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Methyl 4-methyl-2-oxo-3,4-dihydrodibenzo[*b*,*d*]-furan-4a(2*H*)-carboxylate

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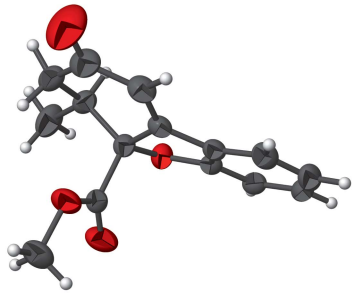
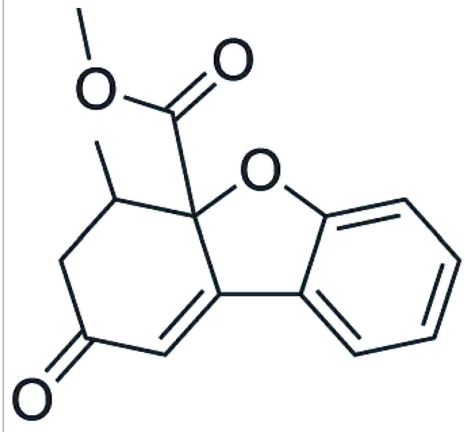
The title compound, $C_{15}H_{14}O_4$, has structural similarities to the alkaloid galanthamine, used in the treatment of Alzheimer's disease. The structure consists of a fused three-ring system comprising benzene and cyclohexenone fused to a central furan ring. The furan ring exhibits an envelope conformation with the carboxylate-substituted C atom as the flap, deviating by 0.352 (3) Å from the mean plane of other four furan-ring atoms. The cyclohexenone ring also exhibits an envelope conformation, with the methyl-substituted C atom as the flap. The methyl and carboxylate groups are on opposite side of the plane of the other five atoms of the cyclohexenone ring. In the crystal, other than van der Waals contacts, there are weak intermolecular C—H···O interactions present linking the molecules to form a one-dimensional zigzag chain along the *b*-axis direction.

3D view



Chemical scheme



Structure description

The title compound has a similar structural framework to that of galanthamine, an alkaloid used in the treatment of Alzheimer's disease, originally extracted from the Caucasian Snowdrop (*Galanthus woronowii*). It can be readily synthesized by Robinson annulation of the Michael adduct of methyl 3-oxo-2,3-dihydrobenzofuran-2-carboxylate and (*E*)-pent-3-en-2-one. For background information and synthesis details, see: Bergonzini & Melchiorre (2012); Marco-Contelles *et al.* (2006); Yamanaka *et al.* (2012).

The molecular structure of the title compound (Fig. 1) has a fused three-ring system comprising benzene and cyclohexenone fused to a central furan. The furan ring exhibits an envelope conformation, with atom C5 as the flap, which deviates by 0.352 (3) Å from the mean plane of other four atoms. This mean plane makes a dihedral angle of 22.80 (3)° with the plane of atoms O2/C5/C6. The cyclohexenone ring also exhibits an envelope conformation, in which atom C4 acts as the flap, deviating from the mean plane of other five atoms of the cyclohexenone ring by 0.597 (2) Å, and this mean plane makes a dihedral angle of 42.64 (3)° with the plane of atoms C3/C4/C5. Atoms C13 of the methyl

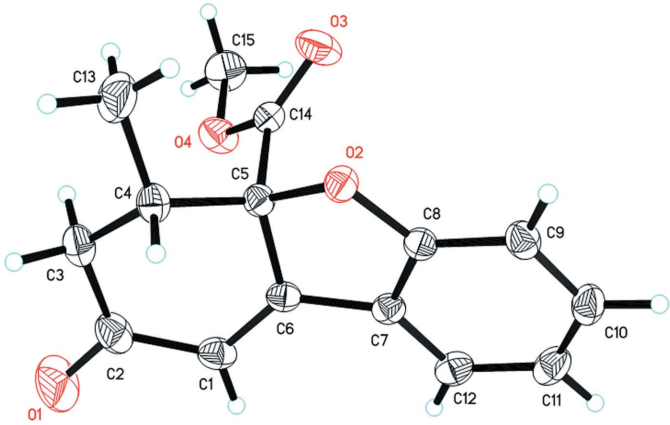


Figure 1
The structure of the title compound. Displacement ellipsoids are drawn at the 50% probability level.

group and C14 of the carboxylate group are displaced from the mean plane of the other five atoms by 0.465 (2) and −1.483 (2) Å, respectively.

In the crystal, there are weak intermolecular C—H···O interactions present linking the molecules to form a one-dimensional zigzag chain along the *b*-axis direction (Table 1 and Fig. 2).

Synthesis and crystallization

$Cu(OTf)_2$ (0.02 mmol, 7.2 mg, 10 mol%) and the ligand bis{2-[(*4S*,*5S*)-4,5-diphenyl-4,5-dihydrooxazol-2-yl]phenyl}amine (10 mol%) were dissolved in toluene (4 ml) at ambient temperature. Methyl 3-oxo-2,3-dihydrobenzofuran-2-carboxylate (0.2 mmol, 38.4 mg) was added and the mixture stirred for 10 minutes, followed by the addition of (*E*)-pent-3-en-2-one (0.22 mmol, 18.5 mg, 1.1 equiv.). The resulting mixture was stirred for 24 h at ambient temperature. After completion of the reaction, the solvent was evaporated under reduced pressure. The resulting crude mixture was purified by flash column chromatography (ethyl acetate/hexane) on silica gel, and the Michael adduct methyl 3-oxo-2-(4-oxopentan-2-yl)-2,3-dihydrobenzofuran-2-carboxylate was obtained. Then, pyrrolidine (0.02 mol, 1.4 mg, 10 mol%) and benzoic acid (0.02 mmol, 2.4 mg, 10 mol%) were dissolved in DCM (4 ml), followed by the addition of methyl 3-oxo-2-(4-oxopentan-2-yl)-2,3-dihydrobenzofuran-2-carboxylate (0.2 mmol, 55.3 mg). The resulting mixture was stirred for a further 24 h at ambient temperature. After completion of the reaction, the solvent was evaporated under reduced pressure. The resulting crude mixture was purified by flash column chromatography (ethyl acetate/hexane) on silica gel, giving

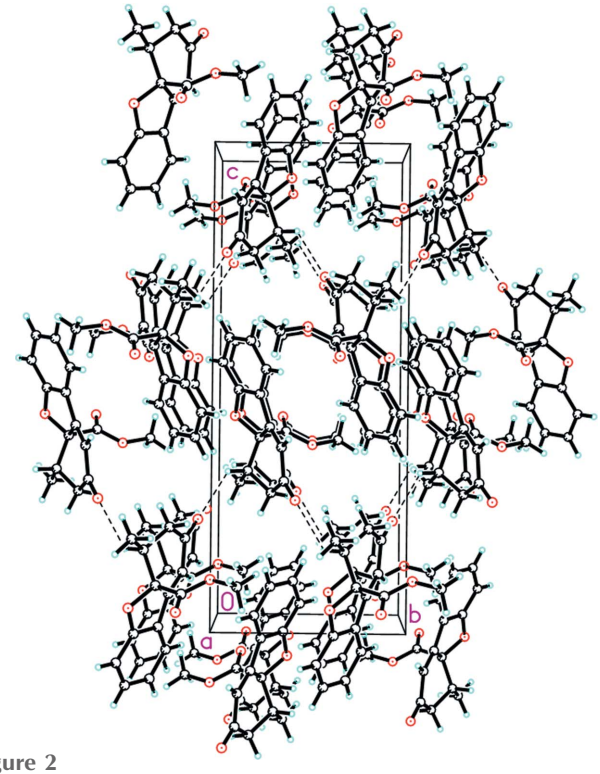


Figure 2
The crystal packing of the title compound viewed down the *a* axis. Hydrogen bonds are shown as dashed lines.

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C15—H15*C*···O3^{i}	0.96	2.65	3.565 (3)	159
C9—H9···O2^{ii}	0.93	2.62	3.455 (2)	149
C1—H1···O3^{iii}	0.93	2.59	3.453 (2)	154

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

Table 2
Experimental details.

Crystal data	
Chemical formula	$C_{15}H_{14}O_4$
M_r	258.26
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	293
a, *b*, *c* (Å)	7.5629 (19), 8.205 (2), 20.587 (5)
β (°)	91.147 (5)
V (Å^3)	1277.3 (6)
Z	4
Radiation type	Mo $K\alpha$
μ (mm^{-1})	0.10
Crystal size (mm)	0.20 × 0.16 × 0.13
Data collection	
Diffractometer	Bruker SMART CCD area detector
Absorption correction	Multi-scan (*SADABS*; Krause *et al.*, 2015)
T_{min}, T_{max}	0.636, 0.746
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	7307, 2514, 2060
R_{int}	0.029
(sin $\theta/\lambda)_{max}$ (Å^{-1})	0.617
Refinement	
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.043, 0.116, 1.04
No. of reflections	2514
No. of parameters	174
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.23, −0.22

Computer programs: *APEX3* and *SAINT* (Bruker, 2013), *SHELXTL* and *SHELXS2013* (Sheldrick, 2008) and *SHELXL2013* (Sheldrick, 2015).

the title compound. Single crystals were obtained by slow evaporation of a dichloromethane solution.

Refinement

Crystal data, data collection and structure refinement details are summarized in Table 2.

Funding information

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full crystallographic data

IUCrData (2017). **2**, x170395 [https://doi.org/10.1107/S2414314617003959]

Methyl 4-methyl-2-oxo-3,4-dihydrodibenzo[*b*,*d*]furan-4a(2*H*)-carboxylate

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Crystal data

$C_{15}H_{14}O_4$
M_r = 258.26
Monoclinic, $P2_1/c$
a = 7.5629 (19) Å
b = 8.205 (2) Å
c = 20.587 (5) Å
β = 91.147 (5)°
V = 1277.3 (6) Å^3
Z = 4
$F(000)$ = 544
D_x = 1.343 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å
Cell parameters from 2301 reflections
θ = 5.4–51.1°
μ = 0.10 mm^{-1}
T = 293 K
Prismatic, yellow
0.20 × 0.16 × 0.13 mm

Data collection

Bruker SMART CCD area detector diffractometer
φ and ω scans
Absorption correction: multi-scan (SADABS; Krause *et al.*, 2015)
T_{min} = 0.636, T_{max} = 0.746
7307 measured reflections
2514 independent reflections
2060 reflections with $I > 2\sigma(I)$
R_{int} = 0.029
θ_{max} = 26.0°, θ_{min} = 2.0°
h = −8→9
k = −10→6
l = −25→21

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.043
$wR(F^2)$ = 0.116
S = 1.04
2514 reflections
174 parameters
0 restraints
Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0544P)^2 + 0.3361P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.23 e Å^{-3}
$\Delta\rho_{min}$ = −0.22 e Å^{-3}

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 (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	−0.0877 (2)	0.9292 (3)	0.22792 (8)	0.0940 (6)

O2	0.32975 (13)	0.60786 (13)	0.06049 (5)	0.0365 (3)
O3	0.55387 (16)	0.85572 (17)	0.06209 (7)	0.0600 (4)
O4	0.37667 (15)	1.01442 (15)	0.12004 (6)	0.0501 (3)
C1	−0.0163 (2)	0.8566 (2)	0.12190 (8)	0.0432 (4)
H1	−0.1242	0.8931	0.1051	0.052*
C2	0.0203 (2)	0.8695 (2)	0.19168 (9)	0.0517 (5)
C3	0.1928 (2)	0.8018 (2)	0.21819 (8)	0.0467 (4)
H3A	0.1706	0.7506	0.2597	0.056*
H3B	0.2732	0.8920	0.2262	0.056*
C4	0.2851 (2)	0.6774 (2)	0.17467 (7)	0.0397 (4)
H4	0.2137	0.5778	0.1751	0.048*
C5	0.28479 (19)	0.73901 (18)	0.10436 (7)	0.0327 (3)
C6	0.10214 (18)	0.79335 (17)	0.08177 (7)	0.0331 (3)
C7	0.08941 (19)	0.74126 (18)	0.01420 (7)	0.0336 (3)
C8	0.22453 (19)	0.62851 (18)	0.00562 (7)	0.0326 (3)
C9	0.2450 (2)	0.5433 (2)	−0.05172 (7)	0.0399 (4)
H9	0.3332	0.4655	−0.0563	0.048*
C10	0.1270 (2)	0.5802 (2)	−0.10195 (7)	0.0456 (4)
H10	0.1378	0.5268	−0.1415	0.055*
C11	−0.0068 (2)	0.6944 (2)	−0.09503 (8)	0.0486 (4)
H11	−0.0823	0.7174	−0.1301	0.058*
C12	−0.0291 (2)	0.7744 (2)	−0.03651 (8)	0.0433 (4)
H12	−0.1210	0.8483	−0.0313	0.052*
C13	0.4676 (3)	0.6326 (3)	0.20074 (9)	0.0636 (6)
H13A	0.5213	0.5560	0.1719	0.095*
H13B	0.4577	0.5844	0.2430	0.095*
H13C	0.5395	0.7288	0.2038	0.095*
C14	0.42267 (19)	0.87457 (19)	0.09257 (7)	0.0359 (4)
C15	0.4953 (3)	1.1509 (2)	0.11045 (10)	0.0623 (6)
H15A	0.6117	1.1228	0.1262	0.093*
H15B	0.4532	1.2440	0.1338	0.093*
H15C	0.4996	1.1764	0.0650	0.093*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0928 (12)	0.1214 (15)	0.0686 (10)	0.0423 (11)	0.0225 (9)	−0.0275 (10)
O2	0.0374 (6)	0.0366 (6)	0.0355 (6)	0.0068 (5)	−0.0021 (4)	−0.0046 (4)
O3	0.0409 (7)	0.0634 (9)	0.0763 (9)	−0.0093 (6)	0.0183 (6)	−0.0091 (7)
O4	0.0501 (7)	0.0399 (7)	0.0608 (7)	−0.0128 (5)	0.0125 (6)	−0.0079 (6)
C1	0.0340 (8)	0.0410 (9)	0.0548 (10)	0.0033 (7)	0.0039 (7)	−0.0048 (8)
C2	0.0566 (11)	0.0479 (10)	0.0513 (10)	0.0026 (8)	0.0157 (8)	−0.0119 (8)
C3	0.0581 (11)	0.0477 (10)	0.0346 (8)	−0.0037 (8)	0.0085 (7)	−0.0038 (7)
C4	0.0469 (9)	0.0387 (8)	0.0335 (8)	−0.0006 (7)	0.0026 (7)	0.0030 (7)
C5	0.0336 (8)	0.0323 (8)	0.0323 (7)	0.0022 (6)	0.0018 (6)	−0.0030 (6)
C6	0.0310 (7)	0.0285 (7)	0.0400 (8)	−0.0032 (6)	0.0015 (6)	0.0005 (6)
C7	0.0331 (7)	0.0309 (8)	0.0366 (8)	−0.0053 (6)	0.0002 (6)	0.0027 (6)
C8	0.0336 (7)	0.0319 (8)	0.0325 (7)	−0.0055 (6)	0.0025 (6)	0.0025 (6)

C9	0.0441 (9)	0.0371 (9)	0.0387 (8)	−0.0050 (7)	0.0075 (7)	−0.0029 (7)
C10	0.0570 (10)	0.0480 (10)	0.0320 (8)	−0.0168 (8)	0.0033 (7)	−0.0012 (7)
C11	0.0538 (10)	0.0519 (11)	0.0396 (9)	−0.0117 (9)	−0.0124 (7)	0.0088 (8)
C12	0.0406 (9)	0.0403 (9)	0.0487 (9)	−0.0013 (7)	−0.0060 (7)	0.0060 (7)
C13	0.0703 (13)	0.0781 (15)	0.0421 (10)	0.0174 (11)	−0.0085 (9)	0.0066 (9)
C14	0.0323 (8)	0.0428 (9)	0.0325 (7)	−0.0011 (7)	−0.0025 (6)	0.0000 (6)
C15	0.0677 (13)	0.0484 (12)	0.0709 (13)	−0.0261 (10)	0.0046 (10)	−0.0042 (9)

Geometric parameters (Å, º)

O1—C2	1.220 (2)	C6—C7	1.457 (2)
O2—C8	1.3791 (17)	C7—C12	1.389 (2)
O2—C5	1.4497 (17)	C7—C8	1.392 (2)
O3—C14	1.1946 (19)	C8—C9	1.383 (2)
O4—C14	1.3288 (19)	C9—C10	1.385 (2)
O4—C15	1.451 (2)	C9—H9	0.9300
C1—C6	1.335 (2)	C10—C11	1.389 (3)
C1—C2	1.461 (2)	C10—H10	0.9300
C1—H1	0.9300	C11—C12	1.385 (2)
C2—C3	1.510 (3)	C11—H11	0.9300
C3—C4	1.535 (2)	C12—H12	0.9300
C3—H3A	0.9700	C13—H13A	0.9600
C3—H3B	0.9700	C13—H13B	0.9600
C4—C13	1.516 (3)	C13—H13C	0.9600
C4—C5	1.533 (2)	C15—H15A	0.9600
C4—H4	0.9800	C15—H15B	0.9600
C5—C6	1.516 (2)	C15—H15C	0.9600
C5—C14	1.547 (2)		
C8—O2—C5	106.28 (11)	C8—C7—C6	106.35 (12)
C14—O4—C15	116.16 (14)	O2—C8—C9	124.37 (14)
C6—C1—C2	121.34 (15)	O2—C8—C7	112.99 (12)
C6—C1—H1	119.3	C9—C8—C7	122.61 (14)
C2—C1—H1	119.3	C8—C9—C10	116.46 (15)
O1—C2—C1	120.96 (18)	C8—C9—H9	121.8
O1—C2—C3	120.73 (17)	C10—C9—H9	121.8
C1—C2—C3	118.28 (14)	C9—C10—C11	122.02 (15)
C2—C3—C4	115.69 (14)	C9—C10—H10	119.0
C2—C3—H3A	108.4	C11—C10—H10	119.0
C4—C3—H3A	108.4	C12—C11—C10	120.71 (15)
C2—C3—H3B	108.4	C12—C11—H11	119.6
C4—C3—H3B	108.4	C10—C11—H11	119.6
H3A—C3—H3B	107.4	C11—C12—C7	118.21 (16)
C13—C4—C5	113.48 (13)	C11—C12—H12	120.9
C13—C4—C3	112.11 (14)	C7—C12—H12	120.9
C5—C4—C3	109.88 (13)	C4—C13—H13A	109.5
C13—C4—H4	107.0	C4—C13—H13B	109.5
C5—C4—H4	107.0	H13A—C13—H13B	109.5

C3—C4—H4	107.0	C4—C13—H13C	109.5
O2—C5—C6	104.53 (11)	H13A—C13—H13C	109.5
O2—C5—C4	110.34 (12)	H13B—C13—H13C	109.5
C6—C5—C4	111.77 (12)	O3—C14—O4	124.24 (15)
O2—C5—C14	105.59 (11)	O3—C14—C5	123.97 (15)
C6—C5—C14	110.69 (12)	O4—C14—C5	111.78 (12)
C4—C5—C14	113.37 (12)	O4—C15—H15A	109.5
C1—C6—C7	132.26 (14)	O4—C15—H15B	109.5
C1—C6—C5	122.88 (14)	H15A—C15—H15B	109.5
C7—C6—C5	104.42 (12)	O4—C15—H15C	109.5
C12—C7—C8	119.92 (14)	H15A—C15—H15C	109.5
C12—C7—C6	133.59 (15)	H15B—C15—H15C	109.5

C6—C1—C2—O1	179.12 (19)	C5—C6—C7—C12	−168.28 (17)
C6—C1—C2—C3	−2.9 (3)	C1—C6—C7—C8	−156.31 (17)
O1—C2—C3—C4	158.43 (19)	C5—C6—C7—C8	16.00 (15)
C1—C2—C3—C4	−19.5 (2)	C5—O2—C8—C9	169.92 (14)
C2—C3—C4—C13	172.58 (16)	C5—O2—C8—C7	−12.19 (16)
C2—C3—C4—C5	45.4 (2)	C12—C7—C8—O2	−179.36 (13)
C8—O2—C5—C6	21.40 (14)	C6—C7—C8—O2	−2.93 (16)
C8—O2—C5—C4	141.71 (12)	C12—C7—C8—C9	−1.4 (2)
C8—O2—C5—C14	−95.43 (12)	C6—C7—C8—C9	175.00 (13)
C13—C4—C5—O2	68.04 (18)	O2—C8—C9—C10	−179.94 (14)
C3—C4—C5—O2	−165.55 (12)	C7—C8—C9—C10	2.4 (2)
C13—C4—C5—C6	−176.09 (15)	C8—C9—C10—C11	−1.1 (2)
C3—C4—C5—C6	−49.69 (17)	C9—C10—C11—C12	−1.1 (3)
C13—C4—C5—C14	−50.15 (19)	C10—C11—C12—C7	2.1 (2)
C3—C4—C5—C14	76.25 (16)	C8—C7—C12—C11	−0.9 (2)
C2—C1—C6—C7	167.82 (16)	C6—C7—C12—C11	−176.13 (16)
C2—C1—C6—C5	−3.3 (2)	C15—O4—C14—O3	1.0 (2)
O2—C5—C6—C1	150.30 (15)	C15—O4—C14—C5	−178.52 (14)
C4—C5—C6—C1	30.9 (2)	O2—C5—C14—O3	−12.1 (2)
C14—C5—C6—C1	−96.46 (17)	C6—C5—C14—O3	−124.64 (16)
O2—C5—C6—C7	−22.93 (14)	C4—C5—C14—O3	108.85 (17)
C4—C5—C6—C7	−142.28 (13)	O2—C5—C14—O4	167.49 (12)
C14—C5—C6—C7	90.32 (14)	C6—C5—C14—O4	54.91 (16)
C1—C6—C7—C12	19.4 (3)	C4—C5—C14—O4	−71.60 (16)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C15—H15*C*···O3^{i}	0.96	2.65	3.565 (3)	159
C9—H9···O2^{ii}	0.93	2.62	3.455 (2)	149
C1—H1···O3^{iii}	0.93	2.59	3.453 (2)	154

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