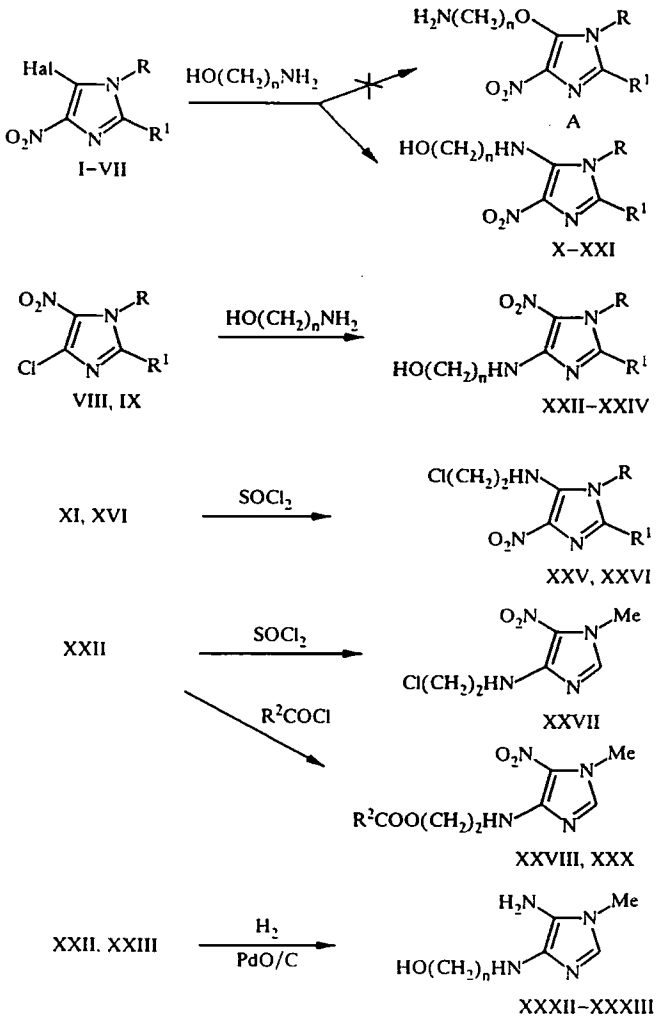


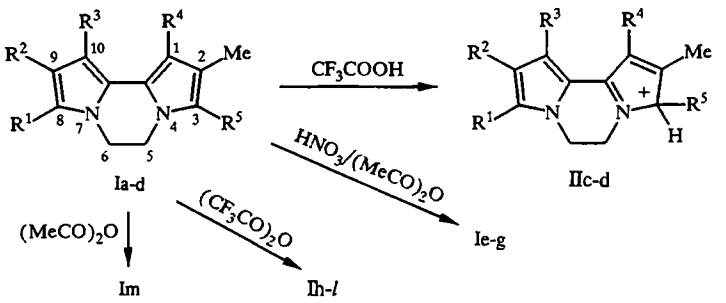
I, III—VI Hal = Cl; II, VII Hal = Br; I, II, X, XI, XVII, XVIII, XVIIIa, XXII, XXIII, XXV R = Me; III, XII, XIX R = Et; IV, XV, XXIV R = Pr; V, XVI, XXVI R = Bu; VI, XIII, XX R = *i*-Bu; VII, XIV, XXI R = $PhCH_2$; I, VIII, X, XVII, XXII, XXIII R^1 = H; II, III, XI, XII, XIV, XVIII, XIX, XXI, XXV R^1 = Me; IV, XV, XXIV R^1 = Et; V, XVI, XXVI R = Pr; VI, XIII, XX R^1 = *i*-Pr; XXVIII R^2 = Me; XXIX R^2 = Pr; XXX R^2 = $CHBrCH_3$; XXXI R^2 = Bu; X—XVI, XXII, XXXII n = 2; XVII—XXI, XXIII, XXIV, XXXIII n = 3

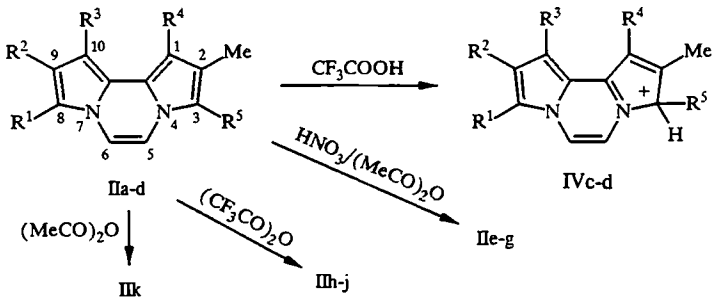
The structure of compounds (X-XXIV) was confirmed by the data from the IR, PMR, and mass spectra and also by certain chemical reactions. Thus, treatment of the hydroxy compounds (XI, XVI, XXII) with thionyl chloride in benzene gave the products from substitution of the hydroxyl group by a chlorine atom, i.e., the 2-chloroethylaminoimidazoles (XXV-XXVII). This rules out the structure of the initial compounds as derivatives of structure A.

The acylation of 1-methyl-4-(2-hydroxyethylmethylamino)-5-nitroimidazole (XXII) by carboxylic acid chlorides in benzene leads to the corresponding esters (XXVIII-XXXI) and not the alternative amides of the initial acids.

Of particular interest are the derivatives of 4,5-diaminoimidazole [9-12]. In order to obtain them we studied the hydrogenation of the nitroaminoimidazoles (XXII) and (XXIII). The reaction takes place readily at atmospheric pressure and room temperature in the presence of palladium oxide on charcoal as catalyst. The obtained derivatives of 4,5-diaminoimidazole (XXXII) and (XXXIII) are extremely labile compounds that readily resinify in air. It was possible to isolate and characterize them in the form of picrates.

The structure of compounds (X-XXXIII) was confirmed by the data from elemental analysis and by spectral methods (Tables 1 and 2). In the IR spectra of the nitro compounds there are absorption bands for the NO_2 group in the region of 1345-1430 and 1530-1570 cm^{-1}. The amino alcohols (X, XI, XV-XVIII, XXII-XXIV) are characterized by the presence of bands for the stretching vibrations of the NH group in the region of 1620-1660 and 3250-3400 cm^{-1} and of the OH group in the region of 3440-3460 cm^{-1}. In the IR spectra of the O-acyl derivatives of the amino alcohols (XXVIII-XXXI) the band of the hydroxyl group disappears, and a distinct band for the ester CO group in the region of 1740-1760 cm^{-1} appears in its place.





Compound	R^1	R^2	R^3	R^4	R^5
Ia	H	H	H	H	H
Ib	CH_3	H	H	H	H
I, IIIc	CH_3	H	H	H	CH_3
I, IIId	CH_3	H	H	CH_3	H
Ie	H	H	H	H	NO_2
If	NO_2	H	H	H	NO_2
Ig	CH_3	H	H	H	NO_2
Ih	CH_3	H	CF_3CO	CF_3CO	CH_3
Ii	CH_3	H	CF_3CO	H	CH_3
Ij	CH_3	CF_3CO	H	CH_3	CF_3CO
Ik	CH_3	H	CF_3CO	CH_3	CF_3CO
Il	CH_3	H	H	CH_3	CF_3CO
Im	CH_3	H	H	CH_3	CH_3CO
IIa	H	H	H	H	H
IIb	CH_3	H	H	H	H
II, IVc	CH_3	H	H	H	CH_3
II, IVd	CH_3	H	H	CH_3	H
IIe	H	H	H	H	NO_2
IIf	NO_2	H	H	H	H
IIg	CH_3	H	H	H	NO_2
IIh	CH_3	H	CF_3CO	CF_3CO	CH_3
IIk	CH_3	H	CF_3CO	H	CH_3
IIj	CH_3	H	CF_3CO	CH_3	CF_3CO
IIk	CH_3	H	H	CH_3	CH_3CO

It was of particular interest to study the reactivity of dipyrrolopyrazines in those cases in which both of the α-pyrrole positions are replaced by alkyl groups. To this end, we synthesized 2,3,8-trimethyl-5,6-dihydrodipyrrolopyrazine Ic and 2,3,8-trimethyldipyrrolopyrazine IIc, and then investigated reactions of protonation, trifluoroacetylation, and acetylation of these compounds.

By analogy with symmetrically constructed dipyrrolopyrazines, where both of the α-positions of the pyrrole ring are occupied [7], we expected that protonation of compounds Ic and IIc would proceed at the free positions 1 or 10. In protonation of these systems in a mixture of CF_3COOH and $CDCl_3$, however, we observed proton attack at the $C_{(3)}$ carbon atom. The PMR spectrum (400 MHz) indicates the presence of a quadruplet 3-H and a doublet 3-CH_3 at 4.76 ppm and 1.62 ppm for the cation of IIIc, and 5.20 ppm and 1.75 ppm for the cation of IVc. Here, the chemical shifts of the 2-CH_3 and 8-CH_3, calculated by an additive scheme and obtained experimentally, are quite close to each other; for the 2-CH_3, $\Delta\delta_{exp\text{-}add} = 0.04$ (IIIc) and $\Delta\delta_{exp\text{-}add} = 0.06$ (IVc); for the 8-CH_3, $\Delta\delta_{exp\text{-}add} = 0.07$ (IIIc) and $\Delta\delta_{exp\text{-}add} = 0.04$ (IVc).

The dipyrrolopyrazines Ic and IIc are less reactive in electrophilic substitution than compounds I-IIa,b,d. For example, the latter compounds are acylated by acetic anhydride within a few hours without any catalyst, giving the corresponding reaction products in yields greater than 50%; in contrast, neither the hydrogenated dipyrrolopyrazine Ic nor the aromatic dipyrrolopyrazine IIc is acylated even under severe conditions. The probable reason for this difference is that the acetyl cation, as a less-strong electrophile, attacks those carbon atoms in the molecule where the highest π-electron density in the HOMO is concentrated, while in the molecules of Ic and IIc these positions are blocked by alkyl substituents.

The trifluoroacetyl cation, being a stronger electrophile, attacks the free positions 1 and 10 of the dipyrrolopyrazine; and as a result, the reactions yield as the main products 1,10-ditrifluoroacetyl-5,6-dihydropyrrolopyrazine Ih and 1,10-ditrifluoroacetyldipyrrolopyrazine IIh. An investigation of the timewise course of this reaction has shown that when the reaction mixture is held at room temperature for 1.5 h, the isomers Ih and IIh are accompanied by the 10-monotrifluoroacetyl derivatives Ii and IIi. When the reaction is continued for a longer time (3-4 days), in the case of the aromatic dipyrrolopyrazine IIc, the percentage ratio between the major isomer IIh and the minor isomer IIi remains the same, whereas in the case of the 5,6-dihydrodipyrrolopyrazine Ic, the only product recovered is the compound Ih. The formation of the substituted dipyrrolopyrazines I-IIi indicates that in the molecules I-IIc, the greatest π-electron density is concentrated on the $C_{(10)}$ atom, which is the site of the initial electrophilic attack of the trifluoroacetyl cation.

With the aim of studying the relationships in the transmission of electronic influence as governed by the presence of substituents on an aryl group introduced into the pyrrole ring of these systems, we synthesized a series of 2-aryl-substituted dipyrrolopyrazines VIa-c and their 5,6-dihydro analogs Va-c.

The introduction of the aryl substituent changes the direction of electrophilic substitution, and in some cases changes the conditions for carrying out the reactions, in the series of dipyrrolopyrazines Va-c and VIa-c in comparison with the 2-methyldipyrrolopyrazines. However, protonation of compounds Va-c and VIa-c still proceeds at position 3 of the dipyrrolopyrazine molecule, giving the thermodynamically stable cations VIIa-c and VIIIa-c, respectively. In contrast, trifluoroacetylation of these heterocycles probably takes place initially at the $C_{(8)}$ atom. Thus, in the reactions of 2-phenyl- and 2-(p-methoxyphenyl)-5,6-dihydrodipyrrolopyrazines Va and Vb with trifluoroacetic anhydride, the expected ditrifluoroacetyl derivatives Vd and Vf are accompanied by the 8-monotrifluoroacetyl derivatives Ve and Vg. The main products from the trifluoroacetylation of the aromatic 2-phenyl- and 2-(p-methoxyphenyl)dipyrrolopyrazines VIa and VIb, in contrast to their 5,6-dihydro analogs, are the 8-monosubstituted trifluoroacetyl isomers VId and VIe. Here, the ditrifluoroacetyldihydropyrrolopyrazines are formed in only very small amounts. Mass spectrometric data on the reaction mixtures indicate the presence, along with the intense peaks of the molecular ions of the compounds VId and VIe (m/z 328 and 358, respectively), weak peaks with m/z 424 and 454 corresponding to ditrifluoroacetyl derivatives of dipyrrolopyrazine VIa and VIb.

Compounds Vc and VIc, which contain an electron-accepting group in the para position of the benzene ring, behave in reactions with trifluoroacetic anhydride somewhat differently in comparison with the phenyl-substituted (V,VIa) and p-methoxyphenyl-substituted (V,VIb) substrates. Trifluoroacetylation of the 5,6-dihydrodipyrrolopyrazine Vc affords the 3,8-ditrifluoroacetyldipyrrolopyrazine Vh, with none of the monotrifluoroacetyl isomer being found in this case. For the aromatic dipyrrolopyrazine VIc, in contrast to compounds VIa and VIb, the main product recovered from the reaction mixture is the 3,8-ditrifluoroacetyl derivative VIf, with the 8-monotrifluoroacetyl isomer VIg as a minor component.

The course of the acetylation reaction, the same as that of trifluoroacetylation, is influenced by the substituent in the para position of the benzene ring. For all of the synthesized 2-aryl-substituted dipyrrolopyrazines, however, the aromatic substrates VIa-c are acetylated more readily than their 5,6-dihydro analogs Va-c. Whereas the dipyrrolopyrazines with a phenyl substituent (VIa) or a p-methoxyphenyl substituent (VIb) react with acetic anhydride over the course of a few hours without

TABLE 1. Properties of Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	M^+	Yield, % (and time)
		C	H	N			
1	2	3	4	5	6	7	8
Ic	$C_{13}H_{16}N_2$	77.18 78,00	7.99 8,00	14.17 14,00	220		25
Id	$C_{13}H_{16}N_2$	78.23 78,00	8.37 8,00	14.19 14,00	140...141		50
Ie	$C_{11}H_{11}N_3O_2$					217	15*
If	$C_{11}H_{10}N_4O_4$					262	2*
Ig	$C_{12}H_{13}N_3O_2$				181...182	231	30
Ih	$C_{17}H_{14}F_6N_2O_2$				207...210	392	28 (1,5 h), 71 (3 days)
Ii	$C_{15}H_{15}F_3N_2O$				233	296	7 (1,5 h)
Ij	$C_{17}H_{14}F_6N_2O_2$	49.58 51,04	3.49 3,57	6.74 7,14	247...248	392	49
Ik	$C_{17}H_{14}F_6N_2O_2$				159...160	392	31
Il	$C_{15}H_{15}F_3N_2O$				Oil	296	3
Im	$C_{15}H_{18}N_2O$	74.53 74,38	8.10 7,43		144...145		66, 68*
IIc	$C_{13}H_{14}N_2$	79.11 78,79	7.07 7,07	14.40 14,14	184...185		52
IId	$C_{13}H_{14}N_2$	79.13 78,79	7.04 7,07	13.82 14,14	112...113		41
IIe	$C_{11}H_9N_3O_2$					215	23
IIf	$C_{11}H_9N_3O_2$					215	5
IIg	$C_{12}H_{11}N_3O_2$	62.85 62,88	5.25 4,80		222...223	229	26
IIh	$C_{17}H_{12}F_6N_3O_2$				265...267	390	50 (1,5 h) 54 (4 days)
IIi	$C_{15}H_{13}F_3N_2O$				Oil	294	5 (1,5 h) 6 (4 days)
IIj	$C_{17}H_{12}F_6N_2O_2$	52.25 52,30	3.07 3,07	6.86 7,17	197		87
IIk	$C_{15}H_{16}N_2O$	74.37 75,00	7.24 6,66	10.79 11,66	194		86, 73*
Va	$C_{16}H_{14}N_2$				145	324	65
Vb	$C_{17}H_{16}N_2O$				220	264	55
Vc	$C_{18}H_{16}N_2O_2$			6.03 5,79	190	276	33
Vd	$C_{20}H_{12}F_6N_2O_2$				110	426	66
Ve	$C_{18}H_{13}F_3N_2O$				155	330	24
Vf	$C_{21}H_{14}F_6N_2O_3$	55.08 55,26	2.97 3,07	5.35 6,10	187		67
Vg	$C_{19}H_{15}F_3N_2O_2$				Oil	360	22
Vh	$C_{22}H_{14}F_6N_2O_3$	56.08 56,41	2.70 2,99	5.54 5,98	230		64

TABLE 1. (continued)

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	M^+	Yield, % (and time)
		C	H	N			
1	2	3	4	5	6	7	8
Vi	$C_{18}H_{16}N_2O$				Oil	276	29
Vj	$C_{18}H_{16}N_2O$				Oil	276	22
Vk	$C_{21}H_{20}N_2O_3$				168	348	35
VIa	$C_{16}H_{12}N_2$				138...140	232	64
VIb	$C_{17}H_{14}N_2O$				210...213	262	90
VIc	$C_{18}H_{14}N_2O$			4,92 5,10	173...175	274	56
VId	$C_{18}H_{11}F_3N_2O$	65,85 66,68	3,35 4,33		190	328	49
VIe	$C_{19}H_{13}F_3N_2O_2$				220...221	358	50
VIf	$C_{22}H_{12}F_6N_2O_3$				223	466	43
VIg	$C_{20}H_{13}F_3N_2O_2$				210	370	11
VIh	$C_{18}H_{14}N_2O$				Oil	274	51
VIi	$C_{18}H_{14}N_2O$					274	24*
VIj	$C_{20}H_{16}N_2O_2$					316	4*
VIk	$C_{19}H_{16}N_2O_2$			8,35 9,20	175...178	304	69
VIl	$C_{19}H_{16}N_2O_2$				220	304	10
VIm	$C_{20}H_{16}N_2O_2$				221 (decomp.)	316	19

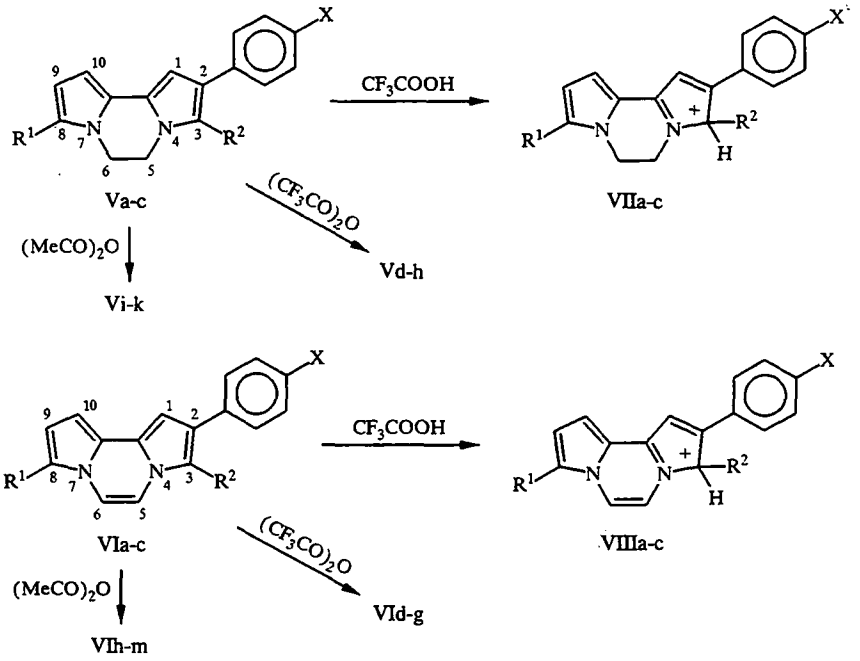
*Compounds Ie,f, IIe,f, and VIi,j could not be isolated in individual form. The yields were calculated on the basis of the ratio of components in the mixture as indicated by PMR spectra (400 MHz).

†Obtained by method B.

any catalyst, giving a mixture of 3- and 8-monoacetyl (VIh, VIi) and 3,8-diacetyl (VIj) products of the reaction (in the case of compound VIa) and a mixture of 3- and 8-monoacetyl isomers VIk and VIl (in the case of compound VIb), we find that the heterocycles Va and Vb enter into this reaction only when a catalyst is introduced into the reaction mixture. Here, the 2-phenyl-5,6-dihydrodipyrrolopyrazine Va forms the 3- and 8-acetyldipyrrolopyrazines Vi and Vj, while the 2-(p-methoxyphenyl)-5,6-dihydrodipyrrolopyrazine Vb forms the 3,8-diacetyl derivative Vk. Acetylation of compound Vc, with an electron-acceptor group in the para position of the benzene ring, does not take place; for its aromatic analog, all that we were able to recover from the reaction mixture, other than the original compound, was 2-(p-acetylphenyl)-8-acetyldipyrrolopyrazine VIm. No catalyst is required to obtain this last product, but the reaction time is somewhat longer in comparison with dipyrrolopyrazines that are not substituted or have the p-methoxyphenyl substituent.

EXPERIMENTAL

The PMR spectra of compounds Ic-m, IIc-k, Va-k, and VIa-m in $CDCl_3$, and also the spectra of protonation of compounds I-IIc,g and V-VIa-c in a mixture of CF_3COOH and $CDCl_3$, were recorded in a Varian VXR-400 instrument, internal standard TMS. The mass spectra of compounds Ie-f, Ii, Ij, IIe-f, IIi, Vc-e, Vg, Vi-k, and VIv-m were recorded in a Kratos MS 890 instrument, those of compounds Ik and Il in an MX-1321A instrument, with direct introduction of the sample into the ion source; the mass spectra of compounds Ig-h, IIg-h, and V-VIa,b were recorded in a Varian MAT-44S chromatograph/mass spectrometer, with an ionization energy of 70 eV. The course of the reaction was monitored by TLC on Silufol UV-254 plates.



Compound	R^1	R^2	X	Compound	R^1	R^2	X
V, VIIa	H	H	H	VI, VIIIb	H	H	OCH_3
V, VIIb	H	H	OCH_3	VI, VIIIc	H	H	CH_3CO
V, VIIc	H	H	CH_3CO	VId	CF_3CO	H	H
Vd	CF_3CO	CF_3CO	H	VIe	CF_3CO	H	OCH_3
Ve	CF_3CO	H	H	VIf	CF_3CO	CF_3CO	CH_3CO
Vf	CF_3CO	CF_3CO	OCH_3	VIg	CF_3CO	H	CH_3CO
Vg	CF_3CO	H	OCH_3	VIh	H	CH_3CO	H
Vh	CF_3CO	CF_3CO	CH_3CO	VIi	CH_3CO	H	H
Vi	H	CH_3CO	H	VIj	CH_3CO	CH_3CO	H
Vj	CH_3CO	H	H	VIk	H	CH_3CO	OCH_3
Vk	CH_3CO	CH_3CO	OCH_3	VIl	CH_3CO	H	OCH_3
VI, VIIIa	H	H	H	VIm	CH_3CO	H	CH_3CO

TABLE 2. PMR Spectra of 2-Alkyl-Substituted Dipyrrolo[1,2-a; 2′,1′-c]pyrazines and Their Derivatives I-IV in $CDCl_3$ (δ, ppm; and J, Hz)

Compound	Substituents on pyrrole ring						Protons of pyrazine ring
	1-R	2-R	3-R	8-R	9-H	10-H	
1	2	3	4	5	6	7	8
Ic	6,02 br.s	2,02 s	2,14 s	2,23 s	5,86 d. q, J_{910} = 3,5	6,08 d, J_{109} = 3,4	4,00 s (5,6-H_2)
Id	2,14 s	2,04 s	6,33 br.s	2,26 d, $J_{CH3,H}$ = 0,86	5,94 d. d, J_{910} = 4,2	6,16 d, J_{109} = 4,3	4,04 m (6-H_2); 4,06 m (5-H_2)
Ie	6,23 s	2,47 br.s		6,78 d. d, J_{89} = 2,6, J_{810} = 1,3	6,28 d. d, J_{910} = 3,7, J_{98} = 2,6	6,55 d. d, J_{109} = 3,7, J_{108} = 1,3	4,26 t (6-H_2); 4,86 t (5-H_2)
If	6,47 s	2,49 d, $J_{CH3,H}$ = 0,7			7,31 d, J_{910} = 4,6	7,06 d	4,92 s (5,6-H_2)
Ig	6,20 d, $J_{H,CH3}$ = 0,7	2,47 br.s		2,30 d, $J_{CH3,H}$ = 0,7	6,00 d. d, $J_{H,CH3}$ = 0,8, J_{910} = 3,7	6,50 d, J_{109} = 3,6	4,15 t (6-H_2); 4,85 t (5-H_2)
Ih		2,13 s	2,23 s	2,31 s	6,47 br.s		4,07 m (5-H_2); 4,15 m (6-H_2)
Ii	7,55 br.s	2,07 s	2,20 s	2,26 s	6,39 m		4,05 s (5,6-H_2)
Ij	2,19 s	2,32 m		2,68 s		6,95 m	4,19 m (6-H_2); 4,80 m (5-H_2)
Ik	1,83 s	2,34 br.s		2,34 br.s	6,57 m		4,00 m (6-H_2); 4,69 m (5-H_2)
Il	2,16 s	2,31 br.s		2,29 m	6,05 d. d, J_{910} = 3,7	6;52 d, J_{109} = 3,7	4,08 m (6-H_2); 4,78 m (5-H_2)
Im	2,15 s	2,33 s	2,47 s	2,29 s	6,00 d, J_{910} = 3,5	6,40 d, J_{109} = 3,5	4,00 t (6-H_2); 4,84 t (5-H_2)
IIc	6,28 s	2,18 d, $J_{CH3,H}$ = 0,5	2,30 s	2,39 d, $J_{CH3,H}$ = 0,9	6,22 d. q, J_{910} = 3,8, $J_{H,CH3}$ = 0,9	6,33 d, J_{109} = 3,8	6,91 d, (5-H), J_{56} = 6,3; 6,93 d, (6-H), J_{65} = 6,3

TABLE 2. (continued)

Compound	Substituents on pyrrole ring						Protons of pyrazine ring
	1-R	2-R	3-R	8-R	9-H	10-H	
1	2	3	4	5	6	7	8
IId	2,30 s	2,14 d, $J_{CH3,H}$ = 0,9	6,70 d, $J_{H,CH3}$ = 0,9	2,37 d, $J_{CH3,H}$ = 0,9	6,23 d. d, J_{910} = 3,6, $J_{H,CH3}$ = 0,9	6,39 d, J_{109} = 3,6	6,77 d. d (6-H), J_{65} = 6,0, J_{610} = 0,6; 6,89 d (5-H), J_{56} = 6,0
IIe	6,50 m	2,62 s		7,27 d. d, J_{89} = 2,7, J_{810} = 1,5	6,74 d. d, J_{98} = 2,7, J_{910} = 3,9	6,84 d. d. d, J_{109} = 3,9	7,40 d. d (6-H), J_{65} = 6,3; 8,69 d (5-H), J_{56} = 6,3
IIf	6,71 br,s	2,31 s	7,08 m		7,61 d, J_{910} = 4,8	6,56 d, J_{109} = 4,8	7,39 d (5-H), J_{56} = 6,2; 8,56 d (6-H), J_{65} = 6,2
IIg	6,44 d, $J_{H,CH3}$ = 0,7	2,58 d, $J_{CH3,H}$ = 0,7		2,45 d, $J_{CH3,H}$ = 0,7	6,47 d. d, J_{910} = 3,8, $J_{H,CH3}$ = 0,7	6,76 d, J_{109} = 3,6	7,25 d (6-H), J_{65} = 6,2; 8,70 d (5-H), J_{56} = 6,3
IIh		2,27 s	2,45 s	2,49 d, $J_{CH3,H}$ = 0,9	6,88 br, s		7,29 d (5-H), J_{56} = 6,0; 7,43 d (6-H), J_{65} = 6,0
IIi	8,00 br,s	2,25 s	2,39 s	2,41 d, $J_{CH3,H}$ = 1,0	6,72 m		7,07 d (5-H), J_{56} = 6,1; 7,26 d (6-H)
IIj	2,11 s	2,51 m		2,53 d, $J_{CH3,H}$ = 0,9	6,99 m, $J_{H,CH3}$ = 0,9		7,21 d (6-H), J_{65} = 6,3; 9,10 d (5-H), J_{56} = 6,3
IIk	2,34 s	2,45 s	2,54 s	2,447 s	6,42 d, J_{910} = 3,8	6,74 d, J_{109} = 3,8	7,04 d (6-H), J_{65} = 6,3; 8,99 d (5-H), J_{56} = 6,2
IIIc	6,70 m	2,45 s	4,76 q, (1H), 1,62 d (3H), $J_{H,CH3}$ = 7,2	2,32 s	6,45 d. d, J_{910} = 4,3	7,24 d, J_{109} = 4,3	4,11 m (6-H_2); 4,35 m (5-H_2)
IIId	2,25 s	2,44 s	4,7 br, s (2H)	2,25 s	6,42 d. d, J_{910} = 4,4	7,40 d, J_{109} = 4,4	4,15 t (6-H_2); 4,32 t (5-H_2)
IVc	6,97 br,s	2,39 d	5,20 q, (1H), 1,75 d (3H), $J_{H,CH3}$ = 7,2	2,67 s	7,14 d, J_{910} = 4,4	7,56 d, J_{109} = 4,8	7,50 d (6-H), J_{65} = 6,0; 7,83 d (5-H), J_{56} = 6,0
IVd	2,36 br,s	2,48 br,s	5,29 s (2H)	2,70 br,s	7,15 d. d, J_{910} = 4,5, $J_{H,CH3}$ = 0,7	7,78 d, J_{109} = 4,5	7,77 d (6-H), J_{65} = 6,0; 8,04 d (5-H), J_{56} = 6,0

TABLE 3. PMR Spectra of 2-Aryl-Substituted Dipyrrolo[1,2-a; 2′,1′-c]pyrazines and Their Derivatives V-VIII in $CDCl_3$ (δ, ppm, and J, Hz)

Compound	Substituents on pyrrole ring					Protons of pyrazine ring	2-Ar
	1-H	3-R	8-R	9-H	10-H		
1	2	3	4	5	6	7	8
Va	6,56 d, J_{13} = 1,6	6,88 d, J_{31} = 1,7	6,61 d. d, J_{89} = 2,6, J_{810} = 1,4	6,20 d. d, J_{910} = 3,5, J_{98} = 2,6	6,31 d. d, J_{109} = 3,5, J_{108} = 1,4	4,25 s (5,6-H_2)	7,16 t (1H, *p*-H); 7,33 t (2H, *m*-H); 7,52 d.d (2H, *o*-H)
Vb	6,50 d, J_{13} = 1,9	6,80 d, J_{31} = 1,7	6,61 d. d, J_{89} = 2,6, J_{810} = 1,5	6,19 d. d, J_{98} = 2,8, J_{910} = 3,6	6,30 d. d, J_{108} = 1,7, J_{109} = 3,6	4,25 s (5,6-H_2)	3,80 s (*p*-OCH_3); 6,89 d (2H, *m*-H); 7,44 d (2H, *o*-H)
Vc	6,61 d, J_{13} = 1,7	7,01 d, J_{31} = 1,8	6,64 d. d, J_{89} = 2,4, J_{810} = 1,3	6,22 d. d, J_{910} = 3,6, J_{98} = 2,7	6,34 d. d, J_{109} = 3,6, J_{108} = 1,6	4,23 s (5,6-H_2)	2,59 s (*p*-CH_3CO); 7,58 d (2H, *m*-H); 7,93 d (2H, *o*-H)
Vd	6,63 s			7,32 m, J_{910} = 4,4	6,64 d, J_{109} = 4,6	4,80 m (5-H_2); 4,93 m (6-H_2)	7,32 m (2H, *m*-H); 7,40 m (3H, *o*-H)
Ve	6,86 d, J_{13} = 1,7	7,08 d, J_{31} = 1,2		7,30 d.d J_{910} = 4,3, $J_{H,CF3}$ = 2,1	6,47 d, J_{109} = 4,3	4,30 t (5-H_2); 4,90 t (6-H_2)	7,24 t (1H, *p-H);* 7,37 t (2H, *m*-H); 7,52 d.d (2H, *o*-H)
Vf	6,59 s			7,31 d. d, J_{910} = 4,4, $J_{H,CF3}$ = 2,0	6,63 d, J_{109} = 4,4	4,78 m (5-H_2); 4,92 m (6-H_2)	3,86 s (*p*-OCH3); 6,93 d (2H, *m*-H); 7,24 d (2H, *o*-H)
Vg	6,80 d, J_{13} = 1,2	7,00 d, J_{31} = 1,7		7,29 d. d, J_{910} = 4,3, $J_{H,CF3}$ = 1,9	6,46 d, J_{109} = 4,3	4,30 t (5-H_2); 4,91 t (6-H_2)	3,85 s (*p*-OCH_3); 6,91 d (2H, *m*-H); 7,43 d (2H, *o*-H)
Vh	6,64 s			7,32 d. d, J_{910} = 4,3, $J_{H,CF3}$ = 2,1	6,66 d, J_{109} = 4,6	4,80 m (6-H_2); 4,95 m (5-H_2)	2,70 s (*p*-CH_3CO); 7,43 d (2H, *m*-H); 8,00 d (2H, *o*-H)
Vi	6,25 s	2,00 s	6,73 d. d	6,20 d. d	6,45 d. d	4,20 t (6-H_2); 4,90 t (5-H_2)	7,40 m (5H, C_6H_5)
Vj	6,75 d, J_{13} = 1,5	7,01 d, J_{31} = 1,5	2,49 s	7,02 d, J_{910} = 4,3	6,34 d, J_{109} = 4,0	4,25 t (5-H_2); 4,90 t (6-H_2)	7,20 t (1H, *p*-H); 7,35 t (2H, *m*-H); 7,52 d.d (2H, *o*-H)
Vk	6,42 s	2,10 s	2,50 s	7,00 d, J_{910} = 4,2	6,43 d, J_{109} = 4,0	4,85 m (5,6-H_2)	3,80 s (*p*-OCH_3); 6,95 d (2H, *m*-H); 7,26 d (2H, *o*-H)

TABLE 3. (continued)

Compound	Substituents on pyrrole ring					Protons of pyrazine ring	2-Ar
	1-H	3-R	8-R	9-H	10-H		
1	2	3	4	5	6	7	8
VIa	6,80 d	7,24 d	6,97 d. d, J_{89} = 2,7, J_{810} = 1,7	6,53 m	6,53 m	7,05 d. d (5,6-H), J_{56} = 6,0, J_{65} = 6,2	7,37 t (2H, *m*-H); 7,60 d. d (2H, *o*-H); 7,22 t (1H, *p*-H)
VIb	6,74 d	7,17 d, J_{31} = 1,7	6,97 m	6,52 m	6,52 m	7,04 d. d (5,6-H), J_{56} = 6,1, J_{65} = 5,8	3,80 s (*p*-OCH_3); 6,92 d (2H, m-H); 7,53 d (2H, *o*-H)
VIc	6,84 d	7,33 d, J_{31} = 1,4	6,99 d. d, J_{89} = 2,7, J_{810} = 1,3	6,54 d, J_{910} = 3,0	6,57 d, J_{109} = 3,1	7,04 d (6-H), J_{65} = 5,7; 7,09 d (5-H), J_{56} = 6,2	2,60 s (*p*-CH_3CO); 7,67 d (2H, m-H); 7,96 d (2H, *o*-H)
VId	7,16 d. d, J_{13} = 1,6, J_{15} = 0,8	7,57 m, J_{31} = 1,6		7,57 m, J_{910} = 4,6, $J_{H,CF3}$ = 2,0	6,74 d. d, J_{109} = 4,7, J_{106} = 0,6	7,43 d. d (5-H), J_{56} = 6,2, J_{51} = 0,8; 8,79 d. d (6-H), J_{65} = 6,2, J_{610} = 0,6	7,30 t (1H, *p*-H); 7,42 t (2H, m-H); 7,64 d. d (2H, *o*-H)
VIe	7,11 br. s	7,51 d, J_{31} = 1,7		7,56 m, J_{910} = 4,4	6,73 d, J_{109} = 5,0	7,43 d (5-H), J_{56} = 6,2; 8,78 d (6-H), J_{65} = 6,1	3,80 s (*p*-OCH_3); 6,96 d (2H, *m*-H); 7,56 m (2H, *o*-H)
VIf	6,90 s			7,72 d, J_{910} = 4,7, $J_{H,CF3}$ = 1,9	7,02 d, J_{109} = 4,7	9,08 d. d (6,5-H), J_{65} = 6,7, J_{56} = 6,5	2,70 s (*p*-CH_3CO); 7,51 d (2H, *m*-H); 8,04 d (2H, *o*-H)
VIg	7,22 d. d, J_{13} = 1,4, J_{15} = 0,7	7,68 d, J_{31} = 1,5		7,60 d. d, J_{910} = 4,6, $J_{H,CF3}$ = 1,9	6,78 d. d, J_{109} = 4,6, J_{106} = 0,5	7,46 d (5-H), J_{56} = 6,2; 8,82 d (6-H), J_{65} = 6,2	2,70 s (*p*-CH_3CO); 7,73 d (2H, m-H); 8,02 d (2H, *o*-H)
VIh	6,56 s	2,05 s	7,18 d. d, J_{810} = 1,4, J_{89} = 2,6	6,66 d. d, J_{910} = 3,8, J_{98} = 2,7	6,74 d, J_{109} = 3,9	7,30 d (6-H), J_{65} = 6,3; 8,90 d (5-H), J_{56} = 6,3	7,44 br. s (5H, C_6H_5)
VIi	7,03 br. s	7,44 d, J_{31} = 1,5	2,50 c	7,31 d, J_{910} = 4,1	6,60 d, J_{109} = 4,3	7,27 m (5-H), J_{56} = 6,3; 8,84 d (6-H), J_{65} = 6,2	7,27 m (1H, *p*-H); 7,40 t (2H, m-H); 7,62 d. d (2H, *o*-H)
VIj*	6,76 br. s	2,10 s	2,52 c		6,74 d, J_{109} = 4,5	9,00 d (5-H), J_{56} = 6,5; 9,07 d (6-H), J_{65} = 6,6	*
VIk	6,53 s	2,10 s	7,17 d. d, J_{810} = 1,1, J_{89} = 2,3	6,64 d. d, J_{910} = 3,7, J_{98} = 2,7	6,72 d. d, J_{109} = 3,5	7,28 d. d (6-H), J_{65} = 6,3, J_{610} = 0,8; 8,90 d. (5-H), J_{56} = 6,4	3,80 s (*p*-OCH_3); 6,97 d (2H, m-H); 7,33 d (2H, *o*-H)

TABLE 3. (continued)

Compound	Substituents on pyrrole ring					Protons of pyrazine ring	2-Ar
	1-H	3-R	8-R	9-H	10-H		
1	2	3	4	5	6	7	8
VIi	6,96 br. s	7,37 d, J_{31} = 1,4	2,60 s	7,31 d, J_{910} = 4,3	6,58 d, J_{109} = 4,1	7,27 d (5-H), J_{56} = 6,4; 8,83 d (6-H), J_{65} = 6,0	3,80 s (p-OCH_3); 6,94 d (2H, m-H); 7,54 d (2H, o-H)
VIm	7,07 d	7,53 d	2,60 s	7,33 d, J_{910} = 4,3	6,63 d, J_{109} = 3,8	7,29 d (5-H), J_{56} = 6,3; 8,87 d (6-H), J_{65} = 6,3	2,70 s (p-CH_3CO); 7,71 d (2H, m-H); 8,00 d (2H, o-H)
VIIa	7,31 s	5,32 s (2H)	7,39 m	6,65 d. d, J_{910} = 4,2, J_{98} = 2,5	7,39 m, J_{109} = 4,0	4,30 t (6-H_2); 4,53 t (5-H_2)	7,55 t (2H, m-H); 7,61 t (1H, p-H); 7,70 d.d (2H, o-H)
VIIb	7,17 s	5,31 s (2H)	7,35 m	6,63 d. d, J_{910} = 4,1, J_{98} = 2,5	7,35 m, J_{109} = 4,2	4,26 t (6-H_2); 4,53 t (5-H_2)	3,97 s (p-OCH_3); 7,10 d (2H, m-H); 7,68 d (2H, o-H)
VIIc	7,43 m	5,41 s (2H)	7,43 m	6,67 d. d, J_{98} = 2,4, J_{910} = 4,3	7,41 d., J_{109} = 4,1	4,39 m (6-H); 4,60 m (5-H_2)	2,80 s (p-CH_3CO); 7,83 d (2H, m-H); 8,19 d (2H, o-H)
VIIIa	7,55 br. s	5,75 s (2H)	8,00 m	7,33 d. d, J_{98} = 2,5, J_{910} = 4,5	7,66 d, J_{109} = 4,5	7,62 m (6-H), J_{65} = 5,7; 8,09 d (5-H), J_{56} = 5,7	7,57 t (2H, m-H); 7,62 m (1H, p-H); 7,74 d (2H, o-H)
VIIIb	7,39 br. s	5,57 s (2H)	7,95 m	7,28 d. d, J_{910} = 4,4, J_{98} = 2,5	7,62 d, J_{109} = 4,4	7,54 d (6-H), J_{65} = 5,8; 8,02 d (5-H), J_{56} = 5,7	3,97 s (p-OCH3); 7,09 d (2H, m-H); 7,71 (2H, o-H)
VIIIc	7,72 br. s	5,80 s (2H)	8,06 m	7,38 d. d., J_{910} = 4,6, J_{98} = 2,5	7,71 d, J_{109} = 4,7	7,69 d (6-H), J_{65} = 5,8; 8,16 d (5-H), J_{56} = 5,2	2,80 s (p-CH_3CO); 7,88 d (2H, m-H); 8,20 d (2H, o-H)

*The signals of the 9-H aromatic protons of compound VIj could not be determined, as they were overlapped by signals of the principal isomer VIi.

The yields and physicochemical constants of the synthesized compounds are listed in Table 1; the spectral characteristics of compounds Ic-m, IIc-k, and III-IVc,d are listed in Table 2, and those of compounds Va-k, VIa-m, and VII-VIIIa-c in Table 3.

2-Methyl-5,6-dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (Ia), 2,8-dimethyl-5,6-dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (Ib), 2-methyldihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (IIa), and 2,8-dimethyldihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (IIb) were synthesized by a procedure given in [2].

5,6-Dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazines (Ic,d and Va-c) and dipyrrolo[1,2-a; 2′,1′-c]pyrazine (IIc,d and VIa-c) were obtained, by a procedure analogous to that of [2], from the corresponding 3,4-dihydropyrrolo[1,2-a]pyrazines or pyrrolo[1,2-a]pyrazines and α-haloketones. Compounds I-IIc,d and V-VIa,b were extracted with chloroform, and compounds V-VIc were then recrystallized from hot ethyl acetate.

Nitro Derivatives of 5,6-Dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (Ie,g) and Dipyrrolo[1,2-a; 2′,1′-c]pyrazine (IIe-g). To a solution of 1 mmole of 5,6-dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (Ia,b) or dipyrrolo[1,2-a; 2′,1′-c]pyrazine (IIa,b) in 10 ml of acetic anhydride, chilled to −10°C, a solution of 0.1 ml of nitric acid (d = 1.42) in 1 ml of acetic anhydride was added dropwise with stirring. The reaction mixture was stirred while still keeping chilled for 30-60 min, until the initial compound disappeared as indicated by TLC; the mixture was then poured into cold water, neutralized to pH ~7 with a saturated sodium carbonate solution, and extracted with chloroform. The chloroform solution was dried over 3 Å molecular sieves, the solvent was driven off, and the resulting compound was chromatographed in a column with SiO_2 (Silpearl) in a 1:1 benzene–heptane system.

Trifluoroacetyl Derivatives of 5,6-Dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (Ih-*l*, Vd-h) and Dipyrrolo[1,2-a; 2′,1′-c]pyrazine (IIh-j, VId-g) were obtained by a procedure analogous to that of [2], from the corresponding 5,6-dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazines (Ic,d, Va-c) or dipyrrolo[1,2-a; 2′,1′-c]pyrazines (IIc,d, VIa-c) and trifluoroacetic anhydride. The mixture of compounds Ih,i or IIh,i was separated in a column with silica gel 40/100 in a 1:1 heptane–ethyl acetate system; the mixture of compounds Ij-*l* was recrystallized from heptane, upon which compound Ij remained in the precipitate; the residue was chromatographed in a column with SiO_2 (Silpearl) in a benzene–heptane system with a gradient from 1:1 to 1:2; compounds IIj and VId were crystallized from heptane. The mixture of compounds Vd,e and Vf,g was chromatographed in a column with SiO_2 (Silpearl) in a 6:1 heptane–ethyl acetate system; compound Vh and the mixture of compounds VIf and VIg were separated in a column with silica gel 100/160 in benzene; compound VIe was recrystallized from ethyl acetate, and the residue was chromatographed in a column with silica gel 100/160 in a 6:1 heptane–ethyl acetate system.

Acetyl Derivatives of 5,6-Dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (Im, Vi-k) and Dipyrrolo[1,2-a; 2′,1′-c]pyrazine (IIk, VIh-m). ***A***. To a solution of 1 mmole of the dipyrrolo[1,2-a; 2′,1′-c]pyrazine (Id) or dipyrrolo[1,2-a; 2′,1′-c]pyrazine (IId, VIa-c) in 10 ml of toluene, 23 mmoles of acetic anhydride was added; the reaction mixture was refluxed for 8-20 h, and then the solvent and excess anhydride were driven off. Compound Im was chromatographed in a column with silica gel 40/100 in a 2:1 heptane–ethyl acetate system; compound IIk was recrystallized from heptane. The mixture of compounds VIh-j was separated in a column with silica gel 40/100 in a heptane–ethyl acetate system with a gradient from 4:1 to 2:1, and the mixture of compounds VIk and VI*l* was separated in a column with SiO_2 (Silpearl) in a heptane–ethyl acetate system with a gradient from 4:1 to 0:1. Compound VIm was chromatographed in a column with silica gel 100/160 in a 4:1 benzene–ethyl acetate system.

B. To a solution of 1 mmole of the 5,6-dihydrodipyrrolo[1,2-a; 2′,1′-c]pyrazine (Id, Vb) or dipyrrolo[1,2-a; 2′,1′-c]pyrazine (IId) in 10 ml of toluene, 23 mmoles of acetic anhydride and 0.02 mmole of magnesium perchlorate were added. The reaction mixture was refluxed for 2-13 h, after which the solvent and excess anhydride were driven off. Compounds Im and IIk were separated by analogy with procedure A. Compound Vk was chromatographed in a column with SiO_2 (Silpearl) in a benzene–ethyl acetate system with a gradient from 4:1 to 1:1.

C. To a solution of 0.25 mmole of compound Va in 10 ml of benzene, 5.3 mmoles of acetic anhydride and 0.02 mmole of magnesium perchlorate were added. The reaction mixture was refluxed for approximately 45-50 h. The solvent and excess anhydride were driven off, and the mixture of compounds Vi and Vj was separated in a column with SiO_2 (Silpearl) in a 1:1 benzene–heptane system, then in straight benzene.

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