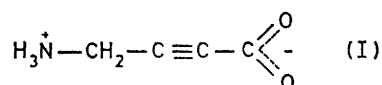


Crystal and Molecular Structure of 4-Aminotetrolic Acid (4-Amino-but-2-ynoic Acid)

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Crystals of the title compound (I) are monoclinic, space group $P2_1/c$, with $a = 7.881(3)$, $b = 6.446(4)$, $c = 11.039(5)$ Å, $\beta = 129.05(3)^\circ$, $Z = 4$. The structure was solved by direct methods and refined by least-squares procedure to $R = 0.056$ for 769 observed diffraction maxima. The molecules are zwitterions linked by a three-dimensional N—H \cdots O hydrogen-bond network.

4-AMINOTETROLIC acid [(I), 4-aminobut-2-ynoic acid], a structural analogue of 4-aminobutanoic acid [(II), GABA] has been shown to have GABA-like action in the feline spinal cord¹ where there is evidence that (II) functions as an inhibitory transmitter.² We report here the crystal structure determination of 4-aminotetrolic acid as part of a study of structure and physiological activity relationships of (II) and its analogues.



EXPERIMENTAL

The acid (I) was synthesized by amination of 4-chlorotetrolic acid prepared from commercial butyne-1,4-diol according to the method of ref. 3. Brown, prismatic crystals were grown by diffusion of ethanol into an aqueous solution.

Crystal Data.— $\text{C}_4\text{H}_5\text{NO}_2$ Monoclinic. $M = 99.1$, $a = 7.881(3)$, $b = 6.446(4)$, $c = 11.039(5)$ Å, $\beta = 129.05(3)^\circ$, $D_c = 1.495$ g cm⁻³, $Z = 4$, $D_m = 1.50(1)$ g cm⁻³, $U = 435.5$ Å³, Mo- K_α radiation, $\lambda = 0.7107$ Å; $\mu(\text{Mo-}K_\alpha) = 1.2$ cm⁻¹. Space group $P2_1/c$ (C_{2h}^5 , No. 14).

Data were corrected for Lorentz and polarization effects but not for absorption or extinction.

Structure Solution and Refinement.—Normalised structure factors $|E|$ were calculated from the observed structure factors by use of the K -curve method, normalising all parity groups of $\pm h, k, l$ separately to obtain the condition $\langle |E|^2 \rangle_{\text{av}} = 1.0$.

An initial set of phases for 128 reflections with $|E| \geq 1.2$ was obtained by use of MULTAN.⁵ An E map calculated with the phases derived from the most consistent solution revealed the positions of all non-hydrogen atoms in the unit cell.

Refinement of the scale factor and overall temperature factor on these atoms gave $R = 0.245$. Three cycles of full-matrix least-squares refinement of positional and isotropic thermal parameters and an overall scale factor for the non-hydrogen atoms gave $R = 0.125$ for the 448 data in the range 2θ 5–45°. Changing to anisotropic thermal parameters and subsequent refinement for two cycles gave $R = 0.080$. At this stage a difference electron-density synthesis clearly revealed all hydrogen atom positions. The final cycles of anisotropic refinement using the 769 observed data, including the hydrogen-atom positional parameters, by full-matrix least-squares were continued until all parameter shifts were $\leq 0.1\sigma$. The function minimised was Σ

TABLE I

Fractional co-ordinates and thermal motion parameters ($\times 10^4$) * derived from least-squares refinement, with estimated standard deviations in parentheses

Atom	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
N(1)	2 429(4)	-3 421(4)	565(3)	197(8)	405(10)	244(6)	-9(8)	162(6)	6(7)
C(4)	2 691(4)	-1 826(5)	1 643(3)	243(9)	442(13)	355(8)	-42(9)	223(7)	-37(8)
C(3)	834(4)	-1 864(5)	1 642(3)	285(9)	376(12)	320(7)	-6(8)	213(7)	-14(8)
C(2)	-700(4)	-1 923(5)	1 607(3)	275(9)	381(9)	301(7)	-32(8)	198(7)	-43(7)
C(1)	-2 555(4)	-2 109(5)	1 636(3)	237(9)	342(11)	305(7)	-20(8)	189(7)	-34(7)
O(1)	-4 325(3)	-2 619(4)	388(3)	290(8)	1 043(16)	372(7)	-183(9)	231(6)	176(8)
O(2)	-2 133(3)	-1 794(4)	2 912(2)	325(7)	446(9)	321(5)	-2(6)	240(6)	-20(6)

* The Debye-Waller factor is defined as $T = \exp[-2\pi^2 \sum_i \sum_j a_i^* a_j^* h_i h_j U_{ij}]$ with U in Å².

Intensity Measurements.—Three-dimensional X-ray diffraction data from a small single crystal ($ca.$ 0.14 \times 0.21 \times 0.42 mm) were collected on a computer-controlled four-circle diffractometer⁴ by use of graphite-monochromated Mo- K_α radiation. A coupled θ — 2θ step scan with $\Delta 2\theta$ 0.04°, a counting time of 10 s per step, and a peak width of 2.0° were used. In the range 2θ 5–60°, 769 diffraction maxima out of a possible 1 377 in a quadrant of reciprocal space ($\pm h, k, l$) had $I \geq 3\sigma(I)$ and were considered observed.

¹ P. M. Beart, D. R. Curtis, and G. A. R. Johnston, *Nature New Biol.*, 1971, **234**, 80.

² D. R. Curtis, A. W. Duggan, D. Felix, and G. A. R. Johnston, *Brain Res.*, 1971, **32**, 69.

³ P. M. Beart and G. A. R. Johnston, *Austral. J. Chem.*, 1972, **25**, 1359.

$w(|F_o| - |F_c|)^2$ with $w = 4I/\sigma^2$ where $\sigma = \sigma(I) \pm 0.05I$. The term $0.05I$ was included in the estimate of σ to allow for the random long-term fluctuation in intensity measurement of a standard reflection which was taken after every 25 observations. Atomic scattering factors for neutral carbon, nitrogen, and oxygen were taken from ref. 6 and for hydrogen from ref. 7. The final R is 0.056. Positional and

⁴ W. R. Busing, R. D. Ellison, H. A. Levy, S. P. King, and P. T. Roseberry, U.S. Atomic Energy Commission Report ORNL **4143**, 1968.

⁵ G. Germain, P. Main, and M. M. Woolfson, *Acta Cryst.*, 1971, **A27**, 368.

⁶ D. T. Cromer and J. T. Waber, *Acta Cryst.*, 1965, **18**, 104.

⁷ 'International Tables for X-Ray Crystallography,' vol. III, Kynoch Press, Birmingham, 1962.

thermal parameters for non-hydrogen atoms are listed in Table 1 and hydrogen atom positions in Table 2. Bond distances and angles are given in Table 3. Observed and

TABLE 2

Fractional co-ordinates for hydrogen atoms ($\times 10^3$) derived from least-squares refinement, with estimated standard deviations in parentheses

Atom	<i>x</i>	<i>y</i>	<i>z</i>
H(1)	404(9)	-212(7)	272(7)
H(2)	276(7)	-39(9)	120(6)
H(3)	258(7)	-474(9)	101(6)
H(4)	101(9)	-330(7)	-45(6)
H(5)	356(8)	-326(7)	43(6)

All hydrogen atoms have U_{iso} 0.051 Å².

TABLE 3

Interatomic distances (Å) and angles (°) for all atoms, with estimated standard deviations in parentheses

(a) Distances			
H(1)-C(4)	1.00(6)	N(1)-C(4)	1.486(4)
H(2)-C(4)	1.06(5)	C(3)-C(4)	1.463(4)
H(3)-N(1)	0.95(6)	C(2)-C(3)	1.186(4)
H(4)-N(1)	0.97(6)	C(1)-C(2)	1.487(4)
H(5)-N(1)	0.99(5)	C(1)-O(1)	1.238(3)
		C(1)-O(2)	1.242(3)
(b) Angles			
H(3)-N(1)-C(4)	107(3)	H(1)-C(3)-H(2)	113(4)
H(4)-N(1)-C(4)	110(3)	N(1)-C(4)-C(3)	110.7(3)
H(5)-N(1)-C(4)	111(3)	C(1)-C(2)-C(3)	176.3(3)
H(1)-C(4)-C(3)	108(3)	C(2)-C(3)-C(4)	178.3(5)
H(2)-C(4)-C(3)	111(3)	C(2)-C(1)-O(1)	115.5(2)
H(4)-N(1)-H(3)	110(4)	C(2)-C(1)-O(2)	116.5(2)
H(5)-N(1)-H(3)	110(4)	O(1)-C(1)-O(2)	127.9(3)
H(4)-N(1)-H(5)	108(4)		

calculated structure factors are listed in Supplementary Publication No. SUP 21550 (3 pp.).*

DISCUSSION

Atomic numbering and perspective drawing of the molecule is shown in Figure 1, and molecular packing and hydrogen bonding in Figure 2 viewed in the direction of *b*.

The C(2)-C(3) triple-bond distance (1.186 Å) is similar to that found in other acetylenic compounds⁸⁻¹⁰ although the short C(3)-C(4) single-bond distance (1.463 Å) indicates a partial multiple-bond.

The location of three hydrogen atoms tetrahedrally surrounding nitrogen confirms the zwitterionic nature of the molecule. These hydrogen atoms enter into hydrogen-bond formation *via* adjacent oxygen atoms, and the details of these interactions are given in Table 4.

* See Notice to Authors, No. 7, in *J.C.S. Perkin II*, 1975, Index Issue.

⁸ R. W. Baker and P. J. Pauling, *J.C.S. Perkin II*, 1973, 1247.

⁹ G. A. Jeffery and J. S. Rollet, *Proc. Roy. Soc.*, 1953, *A*, **86**, 213.

¹⁰ H. Irngartinger, L. Leiserowitz, and G. M. J. Schmidt, *J. Chem. Soc. (B)*, 1970, 497.

Intramolecular N...O distances (5.227 and 5.699 Å) are similar to those found for other γ -aminocarboxy-

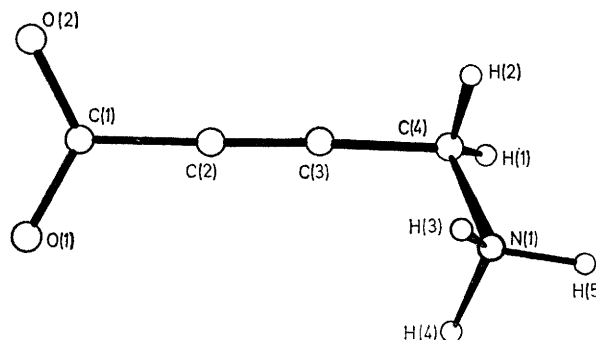


FIGURE 1 Atomic numbering and perspective view of the molecule

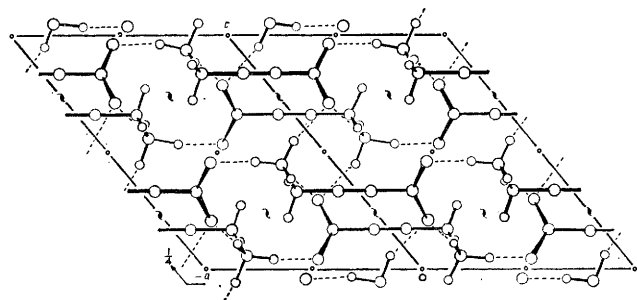
FIGURE 2 Molecular packing viewed in the direction of *b* indicating hydrogen bonds (broken lines)

TABLE 4

Hydrogen bond distances (Å) and angles (°), with estimated standard deviations in parentheses

Distances			
Donor-Acceptor		Angles	
N(1) ... O(1 ^I)	2.734(3)	C(4)-N(1) ... O(1 ^I)	105.2(2)
N(1) ... O(2 ^{II})	2.847(3)	C(4)-N(1) ... O(2 ^{II})	94.4(2)
N(1) ... O(2 ^{III})	2.873(3)	C(4)-N(1) ... O(2 ^{III})	103.7(2)

Roman numerals as superscripts denote the following transformations relative to the reference molecule at *x*, *y*, *z*:
 I $1 + x, y, z$ II $-x, -\frac{1}{2} + y, \frac{1}{2} - z$ III $x, -\frac{1}{2} - y, -\frac{1}{2} + z$
 compounds¹¹⁻¹³ which have GABA-like action at the proposed GABA receptor.

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¹¹ K. Tomita, H. Higashi, and T. Fujiwara, *Bul. Chem. Soc. Japan*, 1973, **46**, 2199.

¹² K. Tomita, M. Harada, and T. Fujiwara, *Bul. Chem. Soc. Japan*, 1973, **46**, 2834.

¹³ L. Brehm, H. Hjeds, and P. Krosgaard-Larsen, *Acta Chem. Scand.*, 1972, **26**, 1298.