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1*H*-Pyrrolo[2,3-*b*]pyridine-3-acetic acid as a molecular probe for use in auxin physiology

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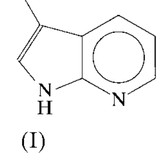
The structural characterization of 1*H*-pyrrolo[2,3-*b*]pyridine-3-acetic acid (alternative name: 7-azaindole-3-acetic acid), $C_9H_8N_2O_2$, reveals similar molecular geometry, *i.e.* with the side chain perpendicular to the 7-azaindole ring, to that of the natural plant growth hormone indole-3-acetic acid (auxin) and its alkylated and halogenated derivatives.

Comment

From the discovery of (hetero)auxin as an endogenous growth factor of grass colepotiles (Went, 1927), its gradual acceptance as a universal plant hormone (Thimann, 1977) and its eventual identification as indole-3-acetic acid (IAA; Bandurski & Schulze, 1974), a multitude of auxin-like plant growth regulators have been synthesized (Jönsson, 1961; Schneider & Wightman, 1978). In most cases, their structures deviate significantly from that of the endogenous hormone and their overall biological properties diverge accordingly. 1*H*-Pyrrolo[2,3-*b*]pyridine-3-acetic acid, (I), retains the auxin activity of IAA (Thimann, 1958) and is thus expected to bind to the proteins involved in the auxin response with about the same efficiency. The structurally similar 7-azatryptophan has been used extensively as a molecular probe in protein biochemistry, mostly exploiting the distinctive fluorescent properties contributed by the 7-azaindole ring system (Smirnov *et al.*, 1997). These properties are shared by (I) and, in conjunction with NMR spectroscopy, should enable the monitoring of auxin–protein interactions without interference from endogenous IAA. Such studies will, however, only afford readily interpretable results if the molecular size and geometry correspond closely with that of natural auxin. We show here that this is indeed the case.



(I)

Compound (I) has no stereogenic centre but crystallizes in the non-centrosymmetric group $Pna2_1$ with two conformers per asymmetric unit, *i.e.* molecules *A* and *B*. Their molecular structures differ slightly with respect to the conformation of the side chain.

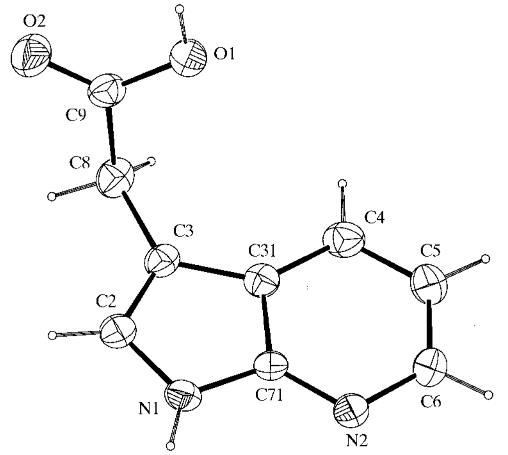


Figure 1
A molecular view of molecule *A* of (I) with the atom-numbering scheme. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

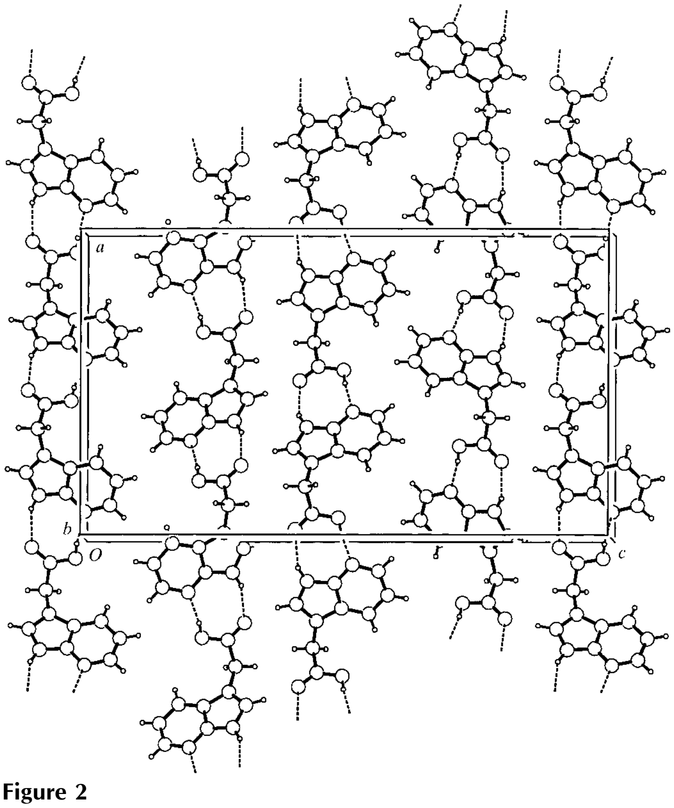


Figure 2
The crystal structure of (I), with the hydrogen-bonding scheme shown as dashed lines.

The overall conformation of the molecule can be described by two torsion angles; C2—C3—C8—C9 [91.5 (6) and 101.3 (6)° for molecules *A* and *B*, respectively; in Table 1 the suffix '2' indicates molecule *B*] defines the relative orientation of the side chain towards the aromatic plane, whereas the orientation of the carboxylic acid group is given by the angle C3—C8—C9—O2 [−119.5 (5) and −107.0 (5)° for *A* and *B*, respectively]. The aromatic 7-azaindole nucleus is planar in both molecules, with maximum deviations of 0.010 (4) (molecule *A*) and 0.007 (5) Å (molecule *B*) for C3 from the best least-squares plane defined by C31/C4/C5/C6/N2/C71/N1/C2/C3. The molecular geometry of the 7-azaindole moiety is characterized by shortening of the C6—N2 [1.345 (6) and 1.335 (6) Å in *A* and *B*, respectively] and N2—C71 bonds [1.329 (6) and 1.334 (6) Å], and shrinkage of the C6—N2—C71 angle [114.3 (4) and 114.7 (4)°]. The same type of distortion has been observed previously in the phenyl part of the indole moiety around C7, but with the substitution of C with N in (I), this distortion becomes more pronounced.

The crystal packing in (I) is determined by two types of hydrogen bond, namely N—H···O and O—H···N. These hydrogen bonds form an eight-membered ring, graph-set notation $R_2^2(8)$ (Bernstein *et al.*, 1995), between two neighbouring molecules of the same conformer (*A*...*A* and *B*...*B*). This pattern is part of infinite *C*(7) (N—H···O) and *C*(10) (O—H···N) chains which run along **a**.

Experimental

Compound (I) was synthesized from 1*H*-pyrrolo[2,3-*b*]pyridine (7-azaindole) *via* 3-(dimethylaminomethyl)-1*H*-pyrrolo[2,3-*b*]pyridine (7-azagramine) and 1*H*-pyrrolo[2,3-*b*]pyridine-3-acetonitrile (7-azaindole-3-acetonitrile; Robison & Robison, 1955, 1956). Crystals of (I) were grown by evaporation from a solution in EtOH–H_2O (1:1 *v*/*v*) over a period of 4 d. A representative crystal was selected for the crystallographic investigation reported here.

Crystal data

$C_9H_8N_2O_2$
$M_r = 176.17$
Orthorhombic, $Pna2_1$
$a = 14.9965$ (7) Å
$b = 4.2170$ (3) Å
$c = 26.022$ (1) Å
$V = 1645.64$ (15) Å^3
$Z = 8$
$D_x = 1.4222$ (1) Mg m^{-3}

Cu $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 11$–19°
$\mu = 0.860$ mm^{-1}
$T = 293$ (2) K
Needle, colourless
0.15 × 0.08 × 0.06 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan (*PLATON*97; Spek, 1997*b*)
$T_{\min} = 0.88$, $T_{\max} = 0.95$
1762 measured reflections
1584 independent reflections
992 reflections with $I > 2\sigma(I)$

$R_{\rm int} = 0.017$
$\theta_{\max} = 74.21°$
$h = -18 \rightarrow 0$
$k = -5 \rightarrow 0$
$l = 0 \rightarrow 32$
3 standard reflections every 87 reflections frequency: 180 min intensity decay: 0.8%

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1···O2$^{\rm i}$	0.86	2.04	2.840 (5)	154
O1—H1*A*···N2$^{\rm ii}$	0.82	1.85	2.662 (5)	171
N12—H12···O22$^{\rm iii}$	0.86	2.10	2.886 (5)	152
O12—H12*A*···N22$^{\rm iv}$	0.82	1.83	2.644 (5)	172

Symmetry codes: (i) $x-\frac{1}{2}, \frac{3}{2}-y, z$; (ii) $\frac{1}{2}+x, \frac{3}{2}-y, z$; (iii) $\frac{1}{2}+x, \frac{1}{2}-y, z$; (iv) $x-\frac{1}{2}, \frac{1}{2}-y, z$.

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.104$
$S = 0.908$
1584 reflections
237 parameters

H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0508P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.001$
$\Delta\rho_{\max} = 0.15$ e Å^{-3}
$\Delta\rho_{\min} = -0.20$ e Å^{-3}

All H atoms were calculated geometrically and refined using a riding model in *SHELXL*97 (Sheldrick, 1997).

Data collection: *CAD*-4 *Software* (Enraf–Nonius, 1989); cell refinement: *CAD*-4 *Software*; data reduction: *HELENA* (Spek, 1997*a*); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97; molecular graphics: *PLATON*97 (Spek, 1997*b*) and *ORTEP* (Johnson, 1965); software used to prepare material for publication: *SHELXL*97.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: AV1034). Services for accessing these data are described at the back of the journal.

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