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tert-Butyl 2-[2-(ethoxycarbothioylamino)-3-pyridyloxy]acetate and *tert*-butyl 2-(3-thioxopyrido[2,1-*c*]-[1,2,4]thiadiazol-8-yloxy)acetate

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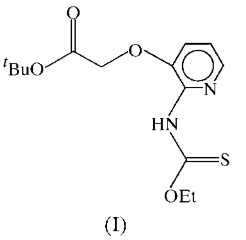
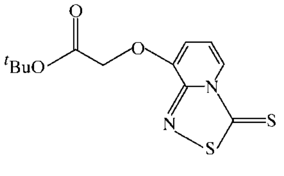
Compounds (I), $C_{14}H_{20}N_2O_4S$, and (II), $C_{12}H_{14}N_2O_3S_2$, are two minor products of the same reaction. Both structures contain identical ester functionalities in similar orientations. Both independent molecules of (I) contain an ethoxycarbothioylamine moiety, whilst (II) possesses a novel exocyclic thione system fused with a pyridine ring.

Comment

An alternative approach to the resolution of racemates involves the development of enantioselective receptors capable of strongly binding substrates (Webb & Wilcox, 1993). The title compounds were synthesized during an on-going scheme of research investigating the preparation of thiourea derivatives as binding sites for the separation of racemic mixtures of carboxylic acid derivatives. Attempts to prepare substituted *N*,*N*′-bis(2-pyridyl) thioureas resulted in the formation of a mixture of products which were separated by column chromatography, concentrated and recrystallized. Two compounds were identified, *i.e.* (I) and (II), providing unexpected results.



(I)



(II)

Compound (I) crystallizes with two independent molecules in the asymmetric unit which are bound together *via* intermolecular hydrogen bonding [*D*···*A* separations N1*A*—H1*A*···N2*B* and N1*B*—H1*B*···O3*A* of 2.920 (3) and 2.9737 (18) Å, respectively]. The two independent molecules possess expected geometries that are similar, but exhibit slight torsional differences in the pendant arms [N1—C1—O1—C2 = −175.15 (14) and −174.11 (13)°, whilst C9—C10—O4—C11 = −174.72 (14) and −179.23 (14)° for *A* and *B*, respectively]. The formation of the ethoxy group in (I) is attributed to the reaction between the isothiocyanate formed and the ethanol present in the chloroform (0.5–1.0% by volume as a stabilizing agent), which is more reactive than the free amine.

The second minor fraction produces the structure of (II), which contains a novel heteroatomic fused-ring system. Both (I) and (II) contain the same ester functionalities which are geometrically virtually identical, including their orientations with respect to the ring systems [O2—C8—C7—C6 = −179.25 (4) and −177.09 (4)° for *A* and *B* in (I), and O1—C4—C3—C2 = 178.28 (2)° in (II)]. The ring system is composed of a pyridine ring fused in the 3 and 4 positions to cyclic thiadiazolo and thione moieties. Inspection of the bond lengths shows a breakdown in the aromaticity of the pyridyl ring to alternating single and double bonds, apart from N1—C5 [1.394 (3) Å compared to 1.329 (3) and 1.330 (3) Å in (I)] which is disturbed by the electronic structure of the five-membered ring. The fused rings approximate planarity, exhibiting an angle from one ring plane normal to the other of 1.72 (5)°. The imine nature of N2 is confirmed by the lack of any peaks in the difference map corresponding to a proton. The five-membered ring system in (II) has not been observed in the solid state before and a search of the Cambridge Structural Database (Allen & Kennard, 1993) shows the structure of 2,4-dimethyl-1,2,4-thiazolidine-3,5-dithione (Raston *et al.*, 1974) to be the closest for comparison, with similar bond lengths and angles for both compounds.

Experimental

Thiophosgene (0.23 ml, 3.0 mmol) was added slowly to a mixture of *tert*-butyl 2-(2-amino-3-pyridyloxy)acetate (1.34 g, 6.0 mmol) in chloroform (40 ml) and 0.4 *M* aqueous potassium carbonate (15 ml, 6.0 mmol). The mixture was heated under reflux for 5 d. After allowing to cool to room temperature, the mixture was transferred into a separating funnel, the organic layer separated and the aqueous layer extracted with chloroform (30 ml). The organic layer was dried over magnesium sulfate and concentrated *in vacuo* to afford a brown oil. The crude product was purified by column chromatography on silica gel, eluting with ethyl acetate–petroleum ether (30:70 *v*/*v*), to produce three fractions. Two of these fractions were recrystallized from methanol where fraction 1 corresponds to compound (II) (60.4 mg, 5%), R_f = 0.28, and fraction 3 corresponds to compound (I) (208.4 mg, 16%), R_f = 0.1. The fractions were additionally characterized by ^{1}H NMR, ^{13}C NMR and mass spectroscopy. (I), ^{1} NMR (300 MHz, CDCl$_3$): δ 8.88 (1H, *s*, NH), 8.10 (1H, *dd*, *J* = 1.8, 4.4 Hz, H$_{\rm pyr}$), 7.05 (2H, *m*, H$_{\rm pyr}$), 4.63 (2H, *q*, *J* = 21.3 Hz, CH$_2$), 4.60 (2H, *s*, CH$_2$), 1.49 [9H, s, (CH$_3$)$_3$], 1.39 (3H, *t*, *J* = 14.3 Hz, CH$_3$);^{13}C NMR (300 MHz, CDCl$_3$): δ 189.0 (0), 167.2 (0), 144.5 (0), 141.6 (0), 140.9 (1), 120.9 (1), 120.4 (1), 83.4 (0), 68.1 (2), 66.9 (2), 28.1 (3), 14.1 (3); LRMS (ESIPOS): *m*/*z* 313 (M + H)$^+$. (II), ^{1} NMR (400 MHz, CDCl$_3$): δ 8.14 (1H, *dd*, *J* = 1, 7.2 Hz, H$_{\rm pyr}$), 6.57 (1H, *dd*, *J* = 7.2, 7.2 Hz, H$_{\rm pyr}$), 6.49 (1H, *dd*, *J* = 0.7, 7.5 Hz, H$_{\rm pyr}$), 4.69 (2H, *s*, CH$_2$), 1.41 [9H, *s*, (CH$_3$)$_3$]; ^{13}C NMR (400 MHz, CDCl$_3$): δ 192.4 (0), 165.1 (0), 148.4 (0), 147.1 (0), 119.1 (0), 112.1 (1), 106.9 (1), 82.3 (0), 65.9 (2), 27.9 (3); LRMS (ESIPOS): m/z 299 $(M + H)^+$, 337 $(M + K)^+$, 339 $(M + CH_3CN)^+$.

Compound (I)

Crystal data

$C_{14}H_{20}N_2O_4S$
$M_r = 312.38$
Triclinic, $P\overline{1}$
$a = 10.661 (2)$ Å
$b = 11.852 (2)$ Å
$c = 13.501 (3)$ Å
$\alpha = 76.85 (3)^\circ$
$\beta = 81.35 (3)^\circ$
$\gamma = 72.12 (3)^\circ$
$V = 1575.1 (5)$ Å^3
$Z = 4$
$D_x = 1.317$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 20603 reflections
$\theta = 1.84$–26.0°
$\mu = 0.222$ mm^{-1}
$T = 150 (2)$ K
Block, colourless
0.2 × 0.1 × 0.1 mm

Data collection

KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (Blessing, 1995)
$T_{\min} = 0.879$, $T_{\max} = 0.986$
20603 measured reflections
6191 independent reflections
4949 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.0465$
$\theta_{\max} = 26^\circ$
$h = -13 \rightarrow 13$
$k = -14 \rightarrow 14$
$l = -16 \rightarrow 16$

Refinement

Refinement on F^2
$R(F) = 0.039$
$wR(F^2) = 0.123$
$S = 0.883$
6191 reflections
388 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1000P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.001$
$\Delta\rho_{\max} = 0.39$ e Å^{-3}
$\Delta\rho_{\min} = -0.39$ e Å^{-3}
Extinction correction: *SHELXL*
Extinction coefficient: 0.0076 (18)

Table 1
Selected geometric parameters (Å, °) for (I).

S1*A*—C1*A*	1.6656 (17)	O2*B*—C8*B*	1.3640 (19)
S1*B*—C1*B*	1.6614 (16)	O2*B*—C9*B*	1.4242 (19)
O1*A*—C1*A*	1.3414 (19)	O3*A*—C10*A*	1.2079 (19)
O1*A*—C2*A*	1.454 (2)	O3*B*—C10*B*	1.1975 (19)
O1*B*—C1*B*	1.3347 (19)	O4*A*—C10*A*	1.3304 (19)
O1*B*—C2*B*	1.4535 (19)	O4*A*—C11*A*	1.487 (2)
O2*A*—C8*A*	1.3693 (19)	O4*B*—C10*B*	1.335 (2)
O2*A*—C9*A*	1.4247 (19)	O4*B*—C11*B*	1.4868 (19)
C1*A*—O1*A*—C2*A*	119.30 (12)	O1*A*—C1*A*—S1*A*	125.32 (12)
C1*B*—O1*B*—C2*B*	118.52 (12)	O1*B*—C1*B*—N1*B*	109.94 (12)
C8*A*—O2*A*—C9*A*	116.91 (12)	O1*B*—C1*B*—S1*B*	125.60 (12)
C8*B*—O2*B*—C9*B*	116.49 (12)	N1*B*—C1*B*—S1*B*	124.46 (12)
C10*A*—O4*A*—C11*A*	120.91 (12)	O3*A*—C10*A*—O4*A*	126.45 (15)
C10*B*—O4*B*—C11*B*	120.00 (12)	O3*A*—C10*A*—C9*A*	124.82 (14)
C1*A*—N1*A*—C4*A*	123.66 (13)	O4*A*—C10*A*—C9*A*	108.74 (13)
C1*B*—N1*B*—C4*B*	122.44 (12)	O3*B*—C10*B*—O4*B*	127.06 (15)
N1*A*—C1*A*—O1*A*	109.31 (13)	O3*B*—C10*B*—C9*B*	124.12 (15)
N1*A*—C1*A*—S1*A*	125.37 (12)	O4*B*—C10*B*—C9*B*	108.82 (13)

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

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
N1*A*—H1*A*···N2*B*	0.86	2.06	2.920 (2)	173
N1*B*—H1*B*···O3*A*	0.86	2.14	2.9737 (18)	163

Compound (II)

Crystal data

$C_{12}H_{14}N_2O_3S_2$
$M_r = 298.37$
Monoclinic, $P2_1/c$
$a = 15.521 (3)$ Å
$b = 6.8270 (10)$ Å
$c = 13.574 (3)$ Å
$\beta = 100.06 (3)^\circ$
$V = 1416.2 (5)$ Å^3
$Z = 4$
$D_x = 1.399$ Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 12963 reflections
$\theta = 2.67$–27.43°
$\mu = 0.381$ mm^{-1}
$T = 150 (2)$ K
Plate, light brown
0.18 × 0.15 × 0.03 mm

Data collection

KappaCCD diffractometer
φ and ω scans
Absorption correction: multi-scan (Blessing, 1995)
$T_{\min} = 0.888$, $T_{\max} = 0.998$
12 963 measured reflections
3159 independent reflections
2304 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.0583$
$\theta_{\max} = 27.43^\circ$
$h = -19 \rightarrow 19$
$k = -8 \rightarrow 8$
$l = -17 \rightarrow 17$

Refinement

Refinement on F^2
$R(F) = 0.039$
$wR(F^2) = 0.122$
$S = 0.807$
3159 reflections
175 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1000P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.005$
$\Delta\rho_{\max} = 0.28$ e Å^{-3}
$\Delta\rho_{\min} = -0.29$ e Å^{-3}

Table 3
Selected geometric parameters (Å, °) for (II).

S1—N2	1.6593 (17)	N1—C1	1.388 (3)
S1—C12	1.712 (2)	N1—C5	1.394 (3)
S2—C12	1.653 (2)	N1—C12	1.393 (3)
O1—C4	1.355 (2)	N2—C5	1.308 (3)
O1—C6	1.426 (2)	C1—C2	1.341 (3)
O2—C7	1.196 (2)	C2—C3	1.434 (3)
O3—C7	1.326 (3)	C3—C4	1.355 (3)
O3—C8	1.481 (3)	C4—C5	1.437 (3)
N2—S1—C12	97.23 (9)	C3—C4—O1	127.14 (18)
C4—O1—C6	116.05 (15)	C3—C4—C5	119.79 (18)
C7—O3—C8	121.40 (17)	O1—C4—C5	113.06 (17)
C1—N1—C5	122.74 (17)	N2—C5—N1	116.92 (17)
C1—N1—C12	124.42 (17)	N2—C5—C4	125.76 (18)
C5—N1—C12	112.84 (16)	N1—C5—C4	117.30 (17)
C5—N2—S1	107.91 (14)	N1—C12—S2	126.63 (16)
C2—C1—N1	118.88 (18)	N1—C12—S1	105.06 (14)
C1—C2—C3	120.99 (19)	S2—C12—S1	128.30 (13)
C4—C3—C2	120.21 (19)		

H atoms were observed in the difference map, but were refined in calculated positions (C—H = 0.93–0.97 Å) using a riding model. No constraints or restraints were applied to the structural models, however, (I) was corrected for extinction effects using a refineable parameter where F_c is multiplied by a modified form of the overall scale factor.

For both compounds, data collection: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* (Hooft, 1998); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 1990).

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