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3-(4-Hydroxy-3-methoxyphenyl)acrylic acid–2,3,5,6-tetramethylpyrazine (2/1)

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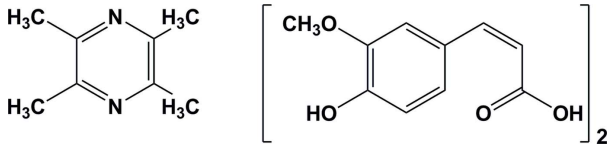
Key indicators: single-crystal X-ray study; T = 100 K; mean σ(C–C) = 0.003 Å; disorder in main residue; R factor = 0.054; wR factor = 0.156; data-to-parameter ratio = 11.5.

The asymmetric unit of the title compound, $C_8H_{12}N_2\cdot 2C_{10}H_{10}O_4$, contains a tetramethylpyrazine molecule, situated about an inversion center, and two substituted acrylic acid derivatives. The dihedral angle between the phenyl and pyrazine rings is 69.45 (9)°. In the crystal, intermolecular O—H···O, O—H···N hydrogen bonds and weak C—H···O interactions lead to the formation of a supramolecular network. The acrylic acid side chain is positionally disordered [occupancy ratio 0.852 (7):0.148 (7)].

Related literature

For the synthesis of the title compound, see: Tan (2004). For the biological properties of the title compound, see: Tan *et al.* (2003).



Experimental

Crystal data

$0.5C_8H_{12}N_2\cdot C_{10}H_{10}O_4$
M_r = 262.28
Monoclinic, $P2_1/n$
a = 9.4696 (7) Å
b = 5.7641 (4) Å
c = 24.3737 (15) Å
β = 93.654 (6)°
V = 1327.70 (16) Å^3
Z = 4
Cu $K\alpha$ radiation
μ = 0.80 mm^{-1}
T = 100 K
0.20 × 0.05 × 0.05 mm

Data collection

Oxford Diffraction Xcalibur Onyx Nova diffractometer
Absorption correction: multi-scan (*CrysAlis PRO*; Oxford Diffraction, 2009)
T_{min} = 0.953, T_{max} = 0.961
4780 measured reflections
2398 independent reflections
2004 reflections with $I > 2\sigma(I)$
R_{int} = 0.030

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.156
S = 1.09
2398 reflections
208 parameters
4 restraints
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.63 e Å^{-3}
$\Delta\rho_{min}$ = −0.40 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
O2—H2···O1^{i}	0.84	1.79	2.613 (5)	167
O4—H4···N1	0.82	1.97	2.749 (2)	158
C3—H3B···O4^{ii}	0.98	2.58	3.553 (3)	174
C14—H14B···O4^{ii}	0.98	2.59	3.465 (2)	148

Symmetry codes: (i) $-x, -y+1, -z$; (ii) $x, y+1, z$.

Data collection: *CrysAlis PRO* (Oxford Diffraction, 2009); cell refinement: *CrysAlis PRO*; data reduction: *CrysAlis PRO*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2*.

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: SU2237).

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supporting information

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3-(4-Hydroxy-3-methoxyphenyl)acrylic acid–2,3,5,6-tetramethylpyrazine (2/1)

Zaiyou Tan, Erjia Zhu, Lin Luo, Zhuohui Lin and Ruisi Yan

S1. Comment

The title compound, tetramethylpyrazine ferulate is a pharmacologically significant compound which we found in some prescriptions of traditional Chinese medicine, and which are used to treat stroke patients. In both the invivo and invitro experiments, tetramethylpyrazine ferulate has a remarkable inhibitory effect on ADP induced platelet aggregation (Tan *et al.*, 2003). In order to study further its pharmacological effects the title compound was synthesized by the reaction of 3-(4-hydroxy-3-methoxyphenyl)-2-acrylicacid with tetrathylpyrazine, and its crystal structure is reported on herein.

X-ray crystallographic analysis confirmed the molecular structure and the atom connectivity for the title compound, as illustrated in Fig. 1. The dihedral angle between the mean planes of the pyrazine ring and phenyl ring (C8—C13) is 69.45 (9)°.

In the crystal intermolecular O—H···N hydrogen bonds and weak C—H···O interactions are observed, leading to the formation of a supra-molecular network (Table 1).

S2. Experimental

The title compound was synthesized according to the published procedure (Tan, 2004). Tetramethylpyrazine (2.8 g) was heated with 3-(4-hydroxy-3-methoxyphenyl)-2-acrylicacid (4.0 g) in acetone (45 ml). After refluxing at 333 K for 1 h, the reaction mixture was left to stand for several days, and yellow crystals were finally isolated.

S3. Refinement

The acid side chain is positionally disordered: occupancy of atoms C6/C6A, C/C5A, O1/O1A and O2/O2A were refined to be 0.852 (7)/0.148 (7). The following restraints were also applied: *DFIX* 1.32. 02 C7 C6 C7 C6A; *DFIX* 1.45. 02 C6 C5 C6A C5A; EADP C5 C5A. The OH and C-bound H-atoms were included in calculated positions and treated as riding atoms: O—H = 0.82 - 0.84 Å, C—H = 0.95 and 0.98Å for CH and CH_3 H-atoms, respectively, with U_{iso}(H) = k × U_{eq}(C), where k = 1.5 for OH and CH_3 H-atoms, and k = 1.2 for all other H-atoms.

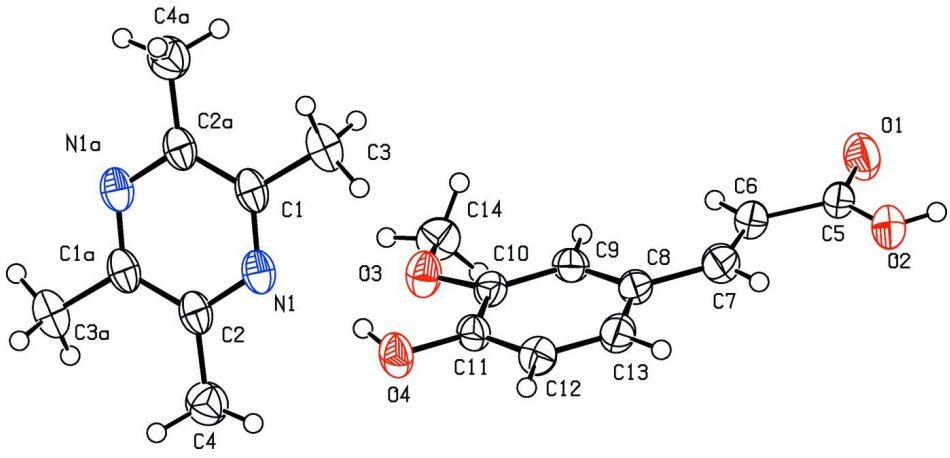

Figure 1

A view of the centrosymmmetric tetramethylpyrazine molecule and one of the ferulate molecules of the title compound. Displacement ellipsoids are drawn at the 50% probability level [Symmetry code: (*a*) = -*x*, -*y*, -*z* + 1; only the major component of the disordered acrylicacid side chain is shown].

3-(4-Hydroxy-3-methoxyphenyl)acrylic acid–2,3,5,6-tetramethylpyrazine (2/1)

Crystal data

$0.5C_8H_{12}N_2{\cdot}C_{10}H_{10}O_4$
M_r = 262.28
Monoclinic, $P2_1/n$
Hall symbol: -P 2yn
a = 9.4696 (7) Å
b = 5.7641 (4) Å
c = 24.3737 (15) Å
β = 93.654 (6)°
V = 1327.70 (16) Å^3
Z = 4
$F(000)$ = 556
D_x = 1.312 Mg m^{-3}
Cu $K\alpha$ radiation, λ = 1.54180 Å
Cell parameters from 2625 reflections
θ = 3.6–71.3°
μ = 0.80 mm^{-1}
T = 100 K
Plate, yellow
0.20 × 0.05 × 0.05 mm

Data collection

Oxford Diffraction Xcalibur Onyx Nova diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
Detector resolution: 8.2417 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (*CrysAlis PRO*; Oxford Diffraction, 2009)
T_{min} = 0.953, T_{max} = 0.961
4780 measured reflections
2398 independent reflections
2004 reflections with $I > 2\sigma i(I)$
R_{int} = 0.030
θ_{max} = 68.2°, θ_{min} = 3.6°
h = −6→11
k = −6→6
l = −29→29

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.054
$wR(F^2)$ = 0.156
S = 1.09
2398 reflections
208 parameters
4 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0848P)^2 + 0.4876P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.003$

$\Delta\rho_{max} = 0.63$ e Å^{-3}
$\Delta\rho_{min} = -0.40$ e Å^{-3}

Special details

Experimental. CrysAlisPro (Oxford Diffraction, 2009) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.

Geometry. Bond distances, angles *etc*. have been calculated using the rounded fractional coordinates. All su's are estimated from the variances of the (full) variance-covariance matrix. The cell e.s.d.'s are taken into account in the estimation of distances, angles and torsion angles

Refinement. Refinement of F^2 against ALL reflections. The weighted *R*-factor *wR* and goodness of fit *S* are based on F^2, conventional *R*-factors *R* are based on *F*, with *F* set to zero for negative F^2. The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating *R*-factors(gt) *etc*. and is not relevant to the choice of reflections for refinement. *R*-factors based on F^2 are statistically about twice as large as those based on *F*, and *R*- factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}	Occ. (<1)
O1	−0.0744 (5)	0.5740 (6)	0.06036 (17)	0.0523 (10)	0.852 (7)
O2	0.0563 (4)	0.2666 (5)	0.03930 (15)	0.0489 (9)	0.852 (7)
O3	−0.11323 (15)	0.0544 (3)	0.33773 (5)	0.0432 (4)	
O4	0.04554 (15)	−0.3292 (2)	0.35223 (6)	0.0444 (5)	
C5	−0.0143 (5)	0.3836 (9)	0.07299 (14)	0.0391 (11)	0.852 (7)
C6	−0.0257 (2)	0.2939 (4)	0.12865 (9)	0.0392 (7)	0.852 (7)
C7	0.0333 (2)	0.1014 (4)	0.14611 (9)	0.0506 (7)	
C8	0.0286 (2)	−0.0041 (4)	0.20015 (8)	0.0404 (6)	
C9	−0.0448 (2)	0.0919 (3)	0.24314 (8)	0.0375 (6)	
C10	−0.04259 (19)	−0.0175 (3)	0.29389 (7)	0.0334 (5)	
C11	0.03695 (19)	−0.2208 (3)	0.30294 (7)	0.0347 (5)	
C12	0.1057 (2)	−0.3180 (4)	0.26015 (8)	0.0395 (6)	
C13	0.1010 (2)	−0.2104 (4)	0.20929 (8)	0.0416 (6)	
C14	−0.2088 (2)	0.2438 (4)	0.32912 (9)	0.0462 (7)	
O1A	−0.051 (2)	0.484 (4)	0.0621 (8)	0.045 (6)	0.148 (7)
O2A	0.1074 (19)	0.249 (3)	0.0201 (7)	0.054 (5)	0.148 (7)
C5A	0.028 (3)	0.322 (5)	0.0629 (11)	0.0391 (11)	0.148 (7)
C6A	0.0587 (13)	0.162 (2)	0.1065 (5)	0.038 (4)	0.148 (7)
N1	0.00905 (17)	−0.1036 (3)	0.44970 (6)	0.0393 (5)	
C1	0.0891 (2)	0.0814 (4)	0.46363 (8)	0.0383 (6)	
C2	−0.0802 (2)	−0.1871 (3)	0.48531 (8)	0.0378 (6)	
C3	0.1847 (2)	0.1711 (4)	0.42178 (9)	0.0479 (7)	
C4	−0.1659 (2)	−0.3952 (4)	0.46761 (10)	0.0503 (7)	
H4	0.01920	−0.24080	0.37590	0.0670*	
H6	−0.07890	0.38050	0.15330	0.0470*	0.852 (7)
H2	0.05430	0.33540	0.00890	0.0730*	0.852 (7)
H14A	−0.27540	0.20980	0.29770	0.0690*	
H14B	−0.15560	0.38480	0.32160	0.0690*	
H14C	−0.26120	0.26690	0.36210	0.0690*	
H7	0.08590	0.01970	0.12040	0.0610*	0.852 (7)
H9	−0.09610	0.23230	0.23740	0.0450*	

H12	0.15630	−0.45930	0.26570	0.0470*	
H13	0.14830	−0.27930	0.18020	0.0500*	
H6AA	0.13470	0.06810	0.09570	0.0450*	0.148 (7)
H6AB	−0.05690	0.17360	0.14590	0.0610*	0.148 (7)
H2A	0.09850	0.34570	−0.00580	0.0810*	0.148 (7)
H3A	0.20300	0.04760	0.39550	0.0720*	
H3B	0.13940	0.30260	0.40220	0.0720*	
H3C	0.27440	0.22170	0.44030	0.0720*	
H4A	−0.12420	−0.46860	0.43620	0.0750*	
H4B	−0.26310	−0.34730	0.45700	0.0750*	
H4C	−0.16650	−0.50610	0.49810	0.0750*	

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0654 (19)	0.053 (2)	0.0387 (12)	0.0041 (16)	0.0046 (11)	0.0104 (15)
O2	0.0630 (18)	0.0519 (12)	0.0320 (15)	−0.0025 (11)	0.0044 (11)	0.0042 (11)
O3	0.0487 (8)	0.0467 (8)	0.0339 (7)	0.0155 (6)	0.0009 (6)	0.0038 (6)
O4	0.0586 (9)	0.0409 (8)	0.0337 (7)	0.0124 (6)	0.0032 (6)	0.0103 (6)
C5	0.046 (2)	0.045 (2)	0.0266 (16)	−0.0126 (18)	0.0039 (12)	−0.0014 (14)
C6	0.0447 (13)	0.0429 (13)	0.0302 (12)	−0.0046 (10)	0.0036 (9)	−0.0014 (9)
C7	0.0541 (12)	0.0586 (14)	0.0381 (12)	−0.0193 (11)	−0.0043 (9)	0.0034 (10)
C8	0.0428 (10)	0.0473 (11)	0.0304 (9)	−0.0178 (9)	−0.0024 (8)	0.0015 (8)
C9	0.0425 (10)	0.0327 (9)	0.0357 (10)	−0.0048 (8)	−0.0090 (8)	0.0055 (7)
C10	0.0367 (9)	0.0343 (9)	0.0286 (9)	0.0002 (7)	−0.0027 (7)	0.0003 (7)
C11	0.0366 (9)	0.0357 (10)	0.0312 (9)	−0.0006 (7)	−0.0018 (7)	0.0046 (7)
C12	0.0372 (10)	0.0422 (11)	0.0389 (10)	0.0010 (8)	0.0017 (8)	−0.0008 (8)
C13	0.0409 (10)	0.0502 (12)	0.0339 (10)	−0.0076 (9)	0.0043 (8)	−0.0041 (8)
C14	0.0463 (11)	0.0405 (11)	0.0516 (12)	0.0110 (9)	0.0011 (9)	−0.0011 (9)
O1A	0.054 (10)	0.050 (15)	0.034 (7)	0.014 (10)	0.025 (7)	0.024 (10)
O2A	0.071 (10)	0.057 (7)	0.035 (7)	0.008 (7)	0.011 (6)	0.015 (6)
C5A	0.046 (2)	0.045 (2)	0.0266 (16)	−0.0126 (18)	0.0039 (12)	−0.0014 (14)
C6A	0.037 (7)	0.042 (8)	0.034 (8)	0.011 (5)	0.003 (5)	0.012 (6)
N1	0.0404 (8)	0.0450 (9)	0.0322 (8)	0.0081 (7)	−0.0007 (7)	0.0108 (7)
C1	0.0365 (9)	0.0450 (11)	0.0331 (9)	0.0087 (8)	0.0010 (7)	0.0140 (8)
C2	0.0356 (9)	0.0446 (11)	0.0327 (9)	0.0072 (8)	−0.0007 (7)	0.0122 (8)
C3	0.0478 (11)	0.0549 (13)	0.0420 (11)	0.0058 (9)	0.0107 (9)	0.0151 (9)
C4	0.0486 (12)	0.0520 (13)	0.0498 (12)	−0.0011 (10)	0.0002 (10)	0.0051 (10)

Geometric parameters (Å, º)

O1—C5	1.265 (6)	C11—C12	1.383 (3)
O1A—C5A	1.20 (4)	C12—C13	1.384 (3)
O2—C5	1.283 (6)	C6—H6	0.9500
O2A—C5A	1.39 (3)	C6A—H6AA	0.9500
O3—C14	1.425 (3)	C7—H7	0.9500
O3—C10	1.361 (2)	C7—H6AB	0.9500
O4—C11	1.352 (2)	C9—H9	0.9500

O2—H2	0.8400	C12—H12	0.9500
O2A—H2A	0.8400	C13—H13	0.9500
O4—H4	0.8200	C14—H14B	0.9800
N1—C1	1.340 (3)	C14—H14C	0.9800
N1—C2	1.339 (2)	C14—H14A	0.9800
C5—C6	1.462 (4)	C1—C3	1.498 (3)
C5A—C6A	1.42 (3)	C1—C2^{i}	1.393 (3)
C6—C7	1.302 (3)	C2—C4	1.496 (3)
C6A—C7	1.068 (12)	C3—H3A	0.9800
C7—C8	1.454 (3)	C3—H3B	0.9800
C8—C13	1.384 (3)	C3—H3C	0.9800
C8—C9	1.407 (3)	C4—H4A	0.9800
C9—C10	1.387 (3)	C4—H4B	0.9800
C10—C11	1.403 (2)	C4—H4C	0.9800

C10—O3—C14	117.19 (15)	C8—C7—H7	116.00
C5—O2—H2	109.00	C8—C7—H6AB	96.00
C5A—O2A—H2A	109.00	C10—C9—H9	120.00
C11—O4—H4	110.00	C8—C9—H9	120.00
C1—N1—C2	119.49 (16)	C13—C12—H12	120.00
O2—C5—C6	118.7 (4)	C11—C12—H12	120.00
O1—C5—C6	118.3 (4)	C8—C13—H13	119.00
O1—C5—O2	123.0 (4)	C12—C13—H13	119.00
O1A—C5A—O2A	126 (2)	H14A—C14—H14C	109.00
O2A—C5A—C6A	106 (2)	H14B—C14—H14C	110.00
O1A—C5A—C6A	128 (2)	H14A—C14—H14B	109.00
C5—C6—C7	123.3 (3)	O3—C14—H14A	109.00
C5A—C6A—C7	147.1 (16)	O3—C14—H14B	109.00
C6A—C7—C8	167.7 (7)	O3—C14—H14C	109.00
C6—C7—C8	128.0 (2)	N1—C1—C3	117.31 (18)
C9—C8—C13	118.77 (18)	N1—C1—C2^{i}	120.61 (17)
C7—C8—C13	117.51 (18)	C2^{i}—C1—C3	122.06 (19)
C7—C8—C9	123.72 (19)	N1—C2—C4	117.03 (17)
C8—C9—C10	120.34 (17)	N1—C2—C1^{i}	119.90 (17)
O3—C10—C9	125.55 (16)	C1^{i}—C2—C4	123.07 (18)
O3—C10—C11	114.63 (15)	C1—C3—H3A	110.00
C9—C10—C11	119.82 (16)	C1—C3—H3B	109.00
O4—C11—C12	118.58 (16)	C1—C3—H3C	109.00
C10—C11—C12	119.59 (17)	H3A—C3—H3B	109.00
O4—C11—C10	121.81 (15)	H3A—C3—H3C	109.00
C11—C12—C13	120.3 (2)	H3B—C3—H3C	109.00
C8—C13—C12	121.10 (19)	C2—C4—H4A	109.00
C7—C6—H6	118.00	C2—C4—H4B	109.00
C5—C6—H6	118.00	C2—C4—H4C	109.00
C5A—C6A—H6AA	107.00	H4A—C4—H4B	110.00
C7—C6A—H6AA	106.00	H4A—C4—H4C	109.00
C6—C7—H7	116.00	H4B—C4—H4C	109.00
C6A—C7—H6AB	96.00		

C14—O3—C10—C9	6.9 (3)	C7—C8—C13—C12	177.84 (19)
C14—O3—C10—C11	−172.83 (16)	C8—C9—C10—C11	2.1 (3)
C1—N1—C2—C4	−179.50 (18)	C8—C9—C10—O3	−177.59 (18)
C2—N1—C1—C2^{i}	0.0 (3)	O3—C10—C11—O4	−2.3 (3)
C1—N1—C2—C1^{i}	0.0 (3)	O3—C10—C11—C12	175.86 (17)
C2—N1—C1—C3	−178.63 (17)	C9—C10—C11—O4	177.98 (17)
O2—C5—C6—C7	0.6 (6)	C9—C10—C11—C12	−3.8 (3)
O1—C5—C6—C7	−179.2 (4)	C10—C11—C12—C13	2.7 (3)
C5—C6—C7—C8	−179.8 (3)	O4—C11—C12—C13	−179.10 (17)
C6—C7—C8—C9	0.3 (3)	C11—C12—C13—C8	0.3 (3)
C6—C7—C8—C13	−179.6 (2)	N1—C1—C2^{i}—N1^{i}	0.0 (3)
C7—C8—C9—C10	−179.05 (18)	N1—C1—C2^{i}—C4^{i}	−179.47 (18)
C9—C8—C13—C12	−2.1 (3)	C3—C1—C2^{i}—N1^{i}	178.56 (18)
C13—C8—C9—C10	0.9 (3)	C3—C1—C2^{i}—C4^{i}	−0.9 (3)

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

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···O1^{ii}	0.84	1.79	2.613 (5)	167
O4—H4···O3	0.82	2.28	2.685 (2)	111
O4—H4···N1	0.82	1.97	2.749 (2)	158
C3—H3*B*···O4^{iii}	0.98	2.58	3.553 (3)	174
C14—H14*B*···O4^{iii}	0.98	2.59	3.465 (2)	148

Symmetry codes: (ii) −*x*, −*y*+1, −*z*; (iii) *x*, *y*+1, *z*.