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Key indicators

 Single-crystal X-ray study
 T = 293 K
 Mean $\sigma(\text{C}-\text{C}) = 0.005 \text{ \AA}$
 R factor = 0.041
 wR factor = 0.110
 Data-to-parameter ratio = 9.5

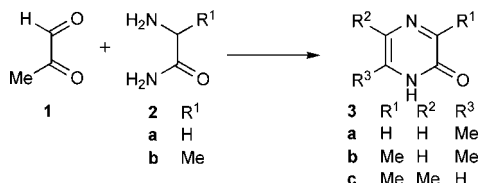
 For details of how these key indicators were
 automatically derived from the article, see
<http://journals.iucr.org/e>.

 Surprising orientation in ring synthesis of
 3,5-dimethylpyrazin-2(1H)-one

 The reaction of pyruvaldehyde with alaninamide gave the title
 compound, $\text{C}_6\text{H}_8\text{N}_2\text{O}$, and not the anticipated 3,6-dimethyl-
 pyrazin-2-one.

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Comment

 One of the standard methods to prepare pyrazin-2-ones is by
 the condensation of a 1,2-dicarbonyl compound with an α -
 amino acid amide (Garg *et al.*, 2002; Jones, 1949; Karmas &
 Spoerri, 1952). For example, pyruvaldehyde (1) (see scheme)
 reacts with glycineamide (2a) to give 6-methylpyrazin-2-one
 (3a) (Yates *et al.*, 1995). The orientation in this ring synthesis
 represents the combination of the amide N atom with the
 ketone carbonyl and of the amine group with the aldehyde
 carbonyl group. In the course of our studies on the dipolar
 cycloaddition reactions of 3-oxidopyraziniums (Kiss *et al.*,
 1987; Allway *et al.*, 1990; Yates *et al.*, 1995), we required 3,6-
 dimethylpyrazin-2-one (3b) and assumed that, by analogy, it
 would result from a reaction of pyruvaldehyde with alani-
 namide (2b).

 Reaction of pyruvaldehyde with alaninamide produced a
 pyrazinone, as anticipated, but standard spectroscopic analysis
 could not unambiguously confirm the structure of the product.
 For example, ^1H NMR spectroscopy revealed two three-
 hydrogen singlet signals corresponding to the two methyl
 groups at δ 2.22 and 2.41 and a one-hydrogen singlet signal for
 the ring C-hydrogen at δ 6.88, but these data are consistent
 both with the anticipated structure (3b) and also with its
 isomer, 3,5-dimethylpyrazin-2-one (3c).

 Suitable crystals were grown from ethyl acetate and an
 X-ray analysis carried out. This showed the product to be 3,5-
 dimethylpyrazin-2(1H)-one (3c) (Fig. 1). Currently, we have
 no explanation for this unexpected regioselectivity; however,
 the moral from this result is that, for each pyrazinone
 synthesized by this method, unambiguous proof of structure
 must be sought.

Experimental

 A solution of L-alaninamide hydrochloride (95%, 0.26 g, 2 mmol) in
 methanol (1.0 ml) was cooled to 243 K and to it was added a solution

of pyruvaldehyde (40%, 0.36 g, 2 mmol) in methanol (0.5 ml) also precooled to 243 K. Next, with stirring, aqueous sodium hydroxide solution (12.5 M, 0.50 ml, 2.5 mmol) was added dropwise while the temperature was maintained below 263 K. The mixture was allowed to stand at 268 K for 2 h, then at r.t. for 3 h. To the mixture was added hydrochloric acid (12 M, 0.5 ml) followed by solid NaHCO₃ (0.25 g) to neutralize excess acid, and the whole was evaporated to dryness in a vacuum at 363 K. The residue was extracted with three portions (2 ml) of boiling chloroform. Evaporation of the extract left a yellow solid (205 mg, 83%). This was recrystallized from ethyl acetate (2 ml) to give colourless crystals (58 mg, 24%; m.p. 417–419 K).

Crystal data

C ₆ H ₈ N ₂ O	$D_x = 1.261 \text{ Mg m}^{-3}$
$M_r = 124.14$	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 12419 reflections
$a = 4.009 (10) \text{ \AA}$	$\theta = 2.3\text{--}24.9^\circ$
$b = 14.59 (3) \text{ \AA}$	$\mu = 0.09 \text{ mm}^{-1}$
$c = 11.59 (3) \text{ \AA}$	$T = 293 (2) \text{ K}$
$\beta = 105.25 (10)^\circ$	Needle, colourless
$V = 654 (3) \text{ \AA}^3$	$0.6 \times 0.1 \times 0.1 \text{ mm}$
$Z = 4$	

Data collection

Rigaku R-Axis diffractometer	$R_{\text{int}} = 0.045$
φ scans	$\theta_{\text{max}} = 24.9^\circ$
Absorption correction: none	$h = 0 \rightarrow 4$
12419 measured reflections	$k = 0 \rightarrow 17$
839 independent reflections	$l = -13 \rightarrow 13$
724 reflections with $I > 2\sigma(I)$	

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0505P)^2 + 0.2114P]$
$R[F^2 > 2\sigma(F^2)] = 0.041$	where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2) = 0.110$	$(\Delta/\sigma)_{\text{max}} < 0.001$
$S = 1.10$	$\Delta\rho_{\text{max}} = 0.18 \text{ e \AA}^{-3}$
839 reflections	$\Delta\rho_{\text{min}} = -0.15 \text{ e \AA}^{-3}$
88 parameters	
H atoms treated by a mixture of independent and constrained refinement	

H atoms bonded to C were included in calculated positions using the riding model, with C–H distances of 0.93 and 0.96 Å and with $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{C})$ for methyl H atoms and $1.2U_{\text{eq}}(\text{C})$ for the other H atoms; atom H1, attached to N1, was found by difference Fourier methods and refined isotropically.

Data collection: *MSC Diffractometer Control Software* (Molecular Structure Corporation, 1992); cell refinement: *DENZO* (Otwinowski & Minor, 1987); data reduction: *DENZO*; program(s) used to solve

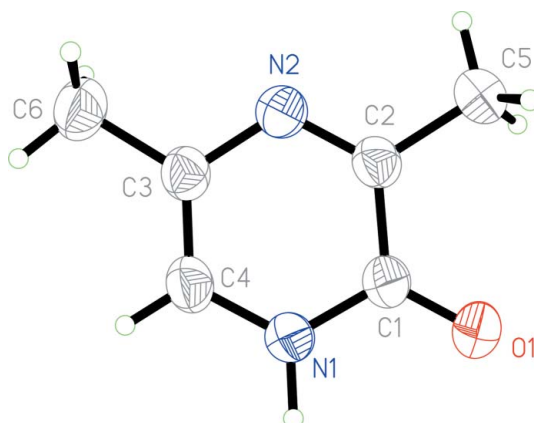


Figure 1 The molecular structure of (3c), with displacement ellipsoids drawn at the 50% probability level.

structure: *SHELXS86* (Sheldrick, 1985); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Bruker, 2001); software used to prepare material for publication: *TEXSAN* (Molecular Structure Corporation, 1995).

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supporting information

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Surprising orientation in ring synthesis of 3,5-dimethylpyrazin-2(1*H*)-one

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3,5-dimethylpyrazin-2(1*H*)-one*Crystal data*

$C_6H_8N_2O$

$M_r = 124.14$

Monoclinic, $P2_1/n$

Hall symbol: $-P\ 2_1n$

$a = 4.009$ (10) Å

$b = 14.59$ (3) Å

$c = 11.59$ (3) Å

$\beta = 105.25$ (10)°

$V = 654$ (3) Å³

$Z = 4$

$F(000) = 264$

$D_x = 1.261$ Mg m⁻³

Melting point = 144–146 K

Mo $K\alpha$ radiation, $\lambda = 0.71069$ Å

Cell parameters from 12419 reflections

$\theta = 2.3$ – 24.9 °

$\mu = 0.09$ mm⁻¹

$T = 293$ K

Needle, colourless

$0.6 \times 0.1 \times 0.1$ mm

Data collection

Rigaku R-AXIS

diffractometer

Radiation source: Rigaku rotating anode

Graphite monochromator

5 and 6° ϕ scans

12419 measured reflections

839 independent reflections

724 reflections with $I > 2\sigma(I)$

$R_{int} = 0.05$

$\theta_{max} = 24.9$ °, $\theta_{min} = 2.3$ °

$h = 0 \rightarrow 4$

$k = 0 \rightarrow 17$

$l = -13 \rightarrow 13$

Refinement

Refinement on F^2

Least-squares matrix: full

$R[F^2 > 2\sigma(F^2)] = 0.041$

$wR(F^2) = 0.110$

$S = 1.10$

839 reflections

88 parameters

0 restraints

Primary atom site location: structure-invariant

direct methods

Secondary atom site location: difference Fourier map

Hydrogen site location: inferred from neighbouring sites

H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0505P)^2 + 0.2114P]$

where $P = (F_o^2 + 2F_c^2)/3$

$(\Delta/\sigma)_{max} < 0.001$

$\Delta\rho_{max} = 0.18$ e Å⁻³

$\Delta\rho_{min} = -0.15$ e Å⁻³

Special details

Geometry. All e.s.d.'s (except the e.s.d. in the dihedral angle between two l.s. planes) are estimated using the full covariance matrix. The cell e.s.d.'s are taken into account individually in the estimation of e.s.d.'s in distances, angles and torsion angles; correlations between e.s.d.'s in cell parameters are only used when they are defined by crystal symmetry. An approximate (isotropic) treatment of cell e.s.d.'s is used for estimating e.s.d.'s involving l.s. planes.

Refinement. Refinement of F^2 against ALL reflections. The weighted R -factor wR and goodness of fit S are based on F^2 , conventional R -factors R are based on F , with F set to zero for negative F^2 . The threshold expression of $F^2 > \sigma(F^2)$ is used only for calculating R -factors(gt) etc. and is not relevant to the choice of reflections for refinement. R -factors based on F^2 are statistically about twice as large as those based on F , and R -factors based on ALL data will be even larger.

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (\AA^2)

	x	y	z	$U_{\text{iso}}^*/U_{\text{eq}}$
O1	−0.2141 (4)	0.49078 (10)	0.34750 (14)	0.0615 (5)
N1	0.1332 (5)	0.60752 (11)	0.44190 (16)	0.0458 (5)
H1	0.171 (6)	0.5743 (16)	0.518 (2)	0.076 (8)*
N2	0.0425 (4)	0.69612 (11)	0.22727 (14)	0.0439 (5)
C1	−0.0691 (5)	0.56613 (13)	0.34268 (18)	0.0435 (5)
C2	−0.1047 (5)	0.61644 (14)	0.23166 (18)	0.0412 (5)
C3	0.2395 (5)	0.73534 (13)	0.33210 (19)	0.0423 (6)
C4	0.2850 (5)	0.69143 (14)	0.4374 (2)	0.0462 (6)
H4	0.4194	0.7180	0.5072	0.055*
C5	−0.3181 (6)	0.57375 (15)	0.11869 (19)	0.0549 (6)
H5A	−0.3500	0.6171	0.0544	0.082*
H5B	−0.5392	0.5564	0.1292	0.082*
H5C	−0.2018	0.5204	0.1001	0.082*
C6	0.3903 (6)	0.82800 (14)	0.3194 (2)	0.0572 (6)
H6A	0.5251	0.8245	0.2623	0.086*
H6B	0.5352	0.8471	0.3954	0.086*
H6C	0.2067	0.8716	0.2925	0.086*

Atomic displacement parameters (\AA^2)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0870 (12)	0.0459 (10)	0.0492 (10)	−0.0219 (9)	0.0141 (8)	−0.0030 (7)
N1	0.0606 (11)	0.0384 (10)	0.0363 (11)	−0.0041 (8)	0.0093 (9)	−0.0023 (8)
N2	0.0501 (10)	0.0378 (10)	0.0429 (11)	0.0010 (8)	0.0107 (8)	−0.0001 (8)
C1	0.0540 (13)	0.0377 (12)	0.0390 (13)	−0.0027 (10)	0.0126 (10)	−0.0055 (10)
C2	0.0459 (12)	0.0387 (12)	0.0383 (13)	0.0007 (9)	0.0101 (10)	−0.0043 (9)
C3	0.0457 (12)	0.0354 (11)	0.0440 (13)	0.0006 (9)	0.0086 (10)	−0.0038 (10)
C4	0.0508 (13)	0.0390 (12)	0.0449 (13)	−0.0036 (10)	0.0055 (10)	−0.0074 (10)
C5	0.0664 (15)	0.0532 (14)	0.0409 (13)	−0.0086 (11)	0.0066 (11)	−0.0043 (10)
C6	0.0612 (15)	0.0424 (13)	0.0652 (16)	−0.0074 (11)	0.0119 (12)	0.0002 (11)

Geometric parameters (\AA , $^\circ$)

O1—C1	1.251 (3)	C3—C6	1.503 (4)
N1—C1	1.362 (4)	C4—H4	0.9300
N1—C4	1.374 (3)	C5—H5A	0.9600
N1—H1	0.98 (3)	C5—H5B	0.9600
N2—C2	1.310 (3)	C5—H5C	0.9600
N2—C3	1.387 (4)	C6—H6A	0.9600
C1—C2	1.456 (4)	C6—H6B	0.9600

C2—C5	1.498 (4)	C6—H6C	0.9600
C3—C4	1.348 (4)		
C1—N1—C4	122.3 (2)	C3—C4—H4	119.9
C1—N1—H1	117.2 (14)	N1—C4—H4	119.9
C4—N1—H1	120.5 (14)	C2—C5—H5A	109.5
C2—N2—C3	119.4 (2)	C2—C5—H5B	109.5
O1—C1—N1	122.1 (2)	H5A—C5—H5B	109.5
O1—C1—C2	122.9 (2)	C2—C5—H5C	109.5
N1—C1—C2	114.9 (2)	H5A—C5—H5C	109.5
N2—C2—C1	122.8 (2)	H5B—C5—H5C	109.5
N2—C2—C5	119.6 (2)	C3—C6—H6A	109.5
C1—C2—C5	117.6 (2)	C3—C6—H6B	109.5
C4—C3—N2	120.5 (2)	H6A—C6—H6B	109.5
C4—C3—C6	123.6 (2)	C3—C6—H6C	109.5
N2—C3—C6	115.9 (2)	H6A—C6—H6C	109.5
C3—C4—N1	120.1 (2)	H6B—C6—H6C	109.5
C4—N1—C1—O1	-178.15 (19)	N1—C1—C2—C5	178.76 (18)
C4—N1—C1—C2	1.5 (3)	C2—N2—C3—C4	1.2 (3)
C3—N2—C2—C1	-0.4 (3)	C2—N2—C3—C6	-178.28 (18)
C3—N2—C2—C5	179.96 (18)	N2—C3—C4—N1	-0.6 (3)
O1—C1—C2—N2	178.72 (19)	C6—C3—C4—N1	178.79 (18)
N1—C1—C2—N2	-0.9 (3)	C1—N1—C4—C3	-0.8 (3)
O1—C1—C2—C5	-1.6 (3)		
