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4,5,6,8,9-Pentachloropyrimido-[1,2-*a*][1,8]naphthyridin-10-one

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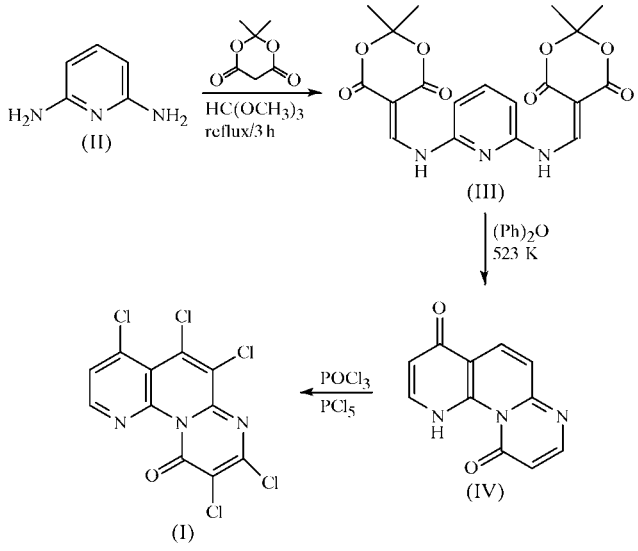
The title compound, $C_{11}H_2Cl_5N_3O$, crystallizes in the monoclinic system with two molecules in the asymmetric unit. The molecules are chemically identical but have different structural parameters. In the three-dimensional packing, the molecules are arranged in dimers that are connected by slipped π–π stacking, and these dimers are connected to one another through several C—H···O and Cl···Cl interactions.

Comment

A variety of pyrimido[1,2-*a*][1,8]naphthyridines are of biological interest because of their antimicrobial (Harper & Wibberley, 1971) and antihypertensive activities (Ferrarini *et al.*, 1990). Naphthyridines containing the pyrimidine moiety, such as pyrimido[2,1-*f*][1,6]naphthyridines, have shown tracheal muscle relaxation activity (Sasaki *et al.*, 1999). We have already investigated extensively the use of 5-arylaminomethylene derivatives of Meldrum's acid as important key intermediates for the synthesis of aza-heterocyclic compounds with potential biological activity (Silva *et al.*, 2002). As an extension of this methodology, we have prepared naphthyridines by a thermal decarboxylation/cyclization process of the bis-adduct (III) in refluxing diphenyl ether, according to the method reported by Cassis *et al.* (1985); this process leads exclusively to 1*H*-pyrimido[1,2-*a*][1,8]naphthyridine-4,10-dione, (IV). Although two possible isomers could be formed, the preferential formation of the angular product (IV) was established from ^{1}H and ^{13}C NMR data.

Halonaphthyridines are prone to nucleophilic aromatic substitution; this makes them important precursors for the introduction of a wide variety of groups containing nucleophilic heteroatoms (O*R*, S*R*, NH*R*, and others). Halonaphthyridines are prepared by several methods, including direct halogenation (Lowe, 1982) of naphthyridines, the Meisenheimer reaction of their *N*-oxides (Paudler & Pokorny, 1971) and the treatment of naphthyridinones with $PCl_5/POCl_3$ (Brown & Plasz, 1971).

As our methodology for the construction of naphthyridine derivatives is based on the preparation of halonaphthyridines, we allowed compound (IV) to react with phosphoryl chloride and phosphorus pentachoride under the reaction conditions used by Carboni *et al.* (1970), in order to obtain the monochloro derivative. However, the product was found, on the basis of elemental analysis, to be a pentachloro derivative. The ^{1}H NMR spectrum showed two doublet signals, at 8.63 and 7.65 p.p.m., with J = 4.8 Hz, indicating a vicinal relationship between two H atoms. We could not safely determine the structure from these data, but we were able to obtain crystals of the product suitable for X-ray analysis, which showed the product to be the title compound, (I). According to the Cambridge Structural Database (Version 5.25; Allen, 2002), this type of heterocyclic system is the second example of a crystal structure of a pyrimido[1,2-*a*][1,8]naphthyridine (Ferrarini *et al.*, 1990).



The asymmetric unit of (I) consists of two independent molecules (Fig. 1). The molecules are chemically identical but have different structural parameters (Table 1), as demonstrated by the different bond angles around atoms N10*A* [C6*A*—N10*A*—C10 = 118.5 (2)°, C6*A*—N10*A*—C1*A* = 120.2 (2)° and C1*A*—N10*A*—C10 = 121.2 (2)°] and N20*A* [C16*A*—N20*A*—C11*A* = 120.8 (2)°, C16*A*—N20*A*—C20 = 119.1 (2)° and C11*A*—N20*A*—C20 = 119.8 (2)°], and by the dihedral angles between the mean planes defined by the rings N1/C2–C4/C4*A*/C1*A* and N7/C8–C10/N10*A*/C6*A* [15.5 (1)°], and N11/C12–C14/C14*A*/C11*A* and N17/C18–C20/N20*A*/C16*A* [25.2 (1)°], in molecules 1 and 2, respectively. The torsion angle involving the N—C bond in the non-aromatic conjugated ring [C6—C6*A*—N10*A*—C10 = 163.2 (3)°] in molecule 1 is 4.8° greater than that in molecule 2 [C16—C16*A*—N20*A*—C20 = 158.5 (3)°]. In addition, the conformational analysis of the ten-membered rings N7/C8–C10/N10*A*/C1*A*/C4*A*/C5/C6/C6*A* [Q = 0.385 (3) Å] in molecule 1 and N17/C18–C20/N20*A*/C11*A*/C14*A*/C15/C16/C16A [Q = 0.464 (3) Å] in molecule 2 shows a significant difference in the total amplitude of the puckering parameter Q (Cremer & Pople, 1975).

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Several forces govern the arrangement of the molecules in the crystal structure of (I). Non-covalent π–π stacking interactions act between the aromatic N11/C12–C14/C14*A*/C11*A* and N1/C2–C4/C4*A*/C1*A* rings, resulting in a dimeric structure (Fig. 2). The geometric parameters are within the acceptable range (Janiak, 2000). The *Cg*1···*Cg*2 distance is 4.595 (2) Å [*Cg*1 is the centroid of the N11-containing ring and *Cg*2 is the centroid of the N1-containing ring at $(1-x, 1-y, 1-z)$, hereafter symmetry code (i)], whereas the *Cg*1···H2 distance is 3.287 Å. The perpendicular distance between the planes is 3.727 (2) Å. The slippage angle γ (defined by the *Cg*1···*Cg*2 vector and the normal to the plane from *Cg*1, and calculated geometrically) is 35.85° and the dihedral angle between the mean planes of the rings is 14.1 (1)°. These parameters demonstrate that the rings are almost coplanar and indicate that slipped π–π stacking governs the dimer formation. The dimeric structures are connected to one another through several halogen bonds, weak C—H···O interactions, and Cl···O and C···O short contacts, forming an intricate three-dimensional network. These intermolecular contacts have values in the range 3.20–3.45 Å for the Cl···Cl bond and 2.30–2.45 Å for the C—H···O interactions (Table 2). In the Cl···O contact, atoms Cl1 and O2$(1-x, y-\frac{1}{2}, \frac{1}{2}-z)$ are separated by 3.224 (3) Å. Unexpected and very short C···O intermolecular contacts are also observed, with a C16···O1^{iv} separation of 2.980 (4) Å and a C16*A*···O1^{iv} separation of 2.810 (4) Å [symmetry code: (iv) $1-x, 2-y, 1-z$], where C16 and C16*A* are Csp^2 atoms. Atom O1 lies 0.252 (5) Å out of the mean plane of the N7/C8–C10/N10*A*/C6*A* ring, towards the neighboring C atoms. A similar C···O intermolecular contact has been observed in other crystal structures (Vila *et al.*, 2002). The geometric parameters of these interactions can be obtained from the archived CIF.

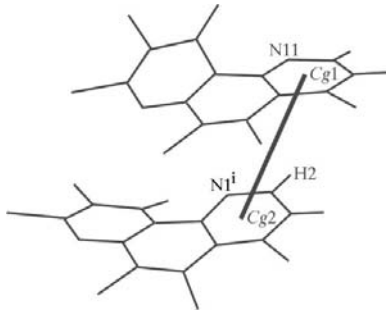

Figure 2
The dimeric structure of (I) formed by π–π stacking. [Symmetry code: (i) $1-x, 1-y, 1-z$.]

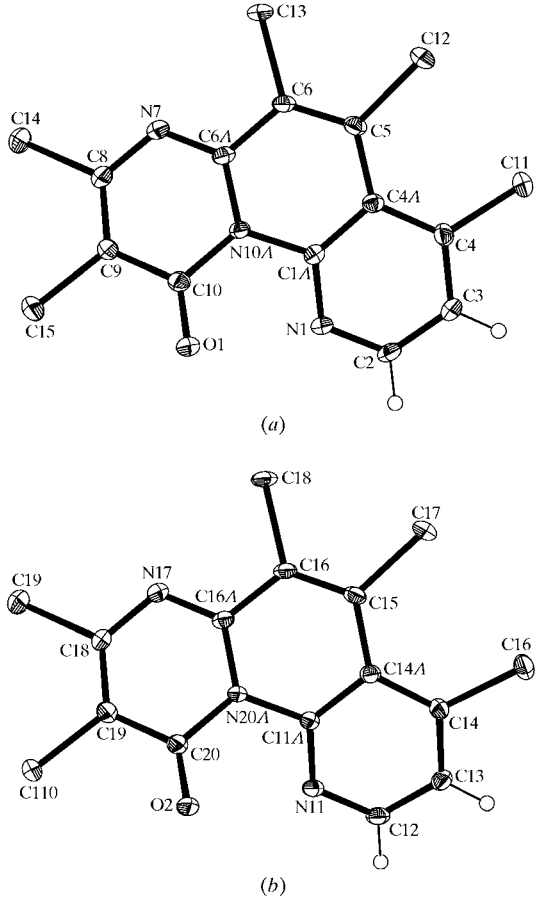

Figure 1
The molecular structure of (I), with the atomic labeling scheme: (*a*) molecule 1 and (*b*) molecule 2. Displacement ellipsoids are shown at the 40% probability level.

Experimental

A solution of (IV) (0.54 g, 2.53 mmol), phosphoryl oxychloride (20 ml) and phosphorus pentachloride (3.00 g, 14.38 mmol) was refluxed for 18 h under N_2. The resulting solution was cooled, poured onto ice–water (40 ml) and neutralized with NH_4OH until the pH was 7. The precipitate was collected by filtration, washed with water, dried and purified by silica-gel chromatography with hexane/ethyl acetate (4:1). Single crystals of (I) suitable for X-ray data collection were obtained by slow evaporation from a hexane/ethyl acetate solution (4:1) [yield 0.80 g, 85%; m.p. 493 K (yellow crystalline solid)]. ^{1}H NMR ($CDCl_3$): δ 7.65 (*d*, *J* = 4.8 Hz, 1H), 8.63 (*d*, *J* = 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ 116.69, 119.10, 128.23, 131.05, 137.05, 143.31, 144.59, 148.35, 148.70, 153.17, 156.31. Analysis calculated for $C_{11}H_2Cl_5N_3O$: C 35.75, H 0.54, N 11.37%; found: C 35.61, H 0.54, N 11.25%.

Crystal data

$C_{11}H_2Cl_5N_3O$
M_r = 369.41
Monoclinic, $P2_1/c$
a = 16.453 (3) Å
b = 7.173 (1) Å
c = 22.368 (3) Å
β = 107.26 (2)°
V = 2520.9 (7) Å^3
Z = 8
D_x = 1.947 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
θ = 10.0–14.0°
μ = 1.15 mm^{-1}
T = 193 (2) K
Irregular block, yellow
0.50 × 0.30 × 0.23 mm

Data collection

Enraf–Nonius CAD-4 diffractometer
ω–2θ scans
Absorption correction: ψ scan (North *et al.*, 1968)
T_{min} = 0.597, T_{max} = 0.777
4607 measured reflections
4476 independent reflections
3857 reflections with $I > 2\sigma(I)$
R_{int} = 0.089
θ_{max} = 25.1°
h = −18 → 19
k = −8 → 0
l = −26 → 0
3 standard reflections
every 200 reflections
intensity decay: 1%

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0703P)^2 + 2.546P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.035$	$(\Delta/\sigma)_{max} = 0.001$
$wR(F^2) = 0.111$	$\Delta\rho_{max} = 0.50$ e Å^{-3}
$S = 1.05$	$\Delta\rho_{min} = -0.41$ e Å^{-3}
4476 reflections	
361 parameters	
H-atom parameters constrained	

Table 1
Selected geometric parameters (Å, °).

C1*A*—N10*A*	1.430 (4)	C11*A*—N20*A*	1.420 (3)
C6*A*—N7	1.306 (4)	C16*A*—N17	1.315 (4)
C6*A*—N10*A*	1.393 (3)	C16*A*—N20*A*	1.378 (3)
C8—N7	1.340 (4)	C18—N17	1.350 (4)
C10—N10*A*	1.450 (4)		
C1*A*—C4*A*—C4	114.3 (2)	C6*A*—N10*A*—C1*A*	120.2 (2)
C1*A*—C4*A*—C5	118.2 (2)	C6*A*—N10*A*—C10	118.5 (2)
C4—C4*A*—C5	127.5 (2)	C1*A*—N10*A*—C10	121.2 (2)
N7—C6*A*—N10*A*	123.9 (3)	C11*A*—N11—C12	117.4 (2)
N7—C6*A*—C6	118.3 (2)	C16*A*—N17—C18	116.9 (2)
N10*A*—C6*A*—C6	117.8 (2)	C16*A*—N20*A*—C11*A*	120.8 (2)
C1*A*—N1—C2	118.0 (2)	C16*A*—N20*A*—C20	119.1 (2)
C6*A*—N7—C8	118.2 (2)	C11*A*—N20*A*—C20	119.8 (2)

Table 2
Hydrogen-bonding geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C2—H2···O2^{ii}	0.95	2.45	3.308 (3)	151
C12—H12···O1^{iii}	0.95	2.30	3.219 (3)	164

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

H atoms were placed in idealized positions and treated using a riding model, with C—H distances of 0.95 Å and U_{eq}(H) values fixed at $1.2U_{iso}$ of the parent atom.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1994); cell refinement: *SET*4 in *CAD*-4 *EXPRESS*; data reduction: *HELENA* (Spek, 1996); program(s) used to solve structure: *SIR*97 (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1788). Services for accessing these data are described at the back of the journal.

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