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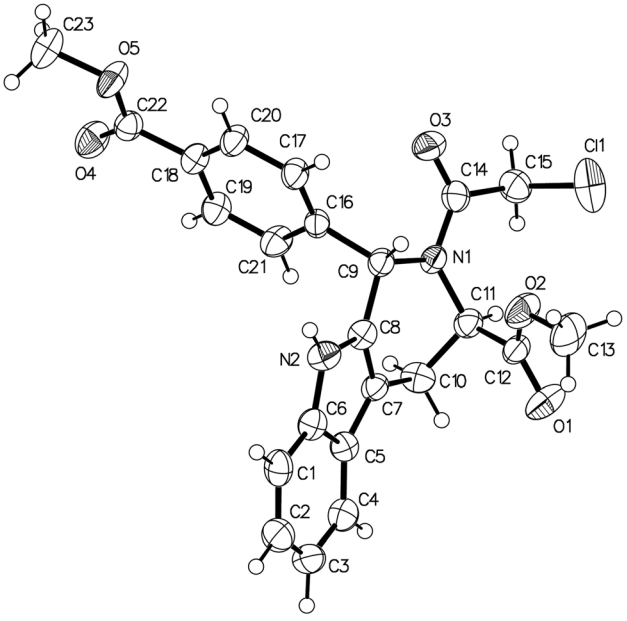
Crystal structure of methyl 2-(2-chloroacetyl)-1-(4-(methoxycarbonyl) phenyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*] indole-3-carboxylate, $C_{23}H_{21}ClN_2O_5$



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Abstract

$C_{23}H_{21}ClN_2O_5$, monoclinic, $P2_1/c$ (no. 14), a = 9.191(3) Å, b = 10.725(5) Å, c = 11.2390(10) Å, β = 109.869(13)°, V = 1041.9(6) Å^3, Z = 2, $R_{gt}(F)$ = 0.0609, $wR_{ref}(F^2)$ = 0.1695, T = 293 K.

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Table 1: Data collection and handling.

Crystal:	Colourless block
Size:	0.19 × 0.15 × 0.12 mm
Wavelength:	Mo *K*α radiation (0.71073 Å)
μ:	0.22 mm^{-1}
Diffractometer, scan mode:	Bruker APEX-II, φ and ω
θ_{max}, completeness:	26.4°, >99%
$N(hkl)_{measured}$, $N(hkl)_{unique}$, R_{int}:	11,717, 4233, 0.087
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2829
$N(param)_{refined}$:	283
Programs:	CrysAlis^{PRO} [1], Olex2 [2], SHELX [3, 4]

The molecular structure is shown in the figure. Table 1 contains crystallographic data and Table 2 contains the list of the atoms including atomic coordinates and displacement parameters.

Source of materials

A mixture of (1*S*,3*R*)-methyl 1-(4-(methoxycarbonyl)phenyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylate hydrochloride (2.00 g, 5 mmol) and triethylamine (1.52 g, 15 mmol) was dissolved in dry dichloromethane (40 mL). The temperature was dropped to 0 °C. Then 2-chloroacetyl chloride (0.78 g, 7 mmol) was added dropwise under stirring. The mixture was stirred for 2 h at room temperature until the TLC indicated the reaction was completed. The solution was concentrated under reduced pressure. The title compound was separated by silica-gel column chromatography with ethyl acetate-petroleum ether (10%) gradient solvent system. The target product was obtained as a white solid. Yield: 93.0%.

Experimental details

The structure was solved with the SHELXT [2] structure solution program and refined on SHELXL [3]. All hydrogen atoms were placed in idealized positions and refined as riding atoms.

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

Atom	*x*	*y*	*z*	U_{iso}*/U_{eq}
C1	0.2645 (7)	0.2216 (6)	0.6401 (5)	0.0426 (15)
H1	0.285300	0.288531	0.698952	0.051*
C2	0.2079 (8)	0.1094 (7)	0.6644 (6)	0.0481 (16)
H2A	0.190859	0.098569	0.742510	0.058*
C3	0.1749 (7)	0.0113 (6)	0.5788 (6)	0.0451 (16)
H3	0.134250	−0.064213	0.598746	0.054*
C4	0.2007 (7)	0.0219 (6)	0.4638 (6)	0.0418 (15)
H4	0.179874	−0.045717	0.405795	0.050*
C5	0.2579 (6)	0.1349 (6)	0.4367 (5)	0.0332 (13)
C6	0.2898 (6)	0.2327 (6)	0.5255 (5)	0.0365 (13)
C7	0.3026 (6)	0.1803 (5)	0.3327 (5)	0.0314 (12)
C8	0.3601 (6)	0.2961 (5)	0.3631 (5)	0.0334 (12)
C9	0.4143 (6)	0.3833 (5)	0.2825 (5)	0.0321 (13)
H9	0.515298	0.420521	0.335548	0.039*
C10	0.3042 (7)	0.1203 (6)	0.2131 (6)	0.0394 (14)
H10A	0.208904	0.141412	0.142153	0.047*
H10B	0.310720	0.028470	0.222698	0.047*
C11	0.4444 (6)	0.1701 (6)	0.1885 (5)	0.0354 (13)
H11	0.442813	0.136165	0.105160	0.042*
C12	0.5882 (7)	0.1219 (6)	0.2881 (6)	0.0378 (14)
C13	0.8295 (8)	0.1653 (8)	0.4436 (7)	0.068 (2)
H13A	0.907332	0.144583	0.405014	0.102*
H13B	0.806145	0.091026	0.484628	0.102*
H13C	0.869466	0.231161	0.506745	0.102*
C14	0.4865 (6)	0.3753 (6)	0.0943 (5)	0.0366 (14)
C15	0.5344 (7)	0.3098 (7)	−0.0085 (6)	0.0468 (16)
H15A	0.513610	0.364401	−0.083512	0.056*
H15B	0.475511	0.231354	−0.035111	0.056*
C16	0.2958 (6)	0.4872 (5)	0.2375 (5)	0.0307 (12)
C17	0.3374 (6)	0.6075 (5)	0.2745 (6)	0.0376 (14)
H17	0.441750	0.626089	0.323329	0.045*
C18	0.0764 (6)	0.6755 (6)	0.1725 (5)	0.0358 (13)
C19	0.0336 (6)	0.5546 (6)	0.1356 (6)	0.0381 (14)
H19	−0.071104	0.536261	0.087695	0.046*
C20	0.2282 (6)	0.7026 (6)	0.2412 (6)	0.0399 (14)
H20	0.258191	0.786100	0.265793	0.048*
C21	0.1410 (6)	0.4605 (6)	0.1676 (6)	0.0391 (14)
H21	0.110442	0.377219	0.142435	0.047*
C22	−0.0450 (6)	0.7746 (6)	0.1379 (5)	0.0355 (13)
C23	−0.1027 (8)	0.9857 (7)	0.1594 (7)	0.0541 (18)
H23A	−0.163124	0.989583	0.068951	0.081*
H23B	−0.049087	1.065147	0.186573	0.081*
H23C	−0.172043	0.969644	0.207419	0.081*
Cl1	0.7351 (2)	0.2778 (3)	0.0582 (2)	0.0841 (8)
N1	0.4391 (5)	0.3099 (4)	0.1784 (4)	0.0309 (10)
N2	0.3530 (5)	0.3302 (5)	0.4795 (4)	0.0382 (12)
H2	0.383633	0.401933	0.517862	0.046*
O1	0.6046 (6)	0.0126 (5)	0.3108 (5)	0.0628 (14)
O2	0.6891 (5)	0.2086 (4)	0.3462 (4)	0.0520 (12)
O3	0.4932 (5)	0.4890 (4)	0.0975 (4)	0.0493 (12)
O4	−0.1783 (5)	0.7561 (4)	0.0792 (4)	0.0505 (11)
O5	0.0094 (5)	0.8865 (4)	0.1820 (4)	0.0480 (12)

Comment

RSL3, chemical name (1S*b*,3*R*)-methyl 2-(2-chloroacetyl)-1-(4-(methoxycarbonyl) phenyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylate, is an inhibitor of the glutathione (GSH) peroxidase 4 (GPX4) (ferroptosis activator), which can inhibit the cysteine/glutamate amino acid transporter system that blocks GSH synthesis and maintaining the reactive oxygen species balance in the body with an IC50 of 100 nM [5]. Many derivatives of 2,3,4,9-tetrahydro-1*H*-pyrido[3,4-b]indole similar to RSL3 were reported [6–11].

In the title structure the chloroacetyl and (methoxycarbonyl)phenyl groups are present instead of two hydrogen atoms of methyl 2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole-3-carboxylate. The bond length C9–C16 and N1–C14 are 1.520(8) Å and 1.362(9) Å, respectively [12]. The plane of the (methoxycarbonyl)phenyl group is almost perpendicular to the indole plane, and the dihedral angle between them is 82.4°. The vertical structure is similar to methyl 1-(2-nitrophenyl)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carboxylate [6], in which the nitrophenyl group plane is almost perpendicular to the indole plane with the dihedral angle: 85.9°.

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Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

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