Table 1. *Selected geometric parameters (Å, °)*

C1—C9a	1.413 (2)	C8—C8′	1.513 (3)
C1—O1′	1.380 (2)	C8a—C9	1.531 (2)
C4—C4a	1.411 (2)	C8a—C10a	1.405 (3)
C4—O4′	1.383 (2)	C9—C91	1.551 (2)
C4a—C9a	1.392 (2)	C9—C9a	1.522 (2)
C4a—C10	1.526 (2)	C9—O9′	1.448 (2)
C5—C10a	1.417 (3)	C10—C11	1.544 (2)
C5—C5′	1.518 (3)	C10—C10a	1.534 (2)
C8—C8a	1.415 (2)	C10—O10′	1.449 (2)
C10—C4a—C9a	122.9 (2)	C10—C10a—C8a	122.7 (2)
C9—C8a—C10a	122.1 (2)	C9—C9a—C4a	122.9 (2)
C8a—C9—C9a	114.9 (2)	C10a—C10—C4a	114.4 (2)
C8a—C9—O9′	104.3 (2)	C4a—C10—O10′	107.1 (2)
C8a—C9—C91	109.8 (2)	C11—C10—C4a	109.4 (2)
C9a—C9—O9′	107.2 (2)	C10a—C10—O10′	104.4 (2)
C91—C9—C9a	109.3 (2)	C11—C10—C10a	110.4 (2)
C91—C9—O9′	111.1 (2)	C11—C10—O10′	111.0 (2)
C6—C5—C5′	116.9 (2)	C7—C8—C8′	115.8 (2)
C10a—C5—C5′	124.8 (2)	C8′—C8—C8a	125.9 (2)
C4—C4a—C9a—C1	0.5 (2)	C8—C8a—C10a—C5	1.5 (2)
C10—C4a—C9a—C9	0.7 (2)	C9—C8a—C10a—C10	1.7 (2)
C9a—C4a—C10—C10a	−1.9 (2)	C10a—C8a—C9—C9a	−2.7 (2)
C4—C4a—C10—C10a	174.1 (2)	C8—C8a—C9—C9a	175.1 (2)
C4a—C10—C10a—C5	−177.0 (2)	C8a—C9—C9a—C1	−174.0 (2)
C4a—C10—C10a—C8a	0.7 (2)	C8a—C9—C9a—C4a	1.6 (2)
C4—C4a—C10—O10′	58.7 (2)	C8—C8a—C9—O9′	58.0 (2)
C4—C4a—C10—C11	−61.7 (2)	C8—C8a—C9—C91	−61.1 (2)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O9′—H9′···O1′	0.950 (2)	1.892 (2)	2.709 (2)	142.5 (2)
O10′—H10′···O4′	0.924 (2)	1.946 (2)	2.699 (2)	137.3 (2)

The title structure was solved by direct methods (*SIR*; Burla *et al.*, 1989) assuming the non-centrosymmetric space group $P1$; an E map revealed all non-H-atom positions, and aromatic H atoms were placed at geometrically calculated positions. The remaining hydroxyl and methyl H atoms emerged in a subsequent difference Fourier map after transformation to the centrosymmetric space group $P\bar{1}$. H atoms were included using a riding model.

Data collection: *CAD*-4 *Operations Manual* (Enraf–Nonius, 1977). Cell refinement: *CAD*-4 *Operations Manual*. Data reduction: *maXus* (Mackay *et al.*, 1998). Program(s) used to refine structure: *maXus*. Molecular graphics: *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *maXus*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: JZ1274). Services for accessing these data are described at the back of the journal.

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Characterization of Quinoline Derivatives. II. 7-(4-Methyl-1-piperazinyl)-6*H*-[1]benzopyrano[3,4-*c*]quinoline†

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(*Received 10 December 1996; accepted 9 March 1998*)

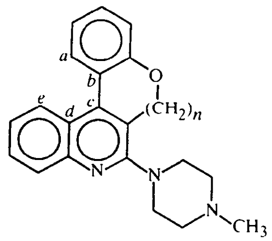
Abstract

The title compound, $C_{21}H_{21}N_3O$, belongs to a new class of novel, potent and selective serotonin 5-HT_3 receptor antagonists based on the arylpiperazine skeleton. The molecular topology is not flat, but the molecule is bent in a helicene-like manner. The pyran ring has a half-boat conformation. This, together with the fusion to the quinoline nucleus, determines the orientation of the fused benzene ring, the role of which is important for the biological activity of the compound. The piperazine ring has a chair conformation. The crystal packing is stabilized by stacking interactions between the quinoline nuclei.

Comment

In the course of a research program aimed at synthesizing new serotonin (5-hydroxytriptamine, 5-HT) receptor ligands, we found that conformationally restrained arylquinoline derivatives may act as antagonists with enhanced selectivity towards the 5-HT_3 receptor subtype (Anzini *et al.*, 1995). We wish to report here on the crystal and molecular structure of 7-(4-methyl-1-piperazinyl)-6*H*-[1]benzopyrano[3,4-*c*]quinoline, (I), the most biologically active member of this class.

† Part I: Giorgi *et al.* (1997).



(I) $n = 1$
(II) $n = 2$

To evaluate the role exerted by the ring at face *c* of the quinoline on the orientation of the fused benzene ring, the data of (I) are compared with those of 6,7-dihydro-8-(4-methyl-1-piperazinyl)[1]benzoxepino[4,5-*c*]-quinoline.0.13H_2O, (II), whose X-ray structure has been published recently (Giorgi *et al.*, 1997). The molecular structure of the title compound is represented in Fig. 1. In the quinoline nucleus, the distances N1—C2 and N1—C10 are 1.318 (3) and 1.374 (3) Å, respectively, in agreement with previously reported data. The quinoline moiety is planar. Atoms C2–C5 and C7 are coplanar within 0.070 Å. In the pyran ring, the distances O1—C11 and O1—C12 are 1.447 (3) and 1.381 (3) Å, respectively. These values are close to the corresponding O—C bond lengths found in analogous arylpyran ethers: 6*H*-benzo[*b*]naphtho[1,2-*d*]-pyran, (III), and its 1,3-dimethyl- and 1,3-dimethoxy-derivatives (Bringmann *et al.*, 1992), in which the distances (H_2)C—O and (Ar)C—O average 1.439 and 1.381 Å, respectively. A comprehensive search of the Cambridge Structural Database (Version 5.11; Allen *et al.*, 1991) for benzopyran ethers yielded 13 unique entries, crystal data being available for nine. The means of the C_{sp^3}—O and (Ar)C—O distances are 1.466 (12) and 1.378 (4) Å, respectively. Similarly, in the three independent molecules of the asymmetric unit of the oxepine derivative (II), these bond lengths average 1.444 (5) and 1.386 (5) Å, respectively (Giorgi *et al.*, 1997).

Both the heterocyclic systems of compounds (I) and (II) are not flat. In Table 2, a comparison between the torsion angles of the 'inner spiral loop' (Bringmann *et al.*, 1992) of (I) and (II) (Fig. 2) and those of some arylpyrans is reported. Compound (I) has an overall value very close to that of 6*H*-benzo[*b*]naphtho[1,2-*d*]pyran (Bringmann *et al.*, 1992), even if the value of the torsion angle γ is significantly lower. This suggests that the outer part of the loop towards the aromatic system is less twisted in quinoline derivative (I) than in the corresponding naphthyl derivative (III). On the other hand, the value of γ found in (I) is very close to that obtained for dinaphtho[2,1-*b*:1′,2′-*d*]-pyran, (IV) (Bringmann *et al.*, 1994). 6-Methoxybenzo-[*b*]naphtho[1,2-*d*]pyran, (V) (Bringmann *et al.*, 1994), shows intermediate values. Owing to the presence of two sp^3-type bridge-C atoms in the oxepine ring, the three atropisomer forms (Eliel *et al.*, 1994) of compound (II) show the highest helical character. On the other hand, it has been found that in solution, the condensed heterocyclic system of (I) shows a higher degree of mobility than that of (II) (Cappelli *et al.*, 1996).

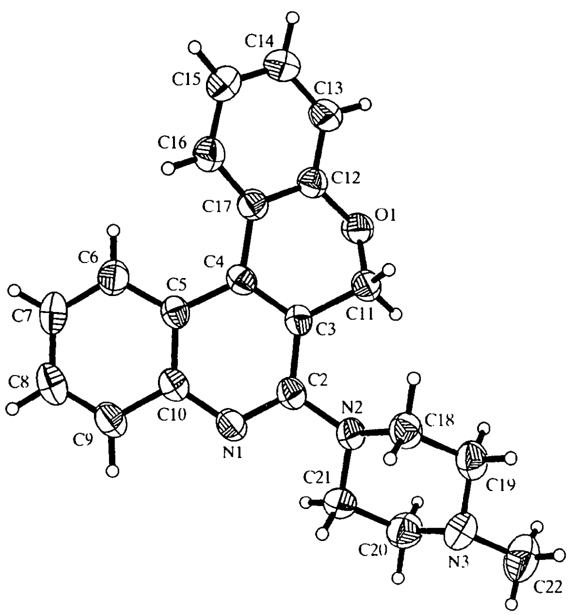


Fig. 1. The molecular structure of (I) showing 50% probability displacement ellipsoids.

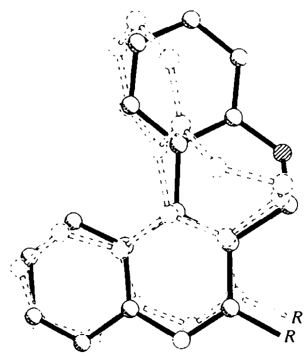


Fig. 2. Superimposition of the heteroaromatic systems of (I) (solid) and one molecule of the asymmetric unit of (II) (dashed) obtained by matching the non-H atoms belonging to the quinoline nuclei.

In (I), the puckering parameters for the pyran ring (Cremer & Pople, 1975) are θ_2 = 73.1 (3), φ_2 = −29.4 (3)° and Q_T = 0.501 (2) Å, indicating a half-boat conformation. Atom C3 is very close to the least-squares plane through the pyran ring, with a deviation of 0.046 (3) Å. Atoms C11, C12 and C17 are on one side, while atoms O1, C3 and C4 are on the other. The dihedral angle between the least-squares plane through the pyran ring and that defined by the fused benzene ring is equal to 162.2 (1)°. The structures containing the benzopyran ether fragment found in the CSD show a wide range for this dihedral angle, as calculated by

GSTAT (Version 5.11; Allen *et al.*, 1991). Its value ranges from 8.6 (LOPHOC: Wani *et al.*, 1980) to 21.0° (YAGZOV: Bringmann *et al.*, 1992).

In the title compound, the dihedral angle between the least-squares planes defined by the quinoline nucleus and the benzene ring fused with the pyran ring is equal to 33.3 (1)°. On the other hand, by replacing the pyran ring with an oxepine ring, this value becomes significantly higher [52.1 (1), 46.0 (1) and 49.4 (1)° in the three molecules of the asymmetric unit of (II)]. As shown in Fig. 2, in (I), the benzene ring fused to the pyran ring is almost coplanar with the quinoline nucleus, while in (II), the two rings are nearly perpendicular to each other.

In (I), the piperazine ring shows a chair conformation with a total puckering amplitude (Q_T) of 0.587 (2) Å (Cremer & Pople, 1975). The dihedral angle between its least-squares plane and that of the quinoline system is 35.2 (1)°, close to the corresponding values found for compound (II) (Giorgi *et al.*, 1997). The crystal packing is stabilized by stacking interactions. For example, molecules lying at (x, y, z) and at $(-x+2, -y+1, -z+1)$ show mean interplanar distances between the quinoline systems of 3.7 Å.

Experimental

The title compound was synthesized and purified as previously reported (Anzini *et al.*, 1995). Single crystals suitable for X-ray data collection were obtained by dissolving 100 mg of powder in 50 ml of *n*-hexane/cyclohexane and allowing the solution to concentrate at room temperature.

Crystal data

$C_{21}H_{21}N_3O$	Mo $K\alpha$ radiation
$M_r = 331.42$	$\lambda = 0.71073$ Å
Monoclinic	Cell parameters from 37 reflections
$P2_1/c$	$\theta = 2–17°$
$a = 12.415$ (2) Å	$\mu = 0.080$ mm^{-1}
$b = 10.806$ (2) Å	$T = 293$ (2) K
$c = 13.253$ (3) Å	Prism
$\beta = 102.83$ (3)°	0.20 × 0.20 × 0.15 mm
$V = 1733.6$ (6) Å^3	Pale yellow
$Z = 4$	
$D_x = 1.270$ Mg m^{-3}	
D_m not measured	

Data collection

Siemens *P*4 diffractometer	$\theta_{max} = 25.01°$
Profile data from ω scans	$h = -14 \rightarrow 14$
Absorption correction: none	$k = -12 \rightarrow 12$
6420 measured reflections	$l = -15 \rightarrow 15$
3031 independent reflections	3 standard reflections every 97 reflections
1973 reflections with $I > 2\sigma(I)$	intensity decay: none
$R_{int} = 0.026$	

Refinement

Refinement on F^2	$(\Delta/\sigma)_{max} = 0.062$
$R(F) = 0.046$	$\Delta\rho_{max} = 0.197$ e Å^{-3}
$wR(F^2) = 0.108$	$\Delta\rho_{min} = -0.155$ e Å^{-3}
$S = 1.092$	Extinction correction: none
3031 reflections	Scattering factors from *International Tables for Crystallography* (Vol. C)
291 parameters	
H atoms: see below	
$w = 1/[\sigma^2(F_o^2) + (0.0708P)^2 + 0.0370P]$ where $P = (F_o^2 + 2F_c^2)/3$	

Table 1. *Selected geometric parameters (Å, °)*

N1—C2	1.318 (3)	C3—C4	1.371 (2)
O1—C11	1.447 (3)	C3—C11	1.505 (3)
O1—C12	1.381 (3)	C4—C17	1.482 (3)
C2—N2	1.409 (3)		
C11—O1—C12	112.0 (2)	C3—C11—O1	110.8 (2)
N1—C2—N2	118.3 (2)	O1—C12—C17	119.7 (2)
C4—C3—C11	117.7 (2)		
C11—O1—C12—C17	−38.1 (3)	C3—C4—C17—C12	26.5 (3)
C3—C11—O1—C12	56.3 (2)		

Table 2. *Comparison of the torsion angles β (abcd) and γ (bcde) (°) of (I) and (II) with those found in analogous cyclic ethers*

	β	γ	β + γ
(I)	33.8 (4)	5.8 (4)	39.6
(II)[a]	−51.1 (6)/−45.0 (4)	−6.0 (6)/−10.1 (5)	−57.1/−55.1
	45.8 (5)	14.2 (5)	60.0
(III)[b]	26.70	12.45	39.15
(IV)[c]	38.56	7.42	45.98
(V)[c]	23.78	10.56	34.34

Notes: (*a*) Giorgi *et al.* (1997); (*b*) Bringmann *et al.* (1992); (*c*) Bringmann *et al.* (1994).

Structure solution was performed by direct methods and Fourier syntheses. Refinement was carried out by full-matrix anisotropic least squares on F^2 for all non-H atoms. H atoms were located in difference Fourier maps and included in the refinement. The isotropic displacement parameters for H atoms belonging to CH or CH_2 groups were refined to a common value of 0.055 (1) Å^2, while those of the methyl groups were refined to 0.102 (6) Å^2.

Data collection: Siemens *P*4 software. Cell refinement: Siemens *P*4 software. Data reduction: Siemens *P*4 software. Program(s) used to solve structure: *SHELXTL-Plus* (Sheldrick, 1990). Program(s) used to refine structure: *SHELXL*93 (Sheldrick, 1993). Molecular graphics: *SHELXTL-Plus*. Geometrical calculations: *SHELXL*93 and *PARST*96 (Nardelli, 1996).

Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1085). Services for accessing these data are described at the back of the journal.

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Acta Cryst. (1998). **C54**, 1130–1131

N,*N*′-Bis(2-pyridylmethyl)dithiooxamide

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(*Received 1 September 1997; accepted 11 February 1998*)

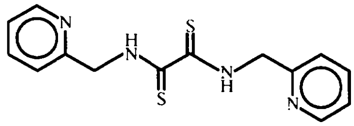
Abstract

Molecules of the title compound (BPDH2, $C_{14}H_{14}N_4S_2$) belong to the C_i point group, with only half of the molecule in an asymmetric unit. The molecule is planar to within 0.006 Å, with intramolecular N—H···S and N—H···N hydrogen bonds [H···N 2.10 (4) and H···S 2.48 (4) Å].

Comment

In the last twenty years, the study of the magnetic properties of polynuclear complexes has attracted considerable interest, due to the occurrence in many such compounds of interactions between the metal centres which considerably alter their magnetic behaviour (Ginsberg, 1971; Daudey *et al.*, 1985). Specifically, many studies have been carried out on dinuclear species, with copper(II) or nickel(II) as metal centres, and with bichelating dianions such as oxalate (Alvarez *et al.*, 1985) or oxamide (Sigel & Martin, 1982) as ligands. However, few compounds in which the ligands are dithiooxamide or its *N*,*N*′-disubstituted derivatives have been studied. Recently, a number of compounds have been designed, synthesized and characterized, which consist of dithiooxamides *N*,*N*′-disubstituted with coordinating groups (Ali Deveci & Irez, 1994; Castiñeiras *et al.*, 1995). In many cases, these compounds, in the presence of copper(II) or nickel(II), yield dinuclear complexes with antiferromagnetic properties (Vidal, 1994).

The title molecule, BPDH2, adopts a *trans* conformation (Fig. 1), which is crystallographically imposed by the inversion centre. This conformation is also found in dithiooxamide (DTO; Wheatley, 1965)



BPDH2

and in some *N*,*N*′-disubstituted dithiooxamides, such as *N*,*N*′-bis(trimethylsilyl)dithiooxamide (BTMDTO; Rinne & Thewalt, 1978), *N*,*N*′-diisopropyldithiooxamide (DIPDTO; Klaska *et al.*, 1980; Drew *et al.*, 1984), *N*,*N*′-diethyldithiooxamide (DEDTO; Drew *et al.*, 1982) and *N*,*N*′-bis(2-hydroxypropyl)dithiooxamide (BHPDTO; Drew *et al.*, 1984).

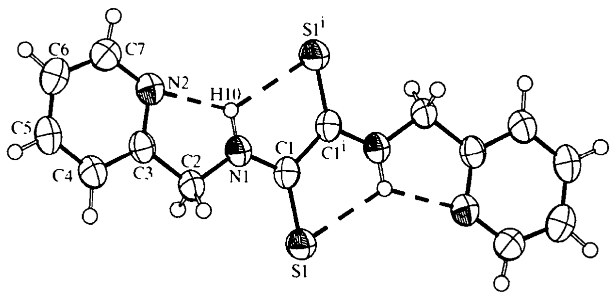


Fig. 1. Plot of BPDH2, showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level, and H atoms are shown as spheres with small arbitrary radii. [Symmetry code: (i) $1 - x$, $1 - y$, $1 - z$.]

The structural parameters found for BPDH2 (Table 1) are comparable to those reported for other *N*,*N*′-disubstituted dithiooxamides (Rinne & Thewalt, 1978; Klaska *et al.*, 1980; Drew *et al.*, 1982, 1984; Jean, 1994), with typical bond distances which do not deviate significantly from those reported for compounds containing the thioamide group (Orpen *et al.*, 1994).

The overall molecule is planar to within 0.006 Å; not only is the dithiooxamide unit planar, as expected for a dithiooxamide function lying across a crystallographic inversion centre, but the pyridine ring also occupies the same plane. This conformation is favoured by the presence of intramolecular hydrogen bonds (Jeffrey &

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