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1,4-Dihydroxyquinoxaline-2,3(1*H*,4*H*)-dione

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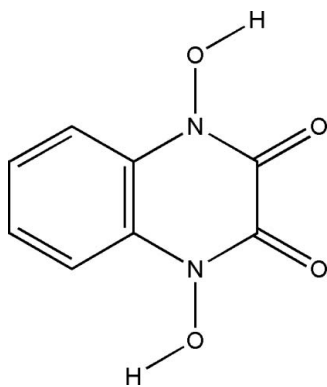
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Key indicators: single-crystal X-ray study; $T = 294$ K; mean $\sigma(\text{C}-\text{C}) = 0.003$ Å; R factor = 0.035; wR factor = 0.072; data-to-parameter ratio = 7.7.

The asymmetric unit of the title compound, $\text{C}_8\text{H}_6\text{N}_2\text{O}_4$, contains one half-molecule; a twofold rotation axis bisects the molecule. The quinoxaline ring is planar, which can be attributed to electron delocalization. In the crystal structure, intermolecular $\text{O}-\text{H}\cdots\text{O}$ hydrogen bonds link the molecules into $R_2^2(10)$ motifs, leading to layers, which interact *via* phenyl-phenyl interactions ($\text{C}\cdots\text{C}$ distances in the range 3.238–3.521 Å).

Related literature

For general background, see: Zarranz *et al.* (2004); Chowdhury *et al.* (2004); Monge *et al.* (1995); Fuchs *et al.* (2001); Dance (1996); Bernstein *et al.* (1995). For related literature, see: Elina & Tsyrl'nikova (1963); Akkurt *et al.* (2004); Mustaphi *et al.* (2001); Oxtoby *et al.* (2005); Ley & Seng (1975); For bond-length data, see: Allen *et al.* (1987);



Experimental

Crystal data

$\text{C}_8\text{H}_6\text{N}_2\text{O}_4$
 $M_r = 194.15$
 Orthorhombic, $C222_1$
 $a = 4.2562$ (6) Å
 $b = 17.630$ (3) Å
 $c = 10.4775$ (17) Å
 $V = 786.2$ (2) Å³
 $Z = 4$
 Mo $K\alpha$ radiation
 $\mu = 0.14$ mm⁻¹
 $T = 294$ (2) K
 $0.50 \times 0.20 \times 0.10$ mm

Data collection

Nicolet P3 diffractometer
 Absorption correction: none
 1004 measured reflections
 529 independent reflections
 437 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.022$
 3 standard reflections
 every 50 reflections
 intensity decay: 2%

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.034$
 $wR(F^2) = 0.071$
 $S = 1.07$
 529 reflections
 69 parameters
 H atoms treated by a mixture of independent and constrained refinement
 $\Delta\rho_{\text{max}} = 0.12$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.15$ e Å⁻³

Table 1

Hydrogen-bond geometry (Å, °).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$\text{O1}-\text{H1}\cdots\text{O2}^i$	0.96 (3)	1.63 (3)	2.584 (2)	174 (3)

Symmetry code: (i) $x, -y + 1, -z$.

Data collection: *P3/PC Data Collection Software* (Siemens, 1991); cell refinement: *P3/PC Data Collection Software*; data reduction: *SHELXTL-Plus* (Sheldrick, 2008); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL-Plus*; software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2003).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: HK2425).

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1,4-Dihydroxyquinoxaline-2,3(1*H*,4*H*)-dione

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Comment

Quinoxalines are of interest owing to their biological activities. They seem to have very interesting anticancer activity (Zarranz *et al.*, 2004). For example, 3-aminoquinoxaline-2-carbonitrile 1,4-dioxide have been studied extensively as bioreductive cytotoxic agent. It was found to be an efficient agent and causes redox-activated DNA damage (Chowdhury *et al.*, 2004), even more active than the first drug clinically used as bioreductive cytotoxic agent (Monge *et al.*, 1995; Fuchs *et al.*, 2001). A nonconvenient synthesis of the title compound, (I), was reported previously (Elina & Tsyruľ nikova, 1963), *via* the hydrolysis of 2-amino-3-hydroxyquinoxaline 1,4-dioxide, which results as a side product (4%) from oxidation of 2-acetamidoquinoxaline with acetic peroxide acid using boiling HCl solution. We report herein a novel simple synthetic method for (I), along with its crystal structure.

The new synthetic strategy for (I), (Fig. 1), is based on the reaction of (1) with NaOH solution, yielding (2) in an S_NAr reaction, which upon hydrolysis with boiling HCl solution, *via* protonation of amine followed by the attack of water molecule, yielded (I) in a good amount (90%).

The asymmetric unit of the title compound, (I), (Fig. 2) contains one half-molecule. The quinoxaline ring is planar, which can be attributed to a wide range of electron delocalization. Bond lengths and angles are in accordance with the corresponding reported values in 1,4-dihydroquinoxaline -2,3-dione core (Oxtoby *et al.*, 2005) and other similar *N*-alkyl quinoxalines (Akkurt *et al.*, 2004; Mustaphi *et al.*, 2001). The existence of (I) in the dione form is evident from C1—O2 [1.226 (3) Å] bond, being smaller than a pure single bond, which confirms the double bond character (Allen *et al.*, 1987). The C1—C1ⁱ [1.503 (4) Å] bond has single bond character compared to multiple bond characters in C2—C2ⁱ [1.381 (4) Å], C2—C3 [1.391 (3) Å], C3—C4 [1.382 (3) Å] and C4—C4ⁱ [1.372 (6) Å] [symmetry code: (i) $-x, y, 1/2 - z$]. The N1—C1 [1.345 (3) Å] bond is significantly shorter than N1—C2 [1.404 (3) Å] and it is an intermediate between those typical for the corresponding single and double bonds, suggesting some degree of delocalization. The N1—C1 bond length is closer to the average $C_{ar}-N_{sp^2}$ (planar) value of 1.353 (7) Å rather than the $C_{ar}-N_{sp^3}$ (pyramidal) value of 1.419 (17) Å (Allen *et al.*, 1987), with the sum of the bond angles around atom N1 [359.81 (18)°], indicating sp^2 hybridization.

In the crystal structure, intermolecular O—H...O hydrogen bonds (Table 1) link the molecules into $R_2^2(10)$ motifs (Fig. 3) (Bernstein *et al.*, 1995) leading to layers running along the *c* axis (Fig. 4). Molecules within layers are further interacting *via* phenyl...phenyl interactions (Dance, 1996), where the layers parallel to *a* axis interact in an offset stacking motif (C...C distances in the range of 3.238–3.521 Å).

Experimental

For the preparation of (I), to a suspension solution of (1) (2.02 g, 10 mmol) (Ley & Seng, 1975) in ethanol (20 ml), NaOH (20 ml, 10%) was added to give a deep blue solution. After refluxing for 5 h, the brown solution was allowed to cool to room temperature. The resulting mixture was then treated with HCl (30 ml, 10%), refluxed for another 5 h and then

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allowed to stand undisturbed. The resulting residual brown solid was filtered off, washed with cold water (5 ml) and then by cold ethanol (5 ml). The title compound, (I), was recrystallized from ethanol solution (yield; 1.76 g, 90%, m.p. 535–536 K decomposition). Analysis found: C 49.45, H 3.27, N 14.41%; $C_8H_6N_2O_4$ requires: C 49.49, H 3.12, N 14.43%. 1H NMR (300 MHz, $DMSO-d_6$): $\delta = 7.36$ (m, 2H; H4/H7), 7.56 (m, 2H; H5/H6); ^{13}C NMR (75 MHz, $DMSO-d_6$): $\delta = 111.6$ (C4/C7), 123.3 (C5/C6), 124.0 (C4a/C7a), 150.4 (C2/C3) p.p.m.. ESI: $m/z = 217.02$ ($C_8H_6N_2O_4Na$).

Refinement

H atom (for OH) was located in a difference synthesis and refined isotropically [$O-H = 0.96$ (3) Å; $U_{iso}(H) = 0.072$ (10) Å²]. The remaining H atoms were positioned geometrically, with $C-H = 0.93$ Å for aromatic H and constrained to ride on their parent atoms, with $U_{iso}(H) = 1.2U_{eq}(C)$.

Figures



Fig. 1. Schematic representation for the steps through which reaction proceeds.

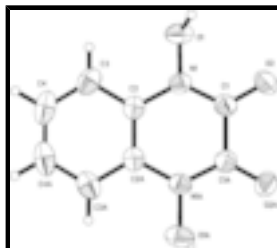


Fig. 2. The molecular structure of the title molecule, with the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

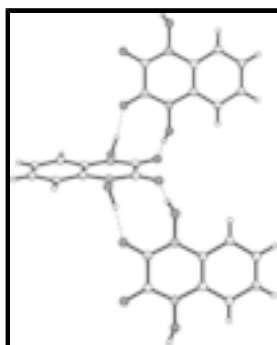


Fig. 3. Part of the crystal structure of (I), showing the formation of $R_2^2(10)$ motifs.

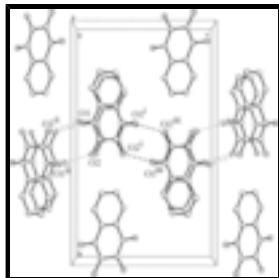


Fig. 4. A packing diagram of (I), showing the layers of molecules parallel to c axis. All hydrogen atoms were omitted for clarity. Hydrogen bonds are shown as dashed lines [symmetry codes: (i) $-x, y, -z + 1/2$, (ii) $x, -y + 1, -z$].

1,4-Dihydroxyquinoxaline-2,3(1*H*,4*H*)-dione

Crystal data

$C_8H_6N_2O_4$

$M_r = 194.15$

Orthorhombic, $C222_1$

Hall symbol: $C\ 2c\ 2$

$a = 4.2562\ (6)\ \text{\AA}$

$b = 17.630\ (3)\ \text{\AA}$

$c = 10.4775\ (17)\ \text{\AA}$

$V = 786.2\ (2)\ \text{\AA}^3$

$Z = 4$

$F_{000} = 400$

$D_x = 1.640\ \text{Mg m}^{-3}$

Mo $K\alpha$ radiation

$\lambda = 0.71073\ \text{\AA}$

Cell parameters from 20 reflections

$\theta = 14\text{--}16^\circ$

$\mu = 0.14\ \text{mm}^{-1}$

$T = 294\ (2)\ \text{K}$

Plates, colourless

$0.50 \times 0.20 \times 0.10\ \text{mm}$

Data collection

Nicolet P3
diffractometer

Radiation source: fine-focus sealed tube

Monochromator: graphite

$T = 294\ (2)\ \text{K}$

Wyckoff scan

Absorption correction: none

1004 measured reflections

529 independent reflections

437 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.022$

$\theta_{\text{max}} = 27.0^\circ$

$\theta_{\text{min}} = 2.3^\circ$

$h = 0 \rightarrow 5$

$k = 0 \rightarrow 22$

$l = -13 \rightarrow 13$

3 standard reflections

every 50 reflections

intensity decay: 2%

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.034$

$wR(F^2) = 0.071$

$S = 1.07$

Hydrogen site location: inferred from neighbouring sites

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0208P)^2 + 0.4073P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{\text{max}} < 0.001$

$\Delta\rho_{\text{max}} = 0.12\ \text{e \AA}^{-3}$

supplementary materials

529 reflections

$$\Delta\rho_{\min} = -0.15 \text{ e } \text{\AA}^{-3}$$

69 parameters

Extinction correction: SHELXL97 (Sheldrick, 2008),

$$F_c^* = kF_c [1 + 0.001 \times F_c^2 \lambda^3 / \sin(2\theta)]^{-1/4}$$

Primary atom site location: structure-invariant direct methods

Extinction coefficient: 0.013 (2)

Secondary atom site location: difference Fourier map

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > 2\sigma(F^2)$ is used only for calculating R -factors(gt) *etc.* and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	<i>x</i>	<i>y</i>	<i>z</i>	$U_{\text{iso}}^*/U_{\text{eq}}$
N1	0.2116 (4)	0.41727 (11)	0.15388 (16)	0.0350 (5)
C1	0.1130 (6)	0.48556 (11)	0.1948 (2)	0.0364 (6)
O1	0.4527 (4)	0.41624 (10)	0.06569 (15)	0.0456 (5)
H1	0.357 (7)	0.4338 (15)	-0.012 (3)	0.072 (10)*
C2	0.1068 (5)	0.34702 (11)	0.2004 (2)	0.0332 (5)
O2	0.1965 (5)	0.54622 (9)	0.14878 (15)	0.0531 (6)
C3	0.2131 (7)	0.27901 (13)	0.1487 (2)	0.0456 (7)
H3	0.3541	0.2788	0.0808	0.055*
C4	0.1046 (7)	0.21177 (13)	0.2002 (2)	0.0557 (8)
H4	0.1745	0.1659	0.1669	0.067*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
N1	0.0369 (10)	0.0401 (9)	0.0279 (8)	0.0022 (10)	0.0011 (9)	-0.0011 (8)
C1	0.0452 (15)	0.0371 (12)	0.0269 (10)	-0.0036 (11)	-0.0014 (13)	-0.0019 (9)
O1	0.0416 (9)	0.0631 (10)	0.0320 (8)	0.0113 (10)	0.0045 (9)	0.0052 (9)
C2	0.0354 (14)	0.0334 (10)	0.0309 (10)	0.0004 (10)	-0.0096 (12)	-0.0007 (8)
O2	0.0823 (16)	0.0374 (8)	0.0397 (9)	-0.0123 (10)	0.0136 (13)	0.0017 (7)
C3	0.0519 (16)	0.0435 (13)	0.0415 (13)	0.0099 (13)	-0.0118 (16)	-0.0077 (10)
C4	0.072 (2)	0.0336 (11)	0.0615 (16)	0.0086 (13)	-0.0242 (18)	-0.0079 (11)

Geometric parameters (\AA , $^\circ$)

N1—C1	1.345 (3)	C2—C2 ⁱ	1.381 (4)
N1—O1	1.381 (2)	C2—C3	1.391 (3)

N1—C2	1.404 (3)	C3—C4	1.382 (3)
C1—O2	1.226 (3)	C3—H3	0.9300
C1—C1 ⁱ	1.503 (4)	C4—C4 ⁱ	1.372 (6)
O1—H1	0.96 (3)	C4—H4	0.9300
C1—N1—O1	117.21 (19)	C2 ⁱ —C2—N1	118.08 (11)
C1—N1—C2	125.42 (18)	C3—C2—N1	121.5 (2)
O1—N1—C2	117.18 (18)	C4—C3—C2	118.6 (2)
O2—C1—N1	124.4 (2)	C4—C3—H3	120.7
O2—C1—C1 ⁱ	119.22 (14)	C2—C3—H3	120.7
N1—C1—C1 ⁱ	116.41 (12)	C4 ⁱ —C4—C3	120.93 (16)
N1—O1—H1	104.2 (17)	C4 ⁱ —C4—H4	119.5
C2 ⁱ —C2—C3	120.47 (15)	C3—C4—H4	119.5
O1—N1—C1—O2	8.8 (3)	C1—N1—C2—C3	177.4 (2)
C2—N1—C1—O2	-176.4 (2)	O1—N1—C2—C3	-7.8 (3)
O1—N1—C1—C1 ⁱ	-170.8 (2)	C2 ⁱ —C2—C3—C4	-1.1 (4)
C2—N1—C1—C1 ⁱ	4.1 (4)	N1—C2—C3—C4	178.9 (2)
C1—N1—C2—C2 ⁱ	-2.5 (4)	C2—C3—C4—C4 ⁱ	0.3 (5)
O1—N1—C2—C2 ⁱ	172.3 (2)		

Symmetry codes: (i) $-x, y, -z+1/2$.

Hydrogen-bond geometry ($\text{\AA}, ^\circ$)

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
O1—H1 \cdots O2 ⁱⁱ	0.96 (3)	1.63 (3)	2.584 (2)	174 (3)

Symmetry codes: (ii) $x, -y+1, -z$.

Fig. 1

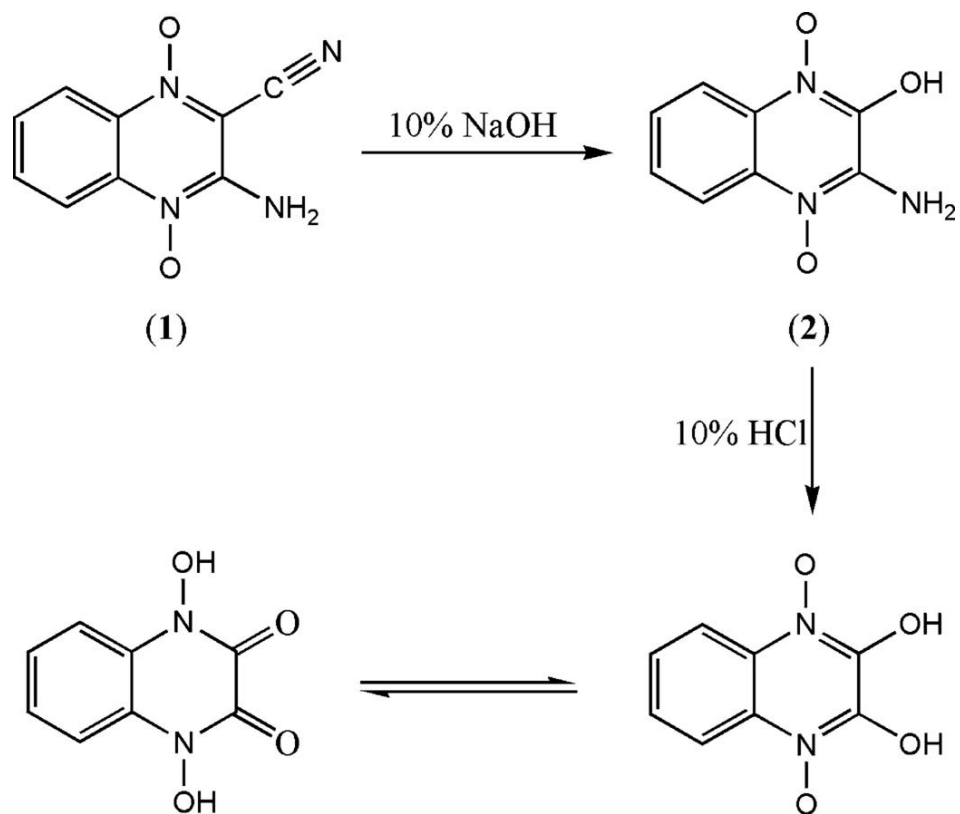


Fig. 2

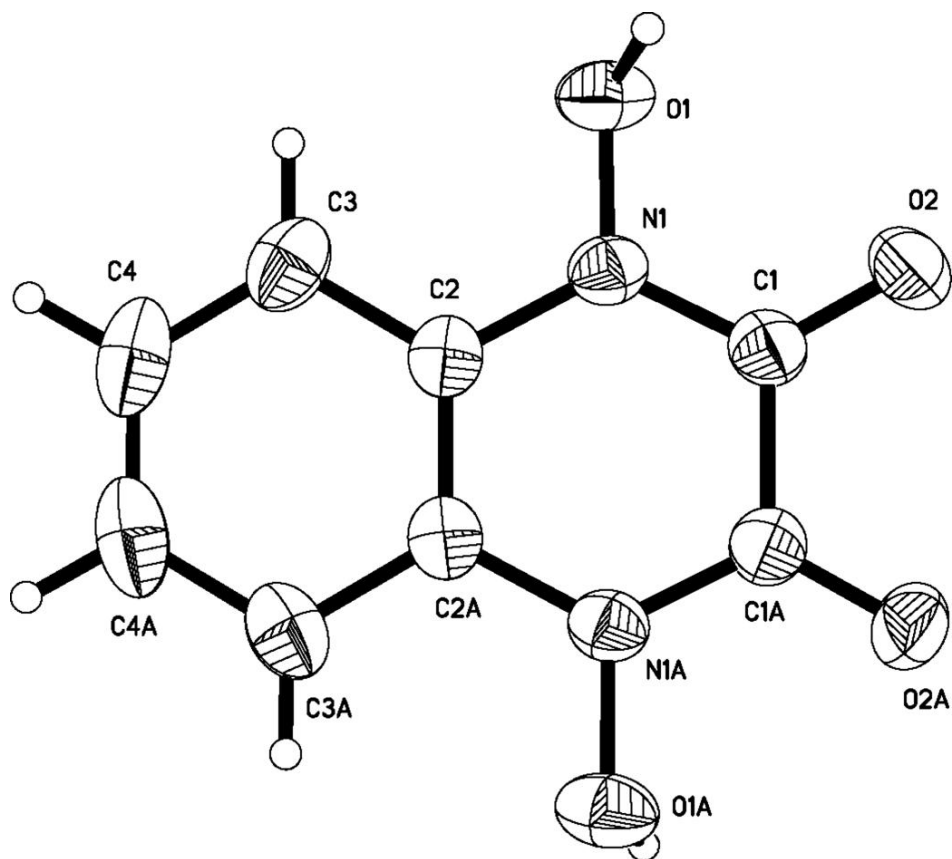


Fig. 3

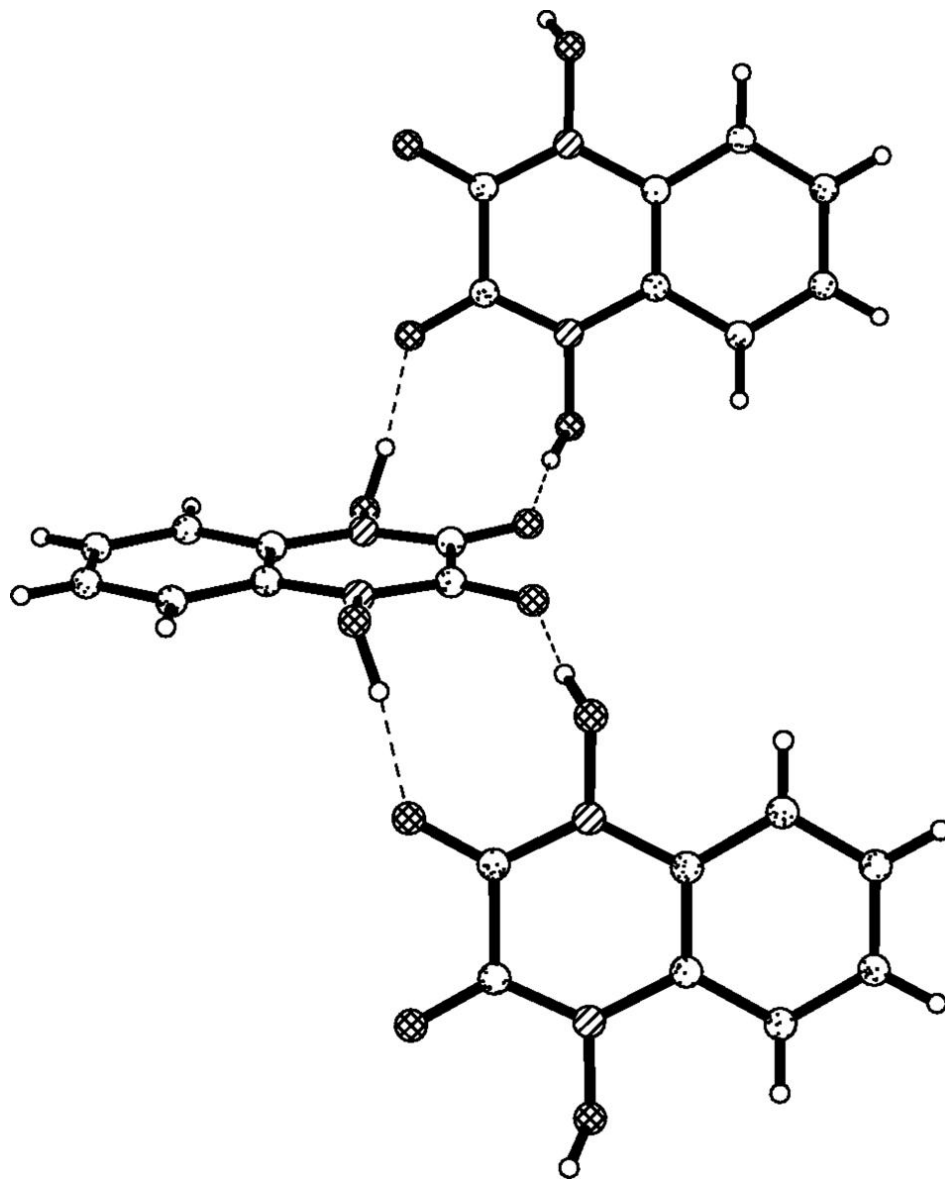


Fig. 4

