Compound (2)

Crystal data

$C_9H_9NO_3S$
$M_r = 211.23$
Monoclinic
$P2_1/n$
$a = 7.149 (4)$ Å
$b = 8.178 (5)$ Å
$c = 16.556 (3)$ Å
$\beta = 93.15 (3)°$
$V = 966.5 (8)$ Å^3
$Z = 4$
$D_x = 1.452$ Mg m^{-3}
D_m not measured

Mo $K\alpha$ radiation
$\lambda = 0.71073$ Å
Cell parameters from 25 reflections
$\theta = 3.5–7.4°$
$\mu = 0.314$ mm^{-1}
$T = 293 (2)$ K
Prism
$0.35 \times 0.25 \times 0.20$ mm
Colourless

Data collection

Rigaku AFC-6S diffractometer
$\omega–2\theta$ scans
Absorption correction: none
1699 measured reflections
1699 independent reflections
1133 reflections with
  $I > 2\sigma(I)$

$\theta_{max} = 24.98°$
$h = 0 \to 8$
$k = 0 \to 9$
$l = -19 \to 19$
3 standard reflections
  every 150 reflections
  intensity decay: $<1\%$

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.044$
$wR(F^2) = 0.108$
$S = 1.025$
1699 reflections
127 parameters
H atoms treated by a
  mixture of independent
  and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.027P)^2 + 0.48P]$
  where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.36$ e Å^{-3}
$\Delta\rho_{min} = -0.23$ e Å^{-3}
Extinction correction: none
Scattering factors from
  International Tables for
  Crystallography (Vol. C)

Table 2. *Selected geometric parameters (Å, °) for (2)*

S1—N1	1.645 (3)	N1—C1	1.291 (4)
S1—C5	1.760 (3)	C1—C4	1.469 (4)
O1—C1	1.311 (3)	C2—C3	1.481 (5)
O1—C2	1.466 (4)	C4—C5	1.384 (4)
N1—S1—C5	96.46 (13)	O1—C2—C3	107.4 (3)
C1—O1—C2	116.3 (2)	C5—C4—C1	109.0 (3)
C1—N1—S1	109.0 (2)	C4—C5—S1	107.1 (2)
N1—C1—O1	123.8 (3)	C8—C7—C6	121.1 (3)
N1—C1—C4	118.4 (3)	C9—C8—C7	121.5 (3)
O1—C1—C4	117.8 (3)	C4—C9—C8	117.8 (3)

For both compounds, data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1995a); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN* (Molecular Structure Corporation, 1995b); program(s) used to solve structures: *TEXSAN*; program(s) used to refine structures: *SHELXL97* (Sheldrick, 1997); molecular graphics: *TEXSAN*; software used to prepare material for publication: *SHELXL97*.

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Complex Network of Hydrogen Bonds in 3-Aminopyrazole-4-carboxylic Acid

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Abstract

3-Aminopyrazole-4-carboxylic acid, $C_4H_5N_3O_2$, crystallized in the non-centrosymmetric space group $P2_1$ in the zwitterionic form. Intermolecular N—H$\cdots$O hydrogen bonds with N$\cdots$O distances of 2.768 (2) and 2.747 (2) Å link molecules into two sets of chains propagating along $[1\bar{1}0]$ and $[110]$. The two sets of chains are crosslinked by strong hydrogen bonds. A complex network of hydrogen bonds ensues. There is a single intramolecular

hydrogen bond. The pyrazole core is closely planar; the dihedral angle between the best-fit core planes of the molecules making up the two chains is 82.2 (1)°. The dihedral angles between the core plane and the planes of the carboxylate group and the amino group are in the region of 2 and 37°, respectively.

Comment

This report on 3-aminopyrazole-4-carboxylic acid is one of a series on hydrogen bonding in amino-substituted N-heterocyclic carboxylic acids. This acid crystallized in the non-centrosymmetric space group $P2_1$ as a zwitter-ion, (I), the carboxy proton having been transferred to the ring N atom.

(I)
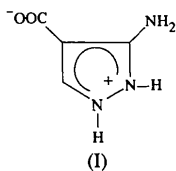
The refined molecule is shown in Fig. 1 together with the numbering scheme. As a consequence of the proton transfer, cyclic carboxylic acid group hydrogen-bonded dimers are not possible. However, hydrogen-bond cycles are formed which involve the carboxylate group O atoms as acceptors and the ring N atoms as donors. Since each molecule has both functionalities, chains of cyclic hydrogen-bonded molecules can occur. Two sets of such chains occur in this structure: one set involves molecules of symmetry type 1 with the chain propagating along [1$\bar{1}$0], while the second set involves molecules of symmetry type 2 with the chain propa-gating along [110]. In contrast to the case of 2-amino-nicotinic acid, which exhibits two sets of such chains which are crosslinked by only C—H···O interactions (Dobson & Gerkin, 1997), the two chains in the present structure are strongly crosslinked. In this structure, each molecule is involved with six neighbors in a total of ten hydrogen bonds; four of these bonds are involved in forming the chain, while six of them are involved in crosslinking. In addition to these intermolecular hydrogen bonds, there is a single intramolecular hydrogen bond. The geometric details of these bonds are given in Table 2. Hydrogen bonds of each type are depicted in Fig. 2, though, for clarity, a single central molecule with all its hydrogen bonds is not shown. Even so, Fig. 2 makes apparent the complex network of hydrogen bonds in this structure. The results of hydrogen-bond graph-set analysis (Bernstein et al., 1995) involving these six hydrogen bonds [for this purpose designated (a) to (f), in the order given in Table 2] for the first- and basic second-level graph sets are presented in Table 3. It is notable that none of the tabulated hydrogen bonds links

molecules in the middle 'column' of molecules shown in Fig. 2 with those in the left 'column'. There are, how-ever, two weaker interactions which do: an N—H···O interaction, N1—H1···O2^{iv} [symmetry code: (iv) $-x$, $y + \frac{1}{2}$, $1 - z$], for which the N···O distance is 3.320 (2) Å and the N—H···O angle 103°, and a C—H···O inter-action, C5—H5···O2^{iv}, for which the C···O distance is 3.236 (3) Å and the C—H···O angle 124°.
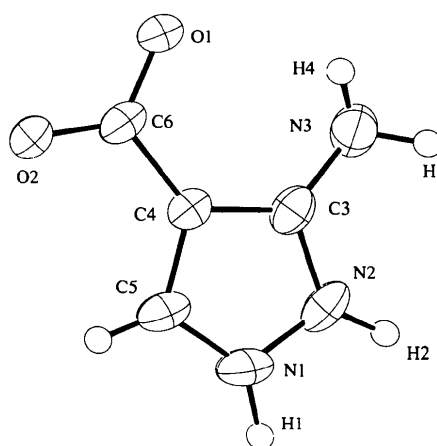

Fig. 1. ORTEPII (Johnson, 1976) drawing of 3-aminopyrazole-4-carboxylic acid showing the numbering scheme. Displacement ellipsoids are drawn for 50% probability for all atoms except hydrogen, for which they have been set artificially small.
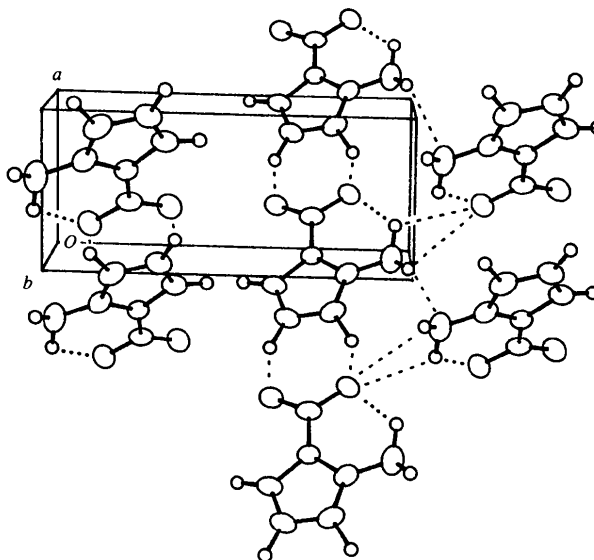

Fig. 2. ORTEPII (Johnson, 1976) packing diagram of 3-amino-pyrazole-4-carboxylic acid. Displacement ellipsoids are drawn for 50% probability for all atoms except hydrogen, for which they have been set artificially small. Intermolecular hydrogen bonds are shown as dashed lines, with intramolecular hydrogen bonds as dotted lines.

The pyrazole core is closely planar: the maximum deviation of a core atom from the best-fit plane describing the core is 0.002 (3) Å, while the average deviation is 0.001 (3) Å. The dihedral angle between the core plane and the carboxylate group plane is in the region of 2°, while that between the core plane and the amino group plane is 37°; the dihedral angle between the carboxylate group plane and the amino group plane is 39°. Furthermore, the entire set of non-H atoms is nearly planar: the maximum deviation of these atoms from the best-fit plane describing them is 0.034 (3) Å; the average deviation is 0.014 (3) Å. The dihedral angle between the core planes of molecules of the two symmetry types is 82.0 (1)°.

Distances and angles of special interest in the title molecule are given in Table 1. On the basis of the compilation and analysis of the structural data for 65 examples of pyrazoles, Bonati & Bovio (1990) formulated six empirical rules for the magnitudes of internal and external angles of pyrazole rings, but found no similar rules for interior and exterior bond lengths. The internal and external angles of the present pyrazole ring satisfy five of the six rules; the sixth rule is not applicable since the substituents at C3 and C5 are not 'of the same type'. Each bond distance in the present pyrazole ring falls within the range of distances for this bond tabulated by Bonati & Bovio (1990); the one C_{ring}—$C_{external}$ bond in the present molecule, C4—C6, is 0.013 (2) Å shorter than the corresponding shortest tabulated bond (of which, it may be noted, there are only seven examples). In summary, the pyrazole ring reported here is unexceptional. The geometry at N3 is distinguishably pyramidal: N3 lies on one side of the pyrazole core plane at a distance of 0.064 (2) Å from it, while the H atoms H3 and H4 lie on the other side of this plane at distances of 0.24 and 0.28 Å from it, respectively.

The closest intermolecular approaches, excluding pairs of atoms within directly hydrogen-bonded groups or involved in the interactions cited above, are between C5 and H5^{iv}, and between C5 and C6^{v} [symmetry code: (v) $x - 1$, y, z], and are merely 0.02 Å less than the corresponding sums of the Bondi (1964) van der Waals radii.

Experimental

3-Aminopyrazole-4-carboxylic acid was obtained as a pale cream-colored powder from Aldrich Chemical Company. This solid was dissolved in hot absolute ethanol, treated with decolorizing carbon and filtered. Slow evaporation of the filtrate at room temperature produced very pale yellow plates, one of which was cut to provide the experimental sample.

Crystal data

$C_4H_5N_3O_2$	Mo $K\alpha$ radiation
$M_r = 127.10$	$\lambda = 0.71073$ Å
Monoclinic	Cell parameters from 25
$P2_1$	reflections
$a = 4.700\,(1)$ Å	$\theta = 9.9–17.3°$
$b = 5.0228\,(8)$ Å	$\mu = 0.134$ mm^{-1}
$c = 10.8995\,(6)$ Å	$T = 296$ K
$\beta = 90.00\,(1)°$	Cut plate
$V = 257.32\,(8)$ Å^3	$0.50 \times 0.50 \times 0.09$ mm
$Z = 2$	Very pale yellow
$D_x = 1.640$ Mg m^{-3}	
D_m not measured	

Data collection

AFC-5S diffractometer	$h = 0 \rightarrow 6$
ω scans	$k = -6 \rightarrow 6$
Absorption correction: none	$l = -14 \rightarrow 14$
1324 measured reflections	6 standard reflections
1183 independent reflections	every 150 reflections
1122 reflections with	intensity variation: ±1.0%
$I > 2\sigma(I)$	(average maximum
$R_{int} = 0.012$	relative intensity)
$\theta_{max} = 27.56°$	

Refinement

Refinement on F^2	Extinction correction:
$R(F) = 0.040$	Zachariasen (1963, 1968)
$wR(F^2) = 0.082$	Extinction coefficient:
$S = 3.57$	$4.9\,(19) \times 10^{-6}$
1177 reflections ($I > 0$)	Scattering factors from
82 parameters	Stewart, Davidson &
H atoms fixed (see below)	Simpson (1965) (H)
$w = 1/\sigma^2(F^2)$	and Creagh & McAuley
$(\Delta/\sigma)_{max} < 0.01$	(1992) (C, N, O)
$\Delta\rho_{max} = 0.20$ e Å^{-3}	
$\Delta\rho_{min} = -0.22$ e Å^{-3}	

Table 1. *Selected geometric parameters (Å, °)*

O1—C6	1.297 (2)	N3—C3	1.360 (2)
O2—C6	1.255 (2)	C3—C4	1.397 (3)
N1—N2	1.359 (2)	C4—C5	1.393 (3)
N1—C5	1.319 (2)	C4—C6	1.446 (3)
N2—C3	1.332 (2)		
O1—C6—O2	123.0 (2)	O2—C6—C4	119.7 (2)
O1—C6—C4	117.2 (2)		

Table 2. *Hydrogen-bonding geometry (Å, °)*

The criteria for inclusion herein are that the donor···acceptor distance is less than 3.3 Å and that the H atom involved is at least as close to the acceptor atom as the donor atom is; it may be noted that some authors adopt an angular cutoff at ~120°. Since the H atoms are fixed, no s.u.'s are given for quantities involving H atoms.

D—H···A	D—H	H···A	D···A	D—H···A
(a) N1—H1···O2^i	0.92	1.91	2.768 (2)	154
(b) N2—H2···O1^i	0.92	1.90	2.747 (2)	152
(c) N3—H3···N3^{ii}	0.92	2.37	3.207 (2)	151
(d) N3—H3···O1^{iii}	0.92	2.82	3.121 (2)	100
(e) N3—H4···O1	0.92	2.39	2.926 (2)	117
(f) N3—H4···O1^{iii}	0.92	2.70	3.121 (2)	109

Symmetry codes: (i) $x - 1$, $1 + y$, z; (ii) $-x$, $\frac{1}{2} + y$, $2 - z$; (iii) $1 - x$, $\frac{1}{2} + y$, $2 - z$.

Table 3. *First- and basic second-level graph-set descriptors involving hydrogen bonds designated (a) to (f)*
(Table 2)

	(a)	(b)	(c)	(d)	(e)	(f)
(a)	$C(6)$	$C(6)[R_2^2(7)]$	$R_4^4(22)$	$C_2^2(9)$	$C_2^2(9)$	$C_2^2(9)$
(b)		$C(6)$	$R_4^4(20)$	$C_2^1(6)$	$C_2^1(6)$	$C_2^1(6)$
(c)			$C(2)$	$C_1^1(6)$	–	$C_2^2(8)$
(d)				$C(6)$	$C_2^1(4)$	$C_2^1(6)[R_2^1(4)]$
(e)					$S(6)$	$C_1^2(2)$
(f)						$C(6)$

The Laue group assignment, systematic absences and non-centrosymmetric intensity statistics indicated space group $P2_1$ uniquely; since refinement proceeded well, it was adopted. Difference Fourier methods were used to locate the initial H-atom positions and the H atoms were then refined isotropically. Subsequently, the H atoms bound to N atoms were moved along the refined N—H bond directions until the distance was 0.92 Å; the isotropic displacement parameters were fixed at 1.2 times those of the attached N atoms. Similarly, H5, bound to C5, was fixed at a distance 0.97 Å from C5, with an isotropic displacement parameter 1.2 times that of C5.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation, 1988). Cell refinement: *MSC/AFC Diffractometer Control Software*. Data reduction: *TEXSAN* (Molecular Structure Corporation, 1995). Program(s) used to solve structure: *SHELXS86* (Sheldrick, 1985). Program(s) used to refine structure: *TEXSAN*. Molecular graphics: *ORTEPII* (Johnson, 1976). Software used to prepare material for publication: *TEXSAN*.

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Crystallographic Evidence of [1,5]Prototropic Shifts Occurring upon Transannular Diels–Alder Reaction of a 14-Membered Macrocycle leading to a 5α-Steroid Skeleton

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Abstract

Reversible prototropic shifts from a stable 14-membered ring macrocycle $(4Z,10E,12Z)$-[$1R^*,14S^*$]-1,8,8-tris-(methoxycarbonyl)-5-methyl-3,17-dioxobicyclo[12.3.0]-heptadeca-4,10,12-triene, $C_{24}H_{30}O_8$, occurred when the compound was heated to form rac-$(5Z,11Z,13Z)$-1,8,8-tris(methoxycarbonyl)-5-methyl-3,17-dioxobicyclo-[12.3.0]heptadeca-5,11,13-triene, $C_{24}H_{30}O_8$. The resulting compound crystallizes in a highly disordered fashion. After a transannular Diels–Alder reaction, the resulting adduct rac-3,3-bis(methoxycarbonyl)-18-oxo-5α,9β-androst-6-en-11,17-dione, $C_{24}H_{30}O_8$, was then easily converted to a 5α-steroid core, rac-3,3-bis-(methoxycarbonyl)-18-oxo-5α-androst-6-en-11,17-dione, $C_{24}H_{30}O_8$. The final adduct is an highly advanced intermediate for the total synthesis of naturally occurring aldosterone.

Comment

The transannular Diels–Alder (TADA) reaction of 14-membered trienes has proved to be highly reliable for the stereoselective construction of *ABC* [6.6.6] tricyclic cores in a single operation (Deslongchamps, 1992). This concept has a broad scope since virtually all possible diastereomeric adducts can be targeted. One exception is the *trans-anti-trans* (TAT) stereochemistry, which cannot be obtained directly due to the inaccessibility of the required chair-boat-chair conformation at the transition state (Lamothe *et al.*, 1988*a,b*). However, since a *trans-syn-cis* (TSC) adduct can readily be obtained from a *trans-cis-cis* (TCC) triene, and provided there is a ketone at the C11 position (steroid numbering), the TSC adduct can be epimerized to the more stable TAT stereochemistry (Marinier & Deslongchamps,