BENZINDOLES.

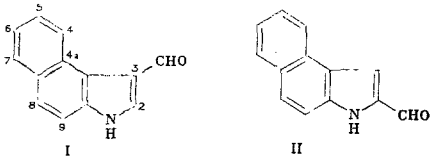
23.* 2-FORMYL- AND 3-FORMYL-4,5-BENZINDOLES

E. I. Voronina, G. M. Ostapchuk,
T. M. Ivanova, T. A. Babushkina,
L. B. Shagalov, and N. N. Suvorov

UDC 547.759.3:541.621.2:543.422

It is shown that, in addition to the usually formed 3-formyl-4,5-benzindole, 2-formyl-4,5-benzindole can be obtained via the Vilsmeier reaction. The IR, PMR, and UV spectra of the 2- and 3-formyl isomers are compared, and their possible conformations are discussed.

3-Formyl-4,5-benzindole (I) was previously obtained by some of us via the Vilsmeier reaction [2]. In the synthesis by this method, in addition to aldehyde I, we isolated high-melting II, which was an isomer of I. The IR spectrum of II in the crystalline state contained bands related to the formyl group and to the indole NH bond; however, it differed from the spectrum of I in the region of skeletal vibrations (Table 1). One might have assumed that we are dealing with different crystalline modifications of the same substance; however, the IR spectra of solutions of the two compounds in $CHCl_3$ and DMSO (Table 1) were also different. We assumed that II is 2-formyl-4,5-benzindole. A comparative analysis of data from the PMR, IR, and UV spectra confirmed this assumption.



I II

In the PMR spectrum of II (Table 2) the spin-spin coupling constant (SSCC) of the proton of the NH group ($^4J_{13}$) was considerably smaller than $^3J_{12}$ in the spectrum of aldehyde I; this is natural for protons that are more remote from one another. Pronounced shielding of the 4-H proton as compared with I, in which this proton is deshielded, is also characteristic for the spectrum of isomer II. In addition, long-range spin–spin coupling ($^5J_{39}$ = 0.73 Hz) is observed in the spectrum of II for the 3-H proton; this sort of coupling between the 2-H and 8-H protons should be substantially weaker ($\leqslant$0.3 Hz) in the case of the 3-substituted compound and therefore is not observed in the spectrum.

The change in the chemical shift of the 3-H proton for isomer II [$\Delta\delta$(3-H) = 0.2 ppm] and the change in the chemical shift of the 2-H proton for isomer I [$\Delta\delta$(2-H) = 0.4 ppm] on passing from a polar solvent (DMSO) to a less polar solvent ($CDCl_3$) are also in agreement with the proposed structures of I and II (Table 2). The existence of a hydrogen bond between the oxygen atom of DMSO and the hydrogen atom of the NH group polarizes this bond and consequently deshields the 2-H proton, which is closest to it.

Let us note that a transoid orientation of the carbonyl group relative to the $C_{(2)}=C_{(3)}$ bond should be energically unfavorable for the 3-substituted isomer because of the substantial nonvalence $O...C_{(4a)}$ interactions in this conformation, and either a coplanar cis form or a structure with a carbonyl group that deviates somewhat from the plane of the rings therefore will evidently be most preferable. These restrictions are absent in the case of the 2-substituted compound. In this connection, one might expect that a transoid orientation of the C=O and $C_{(2)}=C_{(3)}$ bonds with more favorable (than in I) conditions for overlap of the π orbi-

*See [1] for Communication 22.

Institute of Biophysics, Ministry of Public Health of the USSR, Moscow 123182. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 343-345, March, 1984. Original article submitted March 1, 1983; revision submitted September 6, 1983.

TABLE 1, IR Spectrum (cm^{-1}) of 2- and 3-Formyl-4,5-benzindoles

3-Formyl-4,5-benzindole			2-Formyl-4,5-benzindole		
KBr	DMSO	$CHCl_3$	KBr	DMSO	$CHCl_3$
3300—2900 br		3480 int 3250 br	3270 int		3480 int 3250 br
		3050 br 2840 sha 2750 sha	3200—3000 br		
			1690 sh		
	1665 int 1655 sh	1670 int	1670 int	1662 } d 1655 }	1655 sh
1641 int	1650 sh				1650 int
1615 m	1620 w		1625 m	1621 w	1625 w
1580 w			1595 m		
1503 sha	1507 sha		1510 int	1501 sha	
1470 int	1470 sh		1469 vw	1465	
1460 sh	1460 m	1460 sha	1450 w	1450 br	
1431 } d int	1420 w		1435 m		1430 w
1420 }			1420		1420 w
1390 sh		1400 w		1405 int	
1380 int	1385 w	1380 sha	1381 m		1380 vw
	1367 int		1372 m		1350 m
1298 sha	1298 sha	1295 br			
1221 w			1250 m		
1145 m			1145 int		
1132 sha		1135 sh	1135 sh		1137 sha
1126 sha		1112 sha	1090 vw		
960 w		990 m	990 m		
807 } d int					813 int
802 }					800 m sha
760 } d int					779 m sha
750 }					741 int
625 int					618 m

Note: int is intense, w is weak, sh is shoulder, br is broad, d is double, and sha is sharp.

TABLE 2. Chemical Shifts (ppm) and Spin—Spin Coupling Constants (Hz) in the PMR Spectra of 2- and 3-Formyl-4,5-benzindoles (II, I)

Compound	Solvent	NH	2-H (CHO)	3-H (CHO)	8-H	9-H	4-H	5-H	6-H	7-H
I	d_6-DMSO	12,51 $^3J_{12}=3,1$	8,35	9,96	7,63 $^3J_{89}=8,7$	7,70	9,56 $^4J_{46}=1,0$	7,51 $^3J_{45}=7,5$	7,41 $^5J_{47}=0,3$	7,91 $^3J_{56}=6,9$
	$CDCl_3$	9,12	7,96	10,14	7,54	7,76	9,62	7,67	7,53	7,93
II	d_6-DMSO	12,43 $^4J_{13}=1,95$	9,85 $^5J_{39}=$ $=0,73$	8,00	7,48 $^3J_{89}=9,0$	7,80	8,35 $^3J_{45}=7,57$	7,61 $^3J_{56}=7,56$	7,47 $^4J_{46}=1,5$	7,95 $^5J_{47}=0,5$
	$CDCl_3$	9,40	9,86	7,78	7,51	7,79	8,25	7,63	7,50	7,91

tals is realized for isomer II. In fact, in the UV spectrum of isomer II the near absorption band is shifted significantly to the long-wave side as compared with the spectrum of I (Table 3), whereas the frequency of the band of the carbonyl group in the IR spectra of solutions in $CHCl_3$ is appreciably lower for isomer II (1650 cm^{-1}) than for isomer I (1670 cm^{-1}) (Table 1).

EXPERIMENTAL

The IR spectra were recorded with a Perkin—Elmer 180 spectrometer; KBr cuvettes with thicknesses of 0.1 and 1.0 mm were used for measurements of solutions. The accuracy in the measurements was ±1 cm^{-1}. The UV spectra of solutions of the compounds in methanol were recorded in 1-cm-thick quartz cuvettes with a Shimadzu MPS-50 spectrophotometer. The PMR spectra of solutions in $CDCl_3$ and d_6-DMSO were recorded with a Varian HA-100 spectrometer with hexamethyldisiloxane as the internal standard. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 plates.

TABLE 3. UV Spectra of 2- and 3-Formyl-4,5-benzindoles

2-Formyl-4,5-benzindole		3-Formyl-4,5 benzindole	
λ, nm	ε	λ, nm	ε
210	28 000	190	41 000
		216	47 000
236	44 000	249	17 000
231 sh	37 000		
260	10 000	273	30 000
286	16 000		
323	18 000	310	7 000
343	18 200	320	6 000
362	16 800		

2- and 3-Formyl-4,5-benzindoles (II, I). A mixture of these compounds was obtained in 95-98% yield via the Vilsmeier reaction from 4,5-benzindole [2]. The mixture was separated with a column packed with Chemapol silica gel (40/100 μm) by elution with chloroform. The yield of isomer I, with R_f 0.16 [benzene–acetone (4:1)] and mp 189-190°C (mp 185-176°C [2]), was 78-80%. The yield of isomer II, with R_f 0.44 [benzene–acetone (4:1)] and mp 252-253°C, was 6-8%. Found: C 79.6; H 4.8; N 7.9%. $C_{13}H_9NO$. Calculated: C 80.0; H 4.6; N 7.2%.

LITERATURE CITED

1. G. S. Grekova, V. P. Gorbunova, L. B. Shagalov, T. A. Babushkina, A. M. Vasil'ev, and N. N. Suvorov, Khim. Geterotsikl. Soedin., No. 10, 1380 (1980).
2. L. B. Shagalov, T. A. Tkachenko, V. N. Eraksina, and N. N. Suvorov, Tr. Mosk. Khim.-tekhnol. Inst. im. Mendeleeva, 74, 61 (1973).

BENZINDOLES.

24.* SYNTHESIS AND SOME PROPERTIES OF 5,6-BENZOTRYPTAMINE HYDROCHLORIDE

G. M. Ostapchuk, E. I. Voronina,
T. M. Ivanova, T. A. Babushkina,
L. B. Shagalov, and N. N. Suvorov

UDC 547.759.3.07:543.422

An improved method for the synthesis of 5,6-benzotryptamine hydrochloride from 3-hydroxy-2-naphthoic acid was developed; this method makes it possible to obtain the final product and a number of intermediates in high yields. The PMR spectra and the peculiarities of conjugation in the linear benzindole molecule are discussed.

Indolylalkylamines have many-sided biological activity [2-4]. Least study in this case of compounds has been devoted to the physiological action of benzotryptamines [2]; in particular, the literature does not contain any information regarding the properties and activity of 5,6-benzindole derivatives, which is explained by the difficulty involved in the synthesis of these compounds [5]. At the same time, the linear compact 5,6-benzotryptamine molecule, in which the degree of delocalization of the π-electron cloud should be higher than in angular analogs, may prove to be extremely promising from the point of view of its biological activity.

We have developed an improved method for the synthesis of 5,6-benzotryptamine via the following scheme [5]:

*See [1] for communication 23.

Institute of Biophysics, Ministry of Public Health of the USSR, Moscow 123182. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 346-348, March, 1984. Original article submitted June 29, 1983.

