On the Reaction between Potassium Ethoxide and 3-Amino-4-benzoylfurazan: the Crystal Structure of the Intermediate, 5-Phenyl-1,2,4-Oxadiazole-3-carboxamide

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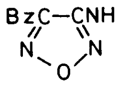
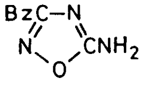
The crystal and molecular structure of 5-phenyl-1,2,4-oxadiazole-3-carboxamide, $C_9H_7N_3O_2$, has been determined by single-crystal *X*-ray analysis. The crystals are triclinic, space group $P\bar{1}$, a = 10.290(2), b = 8.170(2), c = 5.423(1) Å, α = 98.51(1), β = 99.63(1), γ = 95.87(1)°, Z = 2. The structure was solved from diffractometer data by direct methods and refined by full matrix least-squares to R 7.7% for 1 446 reflexions. 5-Phenyl-1,2,4-oxadiazole-3-carboxamide is an intermediate in the reaction between 3-amino-4-benzoylfurazan and potassium ethoxide and its analysis established the structural formula of the final product of the reaction as the corresponding 5-phenyl-1,2,4-oxadiazole-3-carboxylic acid.

SEVERAL authors[1,2] have studied the action of NH_3 on dibenzoylfuroxan. The product is a compound of formula $C_9H_7N_3O_2$, m.p. 135 °C, for which several structural formulae have been proposed; Ponzio and Cerrina[1] have suggested that it is 3-amino-4-benzoylfurazan (I) while Boeseken and Ross van Lennep[2] favoured 5-amino-3-benzoyl-1,2,4-oxadiazole (II).


(I)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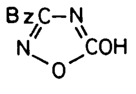
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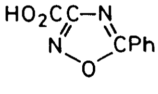
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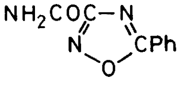
(V)

Recently, Bertelson *et al.*[3] showed that 3,4-diacylfuroxans react with aniline to give, as secondary products, the corresponding 4-acyl-3-anilinofurazans (I; NHPh for NH_2); by analogy, this result favours the structure proposed by Ponzio and Cerrina.

The action of potassium ethoxide on the compound of formula $C_9H_7N_3O_2$ yields a derivative of formula $C_9H_6N_2O_3$, m.p. 120 °C. Boeseken and Ross van Lennep[2] assigned to it the 3-benzoyl-5-hydroxy-1,2,4-oxadiazole structure (III) while Ponzio[4] proposed that it was 5-phenyl-1,2,4-oxadiazole-3-carboxylic acid (IV). Ponzio based his proposal on the fact that he was able to isolate an intermediate product with an amide structure (V) and formula $C_9H_7N_3O_2$, m.p. 160 °C. This product is identical with that[5] of the reaction of water with 3-cyano-5-phenyl-1,2,4-oxadiazole.

The unambiguous determination of the structure of the amide is essential both in the determination of the structural formulae of the compounds $C_9H_7N_3O_2$, m.p. 135 °C, and $C_9H_6N_2O_3$, m.p. 120 °C, and in understanding the mechanism of the reaction of (I) with EtOH.

EXPERIMENTAL

5-Phenyl-1,2,4-oxadiazole-3-carboxamide was prepared, according to Ponzio,[4] from 3-amino-4-benzoylfurazan and recrystallized from tetrahydrofuran as small prismatic crystals. Preliminary Weissenberg photographs established the space group $P\bar{1}$ and approximate cell parameters which were later refined from diffractometer data.

The intensities were collected, using graphite-monochromatized Cu-K_α radiation on a Philips PW 1100 four-circle diffractometer.

The intensities of 1 499 unique reflexions, in the range $2° \leqslant \theta \leqslant 65°$, were measured by the $\theta - 2\theta$ scanning technique; all but 53 reflexions, which had negative measured intensities, were included in the refinement. Lorentz and polarization corrections were applied to yield structure amplitudes $|F_o|$.

Crystal Data.—$C_9H_7N_3O_2$, M = 189. Triclinic, a = 10.290(2), b = 8.170(2), c = 5.423(1) Å, α = 98.51(1), β = 99.63(1), γ = 95.87(1)°, U = 440.75 Å^3, Z = 2, D_c = 1.424 g cm^{-3}, space group $P\bar{1}$. Cu-K_α radiation, λ = 1.541 8 Å, μ(Cu-K_α) = 8.92 cm^{-1}.

Structure Solution and Refinement.—The structure was solved by direct methods using the MULTAN 76[6] system of programs. 1 433 Triple-phase relationships were generated for the 210 largest normalized structure factors ($|E| \geqslant 1.50$). Besides the three origin-defining reflexions five other reflexions were included in the starting set and 32 sets of phases were developed by the tangent formula. The E map computed with the set having the highest combined figure of merit revealed all 14 non-hydrogen atoms, whose positions and individual isotropic temperature factors were initially refined by six full-matrix least-squares cycles, using the SHELX[7] program. The hydrogen atoms were located on a difference map computed after three further cycles in which the components of the anisotropic temperature factors were refined. The hydrogen atoms were then included in the refinement with isotropic temperature factors, but, in order to maintain them in stereochemically plausible positions, the C–H and N–H distances were constrained to their usual values (1.00 ± 0.05 Å). The final cycles with anisotropic temperature factors assigned to all non-hydrogen atoms converged to an R value of 7.7%. The weighting scheme was $w = 1/[\sigma^2(F_o) + qF_o^2]$, where $\sigma(F_o)$ is the estimated standard deviation of the observed amplitudes as derived from counting statistics and q is a variable parameter which is adjusted after each cycle; its final value was 0.09 and the final weighted R factor was 10.6%.

Atomic scattering factors for carbon, nitrogen, and oxygen were from ref. 8 and for hydrogen from ref. 9.

RESULTS AND DISCUSSION

Atomic parameters are listed in the Table. Figure 1 shows the molecule projected on to the plane through the oxadiazole ring and also shows the conventional numbering scheme adopted and the bond distances and angles. Figure 2 illustrates the packing of the molecules in the crystal.

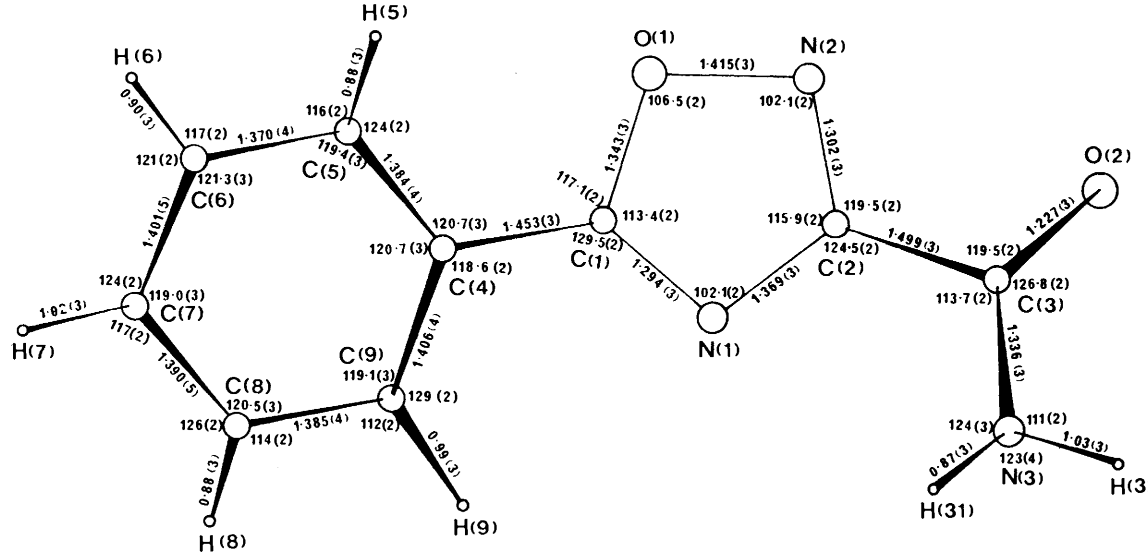

FIGURE 1 Projection of the molecule on the plane of the oxadiazole ring, showing the unconventional numbering scheme and the bond distances and angles with e.s.d.s in parentheses

Observed and calculated structure factors ($\times 10$) and the components of the anisotropic thermal parameters of the non-hydrogen atoms are deposited as Supplementary Publication No SUP 22747 (12 pp.).*

Atomic co-ordinates ($\times 10^3$) and isotropic temperature factors of the hydrogen atoms with e.s.d.'s in parentheses

Atom	x/a	y/b	z/c	U_{iso}
C(1)	0.473 7(2)	0.749 7(3)	−0.071 7(4)	
C(2)	0.286 2(2)	0.824 4(3)	−0.126 5(4)	
C(3)	0.159 1(2)	0.886 1(3)	−0.077 4(4)	
C(4)	0.604 7(2)	0.704 9(3)	0.014 8(5)	
C(5)	0.664 8(3)	0.602 4(4)	−0.146 1(6)	
C(6)	0.787 8(3)	0.561 3(4)	−0.058 2(7)	
C(7)	0.855 3(3)	0.623 6(4)	0.189 8(7)	
C(8)	0.793 5(3)	0.724 7(4)	0.351 3(7)	
C(9)	0.668 3(3)	0.765 7(3)	0.266 9(5)	
N(1)	0.392 7(2)	0.817 2(2)	0.058 4(3)	
N(2)	0.297 6(2)	0.766 7(3)	−0.357 9(4)	
N(3)	0.147 9(2)	0.906 4(3)	0.166 8(4)	
O(1)	0.426 0(2)	0.716 3(3)	−0.322 5(3)	
O(2)	0.077 8(2)	0.912 2(3)	−0.255 5(3)	
H(5)	0.629(4)	0.560(4)	−0.305(7)	0.09(1)
H(6)	0.829(4)	0.506(5)	−0.172(7)	0.10(1)
H(7)	0.945(3)	0.592(4)	0.264(6)	0.09(1)
H(8)	0.828(3)	0.770(3)	0.510(6)	0.07(1)
H(9)	0.638(3)	0.843(4)	0.398(6)	0.08(1)
H(31)	0.203(4)	0.876(4)	0.286(7)	0.10(1)
H(32)	0.056(3)	0.940(4)	0.190(7)	0.10(1)

The longest molecular axis is parallel to the x axis. Approximately along the y axis the molecules are stacked one on top of the other with the five-membered ring of one facing the phenyl ring of the other. Along z they are linked by only one fairly weak hydrogen bond (shown by a dotted line in Figure 2) between N(3) of one molecule and O(2) of another displaced by one unit along z [N(3)–H(32) $\cdots$ O(2) = 2.947 Å].

Both the five- and six-membered rings in the molecule are planar, but they form a dihedral angle of 12.9°. Also the amide group is rotated with respect to the oxadiazole ring, the dihedral angle being 13.0°. The rotations of the phenyl and amide groups are such that the dihedral angle between the two groups is 25.4°. Finally the NH_2 group is rotated by 11° with respect to the amide plane.

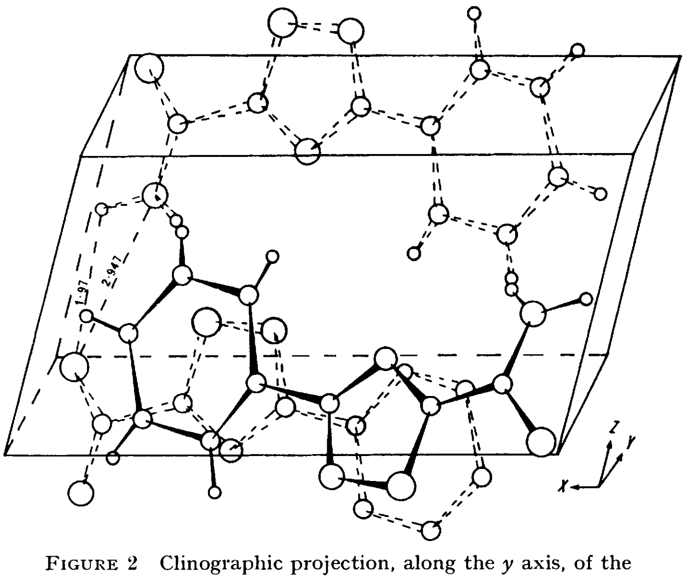

FIGURE 2 Clinographic projection, along the y axis, of the content of a unit cell, showing the packing of the molecules

As far as the geometry of the 1,2,4-oxadiazole ring is

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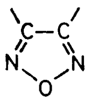
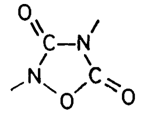
concerned it is not possible to make a direct comparison with any other known compound. In the literature only the structure of 5-methyl-2*H*-[1,2,4]oxadiazole [2,3-*c*]quinazolin-2-one [10] is reported in which the same five-membered ring appears, but fused to a quinazoline system and with a carbonyl oxygen attached to the unshared carbon, thus completely changing the electronic structure of the ring.*

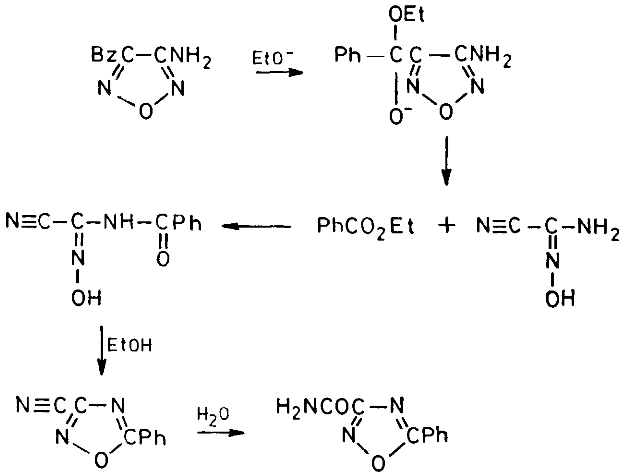


(A)



(B)

Within the ring the sequence of bonds C(1)=N(1)–C(2)=N(2) shows that there is a certain degree of π-delocalization, similar to that found in 1,2,5-oxadiazoles (furazans) (A) [11-15] for the sequence N=C–C=N. The distance N(2)–O(1) is longer than in the furazans implying that the possibility of π-delocalization throughout the whole ring is not significant. The distance C(1)–O(1) corresponds to a partial double bond and the sequence of the two bonds C(1)–O(1)–N(2) is similar to that found in quisqualic acid,[16] where aromaticity in the five-membered ring (B) is excluded.



SCHEME

The geometry of the amide group is similar to that found in most other amides. The only noticeable feature is the angular distortion at C(3), due to the repulsion between the oxygen and nitrogen atoms, which is also present in other amide groups, but it is higher in the present compound.

Reaction Mechanism.—The solution of the structure allowed us to confirm Ponzio's assignment of the structure of the product of the reaction between 3-amino-4-benzoylfurazan and potassium ethoxide, but the mechanism he proposed remains rather doubtful. In fact, although the isomerization of furazans to 1,2,4-oxadiazoles is known,[17] it only takes place under totally different experimental conditions, probably *via* a nitrile oxide and benzonitrile, as indicated by the presence of benzonitrile and phenyl isocyanate among the products.

A more likely mechanism for the reaction is shown in the Scheme. This hypothesis is supported by the fact that Ponzio later described [18] the transformation of 3-benzoyl-4-benzoylaminofurazan, by the action of base, into the amide (V) through a mechanism identical to that in the Scheme; moreover, recently, Brachwitz [19] succeeded in obtaining the amide (V) by nitrosation of the corresponding compound, $N{\equiv}C{-}CH_2{-}NHBz$.

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* After this work was sent for publication a paper by L. Golič, I. Leban, B. Stanovnik, and M. Tišler (*Acta Cryst.*, 1979, **B35**, 2256) appeared describing the structure of 2-amino-3-(5-methyl-1,2,4-oxadiazol-3-yl)pyridine. The geometry of the 1,2,4-oxadiazole ring is very similar to that found by us.