Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Ethyl 2-aminooxazole-5-carboxylate

Alan R. Kennedy,[a]* Abedawn I. Khalaf,[a] Colin J. Suckling[a] and Roger D. Waigh[b]

[a]Department of Pure and Applied Chemistry, University of Strathclyde, Glasgow G1 1XL, Scotland, and [b]Department of Pharmaceutical Sciences, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, Glasgow G4 0NR, Scotland

Correspondence e-mail: a.r.kennedy@strath.ac.uk

Key indicators

Single-crystal X-ray study
T = 150 K
Mean σ(C–C) = 0.003 Å
R factor = 0.050
wR factor = 0.126
Data-to-parameter ratio = 11.9

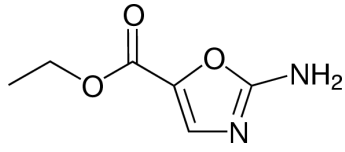
For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

Received 26 July 2001
Accepted 3 August 2001
Online 10 August 2001

The crystal structure of ethyl 2-aminooxazole-5-carboxylate, $C_6H_8N_2O_3$, consists of planar sheets internally connected by intermolecular hydrogen bonding running parallel to the (120) plane. Interactions between the sheets are limited to dipole–dipole interactions between antiparallel carbonyl groups.

Comment

Ethyl 2-aminooxazole-5-carboxylate, (I), was prepared as part of an ongoing investigation of anticancer antibiotic drugs such as distamycin and netropsin (lexitropsins; see Khalaf *et al.*, 2000). Since these drugs exhibit biological activity by binding to specific $(A/T)_4$ sequences in the minor groove of DNA, several analogues with subtly differing binding sites were prepared and tested for activity (Fishleigh *et al.*, 2000). The antiviral activity of (I) was tested *in vitro* by inhibition of plaque formation in cell cultures infected with several RNA and DNA viruses, including Newcastle–Disease and Pseudorabies virus (Ulbricht, 1987).



(I)

The molecular structure of (I) is essentially planar with only the atoms of the ethyl tail showing any significant deviation from the plane defined by the atoms of the five-membered ring [C5 0.163 (6) Å and C6 0.326 (8) Å]. Sheets of coplanar molecules lie parallel to the (120) plane. These sheets are held together internally by in-plane intermolecular hydrogen bonding involving the amine H atoms and all other available acceptor atoms [N2—H2···N1^{i} 2.09 (3), N2—H1···O2^{ii} 2.14 (3) and N2—H1···O1^{ii} 2.63 (3) Å for the H···A distances; symmetry codes: (i) $-x$, $-y$, $-z+2$; (ii) $-x$, $-y$, $-z+1$]. There are dipole–dipole interactions along the *b* direction and between these sheets involving the carbonyl group [O2···C4^{iii} 3.545 (3) Å; symmetry code: (iii) $-x+1$, $-y$, $-z+1$], but no short π interactions involving the ring atoms.

A search of the Cambridge Structural Database (Allen & Kennard, 1993) found no primary amine analogues to (I) but did find a series of secondary and tertiary amines which had been synthesized as aldose reductase inhibitors (Shibata *et al.*, 1982; Ishida *et al.*, 1991). (I) shows several differences in intra-ring bond distances as compared to these compounds. Most notable is the considerable lengthening of the C1—N1 bond

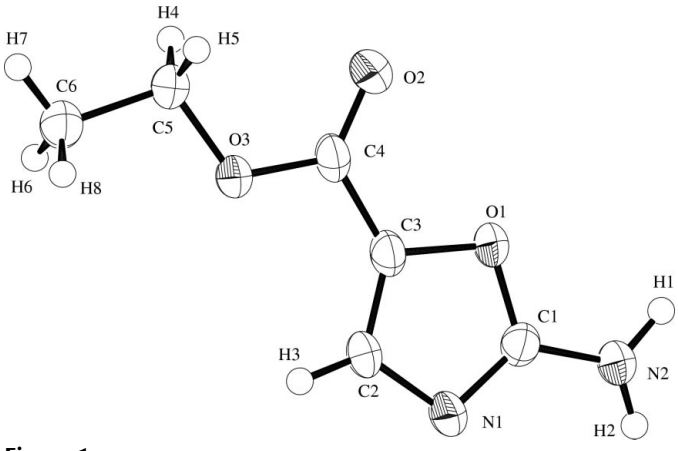


Figure 1
*ORTEP*II (Johnson, 1976) view of (I) with non-H atoms as 50% ellipsoids and H atoms as small spheres of arbitary size.

[1.316 (3) Å *cf*. a range of 1.263–1.294 Å for the five related fragments found] and a shortening of the C2—N1 bond [1.378 (3) Å *cf*. 1.385–1.410 Å]. The bond lengths appear to show that the N2 amine lone pair is considerably conjugated through the ring.

Experimental

Sodium ethoxide (2.44 g, 0.33 mol) was added to diethyl ether (500 ml) and cooled to 273 K with stirring. Ethyl chloroacetate (40.5 g, 0.33 mole) and ethyl formate (24.3 g, 0.33 mol) were added to the reaction mixture over 2 h. The stirring continued overnight at room temperature. The reaction mixture was diluted with ice/water (500 ml) until the sodium salt dissolved. The diethyl ether layer was separated and the water layer was acidified with concentrated HCl and cooled. The precipitated ester was filtered off. After work-up, 43.70 g of crude product was distilled at 5 mmHg (333–338 K). The product, ethyl 2-chloro-3-oxopropanoate $C_5H_7ClO_3$, recrystallized on standing (22.44 g, 45%) as white needles (m.p. 288–293 K). To the above starting material, urea (8.95 g, 0.149 mol) was added followed by 100 ml of ethanol. This mixture was refluxed for 2 h. Ethanol was removed under reduced pressure and then a sodium bicarbonate solution (10%) was added until effervescence ceased. Diethyl ether was added and 20.98 g of ethyl (2*Z*)-3-[(aminocarbonyl)amino]-2-chloro-2-propenoate, $C_6H_9ClN_2O_3$, was removed by filtration (m.p. 484–487 K). The diethyl ether layer was dried over Na_2SO_4 and then the solvent was removed under reduced pressure to leave a green oil. Purification by flash silica-gel column chromatography using ethyl acetate/*n*-hexane (1:2, R_F = 0.2) afforded crystalline (I) (1.72 g, 7.4% yield), m.p. 425–428 K (literature m.p. 428 K; Dornow *et al*., 1953). ^{1}H NMR ($CDCl_3$): 1.35–1.36 (3H, *t*, CH_3); 4.31–4.36 (2H, *q*, CH_2); 5.33 (2H, *s*, NH_2); 7.48 (1H, oxazole); IR (KBr): 3387, 3119, 1715, 1676, 1568, 1408, 1376, 1325, 1261, 1178, 1146 cm^{-1}.

Crystal data

$C_6H_8N_2O_3$	Z = 2
M_r = 156.14	D_x = 1.422 Mg m^{-3}
Triclinic, $P\overline{1}$	Mo $K\alpha$ radiation
a = 6.1295 (6) Å	Cell parameters from 1086 reflections
b = 7.8227 (6) Å	θ = 1.0–26.0°
c = 8.3961 (8) Å	μ = 0.12 mm^{-1}
α = 113.592 (7)°	T = 150 (2) K
β = 93.831 (4)°	Cut needle, colourless
γ = 95.557 (4)°	0.20 × 0.15 × 0.08 mm
V = 364.74 (6) Å^3	

Data collection

Nonius KappaCCD diffractometer	R_{int} = 0.064
φ and ω scans to fill Ewald sphere	θ_{max} = 25.3°
3501 measured reflections	$h = -7 \rightarrow 7$
1300 independent reflections	$k = -9 \rightarrow 9$
905 reflections with $I > 2\sigma(I)$	$l = -10 \rightarrow 9$

Refinement

Refinement on F^2	$w = 1/[\sigma^2(F_o^2) + (0.0599P)^2 + 0.0404P]$ where $P = (F_o^2 + 2F_c^2)/3$
$R[F^2 > 2\sigma(F^2)]$ = 0.050	$(\Delta/\sigma)_{max}$ = 0.001
$wR(F^2)$ = 0.126	$\Delta\rho_{max}$ = 0.21 e Å^{-3}
S = 1.06	$\Delta\rho_{min}$ = −0.20 e Å^{-3}
1300 reflections	
109 parameters	
H atoms treated by a mixture of independent and constrained refinement	

The H1 and H2 atoms of the amine group were placed as found in difference syntheses and refined isotropically. All other H atoms were placed in calculated positions and refined in riding modes.

Data collection: *DENZO* (Otwinowski & Minor, 1997) and *COLLECT* (Hooft, 1988); cell refinement: *DENZO* and *COLLECT*; data reduction: *DENZO* and *COLLECT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *SHELXL*97.

References

Allen, F. H. & Kennard, O. (1993). *Chem. Des. Autom. News*, **8**, 1, 31–37.
Dornow, A., Boberg, F. & Schurer, L. (1953). *Arch. Pharm.* pp. 494–501.
Fishleigh, R. V., Fox, K. R., Khalaf, A. I., Pitt, A. R., Scobie, M., Suckling, C. J., Urwin, J., Waigh, R. D. & Young, S. C. (2000). *J. Med. Chem.* **43**, 3257–3266.
Hooft, R. (1988). *COLLECT*. Nonius BV, Delft, The Netherlands.
Ishida, T., In, Y., Tanaka, C. & Inoue, M. (1991). *Acta Cryst.* B**47**, 806–813.
Johnson, C. K. (1976). *ORTEP*II. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
Khalaf, A. I., Pitt, A. R., Suckling, C. J., Scobie, M., Urwin, J., Waigh, R. D., Fishleigh, R. V. Young, S. C. & Fox, K. R. (2000). *Tetrahedron*, pp. 5225–5239.
Otwinowski, Z. & Minor, W. (1997). *Methods Enzymol.* **276**, 307–326.
Sheldrick, G. M. (1997). *SHELXS*97 and *SHELXL*97. University of Göttingen, Germany.
Shibata, M., Tanaka, C., Inoue, M. & Ishida, T. (1982). *Chem. Pharm. Bull.* **30**, 412–418.
Ulbricht, H. (1987). *Pharmazie*, **42**, 598–601.