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Ethopabate

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Key indicators

Single-crystal X-ray study
T = 203 K
Mean σ(C–C) = 0.002 Å
R factor = 0.037
wR factor = 0.086
Data-to-parameter ratio = 13.6

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

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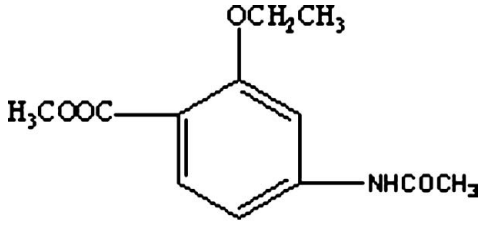
In the title compound (systematic name: methyl 4-acetamido-2-ethoxybenzoate), $C_{12}H_{15}O_4N$, intermolecular N—H···O and C—H···O hydrogen bonds stabilize the crystal packing. An intramolecular C—H···O hydrogen bond generates an *S*(6) motif.

Comment

Ethopabate can be used as an antiprotozoal drug and has a synergetic effect with some anticoccidial drugs. It is often used in conjunction with Nicarbazin, which results in an optimal effect for strengthening its active anticoccidial function. Treatment with toltrazuril, sulphaquinoxaline/pyrimethamine and amprolium/ethopabate has prevented mortality in chickens infected with field isolates of *Eimeria tenella*. Amprolium/ethopabate was the most effective drug in reducing lesions caused by parasites (Chapman, 1989).



(I)

In our work, *p*-aminosalicylic acid has been esterified, acetylated and alkylated to obtain the title compound, (I).

Selected geometric parameters of (I) are listed in Table 1 and the molecular structure is shown in Fig. 1. Atoms O3, C7 and N1 are almost coplanar with the benzene ring. Atom O2 deviates from the mean plane by 0.6092 (3) Å, and atoms C9 and C11 by −0.2053 (3) and 0.1744 (3) Å, respectively. Methyl atoms C8, C10 and C12 deviate from the plane by 0.6083 (3), −0.4626 (3) and 0.1778 (3) Å, respectively. There is an intramolecular C5—H5*A*···O4 hydrogen bond, which forms an *S*(6) motif (Bernstein *et al.*, 1995). In addition, there are two intermolecular hydrogen bonds, *viz*. a strong N—H···O hydrogen bond and a weak C—H···O hydrogen bond (Table 2 and Fig. 2).

Experimental

p-Aminosalicylic acid (26 g, 17 mmol) was added to a cooled mixture of 93% sulfuric acid (65 g, 61.7 mmol) and methanol (163 ml), and the solution was refluxed for 5–6 h. The cooled mass was added to a 5% aqueous solution of sodium carbonate (1300 ml) to yield 24.5 g of methyl *p*-aminosalicylate. This was added to absolute ethanol (50 ml) and heated to 313 K, then acetic anhydride (15.5 g, 15.2 mmol) was

added with the temperature maintained below 323 K. Water (500 ml) was added to the mixture, which was stirred for 1.5 h, filtered and the solid product dried at 330 K to yield 25.8 g methyl *p*-acetylamino-salicylate. This product was dissolved in acetone (300 ml), and potassium carbonate (17 g, 12.3 mmol) and ethyl sulfate (29 g, 18.8 mmol) were added. The mixture was refluxed for 24 h and then about 200 ml of the acetone was distilled. The residue was diluted with 600 ml water, filtered off and washed with water until neutral to give methyl 4-acetamido-2-ethoxybenzoate (24.8 g) with a yield of 84.5%. The product was recrystallized from ethyl acetate by slow evaporation of the solvent at room temperature over several days. Yellow crystals suitable for X-ray crystallography were formed.

Crystal data

$C_{12}H_{15}NO_4$
M_r = 237.25
Orthorhombic, *Pbca*
a = 15.110 (3) Å
b = 9.2097 (19) Å
c = 17.084 (4) Å
V = 2377.3 (9) Å^3
Z = 8
D_x = 1.326 Mg m^{-3}
Mo $K\alpha$ radiation
Cell parameters from 9021 reflections
θ = 2.4–22.0°
μ = 0.10 mm^{-1}
T = 203 (2) K
Block, colorless
0.30 × 0.30 × 0.30 mm

Data collection

Bruker SMART CCD area-detector diffractometer
ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.728, T_{max} = 0.971
9021 measured reflections
2091 independent reflections
1355 reflections with $I > 2\sigma(I)$
R_{int} = 0.048
θ_{max} = 25.0°
$h = -8 \rightarrow 17$
$k = -10 \rightarrow 10$
$l = -20 \rightarrow 20$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.037
$wR(F^2)$ = 0.086
S = 0.87
2091 reflections
154 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0439P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.19 e Å^{-3}
$\Delta\rho_{min}$ = −0.15 e Å^{-3}

Table 1
Selected bond lengths (Å).

O3—C2	1.3549 (19)	N1—C11	1.353 (2)
O3—C9	1.4390 (19)	O1—C7	1.2059 (19)
O4—C11	1.2222 (19)	C7—C1	1.491 (2)
O2—C7	1.328 (2)	C11—C12	1.497 (2)
O2—C8	1.446 (2)	C9—C10	1.499 (2)
C4—N1	1.412 (2)		

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

D—H···A	D—H	H···A	D···A	D—H···A
C5—H5A···O4	0.94	2.29	2.877 (2)	120
N1—H1···O4^{i}	0.87	2.00	2.8652 (18)	173
C8—H8B···O4^{ii}	0.97	2.56	3.505 (2)	166

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

All H atoms were placed in calculated positions and allowed to ride on their parent atoms, with U_{iso}(H) values set to 1.5U_{eq}(parent atom) for the Csp^3-bound H atoms and hydroxyl group O atoms, and

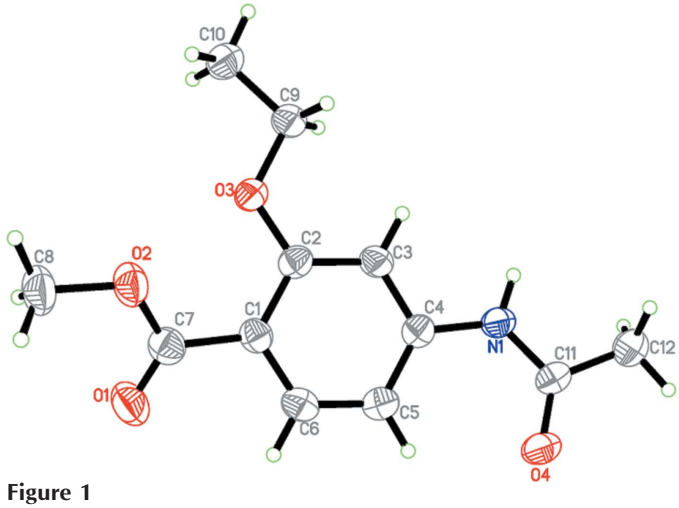


Figure 1
The molecular structure of (I), showing the atom-numbering scheme. Displacement ellipsoids are drawn at the 50% probability level.

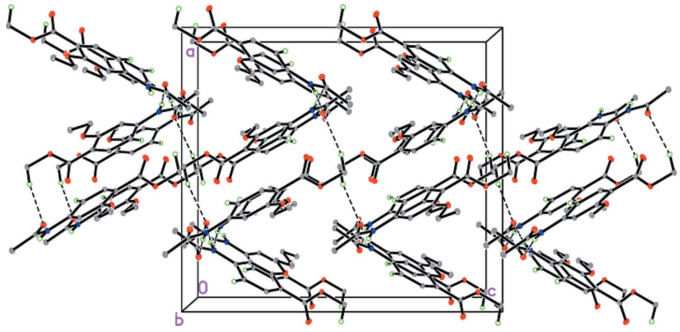


Figure 2
A packing diagram of the compound (I), viewed down the *b* axis. Hydrogen bonds are shown as dashed lines.

1.2U_{eq}(parent atom) for Csp^2-bound H atoms. The C—H distances were in the range 0.94–0.98 Å and the N—H distance was 0.87 Å.

Data collection: *SMART* (Bruker, 2000); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2000); software used to prepare material for publication: *SHELXTL*.

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