CHLORAL AS A FORMYLATING AGENT FOR SOME BRIDGE HETEROSYSTEMS

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UDC 547.446.1'759'785.5'82'833'853:542.953

The interaction of condensed nitrogen-containing bridge systems with chloral has been studied and the high sensitivity of the reaction to the π-excess of the initial heteroaromatic system has been established. It has been shown that chloral is a convenient formylating agent for systems with a moderate π-excess — imidazo-[1,2-a]imidazole, 9H-imidazo[1,2-a]benzimidazole, imidazo[1,2-a]pyridine, imidazo-[1,2-a]naphtho[2,3-d]imidazole. Heterocycles with a high π-excess (indolizine, pyrrolo[1,2-a]benzimidazole) form cyanine dyes under the action of chloral. Systems with a lowered π-excess (1H-imidazo[1,2-a]benzimidazole, imidazo[1,2-a]quinoline, imidazo[2,1-a]isoquinoline, imidazo[1,2-a]perimidine, imidazo[5,1-b]benzoxazole, imidazo[1,2-a]benzothiazole, and imidazo[1,2-a]pyrimidine) do not react with chloral in a neutral medium. However, in a number of cases their formylation can be carried out in an acid medium.

It is known [1] that chloral is capable of adding to aromatic compounds with the formation of trichloroethanols (I), the conditions for this reaction depending on the magnitude of the π-charge on the carbon atoms of the substrate. Thus, while inactivated aromatic compounds (for example, arenes [1, 2]) react with chloral usually in the presence of acid catalysts (H_2SO_4, $AlCl_3$, $ZnCl_2$, etc.), electron-excessive compounds of the type of phenols [3-5], tertiary aromatic amines [6], and hydroxypyrimidines [7, 8] take part in this reaction even in an alkaline medium (potassium carbonate, pyridine).

$$RH + CCl_3CHO \longrightarrow \underset{\text{I}}{RCH(OH)CCl_3} \longrightarrow \underset{\text{II}}{RCHO}$$

In pyridine under the action of bases, the carbinols (I) can split out a molecule of chloroform, and in this case the reaction as a whole is of interest as a method for obtaining aldehydes [1, 9]. However, in contrast to the first stage of this transformation, the transition (I) → (II) in the heterocyclic compound series has hitherto been studied to an extremely small degree. Only for hydroxypyrimidines [7, 8] and hydroxyquinolines [10] has it been shown that this method can be used for the synthesis of the corresponding aldehydes, although their yields are not always high because of side reactions [10].

In 1975, we proposed to use chloral as a convenient formylating agent for a number of bridge imidazole systems: imidazo[1,2-a]pyridine (III), imidazo[1,2-a]imidazole (IV), and 9H-imidazo[1,2-a]benzimidazole (V) [11]. In the present paper we report details of this method and the range of its application.

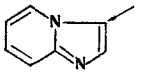
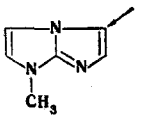
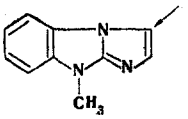
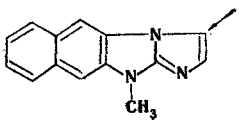
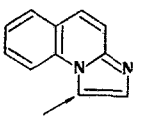
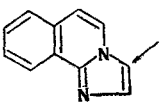
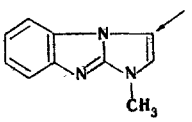
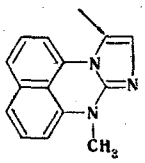
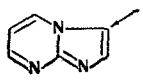
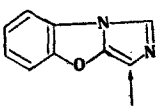
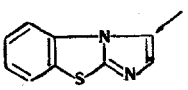
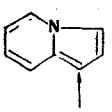
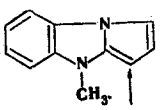
We have established that the possibility and direction of the occurrence of this reaction is largely determined by the π-excess of the bridge system. Table 1 gives the value calculated by means of the simple HMO method of the local (atom with the highest negative charge) and total (total charge on all the atoms) π-excess [12, 13] of heterocycles the behavior of which with chloral has been studied. It must be mentioned that while the calculations were performed for the unsubstituted heterocycles, their C-phenyl or C-methyl derivatives are usually used in the reaction (Table 1).

Compounds with relatively low local π-excesses (charge less than 0.100) do not, as a rule, take part in the reaction with chloral under neutral conditions. These include imidazo[1,2-a]quinoline (VII), imidazo[2,1-a]isoquinoline (VIII), 1H-imidazo[1,2-a]benzimidazole deriva-

Rostov State University and Scientific-Research Institute of Physical and Organic Chemistry, Rostov-na-Donau. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 528-537, April, 1980. Original article submitted June 20, 1979.

0009-3122/80/1604-0409$07.50

TABLE 1. Influence of the π-Excess of Bridge Heterocycles on Their Behavior to Chloral

Type of hetero system*	Derivatives taking part in the reaction (symbol)	π-Excess		Behavior with chloral under neutral conditions
		local	total	
1	2	3	4	5
III 	2-H (III) 2-CH_3 (IIIa) 2-C_6H_5 (IIIb)	−0,102	−0,041	Forms the alcohol (I) and the aldehyde (II)
IV 	6-C_6H_5 (IV)	−0,120	−0,190	The same
V 	2-CH_3 (Va) 2-C_6H_5 (Vb) 2-α-$C_{10}H_7$ (Vc) 2-p-BrC_6H_4 (Vd)	−0,104	−0,158	„ „
VI 	2-C_6H_5 (VI)	−0,100	−0,158	„ „
VII 	2-C_6H_5 (VII)	−0,067	−0,039	Does not react
VIII 	2-C_6H_5 (VIII)	−0,075	−0,055	The same
IX 	2-C_6H_5 (IX)	−0,073	−0,128	„ „
X 	2-C_6H_5 (X)	−0,089	−0,168	„ „
XI 	2-C_6H_5 (XI)	−0,103	+0,213	„ „
XII 	1-C_6H_5	−0,068	−0,042	„ „
XIII 	2-C_6H_5, 7-Br	−0,093	−0,151	„ „
XIV 	2-C_6H_5 (XIV)	−0,163	−0,382	Forms a cyanine dye
XV 	2-C_6H_5 (XV)	−0,202	−0,539	The same

*The arrow shows the position with the highest electron density, at which the addition of chloral takes place in the case of compounds (III-VI, VIII, and XI).

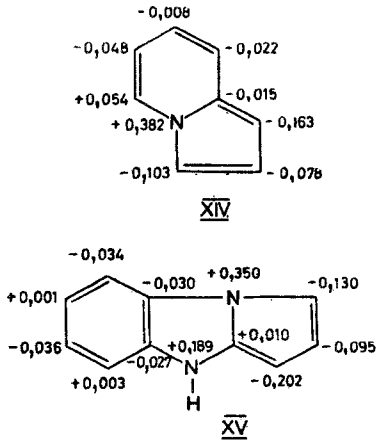


Fig. 1

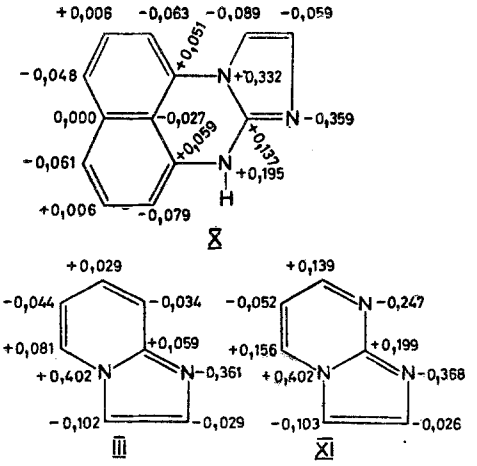


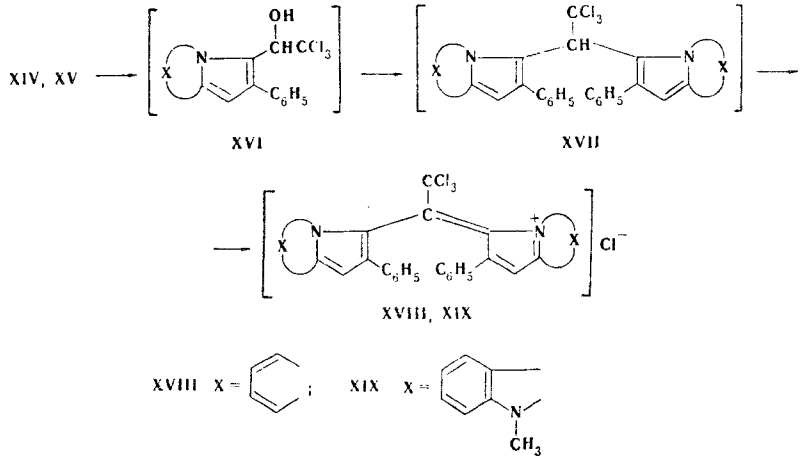
Fig. 2

Fig. 1. Values of the π-charges in the molecules of indolizine (XIV) and pyrrolo[1,2-a]benzimidazole (XV).

Fig. 2. Values of the π-charges in the molecules of imidazo[1,2-a]pyrimidine (X), imidazo[1,2-a]pyridine (III), and imidazo[1,2-a]pyrimidine (XI).

tives (IX), imidazo[1,2-a]perimidine (X), imidazo[5,1-b]benzoxazole (XII), and imidazo[1,2-a]benzothiazole (XIII). An exception is imidazo[1,2-a]pyrimidine (XI), the molecule of which possesses a sufficient local π-excess (−0.103) but which nevertheless does not undergo formylation under neutral conditions. The reasons for this are discussed below.

At the same time, compounds with a very high π-excess, such as indolizine (XIV) or pyrrolo[1,2-a]benzimidazole (XV), react with chloral so readily that even under mild conditions the reaction cannot be stopped at the stage of the formation of the alcohol (I) but the process is completed by the formation of cyanine dyes (XVIII, XIX).



In the course of this transformation, the trichloroethanol derivative (XVI) formed initially takes part in a further interaction with a second molecule of the initial heterocycle, forming the diheteryltrichloroethane (XVII), the rate of the latter reaction probably being considerably higher than the rate of the first stage. By analogy with other diindolizidinylmethanes [14, 15] compounds (XVII) are apparently very unstable and are readily oxidized to the dyes (XVIII and XIX). In the case of compounds (XVII), a hydride-ion acceptor is possibly the chloral itself or one of the intermediate products of its transformation (see [16]).

It must be emphasized that our calculations by the HMO method for indolizine (Fig. 1), in harmony with the results of ^{13}C NMR [17], show a greater electron density in position

TABLE 2. Characteristics of the Carbinols (I) Synthesized

Initial compound	mp, °C[a] (decomp.)	Found, %				Empirical formula	Calculated, %				Yield, %
		C	H	Hal	N		C	H	Hal	N	
III	183—184[b]	41,0	2,9	40,6	10,3	$C_9H_7Cl_3N_2O$	40,7	2,7	40,1	10,6	83
IIIa	179—180[b]	43,1	3,6	38,6	10,2	$C_{10}H_9Cl_3N_2O$	43,0	3,3	38,1	10,0	87—91
IIIb	215—216[b]	52,7	3,3	31,1	8,0	$C_{15}H_{11}Cl_3N_2O$	52,8	3,3	31,1	8,2	80—88
IV	173—175[b]	48,4	3,5	30,4	12,3	$C_{14}H_{12}Cl_3N_3O$	48,6	3,8	30,7	12,1	98
Va	215[c]	47,1	3,9	32,3	12,5	$C_{13}H_{12}Cl_3N_3O$	47,3	3,7	32,0	12,6	92—95
Vb	211—212[b]	54,5	3,9	26,8	10,4	$C_{18}H_{14}Cl_3N_3O$	54,8	3,7	27,0	10,6	95—100
Vc	235[d]	59,4	3,6	23,6	9,3	$C_{22}H_{16}Cl_3N_3O$	59,4	3,6	23,9	9,6	89—92
Vd	276—277[d]	45,8	2,8	39,0	9,0	$C_{18}H_{13}BrCl_3N_3O$	45,6	2,8	39,3	8,7	90
VI	255—256[b]	59,1	3,7	24,3	9,8	$C_{22}H_{16}Cl_3N_3O$	59,4	3,6	23,9	9,5	78—82
VIII	223—224[b]	58,4	3,5	26,9	7,3	$C_{19}H_{13}Cl_3N_2O$	58,3	3,3	27,1	7,2	88
XI	229[d]	48,9	2,9	31,4	12,4	$C_{14}H_{10}Cl_3N_3O$	49,1	2,9	31,0	12,3	86

[a]Melting points were determined by inserting a capillary with the substance into the heated instrument. [b]From ethanol. [c]From benzene. [d]From dimethylformamide.

1,* while the electrophilic substitution reaction for (XIV) takes place predominantly at the C_3 atom [18, 19]. As has now been established [20], a similar relationship is characteristic for the pyrrole molecule, in which the π-charge in the β-position is higher than in the α-position. The noncorrespondence between the direction of electrophilic attack and the value of the negative π-charge is apparently a general phenomenon not only for pyrrole but also for bridge systems based on it. Thus, in addition to (XIV), compound (XV) is also attacked by electrophiles mainly in position 1 (closer to the bridge nitrogen atom [21]) and not at C_3, where the π-electron density is higher (Fig. 1).

The formation of the trichloroethanols (I) and their subsequent conversion into the aldehydes (II) take place most successfully in the case of heterocycles with an intermediate π-excess, the local charge in which is between −0.100 and −0.130 (Table 1) (a somewhat greater charge is perhaps also permissible, but we had no such heterocycles available). These include, apart from the compounds (III-V) already mentioned, the 11H-imidazo[1,2-a]naphtho[2,3-d]imidazole (VI).

A connection between the reactivities of the heterocycles studied in relation to chloral and their total π-excess can also be traced fairly well, but here again there are exceptions. These exceptions are completely understandable, since a large total π-charge may be distributed over several atoms of a polynuclear system. Thus, for example, in compound (X) the comparatively low local π-excess is a consequence of the delocalization of the large negative π-charge in the naphthalene ring (Fig. 2). At the same time, some heterocycles with a small total π-excess can be subjected to formylation because of the high polarization of their π-systems, thanks to which atoms with high negative and positive charges are present in their molecules simultaneously. Characteristic examples are imidazo[1,2-a]pyridine (III) and, particularly, imidazo[1,2-a]pyrimidine (XI) (Fig. 2). The last-mentioned compound is the only heterocycle that we studied which possesses a total π-deficiency because of the presence of two electron-accepting heteroatoms of the pyridine type. Nevertheless, its molecule contains an atom with a considerable π-excess at which formylation can take place, although under different conditions (see below). It may be mentioned, nevertheless, that a decrease in the total π-excess even when a carbon atom with a sufficient local π-excess is present leads to a fall in the reactivity of the heterocycles. Thus, for example, compound (III) is formylated with considerably greater difficulty than compounds (IV-VI), and as already mentioned, compound (XI), is not formylated at all in a neutral medium.

The reaction of compounds (IV-VI) with chloral takes place very readily and can be carried out with an equimolecular ratio of reactants at room temperature both in the absence of a solvent and in an inert solvent (chloroform, benzene, ether, etc.). In the first case, the process is highly exothermic and requires external cooling. The corresponding alcohols of

*Many of the calculations of the molecule (XIV) reported in the literature give preference to the C_3 atom as the position with the highest electron density [18, 19]. But, apparently, the parameters used in these calculations and the final results are incorrect, since they do not agree with the chemical shifts of the ^{13}C nuclei [17].

TABLE 3. Characteristics of the Aldehydes (II) Obtained

Initial compound	mp, °C	ν_{CO}, cm^{-1}	R_f ($CHCl_3$)	Found, %			Empirical formula	Calculated, %			Yield, %
				C	H	N		C	H	N	
III[b]	116—117[b]	1640	0,8	65,5	4,0	20,0	$C_8H_6N_2O$	65,7	4,1	19,8	37
IIIH[c]	340[d]			51,3	3,2	26,0	$C_{14}H_{10}N_6O_4$	51,5	3,1	25,8	
III[a]	121—122[e]	1648	0,82	67,6	4,7	17,2	$C_9H_8N_2O$	67,5	5,0	17,5	76
IIIa-H	260—261[d]			50,6	3,5	28,0	$C_{15}H_{12}N_7O_4$	50,9	3,4	27,7	
IIIa·HCl	257—258[f] (decomp.)			55,3	4,7	13,9	$C_9H_8N_2O\cdot HCl$	54,9	4,7	14,2	
IIIb[g]	147[f]	1645	0,75	75,5	4,5	12,6	$C_{14}H_{10}N_2O$	75,7	4,5	12,6	91
IIIb-H	280—281 (decomp.)[d]			60,0	3,4	21,2	$C_{20}H_{13}N_6O_4$	59,9	3,3	21,0	
IV	86[b,h]	1630	0,85	69,1	4,8	18,8	$C_{13}H_{11}N_3O$	69,3	4,9	18,7	84
IVH	286—287[e] (decomp.)[d]			56,2	3,7	24,0	$C_{19}H_{15}N_7O_4$	56,3	3,7	24,2	
Va[i]	186[e]	1640	0,9	67,7	5,1	19,7	$C_{12}H_{11}N_3O$	67,6	5,2	19,7	92—98
Vb[j]	147[f]	1638	0,9	74,2	4,8	15,4	$C_{17}H_{13}N_3O$	74,2	4,8	15,2	90—95
Vc	254—255[d]	1635	0,85	71,1	4,5	12,7	$C_{21}H_{15}N_3O$	77,1	4,7	12,9	89
Vc-H	>330[d]			64,1	3,6	19,5	$C_{27}H_{19}N_7O_4$	64,2	3,8	19,4	
Vd	199—201[f]	1640	0,9	57,9	3,7	11,6	$C_{17}H_{12}BrN_3O$	57,7	3,4	11,9	78—86
Vd-H	307—308 (decomp.)[d]			52,0	3,3	18,7	$C_{23}H_{16}BrN_7O_4$	51,7	3,0	18,4	
VI	221—222[e]	1650	0,87	77,2	4,4	12,8	$C_{21}H_{15}N_3O$	77,3	4,7	12,9	78
VI-H	310 (decomp.)[d]			64,3	3,8	19,6	$C_{27}H_{19}N_7O_4$	64,1	3,8	19,4	
VIII	177—178[f]	1650	0,9	79,2	4,4	10,2	$C_{18}H_{12}N_2O$	79,4	4,4	10,3	96
VIII-H	>300[d]			63,8	3,8	18,4	$C_{24}H_{16}N_6O_4$	63,7	3,6	18,6	
XI	174[k]	1645	0,9	69,7	4,0	18,9	$C_{13}H_9N_3O$	69,9	4,1	18,8	91
XI-H	270[d]			56,5	3,2	24,5	$C_{19}H_{13}N_3O_4$	56,6	3,2	24,3	

[a]According to the literature [22], mp 117-119°C; yield 17-30%. [b]From petroleum ether. [c]H denotes the 2,4-dinitrophenylhydrazones of the aldehydes. [d]From DMFA. [e]From benzene. [f]From ethanol. [g]According to the literature [23], mp 147-148°C, yield 45%. [h]After prolonged storage, the melting point had risen to 121-122°C, although according to TLC and IR spectroscopy the compound had remained unchanged; an identical aldehyde has also been obtained in our laboratory by Yu. V. Koshchienko with the aid of organometallic synthesis. [i]According to the literature [24], mp 186°C, yield 70%. [j]According to the literature [24], mp 147°C; yield 81-88%. [k]From ethyl acetate.

ype (I) are formed in good yields as the reaction products under these conditions (Table 2). he reaction takes place with rather greater difficulty for imidazo[1,2-a]pyridines (III), s is shown in the greater duration of the process (several days at room temperature) or the ecessity for making the conditions more severe (boiling in benzene or heating in an excess f chloral).

It is known that, depending on the alkaline agent used and its concentration, aryl trihloromethyl carbinols are saponified to glyoxals aryl aldehydes or hydroxy acids [1]. Unike them, the carbinols formed from the heterocycles (III-VI) are readily split under the ction of alkaline agents (aqueous or alcoholic alkali, alkali-metal alkanolates, aqueous soution of sodium carbonate) to the corresponding aldehydes. The formation of aldehydes also akes place under the action of triethylamine, but in this case the reaction proceeds far ore slowly and with a lower yield. The transformation of compounds (III-VI) into aldehydes nder the action of chloral can also be carried out in one stage without the isolation of the alo alcohol. For this purpose, an alkaline agent must be added to the reaction mixture afer the completion of the first stage. The yields of aldehydes usually exceed 80%, and only n individual cases were they lower (Table 3).

It is characteristic that when the above-mentioned systems with methyl groups as substituents were caused to react with chloral, no condensation at these groups took place. The eaction of 2-methylimidazo[1,2-a]pyridine with chloral at the methyl group was reported by ombardino [25] erroneously, as we and other authors [26] have now established. This reacion actually takes place at position 3. However, it must be mentioned that the melting oints of the halo alcohols and aldehydes obtained by Hand et al. [26] differ greatly from hose of the compounds which we isolated when the condensation was carried out both under the onditions that we proposed and also under the conditions of these previous workers [25 and 6] (see the experimental part).

In spite of the fact that compounds (VII-XII) do not react with chloral under neutral conditions, the possibility cannot be excluded of their formylation under other conditions and, for example, in the presence of acid catalysts. It is likely that in the majority of cases conditions can be selected at which the condensation will proceed with satisfactory yields. For example, 2-phenylimidazo[2,1-a]isoquinoline (VIII) and 2-phenylimidazo[1,2-a]-pyridine (XI), which do not react with chloral under neutral conditions, readily form halo alcohols with yields of about 90% in glacial acetic acid. The saponification of these halo alcohols with alkaline agents gave high yields of the corresponding aldehydes (Table 3). The imidazo[1,2-a]benzothiazole (XIII) does not condense with chloral even under these conditions, and the reaction with the imidazo[1,2-a]pyrimidine (X) is accompanied by such pronounced resinification that it was impossible to isolate the desired halo alcohol from the reaction mixture. Heating 2,9-disubstituted imidazo[1,2-a]benzimidazoles with chloral in acetic acid leads, as in the case of aromatic aldehydes [27], to the formation of deeply colored symmetrical methinecyanine dyes.

Thus, we have proposed a convenient method for formylating bridge heterocyclic systems that has substantial advantages (accessibility of the initial reactants, fairly mild reaction conditions, simplicity of performing the synthesis, high yields) over the Vilsmeir method or the organometallic synthesis of aldehydes.

EXPERIMENTAL

The IR spectra were taken on a UR-20 instrument and the PMR spectra on a Tesla BS-467 instrument with a working frequency of 60 MHz using HMDS as internal standard. The course of the reaction was monitored and the individuality of the substances was checked with the aid of TLC on Al_2O_3 of activity grade IV (with chloroform or benzene as the eluent). The quantum-mechanical calculations were performed by the simple HMO method with parameters from the literature for the N and O atoms [28] and the S atom [29].

2-Amino-1-methyl-3-phenacylnapth[2,3-d]imidazolium Bromide. A hot solution of 1.58 g (8 mmole) of 2-amino-1-methylnapth[2,3-d]imidazole in 150 ml of acetone was treated with 1.6 g (8 mmole) of phenacyl bromide. The mixture was carefully stirred, boiled for 3-5 min, and left at room temperature for 3-4 h. The snow-white precipitate of the bromide was filtered off and washed with acetone. Yield 3.1 g (97%), mp 308-309°C (decomp., from ethanol). IR spectrum (paraffin oil), cm^{-1}: 1490, 1600 (C=C), 1675 (C=N), 1695 (C=O), 1550, 3180, 3345 (NH). Found: C 60.8; H 4.8; Br 20.00; N 10.6%. $C_{20}H_{17}N_3O \cdot HBr$. Calculated: C 60.5; H 4.8; Br 20.1; N 10.6%.

11-Methyl-2-phenylimidazo[1,2-a]napth[2,3-d]imidazole (VI). A suspension of 3 g of 2-amino-1-methyl-3-phenacylnapth[2,3-d]imidazolium bromide in 150 ml of concentrated HBr was boiled for 32 h. Then it was cooled and the precipitate was filtered off. The salt obtained was treated with 10% NaOH solution, and the base was extracted with chloroform. The residue after evaporation of the chloroform was purified first by chromatography on a column of Al_2O_3 (with $CHCl_3$ as eluent), the fraction with R_f 0.75 being collected, and then by recrystallization from ethyl acetate. Yield 1.8 g (80%). Slightly yellowish crystals with mp 164-165°C. IR spectrum ($CHCl_3$), cm^{-1}: 1500, 1605, 1615 (C=C, C=N). Found: C 80.8; H 5.1; N 14.2%. $C_{20}H_{15}N_3$. Calculated: C 80.8; H 5.1; N 14.1%.

Reaction of Derivatives of the Heterosystems (III-VI) with Chloral (General Procedures). A. To a solution of 10 mmole of a compound (III-VI) in dry benzene was added 1 ml (1.47 g; 10 mmole) of chloral. The mixture was carefully stirred and was left to stand at room temperature, the course of the reaction being followed chromatographically. After its completion, the precipitate of halo alcohol that had deposited was filtered off and was washed on the filter with benzene and ether. Chloroform, pyridine, or ether can be used as the solvent in this reaction. For the derivatives of systems (IV-VI) the reaction usually takes 3-15 h. In the case of compound (III), the reaction mixture is kept at room temperature for 8-10 days or is boiled for 30-40 h.

B. Equimolar amounts of the initial heterocycle (IV-VI) and chloral were carefully mixed. After the end of the exothermic reaction, the mixture was heated at 40-50°C for 10-15 min. Then it was cooled and the melt was triturated with diethyl ether. The precipitate was filtered off and was washed with benzene and ether. The fusion of compound (VI) was carried out at 105-110°C.

C. A carefully ground mixture of equivalent amounts of compound (V) and chloral hydrate was heated at 70-80°C for 20 min. Then it was cooled and the melt was worked up in a similar manner to that described in method B.

All the halo alcohols were characterized by R_f values of 0.35-0.45 (with chloroform as eluent). In their IR spectra (paraffin oil), the absorption of the OH group was observed in the form of the broad band in the 2500-2750 cm^{-1} region; the CCl_3 group absorbed in the 795-820 cm^{-1} region. Information on the alcohols obtained is given in Table 2.

General Methods of Converting the Halo Carbinols into Aldehydes (Table 3). A. A suspension of 10 mmole of a halo alcohol in 40 ml of 5-10% aqueous NaOH was heated in the boiling water bath for 0.5-2 h. Then it was cooled and the precipitate was filtered off, carefully washed with water, and crystallized from a suitable solvent.

B. The halo alcohol (10 mmole) was added to a solution of 1.5-2 g of NaOH in 30 ml of ethanol, and the mixture was boiled for 20-30 min. Then it was filtered hot from NaCl, the filtrate was evaporated, and the residue was purified by recrystallization.

C. A mixture of 1 mmole of the halo alcohol, 5-8 ml of saturated sodium carbonate or bicarbonate solution, and 1-2 ml of ethanol was boiled for 30-40 min. Then the mixture was cooled, and the aldehyde was filtered off or was extracted with chloroform.

3-Formyl-9-methyl-2-phenylimidazo[1,2-a]benzimidazole (Table 3). A solution of 5 mmole of 9-methyl-2-phenylimidazo[1,2-a]benzimidazole (Vb) in 20 ml of dry chloroform was treated with 0.53 ml (5 mmole) of chloral, and the mixture was carefully stirred and allowed to stand. After the end of the reaction, which was followed chromatographically, 15 ml of 10% aqueous NaOH was added to the reaction flask and the mixture was boiled for 1-2 h. Then it was cooled and the chloroform layer was separated off, washed with water, and dried with anhydrous sodium sulfate, and the chloroform was evaporated off. The residual aldehyde was purified by recrystallization from ethanol. Yield 90%.

3-Formyl-9-methyl-2-naphthylimidazo[1,2-a]benzimidazole (Table 3). Equivalent amounts of compound (Vb) and chloral were mixed at room temperature, and after the end of the exothermic reaction the mixture was heated at 50°C for 15 min, and then an ethanolic solution of caustic soda was added to the melt and it was boiled for 30 min. After cooling, the aldehyde that had deposited was separated off. Yield 89%.

2-Methyl-3-(2,2,2-trichloro-1-hydroxyethyl)imidazo[1,2-a]pyridine. A. A solution of 1.33 g (10 mmole) of 2-methylimidazo[1,2-a]pyridine (IIIa) and 1 ml (10 mmole) of freshly-distilled chloral in 10 ml of dry benzene was left to stand at room temperature, the course of the reaction being followed by TLC. After 8 days the precipitate that had deposited was filtered off and was washed with benzene and ethanol. Yield 2.42 g (87%). Large colorless crystals with mp 179-180°C (decomp., from ethanol). According to the literature [26], unsharp mp: the compound softens and darkens at 92°C and then forms a vitreous mass at 102°C. IR spectrum (paraffin oil), cm^{-1}: 2550-2700 (OH). PMR spectrum ($CDCl_3$), ppm: 2.35 (3 H, s, C–CH_3); 5.63 (1 H, s, C<u>H</u>(OH)); 6.63-7.75 (3 H, m, 6–8-H); 9.06 (1 H, d, H_5).

B. A solution of equimolar amounts of (IIIa) and chloral in benzene was heated for 28 h. Then it was cooled and the precipitate was filtered off. Yield 91%. The compound was identical with that obtained by method A.

C. A mixture of 1 g (7.5 mmole) of (IIIa) and 5 ml of chloral was heated in the boiling water bath for 24 h. Then it was cooled and was triturated with diethyl ether, after which the precipitate was filtered off and was washed repeatedly with ether. This gave 1.1 g (52%) of the carbinol hydrochloride in the form of small colorless needles with mp 226-227°C (decomp., from ethanol). Found: C 38.3; H 3.0; Cl 44.5; N 9.0%. $C_{10}H_9Cl_3N_2O \cdot HCl$. Calculated: C 38.0; H 3.2; Cl 44.9; N 8.9%. The salt obtained was treated in the cold with a mixture of chloroform and aqueous sodium bicarbonate solution. The chloroform layer was separated off and evaporated, and the residue was crystallized from ethanol, giving colorless crystals of the halo carbinol base with mp 179-180°C identical with that described above.

If the fusion of compound (IIIa) with a double amount of chloral was carried out at 95-110°C for 8 h, the yield of hydrochloride rose to 83%. According to Lombardino [25], mp of the hydrochloride 240-241.5°C; according to Hand et al. [26], mp 229°C (decomp.).

3-Formyl-2-methylimidazo[1,2-a]pyridine. A. A mixture of 0.28 g (1 mmole) of halo alcohol, 5 ml of saturated sodium carbonate solution, and 1 ml of ethanol was boiled for 1 h. Then it was cooled and extracted with chloroform. The chloroform extract was evaporated, the residue was dissolved in a small amount of benzene, and the solution was filtered through a layer of Al_2O_3. The benzene was evaporated off and the residue was crystallized from benzene or hexane. Yield 0.12 g. Snow-white needles with mp 121-122°C. According to the literature [26], mp 110-111°C. PMR spectrum ($CDCl_3$), ppm: 2.67 (3 H, s C–CH_3); 6.85-8.0 (3 H, m, 6–8-H); 9.5 (1 H, d, 5-H); 10.02 (1 H, s, CHO).

B. A solution of 1 g of NaOH in 2 ml of water was added to a solution of 1.4 g (5 mmole) of the carbinol in 10 ml of ethanol. The mixture was carefully heated to the boil, and after the end of the vigorous spontaneous reaction it was boiled for another 15-20 min. Then it was cooled, the NaCl was filtered off, the ethanolic solution was evaporated, and the aldehyde was extracted from the residue with benzene or chloroform. Yield 0.7 g. The hydrochloride of the aldehyde was obtained by the addition of concentrated HCl to an alcoholic solution of the base to pH 2-3. Snow-white needles with mp 257-258°C (decomp. from ethanol). According to the literature [26], mp 252°C (decomp.). Found: C 55.1; H 4.7; Cl 18.3; N 13.9%. $C_9H_8N_2O \cdot HCl$. Calculated: C 54.9; H 4.7; Cl 18.0; N 14.2%.

2-Phenyl-3-(2,2,2-trichloro-1-hydroxyethyl)imidazo[2,1-a]isoquinoline (Table 2). A mixture of 0.25 g (1 mmole) of 2-phenylimidazo[2,1-a]isoquinoline, 0.11 ml (1 mmole) of chloral, and 2.5 ml of glacial acetic acid was boiled for 30 min. Then it was cooled and the snow-white macrocrystalline precipitate that deposited on boiling was filtered off and was washed with ether until the odor of acetic acid had disappeared. Yield 0.35 g. IR spectrum (paraffin oil) cm^{-1}: 2600-2700 (OH).

3-Formyl-2-phenylimidazo[2,1-a]isoquinoline (Table 3). A mixture of 0.39 g (1 mmole) of the halo alcohol and 0.12 g (3 mmole) of NaOH in 10 ml of ethanol was boiled for 10-15 min. Then it was cooled and was diluted twofold with water, and the precipitate was filtered off and washed with water. Long silky needles with mp 177-178°C.* Yield 0.26 g.

2-Phenyl-3-(2,2,2-trichloro-1-hydroexyethyl)imidazo[1,2-a]pyrimidine (Table 2). This was obtained by boiling 0.4 g (2 mmole) of 2-phenylimidazo[1,2-a]pyrimidine and 0.22 ml (~2 mmole) of chloral in 3 ml of glacial acetic acid for 10-15 min. After cooling the suspension was diluted twofold with ether and the light lemon yellow precipitate of halo alcohol was filtered off and it was washed with ether and acetone. It did not dissolve in ethanol, benzene, chloroform, and ethyl acetate. Yield 0.6 g. IR spectrum (paraffin oil), cm^{-1}: 2550-2750 (OH).

3-Formyl-2-phenylimidazo[1,2-a]pyrimidine (Table 3). A suspension of 0.51 g (1.5 mmole) of the appropriate halo alcohol in 10 ml of ethanol was treated with 5 ml of a saturated solution of Na_2CO_3, and the mixture was boiled until the crystals of the initial carbinol had completely disappeared. The ethanolic layer was separated off and evaporated. The residue was extracted repeatedly with chloroform. The chloroform extract was evaporated, giving 0.3 g of aldehyde in the form of long slightly yellowish needles. Saponification with aqueous alkali led to a fall in the yield of aldehyde through pronounced resinification and the occurrence of side reactions (see [13]).

Reaction of Compounds (XIV) and (XV) with Chloral. A solution of compound (XIV) or (XV) in benzene was treated with an equimolar amount of chloral. The rapidly darkening reaction mixture was left to stand at room temperature for 1-2 days. The benzene was evaporated off, the oily residue was treated with saturated solution of KCl, and the precipitate was filtered off and washed with water. After drying, it was dissolved in chloroform, and the chloroform solution was passed through a layer of alumina. The upper layer of Al_2O_3 upon which the dye was adsorbed was separated off and was repeatedly extracted with hot ethanol and acetone. Evaporation of the solvents gave dark green crystals of a dye in each case with mp >350°C, the yield of compound (XVIII) being 33% and of compound (XIX) 47%. The dye (XVIII) was also obtained with a yield of 50% by fusing 2-phenylpyrrolo[1,2-a]pyridine with chloral hydrate at 100°C. Found: C 66.0; H 4.0; N 4.7%. $C_{30}H_{20}Cl_4N_2$. Calculated: C 65.5; H 3.7; N 5.1%. For compound (XIX), Found: N 8.8%. $C_{36}H_{26}Cl_4N_4$. Calculated: N 9.0%.

*This compound has also been obtained in our laboratory by T. A. Kuz'menko using the Vilsmeier method.

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