TABLE 1. Characteristics of the Compounds Synthesized

Compound	X	Mp, °C	Found, %			Empirical formula	Calculated, %			Yield, %
			C	H	N		C	H	N	
IIIa	H	225	81,15	5,39	10,29	$C_{37}H_{30}N_4O$	81,32	5,49	10,25	61
IIIb	*p*-Cl	199	71,87	4,32	9,01	$C_{37}H_{28}Cl_2N_4O$	72,07	4,54	9,09	72
IIIc	*p*-Br	206	62,99	3,68	7,86	$C_{37}H_{28}Br_2N_4O$	63,06	3,97	7,95	45
IIId	*m*-Cl	240	71,89	4,42	9,03	$C_{37}H_{28}Cl_2N_4O$	72,07	4,54	9,09	53
IIIe	*m*-Br	212	62,87	3,87	7,86	$C_{37}H_{28}Br_2N_4O$	63,06	3,97	7,95	31
IIIf	*o*-Cl	251	71,97	4,55	8,88	$C_{37}H_{28}Cl_2N_4O$	72,07	4,54	9,09	74
IIIg	*p*-F	239	76,14	4,66	9,49	$C_{37}H_{28}F_2N_4O$	76,28	4,81	9,62	54

Compounds IIIa-g were produced according to a single procedure, described below on the example of compound IIIb.

1,13d-Dimethyl-2-phenyl-4-(p-chlorophenyl)-3-(p-chlorobenzyloxy)-1,2-dihydro-13dH,8H-indolo[3,2-f]pyrazolo[4,3-c]quinoline (IIIb). A mixture of 1.52 g (0.005 mole) 3-p-chlorobenzylidenaminocarbazole, 0.94 g (0.005 mole) antipyrine, 60 ml of alcohol, and 1.5 ml conc. HCl was heated in a flask with a reflux condenser on a boiling water bath for 3 h. At first everything dissolved; after 2 h a precipitate began to form, which was filtered off at the end of the reaction and cooling of the mixture. It was treated with aqueous ammonia, and after drying was recrystallized from a mixture of toluene and methanol (1:1).

In all cases one spot was observed on the thin-layer chromatograms (aluminum oxide, methanol). The characteristics of the compounds synthesized are cited in Table 1.

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SYNTHESIS AND AMINOMETHYLATION OF DERIVATIVES OF PYRAZINO[3.2.1-jk]CARBAZOLE AND DIAZEPINO[3.2.1-jk]CARBAZOLE

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Derivatives of pyrazino- and diazepino[3.2.1-jk]carbazoles were obtained by the Fischer condensation of 1-amino-3-oxo-1,2,3,4-tetrahydroquinoxaline and 1-amino-4-oxo-2,3-dihydrobenzodiazepine(1,5) with cyclohexanone and 3-methylcyclohexanone. A study was carried out on the transformations of derivatives of pyrazino- and diazepino[3.2.1-jk]carbazoles by methylation at the NH group and aminomethylation of the N-methyl derivatives.

In a continuation of a study of the Fischer reaction with the aim of synthesizing condensed heterocycles [1], we obtained derivatives of pyrazino- and diazepino[3.2.1-jk]carbazoles by the reaction of cyclohexanone and 3-methylcyclohexanone with 1-amino-3-oxo-1,2,3,4-

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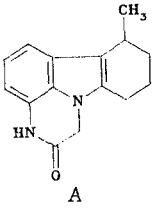
TABLE 1. Derivatives of Pyrazino- and Diazepino[3.2.1-jk] carbazoles

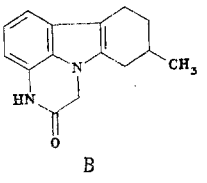
Compound	Mp, °C[a]	Found, %			Chemical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
IIa	285[b]	—	—	—	$C_{14}H_{14}N_2O$	—	—	—	56
IIb	210—212	74,8	6,5	11,9	$C_{15}H_{16}N_2O$	74,9	6,7	11,7	67
IIc	256—258	74,9	6,7	11,7	$C_{15}H_{16}N_2O$	74,9	6,7	11,7	32
IId	226—228	75,8	6,8	11,2	$C_{16}H_{17}N_2O$	75,8	6,8	11,1	31
IIIa	131—133	74,7	6,4	11,6	$C_{15}H_{16}N_2O$	74,9	6,4	11,7	71
IIIb	122—124	75,7	7,3	11,0	$C_{16}H_{18}N_2O$	75,6	7,1	11,0	69
IIIc	245—247	75,4	6,8	11,4	$C_{16}H_{18}N_2O$	75,6	7,1	11,0	85
IVa	155—157	72,6	7,4	14,2	$C_{18}H_{23}N_3O$	72,7	7,8	14,1	30
IVb	152—154	72,7	7,9	13,2	$C_{19}H_{25}N_3O$	73,3	8,1	13,5	33
IVc	180—182	73,6	7,9	13,6	$C_{19}H_{25}N_3O$	73,3	8,1	13,5	42
Va	153—155	70,3	7,4	12,0	$C_{20}H_{25}N_3O_2$	70,8	7,4	12,4	42
Vb	160—162	71,2	7,9	11,7	$C_{21}H_{27}N_3O_2$	71,4	7,7	11,9	57
Vc	178—180	71,3	7,7	11,9	$C_{21}H_{27}N_3O_2$	71,4	7,7	11,9	36

[a]Compounds IIa-d were crystallized from dioxane, while IIIa-c, IVa-c, and Va-c were crystallized from methanol. [b]In accord with the data of Perkin and Riley [2].

tetrahydroquinoxaline (Ia) and 1-amino-4-oxo-2,3-dihydrobenzodiazepine(1,5) (Ib). Compounds Ia and Ib were prepared by the reduction of the previously described nitroso derivatives [2, 3] by zinc in acetic acid and used without separation in the reaction with the ketones. Compounds IIc and IId were obtained in higher yields by the addition of concentration hydrochloric acid or p-toluenesulfonic acid to the acetic acid solution. The Fischer condensation of Ia with 3-methylcyclohexanone may lead to pyrazinocarbazoles with different positions of the methyl group (structures A and B).



A



B

Only IIb was obtained as a result of this reaction. The PMR spectra of its derivatives, IIIb and IVb (in C_6D_5Br), were used to establish the proper structure. If IIIb had structure A, then we would expect complex, partially overlapping signals for the protons C-8, C-9, and C-10 since each of the signals of the methylene protons, in addition to geminal coupling, should also be split due to vicinal coupling with the protons of the adjacent methylene groups. A simpler spectrum would be expected for structure B. The signals for the methylene protons at C-10 for this structure, in addition to geminal coupling, should have splitting only with one vicinal constant due to the proton at C-9. The aliphatic part of the spectrum of IIIb has signals at 102 (d, CH_3, J = 6 Hz), 1.32 (m, 1H), 1.88 (m, 3H); 2.36 (q, 1H, J_1 = 15, J_2 = 4 Hz), 2.68 ppm (m, 2H). The assignment of all the multiplets to the corresponding protons was made using double resonance, which showed that the quartet at 2.36 ppm is related to one of the protons at C-10. The multiplicity of this signal is in accord only with structure B.

We studied the conversions of derivatives of pyrazino- and diazepino[3.2.1-jk]carbazoles (IIa-d) by methylation at the NH group and aminomethylation of the N-methyl derivatives.

7,8,9,10-Tetrahydro-2-oxo-3-methylpyrazino[3.2.1-jk]carbazole (IIIa) was obtained in our previous work [1]. Under analogous conditions, the alkylation of sodium derivatives of IIb and IIc by methyl iodide yielded N-methyl derivatives IIIb and IIIc. The aminomethylation of IIIa-c by bisdimethylaminomethane and bismorpholinomethane in the present work yielded 6-aminomethyl derivatives of pyrazino[3.2.1-jk]carbazole and 7-aminomethyl derivatives of diazepino[3.2.1-jk]carbazole (IV and V).

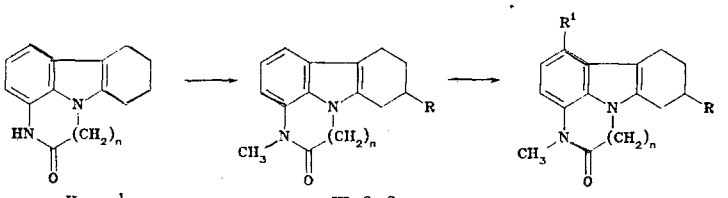
TABLE 2. Chemical Shifts (ppm) in the NMR Spectra of Pyrazino[3.2.1-jk]carbazole Derivatives

Compound	1-CH_2	3-CH_3	4-H	5-H	6-H	8,9-CH_2	7,10-CH_2	6-$CH_2N(CH_3)_2$	Solvent
IIa	4,88	—	6,50	6,94	7,14	1,90 (4H)	2,70 (4H)	—	$CDCl_3$
IIIa	4,88	3,44	6,64	7,0	7,2	1,90 (4H)	2,70 (4H)	—	$CDCl_3$
	5,84	4,26	6,94	7,18	7,36	1,96	2,85	—	$CDCl_3$+Eu(DPM)$_3$; $C_p/C_s \approx 0,5$
	0,96[a]	0,82	0,30	0,18	0,16	0,06	0,15	—	
	4,86	3,46	6,56	6,86	—	1,90 (4H)	2,66 (2H), 2,98 (2H)	3,64, 2,26 (6H)	$CDCl_3$
IVa	5,81	4,23	6,83	7,00	—	1,94 (4H)	2,66 (2H), 3,07 (2H)	3,76, 2,43 (6H)	$CDCl_3$+Eu(DPM)$_3$; $C_p/C_s \approx 0,5$
	0,95[a]	0,77	0,30	0,14	—	0,04		0,12, 0,15	
Va	4,86	3,45	6,57	6,82	—	1,88 (4H)	2,66 (2H), 2,98 (2H)		

* [a] $\Delta\delta = \delta_{(CDCl_3-LSR)} - \delta_{CDCl_3}$.

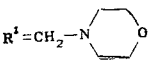
TABLE 3. Chemical Shifts (ppm) in the NMR Spectra of Diazepino[3.2.1-jk]carbazole Derivatives

Compound	1-CH_2	2-CH_2	3-CH_3	5-H	6-H	7-H	8,11-CH_2	9,10-CH_2	7-$CH_2N(CH_3)_2$	Solvent
IIc	3,06	4,28	—	6,66	7,04	7,24	2,72	1,97	—	$CDCl_3$
IVb	2,98	4,22	3,47	6,84	6,95	—	2,68 (2H), 3,06 (2H)	1,90	3,64, 2,27 (6H)	$CDCl_3$



II a-d III a-c (IV, V) a-c

II, III a n=1, R=H; b n=1, R=CH_3; c n=2, R=H; d n=2, R=CH_3. IV a n=1, R=H, R^1=$CH_2N(CH_3)$; b n=1, R=CH_3, R^1=$CH_2N(CH_3)_2$; c n=2, R=H, R^1=$CH_2N(CH_3)_2$;

V a n=1, R=H; b n=1, R=CH_3; c n=2, R=H; a-c R^1=CH_2- 

The position of the aminomethyl substituents in IV and V was also established by PMR spectroscopy through comparison of the spectra of pyrazino[3.2.1-jk]carbazoles IIa and IIIa with IVa and Va and diazepino[3.2.1-jk]carbazoles IIc and IIIc with IVc and Vc. Thus, in the spectrum of IIIa (in $CDCl_3$) the 5-H proton belongs to the triplet at 7.0 ppm (J_{45} = J_{56} = 8 Hz) and 4-H and 6-H give rise to quarters (J_{45} = J_{56} = 8, J_{46} = 2 Hz). The assignment of the latter two signals was made using the PMR spectra of IIIa in $CDCl_3$ with added shift reagent Eu(DPM)$_3$. Table 2 shows that the greatest changes in the chemical shifts $\Delta\delta_H = \delta_{CDCl_3\text{-}LSR} - \delta_{CDCl_3}$ are found for the methyl group at position 3 and the methylene protons at position 1 (0.82-0.96 ppm), while the signals of the aromatic protons are shifted by 0.18-0.3 ppm. Thus, we may assume that the coordination of the shift reagent in the IIIa occurs at the oxygen atom of the carbonyl group. We may expect that the signal for the proton at position 4 in the presence of shift reagent would be displaced more strongly downfield than the signals for the protons at positions 5 and 6. Indeed, the quartet at 6.64 ppm is shifted by 0.3 ppm (Table 2), while the downfield quartet (7.20 ppm) is shifted by only 0.16 ppm and the triplet for the proton at position 5 is shifted by only 0.18 ppm. Hence, the quartet at higher field is assigned to 4-H. The spectrum of aminomethyl derivative IVa has two doublets (J_0 = 8 Hz, 6.56 and 6.86 ppm) in the aromatic proton region, which may be related either to protons 4 and 5 or 5 and 6, depending on the position of entry of the aminomethyl

group (C-6 or C-4). Selection of the proper structure was made by comparison of the spectra of IIa and IVa taken with shift reagent under the conditions described above. The results indicate that complexation of the shift reagent, as in the case of IIIa, occurs at the oxygen atom of the carbonyl group (Table 2). The shift of the aromatic proton signals is 0.3 and 0.14 ppm. These data permit assignment of the signals for IVa to protons 4 and 5 since similar chemical shifts should be observed only for 5-H and 6-H: $\Delta\delta_{5-H} = 0.16$ and $\Delta\delta_{6-H} = 0.18$ ppm (under analogous conditions). Thus, the aminomethylation in pyrazino[3.2.1-jk]-carbazoles IIIa and IIIb proceeds at C-6. Comparison of the spectra of IIIa, IVa, and Va shows that the presence of an aminomethyl group at C-6 leads to a downfield shift of the signals for the 7-H methylene protons by 0.3 ppm apparently as a result of a steric effect, while the signals for protons 8-H-10-H are not shifted. The position of the aminomethyl substituent for diazepino[3.2.1-jk]carbazole derivatives was found by analogy. We should note that the same effect of the introduction of an aminomethyl group on the signals of 7-H methylene protons was observed by comparison of the spectra of IIIb and IVb; the chemical shift of the doublet for the methyl group in the saturated ring is also not altered. This finding indicates a considerable distance between this methyl group and the aminomethyl substituent in IVb, which supports the above conclusion for the location of the methyl group in IVb and IIIb (and, thus, in IIb) at C-9 and not at C-7.

The IR spectra of IIa-c show bands for the NH amide group at 3060-3200 cm^{-1} which disappear in the spectra of N-substituted derivatives IIIa-c and carbonyl group bands at 1650-1680 cm^{-1}. The spectra of IIIa-c show a slight shift of the carbonyl group band toward lower frequencies (1640-1654 cm^{-1}). The UV spectra of these derivatives of pyrazino[3.2.1-jk]carbazole and diazepino[3.2.1-jk]carbazole have three maxima at 220, 250, and 315 nm with log ε 4.31, 4.13, and 3.94, respectively.

EXPERIMENTAL

The IR spectra were taken in vaseline oil on a Perkin-Elmer 457 and UR-10 spectrometers. The UV spectra were taken on an ERS-3 spectrophotometer. The PMR spectra were taken on a Varian XL-200 spectrometer.

1,2,7,8,9,10-Hexahydro-9-methyl-3-oxo-4(H)(1,5)diazepino[3.2.1-jk]carbazole(IId). A sample of 6.5 g (0.1 mole) zinc powder was added with ice cooling and stirring in small portions to a suspension of 3.82 g (0.2 mole) 1-nitroso-4-oxo-2,3-dihydrobenzodiazepine (Ib) in 35 ml glacial acetic acid at $\leq$25°C. The precipitate was filtered off and washed on the filter with 5-10 ml acetic acid. A sample of 2.24 g (0.02 mole) 3-methylcyclohexanone and 3.44 g (0.02 mole) p-toluenesulfonic acid were added to the combined filtrate and stirred for 2 h at 80-90°C, cooled with ice, and poured into water. The crystals were filtered off, washed with water, and recrystallized from dioxane. Products IIb and IIc were obtained analogously (Table 1).

N-Methyl derivatives of pyrazino- and diazepino[3.2.1-jk]carbazoles (IIIb and IIIc, Table 1) were obtained by our previously described method [1].

Aminomethyl derivatives of pyrazino- and diazepino[3.2.1-jk]carbazoles (IVa-c and Va-c). A sample of 0.02 mole bisdialkylaminomethane was added to a solution of 0.01 mole IIIa or IIIb in glacial acetic acid with stirring and cooling to 10°C, maintained at this temperature for 1 h, and then heated on a steam bath for 2 h. The acetic acid was evaporated in vacuum to a small volume. The residue was cooled and brought to pH 8 by the addition of aqueous ammonia. The crystalline precipitate (IV and V) was filtered off, washed with water, and recrystallized from methanol (Table 1).

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