Synthesis and properties of [1,4]diazepino[6,5-*b*]indoles

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1-Aryl-2-oxo-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indole *N*-oxides were synthesized based on 3-(*N*′-aryl-*N*′-chloroacetyl)amino-2-formylindoles. Deoxidation of 2-oxo-1-phenyl-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indole *N*-oxide afforded 1,2,3,6-tetrahydro- and 1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole derivatives. A new approach to the synthesis of pyrido[3,2-*b*]indole and pyrimido[5,4-*b*]indole derivatives was developed.

Key words: 3-arylamino-2-formylindole, [1,4]diazepino[6,5-*b*]indole, *N*-oxide, deoxidation, pyrido[3,2-*b*]indole, pyrimido[5,4-*b*]indole.

Many of indole-containing polycyclic compounds can be used as efficient pharmaceuticals.[1—3] As an example we refer to the following antidepressants: pyrazidole, tetrindole, incazan, the neuroleptic agent carbidine, and antihystamine drugs dimebon and diazolin. It is known that compounds containing the benzo[1,4]diazepine ring are also among important pharmaceuticals. These are anticonvulsive drug clonazepam and numerous tranquilizers of the benzodiazepine series, such as chlozepid, sibazon, phenazepam, hydazepam, *etc*.[1—3] Hence, fused systems involving the indole and [1,4]diazepine rings are of interest from the viewpoint of a search for new biologically active compounds. Thus, some [1,4]diazepino[1,2-*a*]indole derivatives were found to exhibit pronounced psychotropic activity.[4—7] At the same time, [1,4]diazepino[6,5-*b*]indoles remain poorly studied[8] due apparently to the fact that they are difficult to synthesize.

The aim of the present study was to examine the approach to the synthesis of [1,4]diazepino[6,5-*b*]indoles based on 3-(*N*′-aryl-*N*′-chloroacetyl)amino-2-formylindoles, which have been prepared by us previously.[9] It should be noted that we have already used dechloroacetylated 3-*N*′-arylamino-2-formylindole derivatives in the synthesis of three- and tetracyclic systems.[9—11]

We believed that the most simple approach to the synthesis of the target products consists in replacing the Cl atom in the side chain by the amino group followed by cyclization at the 2-formyl group to form the diazepine ring. However, the presence of the reactive chlorine atom simultaneously with the aldehyde fragment in the molecule of an indole derivative can lead to the ambiguous course of the reaction, for example, with ammonia. With this in mind, we chose the procedure, which involves the reaction of 3-(*N*′-aryl-*N*′-chloroacetyl)amino-2-formylindoles **1a,b** with pyridine followed by the pyridine-ring opening in the resulting pyridinium salts **2** under the action of amines[12] to give products containing the primary amino group and subsequent cyclization of the latter compounds.

The reaction of aldehyde **1a** with pyridine readily proceeded even at room temperature. However, (2-oxo-1-phenyl-1,2-dihydropyrido[3,2-*b*]indol-3-yl)pyridinium chloride (**3**) was isolated in quantitative yield instead of the expected salt **2**. Apparently, the initial formation of pyridinium salt **2** led to a substantial increase in the acidity of the resulting CH acid such that intramolecular cyclization involving the formyl group proceeded even under the action of an excess of pyridine to produce δ-carbolinone **3**. Systems of this type are characterized by a substantial upfield shift of the signal for the H(9) proton due to rotation and the anisotropic effect of the phenyl ring at position 1.[10,11] Thus the ^{1}H NMR spectrum of compound **3** has a doublet for the proton at position 9 (with the one-proton intensity) at δ 6.09 (see the Experimental section). Heating of pyridinium salt **3** with benzylamine in methanol proceeded through the pyridinium-ring opening to give 3-amino-2-oxo-1-phenyl-1,2-dihydropyrido[3,2-*b*]indole (**4**), which was characterized also as 3-acetylamino derivative **5**. The structures of compounds **4** and **5** were unambiguously confirmed by the ^{1}H NMR spectra (see the Experimental section).

Hence, the proposed procedure, while providing a way for synthesizing previously inaccessible δ-carbolines, un-

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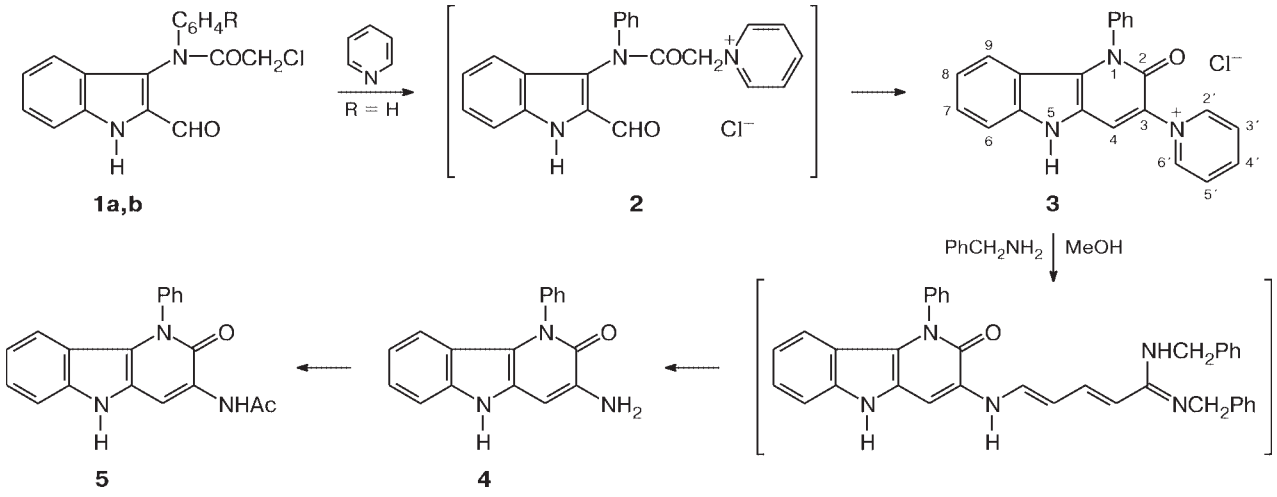
Scheme 1

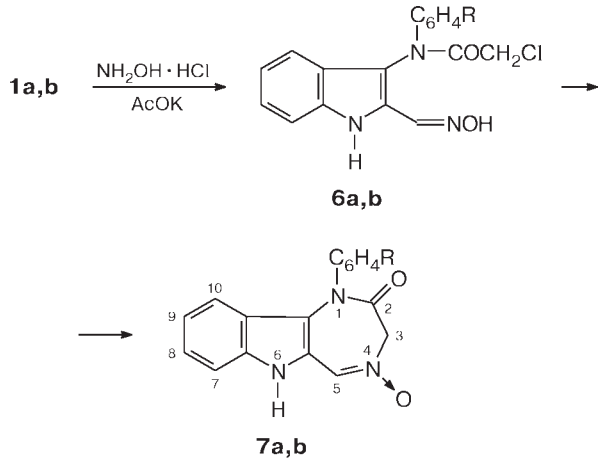


R = H (**a**), 4-Cl (**b**)

fortunately does not allow the preparation of the target [1,4]diazepino[6,5-*b*]indoles.

Because of this, we examined oximation of the starting aldehydes **1a,b**. However, we succeeded in isolating only oxime **6b**, which was characterized by mass spectrometry and ^{1}H NMR spectroscopy (see the Experimental section). It should be noted that we failed to obtain this oxime in the analytically pure form. Oxime **6a** underwent cyclization already in the course of the reaction. Refluxing of compounds **1a,b** with hydroxylamine in ethanol afforded 1-aryl-2-oxo-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indole 4-oxides (**7a,b**) in 90 and 70% yields, respectively.

Scheme 2

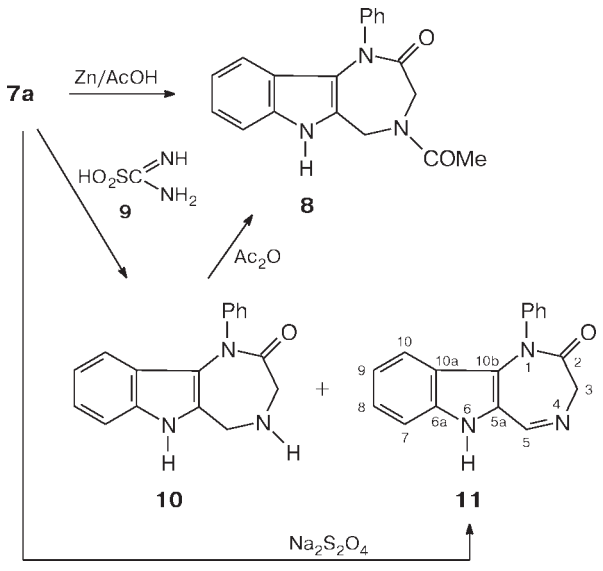


R = H (**a**), 4-Cl (**b**)

The structures of *N*-oxides **7a,b** were confirmed by the data from mass spectrometry and ^{1}H NMR spectroscopy. The mass spectrum of compound **7a** has a low-intensity molecular ion peak $[M]^+$ at *m/z* (I_{rel} (%)) 291 (9). The highest intensity was observed for the ion $[M - 16]^+$ at *m/z* 275 (93). In the mass spectrum of compound **7b**, the molecular ion peak is absent; the most intense peak is observed at *m/z* (I_{rel} (%)) 309 $[M - 16]^+$ (100). In the ^{1}H NMR spectra of compounds **7a** and **7b** (see the Experimental section), the upfield shift of the signal for H(10) ($\delta \approx 6.4$) is noteworthy. This shift is caused by the anisotropic effect of the 1-phenyl or 1-*p*-chlorophenyl fragments and it has been observed previously for carbolinones **3—5**.

The preparation of diazepinoindole *N*-oxides **7a,b** by cyclization gave impetus to the development of a proce-

Scheme 3



dure for the synthesis of the corresponding *N*-deoxidated tricyclic compounds. Generally, these reactions proceed smoothly. However, in the case under consideration, we observed a series of unexpected transformations. First we studied reduction with zinc in acetic acid, which is commonly used in these reactions.[13,14] However, it appeared that the process performed under these conditions was not terminated at the stage of deoxidation of *N*-oxide **7a**, but proceeded further to reduce the 4,5-double bond followed by acetylation of the resulting NH group at position 4 of tricyclic fragment. The ^{1}H NMR spectrum of the 4-acetylamino-2-oxo-1-phenyl-1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole (**8**) that formed is characterized by doubling of most of the expected signals (the spectrum is given in the Experimental section) due to the so-called amide isomerism, *viz.*, the hindered rotation with respect to the N(4)COMe bond.

We also used formamidinesulfinic (**9**) acid, which readily and smoothly reduces carbonyl compounds and sulfoxides,[15] for reduction of the *N*-oxide group. In this case, deoxidation followed by reduction of the C=N bond to form hexahydrodiazepinoindole **10** also proved to be the major direction of the reaction. Compound **10** was subjected to acetylation to obtain the above-described tricyclic compound **8**. At the same time, the reaction with the use of reagent **9** afforded not only compound **10** but

Table 1. Chemical shifts in the ^{13}C NMR spectra (δ) of compounds **4** and **11—13** and the ^{1}H—^{13}C correlations (through two and three bonds) in the HMBC spectrum*

C Atom	δ			
	4	**11**	**12**	**13**
2	156.0 (H(4))	163.2 (3-CH_2)	161.8 (CH_2), 162.1 (CH_2)	155.9 (H(4))
3	137.1 (H(4))	57.6 (H(5))	—	—
4	99.8 (NH)	—	45.5 (CHO) 49.4	143.6
4a	123.6 (H(4), NH)	—	121.0 (NH, 4-CH_2), 121.6 (NH, 4-CH_2)	133.3 (H(4), NH)
5	—	156.5 (3-CH_2)	—	—
5a	135.8 (NH, H(9), H(7))	**	132.0 (NH, H(9), H(7)), 132.1 (NH, H(9), H(7))	136.9 (NH, H(9), H(7))
6	111.1 (H(8))	—	111.6 (H(8)), 112.2 (H(8))	112.4 (H(8))
6a	—	136.6 (NH, H(8), H(9))	—	—
7	121.3 (H(8), H(9))	112.7 (H(9))	120.5 (H(9)), 120.6 (H(9))	125.9 (H(9))
8	118.2 (H(6), H(7))	125.5 (H(10))	119.1 (H(6)), 119.5 (H(6))	119.4 (H(6))
9	116.6 (H(7))	119.8 (H(7))	163.3 (H(7))	119.6 (H(7))
9a	117.0 (NH, H(6), H(8))	—	116.3 (NH, H(6), H(8)), 117.7 (NH, H(6), H(8))	113.8 (NH, H(6), H(8))
9b	114.3 (H(4), NH, H(9))	—	105.3 (NH, H(9)), 106.5 (NH, H(9))	115.6 (NH, H(9))
10	—	119.9 (H(8))	—	—
10a	—	118.9 (NH, H(7), H(9))	—	—
10b	—	124.2 (NH, H(5))	—	—
1′	139.2	140.4	137.4	137.0
2′, 6′	128.4	127.5	128.1	127.8
3′, 5′	129.6	129.0	129.1	129.9
4′	128.7	127.5	128.0	129.6
CHO	—	—	158.8, 161.0	—

* The ordinal numbers of the protons, which show correlation peaks in the HMBC spectrum are given in parentheses.

** The signal is not observed.

Table 2. Physicochemical characteristics of compounds **3—5**, **7a,b**, **8**, and **10—13**

Compound	Yield (%)	M.p./°C (solvent)*	Mol. weight	Found / Calculated (%) C	H	N	Molecular formula	MS, *m/z* (I_{rel} (%))	IR, ν_{max}/cm^{-1} NH (NH_2)	CO
3	99	235—237 decomp. (ether)	373	—	—	11.18 11.24	$C_{22}H_{16}N_3OCl$	—	3310	1620
4	70	275—277 (Pr^iOH)	275	74.21 74.16	5.01 4.76	15.31 15.26	$C_{17}H_{13}N_3O$	275 $[M]^+$ (100), 247 $[M - CO]^+$ (17), 219 $[M - HCO - HCN]^+$ (26), 170 $[M - CO - Ph]^+$ (20)	3423, 3340	1638
5	70	358—360 (Pr^iOH)	317	72.17 71.91	5.00 4.76	13.51 13.24	$C_{19}H_{15}N_3O_2$	317 $[M]^+$ (42), 275 $[M - Ac]^+$ (100), 247 $[M - Ac - CO]^+$ (19), 219 $[M - HCO - HCN]^+$ (35)	3205, 3281	1631, 1669
7a	90	282—283 (DMF)	291	69.87 70.09	4.67 4.49	14.45 14.42	$C_{17}H_{13}N_3O_2$	291 $[M]^+$ (9), 275 $[M - O]^+$ (93), 247 $[M - O - CO]^+$ (33), 246 $[M - O - HCO]^+$ (100), 219 $[M - O - HCO - HCN]^+$ (39), 170 $[M - O - HCO - Ph]^+$ (37)	3141	1668
7b**	70	280—282 (DMF)	325	62.51 62.67	3.65 3.71	12.64 12.90	$C_{17}H_{12}N_3O_2Cl$	309 $[M - O]^+$ (58), 280 $[M - O - HCO]^+$ (100), 254 $[M - O - CO - HCN]^+$ (6), 170 $[M - O - CO - C_6H_4Cl]^+$ (34)	3180	1668
8	38 (***A***) 46 (***B***)	218—220 (EtOAc)	319	71.65 71.45	5.75 5.36	13.20 13.15	$C_{19}H_{17}N_3O_2$	319 $[M]^+$ (64), 305 $[M - CH_2]^+$ (3), 291 $[M - CH_2 - CO]^+$ (3), 276 $[M - Ac]^+$ (6), 260 $[M - Ac - NH_2]^+$ (17), 248 $[M - Ac - NCH_2]^+$ (10), 219 $[M - Ac - COCH_2NH]^+$ (100)	3266	1638, 1671
10	75	252—254 (MeOH)	277	—	—	15.40 15.15	$C_{17}H_{15}N_3O$	277 $[M]^+$ (92), 275 $[M - H_2]^+$ (95), 246 $[M - H_2 - NCH_2]^+$ (90), 219 $[M - COCH_2NH_2]^+$ (100)	3276	1655
11	46 (***A***) 6 (***B***)	249—251 (MeOH)	275	73.99 74.16	5.20 4.76	15.27 15.36	$C_{17}H_{13}N_3O$	275 $[M]^+$ (100), 246 $[M - HCO]^+$ (75), 218 $[M - COCH_2NH]^+$ (22), 170 $[M - HCO - C_6H_5]^+$ (27)	***	1666
12	60	260—262 (MeOH)	291	70.22 70.09	4.70 4.49	14.49 14.42	$C_{17}H_{13}N_3O_2$	291 $[M]^+$ (91), 262 $[M - HCO]^+$ (49), 234 $[M - HCO - CO]^+$ (100)	3443	1628, 1678
13	44	276—278 (EtOH)	261	73.76 73.54	4.43 4.24	16.03 16.08	$C_{16}H_{11}N_3O$	261 $[M]^+$ (100), 233 $[M - CO]^+$ (83), 205 $[M - CO - CH_2N]^+$ (38)	3175	1645

* For recrystallization.

** Found (%): Cl, 10.59; calculated (%): Cl, 10.88.

*** The absorption band of the NH group is observed at 3254 cm^{-1} in the spectrum, which was measured in a film precipitated from chloroform.

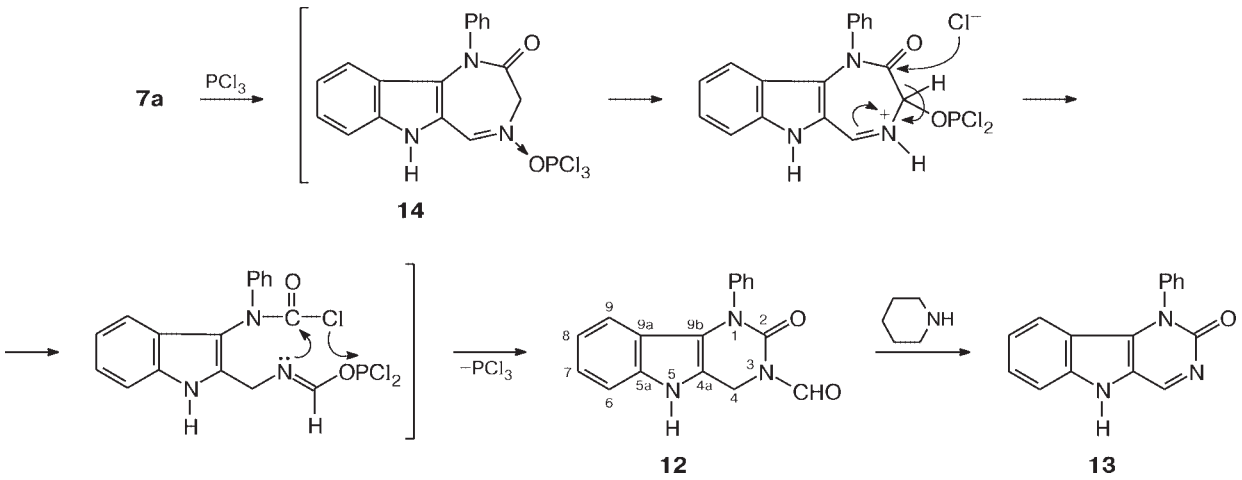
also the target compound, *viz.*, 2-oxo-1-phenyl-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indole (**11**), in low yield. The structure of the latter compound was confirmed by the data from mass spectrometry, ^{1}H NMR spectroscopy, and HMBC* experiments (see the Experimental section, Table 1).

Reduction of *N*-oxide **7a** with sodium hydrosulfide proved to be a more convenient procedure for the synthesis of deoxidated compound **11**. In the latter case, the reaction afforded derivative **11** as the major product in 46% yield.

We studied yet another procedure for deoxidation,[16,17] *viz.*, the reaction of *N*-oxide **7a** with phosphorus trichloride. However, the reaction of compound **7a** with PCl_3 unexpectedly produced 3-formyl-2-oxo-1-phenyl-2,3,4,5-tetrahydro-1*H*-pyrimido[5,4-*b*]indole (**12**). Benzodiazepines are characterized by contraction of the seven-membered ring to the six-membered ring.[18] As far as we know, this contraction under the action of phosphorus halides has not been observed previously. The structure of tricyclic compound **12** was established by mass spectrometry, ^{1}H NMR spectroscopy, and HMBC experiments. The mass spectrum of compound **12** has the ion peak M^+ at *m/z* 291 (100) (Table 2).

* HMBC is heteronuclear multiple-bond connectivity.

Scheme 4



Doubling of most of the signals in the ^{1}H and ^{13}C NMR spectra (see the Experimental section and Table 1) as well as the identity of the correlation peaks for all pair signals observed in the HMBC spectrum suggest the occurrence of the amide isomerism. The signals at δ 8.37 and 8.87 in the ^{1}H NMR spectrum and the signals at δ 158.8 and 161.0 in the ^{13}C NMR spectrum are indicative of the presence of the N—CHO group in compound **12**. Heating of compound **12** with piperidine in methanol led to deformylation followed by aromatization of the pyrimidine ring to form 2-oxo-1-phenyl-1,2-dihydropyrimido[5,4-*b*]indole (**13**). The structure of the latter compound was established by the data from the HMBC experiment, which were compared with those for δ-carbolinone **4**. As can be seen from Table 1, the chemical shifts of the quaternary carbon atoms in compounds **13** and **4** have close values. The observed shift of the signal for the C(4a) atom in the spectrum of pyrimidinone **13** as compared to that for δ-carbolinone **4** (at δ ~10) is apparently associated with the effect of the N atom at position 3. Since the H(4)/C(9b) correlation peak is absent in the spectrum of compound **13**, the structure of **13** was unambiguously established by the NOESY experiment. This spectrum shows the correlation peaks 7.99/12.09 (H(4)/NH) and 7.46/12.09 (H(6)/NH), which indicate that the proton of the NH group is in spatial proximity to the protons of the CH groups at positions 4 and 6. These data provide support for the validity of the structure of **13** and, consequently, of the structure of **12**. The formation of compounds **12** and **13** can be represented by Scheme 4.

Apparently, the first step of this reaction involves the formation of adduct **14** followed by the N→C rearrangement, which is also typical of benzodiazepines (see, for example, the synthesis of the tranquilizer nozepam[19]), the cleavage of the C(2)—C(3) bond, and the pyrimidine-ring closure.

To summarize, we carried out the new synthesis of [1,4]diazepino[6,5-*b*]indoles and studied some properties of these compounds. New procedures were developed for the preparation of previously inaccessible δ-carbolines and pyrimido[5,4-*b*]indoles.

Experimental

The IR spectra were measured on a Perkin—Elmer 457 instrument in Nujol mulls. The mass spectra were obtained on a JSQ-900 mass spectrometer with direct inlet of the sample into the ion source. The ^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer. The 2D HMBC NMR spectra were measured on a Bruker DRX-500 spectrometer using the standard Bruker software. The course of the reactions and the purities of the compounds were monitored on Silufol UV-254 plates using 10 : 1 chloroform—methanol (for compounds **3**, **4**, **5**, **8**, **11**, and **12**), 9 : 1 benzene—methanol (for compounds **6b** and **7a,b**), and 6 : 2.5 : 1.4 : 0.1 ethyl acetate—hexane—ethanol—ammonia (for compound **10**) systems. The physicochemical characteristics and the yields of the compounds are given in Table 2.

(2-Oxo-1-phenyl-1,2-dihydropyrido[3,2-*b*]indol-3-yl)pyridinium chloride (3). A mixture of aldehyde **1a** (2.5 g, 8 mmol) and pyridine (18.7 mL) was stirred at ~20 °C for 48 h. The precipitate was filtered off and washed with pyridine and ether. Then ether was added and the reaction mixture was kept in a refrigerator for 16 h. The yellow precipitate that formed was filtered off and dried at 20 °C. Salt **3** was obtained in a yield of 2.93 g. ^{1}H NMR (DMSO-d_6), δ: 6.09 (d, 1 H, H(9), $J_{9,8}$ = 8.4 Hz); 6.85 (t, 1 H, H(8), $J_{8,7} = J_{8,9}$ = 8.4 Hz); 7.35 (t, 1 H, H(7), $J_{7,6} = J_{7,8}$ = 8.4 Hz); 7.50—7.80 (m, 6 H, H(6) and C_6H_5); 8.33 (m, 2 H, H(3′), H(5′)); 8.79 (m, 1 H, H(4′)); 8.82 (d, 1 H, H(4), $J_{4,5}$ = 1.5 Hz); 9.34 (m, 2 H, H(2′), H(6′)); 12.70 (br.s, 1 H, N(5)H).

3-Amino-2-oxo-1-phenyl-1,2-dihydropyrido[3,2-*b*]indole (4). Benzylamine (2.5 mL, 12 mmol) was added to a solution of pyridinium chloride **3** (0.75 g, 2 mmol) in methanol (6 mL). The reaction mixture was refluxed for 3 h and concentrated to dryness. The resulting oil was washed with low-boiling light petroleum (3×5 mL) and diethyl ether (3×5 mL) and then triturated

with water (30 mL). The precipitate that formed was filtered off, washed with cold propan-2-ol, and dried. Compound **4** was obtained in a yield of 0.34 g. ^{1}H NMR (DMSO-d_6), δ: 5.37 (br.s, 2 H, 3-NH_2); 5.87 (d, 1 H, H(9), $J_{9,8}$ = 8.2 Hz); 6.65 (t, 1 H, H(8), $J_{8,9} = J_{8,7}$ = 8.2 Hz); 6.98 (s, 1 H, H(4)); 6.99 (m, 1 H, H(7)); 7.32 (d, 1 H, H(6), $J_{6,7}$ = 8.2 Hz); 7.43 and 7.64 (both m, 5 H each, C_6H_5); 10.97 (br.s, 1 H, N(5)H).

3-Acetylamino-2-oxo-1-phenyl-1,2-dihydropyrido[3,2-*b*]indole (5). A mixture of 3-amino-δ-carboline **4** (0.07 g, 0.25 mmol) and acetic anhydride (6 mL) was heated on a water bath at 50—60 °C for 5—7 min. The precipitate that formed was filtered off, washed with acetic anhydride and diethyl ether, and dried. Compound **5** was obtained in a yield of 0.03 g. ^{1}H NMR (DMSO-d_6), δ: 2.19 (s, 3 H, COMe); 6.00 (d, 1 H, H(9), $J_{9,8}$ = 8.4 Hz); 6.75 (t, 1 H, H(8), $J_{8,9} = J_{8,7}$ = 8.4 Hz); 7.15 (t, 1 H, H(7), $J_{7,6} = J_{7,8}$ = 8.4 Hz); 7.30—7.90 (m, 6 H, H(6) and C_6H_5); 8.83 (s, 1 H, H(4)); 9.24 (br.s, 1 H, NHCOMe); 11.37 (br.s, 1 H, N(5)H).

3-[*N*´-Chloroacetyl-*N*´-(4-chlorophenyl)]amino-2-formylindole oxime (6b). Aldehyde **1b** (0.3 g, 0.86 mmol) was dissolved in ethanol (10 mL) upon heating and then the reaction solution was cooled to 20 °C. Hydroxylamine hydrochloride (0.066 g, 0.95 mmol) and potassium acetate (0.038 g, 0.95 mmol) were added with stirring. The reaction mixture was kept at 20 °C for 3 days. The precipitate that formed was filtered off and washed with water and ethanol. Oxime **6b** was obtained in a yield of 0.15 g (48%), m.p. 227—229 °C (from ethanol). MS, m/z (I_{rel} (%)): 318 $[M - H - CH{=}NOH]^+$ (50), 241 $[M - H - CH{=}NOH - COCH_2Cl]^+$ (100), 206 $[M - H - C_6H_4Cl]^+$ (40), 129 $[M - H - C_6H_4Cl - COCH_2Cl]^+$ (35). IR, ν/cm^{-1}: 3306 (NH, OH); 1679 (CO). ^{1}H NMR (DMSO-d_6), δ: 4.24 (s, 2 H, $CO\underline{CH_2}Cl$); 7.05 and 7.16 (both t, 2 H each, H(5), H(6), $J_{5,4} = J_{5,6} = J_{6,5} = J_{6,7}$ = 8 Hz); 7.30—7.55 (m, 6 H, H(4), H(7), 4-ClC_6H_4); 7.71 (d, 1 H, $\underline{CH}$=N—OH, J = 2.5 Hz); 11.40 (br.s, 1 H, N(5)H). The signal for the proton of N—$\underline{OH}$ is not observed in the spectrum.

1-Aryl-2-oxo-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indole 4-oxides (7a,b). Aldehyde **1a** (1.92 g, 6.4 mmol) or **1b** (2.14 g, 6.4 mmol) was dissolved in ethanol (67 mL) upon heating and the solution was cooled to 20 °C. Then hydroxylamine hydrochloride (0.48 g, 7 mmol) and potassium acetate (1.36 g, 14 mmol) were added. The reaction mixture was stirred at 20 °C for 1.5 h and then refluxed for 2.5 h. The precipitate that formed was filtered off and washed with water and ethanol. Compounds **7a** and **7b** were obtained in yields of 1.67 and 1.44 g, respectively. ^{1}H NMR of compound **7a** (DMSO-d_6), δ: 4.75 (s, 2 H, 3-CH_2); 6.35 (d, 1 H, H(10), $J_{10,9}$ = 8.2 Hz); 6.78 (t, 1 H, H(9), $J_{9,10} = J_{9,8}$ = 8.2 Hz); 7.15 (t, 1 H, H(8), $J_{8,9} = J_{8,7}$ = 8.2 Hz); 7.20—7.60 (m, 6 H, Ph, H(7)); 8.17 (s, 1 H, H(5)); 11.49 (br.s, 1 H, N(6)H). ^{1}H NMR of compound **7b** (DMSO-d_6), δ: 4.75 (s, 2 H, 3-CH_2); 6.42 (d, 1 H, H(10), $J_{10,9}$ = 8.2 Hz); 6.85 (t, 1 H, H(9), $J_{9,10} = J_{9,8}$ = 8.2 Hz); 7.17 (t, 1 H, H(8)), $J_{8,7} = J_{8,9}$ = 8.2 Hz); 7.43 (d, 1 H, H(7), $J_{7,8}$ = 8.2 Hz); 7.33, 7.50 (AA´XX´, 4 H, 4-ClC_6H_4); 8.16 (s, 1 H, H(5)); 11.50 (br.s, 1 H, N(6)H).

4-Acetylamino-2-oxo-1-phenyl-1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole (8). Method *A*. A suspension of *N*-oxide **7a** (0.5 g, 1.7 mmol) in glacial acetic acid (10 mL) was heated to boiling. Then zinc dust (0.56 g, 8.5 mmol) was added portionwise, the mixture was refluxed for 1 h, and acetic anhydride (0.16 mL, 1.7 mmol) was added. The reaction mixture was refluxed for 30 min and then poured into a 10-fold excess of cold water. The precipitate that formed was filtered off, washed with water, and dried. Compound **8** was obtained in a yield of 0.21 g. ^{1}H NMR (DMSO-d_6), δ: 2.18 and 2.20 (both s, 3 H each, 4-COMe); 4.30 and 4.32 (both s, 2 H each, 3-CH_2); 4.93 and 5.01 (both s, 2 H each, 5-CH_2); 6.40 (m, 1 H, H(10)); 6.75 (m, 1 H, H(9)); 7.05 (m, 1 H, H(8)); 7.20—7.50 (m, 6 H, H(7) and C_6H_5); 11.35 (br.s, 1 H, N(6)H).

Method *B*. Acetic anhydride (0.05 mL, 0.6 mmol) was added to a solution of compound **10** (0.15 g, 0.54 mmol) in AcOH (5 mL) and the mixture was heated to 50 °C. After 15 min, the reaction solution was cooled and poured into cold water (20 mL). The precipitate that formed was filtered off and washed with water and ether. Compound **8** was obtained in a yield of 0.08 g. A mixture with the sample prepared according to the method ***A*** did not give a melting point depression. The IR spectra of these compounds are identical.

2-Oxo-1-phenyl-1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole (10). A suspension of compound **7a** (0.5 g, 1.7 mmol) in an aqueous solution of NaOH (26 mL), which was prepared from NaOH (0.51 g, 12.75 mmol) and water (43 mL), was mixed with stirring with a solution of formamidinesulfinic acid (**9**) (0.74 g, 6.8 mmol) in the remaining solution of NaOH (~17 mL) at 20 °C. The reaction mixture was heated on a boiling water bath for 1 h 15 min. The suspension was cooled and the precipitate was filtered off and washed with water. Compound **10** was obtained in a yield of 0.36 g. ^{1}H NMR (DMSO-d_6), δ: 3.45 (s, 2 H, 3-CH_2); 4.24 (s, 2 H, 5-CH_2); 6.32 (d, 1 H, H(10), $J_{10,9}$ = 8 Hz); 6.65 (t, 1 H, H(9), $J_{9,10} = J_{9,8}$ = 8 Hz); 6.95 (t, 1 H, H(8), $J_{8,9} = J_{8,7}$ = 8 Hz); 7.20—7.50 (m, 6 H, H(7) and C_6H_5); 11.05 (br.s, 1 H, N(6)H).

2-Oxo-1-phenyl-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indole (11). Method *A*. A solution of sodium hydrosulfite (3.2 g, 15.3 mmol) in water (8 mL) was added with stirring to a suspension of *N*-oxide **7a** (1.5 g, 5.1 mmol) in DMF (38 mL). The reaction mixture was refluxed for 3.5 h and then kept at 20 °C for 16 h. The inorganic precipitate was filtered off, the mother liquor was concentrated to dryness, and the residue was triturated with water. The precipitate was filtered off, washed with water, and dried. A compound, which was isolated in a yield of 1.32 g, was crystallized from MeOH. Compound **11** was obtained in a yield of 0.65 g. ^{1}H NMR (DMSO-d_6), δ: 4.50 (s, 2 H, 3-CH_2); 6.23 (d, 1 H, H(10), $J_{10,9}$ = 8.4 Hz); 6.81 (t, 1 H, H(9), $J_{9,10} = J_{9,8}$ = 8.4 Hz); 7.40—7.60 (m, 7 H, H(7), H(8), C_6H_5); 9.13 (s, 1 H, H(5)); 12.10 (br.s, 1 H, N(6)H).

Method *B*. An aqueous mother liquor, which was obtained after filtration of hexahydro[1,4]diazepino[6,5-*b*]indole (**10**), was acidified with concentrated HCl (5 mL). The precipitate that formed was filtered off and washed with water. Compound **11** was obtained in a yield of 0.03 g.

The ^{1}H NMR spectra of the compounds obtained according to the methods ***A*** and ***B*** are identical. The chemical shifts of the corresponding protons are somewhat different. The spectrum of a mixture of the samples has one set of signals.

3-Formyl-2-oxo-1-phenyl-2,3,4,5-tetrahydro-1*H*-pyrimido[5,4-*b*]indole (12). Phosphorus trichloride (0.9 mL, 10.2 mmol) was added dropwise with stirring to a suspension of *N*-oxide **7a** (1 g, 3.4 mmol) in dry chloroform (12 mL). The reaction mixture was refluxed for 10 min and then cooled. The precipitate that formed was filtered off, washed with chloroform and water, and dried. Compound **12** was obtained in a yield of 0.6 g. ^{1}H NMR (DMSO-d_6), δ: 4.63 and 4.75 (both s, 2 H each,

C(4)H_2); 5.93 (m, 1 H, H(9)); 6.71 (m, 1 H, H(8)); 6.98 (m, 1 H, H(7)); 7.20—7.70 (m, 6 H, H(6), Ph); 8.37 and 8.87 (both s, 1 H each, CHO); 11.50 and 11.75 (both br.s, 1 H each, N(5)H).

2-Oxo-1-phenyl-1,2-dihydropyrimido[5,4-*b*]indole (13). A mixture of compound **12** (0.6 g, 2 mmol), methanol (10 mL), and piperidine (0.78 mL, 8 mmol) was refluxed for 5.5 h. The reaction solution was concentrated to one-half of the initial volume and cooled on an ice bath. The precipitate that formed was filtered off and washed with methanol. Compound **13** was obtained in a yield of 0.23 g. ^{1}H NMR (DMSO-d_6), δ: 6.16 (d, 1 H, H(9), $J_{9,8}$ = 8.4 Hz); 6.83 (t, 1 H, H(8), $J_{8,9}$ = $J_{8,7}$ = 8.4 Hz); 7.28 (t, 1 H, H(7), $J_{7,6}$ = $J_{7,8}$ = 8.4 Hz); 7.46 (d, 1 H, H(6), $J_{6,7}$ = 8.4 Hz); 7.55 and 7.69 (both m, 2 H each, H(2′), H(3′), H(4′), H(5′), H(6′); 7.99 (s, 1 H, H(4)); 12.09 (br.s, 1 H, N(5)H).

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