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4-(4-Bromophenyl)-2,5-diethoxycarbonyl-6-methylthieno[2,3-*b*]pyridine

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.008 Å
R factor = 0.046
wR factor = 0.132
Data-to-parameter ratio = 9.6

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

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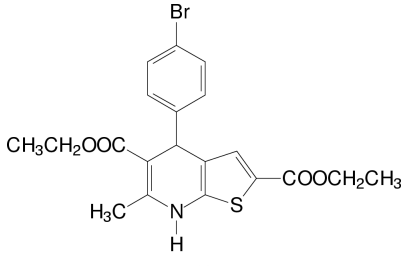
The title compound, alternatively named diethyl 4-(4-bromophenyl)-6-methylthieno[2,3-*b*]pyridine-2,5-dicarboxylate, $C_{20}H_{18}BrNO_4S$, crystallizes with two crystallographically independent molecules in the asymmetric unit. The crystal structure is stabilized by intermolecular and intramolecular C—H···O hydrogen bonds. The thieno[2,3-*b*]pyridine moiety is planar.

Comment

Since the discovery of the pharmacological properties of the 1,4-dihydropyridines (1,4-DHP) as calcium channel blockers, a great deal of work has been directed towards the study of these molecules (Goldmann & Stoltefuss, 1991). In addition to their use in the treatment of cardiovascular diseases, 1,4-DHP derivatives have been recently reported as novel HIV-1 protease inhibitors (Hilgeroth *et al.*, 2000). Besides, thieno[2,3-*b*]pyridines with a different substitution pattern have shown interesting antimicrobial effects (Badr *et al.*, 1991). In a previous study, we reported the crystal structure of 2,5-diethoxycarbonyl-6-methyl-4-phenylthieno[2,3-*b*]pyridine (Novoa de Armas *et al.*, 2003). The title compound, (I), is a 4-(4-bromophenyl)-substituted thieno[2,3-*b*]pyridine, obtained by the reaction of ethyl 4-(4-bromophenyl)-6-chloro-5-formyl-2-methyl-1,4-dihydropyridine-3-carboxylate (Verdecia *et al.*, 1996) with an equimolar amount of ethyl mercaptoacetate in the presence of sodium ethoxide and dry ethanol. Further oxidation of the dihydro derivative produces the corresponding thieno[2,3-*b*]pyridine (Suárez *et al.*, 1997).



(I)

The title compound crystallizes with two crystallographically independent, but chemically equivalent, molecules in the asymmetric unit. In (I), the thieno[2,3-*b*]pyridine moiety is planar and the dihedral angle between the least-squares planes of the thieno[2,3-*b*]pyridine moiety and the 4-bromophenyl ring is 50.1 (2)° [56.0 (2)° in the other independent molecule]. The ester groups, in both independent molecules, are nearly coplanar with the thieno[2,3-*b*]pyridine

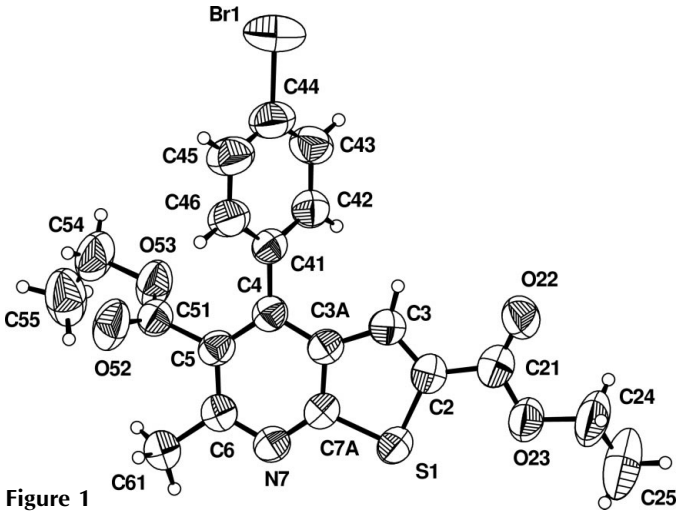


Figure 1
Plot showing the atomic numbering scheme for one of the independent molecules of (I). Displacement ellipsoids are drawn at the 50% probability level for non-H atoms.

moiety. The mean Csp^2-Csp^2 bond length within the 4-bromophenyl ring is 1.386 (4) Å [1.383 (3) Å in the other independent molecule]. The structures are stabilized by intermolecular and intramolecular C—H···O hydrogen bonds (Table 2).

Experimental

A solution of ceric ammonium nitrate (2 mmol) in water (5 ml) was added dropwise to a stirred solution of diethyl 6-methyl-4-(4-bromophenyl)-dihydrothieno[2,3-*b*]pyridine-2,5-dicarboxylate (1 mmol), previously obtained by the reaction of ethyl 4-(4-bromophenyl)-6-chloro-5-formyl-2-methyl-1,4-dihydropyridine-3-carboxylate (1.3 mmol) with ethyl mercaptoacetate (1.8 mmol) in ethanolic sodium ethoxide (prepared from 0.04 g of sodium in 20 ml dry ethanol) in acetone (10 ml). Stirring was continued for 0.5 h and the reaction mixture was partitioned between ethyl acetate and water. Afterwards, the crude product was purified by column chromatography on silica gel (20 g), using hexane–ethyl acetate (4:1) as eluent (yield 90%; m.p. 370–371 K). IR (KBr, cm^{-1}): 1718 (C═O), 1699 (C═O), 1595 (C═C); ^{1}H NMR (DMSO-d_6, p.p.m.): 7.88 (*d*, 2H, H3′, H4′, *J* = 8.5 Hz), 7.62 (*s*, 1H, ═CH), 7.39 (*d*, 2H, H3′, H4′, *J* = 8.5 Hz), 4.33 (*q*, 2H, CH_2), 4.10 (*q*, 2H, CH_2), 2.66 (*s*, 3H, CH_3), 1.30 (*t*, 3H, CH_3), 0.95 (*t*, 3H, CH_3); ^{13}C-NMR (DMSO-d_6, p.p.m.): 167.1 (CO), 162.7 (CO), 161.4 (C6), 155.5 (C4), 143.5 (C1′), 134.3 (C2), 132.9 (C7a), 131.8 (C3′ and C5′), 130.6 (C2′ and C6′), 128.6 (C3a), 127.0 (C3), 125.8 (C5), 122.9 (C4′), 62.0 (CH_2), 61.5 (CH_2), 23.1 (CH_3), 14.1 (CH_3), 13.5 (CH_3); MS, *m*/*z* (intensity %): 447/449 (M^+, 100/95), 402/404 (50/48), 323 (37), 295 (23). Crystals suitable for X-ray analysis were obtained by slow evaporation from methanol.

Crystal data

$C_{20}H_{18}BrNO_4S$
M_r = 448.32
Orthorhombic, $P2_12_12_1$
a = 7.8114 (6) Å
b = 11.2988 (6) Å
c = 45.353 (2) Å
V = 4002.8 (4) Å^3
Z = 8
D_x = 1.488 Mg m^{-3}
Cu Kα radiation
Cell parameters from 67 reflections
θ = 1.9–33.1°
μ = 3.99 mm^{-1}
T = 293 K
Prism, pale yellow
0.44 × 0.38 × 0.11 mm

Data collection

Siemens *P*4 four-circle diffractometer
$\omega/2\theta$ scans
Absorption correction: ψ scan [North *et al.* (1968); *XEMP* (Siemens, 1989)]
T_{min} = 0.126, T_{max} = 0.645
5061 measured reflections
4714 independent reflections
4275 reflections with $I > 2\sigma(I)$
R_{int} = 0.038
θ_{max} = 69.2°
$h = -1 \rightarrow 9$
$k = -1 \rightarrow 13$
$l = -1 \rightarrow 54$
3 standard reflections
every 100 reflections
intensity decay: 3.6%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.046
$wR(F^2)$ = 0.132
S = 1.05
4714 reflections
493 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0862P)^2 + 1.0278P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.001
$\Delta\rho_{max}$ = 0.55 e Å^{-3}
$\Delta\rho_{min}$ = −0.34 e Å^{-3}
Absolute structure: Flack (1983)
Flack parameter = −0.02 (2), 930 Friedel pairs

Table 1
Selected geometric parameters (Å, °).

Br1—C44	1.900 (6)	O53—C54	1.466 (7)
Br2—C344	1.904 (5)	O322—C321	1.197 (10)
S1—C7*A*	1.747 (5)	O323—C321	1.321 (8)
S1—C2	1.735 (5)	O323—C324	1.445 (9)
S31—C32	1.729 (6)	O352—C351	1.198 (7)
S31—C37*A*	1.734 (5)	O353—C354	1.449 (8)
O22—C21	1.208 (7)	O353—C351	1.321 (7)
O23—C24	1.447 (10)	N7—C6	1.328 (6)
O23—C21	1.330 (6)	N7—C7*A*	1.324 (6)
O52—C51	1.192 (8)	N37—C36	1.337 (7)
O53—C51	1.320 (7)	N37—C37*A*	1.329 (7)
C2—S1—C7*A*	90.7 (2)	O52—C51—C5	125.7 (5)
C32—S31—C37*A*	91.0 (2)	O53—C51—C5	110.8 (5)
C21—O23—C24	117.8 (5)	O52—C51—O53	123.3 (5)
C51—O53—C54	117.1 (6)	O53—C54—C55	107.2 (6)
C321—O323—C324	118.7 (6)	S31—C32—C33	113.4 (4)
C351—O353—C354	116.9 (5)	S31—C32—C321	121.8 (4)
C6—N7—C7*A*	115.9 (4)	N37—C36—C35	122.3 (4)
C36—N37—C37*A*	116.2 (4)	N37—C36—C361	115.4 (5)
S1—C2—C21	122.2 (4)	S31—C37*A*—N37	121.9 (4)
S1—C2—C3	113.0 (4)	S31—C37*A*—C33*A*	111.6 (4)
N7—C6—C61	116.0 (4)	N37—C37*A*—C33*A*	126.5 (5)
N7—C6—C5	122.2 (5)	O323—C321—C32	110.3 (6)
N7—C7*A*—C3*A*	127.5 (4)	O322—C321—O323	126.4 (6)
S1—C7*A*—C3*A*	111.1 (3)	O322—C321—C32	123.2 (6)
S1—C7*A*—N7	121.4 (4)	O323—C324—C325	107.8 (8)
O22—C21—C2	123.8 (5)	Br2—C344—C345	120.2 (4)
O23—C21—C2	112.6 (5)	Br2—C344—C343	117.5 (3)
O22—C21—O23	123.6 (5)	O352—C351—O353	124.6 (5)
O23—C24—C25	114.6 (8)	O352—C351—C35	124.3 (5)
Br1—C44—C43	119.6 (6)	O353—C351—C35	111.1 (4)
Br1—C44—C45	119.2 (6)	O353—C354—C355	109.1 (6)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C324—H32*B*···O22^{i}	0.97	2.55	3.431 (8)	151
C54—H54*B*···O52	0.97	2.29	2.660 (9)	102
C24—H24*A*···O22	0.97	2.36	2.688 (9)	99
C324—H32*A*···O322	0.97	2.42	2.742 (9)	99
C354—H35*B*···O352	0.97	2.47	2.675 (9)	91

Symmetry code: (i) $\frac{1}{2}+x, \frac{1}{2}-y, 1-z$.

The short distance for C24—C25 of 1.316 (15) Å [and C354—C355 of 1.425 (12) Å in the other independent molecule] is the the result of

some disorder in the C25 (C55) atom of the terminal methyl groups, as indicated by a rather high anisotropic displacement. H atoms were positioned geometrically and included in the refinement, but were constrained to ride on their parent atoms, with U_{iso}(H) fixed at $1.3U_{eq}$ of their parent atoms.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SIR*92 (Altomare *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *DIAMOND* (Bergerhoff, 1996); software used to prepare material for publication: *PARST* (Nardelli, 1995), *PARSTCIF* (Nardelli, 1991) and *PLATON* (Spek, 1990).

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