SYNTHESIS AND STRUCTURE OF QUATERNARY SALTS OF ACRIDINYLHETARYLMETHANES AND THEIR ANHYDRO BASES

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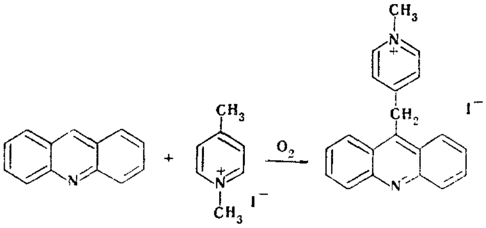
Quaternary salts of 9-acridinylhetarylmethanes were obtained by condensation of acridine with alkiodides of 2- and 4-methyl derivatives of nitrogen heterocycles in the presence of air oxygen. A study of the spectra of the acridinylhetarylmethanes and their quaternary salts and anhydro bases indicates tautomeric transfer of the hydrogen atom of the methylene group to the nitrogen atom of the acridine fragment in monoquaternized acridinylhetarylmethanes.

In a continuation of our research on the condensation of acridines with nucleophiles in the presence of an oxidizing agent [1], we have investigated the reaction of acridine and acridine hydrochloride with alkiodides of nitrogen heterocycles containing a methyl group in the 2- and 4-positions. In dimethylformamide (DMFA) in the presence of air oxygen the condensation takes place at the methyl group and gives acridinylhetarylmethane derivatives, for example,



When heterocycles with most active methyl groups (2- and 4-methylquinolines) are used, side reactions of oxidation of the dihetarylmethane derivative to an acridone and self-condensation of the methylquinolines to cyanines are observed. Oxidation can be avoided when the acridine base is used. Condensation at less active methyl groups (2- and 4-picolines and 1,2-dimethylbenzimidazole) is realized successfully by using acridine hydrochloride. Data on the synthesized compounds are presented in Table 1.

The monoquaternized acridinylhetarylmethanes (I-VI) are converted by alkali to anhydro bases IX-XI and XV-XVII (Table 2), which are close analogs of unsymmetrical cyanine dyes.

The electronic spectra of 9-substituted (amino, aminophenyl, hydroxyphenyl, and aminostyryl derivatives) were investigated in detail in connection with the possible tautomeric amino–imino and oxo–hydroxy forms [2]. There are possibilities in 9-acridinylhetarylmethanes for tautomerism due to transfer of a hydrogen atom of the methylene group situated between two strong acceptors to one of the nitrogen atoms. This sort of tautomerism has been described in the diquinolylmethane series [3].

We made a comparative study of the electronic spectra of the acridinylhetarylmethanes obtained in [1] and of their monoquaternary salts (I-VIII) and anhydro bases (IX-XVII). As one should have expected, the methylene group breaks the conjugation chain in acridinylhetarylmethanes, disrupting the mutual elec-

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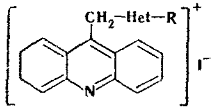
TABLE 1. Quaternary Salts of 9-Acridinylhetarylmethanes



Compound	Het	R	mp,* °C	Empirical formula	λ_{max}, nm (log ε) (in ethanol)	Found, %			Calculated, %			Yield, %
						C	H	N	C	H	N	
I	4-Pyridyl	CH_3	192—193	$C_{20}H_{17}N_2I$	310 (3,68); 554 (3,84)	58,3	4,4	6,5	58,3	4,2	6,8	82
II	4-Pyridyl	C_2H_5	116—117	$C_{21}H_{19}N_2I$	306 (3,67); 552 (3,89)	59,4	4,6	6,7	59,2	4,5	6,5	74
III	4-Pyridyl	C_3H_7	113—114	$C_{22}H_{21}N_2I$	305 (3,66); 555 (3,83)	59,6	5,0	6,4	60,0	4,8	6,4	76
IV	2-Pyridyl	CH_3	223—225	$C_{20}H_{17}N_2I \cdot H_2O$	295 (3,89); 518 (4,08)	56,6	4,9	6,3	56,3	4,5	6,5	79
V	4-Quinolinyl	CH_3	250—252	$C_{24}H_{19}N_2I$	310 (3,94); 644 (4,19)	62,4	4,2	5,9	62,4	4,1	6,1	39
VI	2-Quinolinyl	CH_3	250—252	$C_{24}H_{19}N_2I$	298 (4,91); 588 (4,44)	62,1	4,0	6,1	62,4	4,1	6,1	30
VII	2-Benzothiazolyl	CH_3	235—237	$C_{22}H_{17}N_2IS$	582 (4,39)	56,7	3,9	5,6	56,4	3,7	6,0	46
VIII	2-(1-Methyl)benzimidazolyl	CH_3	300—303	$C_{23}H_{20}N_3I$	290 (3,19); 458 (4,22)	59,6	4,4	9,1	59,4	4,3	9,0	17

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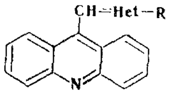
*Compounds I-III were crystallized from water, while IV-VIII were crystallized from ethanol.

TABLE 2. Anhydro Bases of Salts of Acridinylhetarylmethanes



Compound	Het	R	mp, °C (from ethanol)	Empirical formula	λ_{max}, nm (log ε) (in ethanol)	Found, %			Calculated, %		
						C	H	N	C	H	N
IX	4-Pyridyl	CH_3	220—222	$C_{20}H_{16}N_2$	310 (3,97); 554 (3,95)	84,2	5,6	10,2	84,5	5,7	9,8
X	4-Pyridyl	C_2H_5	145—146	$C_{21}H_{18}N_2$	310 (4,17); 556 (3,87)	84,5	6,2	9,7	84,5	6,1	9,4
XI	4-Pyridyl	C_3H_7	174—175	$C_{22}H_{20}N_2$	310 (4,02); 552 (4,17)	84,9	6,5	9,0	84,6	6,4	9,0
XII*	4-Pyridyl	2,4-Dinitrophenyl			285 (4,35)†; 500 (4,19)						
XIII*	4-Pyridyl	9-Acridinyl			300 (4,28); 510 (4,15)						
XIV*	4-Pyridyl	2,7-Dibromo-9-acridinyl			290 (4,28)†; 497 (4,07)						
XV	2-Pyridyl	CH_3	214—216	$C_{20}H_{16}N_2$	295 (3,88); 520 (4,11)	84,0	5,6	9,8	84,5	5,7	9,8
XVI	4-Quinolinyl	CH_3	260—262	$C_{24}H_{19}N_2$	275 (4,07)†; 540 (4,00)	86,3	5,7	8,1	86,2	5,4	8,4
XVII	2-Quinolinyl	CH_3	209—211	$C_{24}H_{19}N_2$	285 (4,28)†; 525 (4,32)	85,7	5,1	8,0	86,2	5,4	8,4

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*Compounds XII-XIV were described in [4].

†These are shoulders.

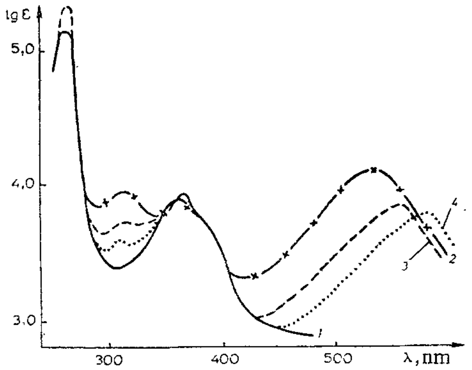


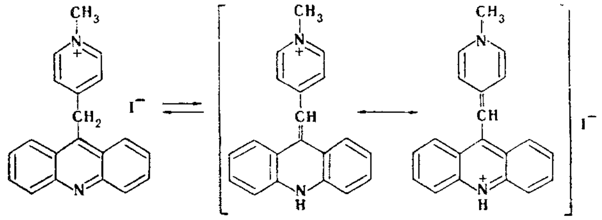
Fig. 1. Electronic spectra of 4-pyridinyl-9-acridinylmethane methiodide (I): 1) in water; 2) in dimethylformamide; 3) in ethanol; 4) in chloroform.

tronic effects of the heterorings. The electronic spectra of the acridinylhetarylmethanes therefore differ little from the spectrum of acridine and contain two absorption bands with maxima at 255 and 355-360 nm. At the same time, the absorption of the introduced heteroring is masked by the more intense absorption of acridine, which is found in the same region.

The electron system of the entire molecule in the anhydro bases is conjugated, and two new bands characteristic for this system arise at 280-320 and 500-600 nm. The maxima experience a hyposchromic shift when the acceptor character of the substituent of the nitrogen of the heteroring increases (IX-XIV) on passing from pyridyl- to quinolinylacridinylmethines (IX, and XVI, XV and XVII). Transfer of the electron density to the acridine fragment of the molecule probably occurs in the excited state in IX-XVII, and the introduction of acceptor substituents that hinder this sort of transfer also causes the observed hypsochromic shift.

The spectra of the monoquaternary salts of acridinylhetarylmethanes contain two new (as compared with the acridine compounds) absorption bands that are characteristic for the completely conjugated system of the anhydro bases (see Tables 1 and 2). The transition from 2- to 4-isomers of pyridine and benzo annelation of the pyridine ring cause a bathochromic shift of the maxima of both bands. An increase in the polarity of the solvent leads to a hypsochromic shift of the maxima, while in water and acetic acid these bands are absent (Fig. 1).

The presence of these absorption bands in the electronic spectrum is probably associated with tautomeric transfer of a hydrogen atom of the methylene group to the nitrogen atom of the acridine residue to give a conjugated system (resonance stabilization of the tautomeric structure promotes this sort of tautomeric transition). For example, for I,



The possibility of this transition is absent in acetic acid, in which both heteroatoms are in the ammonium form, and the spectrum does not contain absorption bands in the regions corresponding to the conjugated structure. The tautomeric equilibrium in water is shifted to the left, apparently due to the formation of strong hydrogen bonds with the nitrogen atom of the acridine fragment. The IR spectra of I-III recorded in chloroform also provide evidence in favor of tautomerism. A distinct absorption band in the region of N–H bond vibrations (3450 cm^{-1}) is observed in these spectra.

EXPERIMENTAL

The UV spectra of 10^{-4}-$5 \cdot 10^{-5}$ mole/liter solutions were recorded with SF-4 and SF-4A spectrophotometers. The IR spectra of saturated solutions of the compounds in chlorform were measured with a UR-20 spectrometer.

Condensation with Alkiodides of 2- and 4-Picolines and 1,2-Dimethylbenzimidazole. Air was bubbled through a solution of 20 mmole of acridine hydrochloride and 40 mmole of the alkiodide in 10-20 ml of DMFA at 120° for 6 h (at 135° in the case of 1,2-dimethylbenzimidazole). The mixture was then cooled, and the resulting precipitate was removed by filtration and refluxed with 50 ml of water. The aqueous mixture was filtered, and the acridone was collected on the filter. Sodium carbonate was added to the filtrate up to pH 10-12, and the resulting precipitate was removed by filtration and crystallized.

Condensation with Methiodides of 2- and 4-Methylquinolines and 2-Methylbenzothiazole. Air was bubbled through a solution of 20 mmole of acridine and 20 mmole of the methiodide in 10-20 ml of DMFA at 120° for 4 h (at 110° in the case of lepidine). At the end of the process, the DMFA was evaporated in a stream of air at the reaction temperature, and the residue was refluxed with 50 ml of acetone. The acetone mixture was cooled, and the resulting precipitate was removed by filtration and crystallized from ethanol. Compounds VI and VII were crystallized fractionally to free them from the side products of the cyanine condensation.

Anhydro Bases of the Quaternary Salts of Acridinylhetarylmethanes (IX-XI, XV, and XVI). A cooled aqueous solution or suspension of I-VI was treated with 10% NaOH solution until the pH was 10-12. The anhydro bases were isolated quantitatively as a resinous mass, which gradually began to crystallize. The solid was removed by filtration and crystallized from ethanol.

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