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2-(2,5-Dimethoxyphenyl)-*N*-[2-(4-hydroxyphenyl)ethyl]acetamide

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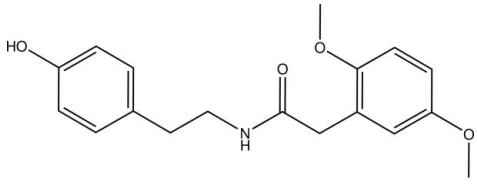
Key indicators: single-crystal X-ray study; T = 296 K; mean σ(C–C) = 0.003 Å; R factor = 0.040; wR factor = 0.088; data-to-parameter ratio = 16.8.

In the title compound, $C_{18}H_{21}NO_4$, the dihedral angles between the acetamide group and the methoxy- and hydroxy-substitured benzene rings are 80.81 (5) and 8.19 (12)°, respectively. The benzene rings are twisted with respect to each other, making a dihedral angle of 72.89 (5)°. In the crystal, N—H···O and O—H···O hydrogen bonds link the molecules into a three-dimensional network.

Related literature

For general background to tyrosinase, see: Kubo *et al.* (2000). For the development of tyrosinase inhibitors, see: Lemic-Stojcevic *et al.* (1995); Battaini *et al.* (2000); Cabanes *et al.* (1994); Thanigaimalai *et al.* (2010).



Experimental

Crystal data

$C_{18}H_{21}NO_4$
M_r = 315.36
Orthorhombic, $P2_12_12_1$
a = 8.1628 (8) Å
b = 12.0701 (11) Å
c = 17.0176 (16) Å
V = 1676.7 (3) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 296 K
0.3 × 0.23 × 0.1 mm

Data collection

Bruker SMART CCD area-detector diffractometer
8417 measured reflections
3638 independent reflections
2352 reflections with $I > 2\sigma(I)$
R_{int} = 0.063

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.040
$wR(F^2)$ = 0.088
S = 0.87
3638 reflections
216 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.11 e Å^{-3}
$\Delta\rho_{min}$ = −0.12 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
N10—H10···O19^{i}	0.88 (2)	2.16 (2)	3.023 (2)	165.4 (19)
O19—H19···O9^{ii}	0.87 (3)	1.76 (3)	2.6289 (19)	174 (3)

Symmetry codes: (i) $x-\frac{1}{2}, -y+\frac{3}{2}, -z+1$; (ii) $-x+\frac{3}{2}, -y+1, z+\frac{1}{2}$.

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: TK5063).

References

Battaini, G., Monzani, E., Casella, L., Santagostini, L. & Pagliarin, R. (2000). *J. Biol. Inorg. Chem.* **5**, 262–268.
Bruker (2002). *SAINT* and *SMART*. Bruker AXS Inc., Madison, Wisconsin, USA.
Cabanes, J., Chazarra, S. & Garcia-Carmona, F. (1994). *J. Pharm. Pharmacol.* **46**, 982–985.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Farrugia, L. J. (1999). *J. Appl. Cryst.* **32**, 837–838.
Kubo, I., Kinst-Hori, I., Chaudhuri, S. K., Kubo, Y., Scanchez, Y. & Ogura, T. (2000). *Bioorg. Med. Chem.* **8**, 1749–1755.
Lemic-Stojcevic, L., Nias, A. H. & Breathnach, A. S. (1995). *Exp. Dermatol.* **4**, 79–81.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Thanigaimalai, P., Le, H. T. A., Lee, K. C., Bang, S. C., Sharma, V. K., Yun, C. Y., Roh, E., Hwang, B. Y., Kim, Y. S. & Jung, S. H. (2010). *Bioorg. Med. Chem. Lett.* **20**, 2991–2993.

supplementary materials

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2-(2,5-Dimethoxyphenyl)-*N*-[2-(4-hydroxyphenyl)ethyl]acetamide

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Comment

Tyrosinase is a copper containing enzyme which acts as a catalyst in two different reactions involving the hydroxylation of monophenols to *o*-diphenols and the oxidation of the *o*-diphenols to *o*-quinones. This class of enzyme is widely distributed in the plant, animal and microorganism kingdoms (Kubo *et al.*, 2000), and its inhibition is one of the major strategies in developing new whitening agents. Over the last few decades, various tyrosinase inhibitors, including azelaic acid (Lemic-Stojcevic *et al.*, 1995), kojic acid (Battaini *et al.*, 2000), arbutin (Cabanes *et al.*, 1994), and *N*-phenylthiourea (PTU) (Thanigaimalai *et al.*, 2010) have been studied. But some of their individual activities are either not potent enough to be considered of practical use or not compatible with safety regulations for food and cosmetic additives. In our continuing search for tyrosinase inhibitors, we have synthesized the title compound, (I), from the reaction of 2,5-dimethoxyphenyl acetyl chloride and tyramine under ambient conditions. Herein, the crystal structure of (I) is described (Fig. 1).

The 2,4-dimethoxyphenyl and 3-hydroxyphenyl moieties are almost planar with r.m.s. deviations of 0.008 and 0.009 Å, respectively, from their corresponding least-squares planes. The dihedral angles between the acetamide group (C7–N10) and the benzene rings (C1–C6 + O20 and O22; and C12–O19) are 80.81 (5) and 8.19 (12)°, respectively. The benzene groups are twisted with respect to each other making a dihedral angle of 72.89 (5)°. The presence of intermolecular N10—H10···O19^{i} and O19—H19···O9^{ii} [symmetry codes: (i) *x* - 1/2, -*y* + 3/2, -*z* + 1, (ii) -*x* + 3/2, -*y* + 1, *z* + 1/2] hydrogen bonds link the molecules into a three-dimensional network (Fig. 2 and Table 1).

Experimental

The starting materials, 2,5-dimethoxyphenyl acetyl chloride and tyramine, were purchased from Sigma Chemical Co. Solvents for organic synthesis were redistilled before use. All other chemicals and solvents were of analytical grade and were used without further purification. The title compound was prepared from the reaction of 2,5-dimethoxyphenyl acetyl chloride (0.21 g, 1.0 mmol) and tyramine (0.14 g, 1.0 mmol) by simple substitution in THF (6 ml) triethylamine (0.12 g, 1.2 mmol). The solvent was removed under reduced pressure. The mixture was purified by column chromatography on silica gel (2:1 dichloromethane/ethylacetate) to give the title compound. Colourless crystals were obtained by slow evaporation of its ethanol solution at room temperature.

Refinement

H atoms of the NH and OH groups were located in a difference Fourier map and refined freely (N—H = 0.88 (2) Å and O—H = 0.87 (3) Å]. Other H atoms were positioned geometrically and refined using a riding model, with C—H = 0.93–0.97 Å, and with U_{iso}(H) = 1.2U_{eq}(C) for aromatic and methylene, and 1.5U_{eq}(C) for methyl H atoms. In the absence of significant anomalous scattering effects, 1471 Friedel pairs were averaged in the final refinement.

Computing details

Data collection: *SMART* (Bruker, 2002); cell refinement: *SAINT* (Bruker, 2002); data reduction: *SAINT* (Bruker, 2002); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 1997); software used to prepare material for publication: *WinGX* (Farrugia, 1999).

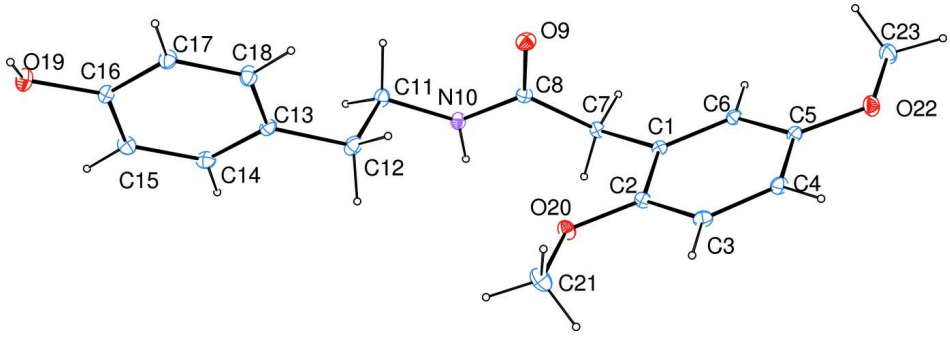

Figure 1

Molecular structure of the title compound, showing the atom-numbering scheme and 30% probability ellipsoids.

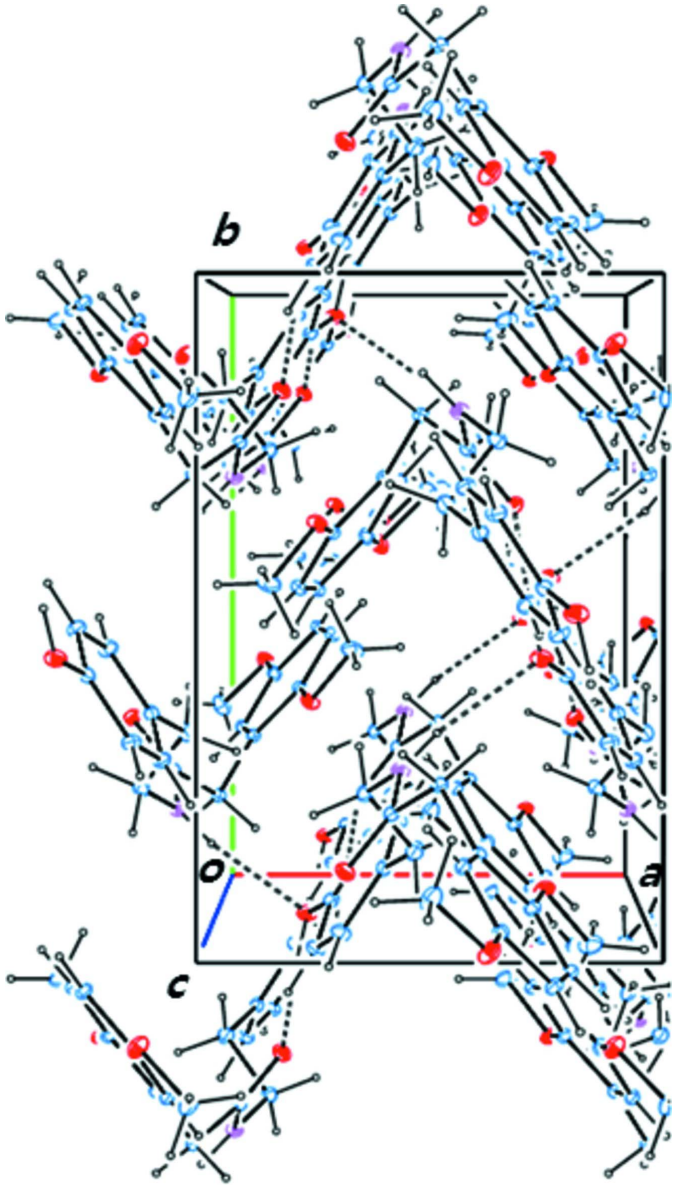

Figure 2

Part of the packing diagram of the title compound, showing a three-dimensional network of molecules linked by intermolecular N—H···O and O—H···O hydrogen bonds (dashed lines).

2-(2,5-Dimethoxyphenyl)-*N*-[2-(4-hydroxyphenyl)ethyl]acetamide

Crystal data

$C_{18}H_{21}NO_4$
$M_r = 315.36$
Orthorhombic, $P2_12_12_1$
Hall symbol: P 2ac 2ab
$a = 8.1628\ (8)$ Å
$b = 12.0701\ (11)$ Å
$c = 17.0176\ (16)$ Å
$V = 1676.7\ (3)$ Å^3
$Z = 4$

$F(000) = 672$
$D_x = 1.249$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 2320 reflections
$\theta = 2.9$–$23.6°$
$\mu = 0.09$ mm^{-1}
$T = 296$ K
Block, colourless
0.3 × 0.23 × 0.1 mm

Data collection

Bruker SMART CCD area-detector diffractometer
Graphite monochromator
φ and ω scans
8417 measured reflections
3638 independent reflections
2352 reflections with $I > 2\sigma(I)$
$R_{int} = 0.063$
$\theta_{max} = 27.5°$, $\theta_{min} = 2.8°$
$h = -4 \rightarrow 10$
$k = -15 \rightarrow 7$
$l = -18 \rightarrow 21$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.040$
$wR(F^2) = 0.088$
$S = 0.87$
3638 reflections
216 parameters
0 restraints
Primary atom site location: structure-invariant direct methods
Secondary atom site location: difference Fourier map
Hydrogen site location: inferred from neighbouring sites
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0365P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.11$ e Å^{-3}
$\Delta\rho_{min} = -0.12$ e Å^{-3}

Special details

Geometry. All s.u.'s (except the s.u. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell s.u.'s are taken into account individually in the estimation of s.u.'s in distances, angles and torsion angles; correlations between s.u.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell s.u.'s is used for estimating s.u.'s involving l.s. planes.

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 $F^2 > 2\sigma(F^2)$ 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}
C1	0.4043 (2)	0.70567 (12)	0.09969 (11)	0.0437 (4)
C2	0.2961 (2)	0.62946 (13)	0.13350 (11)	0.0488 (5)
C3	0.2247 (2)	0.54873 (14)	0.08716 (13)	0.0563 (5)
H3	0.153	0.4979	0.1096	0.068*
C4	0.2590 (2)	0.54310 (14)	0.00842 (12)	0.0562 (5)
H4	0.2107	0.4882	−0.0221	0.067*
C5	0.3644 (2)	0.61811 (14)	−0.02606 (12)	0.0516 (5)
C6	0.4357 (2)	0.69979 (13)	0.02022 (11)	0.0472 (5)
H6	0.5056	0.7513	−0.0028	0.057*
C7	0.4814 (2)	0.79400 (13)	0.15008 (11)	0.0475 (5)
H7A	0.396	0.8424	0.1699	0.057*
H7B	0.5543	0.8383	0.1178	0.057*
C8	0.5769 (2)	0.74773 (14)	0.21872 (12)	0.0496 (5)
O9	0.67141 (17)	0.66858 (11)	0.21107 (9)	0.0710 (4)
N10	0.5600 (2)	0.80014 (13)	0.28703 (10)	0.0532 (4)
H10	0.485 (3)	0.8525 (17)	0.2849 (12)	0.073 (7)*
C11	0.6334 (3)	0.76130 (16)	0.35966 (12)	0.0607 (5)
H11A	0.6477	0.8236	0.395	0.073*

H11B	0.741	0.731	0.3484	0.073*
C12	0.5315 (3)	0.67421 (17)	0.39979 (13)	0.0715 (6)
H12A	0.421	0.7022	0.4064	0.086*
H12B	0.5258	0.6094	0.3662	0.086*
C13	0.5972 (2)	0.64031 (15)	0.47870 (12)	0.0544 (5)
C14	0.5678 (3)	0.70159 (14)	0.54505 (13)	0.0630 (6)
H14	0.5077	0.7668	0.5407	0.076*
C15	0.6242 (3)	0.66973 (15)	0.61796 (13)	0.0624 (6)
H15	0.601	0.7126	0.662	0.075*
C16	0.7159 (2)	0.57352 (14)	0.62542 (12)	0.0514 (5)
C17	0.7467 (3)	0.51175 (15)	0.56022 (12)	0.0623 (5)
H17	0.8067	0.4465	0.5645	0.075*
C18	0.6895 (3)	0.54522 (16)	0.48775 (13)	0.0671 (6)
H18	0.7137	0.5026	0.4437	0.081*
O19	0.7706 (2)	0.54495 (11)	0.69866 (9)	0.0700 (4)
H19	0.794 (4)	0.475 (2)	0.7052 (16)	0.139 (12)*
O20	0.26868 (18)	0.64349 (9)	0.21211 (8)	0.0633 (4)
C21	0.1722 (3)	0.56269 (18)	0.25170 (14)	0.0856 (8)
H21A	0.162	0.5826	0.3061	0.128*
H21B	0.2242	0.4916	0.2475	0.128*
H21C	0.0655	0.5594	0.2282	0.128*
O22	0.38811 (19)	0.60474 (12)	−0.10495 (9)	0.0749 (5)
C23	0.4980 (3)	0.6780 (2)	−0.14310 (14)	0.0836 (7)
H23A	0.5043	0.6595	−0.1979	0.125*
H23B	0.6047	0.6714	−0.1198	0.125*
H23C	0.4595	0.7527	−0.1375	0.125*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
C1	0.0431 (10)	0.0391 (8)	0.0488 (13)	0.0005 (8)	−0.0018 (9)	0.0023 (8)
C2	0.0517 (11)	0.0435 (9)	0.0512 (13)	−0.0025 (8)	0.0037 (10)	0.0049 (9)
C3	0.0487 (11)	0.0460 (9)	0.0743 (15)	−0.0108 (9)	0.0024 (11)	0.0050 (10)
C4	0.0532 (12)	0.0503 (10)	0.0651 (15)	−0.0140 (10)	−0.0054 (11)	−0.0081 (9)
C5	0.0463 (10)	0.0565 (10)	0.0521 (14)	−0.0034 (9)	−0.0060 (10)	−0.0046 (9)
C6	0.0427 (10)	0.0465 (9)	0.0523 (13)	−0.0066 (8)	−0.0032 (9)	0.0015 (8)
C7	0.0550 (12)	0.0409 (8)	0.0465 (12)	−0.0047 (8)	0.0034 (9)	0.0004 (8)
C8	0.0484 (11)	0.0423 (8)	0.0582 (14)	−0.0069 (9)	0.0022 (10)	−0.0024 (9)
O9	0.0680 (9)	0.0593 (8)	0.0858 (11)	0.0182 (7)	−0.0068 (8)	−0.0132 (8)
N10	0.0631 (11)	0.0482 (8)	0.0483 (11)	0.0020 (9)	−0.0041 (9)	0.0003 (8)
C11	0.0649 (13)	0.0622 (11)	0.0552 (13)	−0.0086 (10)	−0.0084 (11)	0.0006 (10)
C12	0.0661 (13)	0.0735 (13)	0.0750 (16)	−0.0123 (12)	−0.0153 (12)	0.0217 (11)
C13	0.0456 (11)	0.0557 (10)	0.0618 (14)	−0.0060 (9)	−0.0070 (10)	0.0102 (10)
C14	0.0607 (13)	0.0487 (10)	0.0795 (17)	0.0101 (10)	0.0030 (12)	0.0125 (11)
C15	0.0743 (14)	0.0474 (10)	0.0656 (15)	0.0058 (10)	0.0069 (12)	−0.0013 (10)
C16	0.0557 (12)	0.0453 (9)	0.0532 (13)	−0.0073 (9)	−0.0089 (10)	0.0053 (9)
C17	0.0690 (13)	0.0551 (10)	0.0628 (14)	0.0164 (10)	−0.0085 (13)	−0.0018 (11)
C18	0.0808 (16)	0.0606 (11)	0.0600 (15)	0.0111 (12)	−0.0088 (12)	−0.0068 (11)
O19	0.0949 (11)	0.0539 (8)	0.0611 (10)	−0.0033 (8)	−0.0192 (9)	0.0029 (7)
O20	0.0770 (9)	0.0559 (7)	0.0569 (9)	−0.0153 (7)	0.0127 (8)	0.0061 (7)

C21	0.113 (2)	0.0654 (13)	0.0782 (17)	−0.0159 (14)	0.0298 (15)	0.0162 (12)
O22	0.0808 (11)	0.0891 (10)	0.0548 (10)	−0.0292 (9)	0.0034 (8)	−0.0165 (8)
C23	0.0788 (17)	0.1105 (18)	0.0614 (16)	−0.0286 (15)	0.0078 (13)	−0.0088 (13)

Geometric parameters (Å, º)

C1—C6	1.378 (2)	C12—H12A	0.97
C1—C2	1.399 (2)	C12—H12B	0.97
C1—C7	1.506 (2)	C13—C14	1.371 (3)
C2—O20	1.367 (2)	C13—C18	1.382 (3)
C2—C3	1.382 (3)	C14—C15	1.378 (3)
C3—C4	1.371 (3)	C14—H14	0.93
C3—H3	0.93	C15—C16	1.387 (3)
C4—C5	1.380 (3)	C15—H15	0.93
C4—H4	0.93	C16—C17	1.360 (3)
C5—O22	1.366 (2)	C16—O19	1.368 (2)
C5—C6	1.390 (2)	C17—C18	1.379 (3)
C6—H6	0.93	C17—H17	0.93
C7—C8	1.511 (3)	C18—H18	0.93
C7—H7A	0.97	O19—H19	0.87 (3)
C7—H7B	0.97	O20—C21	1.423 (2)
C8—O9	1.235 (2)	C21—H21A	0.96
C8—N10	1.331 (2)	C21—H21B	0.96
N10—C11	1.452 (2)	C21—H21C	0.96
N10—H10	0.88 (2)	O22—C23	1.417 (2)
C11—C12	1.504 (3)	C23—H23A	0.96
C11—H11A	0.97	C23—H23B	0.96
C11—H11B	0.97	C23—H23C	0.96
C12—C13	1.503 (3)		

C6—C1—C2	119.14 (16)	C11—C12—H12A	108.9
C6—C1—C7	121.17 (15)	C13—C12—H12B	108.9
C2—C1—C7	119.67 (17)	C11—C12—H12B	108.9
O20—C2—C3	125.22 (16)	H12A—C12—H12B	107.7
O20—C2—C1	115.11 (15)	C14—C13—C18	116.86 (18)
C3—C2—C1	119.67 (18)	C14—C13—C12	121.78 (18)
C4—C3—C2	120.45 (17)	C18—C13—C12	121.36 (19)
C4—C3—H3	119.8	C13—C14—C15	122.16 (17)
C2—C3—H3	119.8	C13—C14—H14	118.9
C3—C4—C5	120.68 (17)	C15—C14—H14	118.9
C3—C4—H4	119.7	C14—C15—C16	119.76 (19)
C5—C4—H4	119.7	C14—C15—H15	120.1
O22—C5—C4	115.38 (16)	C16—C15—H15	120.1
O22—C5—C6	125.57 (17)	C17—C16—O19	123.00 (17)
C4—C5—C6	119.05 (18)	C17—C16—C15	118.94 (18)
C1—C6—C5	120.99 (17)	O19—C16—C15	118.06 (19)
C1—C6—H6	119.5	C16—C17—C18	120.41 (18)
C5—C6—H6	119.5	C16—C17—H17	119.8
C1—C7—C8	113.21 (13)	C18—C17—H17	119.8
C1—C7—H7A	108.9	C17—C18—C13	121.8 (2)

C8—C7—H7A	108.9	C17—C18—H18	119.1
C1—C7—H7B	108.9	C13—C18—H18	119.1
C8—C7—H7B	108.9	C16—O19—H19	115.6 (19)
H7A—C7—H7B	107.7	C2—O20—C21	117.97 (15)
O9—C8—N10	121.66 (18)	O20—C21—H21A	109.5
O9—C8—C7	121.78 (18)	O20—C21—H21B	109.5
N10—C8—C7	116.48 (16)	H21A—C21—H21B	109.5
C8—N10—C11	123.19 (17)	O20—C21—H21C	109.5
C8—N10—H10	112.2 (14)	H21A—C21—H21C	109.5
C11—N10—H10	123.7 (14)	H21B—C21—H21C	109.5
N10—C11—C12	112.56 (16)	C5—O22—C23	117.79 (15)
N10—C11—H11A	109.1	O22—C23—H23A	109.5
C12—C11—H11A	109.1	O22—C23—H23B	109.5
N10—C11—H11B	109.1	H23A—C23—H23B	109.5
C12—C11—H11B	109.1	O22—C23—H23C	109.5
H11A—C11—H11B	107.8	H23A—C23—H23C	109.5
C13—C12—C11	113.50 (18)	H23B—C23—H23C	109.5
C13—C12—H12A	108.9		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N10—H10···O19^{i}	0.88 (2)	2.16 (2)	3.023 (2)	165.4 (19)
O19—H19···O9^{ii}	0.87 (3)	1.76 (3)	2.6289 (19)	174 (3)

Symmetry codes: (i) $x-1/2, -y+3/2, -z+1$; (ii) $-x+3/2, -y+1, z+1/2$.