Acta Crystallographica Section C
Crystal Structure
Communications
ISSN 0108-2701

3-[4-(3,4-Dimethylphenyl)-1,3-thiazol-2-yl]-2-(2-hydroxyphenyl)-1,2,3,4-tetrahydroquinazolin-4-one

Subhash C. Jain,[a] Aparna Bharadvaja,[a] Rohtash Kumar,[a] Deepti Agarwal[a] and William Errington[b]*

[a]Department of Chemistry, University of Delhi, Delhi 110007, India, and
[b]Department of Chemistry, University of Warwick, Coventry CV4 7AL, England
Correspondence e-mail: w.errington@warwick.ac.uk

Received 18 January 2000
Accepted 2 February 2000

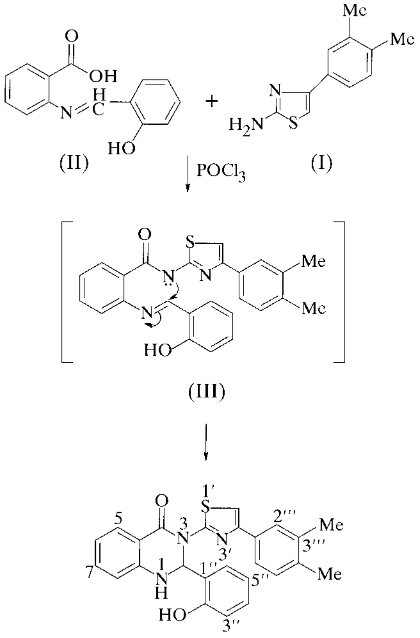
The facile one-pot synthesis of the title compound, $C_{25}H_{21}N_3O_2S$, is described. The six-membered 1,3-diaza ring is puckered with an axial phenyl group in the 2-position. Intermolecular hydrogen bonding between hydroxyl and ketonic O atoms produces infinite one-dimensional chains in the *a* direction.

Comment

Quinazolin-4(1*H*)-ones, commonly known as benzpyrimidinones, form an important class of heterocyclic compounds. Some of them either occur as quinazoline alkaloids (Mohrle & Gundlack, 1970; Baker & McEvoy, 1995) or their precursors (Brown, 1984). In addition, numerous synthetic quinazolinone derivatives are known which exhibit diverse antihistamic (Graham, 1960), diuretic (Cohen *et al.*, 1960), hypnotic (Chappel & von Seeman, 1963) and anti-inflammatory (Saravanan *et al.*, 1998) biological activities.

In view of the multifaceted pharmacological behaviour of this class of heterocyclic compounds, an attempt was made to synthesize some new 2,3-disubstituted benzpyrimidones containing three different biodynamic moieties. For this purpose, synthesis of the title compound, (IV), was anticipated starting from the key intermediate (III), which in turn might be obtained by condensing 2-amino-4-(3,4-dimethylphenyl)-thiazole, (I), with *N*-(2-hydroxybenzylidine)anthranilic acid, (II), in the presence of phosphorus oxychloride. When this reaction was carried out, (IV) was obtained directly, rather than the expected amide (III). The direct formation of (IV) might be explained on the basis that the condensation and cyclization take place in a concerted manner with the final stage involving the facile nucleophilic attack of the amidic nitrogen on the benzylidene carbon. Crystals of (IV) were recrystallized from a mixture of DMF–C_2H_5OH (DMF = dimethylformamide) and its structure was finally confirmed by single-crystal X-ray diffraction.

The molecular structure of the title compound is illustrated in Fig. 1. The bond lengths and angles are largely unremarkable, although the C5′—S1′—C2′ bond angle of 87.98 (9)° is perhaps slightly narrower than expected; a survey of the Cambridge Structural Database (Allen & Kennard, 1993) for 1,3-thiazole rings gave a mean (based upon 1906 observations) value of 90.79 (5)° for this angle. The thiazole ring is flat (r.m.s. deviation 0.005 Å) and is inclined at an angle of 32.7 (1)° to the plane of the attached phenyl group. The 1,3-diaza ring, containing an Csp^3 atom (*i.e.* C2), is non-planar with Cremer–Pople puckering parameters (Cremer & Pople, 1975) of Q_T = 0.418 (2) Å, θ = 61.9 (3) and φ = 44.9 (3)°; the only axial substituent attached to this ring is the hydroxyphenyl group which is inclined at an angle of 86.1 (1)° with respect to the best plane through the diaza ring (r.m.s. deviation 0.171 Å).



The intramolecular O1···S1′ contact of 2.6138 (14) Å is short in comparison with the sum of the van der Waals radii for O and S (3.32 Å); it arises from the planarity of the O1═C4—N3—C2′—S1′ unit (see the appropriate torsion angles in Table 1), an arrangement which minimizes the O···S separation. This

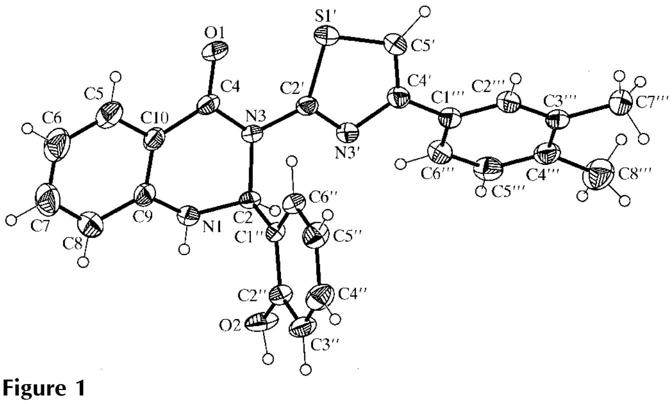


Figure 1
View of the title molecule showing the atomic numbering. Displacement ellipsoids are drawn at the 50% probability level for non-H atoms. H atoms are shown as spheres of arbitrary radii.

planarity is anticipated on the basis of resonance theory which predicts partial double-bond character in the N3—C4 and N3—C2′ bonds, resulting in restricted rotation about these linkages.

Infinite one-dimensional chains are formed *via* hydrogen bonding between hydroxyl groups (O2—H) and ketonic O atoms (O1) in the *a* direction; these O···O distances of 2.7682 (18) Å are significantly shorter than expected from the oxygen van der Waals radius (3.04 Å; Bondi, 1964). A weaker intramolecular hydrogen-bonding interaction between the N1 H atom and the O2 atom is also present.

Experimental

A mixture of 2-amino-4-(3,4-dimethylphenyl)thiazole (1.0 g, 0.005 mol) and *N*-(2-hydroxybenzylidene)anthranilic acid (1.2 g, 0.005 mol) in freshly distilled phosphorus oxychloride (40 ml) was refluxed for 8 h. The progress of the reaction was monitored by thin-layer chromatography. After completion of the reaction, the contents were cooled and poured into ice water. The solid that separated was filtered, washed with water, dried and crystallized from a mixture of DMF–C_2H_5OH as pale-yellow needles (1.7 g, 81% yield, m.p. 502 K). IR (KBr) ν_{max}: 3320, 3030, 2960, 1735, 1698, 1615, 1576, 1419, 1402, 1382, 1297, 1263, 1142, 1089, 1060, 990, 890, 820, 760 cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6): δ (p.p.m.) 2.22 and 2.51 (2*s*, 3H each, 2 × CH_3), 6.59 (*m*, 1H, H-3″), 6.73–6.82 (*m*, 2H, H-8 and H-4″), 6.85–6.91 (*m*, 2H, H-5″ and H-2‴), 7.02–7.15 (*m*, 2H, H-6 and H-5‴), 7.32 (*m*, 1H, H-7), 7.54–7.69 (*m*, 4H, H-2, H-5′, H-6″ and H-6‴), 7.86 (*dd*, 1H, *J* = 7.9 and 1.5 Hz, H-5), 10.2 (*s*, 1H, NH). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ (p.p.m.) 19.0, 19.4, 65.0, 108.8, 112.7, 115.3, 115.5, 117.7, 118.4, 123.0, 125.1, 125.9, 126.7, 127.8, 129.2, 129.6, 131.6, 134.8, 135.8, 136.2, 146.4, 148.3, 154.6, 156.4, 161.4. EIMS *m*/*z* (% int): 427 (M^+, 38), 333 (16), 308 (12), 275 (13), 243 (18), 239 (85), 238 (38), 224 (30), 204 (26), 199 (20), 180 (18), 158 (100), 105 (14), 91 (30), 86 (34) and 69 (19).

Crystal data

$C_{25}H_{21}N_3O_2S$
M_r = 427.51
Triclinic, $P\overline{1}$
a = 8.9439 (9) Å
b = 11.5231 (12) Å
c = 12.0135 (12) Å
α = 63.663 (3)°
β = 68.248 (3)°
γ = 75.966 (3)°
V = 1026.06 (18) Å^3

Z = 2
D_x = 1.384 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 3730 reflections
θ = 1.98–28.55°
μ = 0.186 mm^{-1}
T = 180 (2) K
Block, yellow
0.42 × 0.32 × 0.10 mm

Data collection

Siemens SMART CCD area-detector diffractometer with an Oxford Cryosystems open-flow cryostat (Cosier & Glazer, 1986)
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.926, T_{max} = 0.982

6303 measured reflections
4545 independent reflections
3162 reflections with $I > 2\sigma(I)$
R_{int} = 0.020
θ_{max} = 28.55°
$h = -11 \rightarrow 11$
$k = -14 \rightarrow 9$
$l = -15 \rightarrow 14$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.116
S = 0.957
4545 reflections
294 parameters

H atoms: see below
$w = 1/[\sigma^2(F_o^2) + (0.0603P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.32 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

S1′—C5′	1.716 (2)	S1′—C2′	1.7308 (17)
C5′—S1′—C2′	87.98 (9)		
O1—C4—N3—C2′	3.6 (3)	N3—C2—C1″—C6″	4.6 (2)
C2—N3—C4—O1	167.90 (16)	C5′—C4′—C1‴—C2‴	32.2 (3)
C4—N3—C2′—S1′	6.1 (2)		

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2″*B*···O1^i	0.84 (3)	1.93 (3)	2.7682 (18)	173 (3)
N1—H1*A*···O2	0.80 (2)	2.42 (2)	2.885 (2)	118.4 (18)

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

H atoms bonded to N, O and methyl-C atoms were located from ΔF syntheses, while others bound to C atoms were placed geometrically. H atoms bonded to N and O atoms were refined freely, those in CH_3 groups were treated as part of rigid rotating groups and other H atoms bound to C were constrained to ride on these carrier atoms.

Data collection: *SMART* (Siemens, 1994); cell refinement: *SAINT* (Siemens, 1995); data reduction: *SAINT*; program(s) used to solve structure: *SHELXTL/PC* (Siemens, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *SHELXTL/PC*; software used to prepare material for publication: *SHELXTL/PC*.

We wish to acknowledge the use of the EPSRC's Chemical Database Service at Daresbury Laboratory (Fletcher *et al.*, 1996) for access to the Cambridge Structural Database (Allen & Kennard, 1993). We also thank the Council of Scientific and Industrial Research (CSIR, New Delhi, India) for financial assistance.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: BM1400). Services for accessing these data are described at the back of the journal.

References

Allen, F. H. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 31–37.
Baker, B. R. & McEvoy, F. J. (1995). *J. Org. Chem.* **60**, 136–142.
Bondi, A. (1964). *J. Phys. Chem.* **68**, 441–451.
Brown, D. J. (1984). *Comprehensive Heterocyclic Chemistry*, edited by A. R. Katritzky & C. W. Rees, Vol. III, pp. 57–155. Oxford: Pergamon Press.
Chappel, C. I. & von Seeman, C. (1963). *Prog. Med. Chem.* **3**, 89–145.
Cohen, E., Klarber, B. & Vaughan, J. R. (1960). *J. Am. Chem. Soc.* **82**, 2731–2735.
Cosier, J. & Glazer, A. M. (1986). *J. Appl. Cryst.* **19**, 105–107.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Fletcher, D. A., McMeeking, R. F. & Parkin, D. (1996). *J. Chem. Inf. Comput. Sci.* **36**, 746–749.
Graham, J. D. P. (1960). *Arch. Int. Pharmacodyn. Therap.* **123**, 419–420.
Mohrle, H. & Gundlack, P. (1970). *Tetrahedron Lett.* pp. 3249–3250.
Saravanan, J., Mohan, S. & Manjuanatha, K. S. (1998). *Indian J. Heterocycl. Chem.* **8**, 55–58.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (1997). *SHELXL*97. University of Göttingen, Germany.
Siemens (1994). *SMART* (Version 4.021) and *SHELXTL/PC Reference Manual* (Version 5.0). Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.
Siemens (1995). *SAINT*. Version 4.021. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.