

A REINVESTIGATION OF THE REACTION OF N-(2-BROMOETHYL)ISATOIC ANHYDRIDE WITH METHYLAMINE. ISOLATION AND CRYSTAL STRUCTURE OF 1-(2-HYDROXYETHYL)-3-METHYL-2,4-(1H,3H)-QUINAZOLINEDIONE

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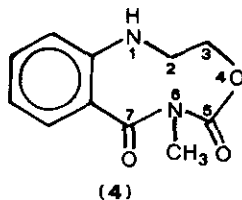
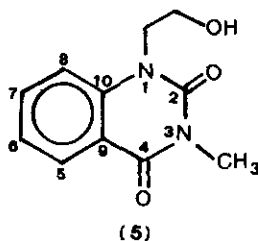
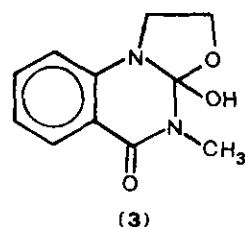
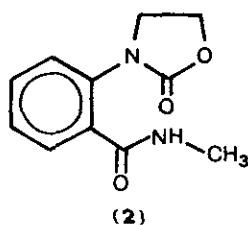
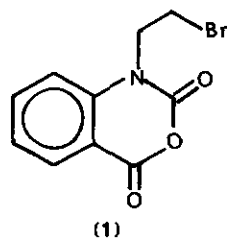
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**Abstract** - The reaction of N-(2-bromoethyl)isatoic anhydride with methylamine affords 1-(2-hydroxyethyl)-3-methyl-2,4-(1H,3H)-quinazolin-2-one, the structure of which has been determined by single crystal X-ray diffraction.

In the context of our studies on the conformation and ring-chain tautomerism of 9- and 10-membered cyclotriptides<sup>1</sup>, the new heterocyclic system (4) described by Barcza *et al.*<sup>2</sup> caught our interest. The 9-membered ring of 2,3-dihydro-6-methyl-4,1,6-benzoxadiazonine-5,7-(1H,6H)-dione (4) contains in fact a free amino group (N-1) and a potentially reactive N-acylurethane carbonyl (C-5) suitably located for studying endoannular interactions and related tetrahedral adducts.

4,1,6-Benzoxadiazonine (4) was obtained by treating N-(2-bromoethyl)isatoic anhydride (1) with methylamine<sup>2</sup>. According to the proposed reaction mechanism<sup>2</sup>, oxazolidinylbenzamide (2) is the species initially formed; this compound, however, is an elusive intermediate which reacts further to give, through the tetrahedral adduct (3), a new heterocyclic system to which structure (4) was assigned on the basis of <sup>1</sup>H-nmr and ir data. The alternative breakdown of the adduct (3) producing N-(2-hydroxyethyl)quinazolin-2-one (5), the ring-chain tautomer of (4), is not discussed by the authors.

We repeated the reaction of (1) with methylamine by following the procedure of Barcza *et al.*<sup>2</sup> Melting point, ir absorptions and <sup>1</sup>H-nmr data of the compound isolated by us<sup>3</sup> are in accordance with the corresponding data reported for (4)<sup>4</sup>. The reaction product, however, does not show basic properties and gives an O-acetyl-



derivative when treated with acetic anhydride/pyridine. Moreover the ir carbonyl frequency ( $\nu_{\text{CO}} = 1700\text{--}1690\text{ cm}^{-1}$ ) seems in accordance with (5) and rather low for a cyclic N-acylurethane such as (4)<sup>5</sup>. Since chemical methods are in general unreliable for the determination of the structure of ring-chain tautomeric compounds and the reported <sup>1</sup>H-nmr data are not decisive to discriminate between (4) and (5), we decided to ascertain the structure of the reaction product by X-ray crystallographic analysis. The molecular structure reported below shows that the isolated product does not correspond to the expected benzoxadiazonine (4) but to its ring-chain tautomer (5).

#### Crystal structure of 1-(2-hydroxyethyl)-3-methyl-2,4-(1H,3H)-quinazolinedione (5).

Suitable single crystals of (5) were obtained by slow evaporation from ethyl acetate<sup>6</sup>. Crystal data:  $\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_3$ ,  $M=220.2$ , tetragonal, s.g.  $P\bar{4}_2c$ ,  $Z=8$ ,  $a=b=17.008$  (5),  $c=7.081(3)\text{ \AA}$ ,  $V=2048(1)\text{ \AA}^3$ ,  $D_c=1.43\text{ g/cm}^3$ ,  $F(000)=928$ ,  $\lambda(\text{Cu-K}\alpha)=1.5418\text{ \AA}$ ,  $\mu(\text{Cu-K}\alpha)=0.9\text{ mm}^{-1}$ ,  $R=0.044$  and  $R_w=0.065$  for 1023 observed independent reflections with  $I>1.5\sigma(I)$ . Intensity data were recorded on an automatic Syntex P2<sub>1</sub> diffractometer equipped with Cu-K $\alpha$  radiation up to a  $2\theta$  value of  $138^\circ$  by the  $\theta$ - $2\theta$  scan technique. The structure has been solved by direct methods using the programme MULTAN 80<sup>7</sup>. An E-map computed with the phases of the set having the highest figures of merit revealed the non hydrogen atoms. A difference Fourier map, computed after isotropic refinement by full-matrix least-squares method, showed a residual electronic density peak of ca.  $2\text{ e}\cdot\text{\AA}^{-3}$  in the vicinity of the hydroxyl group of the N-hydroxy-

ethyl chain. This was interpreted as due to a secondary conformation assumed by the terminal hydroxyl. Refinement was then continued anisotropically, assuming two different positions for the hydroxylic oxygen, with 3/4 and 1/4 occupancy factor respectively. A successive Fourier difference synthesis allowed to detect the hydrogen atoms.

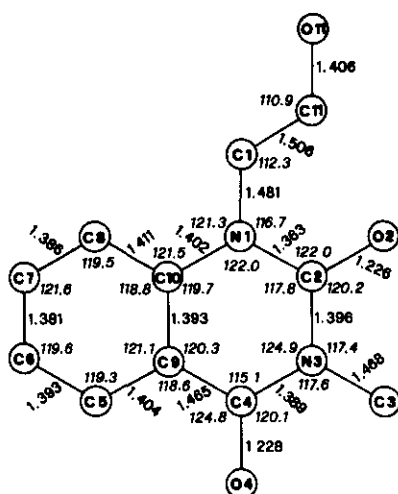


Fig. 1

Atomic numbering, valence bond lengths and angles of (5).

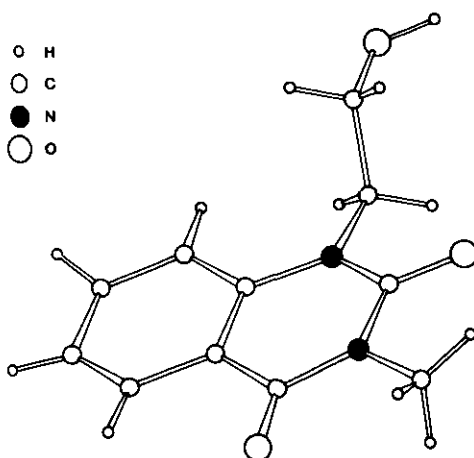


Fig. 2

Perspective molecular view of (5)

The atomic numbering together with the bond lengths and angles and a perspective molecular view of compound (5) are reported in Figure 1 and 2 respectively for the major conformer. The atoms of the heterocyclic ring lie on a plane, the largest deviation from the least squares plane through these atoms, being 0.039 Å for N(3). The hydroxymethyl group is out of the plane of the heterocyclic system with the C(10)-N(1)-C(1)-C(11) torsion angle equal to 90°. In the major conformer the N(1) and O(11) atoms are trans-coplanar with the torsion angle N(1)-C(1)-C(11)-O(11) = -172°, while in the minor conformer the corresponding torsion angle is -78°. Full details of the crystal structure will be given elsewhere.

## ACKNOWLEDGEMENTS

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# REFERENCES AND NOTES

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- S.Barcza, G.M.Coppola, and M.J.Shapiro, J.Het.Chem., 1979, 16, 439.
- Mp 165 - 167°C (CHCl<sub>3</sub>); 60% yield; ir(nujol): 3480, 1700-1690, 1655, 1610 cm<sup>-1</sup>; ir(CHCl<sub>3</sub>): 3480, 1700, 1655, 1610 cm<sup>-1</sup>; <sup>1</sup>H-nmr (Varian EM-390, 90 MHz, DMSO-d<sub>6</sub>): δ = 3.3 (3H,s,CH<sub>3</sub>), 3.6-3.8 (2H,m,CH<sub>2</sub>O), 4.2 (2H,t,J=6.0Hz,CH<sub>2</sub>N), 4.9 (1H,br.t,OH), 7.15-8.2 ppm (4H,m,ArH); <sup>13</sup>C-nmr (Bruker WP 200, 50.28 MHz, CDCl<sub>3</sub>): δ=161.9 (C-4), 152.1(C-2), 140.1(C-10), 135.1(C-7), 129.0(C-5), 123.1(C-6), 115.6(C-9), 113.9(C-8), 60.6(CH<sub>2</sub>O), 46.0(CH<sub>2</sub>-N), 28.4 ppm (CH<sub>3</sub>).  
<sup>1</sup>H- and <sup>13</sup>C-nmr spectra do not show evidence of ring-chain tautomeric equilibria.  
Anal. Calcd. for C<sub>11</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>: C, 59.99; H, 5.49; N, 12.72. Found: C, 60.05; H, 5.52; N, 12.68%.
- Mp 166-168°C (CHCl<sub>3</sub>); ir(nujol): 3480, 1685, 1640 cm<sup>-1</sup>; <sup>1</sup>H-nmr (60 MHz, DMSO-d<sub>6</sub>): δ = 3.3 (3H,s), 3.7 (2H,m), 4.2 (2H,t), 4.9 (1H,br.t), 7.1-8.2 ppm (4H,m). See reference 2.
- (a) N-Benzoyl-N-methyl-tert-butylurethane C<sub>6</sub>H<sub>5</sub>CO-N(CH<sub>3</sub>)-COO-Bu<sup>t</sup> shows ir carbonyl frequency (nujol) at 1730 and 1670 cm<sup>-1</sup> (F.Pinnen and G.Lucente, unpublished results); (b) P.A.Grieco, D.L.Flynn, and R.E.Zelle, J.Am.Chem.Soc., 1984, 106, 6414; (c) C.Shin, Y.Yonezawa, and E.Watanabe, Tetrahedron Lett., 1985, 26, 85.
- These crystals show melting point and spectral data identical to those obtained from chloroform.
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