Acta Crystallographica Section E
Structure Reports
Online

ISSN 1600-5368

N-[(1,3-Benzodioxol-5-yl)methyl]-4-methylbenzamide: an analogue of capsaicin

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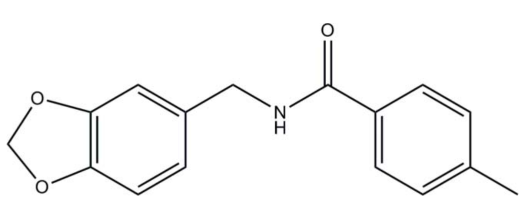
Received 21 January 2013; accepted 22 January 2013

Key indicators: single-crystal X-ray study; T = 290 K; mean σ(C–C) = 0.003 Å; R factor = 0.050; wR factor = 0.149; data-to-parameter ratio = 14.3.

In the title compound, $C_{16}H_{15}NO_3$, the five-membered 1,3-dioxole ring is in an envelope conformation with the methylene C atom as the flap atom [lying 0.202 (3) Å out of the plane formed by the other four atoms]. The benzene ring makes a dihedral angle of 84.65 (4)° with the best least-squares plane through the 1,3-benzodioxole fused-ring system, which substitutes the 2-methoxyphenol moiety in capsaicin. In the crystal, molecules are connected into a zigzag supramolecular chain along the c-axis direction by N—H$\cdots$O hydrogen bonds. These chains are connected into a layer in the ac plane by C—H$\cdots\pi$ interactions.

Related literature

For the biological activity of capsaicin, see: Okamoto *et al.* (2011). For ring conformational analysis, see: Cremer & Pople (1975).



Experimental

Crystal data

$C_{16}H_{15}NO_3$
M_r = 269.29
Monoclinic, $P2_1/c$
a = 4.9810 (2) Å
b = 26.652 (1) Å
c = 10.0545 (3) Å
β = 92.139 (2)°
V = 1333.84 (8) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.09 mm^{-1}
T = 290 K
0.33 × 0.24 × 0.16 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Absorption correction: numerical (*SADABS*; Sheldrick, 1996)
T_{min} = 0.940, T_{max} = 0.951
4550 measured reflections
2602 independent reflections
1698 reflections with $I > 2\sigma(I)$
R_{int} = 0.023

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.149
S = 1.03
2602 reflections
182 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.21 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

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

*Cg*1 and *Cg*2 are the centroids of the C1–C6 and C10–C15 rings, respectively.

D—H$\cdots A$	D—H	H$\cdots A$	$D\cdots A$	D—H$\cdots A$
N1—H1*N*1$\cdots$O3^{i}	0.91	2.08	2.958 (2)	162
C7—H7*A*$\cdots$*Cg*1	0.97	2.74	3.603 (3)	149
C16—H16*C*$\cdots$*Cg*2	0.96	2.96	3.829 (2)	151

Symmetry code: (i) $x, -y+\frac{1}{2}, z-\frac{1}{2}$.

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows* (Farrugia, 2012); software used to prepare material for publication: *Marvinsketch* (Chemaxon, 2010) and *publCIF* (Westrip, 2010).

We thank the Brazilian agencies CNPq (140925/2009–0 to SHM), FAPESP and CAPES for financial support. We also thank Professor Carlos A. De Simone for the data collection.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: TK5191).

References

Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
Chemaxon (2010). *Marvinsketch.* http://www.chemaxon.com.
Cremer, D. & Pople, J. A. (1975). *J. Am. Chem. Soc.* **97**, 1354–1358.
Farrugia, L. J. (2012). *J. Appl. Cryst.* **45**, 849–854.
Nonius (1999). *COLLECT*. Nonius BV, Delft, The Netherlands.
Okamoto, M., Irii, H., Tahara, Y., Ishii, H., Hirao, A., Udagawa, H., Hiramoto, M., Yasuda, K., Takanishi, A., Shibata, S. & Shimizu, I. (2011). *J. Med. Chem.* **54**, 6295–6304.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter Jr & R. M. Sweet, pp. 307–326. New York: Academic Press.
Sheldrick, G. M. (1996). *SADABS*. University of Göttingen, Germany.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.

supplementary materials

Acta Cryst. (2013). E**69**, o332 [doi:10.1107/S1600536813002201]

N-[(1,3-Benzodioxol-5-yl)methyl]-4-methylbenzamide: an analogue of capsaicin

Stella H. Maganhi, Mariana C. F. C. B. Damião, Maurício T. Tavares and Roberto Parise Filho

Comment

Capsaicin is the main pungent compound found in chilli peppers of the genus *Capsicum* and is found to exert multiple pharmacological and physiological effects, including analgesic, anti-cancer, anti-inflammatory, anti-oxidant and anti-obesity (Okamoto *et al.* 2011). This makes capsaicin an excellent scaffold for the rational design of analogues with better biological activity. The title compound (I) is a capsaicin-like derivative where the 2-methoxyphenol ring was substituted with a benzodioxol ring and the amide aliphatic chain was replaced with a 4-methylbenzoyl group. As suitable crystals were obtained from its hexane solution, a crystal structure determination of (I) was undertaken.

In (I), Fig. 1, the 1,3-dioxole five membered ring is in an envelope configuration with the C7 atom lying 0.202 (3) Å out of the plane formed by the other four atoms. The ring puckering parameters are q_2 = 0.128 (2) Å and φ_2 = 149.9 (9)° (Cremer & Pople, 1975).

The crystal packing of (I), Table 1, is sustained by N—H···O and C—H···π interactions, leading to supramolecular layers in the *ac* plane.

Experimental

1-(1,3-Benzodioxol-5-yl)methanamine (0.755 g, 5 mmol) was dissolved in chloroform (20 ml) and then triethylamine (411 μL, 5.5 mmol) and DMF (40 μL, 0,5 mmol) were added. The mixture was stirred for 30 min under argon atmosphere. 4-Methylbenzoyl chloride (661 μL, 5 mmol) was added in portions and stirred over 24 h. The organic layer was washed with 5% HCl aqueous solution, water, brine and dried over anhydrous Na_2SO_4. The solvent was removed under high vacuum and the title compound was obtained after recrystallization from hot hexane. Analytical data: white solid, yield 71.4° (0.96 g, 3.57 mmol). ^{1}H-NMR NMR (300 MHz, DMSO-d6, ppm): δ 8.87 (1*H*, bt, J = 5.8 Hz, 9-NH), 7.79 (2*H*, d, J = 8.2 Hz,12, 13-ArH), 7.27 (2*H*, d, J = 8.2 Hz, 14, 15-ArH), 6.83 (3*H*, m, 4, 5, 7-ArH), 5.98 (2*H*, s, 1-OCH_2O), 4.38 (2*H*, d, J = 6.0 Hz, 8-CH_2), 2.36 (3*H*, s, 15-CH_3). ^{13}C NMR (75 MHz, DMSO-d6, ppm) δ: 165.9 (C9), 147.18 (C2), 145.98 (C1), 141.02 (C13), 133.68 (C10), 131.67 (C5), 128.77 (C12, C14), 127.21 (C11, C15), 120.42 (C4), 107.94 (C3), 107.92 (C6), 100.74 (C7), 42.36 (C8), 20.89 (C16); Anal. calcd. for: $C_{16}H_{15}NO_3$ (269.11): C 71.36, H 5.61, N 5.20, found: C 71.30, H 5.74, N 5.17, mp: 404.7–405.2 K.

Refinement

The H atoms were geometrically placed (C—H = 0.93–0.97 Å) and refined as riding with U_{iso}(H) = 1.2–1.5U_{eq}(C). The N—H H atom was located in a difference map, fixed in this position with U_{iso}(H) = 1.2U_{eq}(N).

Computing details

Data collection: *COLLECT* (Nonius, 1999); cell refinement: *SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO* (Otwinowski & Minor, 1997) and *SCALEPACK*; program(s) used to solve structure: *SIR97* (Altomare *et al.*, 1999); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3 for Windows*

(Farrugia, 2012)\bbr00; software used to prepare material for publication: *Marvinsketch* (Chemaxon, 2010) and *publCIF* (Westrip, 2010).

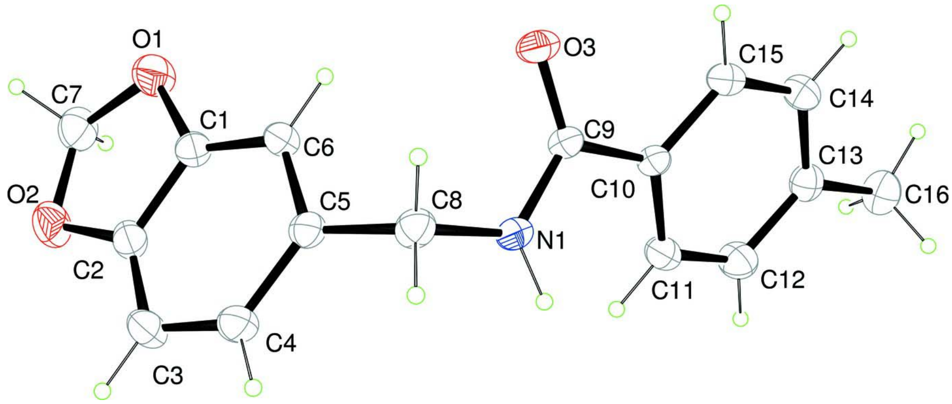


Figure 1

The molecular structure of (I) showing atom labelling scheme and displacement ellipsoids at the 50% probability level (arbitrary spheres for the H atoms).

N-[(1,3-Benzodioxol-5-yl)methyl]-4-methylbenzamide

Crystal data

$C_{16}H_{15}NO_3$
M_r = 269.29
Monoclinic, $P2_1/c$
Hall symbol: -P 2ybc
a = 4.9810 (2) Å
b = 26.652 (1) Å
c = 10.0545 (3) Å
β = 92.139 (2)°
V = 1333.84 (8) Å^3
Z = 4
F(000) = 568
D_x = 1.341 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 5124 reflections
θ = 3.1–27.5°
μ = 0.09 mm^{-1}
T = 290 K
Prism, colourless
0.33 × 0.24 × 0.16 mm

Data collection

Bruker APEXII CCD area-detector diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
Detector resolution: 0 pixels mm^{-1}
φ and ω scans
Absorption correction: numerical (*SADABS*; Sheldrick, 1996)
T_{min} = 0.940, T_{max} = 0.951
4550 measured reflections
2602 independent reflections
1698 reflections with $I > 2\sigma(I)$
R_{int} = 0.023
θ_{max} = 26.0°, θ_{min} = 3.1°
h = −6→6
k = −32→30
l = −12→12

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.050
$wR(F^2)$ = 0.149
S = 1.03
2602 reflections
182 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-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.0859P)^2 + 0.0674P]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ 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 (Å^2)

	x	y	z	U_{iso}*/U_{eq}
O1	−0.0219 (3)	0.06137 (6)	0.88685 (15)	0.0754 (5)
O2	−0.0295 (3)	0.00662 (6)	0.71012 (17)	0.0797 (5)
O3	0.4080 (3)	0.24272 (5)	0.87268 (12)	0.0634 (4)
N1	0.4208 (3)	0.22490 (6)	0.65426 (14)	0.0496 (4)
H1N1	0.3768	0.2357	0.5702	0.060*
C1	0.1365 (4)	0.08000 (7)	0.78849 (19)	0.0525 (5)
C2	0.1354 (4)	0.04694 (8)	0.6838 (2)	0.0585 (5)
C3	0.2867 (5)	0.05485 (8)	0.5769 (2)	0.0733 (6)
H3	0.2878	0.0322	0.5065	0.088*
C4	0.4407 (4)	0.09851 (8)	0.5771 (2)	0.0649 (6)
H4	0.5483	0.1047	0.5053	0.078*
C5	0.4398 (3)	0.13305 (7)	0.68029 (18)	0.0503 (5)
C6	0.2825 (3)	0.12319 (7)	0.79020 (18)	0.0505 (5)
H6	0.2782	0.1453	0.8616	0.061*
C7	−0.1575 (5)	0.01955 (9)	0.8290 (2)	0.0740 (7)
H7A	−0.3444	0.0279	0.8094	0.089*
H7B	−0.1510	−0.0086	0.8903	0.089*
C8	0.5961 (4)	0.18139 (7)	0.6730 (2)	0.0556 (5)
H8A	0.7042	0.1856	0.7545	0.067*
H8B	0.7169	0.1795	0.5997	0.067*
C9	0.3359 (3)	0.25214 (7)	0.75640 (17)	0.0467 (5)
C10	0.1449 (3)	0.29384 (7)	0.72454 (16)	0.0440 (4)
C11	−0.0105 (4)	0.29652 (7)	0.60682 (19)	0.0547 (5)
H11	0.0065	0.2719	0.5422	0.066*
C12	−0.1888 (4)	0.33522 (8)	0.5853 (2)	0.0620 (6)
H12	−0.2918	0.3360	0.5062	0.074*
C13	−0.2198 (4)	0.37300 (7)	0.6775 (2)	0.0535 (5)
C14	−0.0639 (4)	0.37058 (8)	0.7936 (2)	0.0598 (5)
H14	−0.0779	0.3958	0.8570	0.072*
C15	0.1126 (4)	0.33142 (8)	0.81753 (18)	0.0576 (5)
H15	0.2117	0.3303	0.8977	0.069*
C16	−0.4161 (4)	0.41514 (8)	0.6534 (2)	0.0710 (6)
H16A	−0.3634	0.4345	0.5782	0.106*

H16B	−0.4180	0.4363	0.7307	0.106*
H16C	−0.5924	0.4016	0.6358	0.106*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0884 (10)	0.0677 (10)	0.0708 (10)	−0.0258 (8)	0.0130 (8)	−0.0058 (8)
O2	0.0972 (11)	0.0531 (9)	0.0875 (12)	−0.0117 (8)	−0.0135 (9)	−0.0127 (8)
O3	0.0857 (10)	0.0681 (10)	0.0363 (8)	0.0119 (8)	−0.0003 (6)	0.0050 (7)
N1	0.0628 (9)	0.0497 (9)	0.0366 (8)	0.0042 (7)	0.0049 (7)	0.0051 (7)
C1	0.0582 (11)	0.0506 (12)	0.0482 (11)	0.0027 (9)	−0.0053 (9)	−0.0010 (9)
C2	0.0697 (13)	0.0469 (11)	0.0577 (13)	0.0060 (10)	−0.0126 (10)	−0.0048 (10)
C3	0.1024 (17)	0.0590 (14)	0.0577 (14)	0.0133 (13)	−0.0077 (12)	−0.0177 (11)
C4	0.0821 (14)	0.0646 (14)	0.0486 (12)	0.0180 (11)	0.0101 (10)	−0.0022 (10)
C5	0.0545 (11)	0.0504 (11)	0.0459 (11)	0.0121 (9)	0.0000 (8)	0.0027 (9)
C6	0.0592 (11)	0.0481 (11)	0.0440 (11)	0.0028 (9)	0.0003 (8)	−0.0066 (9)
C7	0.0766 (14)	0.0614 (14)	0.0827 (17)	−0.0153 (12)	−0.0136 (13)	−0.0005 (12)
C8	0.0553 (11)	0.0590 (12)	0.0530 (11)	0.0067 (10)	0.0089 (8)	0.0053 (9)
C9	0.0559 (10)	0.0482 (11)	0.0361 (10)	−0.0035 (8)	0.0040 (8)	0.0042 (8)
C10	0.0507 (10)	0.0452 (10)	0.0365 (9)	−0.0044 (8)	0.0069 (7)	0.0020 (8)
C11	0.0632 (11)	0.0533 (12)	0.0474 (11)	0.0016 (9)	−0.0009 (9)	−0.0075 (9)
C12	0.0610 (12)	0.0660 (14)	0.0582 (13)	0.0061 (11)	−0.0090 (9)	−0.0025 (11)
C13	0.0481 (10)	0.0524 (12)	0.0605 (12)	−0.0026 (9)	0.0088 (9)	0.0040 (10)
C14	0.0707 (13)	0.0547 (13)	0.0544 (12)	0.0039 (10)	0.0093 (10)	−0.0095 (10)
C15	0.0712 (13)	0.0598 (13)	0.0417 (11)	0.0020 (10)	−0.0008 (9)	−0.0037 (9)
C16	0.0593 (13)	0.0664 (14)	0.0879 (17)	0.0101 (11)	0.0121 (11)	0.0065 (12)

Geometric parameters (Å, º)

O1—C1	1.380 (2)	C7—H7B	0.9700
O1—C7	1.417 (3)	C8—H8A	0.9700
O2—C2	1.384 (2)	C8—H8B	0.9700
O2—C7	1.418 (3)	C9—C10	1.490 (3)
O3—C9	1.2358 (19)	C10—C15	1.384 (3)
N1—C9	1.339 (2)	C10—C11	1.392 (3)
N1—C8	1.459 (2)	C11—C12	1.373 (3)
N1—H1N1	0.9124	C11—H11	0.9300
C1—C6	1.361 (3)	C12—C13	1.382 (3)
C1—C2	1.372 (3)	C12—H12	0.9300
C2—C3	1.352 (3)	C13—C14	1.380 (3)
C3—C4	1.394 (3)	C13—C16	1.503 (3)
C3—H3	0.9300	C14—C15	1.380 (3)
C4—C5	1.387 (3)	C14—H14	0.9300
C4—H4	0.9300	C15—H15	0.9300
C5—C6	1.403 (3)	C16—H16A	0.9600
C5—C8	1.508 (3)	C16—H16B	0.9600
C6—H6	0.9300	C16—H16C	0.9600
C7—H7A	0.9700		
C1—O1—C7	105.39 (16)	C5—C8—H8A	109.2

C2—O2—C7	105.13 (16)	N1—C8—H8B	109.2
C9—N1—C8	122.43 (15)	C5—C8—H8B	109.2
C9—N1—H1N1	117.9	H8A—C8—H8B	107.9
C8—N1—H1N1	119.5	O3—C9—N1	121.77 (17)
C6—C1—C2	122.7 (2)	O3—C9—C10	121.03 (16)
C6—C1—O1	127.92 (18)	N1—C9—C10	117.19 (15)
C2—C1—O1	109.40 (18)	C15—C10—C11	117.55 (17)
C3—C2—C1	121.5 (2)	C15—C10—C9	118.96 (16)
C3—C2—O2	128.7 (2)	C11—C10—C9	123.47 (17)
C1—C2—O2	109.73 (19)	C12—C11—C10	120.57 (18)
C2—C3—C4	116.89 (19)	C12—C11—H11	119.7
C2—C3—H3	121.6	C10—C11—H11	119.7
C4—C3—H3	121.6	C11—C12—C13	121.98 (18)
C5—C4—C3	122.5 (2)	C11—C12—H12	119.0
C5—C4—H4	118.7	C13—C12—H12	119.0
C3—C4—H4	118.7	C14—C13—C12	117.42 (18)
C4—C5—C6	118.83 (19)	C14—C13—C16	120.94 (19)
C4—C5—C8	120.96 (17)	C12—C13—C16	121.64 (18)
C6—C5—C8	120.17 (17)	C13—C14—C15	121.17 (18)
C1—C6—C5	117.52 (17)	C13—C14—H14	119.4
C1—C6—H6	121.2	C15—C14—H14	119.4
C5—C6—H6	121.2	C14—C15—C10	121.30 (17)
O1—C7—O2	108.35 (18)	C14—C15—H15	119.4
O1—C7—H7A	110.0	C10—C15—H15	119.4
O2—C7—H7A	110.0	C13—C16—H16A	109.5
O1—C7—H7B	110.0	C13—C16—H16B	109.5
O2—C7—H7B	110.0	H16A—C16—H16B	109.5
H7A—C7—H7B	108.4	C13—C16—H16C	109.5
N1—C8—C5	112.19 (14)	H16A—C16—H16C	109.5
N1—C8—H8A	109.2	H16B—C16—H16C	109.5

C7—O1—C1—C6	172.16 (19)	C9—N1—C8—C5	93.3 (2)
C7—O1—C1—C2	−9.7 (2)	C4—C5—C8—N1	108.75 (19)
C6—C1—C2—C3	1.8 (3)	C6—C5—C8—N1	−68.9 (2)
O1—C1—C2—C3	−176.41 (17)	C8—N1—C9—O3	2.1 (3)
C6—C1—C2—O2	179.79 (16)	C8—N1—C9—C10	−176.54 (15)
O1—C1—C2—O2	1.6 (2)	O3—C9—C10—C15	20.0 (3)
C7—O2—C2—C3	−174.9 (2)	N1—C9—C10—C15	−161.38 (17)
C7—O2—C2—C1	7.3 (2)	O3—C9—C10—C11	−158.13 (18)
C1—C2—C3—C4	−0.9 (3)	N1—C9—C10—C11	20.5 (3)
O2—C2—C3—C4	−178.44 (19)	C15—C10—C11—C12	−0.1 (3)
C2—C3—C4—C5	−0.7 (3)	C9—C10—C11—C12	178.03 (17)
C3—C4—C5—C6	1.5 (3)	C10—C11—C12—C13	0.6 (3)
C3—C4—C5—C8	−176.20 (18)	C11—C12—C13—C14	0.0 (3)
C2—C1—C6—C5	−1.0 (3)	C11—C12—C13—C16	−179.77 (18)
O1—C1—C6—C5	176.87 (17)	C12—C13—C14—C15	−1.1 (3)
C4—C5—C6—C1	−0.6 (3)	C16—C13—C14—C15	178.62 (18)
C8—C5—C6—C1	177.12 (16)	C13—C14—C15—C10	1.7 (3)
C1—O1—C7—O2	14.2 (2)	C11—C10—C15—C14	−1.1 (3)

C2—O2—C7—O1	−13.3 (2)	C9—C10—C15—C14	−179.27 (17)

Hydrogen-bond geometry (Å, º)

Cg1 and Cg2 are the centroids of the C1–C6 and C10–C15 rings, respectively.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1—H1*N*1···O3^{i}	0.91	2.08	2.958 (2)	162
C7—H7*A*···*Cg*1	0.97	2.74	3.603 (3)	149
C16—H16*C*···*Cg*2	0.96	2.96	3.829 (2)	151

Symmetry code: (i) x, $-y+1/2$, $z-1/2$.