References

CARRELL, H. L. (1975). *ICRFMLS*. Program in Fortran IV. Local version of *UCLALS4* by P. K. GANTZEL, R. A. SPARKS, R. E. LONG & K. N. TRUEBLOOD.

GLUSKER, J. P., ZACHARIAS, D. E. & CARRELL, H. L. (1976). *Cancer Res.* **36**, 2428–2435.

International Tables for X-ray Crystallography (1962). Vol. III, pp. 201–207. Birmingham: Kynoch Press.

PAULING, L. (1960). *The Nature of the Chemical Bond.* 3rd ed., pp. 198–239. Ithaca: Cornell Univ. Press.

PECK, R. M., TAN, T. K. & PECK, E. B. (1976). *Cancer Res.* **36**, 2423–2427.

STEWART, J. M. (1972). The X-RAY system – version of June 1972. Tech. Rep. TR-192. Computer Science Center, Univ. of Maryland, College Park, Maryland.

STEWART, R. F., DAVIDSON, E. R. & SIMPSON, W. T. (1965). *J. Chem. Phys.* **42**, 3175–3187.

SUTTON, L. E. (1958). Editor, *Tables of Interatomic Distances and Configuration in Molecules and Ions.* Spec. Publ. No. 11. London: The Chemical Society.

WILSON, A. J. C. (1942). *Nature, Lond.* **150**, 151–152.

N,N-Bis(2-hydroxyethyl)glycine

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Abstract. $C_{16}H_{13}O_4N$ (bicine), m.p. 193°C, monoclinic, $P2_1/n$, $a = 9.963$ (2), $b = 11.045$ (3), $c = 7.667$ (1) Å, $\beta = 111.78$ (2)°, $Z = 4$, $M_r = 163.18$, $D_c = 1.38$ g cm^{-3}, observed data $R = 4.7\%$. The conformation of the diethanolamine moiety differs significantly from that observed in other N-diethanolamine structures. The hydroxyethyl moiety adopts a staggered conformation as opposed to the *trans* conformation observed in N-diethanolamine. There are strong hydroxyl hydrogen bonds with the carboxylic O atoms in adjacent molecules.

Introduction. Crystals of bicine were produced as a by-product of crystallization of the thyroid hormone analogue 3,5-diisopropyl-3'-iodo-DL-thyronine with N-diethanolamine in methanol. The melting point of the crystals is 195°C with slight decomposition, in agreement with that previously found for bicine (Stecher, 1968). A 0.1 × 0.1 × 0.2 mm crystal was used to measure the lattice parameters and intensities. The data showed the systematic absences for the space group $P2_1/n$ and the cell constants were determined by least-squares analysis of the angular settings of 45 reflections [at 20°C; λ(Mo $K\alpha$) = 0.7091 Å]. The intensities of 2254 reflexions (1134 reflexions had $I > 2\sigma$) with $2\theta < 60°$ were measured on a Nonius CAD-4 automated diffractometer using Mo $K\alpha$ radiation. After the usual Lorentz and polarization corrections had been applied, normalized structure-factor amplitudes were computed and the structure was solved by application of direct methods with *MULTAN* (Germain, Main & Woolfson, 1971) and *NQEST* (DeTitta, Edmonds, Langs & Hauptman, 1975).

Initially the composition of the crystal was unknown. *MULTAN*, based on 280 reflexions with $E > 1.60$, computed phases for 64 ambiguities which had 16 combined FOM indicators of 2.98. *NQEST* was run on the 64 phase sets from *MULTAN* with the following criteria: $E_{min} = 1.60$, $B_{min} = 0.30$, E_{max} (cross-terms) = 5.00 and E_{min} (cross-terms) = 0.50. This resulted in three values of the *NQEST* indicator of −0.40 from which E maps were computed. The next best *NQEST* indicator was −0.17. An E map calculated from a *MULTAN* solution with an *NQEST* value of −0.40 produced a linear fragment of reasonable geometry. Subsequent Fourier maps produced a molecule that was recognized as bicine.

The atomic parameters were refined by full-matrix least-squares calculations. After three cycles of aniso-tropic refinement, a difference Fourier map was computed which produced positions for all 13 H atoms. The parameters of all atoms including the H atoms were refined for three final cycles. The weights used were the quantities $(1/\sigma_F^2)$ where σ_F is defined by Stout & Jensen (1968, equation H.14) and the instability correction was 0.06 rather than 0.01. The R index, defined as $\Sigma||F_o| - |F_c||/\Sigma|F_o| \times 100$, was 8.2% for all data and 4.7% for the 1134 reflections used in the refinement. The Fourier and least-squares programs are part of the Nonius crystallographic package for the PDP 11/45.

Table 1. *Positional and anisotropic thermal parameters*

The form of the anisotropic thermal parameter is $\exp[-(B_{11}hh + B_{22}kk + B_{33}ll + B_{12}hk + B_{13}hl + B_{23}kl)]$. Standard deviations are given in parentheses.

ATOM	x/a	y/b	z/c	B11	B22	B33	B12	B13	B23
O(7)	0.9538(2)	0.3218(3)	0.3664(3)	0.0088(2)	0.0168(3)	0.0125(3)	-0.0023(4)	0.0034(4)	0.0106(5)
O(1)	0.8688(2)	0.0617(2)	0.5752(3)	0.0086(2)	0.0073(2)	0.0176(4)	-0.0037(3)	0.0014(5)	0.0041(5)
O(43)	3.8026(2)	3.3806(2)	0.7046(3)	0.0089(2)	0.0124(2)	0.0119(3)	0.0088P(4)	0.0033(4)	0.0003(5)
O(44)	0.6639(2)	0.4077(2)	1.0132(3)	0.0091(2)	0.0074(2)	0.0122(3)	0.0047(3)	0.0092(3)	0.0084(4)
N(4)	1.0379(2)	0.2529(2)	0.7354(3)	0.0055(2)	0.0055(2)	0.0085(3)	0.0030(4)	0.0001(4)	-0.0012(4)
C(42)	0.8632(3)	0.3672(2)	0.6701(3)	0.0065(2)	0.0126(4)	0.0081P(4)	0.0035(5)	-0.0001(5)
C(41)	1.0192(3)	0.2905(3)	0.9135(3)	0.0066(2)	0.0091(4)	0.0031(4)	0.0084(5)	-0.0020(5)
C(2)	0.9825(3)	3.0342(3)	0.7354(4)	0.0103(3)	0.0066P(2)	0.0134(5)	-0.0012(5)	0.0047(6)	0.0017(6)
C(3)	1.0468(3)	3.1261(2)	0.7471(2)	0.0070(2)	0.0056(2)	0.0114(4)	0.0025(4)	0.0034(5)	-0.0011(5)
C(5)	1.1232(3)	0.3456(3)	0.6708(4)	0.0077(3)	0.0001(2)	0.0141(4)	-0.0006(4)	0.....(5)	0.0002(6)
C(6)	1.1039(3)	0.3303(3)	0.6717(4)	0.0083(3)	0.0086(3)	0.0158(4)	0.0011(5)	0.0092(5)	0.0046(7)

| ATOM	x/a	y/b	z/c	B150	ATOM	x/a	y/b	z/c	B15G
H(10)	0.785(5)	0.045(4)	0.567(6)	7.5(11)	H(58)	1.223(3)	0.354(3)	0.756(4)	2.9(6)
H(4A)	0.930(3)	0.041(3)	0.841(4)	2.8(6)	H(6A)	1.149(3)	0.402(3)	0.434(5)	3.7(7)
H(2B)	1.012(3)	-0.051(3)	0.736(4)	3.9(7)	H(6B)	1.152(4)	0.256(4)	2.450(5)	5.9(10)
H(3A)	1.127(3)	0.110(3)	0.640(4)	3.6(7)	H(70)	0.936(3)	0.344(3)	0.263(5)	5.1(7)
H(3B)	1.170(3)	0.119(3)	0.857(4)	3.0(6)	H(41A)	1.010(3)	0.221(3)	0.978(5)	4.0(8)
H(4)	0.953(3)	0.255(3)	0.652(4)	2.7(5)	H(41B)	1.005(3)	0.338(3)	0.993(5)	4.2(8)
H(5A)	1.005(3)	0.425(3)	0.696(4)	2.6(6)					
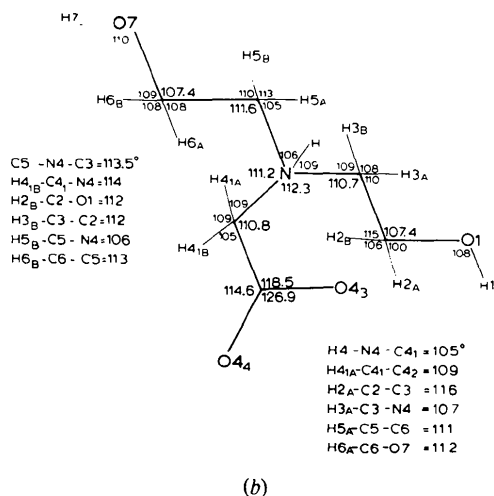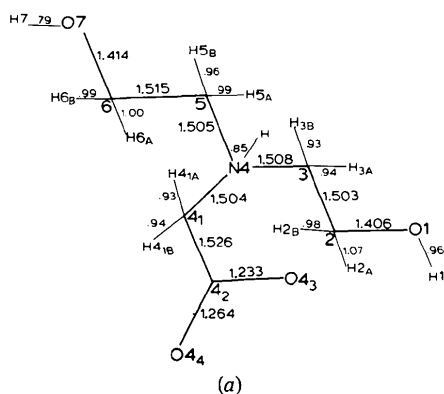
Fig. 1. Bond distances and angles.
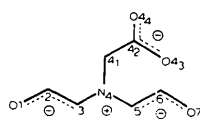
Fig. 2. Charge distribution suggested from the observed structure of bicine.

Scattering factors are from *International Tables for X-ray Crystallography* (1974). The final refined positional and thermal parameters are given in Table 1.*

Discussion. Bicine is widely used as a buffer and chelating agent in many biological investigations (Remizov, 1960; Good, Winget, Winter, Connolly, Izawa & Singh, 1966) and has a pK_a of 8·35. In addition, bicine has many applications in such industrial
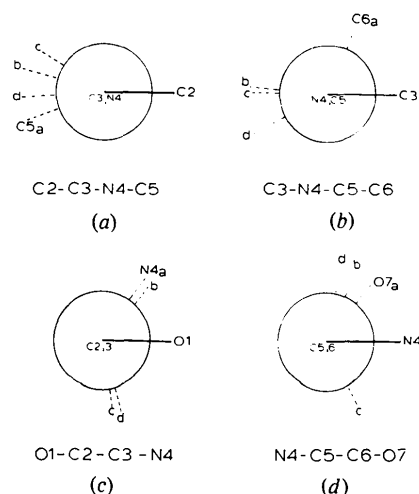
Fig. 3. A comparison of the Newman projections for bicine and N-diethanolamine structures. (a) N,N-Bis(2-hydroxyethyl)glycine. (b) 3,5,3'-Triiodothyroacetic acid N-diethanolamine (1:1) (Cody & Duax, 1973). (c) 3,5-Dibromothyroacetic acid N-diethanolamine (1:1) (Cody, Erman & DeJarnette, 1975). (d) 3,5,3',5'-Tetraiodothyroacetic acid N-diethanolamine (1:1) (Cody & Hazel, 1976).

processes as paper, textile, paint and metal refining and manufacturing. It chelates well with such divalent cations as Mg, Ca, Mn and Cu (Sober, 1968).

The bond lengths and angles calculated from the coordinates in Table 1 are given in Fig. 1. The average estimated standard deviations for the nonhydrogen bond lengths are 0·003 and 0·02 Å for those bonds involving H. The corresponding values for the bond angles are 0·3 and 1·1° respectively.

The C—C bond lengths are all significantly shorter than their expected value of 1·541 Å (Kennard, 1972) indicating a distribution of charge throughout the molecule. The C—O distances in the carboxylic function are indicative of the zwitterion form with the N protonated. The lengthening of the three C—N hydroxyl C—O distances corroborates the charge distribution shown in Fig. 2. This charge distribution was also observed in solution studies of bicine and a number of glycine derivatives (Kostromina, 1972) by proton magnetic resonance techniques. The amount of each partially protonated anion was expressed as the fraction of time during which the particular group was protonated, based on their dissociation constants.

As illustrated in Fig. 3, the conformation of the *N*-diethanolamine moiety of bicine differs significantly from that observed in other *N*-diethanolamine structures. The C—N bonds in *N*-diethanolamine generally

adopt a *trans* configuration while the hydroxyl groups tend to favor a staggered (±60°) conformation. In the case of bicine, the additional substituent on the N moves the hydroxyethyl moiety to a staggered conformation.

Each molecule of bicine is bonded to four others in the lattice through the two distinct hydrogen bonds as illustrated in Table 2 and Fig. 4. Two of the hydrogen bonds bridge translationally related molecules and the others are related by the *n*-glide. There is also a short intramolecular N(4)—H(4)—O(43) interaction in the molecule. From the geometry listed in Table 2, it is questionable whether this represents a true hydrogen bond.

Table 2. *Hydrogen bonds*

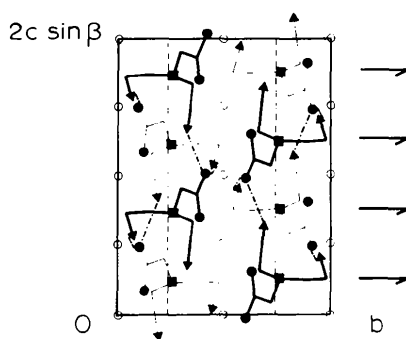|	$X-H$	$H \cdots Y$	$X \cdots Y$	$X-H \cdots Y$
O(7)···O(44)	0·79 Å	1·91 Å	2·69 Å	171°
O(1)···O(44)	0·96	1·75	2·69	164
N(4)···O(43)	0·85	2·19	2·67	116

Fig. 4. Packing diagram of bicine showing the hydrogen-bonding scheme. The dark molecules are above the light ones. The squares are N and the filled circles and triangles are O atoms.

References

CODY, V. & DUAX, W. L. (1973). *Biochem. Biophys. Res. Commun.* **52**, 430–433.

CODY, V., ERMAN, M. & DEJARNETTE, E. (1975). Amer. Cryst. Assoc. Meeting, Charlottesville, Va., **3**, 27.

CODY, V. & HAZEL, J. (1976). Amer. Cryst. Assoc. Meeting, Evanston, Ill., **4**, 51.

DETITTA, G. T., EDMONDS, J. W., LANGS, D. A. & HAUPTMAN, H. A. (1975). *Acta Cryst.* A**31**, 472–479.

GERMAIN, G., MAIN, P. & WOOLFSON, M. M. (1971). *Acta Cryst.* A**27**, 368–376.

GOOD, N. E., WINGET, G. D., WINTER, W., CONNOLLY, T. N., IZAWA, S. & SINGH, R. M. M. (1966). *Biochemistry*, **5**, 467–477.

International Tables for X-ray Crystallography (1974). Vol. IV. Birmingham: Kynoch Press.

KENNARD, O. (1972). *Molecular Structures and Dimensions*, Vol. A1. Utrecht: Oosthoek, Scheltema & Holkema.

KOSTROMINA, N. A. (1972). *Teor. Eksp. Khim.* **8**, 831–836. *Chem. Abs.* **78**, 102686f.

REMIZOV, A. L. (1960). *Biokhimiya*, **25**, 323–327.

SOBER, H. A. (1968). *Handbook of Biochemistry*, p. J-199. Cleveland: The Chemical Rubber Co.

STECHER, P. G. (1968). *The Merck Index*, p. 360. New Jersey: Merck.

STOUT, G. H. & JENSEN, L. H. (1968). *X-ray Structure Determination*, p. 168. New York: Macmillan.