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The crystal structure of (*E*)-2-(4-((4-fluorobenzyl)oxy)styryl)-4,6-dimethoxybenzaldehyde, $C_{24}H_{21}FO_4$

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Abstract

$C_{24}H_{21}FO_4$, triclinic, $P\bar{1}$ (no. 2), $a = 6.9734(5)$ Å, $b = 9.0402(7)$ Å, $c = 16.0963(12)$ Å, $\alpha = 98.977(6)^\circ$, $\beta = 92.867(6)^\circ$, $\gamma = 97.501(6)^\circ$, $V = 991.14(12)$ Å³, $Z = 2$, $R_{gt}(F) = 0.0540$, $wR_{ref}(F^2) = 0.1406$, $T = 273$ K.

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The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of material

To a stirred solution of (*E*)-1-(4-((4-fluorobenzyl)oxy)styryl)-3,5-dimethoxybenzene (0.73 g, 2 mmol) [3], DMF (0.31 mL) in acetonitrile (20 mL) was added $POCl_3$ (1.2 mL) dropwise while cooling with an ice bath. The reaction mixture was stirred at

Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	$0.21 \times 0.17 \times 0.07$ mm
Wavelength:	Mo $K\alpha$ radiation (0.71073 Å)
μ :	0.10 mm^{-1}
Diffractometer, scan mode:	SuperNova, ω
$\theta_{\max}$, completeness:	26.0° , >99%
$N(hkl)_{\text{measured}}$, $N(hkl)_{\text{unique}}$, R_{int} :	6688, 3898, 0.021
Criterion for I_{obs} , $N(hkl)_{\text{gt}}$:	$I_{\text{obs}} > 2 \sigma(I_{\text{obs}})$, 2598
$N(\text{param})_{\text{refined}}$:	264
Programs:	CrysAlis ^{PRO} [1], SHELX [2]

room temperature for 2 h. After completion, the mixture was purified into ice water and neutralized by saturated aq. NaOH. The mixture was stirred overnight and filtered to afford the crude product as yellow solid. After drying, the crude product was purified by column chromatography on silica gel to afford the title compound, using petroleum ether/ethylacetate (4:1, v/v , $R_f = 0.29$) as eluent. Crystals were obtained by slow evaporation from dichloromethane/methanol mixed solution.

Experimental details

All the non-hydrogen atoms were located in successive difference Fourier syntheses. The hydrogen atoms were added theoretically and riding on the concerned atoms.

Comment

Phenolic compounds make up one of the groups of molecules that have been most frequently studied in recent

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Table 2: Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²).

Atom	x	y	z	<i>U</i> _{iso} [*] / <i>U</i> _{eq}
C1	0.5972(3)	1.2267(2)	0.10727(12)	0.0379(4)
C2	0.4099(3)	1.1884(2)	0.06510(12)	0.0395(5)
C3	0.3003(3)	1.0513(2)	0.06741(12)	0.0414(5)
H3	0.1775	1.0275	0.0395	0.050*
C4	0.3739(3)	0.9491(2)	0.11153(12)	0.0398(5)
C5	0.5543(3)	0.9838(2)	0.15437(12)	0.0404(5)
H5	0.5999	0.9147	0.1849	0.048*
C6	0.6693(3)	1.1215(2)	0.15246(12)	0.0379(4)
C7	0.8611(3)	1.1553(2)	0.19862(13)	0.0448(5)
H7	0.9244	1.2533	0.2017	0.054*
C8	0.9530(3)	1.0644(2)	0.23565(13)	0.0492(5)
H8	0.8916	0.9653	0.2302	0.059*
C9	1.1402(3)	1.0978(2)	0.28477(12)	0.0402(5)
C10	1.2654(3)	1.2314(2)	0.28871(12)	0.0415(5)
H10	1.2343	1.3020	0.2558	0.050*
C11	1.4351(3)	1.2625(2)	0.34013(12)	0.0440(5)
H11	1.5165	1.3531	0.3418	0.053*
C12	1.4836(3)	1.1584(2)	0.38909(12)	0.0398(5)
C13	1.3651(3)	1.0220(2)	0.38363(14)	0.0501(6)
H13	1.3984	0.9498	0.4150	0.060*
C14	1.1985(3)	0.9938(2)	0.33183(14)	0.0516(6)
H14	1.1212	0.9008	0.3281	0.062*
C15	1.7612(3)	1.3210(2)	0.45948(15)	0.0613(7)
H15A	1.6841	1.4018	0.4746	0.074*
H15B	1.8226	1.3369	0.4082	0.074*
C16	1.9124(3)	1.3218(2)	0.52927(14)	0.0484(5)
C17	1.8995(3)	1.3974(2)	0.60911(15)	0.0574(6)
H17	1.7925	1.4466	0.6207	0.069*
C18	2.0418(4)	1.4022(3)	0.67276(15)	0.0633(7)
H18	2.0318	1.4539	0.7267	0.076*
C19	2.1950(3)	1.3303(3)	0.65446(17)	0.0675(7)
C20	2.2142(4)	1.2535(4)	0.57634(19)	0.0880(9)
H20	2.3218	1.2046	0.5654	0.106*
C21	2.0708(3)	1.2497(3)	0.51377(16)	0.0743(8)
H21	2.0818	1.1973	0.4601	0.089*
C22	0.7051(3)	1.3726(2)	0.09843(13)	0.0462(5)
H22	0.6400	1.4313	0.0671	0.055*
C23	0.1566(3)	1.2617(3)	−0.01881(15)	0.0554(6)
H23A	0.1489	1.1728	−0.0608	0.083*
H23B	0.1299	1.3457	−0.0452	0.083*
H23C	0.0632	1.2447	0.0218	0.083*
C24	0.3203(3)	0.7009(2)	0.14818(16)	0.0627(7)
H24A	0.4383	0.6757	0.1250	0.094*
H24B	0.2236	0.6129	0.1384	0.094*
H24C	0.3437	0.7358	0.2077	0.094*
F1	2.3377(2)	1.3340(2)	0.71552(11)	0.1143(7)
O1	0.8673(2)	1.42731(16)	0.12631(10)	0.0588(4)
O2	0.34692(19)	1.29427(15)	0.02269(10)	0.0551(4)
O3	0.25379(19)	0.81695(15)	0.10873(10)	0.0550(4)
O4	1.64147(19)	1.17957(15)	0.44637(9)	0.0530(4)

years [4]. Among them, pterostilbene (trans-3,5-dimethoxy-4'-hydroxystilbene) is a natural dimethyl ether analogue to resveratrol, which is classified as a phytoalexin [3]. Up to now,

pterostilbene is found to have diverse biological benefits in the prevention and treatment of many diseases, such as anti-cancer [5–7], anti-inflammation [8–10], anti-diabetes [11], the prevention of cardiovascular and cognitive function degeneration [12]. Consequently, pterostilbene has good potential to be evaluated for therapeutic use.

However, pterostilbene as a natural compound in commercial products has been problematic due to its rapid metabolism, especially when taken orally [13]. Thus, many researchers have attempted to optimize or modify the structures of pterostilbenes in order to achieve better pharmacokinetic characteristics and bioavailability. In our group, we have been working on this subject for many years and diversified derivatives containing pterostilbene have been designed and synthesized [14, 15]. Currently, we have found that pterostilbene-based nitrovinylstilbenes exhibited potential NLRP3 inflammasome activation inhibitory activity. This indicates that this kind of compounds could be candidates to discover new drug for treatment of inflammation-related diseases. During this process, we have optimized the synthetic route of the key intermediate reported here and characterized its structure by single crystal diffraction.

The title compound crystallizes in the triclinic space group $P\bar{1}$. There is one title molecule in the asymmetric unit (see the figure). The C7–C8 bond length [1.3013(30) Å] is consistent with the expected value for a C=C double bond. Similarly, the C22–O1 bond length [1.208(23) Å] is consistent with the expected value for a carbonyl C–O double bond. The angles of C6–C7–C8 and C7–C8–C9 are 127.7(2)° and 128.4(2)° respectively, indicating that it has the *E* configuration (see the figure). All bond lengths and angles are within normal ranges to previously reported structures [16].

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References

1. Oxford Diffraction: CrysAlisPRO, Oxford Diffraction Ltd, Abingdon, Oxfordshire, England (2006).
2. Sheldrick, G. M.: SHELXT – Integrated space-group and crystal-structure determination. *Acta Crystallogr.* **A71** (2015) 3–8.
3. Gomez-Zorita, S.; Fernandez-Quintela, A.; Lasa, A.; Aguirre, L.; Rimando, A. M.; Portillo, M. P.: Pterostilbene, a dimethyl ether derivative of resveratrol, reduces fat accumulation in rats fed an obesogenic diet. *J. Agric. Food Chem.* **62** (2014) 8371–8378.
4. Chen, L.-Z.; Li, Y.; Jiao, M.-M.; Shi, J.-B.; Tan, Y.; Ruan, B.-F.; Liu, X.-H.: Novel resveratrol-based flavonol derivatives: synthesis and anti-inflammatory activity *in vitro* and *in vivo*. *Eur. J. Med. Chem.* **175** (2019) 114–128.

5. Rimando, A. M.; Suh, N.: Biological/chemopreventive activity of stilbenes and their effect on colon cancer. *Planta Med.* **74** (2008) 1635–1643.
6. Jung, J.-H.; Shin, E.-A.; Kim, J.-H.; Sim, D.-Y.; Lee, H.; Park, J.-E.; Lee, H.-J.; Kim, S.-H.: NEDD9 inhibition by miR-25-5p activation is critically involved in co-treatment of melatonin- and pterostilbene-induced apoptosis in colorectal cancer cells. *Cancers* **11** (2019) 1684.
7. Hsiao, Y.-H.; Chen, N.-C.; Koh, Y.-C.; Nagabhushanam, K.; Ho, C.-T.; Pan, M.-H.: Pterostilbene inhibits adipocyte conditioned-medium-induced colorectal cancer cell migration through targeting FABP5-related signaling pathway. *J. Agric. Food Chem.* **67** (2019) 10321–10329.
8. Kosuru, R.; Kandula, V.; Rai, U.; Prakash, S.; Xia, Z.-Y.; Singh, S.: Pterostilbene decreases cardiac oxidative stress and inflammation *via* activation of AMPK/Nrf2/HO-1 pathway in fructose-fed diabetic rats. *Cardiovasc. Drugs Ther.* **32** (2018) 147–163.
9. Xue, E. X.; Lin, J.-P.; Zhang, Y.; Sheng, S.-R.; Liu, H.-X.; Zhou, Y.-L.; Xu, H.: Pterostilbene inhibits inflammation and ROS production in chondrocytes by activating Nrf2 pathway. *Oncotarget* **8** (2017) 41988–42000.
10. Zhang, Y.; Zhang, Y.: Pterostilbene, a novel natural plant conduct, inhibits high fat-induced atherosclerosis inflammation *via* NF- κ B signaling pathway in Toll-like receptor 5 (TLR5) deficient mice. *Biomed. Pharmacother.* **81** (2016) 345–355.
11. Satheesh, M. A.; Pari, L.: The antioxidant role of pterostilbene in streptozotocin-nicotinamide induced type 2 diabetes mellitus in Wistar rats. *J. Pharm. Pharmacol.* **58** (2006) 1483–14904.
12. Joseph, J. A.; Fisher, D. R.; Cheng, V.; Rimando, A. M.; Shukitt-Hale, B.: Cellular and behavioral effects of stilbene resveratrol analogues: implications for reducing the deleterious effects of aging. *J. Agric. Food Chem.* **56** (2008) 10544–10551.
13. Wang, P.; Sang, S.-M.: Metabolism and pharmacokinetics of resveratrol and pterostilbene. *BioFactors* **44** (2018) 16–25.
14. Ruan, B.-F.; Ge, W.-W.; Cheng, H.-J.; Xu, H.-J.; Li, Q.-S.; Liu, X.-H.: Resveratrol-based cinnamic ester hybrids: synthesis, characterization, and anti-inflammatory activity. *J. Enzyme Inhib. Med. Chem.* **32** (2017) 1282–1290.
15. Ruan, B.-F.; Cheng, H.-J.; Ren, J.; Li, H.-L.; Guo, L.-L.; Zhang, X.-X.; Liao, C.-Z.: Novel 2H-chromen-2-one derivatives of resveratrol: design, synthesis, modeling and use as human monoamine oxidase inhibitors. *Eur. J. Med. Chem.* **103** (2015) 185–190.
16. Yao, R.-S.; Lu, X.-Q.; Guan, Q.-X.; Zheng, L.; Lu, X.; Ruan, B.-F.: Novel 2H-chromen-2-one derivatives of resveratrol: design, synthesis, modeling and use as human monoamine oxidase inhibitors. *Eur. J. Med. Chem.* **62** (2013) 222–231.