Formation of a Heterocyclic Cage Compound from Ethylenediamine and Glyoxal

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WE have examined the reaction of ethylenediamine (I) and glyoxal (II) in aqueous solution at room temperature. Interaction of (II) and an excess of (I) in aqueous or alcoholic solution is known[1] to yield decahydropyrazino[2,3-*b*]pyrazine (III). We report that reaction of (I) and (II) in a molar ratio of 2 : 3, in dilute aqueous solution buffered to pH 9 (Na_2HPO_4), gives a new compound (IV) $C_{10}H_{14}N_4O_2$† (m.p. 300—301° after sublimation from ~ 100°) in 20% yield. Compound (IV) is easily isolated by extraction into chloroform, and purified by crystallization from ethanol, or by vacuum sublimation. The product is evidently formed by the interaction of two molecules of (I) and three molecules of (II). The i.r. spectrum of the compound showed the absence of functional groups (C=O, OH, NH). Reaction with 2,4-dinitrophenylhydrazine under the usual acidic conditions gave a quantitative yield of the known bis-2,4-dinitrophenylhydrazone of glyoxal; resistance of (IV) to reaction with lithium aluminium hydride eliminated possible formulae containing an oxiran ring.

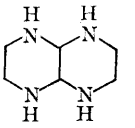
The properties, and particularly the n.m.r. spectrum of (IV) [singlet, τ 4·9 (4H); singlet, τ 5·9 (2H); symmetric AA'BB' multiplet, τ 6·95 (8H)], suggested the novel cage-type structures (IVa) and (IVb), but no decision between the two

† Satisfactory values for C, H, and N, and molecular weight (mass spectrometry) have been obtained for compound (IV).

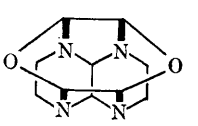
possible structures could be made by chemical or spectroscopic methods. *X*-Ray crystallographic analysis established (IVa) as the correct structure.

Compound (IV) was obtained from ethanol in two different crystal forms (having identical m.p., and i.r. spectrum in chloroform), either clear rods or rhomboids, which, since they form together from the same solution, cannot be polymorphic forms. *X*-Ray crystallographic examination showed that the rods are bundles of parallel single crystals; the rhomboids were not examined with *X*-rays, but appeared to be formed from the rod-shaped crystals by twinning. Recrystallization from a few drops of water resulted in small clear crystals in the shape of thick rods. Their *X*-ray diffraction pattern indicated the space group to be $C2/c$, with unit cell dimensions $a = 11{\cdot}27$ Å, $b = 5{\cdot}98$ Å, $c = 14{\cdot}76$ Å, and $\beta = 106{\cdot}0°$. The unit cell contained four molecules. The molecular structure (IVa) was obtained by applying the symbolic addition procedure[2] to a set of more than 800 diffraction intensities. The details of this analysis will be published elsewhere.

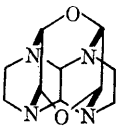
Assuming that the cleavage to the very reactive (II) might also take place *in vivo*, compound (IVa) was screened for physiological activity at the



(III)



(IVa)



(IVb)

Cancer Chemotherapy National Service Centre; however, no significant anti-tumour activity was observed.

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[1] H. C. Chitwood and W. McNamee, U.S.P. 2,345,237/1944 (*Chem. Abs.*, 1944, **38**, 4274); for preparation of (III) by another method, see L. A. Cort and N. R. Francis, *J. Chem. Soc.*, 1964, 2799.
[2] J. Karle and I. L. Karle, *Acta Cryst.*, 1966, **21**, 849.