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2,2,5,5,8,8-Hexamethyl-2,3,5,6,7,8-hexahydroimidazo[1,2-*a*]pyrazine-3,6-dione, a bicyclic product of *α*-aminoisobutyric acid condensation

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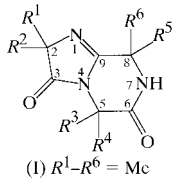
The title compound, $C_{12}H_{19}N_3O_2$, is an unusual product of silica-catalyzed intermolecular condensation of *α*-aminoisobutyric acid. The molecule has three types of C—N bonds: a double bond, a *cis*-amide bond and single bonds, two of which are typical and two having intermediate lengths due to *π*-electron delocalization between C═N and C═O groups. The *cis*-amide moieties interact to form dimers *via* hydrogen bonds which stack in parallel layers.

Comment

The large family of imidazo[1,2-*a*]pyrazines (Basiuk, 1997) includes a few examples of rather exotic bicyclic amidine-type compounds composed of three *α*-amino acid residues.

The formation of this bicyclic amidine system was first reported more than three decades ago (Jones *et al.*, 1963, 1965). During subsequent years, several groups worked on different aspects of the bicyclic amidine chemistry (Titlestad, 1972; Ali *et al.*, 1973; Rothe *et al.*, 1979; Ali & Khatun, 1985; Ali, 1990; Yamada *et al.*, 1993; Saviano *et al.*, 1996). As a result, approximately ten compounds of this class have been reported. The prerequisites of their synthesis have been (1)



(I) R^1–R^6 = Me

the use of tri- to pentapeptide precursors, in some cases along with rather drastic activating reagents such as phosphorus pentachloride or thionyl chloride (Titlestad, 1972; Ali *et al.*, 1973; Ali & Khatun, 1985; Ali, 1990); and (2) the inclusion of sterically hindered *α*-amino acids into molecules of the peptide starting material; such acids include *α*-aminoisobutyric acid (Titlestad, 1972; Ali *et al.*, 1973; Ali & Khatun, 1985; Ali, 1990) and *α*,*α*-diisopropylglycine (Yamada *et al.*, 1993; Saviano *et al.*, 1996). X-ray structures of these compounds are apparently only known for the bicyclic amidine with $R^{1,2,5}$ = ^{i}Pr and $R^{3,4,6}$ = H (Saviano *et al.*, 1996).

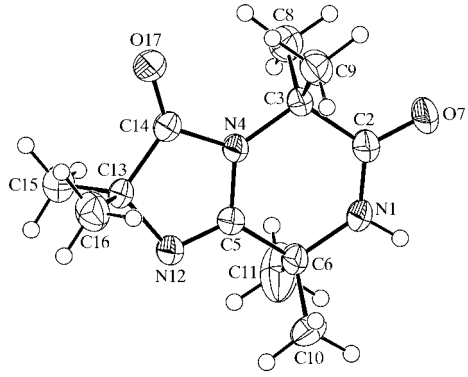


Figure 1
The molecular structure of (I) drawn with 50% probability displacement ellipsoids.

Our recent studies of amino acid pyrolysis products by gas chromatography–FT IR spectroscopy–mass spectrometry revealed that a direct formation of the bicyclic amidines is possible when simple amino acids (*e.g.* *α*-aminoisobutyric acid, alanine, valine, norvaline and leucine) are pyrolyzed at about 773 K (Basiuk, 1998; Basiuk & Navarro-González, 1998; Basiuk *et al.*, 1998*a*), or even at 473–573 K but in the presence of silica gel as a dehydration catalyst (Basiuk & Navarro-González, 1997; Basiuk *et al.*, 1998*b*). In the latter case, bicyclic amidine yields can reach the 1–10% level. Although the amidines form along with many other pyrolysis products, it was possible to separate the *α*-aminoisobutyric acid derivative (R^{1-6} = Me), (I), by means of recrystallization. In this paper we report the results of its X-ray diffraction analysis.

A view of (I) is shown in Fig. 1. In many regards, this compound is similar to the triisopropyl analog reported by Saviano *et al.* (1996). In particular, the double bond lengths are: 1.235 (2) (C2—O7), 1.215 (2) (C14—O17) and 1.271 (2) Å (C5—N12) [*versus* 1.233 (2), 1.215 (2) and 1.276 (2) Å for the triisopropyl analog]. Of the other C—N bonds existing in the molecule, N1—C2 is typical for *cis*-amides [1.331 (2) Å]; N1—C6, N4—C3 and N12—C13 are common single C—N bonds [1.461 (2), 1.480 (2) and 1.477 (2) Å, respectively]. The other two, N4—C5 and N4—C14, exhibit intermediate values [1.397 (2) and 1.390 (2) Å, respectively], thus pointing to an evident *π*-electron delocalization between the C5—N12 and C14—O17 double bonds.

The five-membered ring is planar [0.009 (2) Å], the six-membered ring deviates up to 0.097 (2) Å (C6) and has a slight boat conformation [Cremer & Pople (1975) puckering parameters: Q = 0.143 (2) Å, θ = 112.6 (8), φ = 125.5 (8)°].

Unlike the triisopropyl analog, crystals of the present bicyclic amidine do not display any crystallographic disorder. This is likely due to conformational rigidity of the *α*,*α*-di-

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methyl fragments in the α-aminoisobutyric residues, as compared to their isopropyl counterparts.

As might be expected, the present crystal structure includes a pattern of hydrogen bonding (Fig. 2) similar to that described by Saviano *et al.* (1996). Interaction between *cis*-amide moieties gives rise to the formation of hydrogen-bonded dimers: N1···O7 2.929 (2) Å, N1—H1···O7 161.5 (11)°. The dimers form parallel layers. There is also possible intramolecular bonding between O17 and methyl C8 and C9 groups due to weak C—H···O interactions: C8···O17 3.191 (3) Å and C8—H8*C*···O17 119.1 (8)°; C9···O17 3.116 (3) Å and C9—H9*A*···O17 121.2 (7)°.

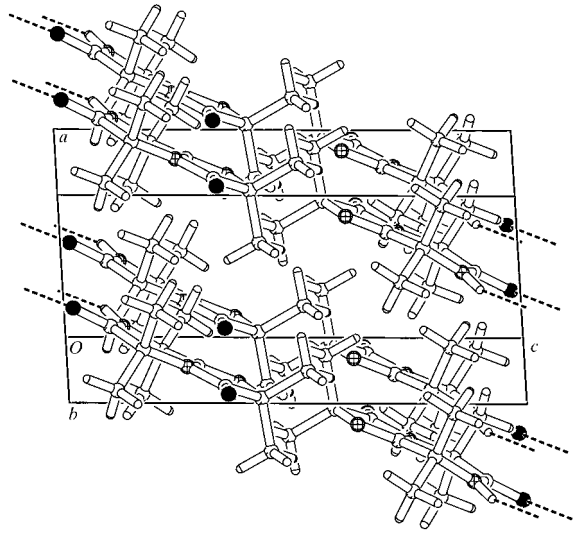

Figure 2
Packing diagram showing hydrogen bonding.

Experimental

α-Aminoisobutyric acid, silica gel and solvents were used without further purification. Crystalline α-aminoisobutyric acid (4 g) was heated in the presence of silica gel (10 g) as dehydration catalyst in a continuously evacuated round-bottom flask under 10^{-1} Torr (1 Torr = 133.322 Pa) at 503–513 K. During heating, the amino acid sublimed, reacted with the silica gel, and the resulting products along with unrelated amino acid condensed in the unheated flask neck. To increase conversion of the starting reagent into condensation products, the flask was opened and the sublimate was returned to the bottom of the flask to again make contact with the silica gel, and the procedure was repeated twice more. This triple sublimation took, in total, about 8 h. Crude sublimate was removed from the flask neck and washed with chloroform (3 × 20 ml). The resulting solution was evaporated to produce 0.27 g of an amorphous, rusty brown substance. Fourfold recrystallization from methanol gave the bicyclic condensation product (I) (yield 23 mg, 0.75%).

Crystal data

$C_{12}H_{19}N_3O_2$	$Z = 2$
$M_r = 237.30$	$D_x = 1.233$ Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
$a = 5.9020$ (10) Å	Cell parameters from 20 reflections
$b = 8.628$ (2) Å	$\theta = 20.03$–$21.42°$
$c = 12.949$ (2) Å	$\mu = 0.086$ mm^{-1}
$\alpha = 95.020$ (10)°	$T = 289$ (2) K
$\beta = 93.340$ (10)°	Needle, colorless
$\gamma = 102.450$ (10)°	0.40 × 0.30 × 0.20 mm
$V = 639.4$ (2) Å^3	

Data collection

Siemens *P*4 diffractometer	$h = -7 \rightarrow 1$
ω scans	$k = -10 \rightarrow 10$
2941 measured reflections	$l = -15 \rightarrow 15$
2234 independent reflections	3 standard reflections
1621 reflections with $I > 2\sigma(I)$	every 97 reflections
$R_{int} = 0.028$	intensity decay: 0.02%
$\theta_{max} = 25°$	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0495P)^2 + 0.1584P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)] = 0.042$	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2) = 0.116$	$\Delta\rho_{max} = 0.17$ e Å^{-3}
$S = 1.013$	$\Delta\rho_{min} = -0.22$ e Å^{-3}
2234 reflections	
167 parameters	
H atoms: see below	

The H1(—N1) atom was constrained to lie on an external bisector of C2—N1—C6, with the N—H distance free to refine and U_{iso}(H1) = 1.2U_{eq}(N1). CH_3 groups were allowed to rotate but not tip, and C—H distances were allowed to refine (same shifts applied along all three C—H bonds in each group), with $U_{iso}(H_{methyl}) = 1.5U_{eq}(C_{methyl})$.

Data collection: *XSCANS* (Siemens, 1994); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *PLATON*99 (Spek, 1999); software used to prepare material for publication: *PLATON*99.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: DA1114). Services for accessing these data are described at the back of the journal.

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