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5-Butyl-5-ethylbarbituric acid: a phase transition at low temperature

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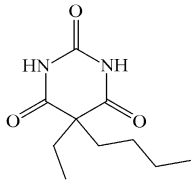
The room-temperature crystal structure of 5-butyl-5-ethylbarbituric acid (generally known as butobarbitone), $C_{10}H_{16}N_2O_3$, was reported in space group $C2/c$ [Bideau (1971). *C. R. Acad. Sci. Paris Ser. C*, **272**, 757–760]. A redetermination at 120 K using synchrotron radiation shows the space group at this temperature to be $P2_1/n$ and not $C2/c$. There are two crystallographically independent molecules in the asymmetric unit, but no solvent. Reported issues concerning possible disorder of the molecule are addressed; the butyl substituent of one of the molecules adopts an unusual conformation in being not fully extended. A subsequent re-collection at room temperature shows that the space group is indeed $C2/c$ ($A2/a$ with the axes selected in this report), and so the crystal structure undergoes a phase change upon cooling to 120 K.

Comment

Derivatives of barbituric acid, often called 'barbiturates', are a well known class of sedative drugs. The parent barbituric acid has no pharmacological activity but its 5,5-disubstituted derivatives do, in particular those with large substituents, for example, ethyl, amyl, butyl or cyclohexyl groups. The molecule must also possess hydrogen-bonding capability to be active, since it is this which facilitates binding of the drug to the acceptor site (Craven *et al.*, 1969).



(I)

Crystals of 5-butyl-5-ethylbarbituric acid, (I), hereafter referred to as 'butobarbitone', were obtained from a failed attempt to react ammonium carbonate with butobarbitone. The crystals were obtained as large plates but were very weakly diffracting, too weak even for a laboratory rotating-anode X-ray source. Data for this crystal were collected at Station 9.8 of the Synchrotron Radiation Source (SRS) at Daresbury Laboratory, Cheshire, England, *via* the EPSRC National X-ray Crystallography Service based in Southampton, England, where rotating-anode screening was carried out.

The structure of (I) at 120 K is presented in Fig. 1. At this temperature, the space group is $P2_1/n$; there are two crystallographically independent butobarbitone molecules in the asymmetric unit, which form an infinite hydrogen-bonded ribbon (Fig. 2 and Table 2). A packing diagram viewed along the *a* axis (Fig. 3) shows how the large butyl substituent and the smaller ethyl substituent act together to separate the hydrogen-bonded ribbons. With the exception of the butyl group torsion angles, discussed below (Table 1), molecular dimensions are unexceptional.

The two molecules in the asymmetric unit have some similar and some different characteristics. Firstly, despite the size of the displacement ellipsoids, which would tend to suggest that the butyl groups are disordered, attempts to model this disorder have brought no improvement. With a disorder model it proved necessary to use geometrical restraints and the final *R* factors are not significantly better than for the ordered model. Secondly, the geometry of the butyl substituent of one molecule is rather unusual; Fig. 4 shows two Newman projections (created with *PLATON*; Spek, 2003) along the C9—C10 and C19—C20 bonds. The positions of atoms C18 and C21 are staggered antiperiplanar with respect to each other, a perfectly normal observation for an alkyl chain. However, atoms C8 and C11 are *gauche*, with a C8—

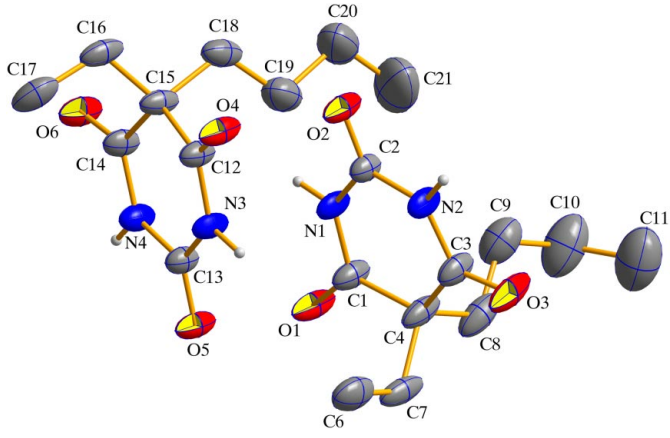


Figure 1
A displacement ellipsoid view (50% probability) of the asymmetric unit of (I). H atoms not involved in hydrogen bonding have been omitted for clarity.

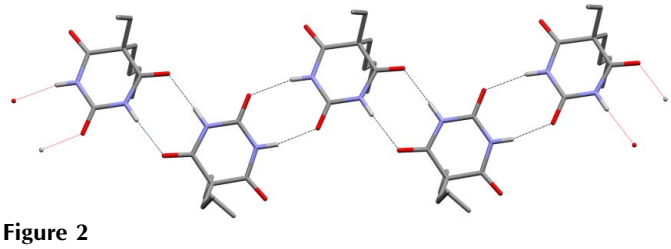


Figure 2
The hydrogen-bonding ribbon motif. H atoms not involved in hydrogen bonding have been omitted for clarity.

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C9—C10—C11 torsion angle of −72.5 (4)°, a rather less common observation for a butyl substituent on a planar ring. The Cambridge Structural Database (CSD; Version 5.26 plus one update; Allen, 2002), searched using *MOGUL* (Bruno *et al.*, 2004), contains only a relatively small number of entries that exhibit such geometry.

After the solution and refinement of the structure, a structural search of the CSD showed that the structure had already been published (CSD refcode ETBBAR; Bideau, 1971). However, it is not found by a search based on the unit-cell parameters. The room-temperature structure is in space group *C*2/*c*, with $Z' = 1$ and $Z = 8$, and the final *R* value is 0.094. The short structural discussion in the previous paper reports unusual geometry of the butyl substituent, which the author attributed to disorder he was unable to resolve. The final sentence of the paper states 'The study of this structure will be repeated at low temperature with the view of specifying the position of C54 [the terminal butyl C atom]'. No such repeated study was ever published, as far as we can tell.

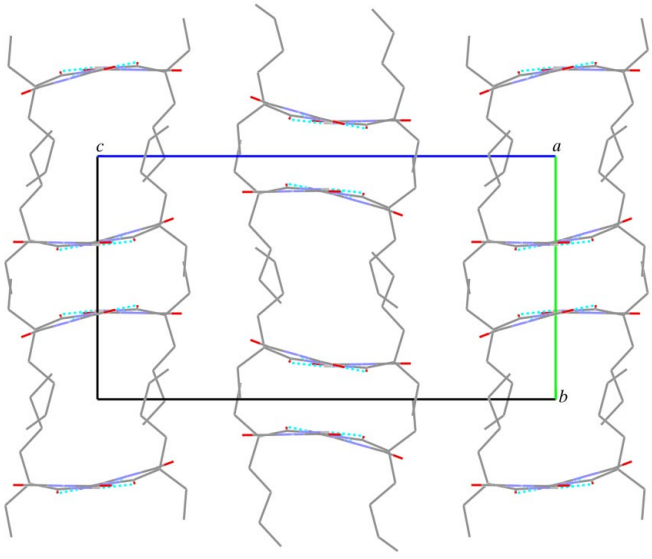

Figure 3
A projection along the *a* axis, showing the separation of the ribbons by the ethyl and butyl substituents. H atoms not involved in hydrogen bonding have been omitted for clarity.

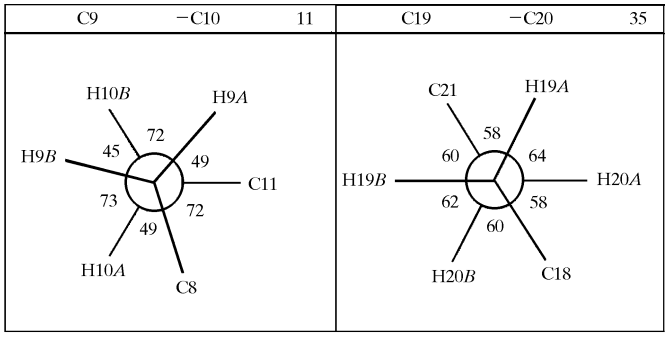

Figure 4
Two Newman projections, showing the difference in torsion angles between the butyl substituents of the two independent molecules.

In changing from room temperature to low temperature, the crystal structure has undergone a phase transition. At 120 K, there is nothing in the data to suggest that a centred unit cell is present. To verify the validity of the original report, we re-collected data at room temperature and found that the structure is indeed in space group *C*2/*c* (actually *A*2/*a* with the choice of axes made here, *a* and *c* being exchanged from those used in the room-temperature study), with $Z' = 1$ and $Z = 8$. This observation, although unusual, is not entirely surprising; we recently determined that barbituric acid dihydrate also undergoes a phase transition at low temperatures (Nichol & Clegg, 2005). Unlike barbituric acid dihydrate, here there is no significant change in the crystal packing between the room-temperature and 120 K structures. The two independent molecules at 120 K become symmetry-equivalent at room temperature, leading to the *C*-centring of the unit cell (with the *a* and *c* axes exchanged from our setting), which otherwise has similar cell parameters. This transition must involve torsional changes in the *n*-butyl groups and could lead to some minor disorder, as reported by Bideau (1971).

Experimental

Equimolar amounts of butobarbitone and ammonium carbonate were dissolved in distilled water and heated until boiling. Colourless crystals of (I) grew over a period of two days when the solution was left to stand at room temperature in a sealed sample vial.

Crystal data

$C_{10}H_{16}N_2O_3$
$M_r = 212.25$
Monoclinic, $P2_1/n$
$a = 10.2220$ (9) Å
$b = 11.0636$ (10) Å
$c = 20.9787$ (18) Å
$\beta = 96.728$ (1)°
$V = 2356.2$ (4) Å^3
$Z = 8$
$D_x = 1.197$ Mg m^{-3}
Synchrotron radiation
$\lambda = 0.6933$ Å
Cell parameters from 7041 reflections
$\theta = 2.3$–30.4°
$\mu = 0.09$ mm^{-1}
$T = 120$ (2) K
Plate, colourless
0.20 × 0.10 × 0.04 mm

Data collection

Bruker APEX2 CCD diffractometer
Thin-slice ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 2003)
$T_{min} = 0.842$, $T_{max} = 0.997$
17 357 measured reflections
4049 independent reflections
3432 reflections with $I > 2\sigma(I)$
$R_{int} = 0.033$
$\theta_{max} = 24.3°$
$h = -12 \rightarrow 12$
$k = -13 \rightarrow 13$
$l = -24 \rightarrow 24$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.062$
$wR(F^2) = 0.175$
$S = 1.05$
4049 reflections
288 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.097P)^2 + 1.2316P]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max} = 0.54$ e Å^{-3}
$\Delta\rho_{min} = -0.30$ e Å^{-3}

Table 1
Selected torsion angles (°).

C7—C4—C8—C9	177.00 (19)	C16—C15—C18—C19	−179.20 (18)
C4—C8—C9—C10	173.7 (2)	C15—C18—C19—C20	175.4 (2)
C8—C9—C10—C11	−72.4 (4)	C18—C19—C20—C21	−178.9 (3)

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

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1···O4	0.83 (2)	2.02 (3)	2.840 (2)	171 (2)
N2—H2···O5^{i}	0.86 (2)	2.00 (3)	2.838 (2)	166 (2)
N3—H3···O1	0.83 (3)	2.03 (3)	2.856 (2)	174 (2)
N4—H4···O2^{ii}	0.86 (3)	2.01 (3)	2.856 (2)	169 (2)

Symmetry codes: (i) $x+1, y, z$; (ii) $x-1, y, z$.

SADABS (Sheldrick, 2003) was used to correct for the synchrotron beam decay through frame scaling; absorption effects are small by comparison. All H atoms were identified in a difference map. CH_2 H atoms were then idealized (C—H = 0.99 Å) and refined as riding [U_{iso}(H) = 1.2U_{eq}(C)]. Methyl H atoms were positioned geometrically (C—H = 0.98 Å) and refined as riding [U_{iso}(H) = 1.5U_{eq}(C)], with free rotation about the C—C bond. N-bound H atoms were refined with unconstrained coordinates [U_{iso}(H) = 1.2U_{eq}(N)]; N—H distances range from 0.83 (3) to 0.86 (3) Å.

Data collection: *APEX2* (Bruker, 2003); cell refinement and data reduction: *SAINT* (Bruker, 2001); program(s) used to solve and refine structure: *SHELXTL* (Sheldrick, 2001); molecular graphics: *DIAMOND* (Brandenburg & Putz, 2004) and *MERCURY* (Bruno *et al.*, 2002); software used to prepare material for publication: *SHELXTL* and local programs.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: SK1827). Services for accessing these data are described at the back of the journal.

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