

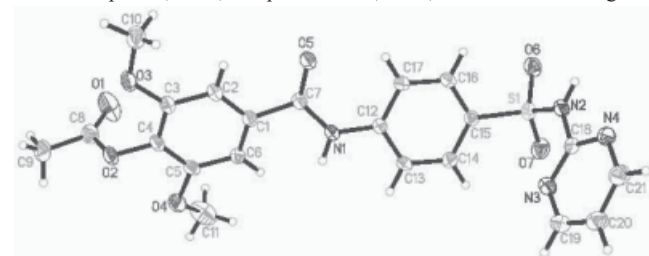
Crystal structure of 2,6-dimethoxy-4-((4-(pyrimidin-2-ylsulfonyl)phenyl)-carbamoyl)phenyl acetate, C₂₁H₂₀N₄O₇S

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Abstract

C₂₁H₂₀N₄O₇S, monoclinic, *P*2₁/*c* (no. 14), *a* = 17.003(2) Å, *b* = 14.403(2) Å, *c* = 9.211(1) Å, β = 97.941(2)°, *V* = 2233.9 Å³, *Z* = 4, *R*_{gt}(*F*) = 0.0461, *wR*_{ref}(*F*²) = 0.1261, *T* = 296 K.

Table 1. Data collection and handling.

Crystal:	colourless blocks, size 0.25×0.30×0.33 mm
Wavelength:	Mo K α radiation (0.71073 Å)
μ :	1.96 cm ⁻¹
Diffractometer, scan mode:	CCD area detector, φ and ω
2 θ _{max} :	50°
<i>N</i> (<i>hkl</i>) _{measured} , <i>N</i> (<i>hkl</i>) _{unique} :	17304, 3936
Criterion for <i>I</i> _{obs} , <i>N</i> (<i>hkl</i>) _{gt} :	<i>I</i> _{obs} > 2 σ (<i>I</i> _{obs}), 2938
<i>N</i> (<i>param</i>) _{refined} :	298
Programs:	SHELX [7]

Source of material

Syringic acid (4-hydroxy-3,5-dimethoxy benzoic acid, 50 g, 250 mmol) was added to acetic anhydride (350 mL) for hydroxyl protecting. The acetylation compound (10.0 g, 38.66 mmol) of syringic acid was poured into SOCl₂ (60 mL) and stirred for 6–7 hours at 80 °C. Then the excess of SOCl₂ was evaporated. The intermediate 3,5-dimethoxy-4-acetoxy-benzoyl chloride was obtained. Then, sulfadiazine (4.23 g, 16.91 mmol), tetrahydrofuran (THF, 43.7 mL) and pyridine (8 mL) were added to the intermediate (4.37 g, 16.90 mmol) and stirred for 24 hours in an ice bath. Among them, pyridine was the catalyst for the reaction [6]. When the reaction was completed, the solvent was evaporated under vacuum, and the residue was washed with water. Recrystallized from methanol and THF for more than 10 days, the title product was obtained. The **m. p.** was determined as 588–590 K using a XT-4 melting point instrument (Beijing Taiké Instrument Co., Ltd, Beijing, China). NMR spectra were recorded on an AVANCE III 300 NMR instrument (Bruker, Germany). ¹H-NMR (300 MHz, DMSO-*d*₆) δ : 2.295 (3H, s, H-9), 3.863 (6H, s, H-10,11), 7.044 (1H, t, *J*=5.0 Hz, H-20), 7.315 (1H, s, H-N2), 7.963 (2H, d, *J*=9.0 Hz, H-13,17), 8.034 (2H, d, *J*=9.0 Hz, H-14,16), 8.517 (2H, d, *J*=5.0 Hz, H-19,21), 10.565 (H, s, H-N1), 11.77 (2H, s, H-2,6); ¹³C-NMR (75 MHz, DMSO-*d*₆) δ : 168.38 (C-18), 165.89 (C-8), 158.81 (C-7), 157.40 (C-3,5), 152.11 (C-19,20), 143.45 (C-12), 135.08 (C-15), 133.13 (C-4),

131.21 (C-1), 129.22 (C-14,16), 120.25 (C-13,17), 116.26 (C-21), 105.27 (C-2,6), 56.71 (C-10,11), 20.57 (C-9). **IR spectra** (potassium bromide) were recorded on a NEXUS 470 Fourier Transform IR spectrophotometer (Thermo Nicolet Corporation, USA). **IR** (ν_{max} , cm⁻¹): 3505, 3461 ($\nu_{\text{N-H}}$); 3191, 3041 ($\nu_{\text{C-H}}$); 1772, 1749 ($\nu_{\text{C=O}}$); 1685, 1670, 1655, 1648, 163, 1532, 1505, 1436 ($\nu_{\text{C=C}}$); 1339, 1174, 1162, 1134, 949, 668, 595, 570, 563, 547, 530, 522, 509, 488, 478, 467, 459, 454, 440, 430, 415, 407. **ESI-MS**: *m/z* 471.1 [M-1]⁺.

Experimental details

All the H atoms were positioned geometrically with *d*(N–H) = 0.86 Å, *d*(C–H) = 0.93–0.96 Å and treated as riding with *U*_{iso}(H) = 1.2 *U*_{eq}(N,C) and *U*_{iso}(H) = 1.5 *U*_{eq}(O).

Discussion

Syringic acid and its derivatives are widely used in perfume, pesticides, pharmacy and organic synthesis industry [1–4]. For medicinal purposes, syringic acid can restrain bacteria and fungus, is a main part of antibacterial ingredients of artemisia stelleriana. On the other hand, it has a sedative and a local anesthetic effect. In our previous studies, it was found that the phenolic acid compounds including syringic acid, chlorogenic acid, ferulic acid, vanillic acid, caffeic acid and protocatechuic acid from Blumea riparia DC play a significant role in the antiplatelet activity [5]. So, sulfonamides were selected as the amine part for synthesizing aromatic amides. The crystal structure of the title compound shows that the pyrimidine ring is almost coplanar with maximal deviation of 0.0123 Å and it makes a dihedral angle of 73.86° with the linker (N2–S1–O5). The presence of a big conjugated system in syringic acid amide can strongly allow it to stabilize through π -electron delocalization. The presence of a –CO–NH– backbone would allow this compound to have some antibacterial activity. The compound exhibits both intermolecular and intramolecular hydrogen bonds, with the former containing N–H⋯O and N–H⋯N, the latter only containing N–H⋯O. The intermolecular and intramolecular hydrogen bonds connect the molecule into a three-dimensional supramolecular architecture.

Table 2. Atomic coordinates and displacement parameters (in Å²).

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso}
H(2A)	4e	0.4477	0.5063	1.0919	0.054
H(2B)	4e	−0.0687	0.7755	0.6503	0.047
H(6B)	4e	−0.0106	0.8872	1.0514	0.045
H(1A)	4e	0.0967	0.8304	1.0173	0.057
H(17A)	4e	0.1429	0.6054	0.9151	0.047
H(16A)	4e	0.2517	0.5232	1.0250	0.045

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Table 2. Atomic coordinates and displacement parameters (in Å²).

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso}
H(14A)	4e	0.3153	0.7362	1.2959	0.060
H(19A)	4e	0.5033	0.8447	1.1628	0.063
H(13A)	4e	0.2067	0.8188	1.1861	0.062
H(10A)	4e	−0.2324	0.8202	0.3818	0.110
H(10B)	4e	−0.1927	0.7497	0.4994	0.110
H(10C)	4e	−0.1401	0.8209	0.4273	0.110
H(20A)	4e	0.6063	0.8248	1.0286	0.070

Table 2. continued.

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> _{iso}
H(21A)	4e	0.6231	0.6800	0.9311	0.068
H(9A)	4e	−0.4070	1.0059	0.8170	0.097
H(9B)	4e	−0.3672	1.0481	0.6881	0.097
H(9C)	4e	−0.3448	1.0863	0.8478	0.097
H(11A)	4e	−0.1267	1.0400	1.2409	0.130
H(11B)	4e	−0.0527	0.9828	1.2082	0.130
H(11C)	4e	−0.1345	0.9331	1.2103	0.130

Table 3. Atomic coordinates and displacement parameters (in Å²).

Atom	Site	<i>x</i>	<i>y</i>	<i>z</i>	<i>U</i> ₁₁	<i>U</i> ₂₂	<i>U</i> ₃₃	<i>U</i> ₁₂	<i>U</i> ₁₃	<i>U</i> ₂₃
S(1)	4e	0.37447(3)	0.55438(4)	1.25024(6)	0.0340(3)	0.0424(3)	0.0450(3)	0.0049(2)	0.0046(2)	0.0049(2)
O(2)	4e	−0.22482(8)	0.99671(9)	0.7802(2)	0.0365(8)	0.0357(8)	0.059(1)	0.0108(6)	0.0102(7)	0.0044(7)
O(5)	4e	0.0358(1)	0.6827(1)	0.8040(2)	0.056(1)	0.049(1)	0.063(1)	0.0204(8)	−0.0149(8)	−0.0185(9)
C(15)	4e	0.2936(1)	0.6214(1)	1.1698(2)	0.0298(9)	0.036(1)	0.039(1)	0.0036(8)	0.0086(9)	−0.0001(9)
O(4)	4e	−0.12955(9)	1.0074(1)	1.0340(2)	0.0520(9)	0.052(1)	0.056(1)	0.0128(7)	0.0095(8)	−0.0148(8)
N(2)	4e	0.4396(1)	0.5573(1)	1.1361(2)	0.0353(9)	0.035(1)	0.065(1)	0.0022(7)	0.0139(9)	−0.0043(9)
C(12)	4e	0.1637(1)	0.7209(1)	1.0408(2)	0.032(1)	0.033(1)	0.046(1)	0.0042(8)	0.0047(9)	−0.0038(9)
O(3)	4e	−0.19883(9)	0.8762(1)	0.5734(2)	0.0530(9)	0.052(1)	0.049(1)	0.0221(7)	−0.0056(8)	−0.0033(7)
C(2)	4e	−0.0793(1)	0.8175(2)	0.7219(2)	0.039(1)	0.035(1)	0.043(1)	0.0071(9)	0.0071(9)	0.0004(9)
O(6)	4e	0.35054(9)	0.4592(1)	1.2462(2)	0.0474(8)	0.0419(9)	0.068(1)	0.0049(7)	0.0122(8)	0.0142(8)
C(6)	4e	−0.0441(1)	0.8846(1)	0.9628(2)	0.032(1)	0.036(1)	0.044(1)	0.0010(8)	0.0054(9)	−0.0013(9)
C(5)	4e	−0.1098(1)	0.9429(1)	0.9368(2)	0.037(1)	0.029(1)	0.051(1)	0.0017(8)	0.015(1)	−0.0034(9)
N(1)	4e	0.0983(1)	0.7754(1)	0.9815(2)	0.040(1)	0.034(1)	0.064(1)	0.0119(8)	−0.0066(9)	−0.0149(9)
C(7)	4e	0.0379(1)	0.7536(1)	0.8766(2)	0.035(1)	0.033(1)	0.044(1)	0.0051(9)	0.0057(9)	−0.001(1)
N(4)	4e	0.5387(1)	0.6160(1)	1.0180(2)	0.039(1)	0.043(1)	0.059(1)	−0.0023(8)	0.0137(9)	−0.0051(9)
C(1)	4e	−0.0294(1)	0.8225(1)	0.8542(2)	0.032(1)	0.032(1)	0.044(1)	0.0029(8)	0.0076(9)	0.0017(9)
C(18)	4e	0.4835(1)	0.6341(1)	1.1032(2)	0.029(1)	0.037(1)	0.052(1)	0.0020(9)	0.0013(9)	−0.001(1)
N(3)	4e	0.4665(1)	0.7161(1)	1.1579(2)	0.044(1)	0.040(1)	0.065(1)	0.0031(8)	0.0116(9)	−0.0049(9)
C(4)	4e	−0.1593(1)	0.9380(1)	0.8047(2)	0.033(1)	0.030(1)	0.050(1)	0.0071(8)	0.0102(9)	0.0046(9)
C(17)	4e	0.1773(1)	0.6317(1)	0.9914(2)	0.039(1)	0.034(1)	0.043(1)	0.0024(9)	−0.0017(9)	−0.0074(9)
C(16)	4e	0.2424(1)	0.5829(1)	1.0571(2)	0.041(1)	0.029(1)	0.042(1)	0.0046(9)	0.0049(9)	−0.0046(9)
O(7)	4e	0.4063(1)	0.5957(1)	1.3855(2)	0.053(1)	0.072(1)	0.047(1)	0.0051(9)	−0.0041(8)	−0.0002(8)
C(3)	4e	−0.1449(1)	0.8755(1)	0.6968(2)	0.038(1)	0.035(1)	0.042(1)	0.0061(9)	0.0045(9)	0.0043(9)
C(14)	4e	0.2808(1)	0.7102(2)	1.2196(3)	0.038(1)	0.048(1)	0.059(2)	0.005(1)	−0.005(1)	−0.018(1)
C(8)	4e	−0.2941(1)	0.9623(2)	0.8173(3)	0.039(1)	0.053(2)	0.062(2)	0.005(1)	0.012(1)	0.001(1)
C(19)	4e	0.5128(1)	0.7860(2)	1.1271(3)	0.056(1)	0.038(1)	0.064(2)	−0.002(1)	0.006(1)	−0.004(1)
C(13)	4e	0.2158(1)	0.7590(2)	1.1539(3)	0.045(1)	0.038(1)	0.070(2)	0.009(1)	−0.003(1)	−0.022(1)
O(1)	4e	−0.2981(1)	0.8863(2)	0.8626(3)	0.062(1)	0.072(1)	0.178(3)	0.011(1)	0.052(2)	0.048(2)
C(10)	4e	−0.1903(2)	0.8116(2)	0.4615(3)	0.070(2)	0.083(2)	0.062(2)	0.029(2)	−0.015(1)	−0.025(2)
C(20)	4e	0.5735(2)	0.7755(2)	1.0456(3)	0.057(1)	0.045(1)	0.074(2)	−0.012(1)	0.015(1)	−0.001(1)
C(21)	4e	0.5836(1)	0.6888(2)	0.9903(3)	0.049(1)	0.057(2)	0.067(2)	−0.011(1)	0.020(1)	−0.004(1)
C(9)	4e	−0.3590(1)	1.0318(2)	0.7902(3)	0.039(1)	0.073(2)	0.080(2)	0.017(1)	0.005(1)	−0.013(2)
C(11)	4e	−0.1092(2)	0.9894(2)	1.1855(3)	0.131(3)	0.076(2)	0.063(2)	0.016(2)	0.049(2)	−0.003(2)

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References

- DeWeerd, K. A.; Saxena, A.; Nagle, D. P. Jr: Metabolism of the 18O-methoxy substituent of 3-methoxybenzoic acid and other unlabeled methoxybenzoic acids by anaerobic bacteria. *Appl. Environ. Microbiol.* **54** (1988). 1237-1242.
- Diao, H. X.; Yi, Y. Q.; Qi, H.; Gao, X. X: Study on anti-cataract effect of gigantol combined with syringic acid and their mechanism. *J. Chin. Mater. Med.* **37** (2012) 2429-2433.
- Guo, X.; Cai, Z.; Tang, J: Study on Synthesis, Characterization and Anti-endotoxic Effect of Syringic Acid-Cu. *J. Anhui Agric. Sci.* **39** (2011) 6-7.
- Ruth, M.; Maria, T. S.; Sagrario, B.: Solubility of Syringic and Vanillic Acids in Supercritical Carbon Dioxide. *J. Chem. Eng. Data.* **49** (2004) 779-782.
- Huang, L.; Lin, C. W.; Li, A. Y.; Wei, B. Y.; Teng, J. W.; Li, L.: Pro-coagulant activity of phenolic acids isolated from blumea riparia. *Nat. Prod. Commun.* **5** (2010) 1-4.
- Wang, X. B.; Jian, H. C.; Zhao, G. S: Synthesis of *N,N*-di(3,4-dihydrocinnamoyl)-1,2-ethylenediamine. *QiLu Pharm. Aff.* **24** (2005) 40-41.
- Sheldrick, G. M.: A short history of SHELX. *Acta Crystallogr.* **A64** (2008) 112-122.