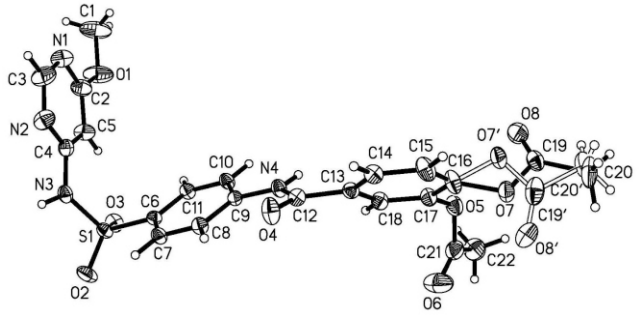
Crystal structure of 3,4-bis(acetyloxy)-*N*-{4-[(6-methoxy-4-pyrimidinyl)aminosulfonyl]phenyl}benzamide, $C_{22}H_{20}N_4O_8S$

Lue Li, Fa-Yan Meng, Li Wang, Zhou-Feng Huang, Shui-Qiang Wei and Cui-Wu Lin*

College of Chemistry and Chemical Engineering, Guangxi University, Guangxi 530004, P. R. China

Received September 14, 2011, accepted and available on-line February 7, 2012; CCDC no. 1267/3681



Abstract

$C_{22}H_{20}N_4O_8S$, triclinic, $P\bar{1}$ (no. 2), a = 8.408(6) Å, b = 9.842(7) Å, c = 15.15(1) Å, α = 108.369(8)°, β = 101.227(9)°, γ = 96.479(8)°, V = 1146.8 Å^3, Z = 2, $R_{gt}(F)$ = 0.042, $wR_{ref}(F^2)$ = 0.130, T = 296 K.

Source of material

Protocatechuic acid (5.0 g, 0.0333 mol) was added to 15 mL acetic anhydride, and allowed to react at 140 °C for 4 h, then concentrated. From the crude product, the white powder of acetyl protocatechuic acid was obtained by recrystallization from ethanol. To the acetyl protocatechuic acid (5.0 g, 0.0210 mol), $SOCl_2$ (15 mL) was added and allowed to react for 5 h under reflux. The excess of $SOCl_2$ was evaporated under vacuum and the crude product was used for the amidation step. A mixture of sulfamonomethoxine (5.9 g, 0.0210 mol) in 30 mL of THF and 5 mL pyridine was added to acetyl protocatechuic chloride and allowed to react for 2 hours in an ice-bath and then kept at room temperature for about 24 hours. When the reaction was complete, the solvent was evaporated under vacuum, and the residue was washed with water and recrystallized from MeOH and THF to afford the title compound.

Experimental details

All H atoms were positioned geometrically with d(C—H) = 0.93-0.96 Å and refined as riding with $U_{iso} = 1.2\ U_{eq}$.

Discussion

Aromatic amides are a large class of organic compounds originating from condensation reaction of aromatic acid and amine [1]. The –CO–NH– backbone gives amides the function of antiproliferative, antiviral, antimalarial, general anesthetics and antimicrobials [2]. Protocatechuic acid is an important component in edible and medicinal plants, exhibiting antioxidant, antitumor, detoxifying enzyme gene expression, possessing free radical-scavenging and antiatherogenic capacity [3-5]. Sulfonamide drugs are a family of synthetic drugs used pharmacologically as antimicrobial agents to treat human and animal infections, in which the amide moiety may exert their effects by modifying the metabolic activity of the invaded pathogenic microorganisms [6-10]. So, we selected the sulfonamide as amine part for synthesizing aromatic amides.

In the title crystal structure, all values of the geometric parameters are normal. The benzene ring is planar within experimental precision. In the case of protocatechuic acid amide, the presence of a –CO–NH– backbone would make this compound antibacterially active. The compound exhibits both intramolecular and intermolecular hydrogen bonding. The intermolecular hydrogen bonds are N3–H3O···O4 with bond length 2.8784 Å, bond angle 125° and symmetry {–x,1–y,1–z}, N4–H6O···O2 with bond length 2.8906 Å, bond angle 145° and symmetry {1+x,y,z}, C18–H18O···O3 with bond length 3.2685 Å, bond angle 169° and symmetry {–x,–y,1–z}, and C22–H22O···N1 with bond length 3.4771 Å, bond angle 168° and symmetry {1+x,y,1+z}. The intramolecular hydrogen bonds are C5–H5O···O3 with bond length 2.9408 Å, bond angle 125°, and C8–H8O···O4 with bond length 2.9210 Å, bond angle 121°.

Table 1. Data collection and handling.

Crystal:	colorless block, size 0.22 × 0.28 × 0.32 mm
Wavelength:	Mo K_α radiation (0.71073 Å)
μ:	1.98 cm^{-1}
Diffractometer, scan mode:	Bruker SMART CCD, φ/ω
$2\theta_{max}$:	50°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	6317, 3952
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 3402
$N(param)_{refined}$:	356
Programs:	SHELXS-97, SHELXL-97, SHELXTL [10]

Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	Occ.	x	y	z	U_{iso}
H(3B)	2*i*		–0.4658	0.1933	0.2863	0.047
H(4A)	2*i*		0.4208	0.2548	0.5383	0.044
H(1B)	2*i*		–0.1948	–0.3692	–0.0786	0.155
H(1C)	2*i*		–0.1127	–0.2063	–0.0540	0.155
H(1D)	2*i*		–0.2992	–0.2615	–0.1085	0.155
H(3C)	2*i*		–0.2921	0.1961	0.0370	0.083
H(5A)	2*i*		–0.3396	–0.1318	0.1857	0.064
H(7A)	2*i*		–0.1748	0.3463	0.5025	0.045
H(8A)	2*i*		0.1013	0.4478	0.5702	0.044
H(10A)	2*i*		0.2226	0.0681	0.4290	0.044
H(11A)	2*i*		–0.0545	–0.0331	0.3602	0.044
H(14A)	2*i*		0.7049	0.6664	0.6578	0.049
H(15A)	2*i*		0.9751	0.6797	0.7347	0.064
H(18A)	2*i*		0.5878	0.2662	0.6710	0.047
H(22A)	2*i*		0.7966	0.0391	0.8767	0.111

* Correspondence author (e-mail: cuiwulin@yahoo.com.cn)

Table 2. Continued.

Atom	Site	Occ.	*x*	*y*	*z*	U_{iso}
H(22B)	2*i*		0.9621	0.0721	0.8478	0.111
H(22C)	2*i*		0.8006	–0.0112	0.7683	0.111
H(20A)	2*i*	0.596(5)	1.4442	0.4306	0.8689	0.126
H(20B)	2*i*	0.596	1.3359	0.4903	0.9406	0.126

Table 2. Continued.

Atom	Site	Occ.	*x*	*y*	*z*	U_{iso}
H(20C)	2*i*	0.596	1.4074	0.5887	0.8885	0.126
H(20D)	2*i*	0.404	1.4168	0.5608	0.8549	0.093
H(20E)	2*i*	0.404	1.3673	0.3906	0.8203	0.093
H(20F)	2*i*	0.404	1.4028	0.4831	0.9296	0.093

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	Occ.	*x*	*y*	*z*	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	2*i*		–0.2675(3)	–0.0019(2)	0.0239(2)	0.073(2)	0.062(1)	0.051(1)	0.005(1)	0.023(1)	0.019(1)
N(2)	2*i*		–0.3427(3)	0.1744(2)	0.1506(2)	0.077(2)	0.043(1)	0.055(1)	0.012(1)	0.017(1)	0.021(1)
N(3)	2*i*		–0.4045(2)	0.1284(2)	0.2814(1)	0.035(1)	0.0344(9)	0.044(1)	0.0117(7)	0.0076(8)	0.0087(8)
N(4)	2*i*		0.3595(2)	0.3193(2)	0.5503(1)	0.0319(9)	0.0318(9)	0.043(1)	0.0092(7)	0.0073(8)	0.0073(7)
O(1)	2*i*		–0.2584(4)	–0.2317(2)	0.0304(2)	0.151(2)	0.052(1)	0.083(2)	0.029(1)	0.076(2)	0.014(1)
O(2)	2*i*		–0.4448(2)	0.1457(2)	0.4393(1)	0.040(1)	0.069(1)	0.058(1)	0.0062(8)	0.0266(8)	0.0097(9)
O(3)	2*i*		–0.3746(2)	–0.0811(2)	0.3394(1)	0.0450(9)	0.0374(8)	0.061(1)	–0.0015(6)	0.0131(8)	0.0182(7)
O(4)	2*i*		0.3775(2)	0.5644(2)	0.6205(1)	0.045(1)	0.0315(8)	0.078(1)	0.0101(7)	–0.0019(9)	0.0095(8)
O(5)	2*i*		0.8713(2)	0.2425(2)	0.7579(1)	0.0405(9)	0.057(1)	0.067(1)	0.0143(7)	0.0131(8)	0.0345(8)
O(6)	2*i*		0.7205(3)	0.2773(3)	0.8680(2)	0.125(2)	0.099(2)	0.087(2)	0.051(2)	0.061(2)	0.052(1)
S(1)	2*i*		–0.35220(6)	0.07463(5)	0.37381(4)	0.0298(3)	0.0365(3)	0.0424(3)	0.0024(2)	0.0128(2)	0.0103(2)
C(1)	2*i*		–0.2124(6)	–0.2704(4)	–0.0603(3)	0.145(4)	0.080(2)	0.084(2)	0.014(2)	0.077(3)	–0.000(2)
C(2)	2*i*		–0.2848(3)	–0.0967(3)	0.0688(2)	0.063(2)	0.046(1)	0.054(2)	0.007(1)	0.025(1)	0.010(1)
C(3)	2*i*		–0.3003(4)	0.1289(3)	0.0682(2)	0.099(2)	0.057(2)	0.059(2)	0.010(2)	0.026(2)	0.028(1)
C(4)	2*i*		–0.3559(3)	0.0756(2)	0.1947(2)	0.034(1)	0.035(1)	0.040(1)	0.0016(8)	0.0036(9)	0.0097(9)
C(5)	2*i*		–0.3289(3)	–0.0635(2)	0.1556(2)	0.072(2)	0.040(1)	0.055(2)	0.013(1)	0.030(1)	0.017(1)
C(6)	2*i*		–0.1408(3)	0.1473(2)	0.4251(2)	0.032(1)	0.035(1)	0.034(1)	0.0057(8)	0.0106(9)	0.0130(8)
C(7)	2*i*		–0.0945(3)	0.2910(2)	0.4880(2)	0.035(1)	0.035(1)	0.041(1)	0.0111(8)	0.0116(9)	0.0095(9)
C(8)	2*i*		0.0704(3)	0.3516(2)	0.5288(2)	0.038(1)	0.029(1)	0.039(1)	0.0071(8)	0.0082(9)	0.0060(8)
C(9)	2*i*		0.1910(2)	0.2680(2)	0.5076(1)	0.030(1)	0.034(1)	0.033(1)	0.0064(8)	0.0072(8)	0.0126(8)
C(10)	2*i*		0.1426(3)	0.1236(2)	0.4438(2)	0.034(1)	0.034(1)	0.042(1)	0.0121(8)	0.0121(9)	0.0084(9)
C(11)	2*i*		–0.0229(3)	0.0626(2)	0.4024(2)	0.036(1)	0.031(1)	0.038(1)	0.0060(8)	0.0088(9)	0.0062(8)
C(12)	2*i*		0.4417(3)	0.4558(2)	0.6079(2)	0.039(1)	0.033(1)	0.038(1)	0.0057(8)	0.0083(9)	0.0122(9)
C(13)	2*i*		0.6170(3)	0.4641(2)	0.6561(2)	0.033(1)	0.035(1)	0.035(1)	0.0033(8)	0.0091(9)	0.0100(8)
C(14)	2*i*		0.7349(3)	0.5894(2)	0.6762(2)	0.042(1)	0.034(1)	0.046(1)	0.0043(9)	0.012(1)	0.0136(9)
C(15)	2*i*		0.8961(3)	0.5980(3)	0.7234(2)	0.036(1)	0.041(1)	0.079(2)	–0.0040(9)	0.011(1)	0.021(1)
C(16)	2*i*		0.9408(3)	0.4861(3)	0.7539(2)	0.030(1)	0.051(1)	0.074(2)	0.003(1)	0.006(1)	0.022(1)
C(17)	2*i*		0.8239(3)	0.3607(2)	0.7330(2)	0.036(1)	0.042(1)	0.047(1)	0.0087(9)	0.010(1)	0.019(1)
C(18)	2*i*		0.6649(3)	0.3502(2)	0.6848(2)	0.036(1)	0.036(1)	0.043(1)	–0.0006(8)	0.008(1)	0.0143(9)
C(21)	2*i*		0.8041(3)	0.2057(3)	0.8249(2)	0.053(2)	0.063(2)	0.050(2)	0.007(1)	0.009(1)	0.028(1)
C(22)	2*i*		0.8445(4)	0.0637(3)	0.8299(2)	0.077(2)	0.083(2)	0.083(2)	0.025(2)	0.022(2)	0.054(2)
O(7)	2*i*	0.596(5)	1.0928(5)	0.5164(3)	0.8280(4)	0.035(2)	0.048(2)	0.047(3)	0.007(1)	0.001(2)	0.009(2)
O(8)	2*i*	0.596	1.1828(4)	0.3358(4)	0.7266(2)	0.060(2)	0.086(3)	0.058(2)	0.033(2)	0.020(2)	0.016(2)
C(19)	2*i*	0.596	1.2105(6)	0.4322(6)	0.8008(5)	0.037(3)	0.046(3)	0.062(3)	0.012(2)	0.013(3)	0.026(3)
C(20)	2*i*	0.596	1.363(2)	0.491(2)	0.882(1)	0.046(7)	0.097(8)	0.098(7)	–0.012(5)	–0.024(5)	0.052(6)
O(7′)	2*i*	0.404	1.1079(6)	0.4745(7)	0.7633(5)	0.029(3)	0.094(4)	0.064(4)	0.000(2)	0.004(3)	0.034(4)
O(8′)	2*i*	0.404	1.0973(9)	0.5164(9)	0.9143(4)	0.078(5)	0.170(7)	0.051(4)	0.015(4)	0.000(3)	0.025(4)
C(19′)	2*i*	0.404	1.175(2)	0.493(1)	0.8539(9)	0.056(6)	0.055(5)	0.080(8)	–0.002(4)	–0.009(6)	0.033(5)
C(20′)	2*i*	0.404	1.358(2)	0.481(2)	0.866(2)	0.05(1)	0.047(6)	0.09(1)	0.020(6)	0.009(7)	0.030(6)

Acknowledgment. This work was supported by grants from the National Natural Science Foundation of China (nos. 20962002 and 20662001).

References

1. Gududuru, V.; Hurch, H.; Dalton, J. T.; Miler, D. D.: Synthesis and antiprofilerative activity of 2-aryl-4-oxo-thiazolidin-3-yl-amides for prostate cancer. Bioorg. Med. Chem. Lett. **14** (2004) 5289-5293.
2. Igor, E. B.; Maksym, V. V.; Yaroshov, V. B.:Synthesis and anti-inflammatory activity of *N*-substituted 2-oxo-2*H*-1-benzopyran-3-carboxamides and their 2-iminoanalogues. Eur. J. Med. Chem. **34** (1999) 997-1001.
3. Tanaka, T.; Tanaka, T.; Tanaka, M.: Potential Cancer Chemopreventive Activity of Protocatechuic Acid. J. Exp. Clin. Med. **3** (2011) 27-33.
4. Wang, D. L.; Zou, T. B. ; Yang, Y.; Yan, X.; Ling, W. H .: Cyanidin-3-*O*-*β*-glucoside with the aid of its metabolite protocatechuic acid, reduces monocyte infiltration in apolipoprotein E-deficient mice. Biochem. Pharmacol. **82** (2011) 713-719.
5. Varì, R.; D'Archivio, M.; Filesi, C.; Carotenuto, S.; Scazzocchio, B.; Santangelo, C.; Giovannini, C.; Masella, R.: Protocatechuic acid induces antioxidant/detoxifying enzyme expression through JNK-mediated Nrf2 activation in murine macrophages. J. Nutr. Biochem. **22** (2011) 409-417.
6. Granja, R. H. M. M.; Nino, A. M. M.; Rabone, F.; Salerno, A. G.: A reliable high-performance liquid chromatography with ultraviolet detection for the determination of sulfonamides in honey. Anal. Chim. Acta **613** (2008) 116-119.
7. Baran, W.; Adamek, E.; Ziemiańska, J.; Sobczak, A.: Effects of the presence of sulfonamides in the environment and their influence on human health. J. Hazard. Mater. **196** (2011) 1-15.
8. de Keizer, W.; Bienenmann-Ploum, M. E.; Bergwerff, A. A., Haasnoot, W.: Flow cytometric immunoassay for sulfonamides in raw milk. Anal. Chim. Acta **620** (2008) 142-149.
9. Priya, B. S.; Nanjunda, S. S.; Tejesvi, M. V.; Basappa; Sarala, G.; Gaonkar, S. L.; Naveen, S.; Shashidhara, J. P.; Rangappa, K. S.: Synthesis, characterization, antimicrobial and single crystal X-ray crystallographic studies of some new sulfonyl, 4-chlorophenoxybenzene and dibenzoazepine substituted benzamides. Eur. J. Med. Chem. **41** (2006) 1262-1270.
10. Sheldrick, G. M.: A short history of SHELX. Acta Crystallogr. **A64** (2008) 112-122.