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2-(2-Ethoxycarbonyl-1,4-benzodioxan-7-yl)-4*H*-1-benzopyran-4-one†

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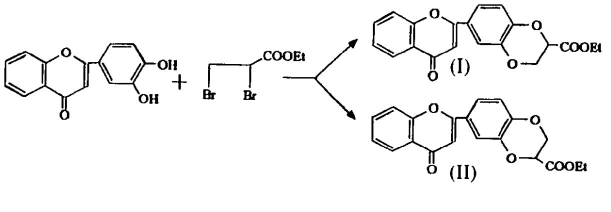
Abstract

The benzopyran ring system of the flavone in the title compound, $C_{20}H_{16}O_6$, is quasi-planar and makes a dihedral angle of 13.9 (4)° with the 2-phenyl substituent. The dioxane ring deviates from planarity. The structure is stabilized by inter- and intramolecular hydrogen bonds.

Comment

It is well known that flavone derivatives exhibit spasmolytic and vasodilatory properties, as well as having potential as anticancer and antiallergy agents (Cody, Middleton & Harborne, 1986; Cody, Middleton, Harborne & Beretz, 1988). In previous studies, we have synthesized flavone derivatives of types (I) and (II) which have a benzodioxane moiety as substituent at position 2 of the benzopyran-4-one skeleton (Ertan, Ertan, Göker & Pindur, 1987). The regioisomers (I) and (II) were separated by fractional crystallization. The structures (regiochemistry and conformation) of (I) and (II) were obtained using various NMR techniques, the NMR spectral data of (I) and (II) being consistent with the structures given in the scheme below. In this study, we confirm the structure of isomer (II) through X-ray analysis.



The displacement ellipsoids of the non-H atoms of (II) are shown in Fig. 1. All bond lengths and angles in the flavone molecule are normal. The benzopyran ring is quasi-planar. The total puckering amplitude (Cremer & Pople, 1975) of the pyrone ring is Q = 0.043 (3) Å. In the generally preferred conformation, the dihedral angle between the phenyl and γ-pyrone rings is expected to be small as shown in 5-hydroxyflavone where the value is 5.2 (9)° (Shoja, 1990). In the title compound, (II), the corresponding dihedral angle increases to 13.9 (4)°.

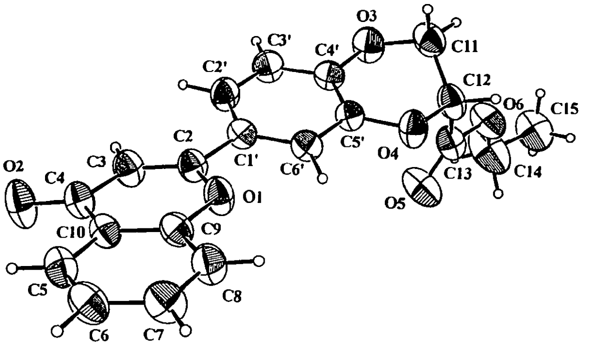


Fig. 1. *ORTEP*II (Johnson, 1976) drawing of $C_{20}H_{16}O_6$ with the atom-numbering scheme. The displacement ellipsoids are drawn at the 50% probability level. H atoms are shown as small circles of arbitrary radii.

Another parameter of interest in flavone structures is the bond length between the benzopyran and phenyl rings. In compound (II), the corresponding C2—C1′ bond length is 1.474 (4) Å. The increase in the dihedral angle has the effect of increasing the length of the C2—C1′ bond. In 5-hydroxyflavone, the dihedral angle is 5.2° and the C1′—C2 bond is 1.465 (4) Å, while in 2′-methyl-3′-nitroflavone, these values are 139.8 (2)° and 1.491 (8) Å, respectively (Kendi, Özbey, Tunçbilek & Ertan, 1996). As we pointed out in 2′-methyl-3′-nitroflavone, the non-coplanarity of the phenyl and pyrone rings supports a decrease in the degree of conjugation between the C1′—C2 bond and the π electrons of the pyrone ring. The ring strain caused by the neighbouring C_{sp^2}—C_{sp^2} atoms causes widening of the angle O1—C9—C10, 121.7 (3)°, and narrowing of C3—C4—C10, 113.5 (3)°. These angles are 122.9 (5) and 114.2 (6)°, respectively, in 2′-methyl-3′-nitroflavone, and 121.2 (2) and 115.6 (2)°, respectively, in morin (Cody & Luft, 1994). The torsion angle which describes the principal degree of freedom of the molecule is O1—C2—C1′—C2 [−167.2 (3)°]. The dioxane ring fused to the phenyl ring deviates from planarity. The puckering parameters if the atomic sequence is chosen from C4′ through O3 to C5′ are Q = 0.484 (3) Å, φ = 135.9 (4) and θ = 53.7 (3)°. The ethoxycarbonyl group attached to the dioxane ring deviates slightly from planarity with torsion angles C14—O6—C13—C12 and C13—O6—C14—C15 of −177.9 (3) and −169.1 (3)°, respectively.

The structure is stabilized by inter- and intramolecular hydrogen bonds, given in Table 2. The molecular packing diagram is shown in Fig. 2. The intramolecular

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† Alternative name: ethyl 7-(4*H*-4-oxo-1-benzopyran-2-yl)-1,4-benzodioxane-2-carboxylate.

hydrogen bond formed between O2 and C5 is also seen in 7-hydroxy-2′,6′-dimethoxyflavone (Wallet, Gaydou, Espinosa, Osorno, Molins & Miravitlles, 1992). It was proposed by Rossi *et al.* (1980) that the hydrogen bonds involving O2 would enhance the electron-withdrawing power of the pyrone ring on the phenyl ring, thus giving C2—C1′ more double-bond character, and force coplanarity in the benzopyran moiety. The other significant hydrogen bonds are C6′···O1 and C14···O5 of which the first determines the torsion of the phenyl ring with respect to the pyrone ring, and the latter is related to the approximate planarity of the ethoxycarbonyl substituent.

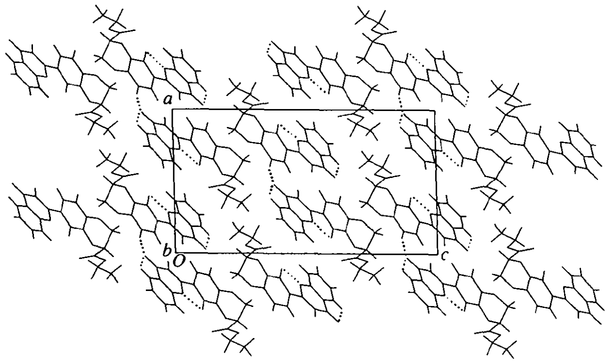

Fig. 2. Diagram of the two-dimensional network of hydrogen bonds in the structure of the title compound.

Experimental

2-(3,4-Dihydroxyphenyl)-4*H*-1-benzopyran-4-one was reacted with ethyl 2,3-dibromopropionate and two regioisomeric products (I) (43%) and (II) (29%) were obtained.

Crystal data

$C_{20}H_{16}O_6$
$M_r = 352.343$
Monoclinic
$P2_1/n$
$a = 11.0244\ (10)$ Å
$b = 7.5621\ (10)$ Å
$c = 19.9172\ (10)$ Å
$\beta = 91.407\ (4)°$
$V = 1659.9\ (3)$ Å^3
$Z = 4$
$D_x = 1.4099$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 11–18°$
$\mu = 0.105$ mm^{-1}
$T = 295$ K
Prismatic
0.48 × 0.20 × 0.16 mm
Colourless

Data collection

Enraf–Nonius CAD-4 diffractometer
$\omega/2\theta$ scans
Absorption correction: empirical *via* ψ scan (*MolEN*; Fair, 1990)
$T_{\min} = 0.930$, $T_{\max} = 1.000$

2145 reflections with $I > \sigma(I)$
$R_{\rm int} = 0.015$
$\theta_{\max} = 26.3°$
$h = 0 \rightarrow 13$
$k = -9 \rightarrow 0$
$l = -24 \rightarrow 24$

3837 measured reflections
3373 independent reflections

3 standard reflections
frequency: 120 min
intensity decay: 1.4%

Refinement

Refinement on F
$R = 0.053$
$wR = 0.050$
$S = 0.80$
2145 reflections
235 parameters
H atoms: see below
$w = 1.0$ if $F >$ threshold, $w = [\text{threshold}/F]^2$ if $F \geq$ threshold, $w = 0$ if $F^2 < \sigma(F^2)$; threshold = 116.69

$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.20$ e Å^{-3}
$\Delta\rho_{\min} = -0.21$ e Å^{-3}
Extinction correction: none
Scattering factors from *International Tables for X-ray Crystallography* (Vol. IV)

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

O1—C2	1.360 (4)	O6—C13	1.337 (4)
O1—C9	1.376 (4)	O6—C14	1.453 (5)
O2—C4	1.232 (4)	C2—C3	1.344 (4)
O3—C11	1.441 (4)	C2—C1′	1.474 (4)
O3—C4′	1.375 (4)	C3—C4	1.439 (5)
O4—C12	1.426 (4)	C11—C12	1.491 (5)
O4—C5′	1.372 (4)	C12—C13	1.530 (5)
O5—C13	1.197 (4)	C14—C15	1.450 (6)
C2—O1—C9	119.5 (2)	C3—C4—C10	113.5 (3)
C11—O3—C4′	111.8 (2)	C2—C1′—C2′	120.9 (3)
C12—O4—C5′	114.8 (2)	O1—C9—C10	121.7 (3)
O1—C2—C3	121.5 (3)	C4—C10—C9	120.2 (3)
O1—C2—C1′	111.4 (2)	O3—C11—C12	110.0 (3)
C3—C2—C1′	127.1 (3)	O4—C12—C11	110.8 (3)
C2—C3—C4	123.5 (3)	O3—C4′—C5′	121.1 (3)
O2—C4—C3	123.9 (3)	O4—C5′—C4′	122.6 (3)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C5—H5···O2	0.95	2.63	2.885 (5)	96
C6′—H6′···O1	0.95	2.35	2.689 (4)	100
C14—H142···O5	0.95	2.53	2.680 (5)	89
C8—H8···O5$^{\rm i}$	0.95	2.53	3.444 (5)	161
C3′—H3′···O2$^{\rm ii}$	0.95	2.62	3.520 (5)	159

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

All non-H atoms were refined with anisotropic displacement parameters. H atoms were placed geometrically 0.95 Å from the corresponding C atoms. For all H atoms, a riding model was used with $U_{\rm iso}({\rm H}) = 1.3U_{\rm eq}({\rm C})$.

Data collection: *CAD*-4 *EXPRESS* (Enraf–Nonius, 1993). Data reduction: *MolEN* (Fair, 1990). Program(s) used to solve structure: *SIR* in *MolEN*. Program(s) used to refine structure: *LSFM* in *MolEN*. Molecular graphics: *MolEN* version of *ORTEP*II (Johnson, 1976). Software used to prepare material for publication: *MolEN* and *PARST*95 (Nardelli, 1995).

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: NA1299). Services for accessing these data are described at the back of the journal.

References

Cody, V. & Luft, R. J. (1994). *J. Mol. Struct.* **317**, 89–97.

Cody, V., Middleton, E. Jr & Harborne, J. B. (1986). Editors. *Plant Flavonoids in Biology and Medicine: Biochemical, Pharmacological and Structure-Activity Relationships.* New York: Alan R. Liss.

Cody, V., Middleton, E. Jr, Harborne, J. B. & Beretz, A. (1988). Editors. *Plant Flavonoids in Biology and Medicine* II: *Biochemical, Cellular and Medicinal Properties.* New York: Alan R. Liss.

Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.

Enraf–Nonius (1993). *CAD-4 EXPRESS.* Version 1.1. Enraf–Nonius, Delft, The Netherlands.

Ertan, M., Ertan, R., Göker, H. & Pindur, U. (1987). *Arch. Pharm. (Weinheim)*, **320**, 1132–1138.

Fair, C. K. (1990). *MolEN. An Interactive Intelligent System for Crystal Structure Analysis.* Enraf–Nonius, Delft, The Netherlands.

Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.

Kendi, E., Özbey, S., Tunçbilek, M. & Ertan, R. (1996). *Cryst. Res. Technol.* **31**, 611–615.

Nardelli, M. (1995). *J. Appl. Cryst.* **28**, 659.

Rossi, M., Cantrell, J. S., Farber, A. J., Dyott, T., Carrell, H. L. & Glusker, J. P. (1980). *Cancer Res.* **40**, 2774–2784.

Shoja, M. (1990). *Acta Cryst.* **C46**, 517–519.

Wallet, J. C., Gaydou, E. M., Espinosa, E., Osorno, O., Molins, E. & Miravitlles, C. (1992). *Acta Cryst.* **C48**, 86–88.

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8-Hydroxyquinoline-*O*-sulfuric Acid and its Monohydrate

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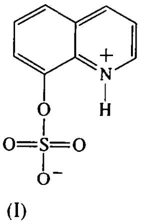
Abstract

8-Hydroxyquinoline-*O*-sulfuric acid exists as a zwitterion in both its anhydrous, $C_9H_7NO_4S$, and monohydrated, $C_9H_7NO_4S.H_2O$, forms. In each case, one of the terminal O atoms of the sulfate group is *trans* to the C8 atom. The structures are stabilized by intermolecular hydrogen bonds.

Comment

It has long been known that many sulfate esters are present in plants and animals (Soda & Hattori, 1931; Soda & Egami, 1943; Mumma & Verlangieri, 1972), and that these esters play an important role in biological processes (Jeffrey & Martin, 1966; Moser, Moser & Orr, 1966; Mumma, 1968; Benesch, Edalji & Benesch, 1976). 8-Hydroxyquinoline-*O*-sulfuric acid is reported to be a good sulfating agent in the synthesis of biologically important compounds, such as D-galactose-*O*-sulfate, adenosine-5′-*O*-sulfate, *etc.* (Nagasawa & Yoshidome, 1974). Kinetic studies of the hydrolysis of 8-hydroxyquinoline-*O*-sulfates catalysed by some divalent and trivalent metal ions have been reported (Hay & Edmonds, 1967; Nagasawa & Yoshidome, 1974).



(I)
(II) = (I).H_2O

8-Hydroxyquinoline-*O*-sulfuric acid, (I), crystallizes as a zwitterion with a protonated N atom and a deprotonated sulfate group (Fig. 1). The deviations of the O1 and S atoms from the quinoline mean plane are 0.012 (3) and 1.167 (4) Å, respectively. The dihedral angle between the quinoline plane and the S, O1, C8 plane is 52.5 (2)°. The S—O1 ester bond length is 1.653 (2) Å, while the non-ester S—O bond lengths range from 1.422 (3) to 1.437 (2) Å (Table 1). The ester O—S—O angles are much narrower than the other O—S—O angles (*cf.* Allen *et al.*, 1991). The O1—C8—C7 angle is significantly wider than the O1—C8—C9 angle [125.0 (3) *versus* 115.8 (3)°]. This may be a result of the intramolecular hydrogen-bond-type interaction between the O1 and N atoms.

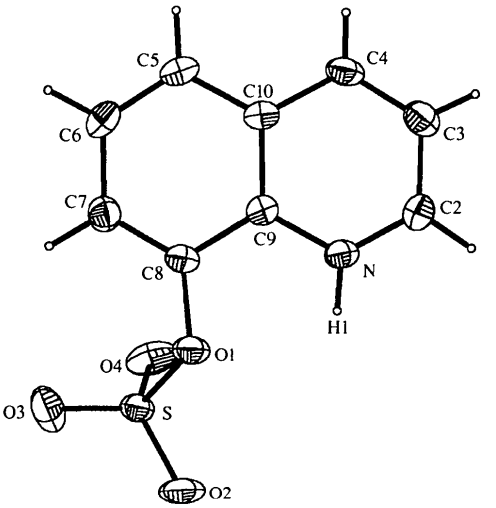


Fig. 1. The molecular structure and numbering scheme of 8-hydroxyquinoline-*O*-sulfuric acid, (I). Displacement ellipsoids are shown at the 50% probability level. H atoms are shown as small spheres of arbitrary radii.