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4-(3-Methoxyphenoxy)butyric acid

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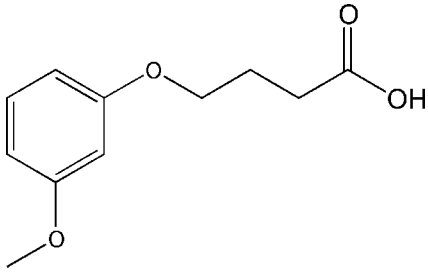
Key indicators: single-crystal X-ray study; T = 173 K; mean σ(C–C) = 0.001 Å; R factor = 0.043; wR factor = 0.120; data-to-parameter ratio = 20.7.

In the title compound, $C_{11}H_{14}O_4$, an intermediate for the synthesis of a new kind of estrogen receptor modulator, all non-H atoms lie on a common plane (r.m.s. deviation = 0.0472 Å). All C—C bonds in the side chain are in a *trans* conformation, and the hydroxyl group is also *trans* to the methylene chain. In the crystal structure, molecules form centrosymmetric dimers showing a head-to-head arrangement which is stabilized by O—H···O hydrogen bonds. A weak C—H···O contact is also present.

Related literature

For the synthesis of 4-(3-methoxy-phenoxy)-butyric acid, see Tandon *et al.* (1990). For estrogen receptor modulators, see Lloyd *et al.* (2004). For a similar carboxylic acid, see: Smith *et al.* (1989).



Experimental

Crystal data

$C_{11}H_{14}O_4$
M_r = 210.22
Monoclinic, $P2_1/n$
a = 9.6509 (6) Å
b = 5.3998 (4) Å
c = 20.2033 (13) Å
β = 90.822 (5)°
V = 1052.74 (12) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.10 mm^{-1}
T = 173 K
0.32 × 0.27 × 0.25 mm

Data collection

Stoe IPDS-II two-circle diffractometer
Absorption correction: none
15489 measured reflections
2945 independent reflections
2458 reflections with $I > 2\sigma(I)$
R_{int} = 0.057

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.120
S = 1.07
2945 reflections
142 parameters
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.31 e Å^{-3}
$\Delta\rho_{min}$ = −0.20 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
O41—H41···O42^{i}	0.927 (18)	1.804 (19)	2.7292 (11)	175.5 (16)
C17—H17B···O42^{ii}	0.98	2.48	3.2477 (14)	135

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

Data collection: *X-AREA* (Stoe & Cie, 2001); cell refinement: *X-AREA*; data reduction: *X-AREA*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *XP* in *SHELXTL-Plus* (Sheldrick, 2008) and *Mercury* (Macrae *et al.*, 2006); software used to prepare material for publication: *SHELXL97* and *PLATON* (Spek, 2009).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: NG2557).

References

Lloyd, D. G., Hughes, R. B., Zisterer, D. M., Williams, D. C., Fattorusso, C., Catalanotti, B., Campiani, G. & Meegan, M. J. (2004). *J. Med. Chem.* **47**, 5612–5615.
Macrae, C. F., Edgington, P. R., McCabe, P., Pidcock, E., Shields, G. P., Taylor, R., Towler, M. & van de Streek, J. (2006). *J. Appl Cryst.* **39**, 453–457.
Sheldrick, G. M. (2008). *Acta Cryst.* A**64**, 112–122.
Smith, G., Shariff, S. M., O'Reilly, E. J. & Kennard, C. H. L. (1989). *Polyhedron*, **8**, 39–43.
Spek, A. L. (2009). *Acta Cryst.* D**65**, 148–155.
Stoe & Cie (2001). *X-AREA*. Stoe & Cie, Darmstadt, Germany.
Tandon, V. K., Khanna, J. M., Arand, N. & Chandra, A. (1990). *Tetrahedron*, **46**, 2871–2882.

supporting information

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4-(3-Methoxyphenoxy)butyric acid

Julia Heilmann-Brohl, Gérard Jaouen and Michael Bolte

S1. Comment

4-(3-Methoxyphenoxy)butyric acid is an intermediate for the synthesis of a new kind of estrogen receptor modulators (Lloyd *et al.*, 2004). All non-H atoms of the title compound (Fig. 1) lie in a common plane (r.m.s. deviation 0.0472 Å). All C—C bonds in the side chain are in a *trans* conformation, and the hydroxyl group is also *trans* to the methylene chain. In the crystal, the molecules form centrosymmetric dimers showing a head-to-head arrangement which is stabilized by O—H···O hydrogen bonds (Fig. 2). In addition to this classical hydrogen bond, there is weak C—H···O contact (Table 1).

Two comparable structures, 4-(4-chlorophenoxy)butanoic acid and 4-(2,4-dichlorophenoxy)butanoic acid, (Smith *et al.*, 1989) adopt a very similar conformation as the title compound. However, the carboxyl group in these structures is slightly twisted out of the molecular plane. The HO—C(O)—CH_2—CH_2 torsion angle is 161.6° and 170.1° in 4-(4-chlorophenoxy)butanoic acid and 4-(2,4-dichlorophenoxy)butanoic acid, respectively, whereas this torsion angle amounts to 174.73 (9)° in the title compound.

S2. Experimental

Synthesis of 4-(3-methoxy-phenoxy)-butyric acid ethyl ester (scheme 2):

Cs_3CO_3 (9.666 mmol, 3.149 g) was added to a solution of 3-methoxyphenol (8.055 mmol, 1.000 g) in acetone (20 ml) and the mixture was stirred for 5 min at r.t.. Ethyl-4-bromobutyrate (8.055 mmol, 1.571 g) was added and the reaction mixture was heated under reflux for 28 h. After cooling to r.t. the slurry was poured onto H_2O/ice/HCl and the aqeous phase was extracted with CH_2Cl_2 (4 *x* 25 ml). The combined organic layers were washed with H_2O (3 *x* 25 ml), dried over $MgSO_4$ and the solvent was removed under reduced pressure to yield the crude product as a slightly yellow oil. The crude product was subjected to a column chromatography (eluent 100% CH_2Cl_2), to obtain the pure product as a slightly yellow oil (1.486 g, 77%). **^{1}H-NMR ($CDCl_3$, 300 MHz):** δ = 7.165 (tr, *J* = 8.1 Hz, 1H, C_6H_4), 6.519 – 6.447 (m, 3H, C_6H_4), 4.146 (q, *J* = 7.2 Hz, 2H, H12), 3.987 (tr, *J* = 6.2 Hz, 2H, H^8), 3.780 (s, 3H, O—CH_3), 2.509 (tr, *J* = 7.2 Hz, 2H H^{10}), 2.145 - 2.055 (m, 2H H^9), 1.259 (tr, *J* = 7.2 Hz, 3H, H^{13}).

Synthesis of 4-(3-methoxy-phenoxy)-butyric acid (scheme 3):

4-(3-methoxy-phenoxy)-butyric acid ethyl ester (2.938 mmol, 0.700 g) is dissolved in acetone (10 ml) and H_2O (5 ml) and 1 *M* NaOH (20 ml) is added. The reaction mixture is stirred at r.t. for 1 h and is then poured into H_2O/HCl (50 ml). The aqeous phase is extracted with CH_2Cl_2 (4 *x* 25 ml), and the combined organic layers are washed with H_2O (2 *x* 30 ml), dried over $MgSO_4$ and the solvent is evaporated. The crude product is obtained as light yellow oil from which colourless crystals – suitable for X-Ray analysis - start to grow within 30 min. Purification of the crude product is conducted by column chromatography. The by-products are removed by elution with CH_2Cl_2. The desired product is then eluted with MeOH. After evaporation of MeOH, the pure product is obtained as an off-white crystalline solid (0.352 g, 58%). **^{1}H-NMR ($CDCl_3$, 300 MHz):** δ = 7.171 (tr, *J* = 8.3 Hz, 1H, C_6H_4), 6.526 - 6.447 (m, 3H, C_6H_4), 4.010 (tr, *J* = 6.0

Hz, 2H, H^8), 3.787 (s, 3H, O—CH_3), 2.592 (tr, J = 7.4 Hz, 2H, H^{10}), 2.174 - 2.073 (m, 2H, H^9), n.o. (COO*H*).

S3. Refinement

H atoms bonded to C were refined with fixed individual displacement parameters [U(H) = 1.2 U_{eq}(C) or U(H) = 1.5 U_{eq}(C_{methyl})] using a riding model with $C_{aromatic}$—H = 0.95 Å, C_{methyl}—H = 0.98 Å, and $C_{methylene}$—H = 0.99 Å. The methyl group was allowed to rotate but not to tip. the hydroxy H atom was freely refined.

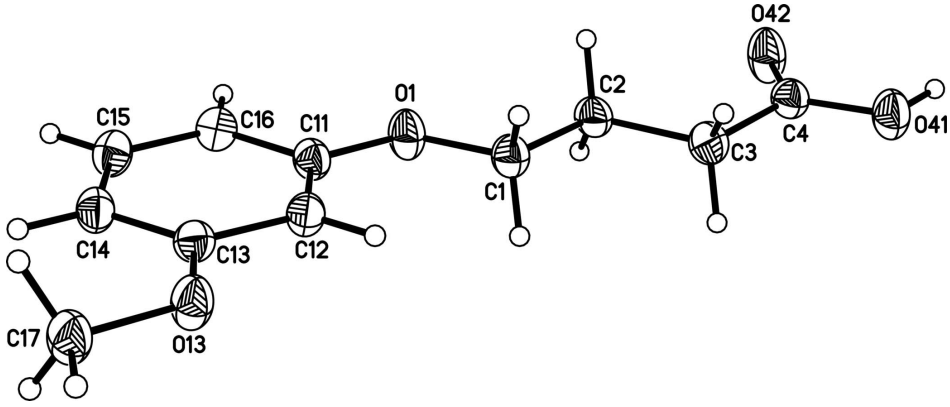

Figure 1

Perspective view of the title compound with the atom numbering scheme; displacement ellipsoids are at the 50% probability level; H atoms are drawn as small spheres of arbitrary radii.

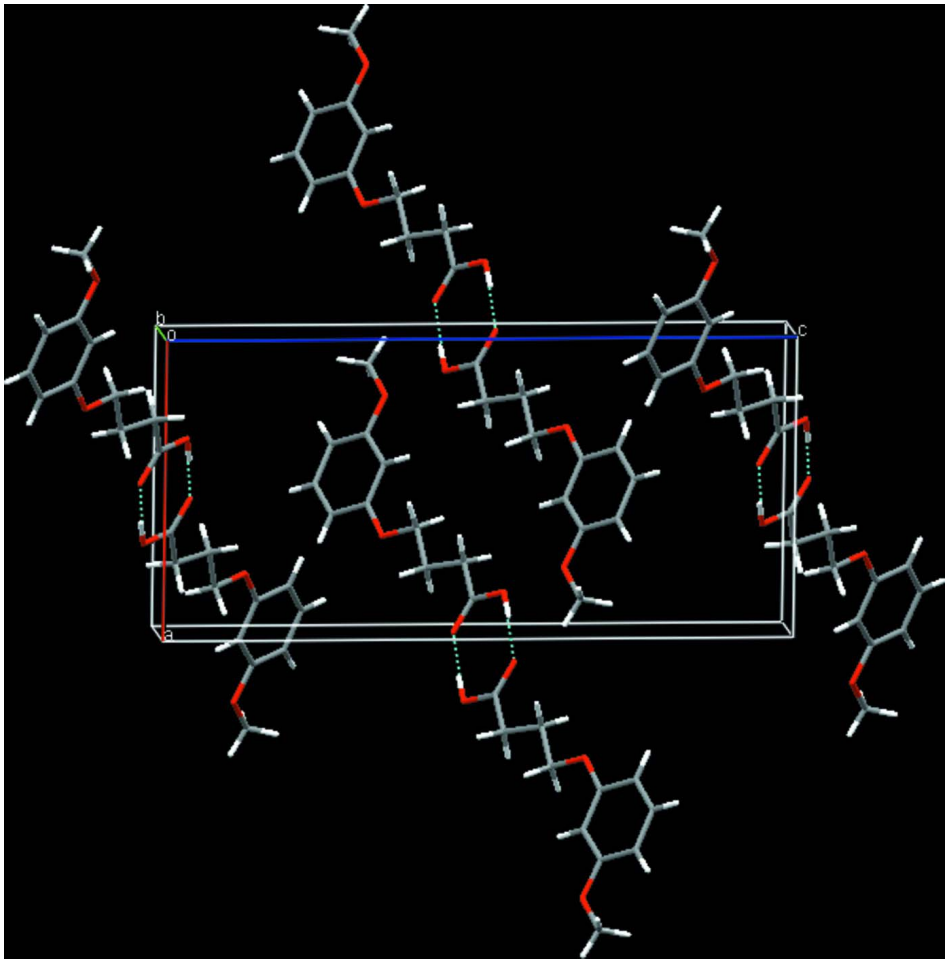

Figure 2

Packing diagram of the title compound with view onto the *ac* plane. Hydrogen bonds shown as dashed lines.

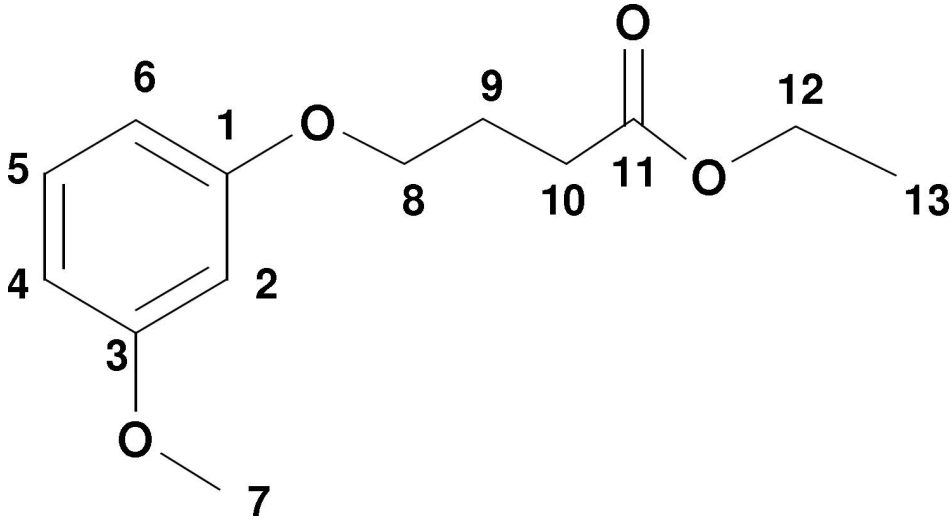

Figure 3

The numbering of the ethyl ester of the title compound.

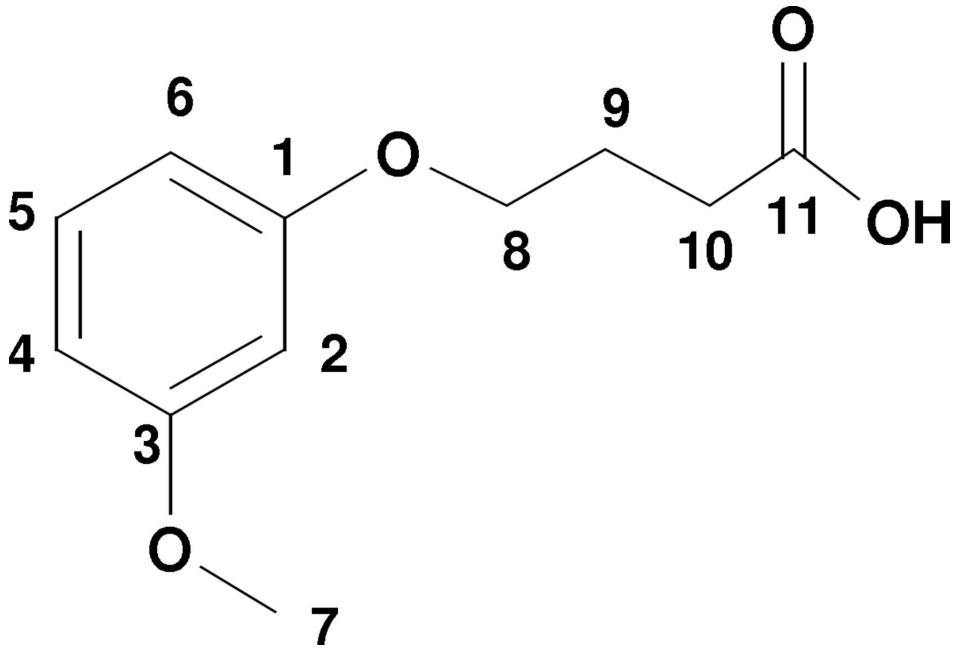

Figure 4

The numbering of the title compound.

4-(3-Methoxyphenoxy)butyric acid

Crystal data

$C_{11}H_{14}O_4$
$M_r = 210.22$
Monoclinic, $P2_1/n$
Hall symbol: -P 2yn
$a = 9.6509$ (6) Å
$b = 5.3998$ (4) Å
$c = 20.2033$ (13) Å
$\beta = 90.822$ (5)°
$V = 1052.74$ (12) Å^3
$Z = 4$
$F(000) = 448$
$D_x = 1.326$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 15224 reflections
$\theta = 3.7$–29.5°
$\mu = 0.10$ mm^{-1}
$T = 173$ K
Block, colourless
0.32 × 0.27 × 0.25 mm

Data collection

Stoe IPDS-II two-circle diffractometer
Radiation source: fine-focus sealed tube
Graphite monochromator
ω scans
15489 measured reflections
2945 independent reflections
2458 reflections with $I > 2\sigma(I)$
$R_{int} = 0.057$
$\theta_{max} = 29.6°$, $\theta_{min} = 3.7°$
$h = -13\rightarrow13$
$k = -7\rightarrow7$
$l = -28\rightarrow25$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.043$
$wR(F^2) = 0.120$
$S = 1.07$
2945 reflections
142 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
$w = 1/[\sigma^2(F_o^2) + (0.0677P)^2 + 0.1161P]$ where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.31$ e Å^{-3}
$\Delta\rho_{min} = -0.20$ e Å^{-3}
Extinction correction: *SHELXL97* (Sheldrick, 2008), $Fc^* = kFc[1+0.001xFc^2\lambda^3/\sin(2\theta)]^{-1/4}$
Extinction coefficient: 0.048 (5)

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'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 $F^2 > \sigma(F^2)$ 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}
O1	0.32321 (7)	0.55314 (15)	0.64594 (4)	0.03035 (19)
C1	0.36009 (11)	0.72446 (18)	0.59488 (5)	0.0263 (2)
H1A	0.3840	0.6344	0.5539	0.032*
H1B	0.4411	0.8248	0.6091	0.032*
C2	0.23475 (10)	0.89015 (19)	0.58265 (5)	0.0265 (2)
H2A	0.2151	0.9860	0.6232	0.032*
H2B	0.1527	0.7866	0.5721	0.032*
C3	0.26116 (11)	1.0679 (2)	0.52546 (5)	0.0286 (2)
H3A	0.3491	1.1572	0.5343	0.034*
H3B	0.2727	0.9704	0.4844	0.034*
C4	0.14701 (11)	1.25525 (19)	0.51430 (5)	0.0269 (2)
O41	0.17803 (9)	1.41971 (15)	0.46803 (4)	0.0342 (2)
H41	0.1036 (18)	1.526 (3)	0.4617 (8)	0.056 (5)*
O42	0.03810 (8)	1.25686 (16)	0.54438 (5)	0.0382 (2)
C11	0.42179 (10)	0.38789 (18)	0.66811 (5)	0.0245 (2)
C12	0.55358 (10)	0.36401 (18)	0.64103 (5)	0.0253 (2)
H12	0.5814	0.4682	0.6058	0.030*
C13	0.64437 (10)	0.18317 (18)	0.66685 (5)	0.0243 (2)
C14	0.60524 (11)	0.02991 (19)	0.71884 (5)	0.0263 (2)
H14	0.6668	−0.0927	0.7358	0.032*
C15	0.47284 (10)	0.06066 (19)	0.74563 (5)	0.0278 (2)
H15	0.4454	−0.0420	0.7813	0.033*
C16	0.38130 (11)	0.23721 (19)	0.72120 (5)	0.0270 (2)
H16	0.2923	0.2562	0.7401	0.032*
O13	0.77149 (8)	0.17389 (15)	0.63728 (4)	0.0316 (2)
C17	0.86678 (11)	−0.0111 (2)	0.66159 (5)	0.0334 (3)
H17A	0.8863	0.0179	0.7087	0.050*
H17B	0.9532	−0.0014	0.6369	0.050*
H17C	0.8257	−0.1758	0.6558	0.050*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0250 (4)	0.0310 (4)	0.0350 (4)	0.0067 (3)	0.0021 (3)	0.0095 (3)
C1	0.0255 (5)	0.0255 (5)	0.0277 (5)	0.0032 (4)	−0.0012 (4)	0.0029 (4)
C2	0.0262 (5)	0.0251 (5)	0.0281 (5)	0.0052 (4)	−0.0032 (4)	0.0004 (4)
C3	0.0290 (5)	0.0275 (5)	0.0294 (5)	0.0056 (4)	−0.0011 (4)	0.0014 (4)
C4	0.0291 (5)	0.0247 (5)	0.0268 (5)	0.0022 (4)	−0.0036 (4)	0.0007 (4)
O41	0.0362 (4)	0.0313 (4)	0.0351 (4)	0.0080 (3)	0.0025 (3)	0.0096 (3)
O42	0.0318 (4)	0.0371 (5)	0.0458 (5)	0.0105 (3)	0.0055 (4)	0.0148 (4)
C11	0.0238 (4)	0.0231 (4)	0.0266 (5)	0.0024 (3)	−0.0027 (4)	0.0014 (4)
C12	0.0263 (5)	0.0255 (5)	0.0240 (4)	0.0018 (3)	−0.0002 (3)	0.0035 (3)
C13	0.0237 (4)	0.0257 (4)	0.0235 (4)	0.0021 (3)	−0.0008 (3)	−0.0002 (4)
C14	0.0273 (5)	0.0250 (5)	0.0265 (5)	0.0018 (4)	−0.0033 (4)	0.0035 (4)
C15	0.0280 (5)	0.0282 (5)	0.0273 (5)	−0.0025 (4)	−0.0011 (4)	0.0050 (4)
C16	0.0245 (5)	0.0286 (5)	0.0280 (5)	−0.0010 (4)	0.0002 (4)	0.0020 (4)
O13	0.0266 (4)	0.0380 (4)	0.0303 (4)	0.0100 (3)	0.0048 (3)	0.0095 (3)
C17	0.0301 (5)	0.0382 (6)	0.0319 (5)	0.0128 (4)	0.0026 (4)	0.0059 (4)

Geometric parameters (Å, º)

O1—C11	1.3747 (11)	C11—C16	1.4061 (14)
O1—C1	1.4343 (12)	C12—C13	1.4072 (13)
C1—C2	1.5219 (13)	C12—H12	0.9500
C1—H1A	0.9900	C13—O13	1.3732 (12)
C1—H1B	0.9900	C13—C14	1.3935 (14)
C2—C3	1.5263 (14)	C14—C15	1.4047 (14)
C2—H2A	0.9900	C14—H14	0.9500
C2—H2B	0.9900	C15—C16	1.3858 (14)
C3—C4	1.5103 (14)	C15—H15	0.9500
C3—H3A	0.9900	C16—H16	0.9500
C3—H3B	0.9900	O13—C17	1.4394 (12)
C4—O42	1.2217 (13)	C17—H17A	0.9800
C4—O41	1.3268 (13)	C17—H17B	0.9800
O41—H41	0.927 (18)	C17—H17C	0.9800
C11—C12	1.3977 (13)		
C11—O1—C1	118.38 (8)	O1—C11—C16	115.18 (9)
O1—C1—C2	106.92 (8)	C12—C11—C16	120.64 (9)
O1—C1—H1A	110.3	C11—C12—C13	118.96 (9)
C2—C1—H1A	110.3	C11—C12—H12	120.5
O1—C1—H1B	110.3	C13—C12—H12	120.5
C2—C1—H1B	110.3	O13—C13—C14	124.03 (9)
H1A—C1—H1B	108.6	O13—C13—C12	114.80 (8)
C1—C2—C3	110.58 (8)	C14—C13—C12	121.16 (9)
C1—C2—H2A	109.5	C13—C14—C15	118.56 (9)
C3—C2—H2A	109.5	C13—C14—H14	120.7
C1—C2—H2B	109.5	C15—C14—H14	120.7

C3—C2—H2B	109.5	C16—C15—C14	121.53 (9)
H2A—C2—H2B	108.1	C16—C15—H15	119.2
C4—C3—C2	113.88 (9)	C14—C15—H15	119.2
C4—C3—H3A	108.8	C15—C16—C11	119.14 (9)
C2—C3—H3A	108.8	C15—C16—H16	120.4
C4—C3—H3B	108.8	C11—C16—H16	120.4
C2—C3—H3B	108.8	C13—O13—C17	116.57 (8)
H3A—C3—H3B	107.7	O13—C17—H17A	109.5
O42—C4—O41	123.38 (9)	O13—C17—H17B	109.5
O42—C4—C3	124.16 (9)	H17A—C17—H17B	109.5
O41—C4—C3	112.46 (9)	O13—C17—H17C	109.5
C4—O41—H41	109.2 (11)	H17A—C17—H17C	109.5
O1—C11—C12	124.18 (9)	H17B—C17—H17C	109.5

C11—O1—C1—C2	−177.45 (8)	C11—C12—C13—C14	−0.36 (15)
O1—C1—C2—C3	−176.12 (8)	O13—C13—C14—C15	178.91 (9)
C1—C2—C3—C4	−174.52 (9)	C12—C13—C14—C15	−0.52 (15)
C2—C3—C4—O42	−5.13 (16)	C13—C14—C15—C16	0.51 (16)
C2—C3—C4—O41	174.73 (9)	C14—C15—C16—C11	0.38 (16)
C1—O1—C11—C12	−4.53 (15)	O1—C11—C16—C15	178.32 (9)
C1—O1—C11—C16	175.88 (9)	C12—C11—C16—C15	−1.28 (15)
O1—C11—C12—C13	−178.30 (9)	C14—C13—O13—C17	1.43 (15)
C16—C11—C12—C13	1.27 (15)	C12—C13—O13—C17	−179.11 (9)
C11—C12—C13—O13	−179.83 (9)		

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O41—H41···O42^{i}	0.927 (18)	1.804 (19)	2.7292 (11)	175.5 (16)
C17—H17*B*···O42^{ii}	0.98	2.48	3.2477 (14)	135

Symmetry codes: (i) −*x*, −*y*+3, −*z*+1; (ii) *x*+1, *y*−1, *z*.