Reactions of 3-[*N*-chloroacetylamino-*N*-(4-nitrophenyl)]-2-formylindole with alkylamines*

*S. Yu. Ryabova,[a] A. S. Shashkov,[b] L. M. Alekseeva,[a] E. A. Lisitsa,[a] and V. G. Granik[a]**

[a]*State Scientific Center for Antibiotics,*
3a ul. Nagatinskaya, 117003 Moscow, Russian Federation.
Fax: +7 (495) 225 6104. E-mail: vggranik@mail.ru
[b]*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,*
47 Leninsky prosp., 119991 Moscow, Russian Federation.
Fax: +7 (499) 135 5328

The reactions of 3-[*N*-chloracetylamino-*N*-(4-nitrophenyl)]-2-formylindole (**1a**) with 2-(*N*,*N*-dialkylamino)ethylamines afford complex condensation products **7b,c** consisting of two similar but not identical diazepinoindole fragments. For the reaction of compound **1a** with 3-(*N*,*N*-diethylamino)propylamine, the process occurs in a different manner, and the predominant product is 4-ethylaminopropyl-1-(4-nitrophenyl)-2-oxo-1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole hydrocloride (**14**). Two routes of these unexpected transformations were proposed. The structures of the synthesized products were proved by the ^{1}H and ^{13}C NMR, HMBC, and HSQC (direct proton-carbon correlation) spectra.

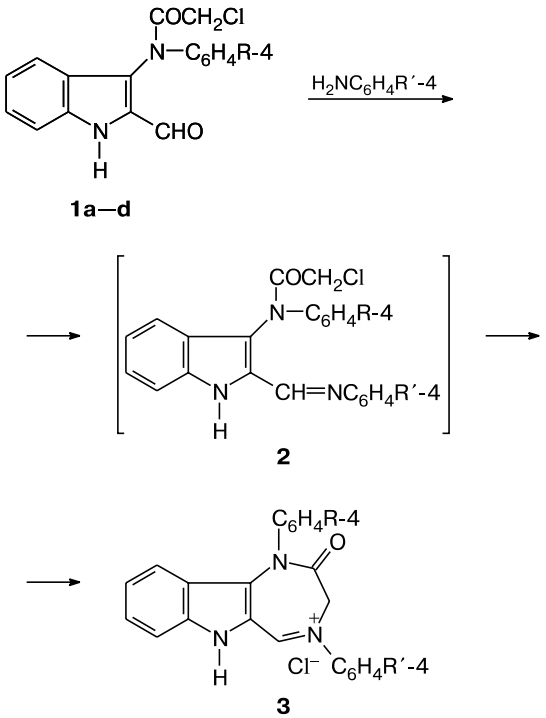
Key words: 3-[*N*-chloroacetylamino-*N*-(4-nitrophehyl)]-2-formylindole, ethanolamine, benzylamine, 2-(diethylamino)ethylamine, 2-(dimethylamino)ethylamine, 3-(diethylamino)propylamine, condensation, cyclization, 1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indoles, 1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indoles.

In the recent years, we have studied the synthesis, properties, and transformations of differently substituted 3-*N*-arylamino-2-formylindoles.[1,2] The use of these compounds in heterocyclic synthesis provided the development of novel, often unusual approaches to the preparation of a whole series of indole-containing heterocycles, such as pyrido[3,2-*b*]indoles, indolo[3,2-*b*]quinolines, pyrrolo[1,2-*a*]indoles, [1,4]diazepino[6,5-*b*]indoles, and pyrimido[5,4-*b*]indoles, and a series of heterotetracyclic compounds, including representatives of new heterocyclic systems.

We have recently studied the reactions of 3-(*N*-aryl-*N*-chloroacetylamino)-2-formylindoles **1** with *para*-substituted anilines (Scheme 1) resulting in the synthesis (without isolation of intermediate compounds **2**) of earlier unknown 1,4-diaryl-2-oxo-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indolium-4 chlorides (**3**).[3] They manifested antihypoxic activity on the models for hypoxic and hypobaric hypoxia at the level of the Pyracetam drug.

It is quite evident that the stabilization of intermediate **2** and final product **3** is caused, to a great extent, by the conjugation with the aromatic ring. Therefore, when aliphatic amines are introduced into the reaction with formylindole **1a**, some unexpected phenomena could be

Scheme 1



R = NO_2 (**a**), H (**b**), Cl (**c**), OEt (**d**)
R′ = H, OMe, Cl

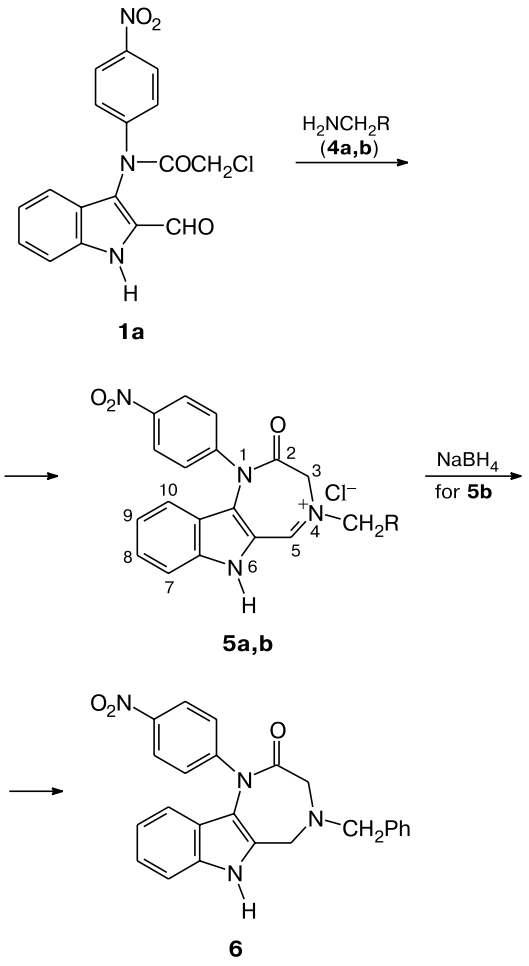
* Dedicated to Academician V. A. Tartakovsky on the occasion of his 75th birthday.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1536—1542, August, 2007.

predicted due to the absence of this conjugation and new biologically active compounds of the diazepinoindole series could be synthesized by the analogous[3] process.

The reactions of compound **1a** with equimolar amounts of ethanolamine (**4a**), benzylamine (**4b**), 2-(*N*,*N*-diethylamino)ethylamine (**4c**), 2-(*N*,*N*-dimethylamino)ethylamine (**4d**), and 3-(*N*,*N*-diethylamino)propylamine (**4e**) were carried out, as with arylamines, on reflux in isopropyl alcohol.[3] It turned out that the direction of these reactions depends on the structure of amine used. For the reactions of 2-formylindole **1a** with ethanolamine and with benzylamine, the process was similar to the reactions with arylamines,[3] and the corresponding 4-substituted 1-(4-nitrophenyl)-2-oxo-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indolium-4 chlorides (**5a,b**) were isolated. Chloride **5b** was reduced with sodium borohydride according to a described method[3] to form 4-benzyl-1-(4-nitrophenyl)-3-oxo-1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole (**6**) (Scheme 2).

Scheme 2



R = CH_2OH (**a**), Ph (**b**)

An insignificant amount of undissolved by-product **7a** containing no chlorine was separated upon the recrystallization of chloride **5b** from methanol. In the mass spectrum of compound **7a** the most intense was the peak corresponding to the peak 411 $[M - HCl + H]^+$ in the mass spectrum of the major substance **5b**. However, the low-intensity peak 821 $[M + H]^+$ and the cluster peaks 843 $[M + Na]^+$ and 859 $[M + K]^+$ were observed, indicating the formation of a dimer. The IR spectrum of compound **7a**, as compared to the spectrum of compound **5b**, contained no absorption band at 1690 cm^{-1} ($C{=}N^+$) and exhibited two bands at 1674 and 1664 cm^{-1} corresponding to two carbonyl groups (Table 1). The ^1H NMR spectrum of compound **7a** also differed substantially from the spectrum of the major substance **5b**: the spectrum exhibited a double set of the same-type signals from protons in both the aromatic and aliphatic regions. The total body of the physicochemical data assumed that a molecule of by-product **7a** contained two structurally similar but not identical fragments.

The reactions of 2-formylindole **1a** with diethylaminoethylamine **4c** and with dimethylaminoethylamine **4d** gave no expected [1,4]diazepino[6,5-*b*]indolium-4 chlorides of the type **5**. The major products obtained in satisfactory yields are dihydrochlorides **7b,c** (Scheme 3), whose ^1H NMR spectra are analogous (doubling of the most part of signals) to the spectrum of by-product **7a**.

The structures of compounds **7a—c** as 16,28-disubstituted 12,19-bis(4-nitrophenyl)-1,4,12,16,19,28-hexaazaheptacyclo[13.11.1.$1^{2,14}$.$0^{3,11}$.$0^{5,10}$.$0^{20,27}$.$0^{21,26}$]octacosa-3(11),5(10),6,8,20(27),21,(26),22,24-octaene-13,18-diones were determined on the basis of the detailed consideration of the ^1H NMR and HMBC spectra of these compounds. The ^1H NMR spectra of all three compounds contain, along with the doubled same-type signals (see Experimental), "unpaired signals": the signal from N(4)H (δ 11.28, 11.61, and 11.56), the signal from the protons of one methylene group $H_2C(17)$ in the form of the AB system (δ 3.67 and 4.40, 3.62 and 4.35, 3.63 and 4.31, J_{gem} = 15.0—15.4 Hz), the mutually split doublets of the H(14) and H(15) protons (δ 3.57 and 4.35, 3.80 and 4.59, 3.77 and 4.56, J_{vic} = 7.2—7.5 Hz), and the singlet of the H(2) proton (δ 7.10, 7.58, and 7.41).* Note that the appearance of the singlet signal in the region of aromatic protons seems strange, because the signals of protons of the benzene fragments and protons of the aryl and phenyl substituents cannot be singlets. This signal belongs to the proton at the sp^3-hybridized C(2)carbon atom** and it is so downfield due to some strong deshielding effects. The

* The chemical shift of the proton (δ 7.10) was calculated by the correlation peak in the HMBC spectrum.

** The HSQC spectrum (direct proton—carbon correlation) of compound **7b** contains the correlation peak H(2)/C(14) 7.58/68.8 ppm.

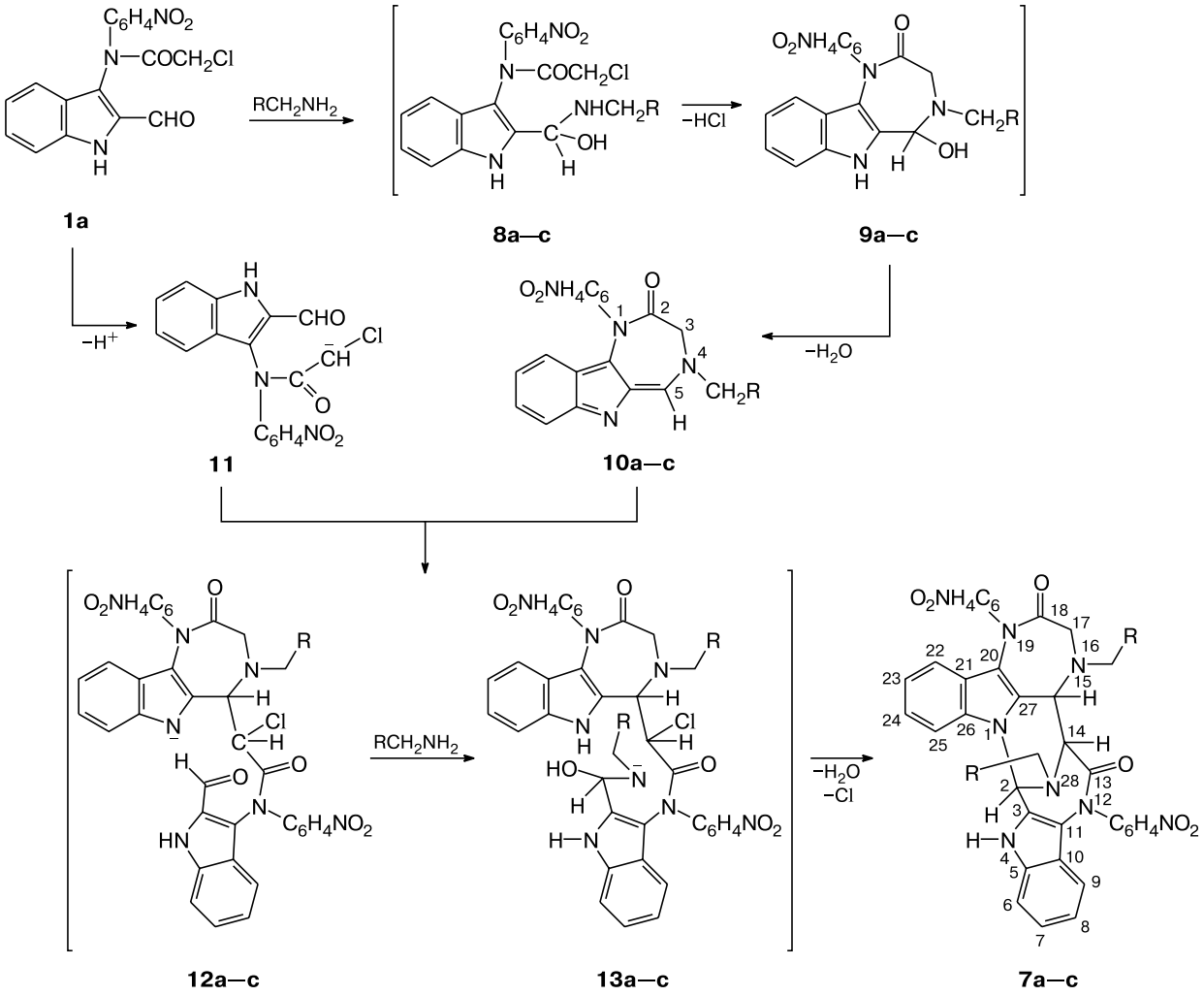
Table 1. Yields, elemental analysis data, and mass and IR spectra of the synthesized compounds

Compound	Yield (%)	M.p./°C (solvent)	Mol. weight	Found / Calculated (%)			Molecular formula	MS, *m/z*	IR, ν_{max}/cm^{-1}		
				C	H	N			NH (OH)	C=N$^+$ (N+H)	CO
5a	84	242—243 (decomp. EtOH)	400	56.44 56.93	4.36 4.28	13.75 13.98	$C_{19}H_{17}ClN_4O_4$	365 [M – HCl + H]$^+$, 337 [M – HCl + H – – CO]$^+$, 729 [2 M – – 2 HCl + H]$^+$	3533, 3477, 3311	1680	1645
5b	46	253—254 (decomp. MeOH)	446	64.30 64.50	4.44 4.29	12.54 12.54	$C_{24}H_{19}ClN_4O_3$	411 [M – HCl + H]$^+$, 383 [M – HCl + H – – CO]$^+$, 433 [M – HCl – + Na]$^+$, 821 [2 M – – 2 HCl + H]$^+$	3520—3470	1690	1635
6	91	204—206 (MeOH)	412	69.86 69.89	4.67 4.89	13.15 13.58	$C_{24}H_{20}N_4O_3$	413 [M + H]$^+$, 435 [M + Na]$^+$, 451 [M + K]$^+$, 825 [2 M + + H]$^+$, 847 [2 M + + Na]$^+$, 863 [2 M + K]$^+$	3350	—	1678
7a	2.4	238—240 (MeOH)	820	—	—	—	$C_{48}H_{36}N_8O_6$	821 [M+H]$^+$, 843 [M + Na]$^+$, 859 [M + + K]$^+$, 411 [M/2 + H]$^+$	3664, 3524, 3470	—	1674, 1664
7b	70	242—243 (MeOH)	910	60.15 60.59	6.06 5.75	15.11 15.36	$C_{46}H_{26}Cl_2N_{10}O_6$	420 [(M– 2 HCl)/2 + + H]$^+$, 839 [M – 2 HCl + H]$^+$	3600, 3470, 3120	2557—2425	1690, 1674
7c	37	238—240 (MeOH)	854	55.73 55.44	5.59 5.54	15.46 15.40	$C_{42}H_{44}Cl_2N_{10}O_6 \cdot 3\ H_2O$	821 [M – 2 HCl + K]$^+$, 805 [M – 2 HCl + Na]$^+$, 783 [M – 2 HCl + H]$^+$, 392 [(M– 2 HCl)/2 + + H]$^+$	3429	2463	1670
14	27	238—240 (MeOH)	443	59.59 59.52	5.95 5.90	15.75 15.78	$C_{22}H_{26}ClN_5O_3$	408 [M – HCl + H]$^+$, 815 [2 (M – HCl) + H]$^+$	3234	2478	1680

strong shift of the H(2) signal in the spectrum can be related to both the immediate closeness to two nitrogen atoms and (most likely, this is the main reason) an anisotropic effect of the circular currents of two aromatic (indole) parts of the molecule, which are geminal toward this proton.

The consideration of the ^{1}H NMR spectra of compounds **7a—c** show that the rather non-standard condensation of two diazepinoindole molecules occurs in these cases: for one of the molecules the nitrogen atom and one of the methylene groups of the diazepine cycle are "cross-linking" sites, whereas for another molecule the both methylene groups are these sites. The ^{13}C NMR spectra of compounds **7a,b** also exhibit a double set of signals for the same-type carbon atoms and signals of the "unpaired" carbon atoms linked with the "unpaired" protons. The signals were assigned (see Experimental) according to the HSQC (for protonated atoms) and HMBC (for quaternary atoms) spectra. We did not assign the signals of the carbon atoms of the indole and substituents to some certain diazepinoindole fragment, because the spectra are intricate and, in addition, the detailed decoding of these fragments did not solve the problems of structure determination. Structures **7a,b** were unambiguously proved by the HMBC spectra. In the spectrum of dimer **7a** (the chemical shifts are given in Experimental), one of the protons of the $H_2C(17)$ group has a correlation peak with the carbon atom of N(16)$\underline{C}H_2$Ph; both protons of $H_2C(17)$ have correlation peaks with the C(15) and C(18) atoms; H(14) has correlation peaks with N(28)$\underline{C}H_2$Ph, C(2), C(13), and C(15); H(15) has correlation peaks with N(16)$\underline{C}H_2$Ph and the C(13), C(14), C(17), C(20), and C(27) carbon atoms; H(2) has a correlation peak with C(14). Similar correlation peaks for the protons in positions 2, 14, 15, and 17 are also observed in the HMBC spectrum of compound **7b** (see Experimental). Since in the spectra of compound **7b** the signal from H(2) is not overlapped by other aromatic signals, we can determine the quaternary carbon atoms having correlation peaks with this proton in the aromatic spectral region: these are C(11),

Scheme 3



R = Ph (**a**), $CH_2N^+Et_2Cl^-$ (**b**), $CH_2N^+Me_2Cl^-$ (**c**)

C(3), C(27), and C(26) (δ 114.3, 124.7, 126.9, and 135.1, respectively).

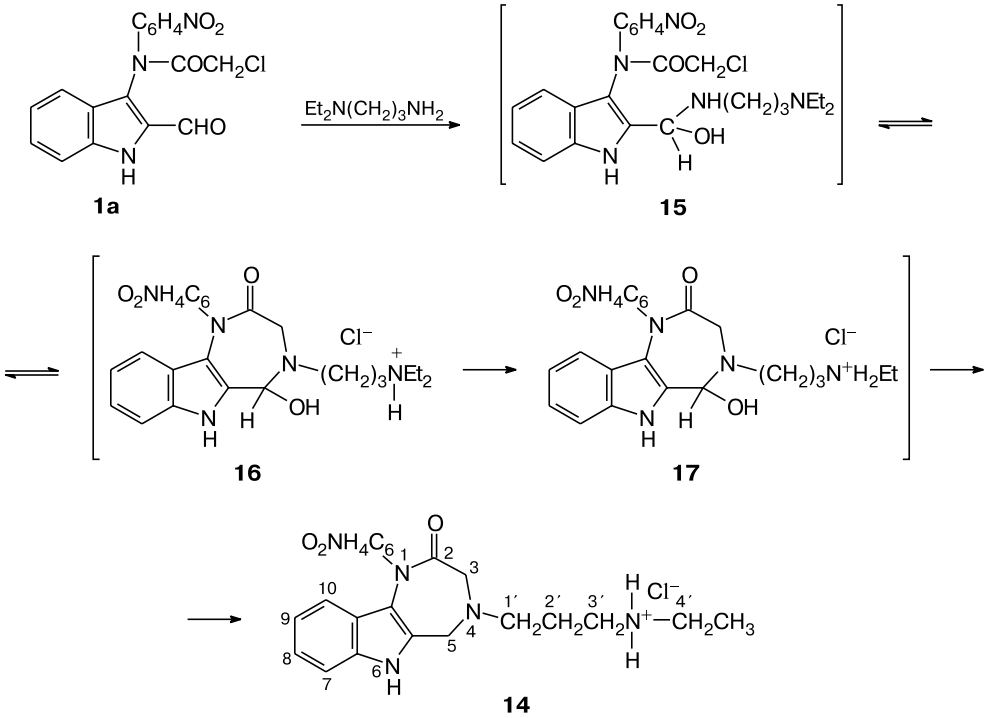
The structure of compound **7c** was determined on the basis of similarity of its ^{1}H NMR spectra to the above discussed spectra of compounds **7a,b**.

One more important fact should be mentioned: the yields of the products isolated in these ambiguously occurring processes are not quantitative. The mother liquors contain intricate mixtures of substances, and the study of their spectra gave no reliable data on the structure of the by-products. Therefore, assumptions on probable schemes of the processes are based on general concepts and the structures of the final products.

When describing the formation of these compounds *via* Scheme 3, we took into account that amines taken in some excess were introduced into all reactions and the excess created a certain basic level of the reaction medium. Unambiguously, the first step of the reaction is the condensation of the formyl group at the amino group of the reactant, resulting in the preliminary formation of the corresponding carbinolamine **8**. If aromatic amine was chosen as the reactant,[3] than, as mentioned above, the condensation was followed by fast dehydration to form the Schiff base stabilized by the conjugation.

In this case, this stabilization does not occur and carbinolamine **8** is further transformed into diazepinoindole **9** and then into compound **10** including the aromatized 10-π-electron system. In parallel, most likely, the starting compound **1a** is transformed into carbanion **11** capable of attacking the electron-deficient position 5 of compound **10** to form anion **12**, which is further subjected to the attack of the initial amine yielding anions **13** and then polycyclic compounds **7a—c**. Note that compounds **7b** and **7c** were isolated as dihydrochlorides, which are formed due to the presence of the $—NEt_2$ and $—NMe_2$ groups.

Scheme 4



The reaction of 2-formylindole **1a** with diethylaminopropylamine **2d** proceeded in a different manner and afforded 4-ethylaminopropyl-1-(4-nitrophenyl)-2-oxo-1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole (**14**) hydrochloride (Scheme 4). The ^{1}H NMR spectrum of this compound (see Experimental) exhibits the signal from one methyl group, the signals from the methylene groups of the $CH_2CH_2CH_2(N^+H_2)CH_2CH_3$ substituent (see Scheme 4), the signal from $H_2C(2')$, which is the most upfield and followed by $H_2C(1')$, the signals from $H_2C(3')$ and $H_2C(4')$ manifesting the downfield shifts (one signal with the intensity 4 H), and the signal from the (N^+H_2) group. The structure of the substituent in position 4 also agrees with the HMBC spectrum: the protons of $H_2C(1')$ have correlation peaks with C(3), C(5), C(3′), C(2′); the protons of $H_2C(2')$ have correlation peaks with C(1′) and C(3′); the general signal from $H_2C(3')$ and $H_2C(4')$ has correlation peaks with CH_3, C(1′), C(2′), C(3′), and C(4′).

It seems probable that in the first step in this case (as well as for the synthesis of compounds **7a—c**) carbinolamine **15** is formed and then undergoes intramolecular cyclization to diazepinoindole **16**.* Then, judging from the structure of the final product, de-ethylation occurs with the rejection of ethylene or ethyl chloride and formation of compound **17**, which is further transformed into diazepinoindole hydrochloride **14**. The generalized scheme of formation of compound **14** is shown in Scheme 4.

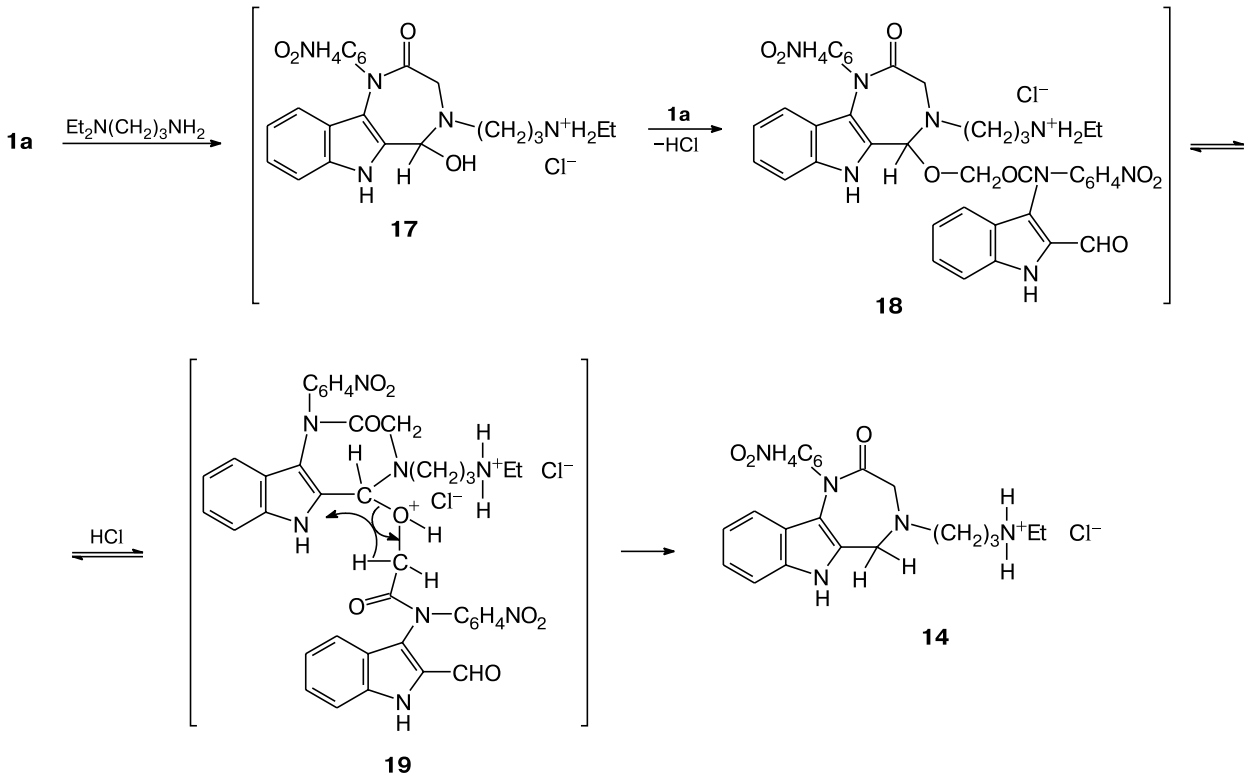
Questions that need special interpretation arise when considering this scheme. First, it is necessary to answer why the difference between the reactions of compound **1a** with diethylaminoethyl- and diethylaminopropylamines is so considerable. It cannot be excluded that the essence is in the ratio of rates of particular reactions, which can depend on the basicity of the reactants, rather than in the dramatic change in the directions of the processes.

Another problem that cannot be explained on the basis of Scheme 4 is a reason for which the tricyclic compound containing the hexahydrodiazepine ring is formed finally in the absence of solvents. It is reasonable to assume that tricycle **14** is formed through the O-alkylation of compound **17** by the starting compound **1a** to form derivative **18**, which further undergoes O-protonation to compound **19** and prototropic shift to form diazepinoindole **14** (Scheme 5).

Very unusual transformations described in the present publication and subsequent assumptions undoubtedly need further detailed investigation.

* Perhaps, the predominant formation of compound **16**, in this case, compared to process **9**→**10** postulated in Scheme 3, is due to a higher basicity of 3-(diethylamino)propylamine (**4e**)[4] than that of 2-(diethylamino)ethylamine (**4c**)[5] (by the first step pK_a = 10.44 (**4e**) and 9.15 (**4c**), and by the second step pK_a = 8.34 (**4e**) and 7.07 (**4c**)).

Scheme 5



Experimental

IR spectra of the synthesized compounds were recorded on an FSM-1201 instrument in Nujol. Mass spectra of the compounds were measured on a Waters ZQ-2000 mass spectrometer (electrospray, sample injection missing the chromatographic column). ^{1}H NMR spectra were obtained on a Bruker AC-300 spectrometer in DMSO-d_6 using standard procedures of the Company. ^{13}C NMR, HMBC, and HSQC spectra were recorded on a Bruker DRX-500 spectrometer in DMSO-d_6. The course of the reactions and individual character of the substances were monitored on Silicagel 60 F_{254} plates (Merck) in chloroform—methanol (10 : 1) and ethyl acetate—isopropyl alcohol—ammonia (5 : 3 : 1) systems. The yields, elemental analysis data, and other physicochemical characteristics of the synthesized compounds are presented in Table 1.

4-Hydroxyethyl-1-(4-nitrophenyl)-2-oxo-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indolium-4 chloride (5a). Ethanolamine (0.093 mL, 1.54 mmol) was added with stirring to a suspension of 2-formylindole **1a** (0.5 g, 1.4 mmol) in Pr^{i}OH (10 mL), and the mixture was refluxed for 20 min. The mixture was cooled, and the precipitate was filtered off, washed with isopropyl alcohol and acetone, and dried. Chloride **5a** was obtained in a yield of 0.3 g. ^{1}H NMR, δ: 3.82, 4.26 (both br.t, 2 H each, $\underline{CH_2}\underline{CH_2}OH$, J = 4.5 Hz); 4.83 (s, 2 H, $H_2C(3)$); 5.36 (br.s, 1 H, OH); 6.32 (d, 1 H, H(10), J_o = 8.4 Hz); 6.94 (t, 1 H, H(9), J_o = 8.4 Hz); 7.44 (t, 1 H, H(8), J_o = 8.4 Hz); 7.61 (m, 3 H, H(7), H(3′), H(5′)); 8.38 (d, 2 H, H(2′), H(6′), J_o = 9.0 Hz); 9.49 (s, 1 H, H(5)); 12.76 (br.s, 1 H, N(6)H).

4-Benzyl-1-(4-nitrophenyl)-2-oxo-1,2,3,6-tetrahydro[1,4]diazepino[6,5-*b*]indolium-4 chloride (5b). Benzylamine (0.17 mL, 1.54 mmol) was added with stirring and reflux to a suspension of 2-formylindole **1a** (0.5 g, 1.4 mmol) in Pr^{i}OH (10 mL). The mixture was refluxed for 1 h. A hot new precipitate that formed was filtered off, washed with isopropyl alcohol and acetone, and dried. Chloride **5b** was obtained (0.39 g) and further used without purification. Methanol (60 mL) was added, and the mixture was refluxed for 10 min. An insoluble residue of **7a** was filtered off. **16,28-Dibenzyl-12,19-bis(4-nitrophenyl)-1,4,12,16,19,28-hexaazaheptacyclo[13.11.1.1^{2,14}.0^{3,11}.0^{5,10}.0^{20,27}.0^{21,26}]octacosa-3(11),5(10),6,8,20(27),21,(26),22,24-octaene-13,18-dione (7a)** was obtained in a yield of 0.02 g. ^{1}H NMR, δ: 3.22, 3.58, 3.66, 3.91 (all d, 1 H each, N(16)$\underline{CH_2}$Ph, N(28)$\underline{CH_2}$Ph, J_{gem} = 14.0 Hz, J_{gem} = 12.9 Hz); 3.67, 4.40 (both d, 1 H each, $H_2C(17)$, J_{gem} = 15.0 Hz); 3.57, 4.35 (both d, 1 H each, H(14)), H(15)), J_{vic} = 7.5 Hz); 5.58, 6.36 (both d, 1 H each, 2 H of benzene fragments, J_o = 8.3 Hz); 6.71, 6.94, 7.04, 7.91 (three t, one d, 1 H each, 4 H of benzene fragments, J_o = 8.6 Hz); 7.08—7.29 (m, 13 H, Ph, Ph, 2 H of benzene fragments, H(2)); 7.38, 7.72, 8.29, 8.32 (all d, 2 H each, N(12)C_6H_4 NO_2, N(19)$C_6H_4NO_2$, J_o = 8.6 Hz); 11.28 (br.s, 1 H, N(4)H).

^{13}C NMR, δ: 53.0 (C(15)); 55.2 (C(17)); 56.5, 57.7 (N(16)$\underline{C}H_2$Ph, N(28)$\underline{C}H_2$Ph); 67.2 (C(2)); 68.2 (C(14)); 111.2, 111.7, 118.6, 118.8, 119.5, 120.2, 122.0, 122.6, 123.9, 124.0, 127.5, 128.1, 128.2, 128.3, 128.4, 129.0 (C(6)—C(9)), C(22)—C(25)), (N(12)$\underline{C}_6H_4NO_2$ and N(19)$\underline{C}_6H_4NO_2$, N(16)$CH_2\underline{Ph}$ and N(28)$CH_2\underline{Ph}$)*); 114.0, 114.4, 120.0, 121.0,

* The chemical shifts of the signals from the protonated atoms.

125.2, 127.5, 134.8, 136.1, 136.7, 137.3, 144.9, 145.0, 145.9, 146.8, 169.2, 170.3 (C(10), C(20), C(11), C(21), C(3), C(27), C(5), C(26)), (N(16)CH_2Ph and N(28)CH_2Ph, N(12)$C_6H_4NO_2$ and N(19)$C_6H_4NO_2$)*), C(13), C(18).

HMBC, δ: 4.40/56.5 H(17)/N(16)CH_2Ph; 3.67, 4.40/53.0 H_2C(17)/C(15); 3.67, 4.40/170.3 H_2C(17)/C(18); 3.57/57.7 H(14)/N(28)CH_2Ph; 3.57/53.0 H(14)/C(15); 3.57/67.2 H(14)/C(2); 3.57/169.2 H(14)/C(13); 4.35/56.5 H(15)/N(16)CH_2Ph; 4.35/55.2 H(15)/C(17); 4.35/68.2 H(15)/C(14); 4.35/169.2 H(15)/C(13); 4.35/114.0 H(15)/C(20); 4.35/127.5 H(15)/C(27); 7.10/68.2 H(2)/(C(14).

After compound **7a** was separated, the mother liquor was clarified with active carbon and evaporated by 1/4 of the volume, and a precipitate of chloride **5b** was filtered off (0.29 g, 46%). ^{1}H NMR, δ: 4.67 (s, 2 H, H_2C(3)); 5.46 (s, 2 H, CH_2Ph); 6.28 (d, 1 H, H(10), J_o = 8.4 Hz); 6.92 (t, 1 H, H(9), J_o = 8.4 Hz); 7.40—7.64 (m, 9 H, H(8), H(3′), H(5′), H(7), Ph); 8.35 (d, 2 H, H(2′), H(6′), J_o = 9.0 Hz); 9.91 (s, 1 H, H(5)); 13.10 (br.s, 1 H, N(6)H).

4-Benzyl-1-(4-nitrophenyl)-2-oxo-1,2,3,4,5,6-hexahydro-[1,4]diazepino[6,5-*b*]indole (6). Sodium borohydride (0.03 g, 0.79 mmol) was slowly added with stirring in small portions to a suspension of chloride **5b** (0.18 g, 0.4 mmol) in methanol (10 mL). A solution was formed in 15 min, and a new precipitate began to form in 30 min. The reaction mixture was additionally stirred for 30 min at ambient temperature. The precipitate was filtered off, washed with methanol, and dried. Compound **6** was obtained in a yield of 0.15 g. ^{1}H NMR, δ: 3.85 (s, 2 H, H_2C(3)); 3.98 (s, 2 H, H_2C(5)); 3.97 (s, 2 H, CH_2Ph); 6.46 (d, 1 H, H(10), J_o = 8.4 Hz); 6.83 (t, 1 H, H(9), J_o = 8.4 Hz); 7.08 (t, 1 H, H(8), J_o = 8.4 Hz); 7.22—7.44 (m, 6 H, H(7), CH_2Ph); 7.57 (d, 2 H, H(3′), H(5′), J_o = 8.4 Hz); 8.26 (d, 2 H, H(2′), H(6′), J_o = 9.0 Hz); 11.53 (br.s, 1 H, N(6)H).

16,28-Bis[2-*N*,*N*-diethylamino)ethyl]-12,19-bis(4-nitrophenyl)-1,4,12,16,19,28-hexaazaheptacyclo-[13.11.1.1^{2,14}.0^{3,11}.0^{5,10}.0^{20,27}.0^{21,26}]octacosa-3(11),5(10),6,8,20(27),21,(26),22,24-octaene-13,18-dione dihydrochloride (7b). 2-(Diethylamino)ethylamine (0.16 mL, 1.11 mmol) was added with stirring and reflux to a suspension of 2-formylindole **1a** (0.36 g, 1.01 mmol) in Pr^{i}OH (10 mL), and the mixture was refluxed for 10 min. The mixture was cooled down, and the precipitate was washed with Pr^{i}OH and acetone, and dried. Compound **7b** was obtained in a yield of 0.32 g. ^{1}H NMR, δ: 1.04—1.19, 2.63—3.51 (both m, 28 H, N(16)$C_2H_4N^+HEt_2$ and N(28)$C_2H_4N^+HEt_2$); 3.62, 4.35 (both d, 1 H each, H_2C(17), J_{gem}=15.4 Hz); 3.80, 4.59 (both d, 1 H each, H(14), H(15), J_{vic}=7.2 Hz); 6.14, 6.34, 7.35, 8.18 (all d), 6.73, 6.93 7.07, 7.30 (all t) (all d and t; 1 H each, H(6)—H(9), H(22)—H(25), J_o=8.3 Hz); 7.58 (s, 1 H, H(2)); 7.64, 7.83, 8.26, 8.37 (all d, 2 H each, N(12)$C_6H_4NO_2$ and N(19)$C_6H_4NO_2$, J_o=8.8 Hz); 10.46, 10.57 (both br.s, 1 H each, N(16)$C_2H_4N^+HEt_2$ and N(28)$C_2H_4N^+HEt_2$); 11.61 (br.s, 1 H, N(4)H).

^{13}C NMR, δ: 8.18—8.56 (N(16)$(CH_2)_2N^+H(CH_2Me)_2$ and N(28)$(CH_2)_2N^+H(CH_2Me)_2$); 46.2—49.3 (N(16)$CH_2CH_2N^+H(CH_2Me)_2$ and N(28)$CH_2CH_2N^+H(CH_2Me)_2$); 53.0 (C(17)); 57.4 (C(15)); 67.2 (C(2)); 68.8 (C(14)); 111.4, 111.9, 118.3, 119.2, 119.5, 120.3, 122.3, 122.7, 124.0, 124.1, 128.0, 129.3 (C(6)—C(9), C(22)—C(25), (N(12)$C_6H_4NO_2$ and N(19)$C_6H_4NO_2$)*); 114.0, 114.3, 120.1, 121.0, 124.9, 126.9, 135.1, 135.8, 145.0, 145.6, 145.7, 146.6, 169.8, 170.3 (C(10), C(20), C(11), C(21), C(3), C(27), C(5), C(26), (N(12)$C_6H_4NO_2$ and N(19)$C_6H_4NO_2$)**; C(18); C(13)).

HMCB, δ: 4.35/48.7 H(17)/N(16)$CH_2CH_2N^+H(CH_2Me)_2$; 3.62, 4.35/57.4 H_2C(17)/C(15); 3.62, 4.35/169.8 H_2C(17)/C(18); 3.80/49.3 H(14)/N(28)$CH_2CH_2N^+H(CH_2Me)_2$; 3.80/57.4 H(14)/C(15); 3.80/67.2 H(14)/C(2); 3.80/170.0 H(14)/C(13); 4.59/48.7 H(15)/N(16)$CH_2CH_2N^+H(CH_2Me)_2$; 4.59/53.0 H(15)/C(17); 4.59/68.8 H(15)/C(14); 4.59/170.3 H(15)/C(13); 4.59/114.0 H(15)/C(20); 4.59/127.0 H(15)/C(27); 7.58/68.8 H(2)/C(14); 7.58/114.3 H(2)/C(11); 7.58/124.7 H(2)/C(3); 7.58/128.9 H(2)/C(27); 7.58/135.8 H(2)/C(26).

16,28-Bis[2-*N*,*N*-dimethylamino)ethyl]-12,19-bis(4-nitrophenyl)-1,4,12,16,19,28-hexaazaheptacyclo-[13.11.1.1^{2,14}.0^{3,11}.0^{5,10}.0^{20,27}.0^{21,26}]octacosa-3(11),5(10),6,8,20(27),21,(26),22,24-octaene-13,18-dione dihydrochloride (7c). 2-(Dimethylamino)ethylamine (0.066 mL, 0.55 mmol) was added with stirring and reflux to a suspension of 2-formylindole **1a** (0.18 g, 0.5 mmol) in Pr^{i}OH (10 mL), and the mixture was refluxed for 30 min. The mixture was cooled down, and the precipitate was filtered off, washed with isopropanol and acetone, and dried. Compound **7c** was obtained in a yield of 0.08 g. ^{1}H NMR, δ: 2.56—3.56 (m, 20 H, (N(16)$C_2H_4N^+HMe_2$ and N(28)$C_2H_4N^+HMe_2$); 3.63, 4.31 (both d, 1 H each, H_2C(17), J_{gem} = 15.4 Hz); 3.77, 4.56 (both d, 1 H each, H(14), H(15), J_{vic} = 7.1 Hz); 6.15, 6.33, 7.39, 8.16 (all d), 6.74, 6.93 7.08, 7.30 (all t) (all 1 H, H(6)—H(9), H(22)—H(25), J_o = 8.3 Hz); 7.41 (s, 1 H, H(2)); 7.62, 7.83, 8.26, 8.36 (all d, 2 H each, N(12)$C_6H_4NO_2$ and N(19)$C_6H_4NO_2$, J_o = 8.9 Hz); 10.37 (br.s, 2 H, N(16)$C_2H_4N^+HMe_2$ and N(28)$C_2H_4N^+HMe_2$)); 11.58 (br.s, 1 H, N(4)H).

4-Ethylaminopropyl-1-(4-nitrophenyl)-2-oxo-1,2,3,4,5,6-hexahydro[1,4]diazepino[6,5-*b*]indole hydrochloride (14). 3-(Diethylamino)propylamine (0.09 mL, 0.55 mmol) was added with stirring and reflux to a suspension of 2-formylindole **1a** (0.18 g, 0.5 mmol) in Pr^{i}OH (10 mL), and the mixture was refluxed for 2 h. The mixture was cooled down, and the precipitate that formed was filtered off. The mother liquor was evaporated, the residue was triturated with ether, and the precipitate was filtered off. Compound **14** was obtained in a yield of 0.06 g.

^{1}H NMR, δ: 1.20 (t, 3 H, CH_2CH_3, J_o = 7.5 Hz); 1.88 (m, 2 H, H_2C(2′)); 2.77 (t, 2 H, H_2C(1′)); 2.92 (m, 4 H, H_2(3′), H_2C(4′)); 3.39 (s, 2 H, H_2(3)); 4.09 (s, 2 H, H_2C (5)); 6.43 (d), 6.82, 7.07 (both t), 7.40 (d) (1 H each, H(10)—H(7), J_o = 8.4 Hz); 7.57, 8.25 (both d, 2 H each, $C_6H_4NO_2$, J_o = 9.0 Hz); 8.82 (br.s, 2 H, $C_2H_4N^+H_2Et$).

^{13}C NMR, δ: 10.9 (CH_3); 23.6 (C(2′)); 41.8 (C(4′)); 44.2 (C(3′)); 49.1 (C(5)); 53.5 (C(1′)); 57.4 (C(3)); 111.9, 117.3, 119.4, 121.6 (C(7), C(10), C(9), C(8)); 124.3, 126.3, 144.3, 145.7 ($C_6H_4NO_2$); 114.5, 120.7, 130.0, 134.3 ($C(10_b)$, $C(10_a)$, $C(5_a)$, $C(6_a)$).

* The chemical shifts of the signals from the quaternary atoms.

* The chemical shifts of the signals from the protonated atoms.

** The chemical shifts of the signals from the quaternary atoms.

References

1. S. Yu. Ryabova, Doc. Sci. (Chem.) Thesis, State Scientific Center for Antibiotics, Moscow, 2005, 451 pp. (in Russian).
2. K. F. Suzdalev and M. N. Babakova, in *Izbrannye metody sinteza i modifikatsii geterotsiklov. Khimiya sinteticheskikh indol´nykh sistem* [*Selected Methods for Synthesis and Modifications of Heterocycles. Chemistry of Synthetic and Indole Systems*], Ed. V. G. Kartsev, IBS PRESS, Moscow, 2004, **3**, 403 (in Russian).
3. S. Yu. Ryabova, L. M. Alekseeva, N. A. Rastorgueva, E. A. Lisitsa, D. M. Papakhin, V. A. Parshin, and V. G. Granik, *Izv. Akad. Nauk*, *Ser. Khim*., 2006, 2193 [*Russ. Chem. Bull., Int. Ed.*, 2006, **55**, 2278].
4. C. Tissier and P. Barillier, *Compt. Rend. C*, 1969, **268**, 1953.
5. J. Bjerrum, G. Schwarzenbach, and L. G. Sillen, *Stability Constants*, London, Chem. Soc., 1957, 105 pp.

Received January 31, 2007;
in revised form February 26, 2007