

N-(3,4-Difluorophenyl)-3,4-dimethoxybenzenesulfonamide

Hyon Pil You,^a Byung Hee Han,^{a*} Sung Kwon Kang,^a Chang Keun Sung^b and Sang Ook Kang^c

^aDepartment of Chemistry, Chungnam National University, Daejeon 305-764, Republic of Korea, ^bDepartment of Food Science and Technology, Chungnam National University, Daejeon 305-764, Republic of Korea, and ^cDepartment of Materials Chemistry, Korea University, 208 Seochang, Chochidwon, Chungnam 339-700, Republic of Korea

Correspondence e-mail: bhhan@cnu.ac.kr

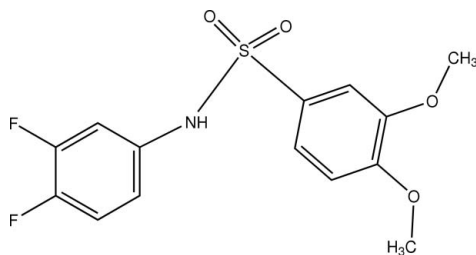
Received 3 April 2008; accepted 30 April 2008

Key indicators: single-crystal X-ray study; $T = 295$ K; mean $\sigma(\text{C}-\text{C}) = 0.004$ Å; R factor = 0.044; wR factor = 0.127; data-to-parameter ratio = 16.2.

In the title sulfonamide derivative, $\text{C}_{14}\text{H}_{13}\text{F}_2\text{NO}_4\text{S}$, the dihedral angle between the benzene rings is 66.05 (9°). The crystal structure is stabilized by weak intermolecular N—H \cdots O hydrogen bonds involving the amine and methoxy groups, which link the molecules into a one-dimensional chain. No significant interchain contacts are observed.

Related literature

For general background on skin-whitening agents, see: Dawley & Flurkey (1993); Nerya *et al.* (2003); Juana *et al.* (1994); Briganti *et al.* (2003). For the synthesis, see: Hussain *et al.* (2003).



Experimental

Crystal data

$\text{C}_{14}\text{H}_{13}\text{F}_2\text{NO}_4\text{S}$
 $M_r = 329.31$

Monoclinic, $P2_1/c$
 $a = 12.2886$ (10) Å

$b = 8.5662$ (7) Å
 $c = 14.5546$ (12) Å
 $\beta = 109.655$ (2) $^\circ$
 $V = 1442.8$ (2) Å³
 $Z = 4$

Mo $K\alpha$ radiation
 $\mu = 0.26$ mm⁻¹
 $T = 295$ (2) K
 $0.25 \times 0.18 \times 0.15$ mm

Data collection

Bruker SMART CCD area-detector diffractometer
Absorption correction: multi-scan (SADABS; Bruker, 2002)
 $T_{\min} = 0.928$, $T_{\max} = 0.957$

9690 measured reflections
3308 independent reflections
1700 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.042$

Refinement

$R[F^2 > 2\sigma(F^2)] = 0.044$
 $wR(F^2) = 0.126$
 $S = 0.99$
3308 reflections
204 parameters

H atoms treated by a mixture of independent and constrained refinement
 $\Delta\rho_{\text{max}} = 0.19$ e Å⁻³
 $\Delta\rho_{\text{min}} = -0.21$ e Å⁻³

Table 1

Hydrogen-bond geometry (Å, $^\circ$).

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
$N7-H7\cdots O17^i$	0.76 (3)	2.48 (3)	3.180 (3)	155 (3)
$N7-H7\cdots O19^i$	0.76 (3)	2.61 (3)	3.256 (3)	144 (3)

Symmetry code: (i) $-x + 2, y + \frac{1}{2}, -z + \frac{1}{2}$.

Data collection: SMART (Bruker, 2002); cell refinement: SAINT (Bruker, 2002); data reduction: SAINT; program(s) used to solve structure: SHELXS97 (Sheldrick, 2008); program(s) used to refine structure: SHELXL97 (Sheldrick, 2008); molecular graphics: ORTEP-3 for Windows (Farrugia, 1997); software used to prepare material for publication: WinGX (Farrugia, 1999).

This work was partially supported by Chungnam National University, the Fund of New Universities for Regional Innovation (05-Na-A-01) from the Ministry of Education and Human Resources Department, Republic of Korea, and the DBIO Co. Ltd.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: BH2170).

References

- Briganti, S., Camera, E. & Picardo, M. (2003). *Pigment Cell Res.* **16**, 101–110.
Bruker (2002). *SADABS, SAINT and SMART*. Bruker AXS Inc., Madison, Wisconsin, USA.
Dawley, R. M. & Flurkey, W. H. (1993). *J. Food Sci.* **58**, 609–610.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Hussain, H. H., Babic, G., Durst, T., Wright, J. S., Flueraru, M., Chichirau, A. & Chepelev, L. L. (2003). *J. Org. Chem.* **68**, 7023–7032.
Juana, C., Soledad, C. & Francisco, G. (1994). *J. Pharm. Pharmacol.* **46**, 983–985.
Nerya, O., Vaya, J., Musa, R., Izrael, S., Ben-Arie, R. & Tamir, S. (2003). *J. Agric. Food Chem.* **51**, 1201–1207.
Sheldrick, G. M. (2008). *Acta Cryst.* **A64**, 112–122.

supplementary materials

Acta Cryst. (2008). E64, o994 [doi:10.1107/S1600536808012610]

***N*-(3,4-Difluorophenyl)-3,4-dimethoxybenzenesulfonamide**

H. P. You, B. H. Han, S. K. Kang, C. K. Sung and S. O. Kang

Comment

Most skin whitening agents currently on the market (Dawley & Flurkey, 1993; Nerya *et al.*, 2003) contain hydroquinone, ascorbic acid, kojic acid (Juana *et al.*, 1994), arbutin, azealic acid, and glycyrrhetic acid. They include aromatic, methoxy, hydroxyl and carbonyl functional groups in their structures. They are acting as a direct inhibitors of tyrosinase, the enzyme in the skin pigment cells (melanocytes) producing melanin.

Tyrosinase is the key enzyme converting the amino acid *L*-tyrosine to melanin, and its inhibitors are target molecules to develop anti-pigmentation agents for skin treatment after sunburn (Briganti *et al.* 2003). The melanin formation by the tyrosinase activity after sunlight exposure causes some dermatological disorders associated with freckles and melasma. Therefore, potent inhibitory agents on melanin formation and tyrosinase should be cosmetically useful for treatment of dermatological disorders.

However, most skin whitening agents have some problems, due to toxicity, low stability of formulation and poor skin permeation. In our work on the development of new whitening agents to complement the inadequacy of current whitening agents and maximize the inhibitory effects of melanin creation, we synthesized the title compound (Fig. 1), *via* a general chemical reaction (Hussain *et al.*, 2003) of 3,4-difluoroaniline with aromatic sulfonyl chloride, and studied its X-ray crystal structure.

The 3,4-dimethoxybenzenesulfonyl and 3,4-difluoroaniline moieties are essentially planar, with a mean deviation of 0.004 Å and 0.010 Å, respectively, from the corresponding least-squares planes. The dihedral angle between benzene rings is 66.05 (9)°. The intermolecular N7—H7¹···O17¹ and O19¹ [symmetry code: (i) $-x + 2, y + 1/2, -z + 1/2$] hydrogen bonds (involving the H atom of the amine and O atoms of methoxy groups) allow to form an extensive one-dimensional network along the *b* axis, which stabilizes the crystal structure.

Experimental

3,4-difluoroaniline and 3,4-dimethoxy benzenesulfonyl chloride were purchased from Sigma Chemical Co. Solvents used for organic synthesis were redistilled before used. All other chemicals and solvents were of analytical grade and used without further purification. The title compound was prepared by the reaction of 3,4-difluoroaniline (1 mmol) with aromatic sulfonyl chloride (1.2 mmol) in triethylamine as a solvent, under stirring. Evaporation of solvent, treatment with water, extraction with methylene chloride and chromatography of the dried solution (MgSO₄) on silica gel column (2 / 1 = hexane / ethyl acetate) gave the title compound in 56% yield. Colourless single crystals were obtained by slow evaporation from an ethyl acetate solution, at room temperature.

Refinement

The amine H atom H7 was located in a difference map and refined freely. The other H atoms were positioned geometrically and refined using a riding model, with C—H = 0.93 Å for aromatic H atoms and 0.96 Å for methyl H atoms, and with $U_{\text{iso}}(\text{H}) = 1.2U_{\text{eq}}(\text{C})$ for aromatic and $1.5U_{\text{eq}}(\text{C})$ for methyl H atoms.

Figures

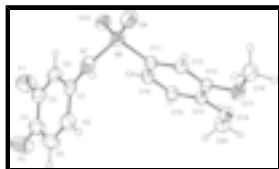


Fig. 1. The molecular structure of the title compound, showing the atom-numbering scheme and 30% probability ellipsoids.

N-(3,4-Difluorophenyl)-3,4-dimethoxybenzenesulfonamide

Crystal data

$\text{C}_{14}\text{H}_{13}\text{F}_2\text{NO}_4\text{S}$

$M_r = 329.31$

Monoclinic, $P2_1/c$

Hall symbol: -P 2ybc

$a = 12.2886$ (10) Å

$b = 8.5662$ (7) Å

$c = 14.5546$ (12) Å

$\beta = 109.655$ (2)°

$V = 1442.8$ (2) Å³

$Z = 4$

$F_{000} = 680$

$D_x = 1.516$ Mg m⁻³

Mo $K\alpha$ radiation

$\lambda = 0.71073$ Å

Cell parameters from 1598 reflections

$\theta = 2.8$ – 23.5 °

$\mu = 0.26$ mm⁻¹

$T = 295$ (2) K

Block, colourless

$0.25 \times 0.18 \times 0.15$ mm

Data collection

Bruker SMART CCD area-detector diffractometer

φ and ω scans

Absorption correction: multi-scan (SADABS; Bruker, 2002)

$T_{\text{min}} = 0.928$, $T_{\text{max}} = 0.957$

9690 measured reflections

3308 independent reflections

1700 reflections with $I > 2\sigma(I)$

$R_{\text{int}} = 0.042$

$\theta_{\text{max}} = 27.5$ °

$\theta_{\text{min}} = 1.8$ °

$h = -15 \rightarrow 14$

$k = -11 \rightarrow 9$

$l = -18 \rightarrow 18$

Refinement

Refinement on F^2

H atoms treated by a mixture of independent and constrained refinement

Least-squares matrix: full

$$R[F^2 > 2\sigma(F^2)] = 0.044$$

$$wR(F^2) = 0.126$$

$$S = 0.99$$

3308 reflections

204 parameters

$$w = 1/[\sigma^2(F_o^2) + (0.0426P)^2 + 0.5561P]$$

$$\text{where } P = (F_o^2 + 2F_c^2)/3$$

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

$$\Delta\rho_{\max} = 0.19 \text{ e } \text{\AA}^{-3}$$

$$\Delta\rho_{\min} = -0.21 \text{ e } \text{\AA}^{-3}$$

Extinction correction: SHELXL97 (Sheldrick, 2008),

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

Extinction coefficient: 0.0349 (19)

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

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
F1	0.37106 (16)	0.1400 (3)	-0.04021 (13)	0.0975 (7)
F2	0.3788 (2)	0.0318 (3)	0.13264 (17)	0.1271 (9)
C1	0.6212 (2)	0.3457 (3)	0.11332 (19)	0.0492 (7)
C2	0.5338 (2)	0.2966 (3)	0.0306 (2)	0.0584 (8)
H2	0.5288	0.3352	-0.0304	0.07*
C3	0.4554 (2)	0.1914 (4)	0.0395 (2)	0.0609 (8)
C4	0.4593 (3)	0.1366 (4)	0.1281 (2)	0.0753 (10)
C5	0.5430 (3)	0.1849 (5)	0.2102 (2)	0.0885 (12)
H5	0.5454	0.1475	0.2708	0.106*
C6	0.6248 (2)	0.2906 (4)	0.2030 (2)	0.0692 (9)
H6	0.6826	0.3245	0.2591	0.083*
N7	0.7042 (2)	0.4591 (3)	0.1068 (2)	0.0595 (7)
H7	0.738 (2)	0.489 (4)	0.158 (2)	0.062 (10)*
S8	0.78080 (6)	0.43912 (9)	0.03547 (5)	0.0595 (3)
O9	0.84833 (17)	0.5777 (2)	0.04834 (17)	0.0802 (7)
O10	0.70295 (15)	0.3991 (3)	-0.05866 (13)	0.0709 (6)
C11	0.8750 (2)	0.2809 (3)	0.07756 (18)	0.0490 (7)
C12	0.9910 (2)	0.3073 (3)	0.13211 (17)	0.0478 (6)
H12	1.0184	0.4087	0.1468	0.057*
C13	1.0644 (2)	0.1829 (3)	0.16380 (17)	0.0472 (6)
C14	1.0231 (2)	0.0296 (3)	0.14189 (18)	0.0480 (6)
C15	0.9086 (2)	0.0050 (3)	0.0875 (2)	0.0559 (7)
H15	0.8809	-0.0962	0.0724	0.067*
C16	0.8350 (2)	0.1300 (3)	0.0554 (2)	0.0566 (7)
H16	0.7579	0.1128	0.0187	0.068*
O17	1.17904 (15)	0.1936 (2)	0.21844 (13)	0.0614 (5)
C18	1.2333 (2)	0.3419 (4)	0.2277 (2)	0.0669 (9)
H18A	1.3129	0.3326	0.2681	0.1*
H18B	1.1949	0.4141	0.2569	0.1*
H18C	1.2288	0.3792	0.1643	0.1*
O19	1.10296 (15)	-0.0832 (2)	0.17753 (14)	0.0599 (5)
C20	1.0682 (3)	-0.2409 (3)	0.1507 (2)	0.0668 (8)
H20A	1.132	-0.3098	0.1805	0.1*
H20B	1.0441	-0.2514	0.0811	0.1*
H20C	1.005	-0.2674	0.1727	0.1*

supplementary materials

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
F1	0.0780 (12)	0.1205 (18)	0.0749 (12)	-0.0470 (12)	0.0005 (10)	-0.0069 (11)
F2	0.1139 (17)	0.160 (2)	0.1037 (16)	-0.0684 (17)	0.0321 (14)	0.0185 (15)
C1	0.0374 (13)	0.0490 (16)	0.0540 (17)	0.0026 (12)	0.0060 (12)	-0.0074 (13)
C2	0.0499 (16)	0.0634 (19)	0.0522 (17)	-0.0065 (14)	0.0044 (13)	0.0047 (14)
C3	0.0480 (16)	0.069 (2)	0.0555 (18)	-0.0104 (15)	0.0037 (14)	-0.0058 (15)
C4	0.0615 (19)	0.088 (3)	0.075 (2)	-0.0210 (18)	0.0223 (17)	0.0036 (19)
C5	0.074 (2)	0.134 (4)	0.057 (2)	-0.015 (2)	0.0207 (18)	0.008 (2)
C6	0.0520 (17)	0.096 (3)	0.0530 (19)	-0.0028 (17)	0.0093 (14)	-0.0121 (17)
N7	0.0462 (13)	0.0581 (16)	0.0618 (17)	-0.0029 (12)	0.0019 (12)	-0.0102 (13)
S8	0.0460 (4)	0.0573 (5)	0.0647 (5)	-0.0070 (4)	0.0048 (3)	0.0101 (4)
O9	0.0582 (12)	0.0579 (14)	0.1098 (18)	-0.0137 (10)	0.0090 (12)	0.0198 (12)
O10	0.0543 (11)	0.0896 (17)	0.0556 (12)	-0.0054 (10)	0.0009 (9)	0.0153 (11)
C11	0.0422 (14)	0.0530 (17)	0.0480 (15)	-0.0059 (13)	0.0102 (12)	0.0031 (13)
C12	0.0480 (14)	0.0453 (16)	0.0459 (15)	-0.0115 (12)	0.0102 (12)	-0.0005 (12)
C13	0.0420 (14)	0.0526 (17)	0.0427 (14)	-0.0059 (13)	0.0084 (11)	0.0005 (12)
C14	0.0469 (14)	0.0473 (17)	0.0482 (15)	-0.0036 (13)	0.0138 (12)	0.0015 (12)
C15	0.0509 (16)	0.0509 (17)	0.0643 (18)	-0.0130 (14)	0.0171 (14)	-0.0060 (14)
C16	0.0418 (14)	0.062 (2)	0.0598 (18)	-0.0137 (14)	0.0092 (13)	-0.0027 (15)
O17	0.0470 (10)	0.0523 (12)	0.0707 (13)	-0.0082 (9)	0.0010 (9)	0.0051 (10)
C18	0.0486 (16)	0.061 (2)	0.078 (2)	-0.0199 (14)	0.0042 (14)	0.0031 (16)
O19	0.0563 (11)	0.0441 (12)	0.0732 (13)	-0.0037 (9)	0.0138 (10)	-0.0016 (9)
C20	0.0727 (19)	0.0473 (18)	0.081 (2)	-0.0054 (16)	0.0270 (17)	-0.0061 (16)

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

F1—C3	1.343 (3)	C11—C12	1.398 (3)
F2—C4	1.354 (3)	C12—C13	1.372 (4)
C1—C6	1.375 (4)	C12—H12	0.93
C1—C2	1.382 (3)	C13—O17	1.369 (3)
C1—N7	1.434 (4)	C13—C14	1.405 (4)
C2—C3	1.357 (4)	C14—O19	1.350 (3)
C2—H2	0.93	C14—C15	1.379 (3)
C3—C4	1.359 (4)	C15—C16	1.378 (4)
C4—C5	1.352 (4)	C15—H15	0.93
C5—C6	1.383 (4)	C16—H16	0.93
C5—H5	0.93	O17—C18	1.420 (3)
C6—H6	0.93	C18—H18A	0.96
N7—S8	1.628 (3)	C18—H18B	0.96
N7—H7	0.76 (3)	C18—H18C	0.96
S8—O10	1.424 (2)	O19—C20	1.431 (3)
S8—O9	1.424 (2)	C20—H20A	0.96
S8—C11	1.754 (3)	C20—H20B	0.96
C11—C16	1.381 (4)	C20—H20C	0.96
C6—C1—C2	119.3 (3)	C13—C12—C11	119.6 (2)

C6—C1—N7	119.9 (2)	C13—C12—H12	120.2
C2—C1—N7	120.7 (3)	C11—C12—H12	120.2
C3—C2—C1	119.2 (3)	O17—C13—C12	125.1 (2)
C3—C2—H2	120.4	O17—C13—C14	114.6 (2)
C1—C2—H2	120.4	C12—C13—C14	120.3 (2)
F1—C3—C2	120.1 (3)	O19—C14—C15	125.5 (2)
F1—C3—C4	118.5 (3)	O19—C14—C13	114.9 (2)
C2—C3—C4	121.4 (3)	C15—C14—C13	119.6 (3)
C5—C4—F2	120.7 (3)	C16—C15—C14	120.1 (3)
C5—C4—C3	120.4 (3)	C16—C15—H15	119.9
F2—C4—C3	118.9 (3)	C14—C15—H15	119.9
C4—C5—C6	119.3 (3)	C15—C16—C11	120.5 (2)
C4—C5—H5	120.3	C15—C16—H16	119.8
C6—C5—H5	120.3	C11—C16—H16	119.8
C1—C6—C5	120.3 (3)	C13—O17—C18	118.3 (2)
C1—C6—H6	119.8	O17—C18—H18A	109.5
C5—C6—H6	119.8	O17—C18—H18B	109.5
C1—N7—S8	123.2 (2)	H18A—C18—H18B	109.5
C1—N7—H7	109 (2)	O17—C18—H18C	109.5
S8—N7—H7	115 (2)	H18A—C18—H18C	109.5
O10—S8—O9	120.03 (13)	H18B—C18—H18C	109.5
O10—S8—N7	107.04 (13)	C14—O19—C20	117.3 (2)
O9—S8—N7	105.36 (14)	O19—C20—H20A	109.5
O10—S8—C11	107.51 (13)	O19—C20—H20B	109.5
O9—S8—C11	108.15 (12)	H20A—C20—H20B	109.5
N7—S8—C11	108.29 (13)	O19—C20—H20C	109.5
C16—C11—C12	119.9 (2)	H20A—C20—H20C	109.5
C16—C11—S8	120.0 (2)	H20B—C20—H20C	109.5
C12—C11—S8	120.0 (2)		

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

$D-H\cdots A$	$D-H$	$H\cdots A$	$D\cdots A$	$D-H\cdots A$
N7—H7 \cdots O17 ⁱ	0.76 (3)	2.48 (3)	3.180 (3)	155 (3)
N7—H7 \cdots O19 ⁱ	0.76 (3)	2.61 (3)	3.256 (3)	144 (3)

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

Fig. 1

