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THE STRUCTURE OF THE PRODUCT FROM THE REACTION OF o-AMINOBENZALDOXIME AND ACETIC ANHYDRIDE

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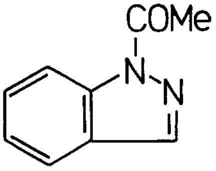
Auwers [1,2] reported the preparation of three acetylated indazoles. Two of them were prepared by acetylation of indazole and the third compound was obtained from treatment of o-aminobenzaldoxime with acetic anhydride. For the later compound the structure of 1-acetyl indazole (1) was proposed on hand of its formation and since it could be hydrolized into o-acetylaminobenzaldoxime. The alleged 1-acetylindazole had m.p. 169-171° and was different from the other two acetylindazoles, one (m.p. 42-43°) being obtained when indazole was treated with acetic anhydride, and the other (m.p. 106°) from the reaction of the silver salt of indazole and acetyl chloride, or by acetylation of indazole in the presence of pyridine. The later compound was designated as "labile" 2-acetyl-indazole and it was claimed that after standing it is transformed into the stable 2-acetylindazole, m.p. 42-43° [1].

Later, Meisenheimer [3] based on chemical evidence, claimed that the compound with m.p. 169-171° is not 1-acetylindazole, but a derivative of benzoxadiazepine (2). Similarly, for 1-acetyl-3-methylindazole he proposed the structure coresponding to the 5-methyl analog of 3,1,4-benzoxadiazepine 2 [4]. Further investigations, conducted by both, Auwers and Meisenheimer group, gave evidence much in favour of the benzoxadiazepine structure and this was then accepted [4,5] This view was also accepted in a review [6] where it is stated that 1-acylindazoles, described in the literature before 1925 should be regarded most probably as benzoxadiazepines.

Recently, it was found that irradiation of quinazoline-1-oxides gives 1-acetylindazole [7] and the reaction has been explained by the intermediate formation of a 3,1,4-benzoxadiazepine compound. This was supported also by the observation that a 3,1,4-benzoxadiazepine derivative was transformed upon irradiation into an 1-acylindazole derivative

Sternbach et al. [8] afforded chemical evidence that compounds obtained by dehydration of o-acylaminobenzoketoximes with a Beckmann mixture are not derivatives of 3,1,4-benzoxadiazepines but quinazoline 3-oxides. No spectroscopic data were available for the investigated compounds.

Taking into account that the above mentioned 1-acetylindazole with m.p. 169-171° could possibly not have this the 3,1,4-benzoxadiazepine structure (2), but that it is a derivative of quinazoline-3-oxide (3), prompted us to investigate the compound by X-ray analysis. Moreover, this was strongly desirable when taking into account the relative instability of quinazoline-3-oxide. It was found that quinazoline-3-oxide easily adds water and after succesive ring fission and hydrolysis is transformed into 2-aminobenzaldoxime[9]. The compound was prepared according to the literature[1,2] from o-aminobenzaldoxime and acetic anhydride in the presence of hydrogen chloride at room temperature after 6 days. The compound was crystallized from benzene and for X-ray analysis the crystals were obtained by slow cooling of a saturated n-heptane solution, m p. 170-172°. Mass spectrum $M^+ = 160$, NMR ($CDCl_3$) $\delta = 1.11$ (s, H_4), 2.05-2.4 (m, H_5, H_6, H_7, H_8), 7.12 (s, 2-Me). (Anal.Calcd. for $C_9H_8N_2O$ C, 67.48, H, 5.03, N, 17.49 %). Found C, 67.12, H, 5.08, N, 17.80.



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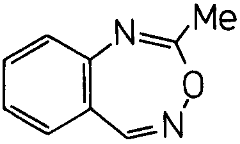

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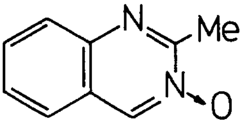


III

Conclusive evidence for the 2-methyl-quinazoline-3-oxide structure was obtained from X-ray analysis. The crystal is triclinic, space group $P\bar{1}$, with two molecules in an unit cell of dimensions $a = 3\ 94\ (1)$, $b = 9.02\ (1)$, $c = 11.03\ (1)$ Å, $\alpha = 79.8\ (1)$, $\beta = 99.6\ (1)$, $\gamma = 92.5\ (1)^\circ$, $V = 380.4$ Å. $D_{calc} = 1.40$ g cm^{-3}, $D_{obs} = 1.39\ (6)$ g cm^{-3} (flotation).

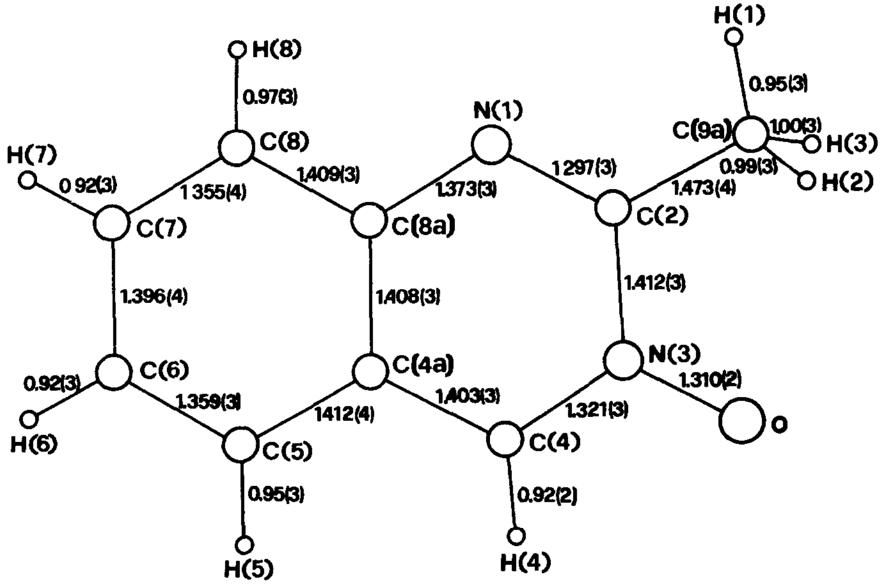
Intensity data of 1731 independent reflections in the range $1.5^\circ \leq \vartheta \leq 27.5^\circ$ were measured on an Euraf-Nonius CAD-4 automatic diffractometer with $\omega - 2\vartheta$ scan and MoK_α radiation. 1031 reflections with $I_o > 1.5\,\sigma\,(I_o)$ (calculated from counting statistics) were used for the structure analysis The crystal structure was solved by direct methods using the program MULTAN of Declerq, Germain, Main and Woolfson[10] using 250 highest E's and 2000 Σ_2 relationships. Three dimensional E map revealed all the non-hydrogen atoms in correct orientation but displaced from the right position. This structure information was used to estimate the phase and variance of Σ_2 relationships by the procedure of Main[11]. MULTAN program was reentered at the convergence stage and 32 sets of phases were generated. The set with the lowest psi-zero value gave the correct structure. The positions of hydrogen atoms of methyl group were obtained from difference electron-density map, while the hydrogens attached to the rings were put to the calculed positions. The positions of all atoms, anisotropic thermal parameters of non-hydrogen atoms and isotropic thermal parameters of hydrogen atoms were then refined by fullmatrix least-squares program. The final conventional R and R_w for 1031 reflections are 0.045 and 0.040, respectively.

A list of structure factors can be obtained from the authors, the final atomic parameters are given in table.

Table of positional and thermal parameters (x10^4)

Thermal parameters are given according to the expression $T=\exp[-2\pi^2(a^{*2}h^2U_{11}+\ldots+2a^*b^*hkU_{12}+\ldots)$

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
O	5504(4)	-1101(2)	3717(2)	552(9)	540(10)	599(10)	-141(7)	274(7)	8(7)
N(1)	9496(4)	1256(2)	1444(2)	319(8)	416(10)	404(10)	- 16(7)	108(7)	- 44(8)
C(2)	7992(5)	104(2)	2023(2)	287(9)	414(12)	393(11)	16(8)	88(8)	- 53(9)
N(3)	7172(4)	78(2)	3225(2)	301(8)	422(10)	415(9)	2(7)	120(6)	- 14(8)
C(4)	8118(5)	1218(2)	3817(2)	359(10)	499(13)	319(12)	49(9)	105(8)	- 57(10)
C(4a)	9835(5)	2475(2)	3246(2)	262(9)	475(12)	389(12)	51(8)	52(8)	- 79(9)
C(5)	10925(6)	3734(3)	3818(3)	404(11)	529(14)	521(15)	52(9)	35(10)	-201(11)
C(6)	12419(6)	4936(3)	3172(3)	429(12)	458(14)	773(18)	- 27(11)	25(11)	-231(14)
C(7)	12912(5)	4943(3)	1947(3)	442(12)	453(14)	691(18)	- 73(10)	122(11)	- 63(12)
C(8)	11980(5)	3741(2)	1378(2)	407(11)	456(13)	465(13)	- 35(9)	120(9)	- 51(10)
C(8a)	10421(5)	2477(2)	2021(2)	257(9)	386(11)	439(13)	4(8)	58(8)	- 57(9)
C(9a)	7024(6)	-1253(3)	1466(3)	463(13)	481(14)	554(15)	- 92(10)	159(11)	-146(12)
H(1)	7847(59)	-1164(24)	692(23)	479(59)					
H(2)	7886(63)	-2161(31)	2060(25)	638(68)					
H(3)	4473(86)	-1378(32)	1311(26)	835(79)					
H(4)	7608(48)	1149(21)	4605(20)	359(52)					
H(5)	10634(60)	3686(26)	4665(27)	561(66)					
H(6)	13098(62)	5781(33)	3506(24)	587(70)					
H(7)	13721(68)	5818(35)	1510(25)	680(81)					
H(8)	12363(52)	3717(21)	535(22)	417(55)					



Bond lenghts with their estimated standard deviations and the molecule are presented in figure. The six-membered carbon ring has a mean carbon bond distance of 1.390 Å and a mean angle of 120.0° with the minimum value at C(4a) of 118.9(2)° and maximum value at C(7) of 121.0(2)°. These values are similar to those in 3-phenyl-2,4(1H,3H)-quinazolinedione[12] or tricycloquinazoline [13]. The mean value of 1.309 Å for bond lenghts N(1)-C(2) and N(3)-C(4) clearly indicates double-bond character contrary to the mean value of 1.392 Å for N(1)-C(8a) and N(3)-C(2) bond lenghts which are usually observed in heterocyclic rings. Although the N(3)-O bond lenght (1.310 Å) is somewhat short it is in a good agreement with the values reported in the literature[14,15]. Bond lenghts involving hydrogen atoms are found to be in the range of 0.92 to 1.00 Å. Apart from hydrogens in the methyl group they lie in the plane of the bicycle. The temperature factors for hydrogens are in the range of 0.036 to 0.083 (U), maximum value is for methyl hydrogen atom H(3). Valency angles are between 116.0 and 123.8° with the maximum estimated standard deviation being 0.3°.

The equation of the least-squares plane (in direct space) through all the non-hydrogen atoms is.

$$-3.3567x + 3.5172y - 1.8779z = -3.0100.$$

The largest deviations are 0.08 Å for the oxygen atom and -0.06 Å for methyl carbon atom (oxygen atom is above, methyl carbon atom below the plane). The mean plane of the atoms N(1), C(2), N(3), C(4), C(4a) and C(8a) is given by the equation

$$-3.3429x + 3.5772y - 1.8870z = -2.9974$$

with the deviations from the plane -0.0002, -0.0187, 0.0190, -0.0012, -0.0174 and 0.0185 Å respectively. The equation of the mean plane through atoms C(4a), C(5), C(6), C(7), C(8) and C(9a) is

$$-3.4230x + 3.4826y - 1.4797z = -2.9970$$

with the deviations 0.0123, -0.0070, -0.0043, 0.0105, -0.0049 and -0.0065 Å, respectively. The dihedral angle between last two planes is 2.5°. The distortion from the plane in heterocyclic ring is the same as in lumazine hydrate[16].

The molecules of the compound are held together in the structure only by van der Waals forces.

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