

# Crystal structure of 4-(4-(*N*-(5,6-dimethoxypyrimidin-4-yl)sulfamoyl)phenylcarbamoyl)-2,6-dimethoxyphenyl acetate, C<sub>23</sub>H<sub>24</sub>N<sub>4</sub>O<sub>9</sub>S

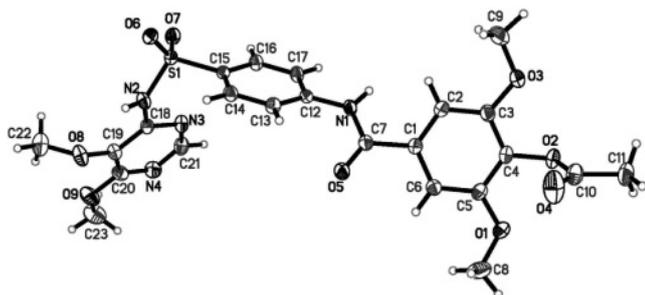
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## Abstract

C<sub>23</sub>H<sub>24</sub>N<sub>4</sub>O<sub>9</sub>S, triclinic,  $P\bar{1}$  (no. 2),  $a = 8.297(1)$  Å,  $b = 11.199(1)$  Å,  $c = 13.876(2)$  Å,  $\alpha = 88.856(2)^\circ$ ,  $\beta = 76.540(2)^\circ$ ,  $\gamma = 80.098(2)^\circ$ ,  $V = 1235.0$  Å<sup>3</sup>,  $Z = 2$ ,  $R_{\text{gt}}(F) = 0.0405$ ,  $wR_{\text{ref}}(F^2) = 0.1084$ ,  $T = 296$  K.

Table 1. Data collection and handling.

Crystal:	colourless blocks, size 0.11×0.33×0.36 mm
Wavelength:	Mo $K_{\alpha}$ radiation (0.71073 Å)
$\mu$ :	1.91 cm <sup>-1</sup>
Diffractionmeter, scan mode:	Bruker APEX-II CCD, $\varphi$ and $\omega$
$2\theta_{\text{max}}$ :	50°
$N(hkl)_{\text{measured}}$ , $N(hkl)_{\text{unique}}$ :	9804, 4332
Criterion for $I_{\text{obs}}$ , $N(hkl)_{\text{gt}}$ :	$I_{\text{obs}} > 2\sigma(I_{\text{obs}})$ , 3294
$N(\text{param})_{\text{refined}}$ :	334
Programs:	SHELX [11]

## Source of material

6000mg (about 30 mmol) of syringic acid (4-hydroxy-3,5-dimethoxybenzoic acid) in 50mL of acetic anhydride was magnetic stirred and refluxed at 120°C for 2h. 900mL of water was added to the above solution to get precipitates (5535mg) by the method of pumping filtration. 5000mg (about 20mmol) of the above dry precipitates in 40mL of thionyl chloride was magnetic stirred and refluxed at 80°C for 6h under anhydrous conditions. The solution was removed under reduced pressure to get a residue of 5692mg. 5173mg (20mmol) of the residue, 6207mg (20mmol) of sulfadimoxine(4-amino-*N*-(5,6-dimethoxy-pyrimidin-4-yl)-benzenesulfonamide) and 10mL of pyridine in 400mL of THF were magnetic stirred at 0°C for 2h and then at room temperature. 8000mL of water was added to the above reaction solution to get 7760mg of precipitates after pumping filtration. The product was redissolved in a mixed solution of THF and methanol and then left for evaporation at room temperature. After crystallization and recrystallization from the mixed solution, colourless crystals suitable for X-ray analysis was obtained. The melting point of the crystals was determined as 565–567 K using a XT-4 melting point instrument (Beijing Taike Instrument Co., Ltd, Beijing, China).

NMR spectra were obtained on a AVANCE III 300 NMR instrument (Bruker, Germany). <sup>1</sup>H-NMR (300 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 7.31 (2H, s, H-2,6), 3.86 (6H, s, H-8,9), 2.29(3H, s, H-11), 7.95 (2H, d,  $J=9.0$  Hz, H-13,17), 8.03 (2H, d,  $J=9.0$  Hz, H-14,16), 8.14(1H, s, H-21), 3.72(3H, s, H-22), 3.91(3H, s, H-23), 10.58 (1H, s, H-N1), 11.09 (1H, s, H-N2); <sup>13</sup>C-NMR (75 MHz, DMSO-*d*<sub>6</sub>)  $\delta$ : 129.1 (C-1), 105.3 (C-2), 150.8 (C-3), 127.7 (C-4), 150.8 (C-5), 105.3 (C-6), 165.9 (C-7), 56.7 (C-8), 56.7 (C-8), 168.3 (C-10), 20.6 (C-11), 135.4 (C-12), 120.2 (C-13), 120.2 (C-14), 133.1 (C-15), 120.2 (C-16), 120.2 (C-17), 143.5 (C-18), 131.2 (C-19), 162.0 (C-20), 152.1 (C-21), 60.7 (C-22), 54.5 (C-23). IR spectra (potassium bromide) were recorded on a NEXUS 470 Fourier Transform IR spectrophotometer (Thermo Nicolet Corporation, USA). IR ( $\nu_{\text{max}}$ , cm<sup>-1</sup>): 3639, 3566 ( $\nu_{\text{N-H}}$ ); 3190 ( $\nu_{\text{C-H}}$ ); 1762, 1725, 1710 ( $\nu_{\text{C=O}}$ ); 1669, 1662, 1647, 1538, 1507 ( $\nu_{\text{C=C}}$ ); 1338, 1166, 858, 812, 720, 690, 651, 641, 603, 591, 568, 544, 497, 489, 481, 443.

## Experimental details

H atoms bonded to C and N atoms were positioned geometrically with  $d(\text{N-H}) = 0.86$  Å,  $d(\text{C-H}) = 0.93$  (aromatic CH) or 0.96 Å (methyl CH<sub>3</sub>), and treated as riding atoms. For all H atoms, isotropic displacement parameters were calculated as  $U_{\text{iso}}(\text{H}) = 1.2 U_{\text{eq}}(\text{N}, \text{C})$ .

## Discussion

Syringic acid, a natural compound occurring in many kinds of plant species, showed antifungal activity at high concentration [1], anti-endotoxic effects [2], hepatoprotective effect [3,4,5], sulfadoxine was usually used as anti-malarial drug [6,7,8,9], but drug resistance occurred in recent years [10]. Modifying the chemical structure of sulfadoxine with benzoyl group (such as syringic acid) or other groups may reduce the resistance to malaria or obtain some novel properties (such as combining the activities of syringic acid with those of sulfadoxine), which should be investigated in future. The title crystal structure is only built up by the C<sub>23</sub>H<sub>24</sub>N<sub>4</sub>O<sub>9</sub>S (m.p. 565–567K) molecules, in which all values of the geometric parameters are normal. The benzene rings make a dihedral angle of 66.5° and the pyrimidine ring is twisted by 70.1° from the central benzene ring. The crystal packing is stabilized by intermolecular hydrogen bonds: N2–H2A⋯O5 ( $d(\text{N2-H2A}\cdots\text{O5}) = 2.887$  Å;  $\angle\text{N2-H2A}\cdots\text{O5} = 151.20^\circ$ ), N1–H1A⋯O6 ( $d(\text{N1-H1A}\cdots\text{O6}) = 3.069$  Å,  $\angle\text{N1-H1A}\cdots\text{O6} = 136.90^\circ$ ), N1–H1A⋯O1 ( $d(\text{N1-H1A}\cdots\text{O1}) = 3.216$  Å,  $\angle\text{N1-H1A}\cdots\text{O1} = 133.07^\circ$ ).

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**Table 2.** Atomic coordinates and displacement parameters (in Å<sup>2</sup>).

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>iso</sub>
H(2A)	2i	0.4447	0.2237	0.2856	0.048
H(1A)	2i	-0.0048	-0.0243	0.7670	0.044
H(17A)	2i	-0.0984	0.1405	0.6706	0.045
H(14A)	2i	0.3812	0.0133	0.4262	0.044
H(16A)	2i	-0.0680	0.2275	0.5160	0.044
H(6B)	2i	0.3261	-0.0662	0.9472	0.047
H(13A)	2i	0.3495	-0.0744	0.5800	0.045
H(2B)	2i	-0.0418	-0.1852	0.8527	0.049
H(21A)	2i	0.1546	0.5478	0.5361	0.058
H(11A)	2i	0.0759	-0.4897	1.2886	0.096
H(11B)	2i	-0.1039	-0.4331	1.2756	0.096
H(11C)	2i	-0.0062	-0.3584	1.3295	0.096

**Table 2.** continued.

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>iso</sub>
H(8A)	2i	0.4329	-0.1020	1.1796	0.119
H(8B)	2i	0.4104	-0.0356	1.0819	0.119
H(8C)	2i	0.4827	-0.1747	1.0786	0.119
H(22A)	2i	0.7103	0.4058	0.1023	0.112
H(22B)	2i	0.6405	0.5299	0.1599	0.112
H(22C)	2i	0.5165	0.4557	0.1284	0.112
H(9A)	2i	-0.3354	-0.3584	0.9678	0.116
H(9B)	2i	-0.1624	-0.3629	0.8914	0.116
H(9C)	2i	-0.2889	-0.2402	0.9143	0.116
H(23A)	2i	0.6480	0.7807	0.3252	0.117
H(23B)	2i	0.5663	0.7360	0.4301	0.117
H(23C)	2i	0.4526	0.7868	0.3577	0.117

**Table 3.** Atomic coordinates and displacement parameters (in Å<sup>2</sup>).

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> <sub>11</sub>	<i>U</i> <sub>22</sub>	<i>U</i> <sub>33</sub>	<i>U</i> <sub>12</sub>	<i>U</i> <sub>13</sub>	<i>U</i> <sub>23</sub>
S(1)	2i	0.18790(6)	0.19387(4)	0.33939(3)	0.0357(3)	0.0365(3)	0.0292(3)	-0.0079(2)	-0.0056(2)	0.0031(2)
C(15)	2i	0.1614(2)	0.1306(2)	0.4577(1)	0.034(1)	0.0309(9)	0.0288(9)	-0.0104(8)	-0.0070(8)	0.0008(7)
O(2)	2i	-0.0151(2)	-0.2612(1)	1.1617(1)	0.0512(9)	0.0446(8)	0.0327(7)	-0.0025(7)	-0.0049(6)	0.0105(6)
O(7)	2i	0.0422(2)	0.2811(1)	0.3365(1)	0.0404(8)	0.0508(8)	0.0409(8)	-0.0011(7)	-0.0098(6)	0.0094(6)
O(5)	2i	0.3669(2)	-0.0697(1)	0.7531(1)	0.0337(8)	0.063(1)	0.0422(8)	-0.0088(7)	-0.0070(6)	0.0112(7)
N(2)	2i	0.3523(2)	0.2603(2)	0.3229(1)	0.0368(9)	0.0365(9)	0.0396(9)	-0.0082(7)	0.0046(7)	-0.0021(7)
O(6)	2i	0.2399(2)	0.0968(1)	0.26739(9)	0.0466(8)	0.0479(8)	0.0325(7)	-0.0112(7)	-0.0058(6)	-0.0056(6)
N(1)	2i	0.0979(2)	-0.0231(2)	0.7369(1)	0.0292(8)	0.0461(9)	0.0338(9)	-0.0080(7)	-0.0037(7)	0.0097(7)
C(17)	2i	-0.0011(2)	0.1158(2)	0.6216(1)	0.033(1)	0.041(1)	0.033(1)	-0.0032(8)	0.0003(8)	0.0023(8)
C(12)	2i	0.1243(2)	0.0271(2)	0.6418(1)	0.032(1)	0.033(1)	0.0304(9)	-0.0112(8)	-0.0067(8)	0.0031(8)
O(1)	2i	0.2399(2)	-0.1361(2)	1.1333(1)	0.058(1)	0.076(1)	0.0341(8)	-0.0219(8)	-0.0164(7)	0.0033(7)
C(7)	2i	0.2167(2)	-0.0694(2)	0.7859(1)	0.037(1)	0.035(1)	0.033(1)	-0.0075(8)	-0.0063(8)	0.0018(8)
N(3)	2i	0.2340(2)	0.4111(2)	0.4460(1)	0.049(1)	0.041(1)	0.0364(9)	-0.0070(8)	-0.0012(8)	0.0032(7)
O(3)	2i	-0.1710(2)	-0.2888(2)	1.0192(1)	0.069(1)	0.076(1)	0.0464(9)	-0.0420(9)	-0.0158(8)	0.0183(8)
O(8)	2i	0.6015(2)	0.3880(1)	0.2429(1)	0.0498(9)	0.0470(9)	0.056(1)	-0.0091(7)	0.0117(7)	0.0024(7)
C(19)	2i	0.4769(2)	0.4385(2)	0.3205(2)	0.039(1)	0.039(1)	0.041(1)	-0.0071(9)	-0.0028(9)	0.0020(9)
C(14)	2i	0.2855(2)	0.0394(2)	0.4758(1)	0.033(1)	0.040(1)	0.034(1)	-0.0042(8)	-0.0018(8)	-0.0002(8)
C(16)	2i	0.0165(2)	0.1681(2)	0.5294(1)	0.035(1)	0.035(1)	0.036(1)	-0.0012(8)	-0.0049(8)	0.0053(8)
O(9)	2i	0.5780(2)	0.6211(2)	0.3213(1)	0.061(1)	0.0461(9)	0.089(1)	-0.0267(8)	-0.0039(9)	-0.0037(9)
C(1)	2i	0.1508(2)	-0.1189(2)	0.8857(1)	0.038(1)	0.035(1)	0.033(1)	-0.0055(8)	-0.0069(8)	0.0034(8)
C(18)	2i	0.3540(2)	0.3724(2)	0.3648(1)	0.038(1)	0.033(1)	0.034(1)	-0.0050(8)	-0.0072(8)	0.0051(8)
C(6)	2i	0.2333(3)	-0.1052(2)	0.9598(1)	0.038(1)	0.042(1)	0.038(1)	-0.0079(9)	-0.0072(9)	0.0026(9)
C(13)	2i	0.2668(2)	-0.0127(2)	0.5677(1)	0.035(1)	0.037(1)	0.037(1)	0.0002(8)	-0.0073(8)	0.0031(8)
C(2)	2i	0.0134(3)	-0.1778(2)	0.9028(1)	0.047(1)	0.045(1)	0.035(1)	-0.012(1)	-0.0133(9)	0.0065(9)
N(4)	2i	0.3448(2)	0.5936(2)	0.4432(1)	0.056(1)	0.041(1)	0.053(1)	-0.0070(9)	-0.0109(9)	-0.0034(8)
C(5)	2i	0.1759(3)	-0.1503(2)	1.0527(1)	0.046(1)	0.039(1)	0.033(1)	-0.0028(9)	-0.0099(9)	-0.0010(8)
C(4)	2i	0.0411(3)	-0.2118(2)	1.0690(1)	0.046(1)	0.036(1)	0.030(1)	-0.0043(9)	-0.0045(8)	0.0052(8)
C(3)	2i	-0.0410(3)	-0.2257(2)	0.9948(2)	0.043(1)	0.038(1)	0.039(1)	-0.0116(9)	-0.0072(9)	0.0063(9)
C(21)	2i	0.2373(3)	0.5197(2)	0.4799(2)	0.057(1)	0.042(1)	0.040(1)	-0.002(1)	-0.002(1)	-0.0023(9)
C(10)	2i	0.0811(3)	-0.3657(2)	1.1810(2)	0.064(2)	0.041(1)	0.048(1)	-0.003(1)	-0.010(1)	0.008(1)
C(20)	2i	0.4644(3)	0.5522(2)	0.3638(2)	0.043(1)	0.040(1)	0.055(1)	-0.0105(9)	-0.013(1)	0.004(1)
O(4)	2i	0.2092(3)	-0.4077(2)	1.1256(2)	0.090(2)	0.067(1)	0.090(2)	0.024(1)	0.015(1)	0.024(1)
C(11)	2i	0.0050(4)	-0.4162(2)	1.2772(2)	0.083(2)	0.057(1)	0.054(2)	-0.015(1)	-0.017(1)	0.024(1)
C(8)	2i	0.4047(3)	-0.1100(3)	1.1170(2)	0.047(2)	0.140(3)	0.050(2)	-0.009(2)	-0.013(1)	-0.024(2)
C(22)	2i	0.6186(4)	0.4499(3)	0.1508(2)	0.083(2)	0.080(2)	0.052(2)	-0.013(2)	0.002(1)	0.004(1)
C(9)	2i	-0.2454(4)	-0.3146(3)	0.9420(2)	0.088(2)	0.096(2)	0.061(2)	-0.059(2)	-0.012(1)	-0.001(2)
C(23)	2i	0.5597(4)	0.7411(2)	0.3619(3)	0.084(2)	0.045(1)	0.109(2)	-0.026(1)	-0.022(2)	-0.003(1)

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