA) is an important dopamine metabolite produced from a deaminated metabolite of dopamine, 3,4-dihydroxyphenylacetic acid, by the catalytic action of catechol-*o*-methyltransferase (Soares-da-Silva & Garrett, 1990; Kopin, 1985; Ishimitsu & Hirose, 1981). The crystal structures of dopamine (Bergin & Carlström, 1968; Giesecke, 1980) and other related compounds (Barlow, Johnson, Howard, Walton & Koellner, 1989; Seiler, Markstein, Walkinshaw & Boelsterli, 1989) have been determined. It is also important to determine the detailed structure of dopamine metabolites for understanding its metabolic pathway. For this reason, we report here the crystal structure of homovanillic acid.

Experimental. Crystallized from 50% methanol solution (0·2 *M*) as platelets, 0·4 × 0·4 × 0·2 mm. Rigaku AFC5R automated four-circle diffractometer with graphite-monochromated Mo $K\alpha$ radiation; lattice parameters determined by least-squares fit of 2θ values of 25 reflections ($24.99 < 2\theta < 38.69°$); intensity data up to 2θ = 55·0° collected, ω scan, scan speed 32·0°(ω) min^{-1}, scan width (0·88 + 0·30tanθ)°, the ratio of peak counting time to background counting time was 2:1 at 50 kV and 180 mA; h 0–12,

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