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(1*R*,3*S*)-3-(1*H*-Benzo[*d*]imidazol-2-yl)-1,2,2-trimethylcyclopentane-1-carboxylic acid as a new anti-diabetic active pharmaceutical ingredient

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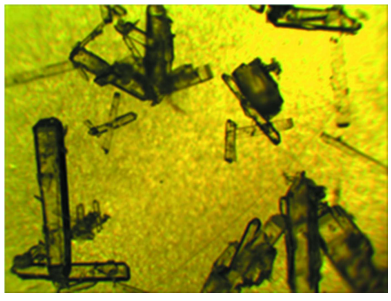
Supporting information: this article has supporting information at journals.iucr.org/e

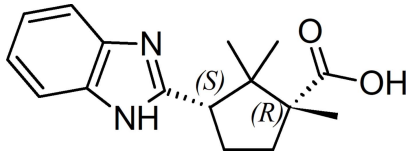
The chiral title compound, $C_{16}H_{20}N_2O_2$, which can be used for producing active pharmaceutical ingredients for treatment of type 2 pancreatic diabetes and other pathologies dependent on insulin resistance, was prepared from (1*R*,3*S*)-camphoric acid and *o*-phenylenediamine. It crystallized from an ethanol solution in the chiral monoclinic $P2_1$ space group. The five-membered ring adopts a twisted conformation with the methyl-substituted C atoms displaced by −0.273 (5) and 0.407 (5) Å from the mean plane through the other three atoms. In the crystal, molecules are linked by O—H···N hydrogen bonds, forming chains along the *a*-axis direction. Hirshfeld surface analysis and two-dimensional fingerprint plots were used to analyze the intermolecular contacts present in the crystal.

1. Chemical context

The incidence of diabetes has taken on the character of an epidemic in the world. According to the forecasts of the World Health Organization, the number of patients with diabetes will double and reach 300 million people by 2025 (Zimmet *et al.*, 2001). In this regard, developing and introducing new anti-diabetic drugs is of great importance.

A great number of camphoric acid as well as benzimidazole derivatives exhibit different types of biological activities (Merzlikin *et al.*, 2008; Ivachtchenko *et al.*, 2002, 2019; Kovalenko *et al.*, 1998).





Our research on the molecular design, construction and synthesis of new benzimidazole derivatives of 1,2,2,3-tetramethylcyclopentane-1-carboxylic acid has shown that (1*R*,3*S*)-3-(1*H*-benzo[*d*]imidazol-2-yl)-1,2,2-trimethylcyclopentane-1-carboxylic acid, **4**, exhibits pronounced antidiabetic activity and, in particular, antihyperglycemic effect, which reduces insulin resistance and restores the physiological function of pancreatic β-cells (Jain *et al.*, 2009; Chuev *et al.*, 2017).

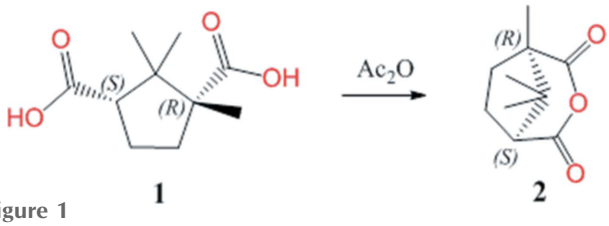


Figure 1
Synthesis of (1*R*,5*S*)-1,8,8-trimethyl-3-oxabicyclo[3.2.1]octane-2,4-dione, **2**.

Racemic and enantiomeric crystals are known to possess different activities, which is very important in the pharmaceutical industry. We have found that the disadvantage of the (±) and (-) forms of compound **4** described in the patent of Merzlikin *et al.* (2009) is their poor bioavailability as compared to the (+) form. To obtain (1*R*,3*S*)-3-(1*H*-benzo[*d*] imidazol-2-yl)-1,2,2-trimethylcyclopentane-1-carboxylic acid **4**, the enantiomerically pure (1*R*,3*S*)-camphoric acid **1** was used.

In the first stage, (1*R*,5*S*)-1,8,8-trimethyl-3-oxabicyclo[3.2.1]octane-2,4-dione [D-(+)-camphoric anhydride] **2** was obtained by refluxing a mixture of (1*R*,3*S*)-camphoric acid and acetic anhydride for 2 h (Dong *et al.*, 2016) (Fig. 1).

In the second stage, the synthesis of (1*R*,3*S*)-3-(1*H*-benzo[d]imidazol-2-yl)-1,2,2- trimethylcyclopentane-1-carboxylic acid **4** was carried out according to Fig. 2 *via* cyclocondensation of D-(+)-camphoric anhydride **2** with *o*-phenylenediamine **3** in a mixture of toluene and DMF (383 K) by refluxing for several hours (Fig. 2).

It should be noted that during the synthesis, the configuration of the chiral centers did not change and the structure of the title molecule was unambiguously confirmed by X-ray analysis.

2. Structural commentary

The asymmetric unit contains one molecule of the title compound **4** (Fig. 3). The bicyclic fragment is planar with a maximum deviation of 0.016 (6) Å (for atom C16). The saturated five-membered ring adopts a twisted conformation in which the deviations of atoms C11 and C12 from the mean-square plane through the remaining ring atoms are −0.273 (5) and 0.407 (5) Å, respectively. The cyclopentane ring is turned in relation to the N1—C1 endocyclic bond, the N1—C1—C8—C9 torsion angle being −30.0 (7)°. It can be assumed that the weak intramolecular C9—H9*B*···N1 (H···N = 2.53 Å, C—H···N = 108°) hydrogen bond additionally stabilizes such a location of the saturated ring. The methyl group on the C11 atom is located in the axial position [C9—C10—C11—C15 = 87.5 (6)°]. The carboxyl group has an equatorial orientation and is almost coplanar to the endocyclic C10–C11 bond [the C9—C10—C11—C16 and C10—C11—C16—O1 torsion angles are −150.8 (5) and 13.9 (8)°, respectively]. This position is stabilized by the formation of weak intramolecular C10—H10*A*···O1 and C15—H15*B*···O2 hydrogen bonds between the vicinal and geminal substituents (H···O = 2.43 and 2.42 Å, C—H···O = 103 and 100°, respectively). The presence of geminal substituents on neighboring atoms of the pentane ring leads to significant steric repulsion (the shortened intramolecular contacts are given in Table 1), which causes elongation of the C8—C12 bond to 1.571 (7) Å, compared with its mean value of 1.556 Å (Burgi *et al.*, 1994).

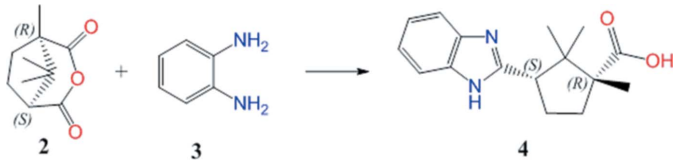


Figure 2
Synthesis of (1*R*,3*S*)-3-(1*H*-benzo[*d*]imidazol-2-yl)-1,2,2- trimethylcyclopentane-1-carboxylic acid, **4**.

Table 1
Intramolecular short contacts (Å) in compound **4** together with the sums of the respective van der Waals radii.

The van der Waals radii sum values (Zefirov *et al.*, 1997) are given in parentheses.

H8···H15*A*	2.26 (2.34)	H15*B*···H14*C*	2.32 (2.34)
H13*C*···C1	2.57 (2.87)	H13*B*···C16	2.54 (2.87)

Table 2
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···N1^{i}	0.82	1.82	2.631 (6)	170
N2—H2*A*···O1^{ii}	0.86	2.16	2.871 (6)	140
C14—H14*C*···C2^{iii}	0.96	2.81	3.439 (8)	124

3. Supramolecular features

In the crystal, molecules of **4** form layers parallel to the (100) plane as a result of the strong N2—H···O1 and O2—H···N1 and weak C14—H14*C*···C2(π) intermolecular hydrogen bonds (Table 2, Fig. 4*a*,b). The neighboring layers are not bound any specific interactions (Fig. 4*a*). It is interesting to note that the molecules are linked by hydrogen bonds that use the O—H···N heterosynthon instead of the carboxylic acid dimer homosynthon. Despite the presence of an aromatic ring in the molecule, no stacking interactions are observed in the crystal of **4**. Instead of π– π interactions, C—H···π interactions are formed (Table 2, Fig. 4*b*).

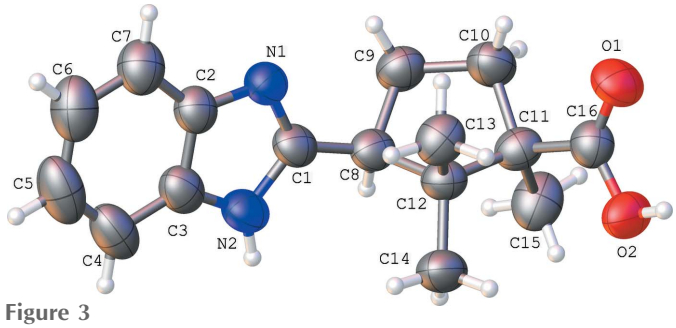


Figure 3
The molecular structure of the title compound **4** with the atom labeling. Displacement ellipsoids are drawn at the 50% probability level.

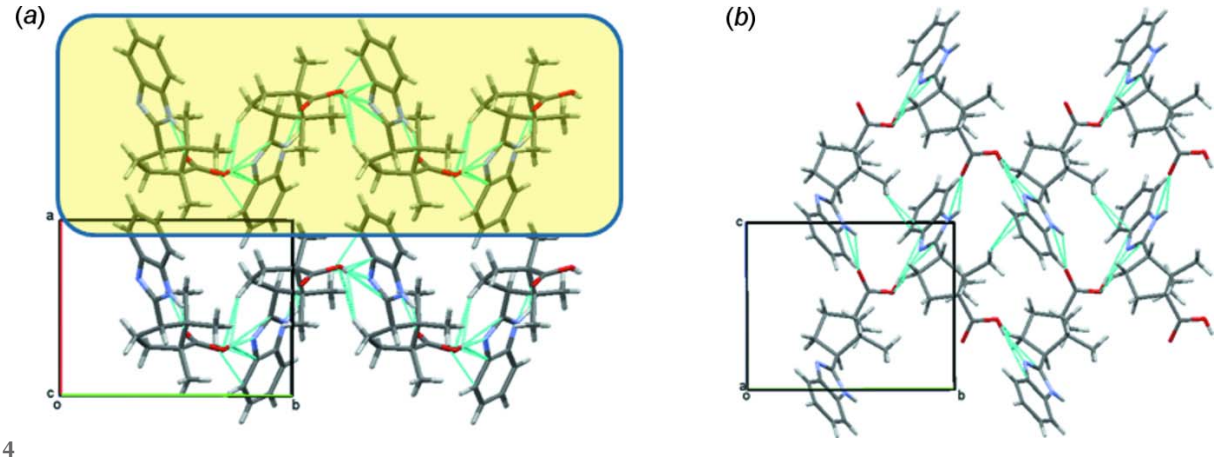


Figure 4
(*a*) View of the structure of compound **4** down the *b* axis and (*b*) hydrogen bonds within a layer in the crystal of **4**.

4. Hirshfeld surface analysis

Crystal Explorer 17.5 (Turner *et al.*, 2017) was used to analyze the interactions in the crystal and fingerprint plots mapped over d_{norm} (Figs. 5 and 6) were generated. The molecular Hirshfeld surfaces were obtained using a standard (high) surface resolution with the three-dimensional d_{norm} surfaces mapped over a fixed color scale of −0.716 (red) to 1.406 (blue) a.u. The red spots indicate regions of donor–acceptor interactions or short contacts. There are three red spots in the d_{norm} surface for **4** (Fig. 5), which correspond to the interactions listed in Table 2.

All of the intermolecular interactions of the title compound are shown in the two-dimensional fingerprint plot presented in Fig. 6*a*. The fingerprint plots indicate that the principal contributions are from H···H (61.7%; Fig. 6*b*), C···H/H···C (18.1%; Fig. 6*c*), O···H/H···O (13.5%; Fig. 6*d*) and N···H/H···N (6.6%; Fig. 6*e*) contacts. The H···H interactions appear in the middle of the plot scattered over a large area, while the C···H/H···C contacts are represented by the 'wings' of the plot. O···H/H···O interactions appear as inner spikes and the N···H/H···N contacts, corresponding to the O—H···N interaction, are represented by a pair of sharp outer spikes, which indicate they are the strongest interactions in the crystal of **4**.

5. Database survey

A search of the Cambridge Structural Database (CSD, Version 5.41, November 2019; Groom *et al.*, 2016) for the 1,2,2-trimethylcyclopentane-1-carboxylic acid skeleton yielded 27 hits. Only one structure involves a benzothiazol-2′-yl ring in position 3, *viz.* (1*R*,3*S*)-(+)-*cis*-1,3-bis(benzothiazol-2′-yl)-1,2,2-trimethylcyclopentane (CSD refcode XUMXIM; Gilbert *et al.*, 2002). The cyclopentane ring has the twist conformation with the atoms C1 and C4 displaced by 0.48 (1) and −0.26 (2) Å from the mean plane through the other three atoms [*cf.* 0.407 (5) Å and −0.273 (5) Å in the title compound].

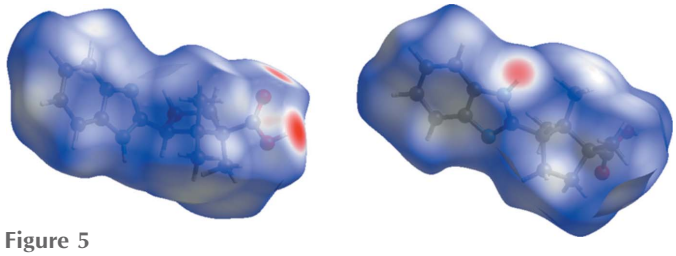


Figure 5
Two orientations of the Hirshfeld surface for the title compound mapped over d_{norm}.

6. Synthesis and crystallization

(1*R*,3*S*)-3-(1*H*-Benzo[*d*]imidazol-2-yl)-1,2,2-trimethylcyclopentane-1-carboxylic acid, **4**

In a glass reactor equipped with a Dean–Stark receiver, D-(+)-camphoric anhydride **2** (2.20 kg, 12.1 mol), *o*-phenylenediamine **3** (1.31 kg, 12.1 mol), toluene (11.46 L) and dimethylformamide (0.91 L) were charged. Under stirring, the reaction mixture was heated to boiling (383 K). The mixture was refluxed and the released water was collected in the Dean–Stark receiver. When the removal of water had finished, the reaction mixture was cooled to room temperature. The

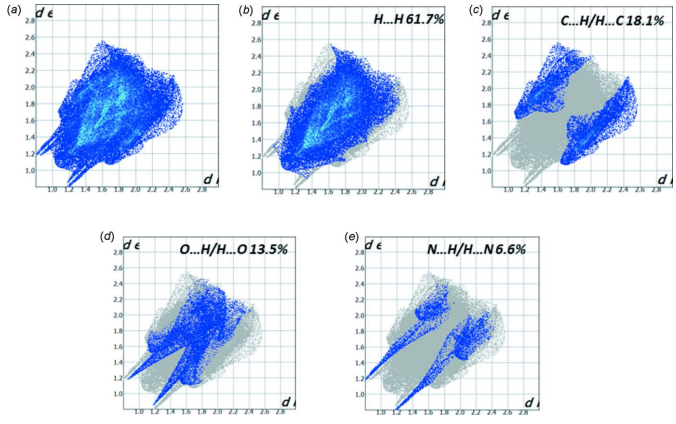


Figure 6
(*a*) The two-dimensional fingerprint plot for compound **4**, and those delineated into (*b*) H···H (61.7%), (*c*) C···H/H···C (18.1%), (*d*) O···H/H···O (13.5%) and (*e*) N···H/H···N (6.6%) contacts.

precipitate that formed was filtered *in vacuo* using a Nutsche filter. The precipitate was thoroughly squeezed, washed twice with toluene (1.4 L) and re-squeezed. Then the precipitate was washed on the filter with 70% water–ethanol (3.7 L), heated to a temperature of 348±5 K. Finally, the precipitate of the product **4** was thoroughly squeezed and dried at 343 K for 4 h, yielding 2.41 kg (73.2%) of a white crystal-like powder that is practically insoluble in water, soluble in 96% alcohol, m.p. 527–528 K. UV (ethanol) λmax (ε): 204 nm (48960), 245 nm (6800), 275 nm (9160), 281 nm (9320); IR (KBr): ν (cm^{-1}) 3450 (O—H), 3286 (N—H), 2970, 2935, 2887 (C—H), 1673 (C═O), 1529, 1456, 1436, 1373, 1279, 1358, 1167, 1124, 1057, 740; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.22 (*s.br*, 1H, OH), 12.10 (*s.br*, 1H, NH), 7.52 (*s.br*, 1H, H-4, H-7), 7.44 (*s.br*, 1H, H-4, H-7), 7.10 (*t*, *J* = 4.5 Hz, 2H, H-5, H-6), 3.41–3.31 (*m*, 1H, CH), 2.64–2.54 (*m*, 1H,CH), 2.43–2.33 (*m*, 1H, CH), 2.05–1.95 (*m*, 1H, CH), 1.55–1.45 (*m*, 1H, CH), 1.25 (*s*, 3H, CH3), 1.14 (*s*, 3H, CH_3), 0.61 (*s*, 3H, CH_3); LC/MS *m*/*z* (%): 273.2 [*M*H]+ (100); found, %: C 70.88; H 7.83; N 10.55. $C_{16}H_{20}N_2O_2$. Calculated, %: C 70.56; H 7.40; N 10.29.

Further crystallization by slow evaporation of an ethanol solution was carried out to provide single block-like colorless crystals (Fig. 7) suitable for X-ray diffraction analysis.

7. Refinement

Crystal data, data collection and structure refinement details are summarized in Table 3. H atoms were included in calculated positions and treated as riding on their parent C atom: C—H = 0.82–0.98 Å with U_{iso}(H) = 1.5U_{eq}(C-methyl and O-hydroxyl) and 1.2U_{eq}(C) for other H atoms. The Flack parameter cannot be determined reliably, because there is no X-ray anomalous scattering because of the absence of heavy atoms in the molecule.

References

Burgi, H.-B. & Dunitz, J. D. (1994). *Structure correlation*, Vol. 2, pp. 741-784. Weinheim: VCH.

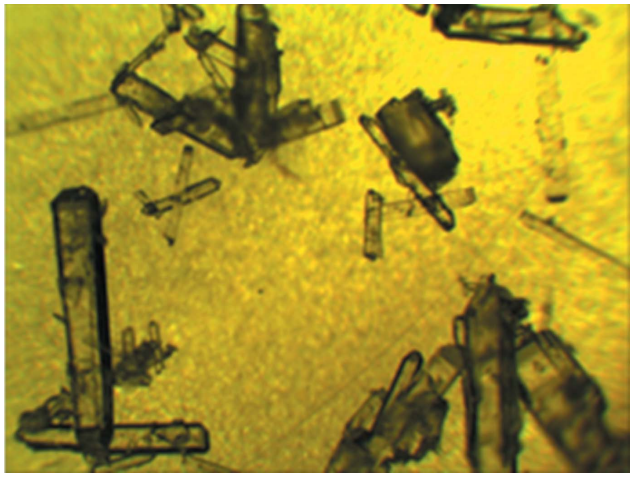


Figure 7
Crystals of the title compound **4**.

Table 3
Experimental details.

Crystal data	
Chemical formula	$C_{16}H_{20}N_2O_2$
M_r	272.34
Crystal system, space group	Monoclinic, $P2_1$
Temperature (K)	293
a, *b*, *c* (Å)	7.9805 (7), 10.8671 (8), 8.4912 (7)
β (°)	94.056 (7)
V (Å^3)	734.55 (10)
Z	2
Radiation type	Mo *Kα*
μ (mm^{-1})	0.08
Crystal size (mm)	0.3 × 0.2 × 0.1
Data collection	
Diffractometer	Rigaku Oxford Diffraction Xcalibur, Sapphire3
Absorption correction	Multi-scan (*CrysAlis PRO*; Rigaku OD, 2018)
T_{min}, T_{max}	0.182, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	4859, 2455, 1731
R_{int}	0.058
(sin θ/λ)$_{max}$ (Å^{-1})	0.594
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, *S*	0.065, 0.180, 1.04
No. of reflections	2455
No. of parameters	185
No. of restraints	1
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.15, −0.19
Absolute structure	Flack *x* determined using 459 quotients $[(I^+)-(I^-)]/[(I^+)+(I^-)]$ (Parsons et al., 2013)
Absolute structure parameter	−1.8 (10)

Computer programs: *CrysAlis PRO* (Rigaku OD, 2018), *SHELXT* (Sheldrick, 2015*a*), *SHELXL* (Sheldrick, 2015*b*), *OLEX2* (Dolomanov *et al.*, 2009).

Chuev, V. P., Buzov, A. A., Kovalenko, S. N., Merzlikin, S. I. & Shtrygol, S. Yu. (2017). Pharmaceutical antidiabetic composition based on (+)-*cis*-3-(*1H*-benzimidazol-2-yl)-1,2,2-trimethylcyclopentane carboxylic acid. Patent RU 2624872, C1, 07 July 2017.

Dolomanov, O. V., Bourhis, L. J., Gildea, R. J., Howard, J. A. K. & Puschmann, H. (2009). *J. Appl. Cryst.* **42**, 339–341.

Dong, Y., Li, Q., Wang, J., Lu, L., Wang, Y., Bao, L., Wang, Z. & Zhang, Y. (2016). *Mendeleev Commun.* **26**, 166–168.

Gilbert, J. G., Addison, A. W., Palaniandavar, M. & Butcher, R. J. (2002). *J. Heterocycl. Chem.* **39**, 399–404.

Groom, C. R., Bruno, I. J., Lightfoot, M. P. & Ward, S. C. (2016). *Acta Cryst.* B**72**, 171–179.

Ivachtchenko, A., Kovalenko, S., Parkhomenko, O. & Chernykh, V. (2002). *Heterocycl. Commun.* **8**, 329–330.

Ivachtchenko, A. V., Mitkin, O. D., Kravchenko, D. V., Kovalenko, S. M., Shishkina, S. V., Bunyatyan, N. D., Konovalova, I. S., Ivanov, V. V., Konovalova, O. D. & Langer, T. (2019). *Crystals*, **9**, 644–660.

Jain, M., Merzlikin, S. I. & Merzlikin, D. S. (2009). Benzimidazole derivatives and the use thereof, PCT Int. Appl., WO 2009/093990, 30 July 2009.

Kovalenko, S. N., Vasil'ev, M. V., Sorokina, I. V., Chernykh, V. P., Turov, A. V. & Rudnev, S. A. (1998). *Chem. Heterocycl. Compd.* **34**, 1412–1415.

Merzlikin, S. I. & Jain, M. (2009). Method for the treatment of metabolic syndrome X, PCT Int. Appl., WO 2009005483, A1, 08 January 2009.

Merzlikin, S. I. & Podgayny, D. G. (2008). *Zh. Org. Farmats. Khim.* **6**, 67–71.

Parsons, S., Flack, H. D. & Wagner, T. (2013). *Acta Cryst.* B**69**, 249–259.

Rigaku OD (2018). *CrysAlis PRO*. Rigaku Oxford Diffraction, Yarnton, England.
Sheldrick, G. M. (2015*a*). *Acta Cryst.* A**71**, 3–8.
Sheldrick, G. M. (2015*b*). *Acta Cryst.* A**71**, 3–8.
Turner, M. J., McKinnon, J. J., Wolff, S. K., Grimwood, D. J., Spackman, P. R., Jayatilaka, D. & Spackman, M. A. (2017). *CrystalExplorer17*. University of Western Australia. http://hirshfeldsurface.net.
Zefirov, Yu. V. (1997). *Kristallographiya*, **42**, 936-958.
Zimmet, P., Alberti, K. G. M. M. & Shaw, J. (2001). *Nature*, **414**, 782–787.

supporting information

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(1*R*,3*S*)-3-(1*H*-Benzo[*d*]imidazol-2-yl)-1,2,2-trimethylcyclopentane-1-carboxylic acid as a new anti-diabetic active pharmaceutical ingredient

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Computing details

Data collection: *CrysAlis PRO* (Rigaku OD, 2018); cell refinement: *CrysAlis PRO* (Rigaku OD, 2018); data reduction: *CrysAlis PRO* (Rigaku OD, 2018); program(s) used to solve structure: ShelXT (Sheldrick, 2015a); program(s) used to refine structure: *SHELXL* (Sheldrick, 2015b); molecular graphics: *OLEX2* (Dolomanov *et al.*, 2009); software used to prepare material for publication: *OLEX2* (Dolomanov *et al.*, 2009).

(1*R*,3*S*)-3-(1*H*-Benzo[*d*]imidazol-2-yl)-1,2,2-trimethylcyclopentane-1-carboxylic acid

Crystal data

$C_{16}H_{20}N_2O_2$
$M_r = 272.34$
Monoclinic, $P2_1$
$a = 7.9805$ (7) Å
$b = 10.8671$ (8) Å
$c = 8.4912$ (7) Å
$\beta = 94.056$ (7)°
$V = 734.55$ (10) Å^3
$Z = 2$
$F(000) = 292$
$D_x = 1.231$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 748 reflections
$\theta = 3.6$–20.3°
$\mu = 0.08$ mm^{-1}
$T = 293$ K
Plate, colourless
0.3 × 0.2 × 0.1 mm

Data collection

Rigaku Oxford Diffraction Xcalibur, Sapphire3 diffractometer
Radiation source: fine-focus sealed X-ray tube, Enhance (Mo) X-ray Source
Graphite monochromator
Detector resolution: 16.1827 pixels mm^{-1}
ω scans
Absorption correction: multi-scan (CrysAlisPro; Rigaku OD, 2018)
$T_{min} = 0.182$, $T_{max} = 1.000$
4859 measured reflections
2455 independent reflections
1731 reflections with $I > 2\sigma(I)$
$R_{int} = 0.058$
$\theta_{max} = 25.0°$, $\theta_{min} = 3.1°$
$h = -9\rightarrow8$
$k = -12\rightarrow11$
$l = -9\rightarrow10$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.065$
$wR(F^2) = 0.180$
$S = 1.04$
2455 reflections
185 parameters
1 restraint
Primary atom site location: dual
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0794P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.15$ e Å^{-3}

$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Absolute structure: Flack *x* determined using 459 quotients [(I^+)-(I^-)]/[(I^+)+(I^-)] (Parsons et al., 2013)
Absolute structure parameter: −1.8 (10)

Special details

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

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å^2)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.3639 (6)	0.5406 (4)	0.7106 (5)	0.0801 (12)
O2	0.2632 (6)	0.7051 (3)	0.5806 (5)	0.0755 (12)
H2	0.289977	0.738749	0.665107	0.113*
N1	0.6692 (5)	0.3376 (4)	0.1635 (5)	0.0593 (11)
N2	0.5767 (6)	0.4717 (4)	−0.0168 (5)	0.0673 (13)
H2A	0.510294	0.522765	−0.067258	0.081*
C1	0.5454 (7)	0.4112 (5)	0.1190 (6)	0.0584 (13)
C2	0.7894 (7)	0.3527 (5)	0.0550 (7)	0.0604 (14)
C3	0.7336 (8)	0.4365 (5)	−0.0588 (7)	0.0654 (14)
C4	0.8269 (10)	0.4678 (6)	−0.1848 (8)	0.0831 (19)
H4	0.786965	0.523797	−0.261269	0.100*
C5	0.9807 (11)	0.4124 (8)	−0.1914 (9)	0.096 (2)
H5	1.047951	0.432369	−0.272757	0.115*
C6	1.0379 (9)	0.3261 (7)	−0.0773 (9)	0.090 (2)
H6	1.142413	0.289532	−0.084821	0.108*
C7	0.9429 (8)	0.2942 (7)	0.0460 (8)	0.0759 (17)
H7	0.980342	0.235604	0.120267	0.091*
C8	0.3928 (7)	0.4359 (5)	0.2036 (6)	0.0580 (13)
H8	0.300846	0.455808	0.125078	0.070*
C9	0.3372 (7)	0.3271 (5)	0.3025 (7)	0.0679 (15)
H9A	0.245558	0.283181	0.246369	0.082*
H9B	0.429868	0.270412	0.324145	0.082*
C10	0.2806 (9)	0.3803 (5)	0.4556 (8)	0.0716 (16)
H10A	0.360495	0.359711	0.543071	0.086*
H10B	0.171604	0.347548	0.477382	0.086*
C11	0.2707 (6)	0.5205 (5)	0.4334 (7)	0.0597 (14)
C12	0.4144 (6)	0.5465 (5)	0.3225 (6)	0.0575 (12)
C13	0.5865 (7)	0.5408 (6)	0.4150 (7)	0.0707 (15)
H13A	0.597970	0.463626	0.469595	0.106*
H13B	0.595652	0.606974	0.490044	0.106*
H13C	0.673547	0.548409	0.343119	0.106*
C14	0.3983 (9)	0.6692 (5)	0.2366 (8)	0.0764 (17)
H14A	0.491174	0.679383	0.171902	0.115*
H14B	0.398423	0.734744	0.312382	0.115*
H14C	0.295039	0.670837	0.171336	0.115*

C15	0.0964 (7)	0.5560 (7)	0.3588 (8)	0.0811 (18)
H15A	0.079109	0.518462	0.256632	0.122*
H15B	0.089416	0.643848	0.348102	0.122*
H15C	0.011624	0.527941	0.425166	0.122*
C16	0.3042 (6)	0.5877 (5)	0.5895 (7)	0.0612 (15)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.100 (3)	0.086 (3)	0.053 (2)	0.005 (2)	−0.011 (2)	0.006 (2)
O2	0.103 (3)	0.063 (2)	0.058 (3)	0.012 (2)	−0.014 (2)	−0.0111 (18)
N1	0.067 (3)	0.060 (3)	0.051 (3)	0.004 (2)	0.001 (2)	0.001 (2)
N2	0.083 (3)	0.067 (3)	0.050 (3)	0.003 (2)	−0.004 (2)	0.006 (2)
C1	0.070 (3)	0.060 (3)	0.043 (3)	−0.001 (3)	−0.006 (2)	−0.001 (2)
C2	0.063 (3)	0.066 (3)	0.051 (3)	−0.002 (3)	0.000 (2)	−0.006 (3)
C3	0.078 (4)	0.063 (3)	0.055 (3)	−0.010 (3)	0.004 (3)	−0.005 (3)
C4	0.104 (5)	0.088 (4)	0.059 (4)	−0.026 (4)	0.016 (3)	−0.001 (3)
C5	0.098 (5)	0.119 (6)	0.073 (5)	−0.039 (5)	0.027 (4)	−0.019 (4)
C6	0.075 (4)	0.113 (6)	0.083 (5)	−0.011 (4)	0.012 (4)	−0.026 (5)
C7	0.071 (4)	0.090 (4)	0.066 (4)	0.000 (3)	0.001 (3)	−0.011 (3)
C8	0.068 (3)	0.056 (3)	0.049 (3)	0.002 (2)	−0.007 (2)	−0.002 (2)
C9	0.074 (4)	0.055 (3)	0.074 (4)	−0.001 (3)	0.003 (3)	−0.001 (3)
C10	0.088 (4)	0.061 (3)	0.066 (4)	−0.005 (3)	0.008 (3)	0.005 (3)
C11	0.056 (3)	0.055 (3)	0.067 (4)	0.003 (2)	−0.004 (2)	0.000 (3)
C12	0.061 (3)	0.052 (3)	0.058 (3)	0.001 (2)	−0.002 (2)	0.003 (2)
C13	0.064 (3)	0.071 (3)	0.075 (4)	0.000 (3)	−0.005 (3)	−0.010 (3)
C14	0.102 (5)	0.058 (3)	0.069 (4)	0.007 (3)	0.003 (3)	0.007 (3)
C15	0.063 (3)	0.097 (4)	0.081 (4)	0.005 (4)	−0.012 (3)	−0.019 (4)
C16	0.057 (3)	0.068 (4)	0.058 (4)	0.001 (3)	0.001 (3)	−0.005 (3)

Geometric parameters (Å, º)

O1—C16	1.216 (6)	C5—C6	1.401 (11)
O2—C16	1.319 (6)	C6—C7	1.380 (9)
N1—C1	1.307 (7)	C8—C9	1.533 (8)
N1—C2	1.386 (7)	C8—C12	1.571 (7)
N2—C1	1.366 (7)	C9—C10	1.520 (9)
N2—C3	1.381 (8)	C10—C11	1.536 (8)
C1—C8	1.481 (8)	C11—C12	1.560 (8)
C2—C3	1.378 (8)	C11—C15	1.537 (7)
C2—C7	1.387 (8)	C11—C16	1.520 (8)
C3—C4	1.388 (8)	C12—C13	1.534 (7)
C4—C5	1.372 (10)	C12—C14	1.521 (8)
C1—N1—C2	106.3 (5)	C10—C9—C8	106.8 (5)
C1—N2—C3	107.9 (5)	C9—C10—C11	106.7 (5)
N1—C1—N2	111.0 (5)	C10—C11—C12	102.7 (4)
N1—C1—C8	127.0 (5)	C10—C11—C15	109.7 (5)

N2—C1—C8	121.9 (5)	C15—C11—C12	112.9 (5)
N1—C2—C7	129.6 (6)	C16—C11—C10	111.4 (5)
C3—C2—N1	109.9 (5)	C16—C11—C12	110.4 (4)
C3—C2—C7	120.5 (6)	C16—C11—C15	109.7 (4)
N2—C3—C4	132.6 (6)	C11—C12—C8	101.4 (4)
C2—C3—N2	104.9 (5)	C13—C12—C8	110.6 (4)
C2—C3—C4	122.5 (6)	C13—C12—C11	110.7 (4)
C5—C4—C3	117.0 (7)	C14—C12—C8	111.1 (4)
C4—C5—C6	120.9 (6)	C14—C12—C11	114.0 (5)
C7—C6—C5	121.6 (7)	C14—C12—C13	108.8 (5)
C6—C7—C2	117.5 (7)	O1—C16—O2	122.4 (5)
C1—C8—C9	113.9 (5)	O1—C16—C11	124.8 (5)
C1—C8—C12	113.2 (4)	O2—C16—C11	112.8 (5)
C9—C8—C12	105.1 (4)		

N1—C1—C8—C9	−30.0 (7)	C7—C2—C3—N2	177.5 (5)
N1—C1—C8—C12	90.0 (6)	C7—C2—C3—C4	−1.0 (8)
N1—C2—C3—N2	−0.1 (6)	C8—C9—C10—C11	10.7 (7)
N1—C2—C3—C4	−178.6 (5)	C9—C8—C12—C11	−35.1 (5)
N1—C2—C7—C6	179.1 (5)	C9—C8—C12—C13	82.4 (6)
N2—C1—C8—C9	153.8 (5)	C9—C8—C12—C14	−156.6 (5)
N2—C1—C8—C12	−86.2 (6)	C9—C10—C11—C12	−32.7 (6)
N2—C3—C4—C5	−178.8 (6)	C9—C10—C11—C15	87.5 (6)
C1—N1—C2—C3	−1.0 (6)	C9—C10—C11—C16	−150.8 (5)
C1—N1—C2—C7	−178.3 (6)	C10—C11—C12—C8	41.1 (5)
C1—N2—C3—C2	1.1 (6)	C10—C11—C12—C13	−76.3 (5)
C1—N2—C3—C4	179.4 (6)	C10—C11—C12—C14	160.6 (5)
C1—C8—C9—C10	140.0 (5)	C10—C11—C16—O1	13.9 (8)
C1—C8—C12—C11	−160.0 (4)	C10—C11—C16—O2	−166.9 (5)
C1—C8—C12—C13	−42.5 (6)	C12—C8—C9—C10	15.6 (6)
C1—C8—C12—C14	78.5 (6)	C12—C11—C16—O1	−99.5 (6)
C2—N1—C1—N2	1.7 (6)	C12—C11—C16—O2	79.7 (5)
C2—N1—C1—C8	−174.8 (5)	C15—C11—C12—C8	−76.9 (5)
C2—C3—C4—C5	−0.8 (9)	C15—C11—C12—C13	165.7 (5)
C3—N2—C1—N1	−1.8 (6)	C15—C11—C12—C14	42.6 (6)
C3—N2—C1—C8	174.9 (5)	C15—C11—C16—O1	135.5 (6)
C3—C2—C7—C6	2.0 (8)	C15—C11—C16—O2	−45.3 (7)
C3—C4—C5—C6	1.4 (10)	C16—C11—C12—C8	160.0 (4)
C4—C5—C6—C7	−0.4 (10)	C16—C11—C12—C13	42.6 (6)
C5—C6—C7—C2	−1.3 (9)	C16—C11—C12—C14	−80.5 (5)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···N1^{i}	0.82	1.82	2.631 (6)	170

N2—H2*A*···O1^{ii}	0.86	2.16	2.871 (6)	140
C14—H14*C*···C2^{iii}	0.96	2.81	3.439 (8)	124

Symmetry codes: (i) −*x*+1, *y*+1/2, −*z*+1; (ii) *x*, *y*, *z*−1; (iii) −*x*+1, *y*+1/2, −*z*.