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Pseudomerohedral twinning, pseudosymmetry and complex hydrogen-bonded sheets in 2-methoxy-4-(pyrrolo-[1,2-a]quinoxalin-4-yl)phenol

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The title compound, $C_{18}H_{14}N_2O_2$, crystallizes as a nonmerohedral twin, but the structure can be satisfactorily refined as a merohedral twin, in which a monoclinic unit cell with a cell angle β close to 90° emulates a metrically orthorhombic cell. The two molecules in the asymmetric unit are very similar in structure and they are related by an approximate pseudo-screw axis. The molecules are linked into complex sheets by a combination of two O—H···N hydrogen bonds and four C—H···O hydrogen bonds.

Comment

Pyrrolo[1,2-a]quinoxaline constitutes a privileged heterocyclic system because of its potential bioactivity; some compounds containing this system have shown antiproliferative activity against human leukaemia and breast cancer (Desplat *et al.*, 2010) and antileishmanial activity (Guillon *et al.*, 2007). They also show promise as anti-ulcer agents because they are potential bacterial multidrug resistance pump inhibitors (Vidaillac Guillon, Arpin *et al.*, 2007; Vidaillac Guillon, Moreau *et al.*, 2007). We report here the molecular and supramolecular structure of the title compound, (I), which was prepared by simple cyclocondensation of 1-(2-aminophenyl)pyrrole with an aromatic aldehyde catalysed with L-proline.

Compound (I) (Fig. 1) crystallizes with $Z' = 2$ in the centrosymmetric space group $P2_1/c$, with a unit cell having the cell angle $\beta = 90.326$ (12)°, *i.e.* fairly close to 90°. Although analysis of the reflection data indicated that (I) had crystallized as a nonmerohedral twin, the form of the twinning matrix showed that the twinning was close to merohedral, emulating a metrically orthorhombic cell. In fact, it proved possible to refine the structure either as a nonmerohedral twin using a

modified reflection file, or as a merohedral twin using an unmodifed reflection file, and we report both refinements here, denoted (Inm) and (Im) for the nonmerohedral and merohedral twin models, respectively. As the atomic coordinates and geometric parameters derived from them are extremely similar for the two refinements, we discuss here only the results of the refinement as a nonmerohedral twin.

(I)
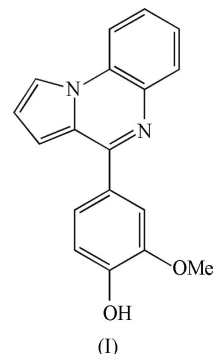
The bond lengths and angles in the two independent molecules are very similar (Table 1), and the conformations of the two molecules in the selected asymmetric unit, as indicated by the key torsion angles (Table 1), are almost identical, but a search for possible additional crystallographic symmetry revealed none. However, the coordinates of pairs of corresponding atoms in the two molecules of the selected asymmetric unit are approximately related by the transformation $(\frac{1}{2} + x, \frac{1}{2} - y, 1.36 - z)$, corresponding to an approximate, but noncrystallographic, pseudo-screw axis along the line $(x, \frac{1}{4}, 0.68)$ (Fig. 2).

Within the fused tricyclic component of the molecules, the bond distances (Table 1) indicate some interesting patterns. In the five-membered rings, the C—C distances span ranges of less than 0.04 Å, even though $Cx2—Cx3$ ($x = 1$ or 2) are formally single bonds, while $Cx1—Cx2$ and $Cx3—Cx3a$ are formally double bonds, thus indicating a degree of 6π electron delocalization in these rings. In the carbocyclic rings, the bond distances support aromatic delocalization, but with some slight bond fixation in the $Cx6—Cx7$ and $Cx8—Cx9$ bonds, while in the central rings there are clearly localized double bonds at the $Cx4—Nx5$ bonds. Overall, therefore, the pattern of two 6π circuits in the two outer rings of the fused system, with a localized double bond in the central ring, is reminiscent of the electronic structure of phenanthrene and related molecules (Glidewell & Lloyd, 1984, 1986).
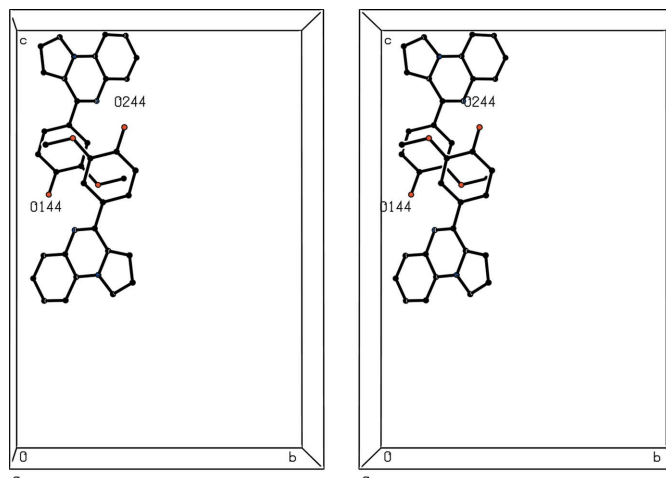
Just three torsion angles (Table 1) suffice to define the molecular conformation. In each molecule, atom $Cx47$ ($x = 1$ or 2) of the methoxy group is almost coplanar with the adjacent ring, with deviations from the mean planes of 0.102 (3) and 0.063 (3) Å for atoms C147 and C247, respectively. Accordingly, the exocyclic C—C—O angles at each atom $Cx45$ show the usual difference of *ca* 10° (Seip & Seip, 1973; Ferguson *et al.*, 1996). The pendent aryl rings make dihedral angles with the adjacent heterocyclic rings of 33.8 (2) and 35.7 (2)° in the type 1 and 2 molecules (for which $x = 1$ or 2,

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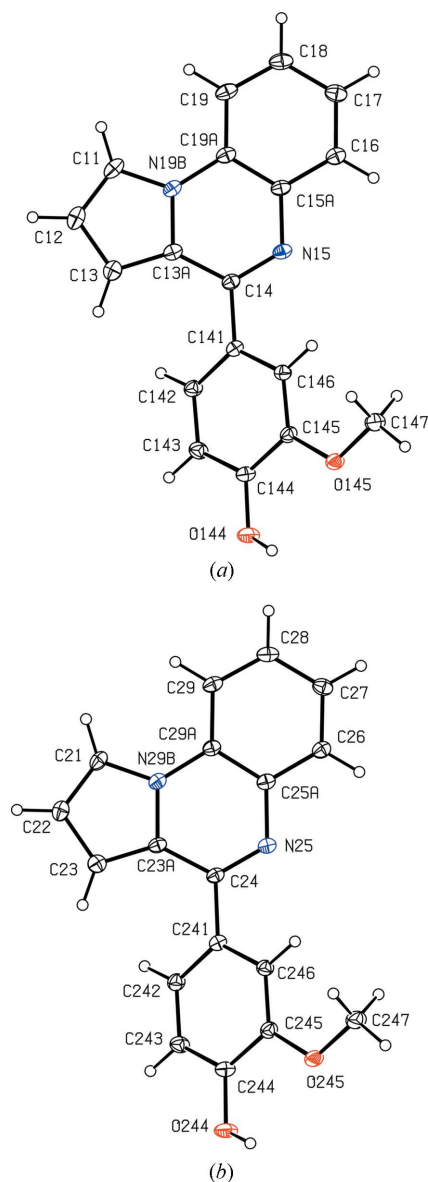
Figure 1
The independent molecular components of (I), showing the atom-labelling scheme for (a) molecule 1, containing atom N15, and (b) molecule 2, containing atom N25. Displacement ellipsoids are drawn at the 30% probability level and H atoms are shown as small spheres of arbitrary radii.

Figure 2
A stereoview of the selected asymmetric unit of (I), showing the pseudosymmetric relationship of the two independent molecules. For the sake of clarity, all H atoms have been omitted.
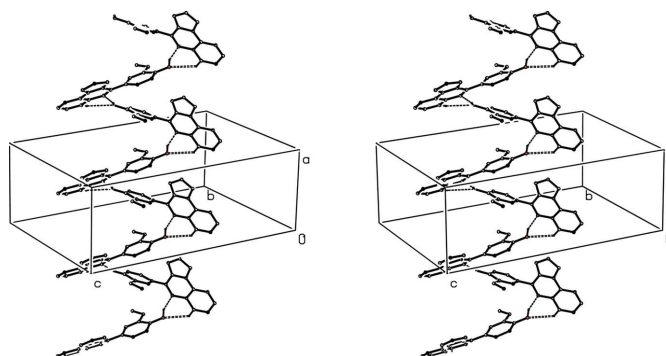
Figure 3
A stereoview of part of the crystal structure of (I), showing the formation of a chain of rings parallel to [100] and built from two O—H···N hydrogen bonds and two C—H···O hydrogen bonds. For the sake of clarity, H atoms not involved in the motifs shown have been omitted.

respectively), and even the H—O—C—C torsion angles are very similar in the two molecules. These conformations mean that the molecules have no internal symmetry, and hence that they are conformationally chiral, but the centrosymmetric space group accommodates equal numbers of the two conformational enantiomers for each type of molecule.

The supramolecular structure of (I) is built by two O—H···N hydrogen bonds and four C—H···O hydrogen bonds, which utilize all four of the O atoms present in the asymmetric unit (Table 2). The resulting sheet formation can be readily analysed in terms of two one-dimensional substructures (Ferguson *et al.*, 1998*a*,*b*; Gregson *et al.*, 2000). Just as atom O144 acts as hydrogen-bond donor to atom N25 within the

selected asymmetric unit, so also atom O244 at (x, y, z) acts as hydrogen-bond donor to atom N15 at $(1 + x, y, z)$, so forming a $C_2^2(16)$ chain (Bernstein *et al.*, 1995) running parallel to the [100] direction. The formation of the one-dimensional substructure along [100] is augmented by two of the C—H···O hydrogen bonds. Atom C26 acts as hydrogen-bond donor to hydroxy atom O144 within the selected asymmetric unit, and atom C16 at (x, y, z) acts as donor to hydroxy atom O244 at $(-1 + x, y, z)$, so that these two hydrogen bonds form a $C_2^2(20)$ chain, also parallel to [100] but antiparallel to the $C_2^2(16)$ motif. The combination of all four of these hydrogen bonds generates a $C_2^2(16)C_2^2(20)[R_2^2(6)][R_2^2(6)]$ chain of rings along [100] (Fig. 3).

Two further C—H···O hydrogen bonds generate a second one-dimensional substructure in the form of a chain of edge-fused rings, itself built from two independent simple chain motifs. Atom C11 in the type 1 molecule at (x, y, z) acts as hydrogen-bond donor to methoxy atom O145 at $(x, \frac{1}{2} - y, \frac{1}{2} + z)$,
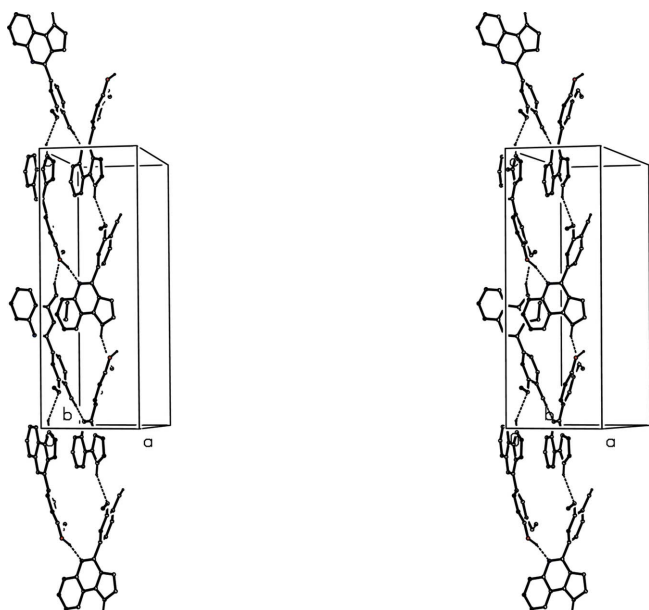
Figure 4
A stereoview of part of the crystal structure of (I), showing the formation of a chain of edge-fused rings parallel to [001] and built from one O—H⋯N hydrogen bond and two C—H⋯O hydrogen bonds. For the sake of clarity, H atoms bonded to C atoms but not involved in the motifs shown have been omitted.

so forming a $C(9)$ chain built from type 1 molecules related by the c-glide plane at $y = \frac{1}{4}$ and thus running parallel to the [001] direction. In a similar way, atom C21 in the type 2 molecule at (x, y, z) acts as hydrogen-bond donor to methoxy atom O245 at $(x, \frac{1}{2} - y, -\frac{1}{2} + z)$, so forming a second $C(9)$ chain along [001], this time containing only type 2 molecules and running antiparallel to the chain containing type 1 molecules. These two chains are linked by the O—H⋯N hydrogen bond within the asymmetric unit to form a ribbon, or a chain of edge-fused $R_4^4(28)$ rings running parallel to [001] (Fig. 4). The combination of the two chains of rings along [100] and [001] produces a complex sheet lying parallel to (010).

Experimental

A mixture of 1-(2-aminophenyl)pyrrole (1 mmol), 4-hydroxy-3-methoxybenzaldehyde (1 mmol), L-proline (20% w/w with respect to the pyrrole), Pd/C (50% w/w with respect to the pyrrole) and acetonitrile (2 ml) was stirred at ambient temperature for 48 h. The progress of the reaction was monitored by thin-layer chromatography, and when the reaction was thus judged to be complete the Pd/C was removed by filtration and the solvent was removed under reduced pressure. The resulting solid product, (I), was purified by column chromatography on silica gel using dichloromethane as the eluent. Yellow crystals of (I) suitable for single-crystal X-ray diffraction were grown by slow evaporation, at ambient temperature and in air, of a solution in ethanol (83% yield, m.p. 414 K). MS (70 eV) m/z (%): 290 (100) [M^+], 275 (8), 261 (9); elemental analysis found: C 74.4, H 5.0, N 9.6%; $C_{18}H_{14}N_2O_2$ requires: C 74.5, H 4.86, N 9.7%.

Twin form (Inm)

Crystal data

$C_{18}H_{14}N_2O_2$	$V = 2717.0$ (6) Å^3
$M_r = 290.31$	$Z = 8$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 7.9278$ (8) Å	$\mu = 0.09$ mm^{-1}
$b = 15.2929$ (18) Å	$T = 120$ K
$c = 22.410$ (4) Å	$0.50 \times 0.26 \times 0.18$ mm
$\beta = 90.326$ (12)°	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	5057 measured reflections
	5057 independent reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)	3891 reflections with $I > 2\sigma(I)$
$T_{min} = 0.944$, $T_{max} = 0.983$	$R_{int} = 0.000$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.054$	400 parameters
$wR(F^2) = 0.159$	H-atom parameters constrained
$S = 1.04$	$\Delta\rho_{max} = 0.21$ e Å^{-3}
5057 reflections	$\Delta\rho_{min} = -0.26$ e Å^{-3}

Twin form (Im)

Crystal data

$C_{18}H_{14}N_2O_2$	$V = 2717.0$ (6) Å^3
$M_r = 290.31$	$Z = 8$
Monoclinic, $P2_1/c$	Mo $K\alpha$ radiation
$a = 7.9278$ (8) Å	$\mu = 0.09$ mm^{-1}
$b = 15.2929$ (18) Å	$T = 120$ K
$c = 22.410$ (4) Å	$0.50 \times 0.26 \times 0.18$ mm
$\beta = 90.326$ (12)°	

Data collection

Bruker–Nonius KappaCCD area-detector diffractometer	34020 measured reflections
	5057 independent reflections
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)	3891 reflections with $I > 2\sigma(I)$
$T_{min} = 0.944$, $T_{max} = 0.983$	$R_{int} = 0.061$

Table 1
Selected geometric parameters (Å, °) for twin form (Inm).

C11—C12	1.361 (5)	C21—C22	1.370 (4)
C12—C13	1.398 (4)	C22—C23	1.395 (4)
C13—C13a	1.378 (4)	C23—C23a	1.376 (4)
C13a—C14	1.424 (4)	C23a—C24	1.419 (4)
C14—N15	1.303 (4)	C24—N25	1.299 (4)
N15—C15a	1.389 (4)	N25—C25a	1.393 (3)
C15a—C16	1.389 (4)	C25a—C26	1.391 (4)
C16—C17	1.373 (4)	C26—C27	1.369 (4)
C17—C18	1.385 (4)	C27—C28	1.388 (4)
C18—C19	1.361 (4)	C28—C29	1.363 (4)
C19—C19a	1.384 (4)	C29—C29a	1.385 (4)
C19a—N19b	1.382 (4)	C29a—N29b	1.386 (4)
N19b—C11	1.350 (4)	N29b—C21	1.355 (4)
C13a—N19b	1.386 (4)	C23a—N29b	1.393 (3)
C15a—C19a	1.395 (4)	C25a—C29a	1.391 (4)
O145—C145—C144	115.6 (2)	O245—C245—C244	115.0 (2)
O145—C145—C146	124.3 (3)	O245—C245—C246	124.8 (3)
C145—O145—C147	116.7 (2)	C245—O245—C247	116.9 (2)
C13a—C14—C141—C142	35.5 (4)	C23a—C24—C241—C242	37.3 (4)
C144—C145—O145—C147	−172.5 (3)	C244—C245—O245—C247	−173.6 (3)
C143—C144—O144—H144	−158	C243—C244—O244—H244	−161

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Table 2
Hydrogen-bond geometry (Å, °) for twin form (Inm).

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
O144—H144$\cdots$N25	0.98	1.77	2.703 (3)	158
O244—H244$\cdots$N15[i]	0.95	1.86	2.725 (3)	150
C11—H11$\cdots$O145[ii]	0.95	2.57	3.451 (4)	154
C16—H16$\cdots$O244[iii]	0.95	2.49	3.212 (4)	133
C21—H21$\cdots$O245[iv]	0.95	2.49	3.380 (3)	156
C26—H26$\cdots$O144	0.95	2.53	3.249 (3)	133

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

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.053$	400 parameters
$wR(F^2) = 0.159$	H-atom parameters constrained
$S = 1.05$	$\Delta\rho_{max} = 0.22$ e Å^{-3}
5057 reflections	$\Delta\rho_{min} = -0.27$ e Å^{-3}

The initial refinement converged to a high R index of 0.103 and analysis of the .fcf data indicated that the refinement should be handled as a nonmerohedral twin, with twinning matrix (-1.000, 0.000, -0.004/0.000, -1.000, 0.000/0.000, 0.000, 1.000). From the original HKLF file (38 684 measured reflections, of which 6234 were unique with a merging index of 0.0661), a modified file was prepared by use of the TwinRotMat option in *PLATON* (Spek, 2009) for use in the final refinement as a nonmerohedral twin, to give twin fractions of 0.1234 (13) and 0.8766 (13).

All H atoms were located in difference maps. H atoms bonded to C atoms were then treated as riding in geometrically idealized positions, with C—H = 0.95 (all ring atoms) or 0.98 Å (methyl), and with U_{iso}(H) = kU_{eq}(C), where k = 1.5 for the methyl groups, which were permitted to rotate but not to tilt, and 1.2 for all other H atoms bonded to C atoms. H atoms bonded to atoms O144 and O244 were permitted to ride at the positions deduced from difference maps, with U_{iso}(H) = 1.5U_{eq}(O), giving O—H distances of 0.98 and 0.95 Å, respectively.

The form of the twinning matrix suggested that the twinning was pseudomerohedral, as the twinning matrix approximated to (-1, 0, 0/0, -1, 0/0, 0, 1), equivalent to a twofold rotation about [001] and thus corresponding to a monoclinic cell having the cell angle β close to 90°, emulating a metrically orthorhombic cell. Accordingly, the structure was also refined as a merohedral twin, to give twin fractions of 0.1228 (13) and 0.8772 (13). The H atoms were handled exactly as for the nonmerohedral twin, now giving O—H distances of 0.97 and 0.96 Å, respectively. For refinements conducted under otherwise identical conditions, the merohedral twin actually gave a slightly smaller R factor, but the atomic coordinates and derived intramolecular geometric parameters from the two refinements are virtually indistinguishable, apart from the O—H distances.

For both twin forms, data collection: *COLLECT* (Nonius, 1999); cell refinement: *DIRAX/LSQ* (Duisenberg et al., 2000); data reduc-

tion: *EVALCCD* (Duisenberg et al., 2003); program(s) used to solve structure: *SIR2004* (Burla et al., 2005); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK3375). Services for accessing these data are described at the back of the journal.

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