Nitrogen Configuration Determined by X-ray Analysis on an Homogeneous Series of 3-Indolinones

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The X-ray diffraction analyses of 2-methyl-2-phenylindolin-3-one **1**, 1,2-dimethyl-2-phenylindolin-3-one **2**, 1-hydroxy-2-methyl-2-phenylindolin-3-one **3** and 1-methoxy-2-methyl-2-phenylindolin-3-one **4** have been carried out and the structural data were compared with those of 1-oxyl-2-methyl-2-phenylindolin-3-one **5**. The results demonstrate that only compounds **2** and **5** show planar trigonal geometry which is coplanar with the conjugated benzene ring of the indolinic nucleus, whereas compounds **3** and **4** show a marked pyramidality of the nitrogen. Even if compound **1** shows a certain pyramidality of the nitrogen, it has been considered similar to compound **2**. The reactivity of all studied compounds fit the structural data.

3-Indolinones have been prepared in different ways and may be considered as precursors of indoline and indole derivatives [1-4]. The method followed by us for their synthesis concerns the addition of Grignard reagents to 3*H*-indole-3-one [5] or to 3*H*-indole-3-arylimino and subsequent hydrolysis [5]. 2-Methyl-2-phenylindolin-3-one **1** [5,6], 1,2-dimethyl-2-phenylindolin-3-one **2** [6], 1-hydroxy-2-methyl-2-phenylindolin-3-one **3** [7], 1-methoxy-2-phenylindolin-3-one **4** [8] and 1-oxyl-2-methyl-2-phenylindolin-3-one **5** [7] constitute an indolinonic homogeneous
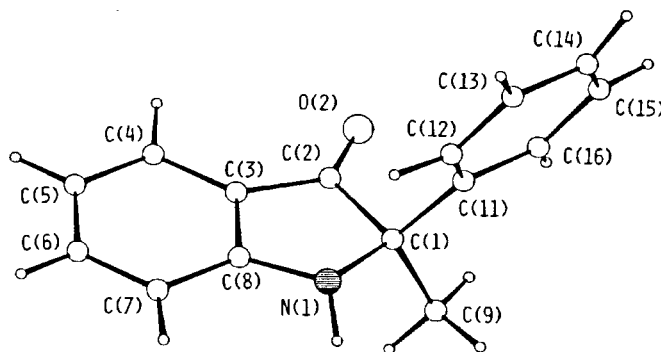

Figure 1. Perspective view of 2-methyl-2-phenylindolin-3-one, **1**.
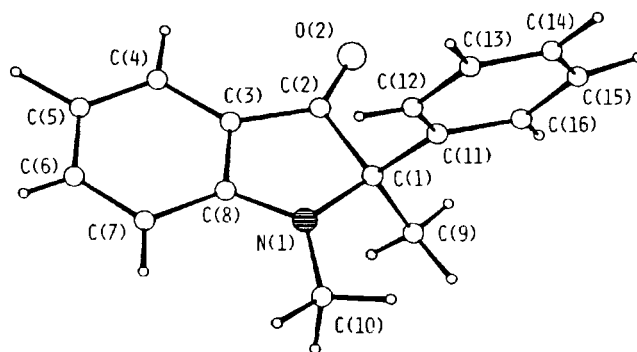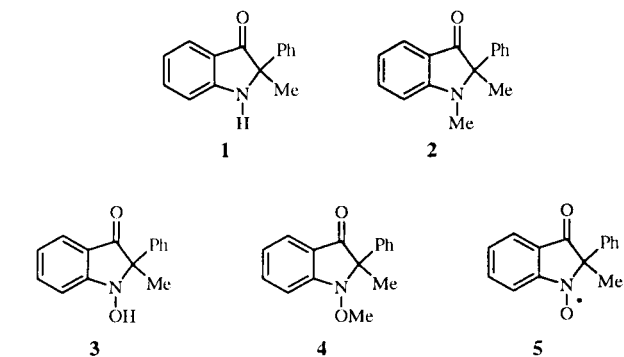

1   **2**

3   **4**   **5**

Figure 2. Perspective view of 1,2-dimethyl-2-phenylindolin-3-one, **2**.

series in which the only difference lies in the substituents at the nitrogen atom. The present paper deals with the pyramidality of the nitrogen atom of the indolinic nucleus as a function of the substituent bonded to the nitrogen

Molecular Geometry.

Table 1 collects the experimental and crystallographic data for all four compounds. Selected bond distances and angles and torsion angles are reported in Table 2.

The numbering scheme used in the crystal analysis is shown in Figures 1-4, which represent perspective views of

the compounds **1, 2, 3** and **4**, respectively. The two independent molecules forming the asymmetric unit of **4** are quite similar in their geometry, the main difference concerning the degree of pyramidality of the nitrogen atom. The intramolecular bond distances and angles, in line with the hybridization expected for the atoms involved, are in good agreement with related compounds previously studied [9-12].

Table 1

Experimental Data for the X-ray Diffraction Studies on Crystalline Compounds 1, 2, 3 and 4

compound	1	2	3	4
formula	$C_{15}H_{13}NO$	$C_{16}H_{15}NO$	$C_{15}H_{13}NO_2$	$C_{16}H_{15}NO_2$
cryst habit	prisms	orthorhombic bipyramids	prisms	prisms
cryst colour	light green-azure	light green-azure	dark-yellow	green
fw F(000)	223.3 472	237.3 504	239.3 1008	253.3 536
cryst syst	monoclinic	orthorhombic	orthorhombic	triclinic
space group	$P\,2_1/C$	$P\,2_1\,2_1\,2_1$	$P\,b\,c\,a$	$P\,\bar{1}$
cell parameters at 295 K[a]				
a, Å	10.099(2)	13.156(3)	20.952(4)	12.108(3)
b, Å	11.576(2)	10.255(2)	9.160(2)	10.534(2)
c, Å	10.726(2)	9.631(2')	13.066(3)	10.884(2)
α, deg	90	90	90	101.6(1)
β, deg	102.3(1)	90	90	90.5(1)
γ, deg	90	90	90	86.2(1)
V, Å³	1225.2(6)	1299.4(5)	2507.6(9)	1356.9(7)
Z	4	4	8	4
d_{calc} g cm⁻¹	1.21	1.21	1.27	1.24
cryst dimens, mm	0.19 x 0.33 x 0.38	0.33 x 0.38 x 0.48	0.19 x 0.33 x 0.57	0.19 x 0.29 x 0.29
linear abs coeff, cm⁻¹	6.0	5.9	6.8	6.6
diffractometer	Siemens AED	Siemens AED	Siemens AED	Siemens AED
diffraction geometry	equatorial	equatorial	equatorial	equatorial
scan type	ω-2θ	ω-2θ	ω-2θ	ω-2θ
scan width, deg	b	b	b	b
radiation	c	c	c	c2
2θ range colln, deg	6-140	6-140	6-140	6-140
hkl range	±h,k,l	±h,k,l	±h,k,l	±h,±k,l
unique total data	2586	2778	5294	5174
criterion of obsn	I>2σ(I)	I>2σ(I)	I>2σ(I)	I>2σ(I)
unique obs data (NO)	1678	1394	1853	3140
no. of refined par (NV)	206	223	215	232
overdetermn ratio (NO/NV)	8.1	6.3	8.6	13.5
absorption	d	d	d	d
solution	e	e	e	e
H atoms	f	f	f	f
R	0.041	0.039	0.048	0.043
R_w	0.050	0.045	0.052	0.054
GOF	0.802	0.709	0.818	0.221
largest shift/esd	0.02	0.03	0.03	0.02
largest peak, eÅ⁻³	0.11	0.14	0.17	0.14
computer and programs	g	g	g	g

[a] unit cell parameters were obtained by least-sauares analys;is of the setting angles of 30 carefully centered reflections chosen from diverse regions of reciprocal space. [b] from (θ-0.6) to [θ+(0.6+Δθ)°; Δθ = [(λα₂-λα₁)/λ]tanθ. [c] Ni-filtered CuKα λ = 1.54178 Å. [d] no correction applied. [e] direct methods. [f] located in DF map and isotropically refined. [g] ENCORE e91, SHELXS86 [23], SHELX76 [24], PARST [25].   R = Σ|ΔF|/Σ|F₀|
$R_w = [\Sigma W(\Delta F^2)^2/\Sigma w(F_o^2)^2]^{1/2}$ $GOF = [\Sigma w|\Delta F|^2/(NO-NV)]^{1/2}$.

The conformational study by torsion angles and the analysis of the planarity indicate that the main differences between the four compounds lie in the geometry of the five-membered ring, which can be considered planar even in the presence of small, though significant, distortions, only in compound 2. The planarity of this ring is correlated to the bond arrangement of the N(1) atom and to the nature of its substituent. In fact, when the coordination geometry of the N(1) is trigonal planar as in 5 [10] then also the ring is strictly planar and the substituent at N atom lies on this plane. In Table 3 the values are reported which correlate the pyramidality of the N atom in terms of sum of its valence angles and the out-of-plane with respect to the three bonded atoms, the distance of the sub-

stituent at N atom from the pyrroline mean plane, the sum(d/s)² as a value indicating the planarity of the pyrroline ring and finally the angle between the mean planes of the five and six membered rings in the two condensed ring moiety for all the five homogeneous compounds. It is worth noting that the pyramidality of the N atom progressively increases in the compounds 2, 1, 3 and 4 and at the same time the distortion of the five membered ring, the distance from its mean plane of the substituent at N and the angle between the two mean planes of the indolinic system increase. This increase in deviation from the planarity of the indolinic system can be linked to the nature of the N substituent: in fact, possibly it seems that a slight electron-donor effect of the substituent, as in the case of
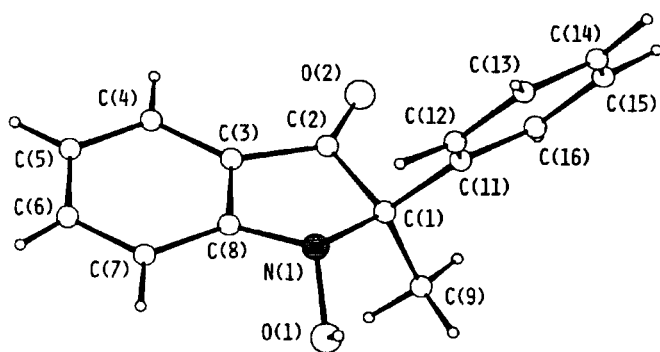
Figure 3. Perspective view of 1-hydroxy-2-methyl-2-phenylindolin-3-one, 3.

methyl, or a very small electron interaction, as in the case of the hydrogen, with a consequent further delocalization of the N electron lone pair on the adjacent benzene ring and shortening of N(1)-C(8) bond, can justify a decrease in the pyramidality of N atom with increasing the planarity of all the indoline moiety.

All the benzene rings are planar within the experimental errors. Molecular packing of compound 3 is determined by an intermolecular hydrogen bond of the type O-H...O bridging the O(1) atom with the O(2) one in the
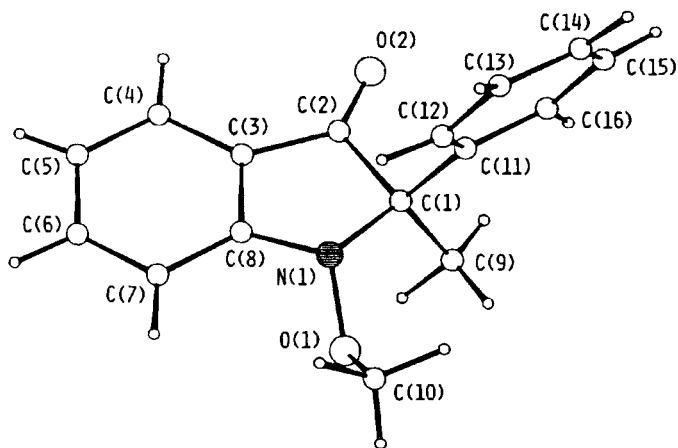

Figure 4. Perspective view of 1-methoxy-2-methyl-2-phenylindolin-3-one, 4.

x, 1/2-y, 1/2+z position [O(1)-H(1) 1.08(3), O(1)...O(2) 2.700(2), H(1)...O(2) 1.63(3) Å; O(1)-H(1)...O(2) 171.9(22)°]. The molecular packing of the other three compounds is consistent with van der Waals interactions.

Discussion.

It is well known that secondary aromatic amines 6 are used as antioxidants in polymer stabilization and that they react with peroxyl radicals affording the corresponding aminyls 7, which in turn, may lead to the formation of tertiary amines (alkylated amines) 8 or of aminoxyls 9 [13]. The latter compounds by hydrogen abstraction, form hydroxylamines 10 or by coupling with C-centered radicals, form alkylated hydroxylamines 11, according to Scheme 1 [13,14]. All compounds 6-11 may also react at the conjugated position of the benzene ring.

Thus, compound 1, which gives rise to the very stable aminoxyl 5, may be considered a good model compound to study the reactivity shown in Scheme 1 and that involving the conjugated benzene moiety. In order to determine whether the chemical behaviour of compounds 1-5 could depend to some extent on changes in the degree of pyramidality at the nitrogen atom, an X-ray analysis of compounds 1-4 was carried out, since that of aminoxyl 5 has already been studied [14]. A planar configuration of nitrogen was observed only for aminoxyl 5; that of the nitrogen in compound 2 is almost planar, whereas all the other compounds 1, 3 and 4 show significant pyramidality [15]. The trigonal planar geometry of the nitrogen atom in compound 5, which is coplanar with the benzene ring, may justify the great stability of this aminoxyl and its reactivity at the conjugated position of the indolinic benzene.

The unpaired electron delocalization, favoured by the coplanar configuration, makes these compounds highly reactive with all oxygen centered radicals, thus enhancing their antioxidant properties. In fact, aminoxyls of the 3-indolinonic and 3-arylimino indolinonic series react efficiently with alkylperoxyl radicals [16] and alkoxyl radicals [8] exerting protection against thermal degradation during polypropylene processing [17] and inhibiting autoxidation processes in lipids [18], low density
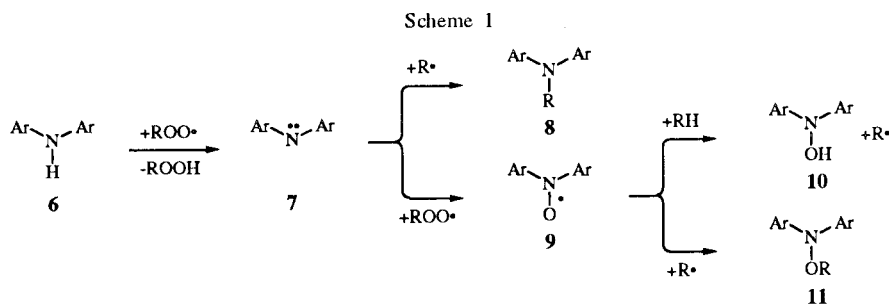

Scheme 1

Table 2
Selected Bond Distances (Å), Angles (o) and Torsion Angles (°) with e.s.d.'s in Parentheses

Compound	1	2	3	4	
	X=H	X=C(10)	X=O(1)	X=O(l)	X=O(l)
X-N(1)	0.93(2)	1.445(5)	1.415(2)	1.423(3)	1.412(3)
O(1)-C(10)				1.416(5)	1.424(5)
O(2)-C(2)	1.224(2)	1.213(3)	1.223(2)	1.212(3)	1.215(4)
N(1)-C(1)	1.465(2)	1.471(4)	1.479(2)	1.489(3)	1.484(3)
N(1)-C(8)	1.373(3)	1.362(4)	1.381(2)	1.388(3)	1.392(3)
C(1)-C(2)	1.547(3)	1.552(3)	1.540(2)	1.550(4)	1.558(4)
C(1)-C(9)	1.535(3)	1.525(5)	1.536(3)	1.526(4)	1.524(4)
C(1)-C(11)	1.521(3)	1.526(3)	1.525(3)	1.531(4)	1.523(4)
C(2)-C(3)	1.443(3)	1.444(3)	1.455(3)	1.447(4)	1.442(4)
C(3)-C(4)	1.399(3)	1.400(4)	1.400(3)	1.404(4)	1.394(4)
C(3)-C(8)	1.396(3)	1.383(4)	1.397(2)	1.383(4)	1.384(4)
C(4)-C(5)	1.373(4)	1.362(6)	1.379(3)	1.359(4)	1.379(5)
C(5)-C(6)	1.386(5)	1.372(7)	1.406(4)	1.393(5)	1.386(5)
C(6)-C(7)	1.375(4)	1.397(6)	1.369(3)	1.389(5)	1.368(5)
C(7)-C(8)	1.402(3)	1.408(4)	1.399(3)	1.396(4)	1.397(4)
N(1)-O(1)-C(l0)				109.6(3)	109.8(3)
X-N(1)-C(1)	120.1(13)	122.5(3)	115.5(1)	114.6(2)	114.7(2)
X-N(1)-C(8)	116.7(14)	125.6(3)	114.6(1)	112.1(2)	113.4(2)
C(1)-N(1)-C(8)	109.7(2)	110.6(2)	109.7(2)	109.2(2)	109.1(2)
N(1)-C(1)-C(2)	103.0(1)	102.2(2)	102.0(1)	102.1(2)	101.4(2)
N(1)-C(1)-C(9)	110.6(1)	111.2(2)	111.7(2)	112.4(2)	112.3(2)
N(1)-C(1)-C(11)	112.6(1)	111.1(2)	111.7(2)	110.9(2)	110.7(2)
C(9)-C(1)-C(11)	113.4(1)	114.0(2)	112.8(2)	113.4(2)	114.0(2)
C(2)-C(1)-C(9)	108.6(1)	108.3(2)	107.9(2)	108.3(2)	107.9(3)
C(2)-C(1)-C(11)	108.1(2)	109.4(2)	110.3(1)	109.1(2)	109.8(2)
O(2)-C(2)-C(1)	123.9(1)	123.7(2)	123.7(1)	123.7(2)	124.1(3)
O(2)-C(2)-C(3)	129.1(1)	129.8(2)	128.8(2)	129.0(3)	128.6(3)
C(1)-C(2)-C(3)	107.0(2)	106.5(2)	107.6(2)	107.3(2)	107.3(2)
C(2)-C(3)-C(8)	107.5(2)	108.5(2)	107.3(1)	108.2(2)	108.1(2)
C(4)-C(3)-C(8)	121.4(2)	122.2(2)	121.3(2)	120.9(2)	120.7(2)
C(3)-C(4)-C(5)	117.6(2)	118.1(3)	118.0(2)	118.4 (3)	118.5(3)
C(4)-C(5)-C(6)	120.8(3)	120.2(4)	120.3(2)	120.8(3)	120.0(3)
C(5)-C(6)-C(7)	122.8(3)	123.6(4)	122.2(2)	122.0(3)	122.3(3)
C(6)-C(7)-C(8)	117.0(2)	116.2(3)	117.9(2)	116.9(3)	117.7(3)
N(1)-C(8)-C(3)	112.3(2)	111.9(2)	111.7(1)	111.9(2)	111.7(2)
C(3)-C(8)-C(7)	120.3(2)	119.8(2)	120.4(2)	121.0(2)	120.7(2)
X-N(1)-C(1)-C(9)		57.7(4)	29.8(2)	-21.1(3)	28.7(3)
X-N(1)-C(1)-C(11)		-70.4 (4)	-97.5 (2)	107.0 (2)	-99.9 (3)
C(8)-N(1)-C(1)-C(2)	-6.1(2)	5.4(3)	13.5(2)	-10.3 (3)	15.1(3)
C(1)-N(1)-C(8)-C(3)	7.9(2)	-6.1(3)	-13.5 (2)	12.6 (3)	-14.8 (3)
N(1)-C(1)-C(2)-C(3)	2.5(2)	-3.0(2)	-9.1(2)	4.9 (3)	-10.8 (3)
C(9)-C(1)-C(2)-O(2)	64.5 (2)	-63.8 (3)	-70.5 (2)	64.2 (3)	-72.0 (4)
C(11)-C(1)-C(2)-O(2)	-58.9(2)	61.0(3)	53.1(2)	-59.6(3)	52.8(4)
C(1)-C(2)-C(3)-C(8)	1.8(2)	-0.3 (3)	1.9 (2)	2.0(3)	2.9(3)
C(2)-C(3)-C(8)-N(1)	-6.0(3)	3.9(3)	7.0(2)	-9.0(3)	7.2(3)

Table 3
Analysis of the Pyramidality of the Indolinic Nitrogen Atom

Compound	1	2	3	4		5
a	346.5(10)	358.7(3)	339.8(1)	335.9(2)	337.3(2)	360.0(1)
b	-0.256(1)	0.094(3)	-0.377(2)	0.415(2)	-0.401(2)	0.012(2)
c	-0.431(22)	0.114(5)	0.683(2)	0.828(2)	0.714(2)	0.008(2)
d	1549	433	4537	1967	3653	49
e	4.4(1)	3.0(1)	4.2(1)	5.1(1)	4.9(1)	2.1(1)

[a] sum of valence angles of N(1). [b] out-of-plane of N(1) with respect to the plane through its three bonded atoms. [c] distance of the N(1) substituent from the mean plane of the pyrroline ring. [d] sum(d/s)^2 of the pyrroline mean plane. [e] the folding angle of the indoline ring along the C(3)-C(8) bond.

lipoproteins [19] and proteins [20]. Compounds **1** and **2** under oxidation afford the corresponding radical cations which lead first to the formation of dimer radical cations as demonstrated by a chemical and electrochemical study [21]. The fact that the dimerization of radical cations such as **1**[+*] and **2**[+*] occurs through the C5-C5' position and that electrophilic reactions are oriented mainly at C5 [21], confirms that the delocalization of the unpaired electron in the first case and of the lone pair in the second, is high as suggested from the results of the X-ray analyses.

The pyramidality of the nitrogen of compound **3** and **4**, which could be due to the lone pairs interactions of the two adjacent heteroatoms, agrees with the tendency of these compounds to regenerate aminoxyl **5** through hydrogen released from compound **3** and homolytic dealkylation from compound **4** [22].

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