

Conformational isomerism in 3-(*Z*)-isobutylidene-1-acetylpiperazine-2,5-dione

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Key indicators

Single-crystal X-ray study

T = 295 K

Mean $\sigma(\text{C}-\text{C}) = 0.004 \text{ \AA}$

R factor = 0.053

wR factor = 0.188

Data-to-parameter ratio = 14.2

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

The title compound, $\text{C}_{10}\text{H}_{14}\text{N}_2\text{O}_3$, (I), is a key intermediate in the synthesis of the cyclic dehydropeptide albonoursin, which has been found to exhibit useful biological and pharmacological properties. It crystallizes with two molecules in the asymmetric unit with different conformational structures. The methylpropylidene side chain is found to be in the *Z* configuration about the $\text{C}=\text{C}$ double bond for both molecules.

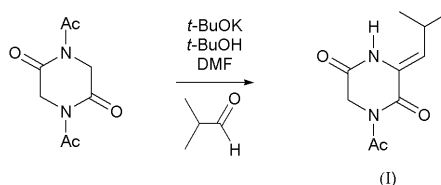
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Comment

Several cyclic dehydropeptides, such as roquefortine (Barrow *et al.*, 1979; Chen & Joullie, 1998) and albonoursin (Shin *et al.*, 1980) exhibit biological and pharmacological properties. In particular, interest in the latter has led to the syntheses and assignment of configurations of albonoursin and its geometric isomers (Villemin & Ben Alloum, 1990; Shin *et al.*, 1977). The title monoalkylidene piperazine-2,5-dione, (I), is a key intermediate in the synthesis of albonoursin. The solution structure determination of (I) has relied on the assignment of the configuration of the double bond by NMR spectroscopy (Shin *et al.*, 1977; Gallina & Liberatori, 1974). We report here the first solid-state structural elucidation of (I), which allows direct correlation between the solution and solid-state structures for assignment of the double-bond geometry. In addition, this represents one of the first accounts of a solid-state structure for a monoalkylidene piperazine-2,5-dione. Compound (I) was obtained by a modification of a procedure (Gallina & Liberatori, 1973) where 1,3-diacetylpiperazine-2,5-dione (Marcuccio & Elix, 1984) was condensed with 2-methylpropionaldehyde in the presence of a strong base, namely potassium *tert*-butoxide.



The crystal structure of (I) contains two independent molecules (*Ia* and *Ib*) in the asymmetric unit, the structures of which are shown in Fig. 1. In both molecules, the methylpropylidene side chain adopts a *Z* configuration about the double bond, confirming the NMR assignment in the solution state. Both molecules associate as pairs of centrosymmetrically related molecules through classical $R_2^2(8)$ (Bernstein *et al.*, 1995) $\text{N}-\text{H}\cdots\text{O}$ hydrogen-bonding interactions between N2 and O3 [for molecule *Ia*: $\text{H}\cdots\text{O}3\text{A}^{\text{i}} = 2.00 \text{ \AA}$, $\text{N}2\text{A}^{\text{i}}\cdots\text{O}3\text{A}^{\text{i}} =$

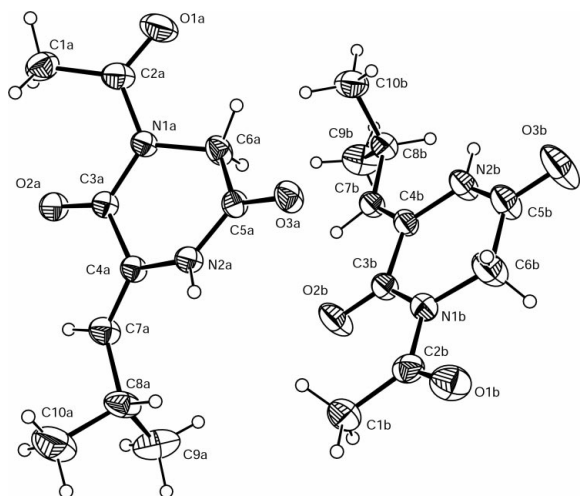


Figure 1
ORTEP-3 (Farrugia, 1997) plot, showing the atomic numbering scheme for molecules (1a) and (1b). Displacement ellipsoids for non-H atoms are drawn at the 30% probability level.

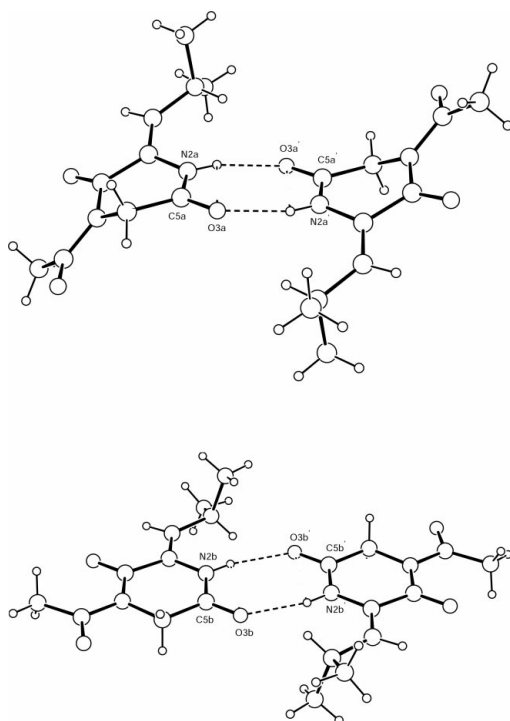


Figure 2
ORTEP-3 plot showing the hydrogen-bonding arrangement for molecules (1a) (above) and (1b) (below).

2.836 (2) Å and N2A—H···O3Aⁱ = 167°; symmetry code: (i) $-x, 2-y, 2-z$; for molecule 1b: H···O3Bⁱⁱⁱ = 2.07 Å, N2B···O3Bⁱⁱⁱ = 2.908 (3) Å and N2B—H···O3Bⁱⁱⁱ = 167°; symmetry code: (ii) $-x, 1-y, 1-z$] (Fig. 2). This hydrogen-bonding feature is observed in the structures of other piperazinedione systems (Ongania *et al.*, 1985; Ajo *et al.*, 1985).

The piperazinedione ring in molecule (1a) adopts a puckered conformation with the peripheral isopropyl and keto substituents lying well out of the plane defined by the inter-

molecular N—H···O hydrogen bonding. In the crystal lattice (Fig. 3), the dimers of (1a) lie approximately in the *ac* plane at $b \sim 0$, with the long axis of the dimer oriented along the crystallographic *a* axis. In contrast, the conformational structure of (1b) is essentially planar for all non-H atoms other than the C9 and C10 methyl groups. As in (1a), the dimers of (1b) lie approximately in the *ac* plane but at $b \sim \frac{1}{2}$, with the long axis oriented along the *c* axis. The bond lengths for both molecules (Table 1) are in accord with conventional values (Allen *et al.*, 1987), with differences between corresponding values in the two molecules no greater than 0.01 Å. Greater diversity is apparent in the bond angles, with the greatest differences observed for the angles about N1 and C6.

Experimental

Potassium *tert*-butoxide (0.567 g, 5.053 mmol) in *tert*-butanol (10 ml, 0.105 mol) was added to a stirred solution of 2-methylpropionaldehyde (1.80 ml, 0.020 mol) and 1,4-diacetyl-piperazine-2,5-dione (1.054 g, 5.328 mmol) in dry DMF (10.50 ml, 0.136 mol) at 273 K. The mixture was stirred at room temperature for 24 h and worked up as described elsewhere (Gallina & Liberatori, 1973). The crude product was recrystallized (ethyl acetate/hexane), giving (I) as white crystals (263 mg, 24%). Colourless crystals of (I) [m.p. 419.9–420.3 K; literature 419.2–420.2 K (Gallina & Liberatori, 1973, 1974) and 423.2–424.2 K (Shin *et al.*, 1977)] were isolated by slow evaporation of a hexane–ethyl acetate solution of (I). Analysis found: C 57.41, H 6.77, N 13.45%; calculated for C₁₀H₁₄N₂O₃: C 57.13, H 6.71, N 13.33%. ν_{\max} (KBr)/cm⁻¹: 3390, 3196 (NH), 1687, 1650, (CO), 1636, (C=C). δ_H (200 MHz, CDCl₃, p.p.m.): 8.10 (1H, *brs*, NH), 6.18 (1H, *d*, $J_{7,8} = 10$ Hz, 7-H), 4.44 (2H, *s*, 6-H), 2.75–2.60 (1H, *m*, 8-H), 2.61 (3H, *s*, 1-H), 1.10 (6H, *d*, $J_{9/10,8} = 6.5$ Hz, 9-H, 10-H). δ_C (50 MHz, CDCl₃, p.p.m.): 172.7 (C2), 164.2 (C5), 160.2 (C3), 131.6 (C4), 124.5 (C7), 46.0 (C6), 27.2 (C9 and C10), 25.9 (C8), 22.0 (C1). ESMS⁺: 209 (MH⁺, 100%), 233 (MNa⁺, 100%).

Crystal data

C₁₀H₁₄N₂O₃
 $M_r = 210.23$
 Triclinic, $P\bar{1}$
 $a = 10.7310$ (18) Å
 $b = 10.827$ (3) Å
 $c = 9.7916$ (14) Å
 $\alpha = 95.607$ (17)°
 $\beta = 94.680$ (13)°
 $\gamma = 76.484$ (17)°
 $V = 1098.8$ (4) Å³

$Z = 4$
 $D_x = 1.271$ Mg m⁻³
 Mo K α radiation
 Cell parameters from 25 reflections
 $\theta = 19.4$ – 20.0°
 $\mu = 0.10$ mm⁻¹
 $T = 295$ K
 Prism, colourless
 0.60 × 0.50 × 0.30 mm

Data collection

Rigaku AFC-7R diffractometer
 ω – 2θ scans
 Absorption correction: none
 4100 measured reflections
 3872 independent reflections
 2691 reflections with $I > 2\sigma(I)$
 $R_{\text{int}} = 0.019$

$\theta_{\max} = 25.0^\circ$
 $h = 0 \rightarrow 12$
 $k = -12 \rightarrow 12$
 $l = -11 \rightarrow 11$
 3 standard reflections
 every 150 reflections
 intensity decay: 1.3%

Refinement

Refinement on F^2
 $R[F^2 > 2\sigma(F^2)] = 0.053$
 $wR(F^2) = 0.188$
 $S = 1.09$
 3872 reflections
 272 parameters
 H-atom parameters constrained

$w = 1/[\sigma^2(F_o^2) + (0.1241P)^2 + 0.0666P]$
 where $P = (F_o^2 + 2F_c^2)/3$
 $(\Delta/\sigma)_{\max} < 0.001$
 $\Delta\rho_{\max} = 0.26$ e Å⁻³
 $\Delta\rho_{\min} = -0.26$ e Å⁻³
 Extinction correction: SHELXL97
 Extinction coefficient: 0.032 (7)

Table 1
Selected geometric parameters (Å, °).

O1A—C2A	1.210 (3)	O1B—C2B	1.214 (4)
O2A—C3A	1.203 (3)	O2B—C3B	1.214 (3)
O3A—C5A	1.233 (3)	O3B—C5B	1.224 (4)
N1A—C2A	1.408 (3)	N1B—C6B	1.458 (4)
N1A—C3A	1.394 (3)	N1B—C2B	1.417 (3)
N1A—C6A	1.463 (3)	N1B—C3B	1.380 (3)
N2A—C4A	1.408 (3)	N2B—C5B	1.328 (4)
N2A—C5A	1.335 (3)	N2B—C4B	1.406 (3)
C1A—C2A	1.484 (4)	C1B—C2B	1.483 (4)
C3A—C4A	1.501 (3)	C3B—C4B	1.495 (3)
C4A—C7A	1.332 (3)	C4B—C7B	1.325 (3)
C5A—C6A	1.494 (3)	C5B—C6B	1.485 (4)
C7A—C8A	1.500 (3)	C7B—C8B	1.505 (3)
C8A—C10A	1.513 (4)	C8B—C9B	1.507 (4)
C8A—C9A	1.519 (5)	C8B—C10B	1.525 (4)
C2A—N1A—C3A	124.14 (18)	C2B—N1B—C3B	125.08 (19)
C2A—N1A—C6A	117.28 (17)	C2B—N1B—C6B	112.6 (2)
C3A—N1A—C6A	118.47 (16)	C3B—N1B—C6B	122.3 (2)
C4A—N2A—C5A	123.42 (17)	C4B—N2B—C5B	125.4 (2)
O1A—C2A—N1A	118.1 (3)	O1B—C2B—N1B	117.6 (2)
O1A—C2A—C1A	122.7 (3)	O1B—C2B—C1B	121.3 (2)
N1A—C2A—C1A	119.22 (19)	N1B—C2B—C1B	121.1 (3)
N1A—C3A—C4A	114.57 (17)	N1B—C3B—C4B	117.91 (18)
O2A—C3A—N1A	123.49 (19)	O2B—C3B—N1B	122.0 (2)
O2A—C3A—C4A	121.94 (18)	O2B—C3B—C4B	120.1 (2)
N2A—C4A—C3A	117.33 (17)	N2B—C4B—C3B	117.90 (19)
N2A—C4A—C7A	123.57 (19)	N2B—C4B—C7B	122.30 (19)
C3A—C4A—C7A	118.96 (19)	C3B—C4B—C7B	119.80 (19)
O3A—C5A—N2A	123.26 (19)	O3B—C5B—N2B	123.4 (3)
N2A—C5A—C6A	115.91 (18)	N2B—C5B—C6B	118.8 (3)
O3A—C5A—C6A	120.83 (18)	O3B—C5B—C6B	117.8 (3)
N1A—C6A—C5A	113.11 (17)	N1B—C6B—C5B	117.3 (3)
C4A—C7A—C8A	128.6 (2)	C4B—C7B—C8B	127.71 (19)
C7A—C8A—C9A	109.8 (2)	C7B—C8B—C9B	111.14 (19)
C7A—C8A—C10A	110.1 (3)	C7B—C8B—C10B	110.18 (19)
C9A—C8A—C10A	109.3 (2)	C9B—C8B—C10B	110.4 (2)

H atoms were constrained in the riding-model approximation, with C—H distances set at 0.95 Å and N—H set at 0.85 Å. U_{iso} values for the H atoms were set at $1.2U_{\text{eq}}$ of the parent atom.

Data collection: *MSC/AFC-7 Diffractometer Control Software* (Molecular Structure Corporation, 1999); cell refinement: *MSC/AFC-7 Diffractometer Control Software*; data reduction: *TEXSAN for Windows* (Molecular Structure Corporation, 1997–2001); program(s) used to solve structure: *TEXSAN for Windows*; program(s) used to refine structure: *TEXSAN for Windows* and *SHELXL97* (Sheldrick, 1997); molecular graphics: *PLATON* (Spek, 2001) and *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *TEXSAN for Windows* and *PLATON*.

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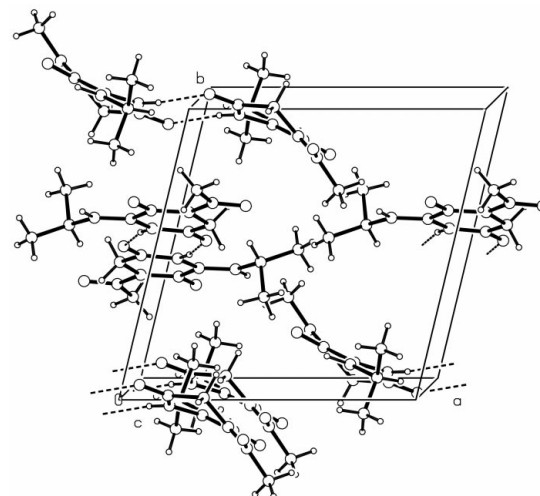


Figure 3
Crystal packing diagram for (I), viewed down the *c* axis with *a* horizontal and *b* vertical.

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