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5-(2-Chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate

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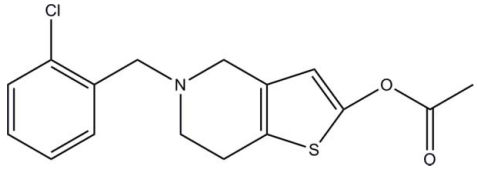
Key indicators: single-crystal X-ray study; T = 113 K; mean σ(C–C) = 0.002 Å; R factor = 0.030; wR factor = 0.086; data-to-parameter ratio = 14.2.

In the title compound, $C_{16}H_{16}ClNO_2S$, the benzene and thiophene rings make a dihedral angle of 72.60 (4)°. In the crystal, weak C—H···O interactions are observed.

Related literature

The title compound is a derivative of the antiplatelet agent clopidogrel [systematic name (+)-(*S*)-methyl 2-(2-chloro phenyl)-2-(6,7-dihydrothieno[3,2-*c*]pyridin-5(4*H*)-yl)acetate]. For background to the bioactivity and applications of clopidogrel, see: Muller *et al.* (2003); Savi *et al.* (1994); Sharis *et al.* (1998). For the synthesis of the title compound, see: Roquettes *et al.* (1993).



Experimental

Crystal data

$C_{16}H_{16}ClNO_2S$
M_r = 321.81
Monoclinic, $P2_1/n$
a = 14.526 (3) Å
b = 6.1065 (12) Å
c = 17.490 (3) Å
β = 99.098 (3)°
V = 1532.0 (5) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.39 mm^{-1}
T = 113 K
0.20 × 0.18 × 0.10 mm

Data collection

Rigaku Saturn CCD area-detector diffractometer
Absorption correction: multi-scan (*CrystalClear*; Rigaku/MSC, 2005)
T_{min} = 0.926, T_{max} = 0.962
10686 measured reflections
2704 independent reflections
2397 reflections with $I > 2\sigma(I)$
R_{int} = 0.033

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.030
$wR(F^2)$ = 0.086
S = 1.07
2704 reflections
191 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.18 e Å^{-3}
$\Delta\rho_{min}$ = −0.31 e Å^{-3}

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

D—H···A	D—H	H···A	D···A	D—H···A
C15—H15···O1^{i}	0.95	2.52	3.364 (2)	148

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

Data collection: *CrystalClear* (Rigaku/MSC, 2005); cell refinement: *CrystalClear*; data reduction: *CrystalClear*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *CrystalStructure* (Rigaku/MSC, 2005).

The authors thank Mr Hai-Bin Song at Nankai University for the X-ray crystallographic determination and helpful suggestions.

Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: KP2393).

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supplementary materials

Acta Cryst. (2012). E**68**, o1053 [doi:10.1107/S1600536812010045]

5-(2-Chlorobenzyl)-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-2-yl acetate

Jing Yang, Na Chen, Hao Sun, Xiao-Xia Cao and Deng-Ke Liu

Comment

Clopidogrel is an oral, thienopyridine class of antiplatelet agent used to inhibit blood clots in coronary artery disease, peripheral vascular disease, and cerebrovascular disease (Muller *et al.*, 2003; Savi *et al.*, 1994; Sharis *et al.*, 1998). The molecular structure of the title compound, a derivative of clopidogrel, is reported here. The thiophene and benzene rings make a dihedral angle of 72.60 (4)°; the tetrahydropyridine ring adopts a half-chair conformation (Fig. 1). In the crystal structure, the packing is realsied by weak intramolecular C—H···Cl and C—H···N, and intermolecular C—H···O interaction (Table 1).

Experimental

We used the method of Roquettes *et al.* (1993) to sythesize the title compound. 8.85 g (0.0316 mol) of 5-(2-chloro-benzyl)-5,6,7,7a-tetrahydro-4*H*-thieno [3,2-*c*] pyridine-2-one are dissolved in 120 mL of isopropenyl acetate with 7.8 g (0.0411 mol) of *p*-toluenesulphonic acid; the medium is stirred at 363 K for 6 h. After cooling to about 293 K, 2 volumes of water are introduced into the medium, the pH is made basic by adding saturated aqueous $NaHCO_3$ solution and the desired product is extracted with ethyl acetate. After removal of the solvent, the oil, dissolved in CH_2Cl_2, is filtered on silica to give a 68% yield of the target compound. Colourless single crystals were grown from a methanol solution.

Refinement

All H atoms were positioned geometrically and refined using a riding model, with d(C—H) = 0.95 - 0.99 Å, and U_{iso}(H) = 1.5 or 1.2U_{eq}.

Computing details

Data collection: *CrystalClear* (Rigaku/MSC, 2005); cell refinement: *CrystalClear* (Rigaku/MSC, 2005); data reduction: *CrystalClear* (Rigaku/MSC, 2005); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *SHELXTL* (Sheldrick, 2008); software used to prepare material for publication: *CrystalStructure* (Rigaku/MSC, 2005).

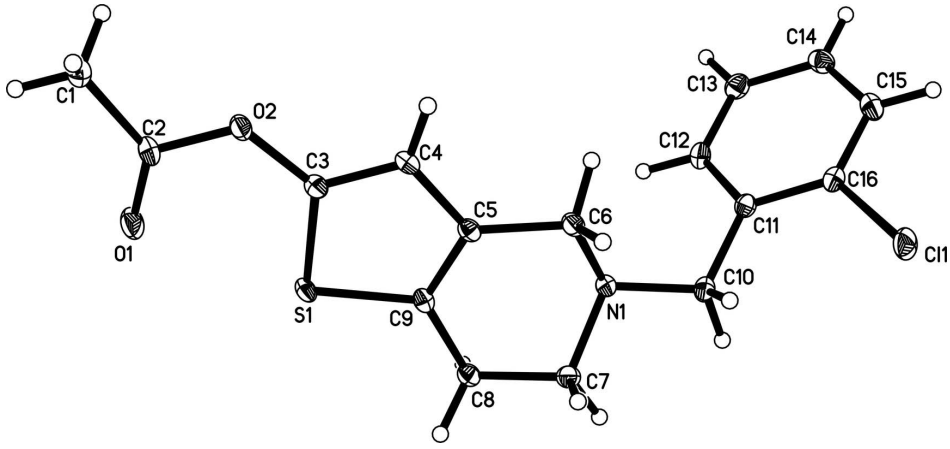

Figure 1

The molecular structure of (I), with the atom-numbering scheme and 50% probability displacement ellipsoids.

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Crystal data

$C_{16}H_{16}ClNO_2S$
$M_r = 321.81$
Monoclinic, $P2_1/n$
Hall symbol: -P 2yn
$a = 14.526$ (3) Å
$b = 6.1065$ (12) Å
$c = 17.490$ (3) Å
$\beta = 99.098$ (3)°
$V = 1532.0$ (5) Å^3
$Z = 4$
$F(000) = 672$
$D_x = 1.395$ Mg m^{-3}
Mo $K\alpha$ radiation, $\lambda = 0.71073$ Å
Cell parameters from 4955 reflections
$\theta = 1.7$–27.9°
$\mu = 0.39$ mm^{-1}
$T = 113$ K
Prism, colourless
0.20 × 0.18 × 0.10 mm

Data collection

Rigaku Saturn CCD area-detector diffractometer
Radiation source: rotating anode
Multilayer monochromator
Detector resolution: 14.63 pixels mm^{-1}
ω and φ scans
Absorption correction: multi-scan (*CrystalClear*; Rigaku/MSC, 2005)
$T_{min} = 0.926$, $T_{max} = 0.962$
10686 measured reflections
2704 independent reflections
2397 reflections with $I > 2\sigma(I)$
$R_{int} = 0.033$
$\theta_{max} = 25.0°$, $\theta_{min} = 1.7°$
$h = -17\rightarrow17$
$k = -7\rightarrow5$
$l = -20\rightarrow20$

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)] = 0.030$
$wR(F^2) = 0.086$
$S = 1.07$
2704 reflections
191 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
$w = 1/[\sigma^2(F_o^2) + (0.0514P)^2 + 0.2496P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.18$ e Å^{-3}
$\Delta\rho_{min} = -0.31$ e Å^{-3}

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}
Cl1	0.64701 (3)	0.34141 (7)	0.05214 (2)	0.03277 (14)
S1	0.08191 (2)	0.16665 (6)	0.14645 (2)	0.01970 (13)
O1	−0.07808 (8)	−0.0621 (2)	0.12690 (7)	0.0350 (3)
O2	0.03009 (7)	−0.21624 (17)	0.06530 (6)	0.0227 (2)
N1	0.38577 (8)	0.2952 (2)	0.15330 (6)	0.0197 (3)
C1	−0.11190 (11)	−0.4038 (3)	0.05983 (9)	0.0262 (4)
H1A	−0.1710	−0.4020	0.0802	0.039*
H1B	−0.0773	−0.5373	0.0771	0.039*
H1C	−0.1245	−0.4005	0.0031	0.039*
C2	−0.05566 (10)	−0.2093 (3)	0.08876 (8)	0.0232 (3)
C3	0.09637 (10)	−0.0575 (2)	0.08845 (8)	0.0189 (3)
C4	0.18265 (10)	−0.0674 (2)	0.06854 (8)	0.0192 (3)
H4	0.2022	−0.1776	0.0362	0.023*
C5	0.24081 (10)	0.1077 (2)	0.10193 (7)	0.0180 (3)
C6	0.34116 (10)	0.1424 (2)	0.09400 (8)	0.0209 (3)
H6A	0.3745	0.0004	0.0994	0.025*
H6B	0.3451	0.2017	0.0419	0.025*
C7	0.32906 (10)	0.4937 (3)	0.15410 (8)	0.0212 (3)
H7A	0.3132	0.5520	0.1008	0.025*
H7B	0.3651	0.6070	0.1865	0.025*
C8	0.23974 (10)	0.4424 (2)	0.18630 (8)	0.0205 (3)
H8A	0.2543	0.4127	0.2426	0.025*
H8B	0.1965	0.5686	0.1782	0.025*
C9	0.19592 (10)	0.2454 (3)	0.14461 (8)	0.0187 (3)
C10	0.47954 (10)	0.3512 (2)	0.13892 (9)	0.0243 (4)
H10A	0.5017	0.4817	0.1701	0.029*
H10B	0.4764	0.3902	0.0836	0.029*
C11	0.54919 (10)	0.1683 (2)	0.15836 (8)	0.0199 (3)
C12	0.54030 (10)	0.0141 (3)	0.21553 (8)	0.0245 (3)
H12	0.4874	0.0207	0.2412	0.029*
C13	0.60608 (11)	−0.1481 (3)	0.23609 (9)	0.0258 (4)
H13	0.5982	−0.2505	0.2754	0.031*
C14	0.68378 (11)	−0.1607 (3)	0.19890 (9)	0.0264 (4)
H14	0.7289	−0.2724	0.2125	0.032*
C15	0.69503 (11)	−0.0102 (3)	0.14218 (8)	0.0259 (4)
H15	0.7480	−0.0172	0.1166	0.031*
C16	0.62835 (10)	0.1509 (2)	0.12296 (8)	0.0208 (3)

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
Cl1	0.0313 (2)	0.0369 (3)	0.0341 (2)	0.00271 (18)	0.01724 (18)	0.01129 (18)
S1	0.0156 (2)	0.0234 (2)	0.0206 (2)	0.00371 (15)	0.00426 (15)	−0.00402 (15)
O1	0.0202 (6)	0.0410 (7)	0.0459 (7)	−0.0015 (5)	0.0117 (5)	−0.0193 (6)
O2	0.0158 (5)	0.0253 (6)	0.0273 (5)	0.0010 (4)	0.0048 (4)	−0.0066 (5)
N1	0.0158 (6)	0.0185 (6)	0.0250 (7)	0.0012 (5)	0.0039 (5)	0.0012 (5)
C1	0.0193 (8)	0.0292 (9)	0.0295 (8)	−0.0003 (7)	0.0019 (6)	−0.0017 (7)
C2	0.0144 (7)	0.0307 (9)	0.0240 (7)	0.0029 (7)	0.0017 (6)	0.0001 (7)
C3	0.0178 (7)	0.0210 (8)	0.0176 (7)	0.0025 (6)	0.0014 (5)	−0.0023 (6)
C4	0.0187 (8)	0.0201 (8)	0.0189 (7)	0.0054 (6)	0.0031 (6)	−0.0010 (6)
C5	0.0177 (7)	0.0200 (7)	0.0161 (7)	0.0043 (6)	0.0021 (5)	0.0027 (6)
C6	0.0197 (8)	0.0215 (8)	0.0224 (7)	0.0032 (6)	0.0061 (6)	0.0005 (6)
C7	0.0229 (8)	0.0185 (8)	0.0223 (7)	0.0012 (6)	0.0042 (6)	0.0007 (6)
C8	0.0206 (8)	0.0211 (8)	0.0206 (7)	0.0024 (6)	0.0057 (6)	−0.0016 (6)
C9	0.0155 (7)	0.0226 (8)	0.0178 (7)	0.0027 (6)	0.0028 (5)	0.0015 (6)
C10	0.0180 (8)	0.0233 (8)	0.0325 (8)	−0.0011 (6)	0.0063 (6)	0.0047 (7)
C11	0.0166 (7)	0.0210 (8)	0.0212 (7)	−0.0030 (6)	0.0003 (6)	−0.0018 (6)
C12	0.0206 (8)	0.0282 (9)	0.0256 (7)	−0.0031 (7)	0.0069 (6)	0.0022 (7)
C13	0.0265 (9)	0.0251 (9)	0.0251 (8)	−0.0022 (7)	0.0019 (6)	0.0048 (7)
C14	0.0219 (8)	0.0252 (9)	0.0302 (8)	0.0046 (7)	−0.0015 (6)	−0.0015 (7)
C15	0.0199 (8)	0.0315 (9)	0.0268 (8)	0.0018 (7)	0.0047 (6)	−0.0036 (7)
C16	0.0212 (8)	0.0227 (8)	0.0187 (7)	−0.0045 (6)	0.0038 (6)	−0.0003 (6)

Geometric parameters (Å, º)

Cl1—C16	1.7515 (15)	C7—C8	1.526 (2)
S1—C9	1.7298 (15)	C7—H7A	0.9900
S1—C3	1.7362 (14)	C7—H7B	0.9900
O1—C2	1.1946 (19)	C8—C9	1.496 (2)
O2—C2	1.3722 (17)	C8—H8A	0.9900
O2—C3	1.3810 (18)	C8—H8B	0.9900
N1—C10	1.4641 (18)	C10—C11	1.509 (2)
N1—C7	1.4671 (19)	C10—H10A	0.9900
N1—C6	1.4676 (19)	C10—H10B	0.9900
C1—C2	1.485 (2)	C11—C16	1.393 (2)
C1—H1A	0.9800	C11—C12	1.394 (2)
C1—H1B	0.9800	C12—C13	1.384 (2)
C1—H1C	0.9800	C12—H12	0.9500
C3—C4	1.354 (2)	C13—C14	1.391 (2)
C4—C5	1.429 (2)	C13—H13	0.9500
C4—H4	0.9500	C14—C15	1.381 (2)
C5—C9	1.358 (2)	C14—H14	0.9500
C5—C6	1.501 (2)	C15—C16	1.384 (2)
C6—H6A	0.9900	C15—H15	0.9500
C6—H6B	0.9900		
C9—S1—C3	90.21 (7)	H7A—C7—H7B	108.1
C2—O2—C3	120.95 (12)	C9—C8—C7	107.84 (12)

C10—N1—C7	110.35 (12)	C9—C8—H8A	110.1
C10—N1—C6	110.24 (11)	C7—C8—H8A	110.1
C7—N1—C6	110.26 (11)	C9—C8—H8B	110.1
C2—C1—H1A	109.5	C7—C8—H8B	110.1
C2—C1—H1B	109.5	H8A—C8—H8B	108.5
H1A—C1—H1B	109.5	C5—C9—C8	124.19 (13)
C2—C1—H1C	109.5	C5—C9—S1	112.48 (11)
H1A—C1—H1C	109.5	C8—C9—S1	123.33 (11)
H1B—C1—H1C	109.5	N1—C10—C11	113.41 (12)
O1—C2—O2	122.06 (14)	N1—C10—H10A	108.9
O1—C2—C1	127.46 (14)	C11—C10—H10A	108.9
O2—C2—C1	110.48 (13)	N1—C10—H10B	108.9
C4—C3—O2	121.60 (13)	C11—C10—H10B	108.9
C4—C3—S1	112.82 (11)	H10A—C10—H10B	107.7
O2—C3—S1	125.56 (10)	C16—C11—C12	116.34 (14)
C3—C4—C5	111.90 (13)	C16—C11—C10	121.82 (13)
C3—C4—H4	124.1	C12—C11—C10	121.76 (13)
C5—C4—H4	124.1	C13—C12—C11	122.09 (14)
C9—C5—C4	112.57 (13)	C13—C12—H12	119.0
C9—C5—C6	121.40 (13)	C11—C12—H12	119.0
C4—C5—C6	126.01 (13)	C12—C13—C14	119.74 (14)
N1—C6—C5	110.56 (11)	C12—C13—H13	120.1
N1—C6—H6A	109.5	C14—C13—H13	120.1
C5—C6—H6A	109.5	C15—C14—C13	119.75 (15)
N1—C6—H6B	109.5	C15—C14—H14	120.1
C5—C6—H6B	109.5	C13—C14—H14	120.1
H6A—C6—H6B	108.1	C14—C15—C16	119.31 (14)
N1—C7—C8	110.19 (12)	C14—C15—H15	120.3
N1—C7—H7A	109.6	C16—C15—H15	120.3
C8—C7—H7A	109.6	C15—C16—C11	122.76 (14)
N1—C7—H7B	109.6	C15—C16—Cl1	117.60 (12)
C8—C7—H7B	109.6	C11—C16—Cl1	119.63 (12)

C3—O2—C2—O1	3.4 (2)	C6—C5—C9—S1	−178.61 (10)
C3—O2—C2—C1	−176.85 (12)	C7—C8—C9—C5	15.76 (19)
C2—O2—C3—C4	177.09 (13)	C7—C8—C9—S1	−164.89 (10)
C2—O2—C3—S1	−1.09 (19)	C3—S1—C9—C5	0.20 (11)
C9—S1—C3—C4	−0.86 (11)	C3—S1—C9—C8	−179.22 (12)
C9—S1—C3—O2	177.46 (12)	C7—N1—C10—C11	164.39 (12)
O2—C3—C4—C5	−177.12 (12)	C6—N1—C10—C11	−73.58 (15)
S1—C3—C4—C5	1.27 (15)	N1—C10—C11—C16	154.60 (13)
C3—C4—C5—C9	−1.12 (17)	N1—C10—C11—C12	−28.7 (2)
C3—C4—C5—C6	177.91 (13)	C16—C11—C12—C13	−0.2 (2)
C10—N1—C6—C5	−172.40 (12)	C10—C11—C12—C13	−177.04 (14)
C7—N1—C6—C5	−50.32 (15)	C11—C12—C13—C14	−0.3 (2)
C9—C5—C6—N1	15.88 (18)	C12—C13—C14—C15	0.5 (2)
C4—C5—C6—N1	−163.07 (12)	C13—C14—C15—C16	−0.2 (2)
C10—N1—C7—C8	−167.59 (12)	C14—C15—C16—C11	−0.2 (2)
C6—N1—C7—C8	70.39 (14)	C14—C15—C16—Cl1	178.66 (11)

N1—C7—C8—C9	−49.62 (14)	C12—C11—C16—C15	0.5 (2)
C4—C5—C9—C8	179.88 (12)	C10—C11—C16—C15	177.29 (14)
C6—C5—C9—C8	0.8 (2)	C12—C11—C16—Cl1	−178.42 (11)
C4—C5—C9—S1	0.47 (16)	C10—C11—C16—Cl1	−1.6 (2)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C10—H10*B*···Cl1	0.99	2.64	3.0648 (16)	106
C12—H12···N1	0.95	2.58	2.898 (2)	100
C15—H15···O1^{i}	0.95	2.52	3.364 (2)	148

Symmetry code: (i) *x*+1, *y*, *z*.