Single Crystal X-ray Diffraction Analysis of 2,3a,4,5-Tetrahydro-7,8-dimethoxy-3a-methyl-3*H*-benz[*g*]indazol-3-one Hemihydrate (1)

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The structure of 2,3a,4,5-tetrahydro-7,8-dimethoxy-3a-methyl-3*H*-benz[*g*]indazol-3-one hemihydrate was unequivocally established by means of an X-ray diffraction analysis of a single crystal. The molecule crystallizes in the space group C2/c with unit cell parameters of a = 18.839(4), b = 7.7694(7), c = 18.211(2) Å and β = 101.06(1). The structure was solved by direct methods and refined by least-squares methods to an R-value of 0.069 for 2689 reflections. The indazol-3-one unit of the molecule is non-planar.

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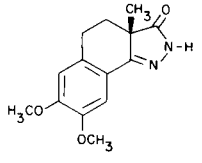
Introduction.

It was reported previously (2) that the title compound **1** exhibited growth inhibitory properties for *Bacillus subtilis* and KB cells. These observations coupled with our interest in the structural as well as biological properties of small nitrogen-containing heterocycles (3,4) prompted us to perform a single crystal X-ray diffraction analysis of 2,3a,4,5-tetrahydro-7,8-dimethoxy-3a-methyl-3*H*-benz[*g*]indazol-3-one (2). Herein we report such an analysis on a crystal of this compound which contained water of crystallization.

Structure I



Crystal and Intensity Data.

Suitable prismatic single crystals were obtained by recrystallization from ethanol. The crystals system is monoclinic and space group is C2/c. The crystal data are: $C_{14}H_{16}N_2O_3 \cdot \frac{1}{2}H_2O$, M = 269.31, a = 18.839(4), b = 7.7694(7), c = 18.211(2) Å, β = 101.06(1)°, V = 2616 Å^3 at 138°K and at room temperature a = 19.03(2), b = 7.725(2), c = 18.534(6) Å, β = 101.83°(5), V = 2667 Å, Z = 8, D_m = 1.316 gm cm^{-3}, D_c = 1.341 g. cm^{-3}, F(000) = 1144.

Integrated intensity data were collected at 138°K on a Nonius CAD-4 diffractometer equipped with a cold-stream cooling device. The intensities of 2689 reflections comprising all unique data with $2\theta < 150°$ were measured using Ni-filtered Cu$K\bar{\alpha}$ radiation (λ = 1.5418 Å). A variable scan width of (1.1 + 0.11 tan θ)°, as determined from the crystal mosaic, and a variable aperture width of (4.0 + 0.86 tan θ)mm were used. The maximum time spent on a measurement was 60 s while a faster scan time was employed for reflections giving 40,000 counts or more.

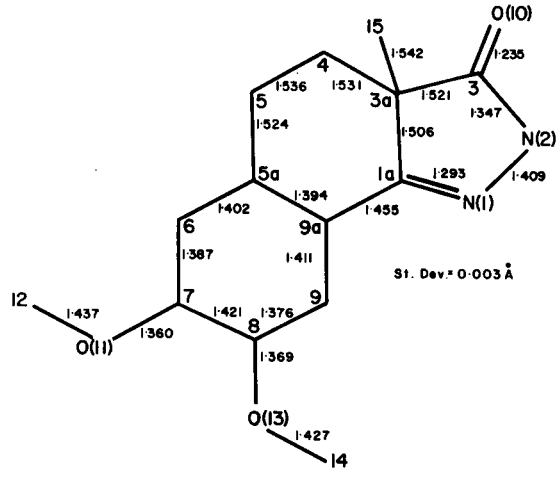


Figure 1. Numbering Scheme and Bond Distances (Å) in 2,3a,4,5-Tetrahydro-7,8-dimethoxy-3a-methyl-3*H*-benz[*g*]-indazol-3-one Hemihydrate (**1**)

The intensity of a monitor reflection, measured after every 25 observations, showed a maximum variation of 3% during data collection. The orientation matrix was checked after every 100 measurements. A total of 426 reflections were considered indistinguishable from background on the basis that net count [= Peak − 2 (left background + right background)] was less than 1.4 σ (I). Lorentz and polarization corrections were applied to individual reflections but no absorption correction was made (μ = 7.83 cm^{-1}). An experimental weight based on counting statistics was assigned to each structure factor (5).

Structure Determination and Refinement.

The structure was solved by direct methods using the computer program MULTAN(6), which yielded all the non-hydrogen atoms in the molecule. The structure was refined by a block-diagonal least squares program, the quantity minimized being $\Sigma W_F(|kFo| - |Fc|)^2$. After a few

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cycles of refinement, a difference Fourier map was calculated which showed the oxygen atom of a water molecule lying on the two-fold axis. All the hydrogen atoms except those in the water molecules were also located from the difference Fourier map. The structure was further refined with isotropic temperature factors for the hydrogen atoms and anisotropic thermal parameters for the carbon, nitrogen and oxygen atoms. The R-value, defined as,

$$\frac{\Sigma\,||kFo| - |Fc||}{\Sigma\,|kFo|}$$

based on the final parameters (Table 1) (7) was 0.056 for the 2211 reflections with $I > 1.4\ \sigma\ (I)$ and 0.069 for all 2689 reflections. The atomic scattering factors for carbon, nitrogen and oxygen were taken from the International Tables for X-ray Crystallography (8) while those for hydrogen were taken from Stewart, Davidson and Simpson (9). A final difference Fourier map showed all residual electron density to be between -0.35 to 0.35 e Å^{-3}. Bond distances involving hydrogen atoms range from 0.86 to 1.06 Å with an average value of 1.04 Å.

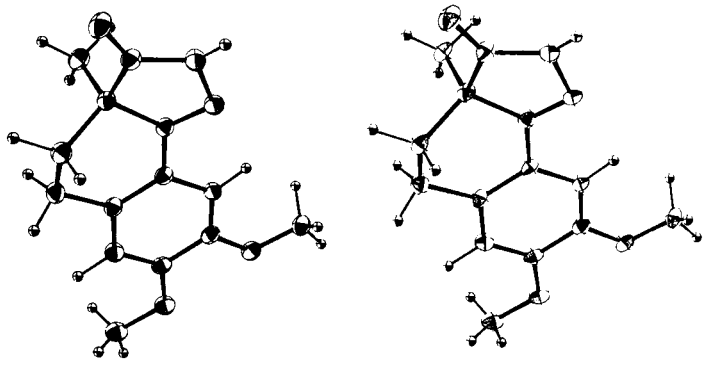


Figure 2. Stereoview (10) of Single Molecule of **1**

Discussion.

The structure of 2,3a,4,5-tetrahydro-7,8-dimethoxy-3a-methyl-3*H*-benz[*g*]indazol-3-one, **1**, is of interest because of its potential use in chemotherapy (2) and is one of a series of indazoles whose structures have been investigated in this laboratory (3,4). Figures 1 and 2 show the numbering scheme with bond distances and a

Table 1

Positional Parameters (× 10^4) for Carbon, Nitrogen and Oxygen Atoms

Atoms	X/A	Y/B	Z/C	Atoms	X/A	Y/B	Z/C
N(1)	4070(1)	11421(2)	3039(1)	C(9)	5546(1)	10753(3)	3880(1)
N(2)	3347(1)	11218(2)	2667(1)	C(9a)	4973(1)	9552(3)	3773(1)
C(3)	3087(1)	9620(3)	2725(1)	C(1a)	4292(1)	9902(3)	3267(1)
C(3a)	3736(1)	8509(3)	3049(1)	C(12)	6969(1)	7100(4)	5717(1)
C(4)	3670(1)	7462(3)	3745(1)	C(14)	6691(1)	13139(3)	4173(1)
C(5)	4413(1)	6732(3)	4106(1)	C(15)	3899(1)	7363(3)	2410(1)
C(5a)	5028(1)	8037(3)	4189(1)	O(10)	2448(1)	9195(2)	2518(1)
C(6)	5664(1)	7731(3)	4713(1)	O(11)	6857(1)	8718(2)	5330(1)
C(7)	6231(1)	8900(3)	4821(1)	O(13)	6759(1)	11505(2)	4538(1)
C(8)	6170(1)	10439(3)	4392(1)	O(W)	5000(0)	3968(9)	2500(0)

Table 2

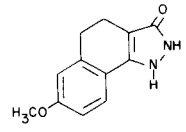
Bond-Angles (Estimated Standard Deviation is 0.2°)

N(1)	– N(2)	– C(3)	113.4°	C(9a)	– C(1a)	– C(3a)	121.1
N(2)	– C(3)	– C(3a)	106.0	N(1)	– C(1a)	– C(9a)	124.5
C(3)	– C(3a)	– C(1a)	99.3	C(9a)	– C(5a)	– C(6)	118.5
C(3a)	– C(1a)	– N(1)	113.9	C(5a)	– C(6)	– C(7)	121.4
C(1a)	– N(1)	– N(2)	106.0	C(5)	– C(5a)	– C(6)	119.3
N(2)	– C(3)	– O(10)	124.8	C(6)	– C(7)	– C(8)	119.6
C(3a)	– C(3)	– O(10)	129.1	C(7)	– C(8)	– C(9)	119.4
C(3)	– C(3a)	– C(15)	107.3	C(8)	– C(9)	– C(9a)	120.5
C(1a)	– C(3a)	– C(15)	112.6	C(9)	– C(9a)	– C(5a)	120.6
C(4)	– C(3a)	– C(15)	112.2	C(9)	– C(9a)	– C(1a)	121.5
C(1a)	– C(3a)	– C(4)	109.1	C(6)	– C(7)	– O(11)	124.9
C(3)	– C(3a)	– C(4)	115.8	C(8)	– C(7)	– O(11)	115.4
C(3a)	– C(4)	– C(5)	109.7	C(7)	– O(11)	– C(12)	116.9
C(4)	– C(5)	– C(5a)	114.2	C(7)	– C(8)	– O(13)	115.2
C(5)	– C(5a)	– C(9a)	122.2	C(9)	– C(8)	– O(13)	125.4
C(5a)	– C(9a)	– C(1a)	117.8	C(8)	– O(13)	– C(14)	116.8

stereoview of the molecule, respectively. The bond angles are presented in Table 2.

It is interesting to compare the pyrazoline ring in the structure of the present compound (**1**) with the 3a-desmethyl compound: 1,2,4,5-tetrahydro-7-methoxy-3*H*-benz[*g*]indazol-3-one (**2**) (4). In the latter compound, the 5-membered pyrazoline ring exists as the 1,2-dihydropyrazole-3-one tautomer, with the significant hybrid being described by two resonance forms in both of which a negative charge exists on the oxygen atom. The methyl substitution on C(3a) in the present compound prevents that particular tautomer and instead the 2,4-dihydropyrazol-3-one tautomer exists for which the carbon atoms C(1a) and C(3) are sp^2 hybridized [sums of bond angles around C(1a) and C(3) are 359.5° and 359.9°, respectively] and a formal double bond exists between C(1a) and N(1). The bond distances in the 5-membered ring compared to those in **2** (in parentheses) reflect this change in tautomeric form: C(1a)-C(3a): 1.506 (1.383) Å; C(3)-C(3a): 1.521 (1.413) Å; C(3)-O(10): 1.235 (1.294) Å; C(3)-N(2): 1.347 (1.359) Å; N(1)-N(2): 1.409 (1.369) Å; N(1)-C(1a): 1.293 (1.344) Å. These dimensions also indicate that the contribution to the hybrid of resonance forms with a negative charge on O(10) are much less important in the present structure and O(10), therefore, will be a worse acceptor for hydrogen bonds in **1** than in **2**. In contrast, O(10) in **2** is the acceptor of *three* strong hydrogen bonds. The hydrogen atom on N(2) behaves normally under least-squares refinement.

Structure 2



The five-membered ring is not perfectly planar. The average deviation of the five ring-atoms from their best plane is 0.044 Å; the maximum deviation being 0.066 Å for atom C(3) (Table 4). The equation of the best plane through the whole molecule is 10.046x − 3.049y − 15.243z + 3.743 = 0. Among the ring-atoms, C(4) deviates maximum from this plane (0.55 Å) (Figure 3). The whole molecule **1** is characterized by a relative flatness, the dihedral angle between the least-squares planes of the five-membered ring and the benzene ring being 21°. The torsion angles of the cyclohexadiene ring (Figure 3) show a half-chair conformation.

The hydrogen bonding is summarized in Table 4. The nitrogen N(2) is involved in a strong hydrogen bond with O(10), while N(1) is the acceptor for an hydrogen bond from the water molecule. The water molecule does not take part in any other hydrogen-bonding. The relative isolation of the water molecule may be responsible for the high thermal vibration of oxygen (water) (Table 1). The O(10), which is the acceptor of 3 hydrogen bonds in compound **2**, is involved in only one hydrogen bond in the present compound.

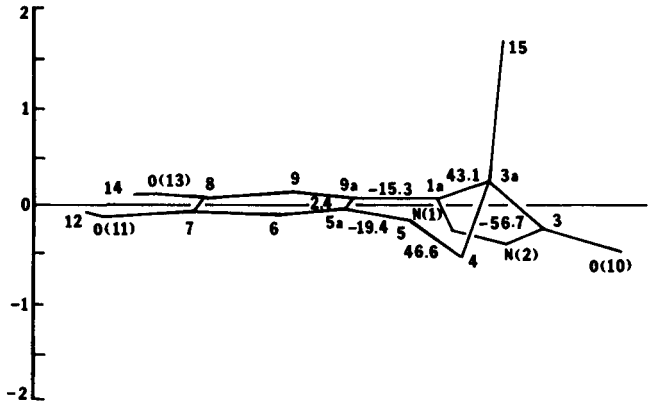


Figure 3. Conformational Angles Around Cyclohexadiene Ring in **1** (view is with respect to the least square plane through the molecule)

Table 3

Distances of atoms from the best plane through the five-membered ring. The atoms used in the L.S. plane are underlined. The equation of the plane is: 8.360 x − 1.237 y − 17.296 z + 3.257 = 0

Atom	Distance(Å)
N(1)	−0.011
N(2)	0.054
C(3)	−0.066
C(3a)	0.054
C(1a)	−0.031
O(10)	−0.188
C(15)	1.437

Table 4

Hydrogen Bonding in **1**

Donor	Acceptor	D...A	H...A
N(2)	O(10) (a)	2.741 Å	1.889 Å
O(W) (b)	N(1)	2.935 Å	(c)

(a) ½ − x, ½ + y, ½ − z. (b) x, y + 1, z. (c) Hydrogen atoms on O(W) were not located.

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