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5-Fluoroindoline-2,3-dione

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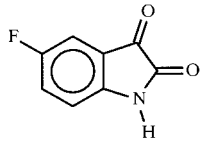
In the title compound (5-fluoroisatin), $C_8H_4FNO_2$, the N atom of one molecule is linked to the amido-O atom of an adjacent molecule across a center of symmetry by a cyclic hydrogen bond [N···O = 2.888 (4) Å].

Comment

Substituted isatin (2,3-indolinedione) compounds display biological (Anastasova, 1997) and cytostatic (Anastasova *et al.*, 2000; Juranic *et al.*, 1990) activity. QSAR studies have correlated the cytostatic activity of the monosubstitued isatins (including 5-fluoroisatin) to the nature and position of the substituent in the molecule. The fluorine substituent at the 5-position enhances antiproliferative activity; for the related uracil systems, the 5-fluro compounds are well known anti-tumor agents (Bretner *et al.*, 1993). The crystal structure of isatin has been well investigated (Frolova *et al.*, 1988; Goldschmidt & Llewellyn, 1950; Palenik *et al.*, 1990; Palmer *et al.*, 1987); the crystal structures of monosubstituted isatins have not been reported, other than for the *N*-acetyl derivative (Zukerman-Schpector *et al.*, 1992); the molecular structures of the title compound, (I), and other 5- and *N*-substitued isatins have been studied by spectroscopic methods (Morales-Rios & Joseph-Nathan, 1991; Naumov & Anastasova, 2000).



(I)

The 5-fluoroisatin molecule is planar and all bond distances and angles are normal, except for the elongated C(═O)—C(═O) single bond of 1.554 (4) Å. Such long bonds are, aside from a number of other reasons (Palmer *et al.*, 1987), attributed to non-bonded lone-pair/lone-pair repulsions (Palenik *et al.*, 1990). A shorter bond [1.538 (2) Å] is found in the *N*-ethyl derivative (Zuckerman-Schpector *et al.*, 1992). In the F-substituted derivative, the amido-N atom of one molecule is linked to the amido-O atom of an adjacent molecule across a center of symmetry [N···O 2.888 (4) Å].

The *ab initio* [HF/6-31G(d,p)] theoretical structure of 5-fluoroisatin reveals a slightly longer N—C(aromatic) bond; otherwise, the molecular structure is insignificantly different from that of isatin itself. Intermolecular (*e.g.* hydrogen bonding) rather than intrinsic factors probably account for the slightly longer 3-carbonyl bond in isatin [2-carbonyl = 1.220 (3) Å and 3-carbonyl = 1.211 (3) Å (Frolova *et al.*, 1988); 2-carbonyl = 1.220 (3) Å and 3-carbonyl = 1.213 (3) Å (Palenik *et al.*, 1990); 2-carbonyl = 1.220 (2) Å and 3-carbonyl = 1.214 (2) Å (Palmer *et al.*, 1987)] and 5-fluoroisatin [3-carbonyl = 1.222 (3) Å and 2-carbonyl = 1.211 (3) Å]. These are indistinguishable in the optimized structures (isatin: 1.184 and 1.183 Å; 5-fluoroisatin: 1.183 and 1.182 Å). The acetyl group in *N*-acetylisatin (Zukerman-Schpector *et al.*, 1992) hinders the formation of isatin-like cetrosymmetric dimers, which explains the reverse order of bond lengths [2-carbonyl = 1.196 (2) Å and 3-carbonyl = 1.207 (2) Å]. The long Csp^2—Csp^2 single bond in isatin and its derivatives allows for the ready cleavage of the five-membered ring in acidic or alkaline media, the reaction can explain the biological activity. *Ab initio* treatment (isatin: 1.555 Å; 5-F isatin: 1.553 Å) supports the insensitivity of this bond to substitution of the hydrogen by fluorine.

Experimental

5-Fluoroisatin was obtained by cyclization of the fluorinated isonitroso precursor; the synthesis will be detailed elsewhere (Anastasova *et al.*, 2000). Theoretical calculations: the molecular geometry of 5-fluoroisatin was first *CNDO*-optimized with *HYPERCHEM* (Hypercube Inc., 1996) and then further optimized at the HF SCF level within the standard basis set 6-31G(d,p) by the analytical gradient method in the *GAUSSIAN*-94*w* package (Frisch *et al.*, 1995). Harmonic vibrational analyses at the same level were performed on the resulting stationary points to ascertain energy minima.

Crystal data

$C_8H_4FNO_2$
M_r = 165.12
Monoclinic, $P2_1/c$
a = 3.789 (7) Å
b = 12.20 (1) Å
c = 14.99 (2) Å
β = 94.41 (1)°
V = 691 (2) Å^3
Z = 4
D_x = 1.587 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 2310 reflections
θ = 2.15–25.97°
μ = 0.134 mm^{-1}
T = 298 (2) K
Parallelepiped, brown
0.30 × 0.25 × 0.25 mm

Data collection

MarResearch Image Plate diffractometer
Method: 95 frames at 2° intervals, counting time 2 min.
2310 measured reflections
1265 independent reflections
851 reflections with $I > 2\sigma(I)$
R_{int} = 0.034
θ_{max} = 25.97°
$h = 0 \rightarrow 4$
$k = -15 \rightarrow 14$
$l = -18 \rightarrow 18$
Intensity decay: none

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0891P)^2 + 0.1412P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.053$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.166$	$\Delta\rho_{max} = 0.20$ e Å^{-3}
$S = 1.074$	$\Delta\rho_{min} = -0.19$ e Å^{-3}
1265 reflections	Extinction correction: *SHELXL*97
110 parameters	Extinction coefficient: 0.04 (1)
H-atom parameters constrained	

Table 1
Hydrogen-bonding geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O2^{i}	0.86	2.06	2.888 (4)	163

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

Data collection: *XDS* (Kabsch, 1988); cell refinement: *XDS*; data reduction: *XDS*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); software used to prepare material for publication: *SHELXL*97.

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References

Anastasova, F. B. (1997). PhD thesis, 'Sv. Kiril i Metodij' University, Skopje, Macedonia.
Anastasova, F., Juranic, Z., Radulovi, S., Panteli, Lj., Stanojkovi, T. & Juranic, I. (2000). Unpublished results.
Bretner, M., Kulikowski, T., Dzik, J. M., Balinska, M., Rode, W. & Shugar, D. (1993). *J. Med. Chem.* **36**, 3611–3617.
Frisch, M. J., Trucks, G. W., Schlegel, H. B., Gill, P. M. W., Johnson, B. G., Robb, M. A., Cheeseman, J. R., Keith, T., Petersson, G. A., Montgomery, J. A., Raghavachari, K., AluLaham, M. A., Zakrzewski, V. G., Ortiz, J. V., Foresman, J. B., Peng, C. Y., Ayala, P. Y., Chen, W., Wong, M. W., Anders, J. L., Replogle, E. S., Gomperts, R., Martin, R. L., Fox, D. J., Binkley, J. S., Defrees, D. J., Baker, J., Stewart, J. P., Head-Gordon, M., Gonzalez, C. & Pople, J. A. (1995). *GAUSSIAN*-94*w*. Revision B.2, Gaussian Inc., Pittsburgh, PA, USA.
Frolova, N. A., Kravtsov, V. H., Biyshkin, B. H., Chumakov, Y. M., Belykova, O. N. & Malinovsky, T. I. (1988). *Zh. Strukt. Khim.* **29**, 155–158.
Goldschmidt, G. H. & Llewellyn, F. J. (1950). *Acta Cryst.* **3**, 294–305.
Hypercube Inc. (1996). *HYPERCHEM*. Hypercube Inc., Waterloo, Ontario, Canada.
Juranic, Z., Anastasova, F., Juranic, I., Stanojkovi, T., Radulovi, S. & Vuleti, N. (1990). *J. Exp. Clin. Cancer Res.* **18**, 317–324.
Kabsch, W. (1988). *J. Appl. Cryst.* **21**, 916–932.
Morales-Rios, M. S. & Joseph-Nathan, P. (1991). *Magn. Reson. Chem.* **29**, 893–896.
Naumov, P. & Anastasova, F. (2000). *Spectrochim. Acta.* Submitted.
Palenik, G. J., Koziol, A. E., Katritzky, A. R. & Fan, W.-Q. (1990). *J. Chem. Soc. Chem. Commun.* pp. 715–716.
Palmer, M. H., Blake, A. J. & Gould, R. O. (1987). *Chem. Phys.* **115**, 219–227.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Zukerman-Schpector, J., Castellano, E. E., Pinto, A. D. C., da Silva, J. F. M. & Barcellos, M. T. F. C. (1992). *Acta Cryst.* C**48**, 760–762.