Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

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

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Key indicators

Single-crystal X-ray study
T = 293 K
Mean σ(C–C) = 0.005 Å
R factor = 0.041
wR factor = 0.110
Data-to-parameter ratio = 9.5

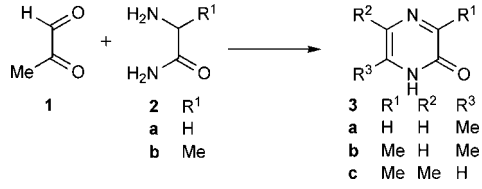
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 27 January 2006
Accepted 1 February 2006

The reaction of pyruvaldehyde with alaninamide gave the title compound, $C_6H_8N_2O$, and not the anticipated 3,6-dimethylpyrazin-2-one.

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 glycinamide (2*a*) to give 6-methylpyrazin-2-one (3*a*) (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 (3*b*) and assumed that, by analogy, it would result from a reaction of pyruvaldehyde with alaninamide (2*b*).



1

2	R^1
a	H
b	Me

3	R^1	R^2	R^3
a	H	H	Me
b	Me	H	Me
c	Me	Me	H

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, ^{1}H 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 (3*b*) and also with its isomer, 3,5-dimethylpyrazin-2-one (3*c*).

Suitable crystals were grown from ethyl acetate and an X-ray analysis carried out. This showed the product to be 3,5-dimethylpyrazin-2(1*H*)-one (3*c*) (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 $NaHCO_3$ (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

$C_6H_8N_2O$	D_x = 1.261 Mg m^{-3}
M_r = 124.14	Mo $K\alpha$ radiation
Monoclinic, $P2_1/n$	Cell parameters from 12419 reflections
a = 4.009 (10) Å	θ = 2.3–24.9°
b = 14.59 (3) Å	μ = 0.09 mm^{-1}
c = 11.59 (3) Å	T = 293 (2) K
β = 105.25 (10)°	Needle, colourless
V = 654 (3) Å^3	0.6 × 0.1 × 0.1 mm
Z = 4	

Data collection

Rigaku R-AXIS diffractometer	R_{int} = 0.045
φ scans	θ_{max} = 24.9°
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	$w = 1/[\sigma^2(F_o^2) + (0.0505P)^2 + 0.2114P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.041	$(\Delta/\sigma)_{max} < 0.001$
$wR(F^2)$ = 0.110	$\Delta\rho_{max}$ = 0.18 e Å^{-3}
S = 1.10	$\Delta\rho_{min}$ = −0.15 e Å^{-3}
839 reflections	
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_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms and 1.2U_{eq}(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 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).

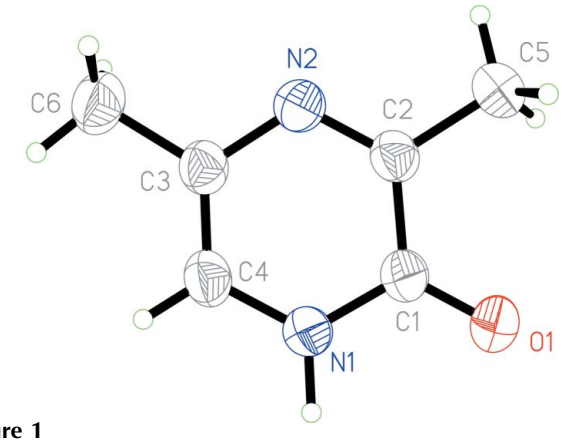


Figure 1
The molecular structure of (3*c*), with displacement ellipsoids drawn at the 50% probability level.

YY gratefully acknowledges a studentship from The University of Manchester.

References

Allway, P. A., Sutherland, J. K. & Joule, J. A. (1990). *Tetrahedron Lett.* **31**, 4781–4783.
Bruker (2001). *SHELXTL*. Version 6.12. Bruker AXS Inc., Madison, Wisconsin, USA.
Garg, N. K., Sarpong, R. & Stoltz, B. N. (2002). *J. Am. Chem. Soc.* **124**, 13179–13184.
Jones, R. G. (1949). *J. Am. Chem. Soc.* **71**, 78–81.
Karmas, G. & Spoerri, P. E. (1952). *J. Am. Chem. Soc.* **74**, 1580–1584.
Kiss, M., Russell-Maynard, J. & Joule, J. A. (1987). *Tetrahedron Lett.* **28**, 2187–2190.
Molecular Structure Corporation (1992). *MSC Diffractometer Control Software*. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Molecular Structure Corporation (1995). *TEXSAN*. Version 1.7. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
Otwinowski, Z. & Minor, W. (1997). *Methods in Enzymology*, Vol. 276, *Macromolecular Crystallography*, Part A, edited by C. W. Carter & R. M. Sweet, pp. 307–326. London: Academic Press.
Sheldrick, G. M. (1985). *SHELXS86*. University of Göttingen, Germany.
Sheldrick, G. M. (1997). *SHELXL97*. University of Göttingen, Germany.
Yates, N. D., Peters, D. A., Allway, P. A., Beddoes, R. L., Scopes, D. I. C. & Joule, J. A. (1995). *Heterocycles*, **40**, 331–347.