STRUCTURE OF THE PRODUCTS OF THE REACTION OF 9,10-DIMETHYLACRIDINIUM SALTS WITH AROMATIC o-HYDROXY ALDEHYDES

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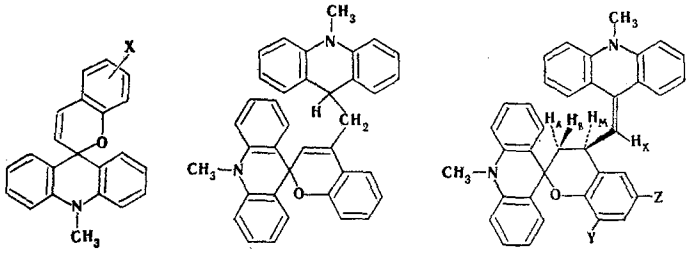
The reaction of 9,10-dimethylacridinium methosulfate with aromatic o-hydroxy aldehydes in alcohol in the presence of piperidine gives 10-methyl-4'-(10-methyl-9-acridanylidenemethyl)-spiro[acridan-9,2'-chromans]. The structure of the compounds obtained was established by means of the PMR, UV, and IR spectra.

Wizinger [1] obtained the corresponding spiropyrans (I-III) by condensation of 9,10-dimethylacridinium methosulfate with salicylaldehyde, 3-methoxysalicylaldehyde, and 2-hydroxynaphthaldehyde in glacial acetic acid.



I-III IVa IVb-Xb

I X=H; II X=8'-OCH_3; III X=5',6'-benzo Z=H, CH_3, OCH_3, NO_2, Br Y=H, OCH_3, Br

Since the synthetic method described by Wizinger [1] was hard to reproduce and gave very low yields, we attempted to carry out this condensation in alcohol with the addition of piperidine [2]. Under these conditions, the reaction proceeded rapidly to give high yields of crystalline, almost colorless substances (IV-X, Table 1) that are readily soluble in low-polarity solvents and have weak thermochromic properties. Solutions of them in p-dimethoxybenzene turn yellow on heating and green on cooling. The color again becomes yellow on reheating. Compounds IV-X dissolve in acetic and trifluoroacetic acids to give intensely yellow or orange salts. The melting points of IV and VIII differed considerably from those indicated in [1] for I and II. The formation of IV and VIII instead of I and II apparently was not associated with any redox processes, since the same compounds were obtained in high yields under argon.

It was found that IV-X are the products of the reaction of two molecules of 9,10-dimethylacridinium methosulfate with one molecule of aldehyde. The presence of two acridine residues in the investigated compounds was established on the basis of a determination of their elementary compositions and molecular weights. The formation of condensation products of this type was previously observed in the preparation of spiropyrans of the indoline series [3]. It was shown that a second indoline residue is found in the 4' position of the pyran ring. In analogy with these data, one should have assumed a structure of the IVa type, which contains a chromene ring, for IV-X. The ready formation of colored salts of IV-X in CH_3COOH, which should be associated with opening of the pyran ring, is, it would seem, in agreement with this.

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TABLE 1. 10-Methyl-4'-(10-methyl-9-acridanylidenemethyl)spiro[acridan-9,2'-chromans] (IVb-Xb)

Compound	Z	Y	mp, °C (dec.)*	Empirical formula†	Found, %			Calc., %			λ_{max}, nm (lg ε)		Yield, %
					C	H	N	C	H	N	dioxane	acetic acid	
IVb	H	H	195—196	$C_{37}H_{30}N_2O$	86,1	6,1	5,5	85,7	5,83	5,4	275—280 (4,41); 368 (4,01)‡	360 (4,39); 426 (3,94)	63
Vb	CH_3	H	195—196	$C_{38}H_{32}N_2O$	85,7	6,2	4,9	85,7	6,1	5,3	228 (4,85); 267 (4,41); 283 (4,42); 368 (4,03)	361 (4,39); 428 (3,95)	60
VIb	OCH_3	H	192—193	$C_{38}H_{32}N_2O_2$	83,9	6,3	—	83,2	5,9	—	225 (4,86); 267 (4,35); 286 (4,37); 368 (3,97)	361 (4,32); 428 (3,84)	69
VIIb	NO_2	H	183—184	$C_{37}H_{29}N_3O_3$	78,5	5,3	—	78,9	5,2	—	229 (4,71); 267 (4,41); 285 (4,42); 366 (4,03)	347 (4,32); 361 (4,49); 427 (4,01)	80
VIIIb	H	OCH_3	147—148	$C_{38}H_{32}N_2O_2$	83,0	6,0	5,3	83,2	5,9	5,1	225 (4,87); 267 (4,36); 368 (3,95)	361 (4,38); 428 (3,92)	70
IXb	Br	H	188—190	$C_{37}H_{29}BrN_2O$	74,4	5,3	4,9	74,4	4,9	4,7	229 (4,85); 268 (4,38); 284 (4,39); 369 (4,00)	361 (4,45); 428 (4,00)	60
Xb	Br	Br	180—183	$C_{37}H_{28}Br_2N_2O$	65,5	4,6	4,1	65,7	4,2	4,1	228 (4,81); 268 (4,37); 283 (4,36); 368 (4,00)	362 (4,43); 428 (3,98)	64

* All of the decomposition points were determined by filling the capillary at 20° below the indicated temperature.

† The molecular weight was confirmed by inverse ebullioscopy, while the compositions of IXb and Xb were also confirmed by determination of the bromine content.

‡ The spectrum of a solution in chloroform was recorded.

However, the long-wave absorption maximum of an acetic acid solution of IV is shifted hypsochromically relative to the absorption maximum of I, and the entire spectrum differs only slightly from the absorption spectrum of the 9,10-dimethylacridinium salt (Fig. 1). Moreover, in contrast to the spectrum of I, an absorption band with a maximum at 368 nm is presented in the absorption spectra of dioxane solutions of IV-X (Table 1 and Fig. 2). This band cannot be due to the acridan residue in IVa, which is not conjugated with the rest of the molecule, since acridans absorb no higher than 300 nm [4, 5]. Only the acridanylidene residue could be responsible for the absorption at ~370 nm. This is attested to by the UV spectra of 9-benzylidene-10-methylacridan (λ_{max} 394 nm) and 9-methylene-10-methylacridan (λ_{max} 384 nm), which, of course, were obtained only in solution.

The IR spectra of IV-X do not contain the absorption bands at 930-950 and 1650-1660 cm^{-1} that are characteristic for the pyran ring of spiropyrans of both the indoline series [6] and the acridine and phenanthridine series.

These facts are incompatible with formula IVa, although a similar structure in the indoline series has up to now been defended by German chemists [7].

We were able to establish the structure of IV-X in an investigation of their PMR spectra (Table 2 and Fig. 3), which showed that these compounds are chroman derivatives (IVb-Xb) rather than chromene derivatives (of the IVa type). The presence of two three-proton singlets of the N-methyl groups is characteristic for chloroform solutions of IV-X; this corresponds to the presence of two acridine residues of different chemical nature. A one-proton doublet (J_{MX} ~ 10 Hz) of a proton attached to the double bond of the acridanylidene residue (H_X) is observed at ~5.5 ppm. The nonequivalent protons in the 3' position (H_A and H_B) give a one-proton doublet at ~2.35 ppm for H_A, the lines of which are split (J_{AM} ~ 4 Hz) due to interaction with 4'-H (H_M), and a one-proton triplet for H_B because of the closeness of the J_{BM} and J_{AB} values (~13 Hz). The 4'-H signal appears as a one-proton multiplet at ~4 ppm.

The PMR spectra of IV-X in trifluoroacetic acid also confirm the structure of IVb-Xb. The N–CH_3 groups give a singlet at 4.2-4.4 ppm. The signals of the CH_2 and CH groups are overlapped by the base of the peak of the N–CH_3 groups and appear as a shoulder on the weak-field side. The overall area of the signal corresponds to the total number of protons of the indicated groups. This same region of the spectrum is characteristic for the N–CH_3 groups of 9,10-dimethyl- and 9-benzyl-10-methylacridinium salts in trifluoroacetic acid. It should be noted that the PMR spectrum of 9-benzylidene-10-methylacridan

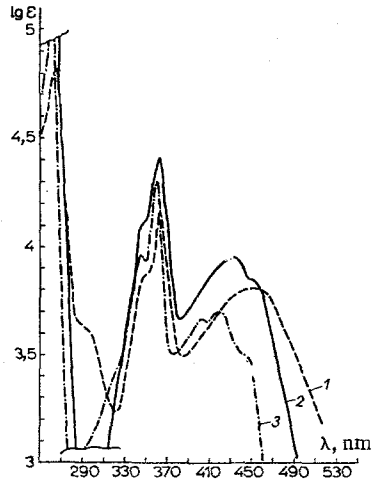


Fig. 1

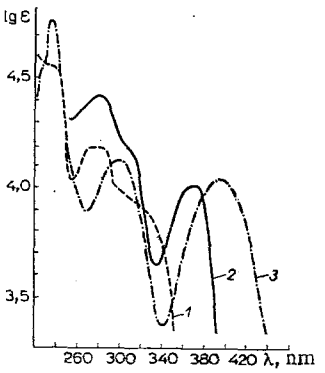


Fig. 2

Fig. 1. Absorption spectra of acridine derivatives (in 12% aqueous acetic acid): 1) 10-methylspiro[acridan-9,2'-chromene] (I); 2) 10-methyl-4'-(10-methyl-9-acridanylidenemethyl)spiro[acridan-9,2'-chroman] (IVb); 3) 9,10-dimethylacridinium methosulfate.

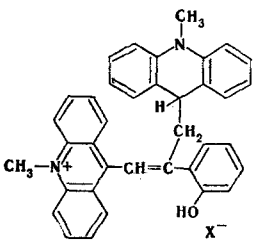
Fig. 2. Absorption spectra of 9-benzylideneacridan and spiro derivatives of acridine (I and IVb): 1) I in dioxane; 2) IVb in chloroform; 3) 10-methyl-9-benzylideneacridan in dioxane.

TABLE 2. PMR Spectra of IVb-Xb

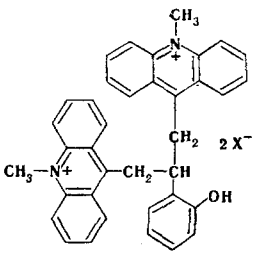
Compound	δ, ppm (CDCl₃)						J, Hz			
	N–CH₃	H_A	H_B	H_M	H_X	CH₃	AB	AM	BM	MX
IVb	3,32, 3,43	2,34	1,79	3,99	5,51	—	13,0	3,9	12,1	10,0
Vb	3,31, 3,42	2,31	1,80	3,95	5,50	2,21	13,5	3,9	12,1	10,0
VIb	3,32, 3,43	2,31	1,77	3,95	5,49	3,66	13,0	3,4	12,6	10,0
VIIb	3,36, 3,47	2,42	1,79	4,05	5,44	—	13,7	3,9	13,6	10,0
VIIIb	3,33, 3,43	2,37	1,80	~4,0*	5,53	3,92	13	4	13	10
IXb	3,35, 3,46	2,34	1,76	3,97	5,44	—	13,0	3,9	13,1	10,0
Xb	3,39, 3,49	2,42	1,75	4,06	5,48	—	13,2	3,6	13,2	9,6

*The multiplet of the H_M proton is partially overlapped by the intense signal of the O–CH_3 group.

in trifluoroacetic acid does not differ from the spectrum of 9-benzyl-10-methylacridinium iodide. This is due to the addition of a proton to the ethylene bond of benzylideneacridan with conversion of the latter to 9-benzyl-10-methylacridinium trifluoroacetate. At the same time, 9,10-dimethylacridan, which does not have basic properties [4], dissolves in CF_3COOH without chemical reaction with it and has the signal of an N–CH_3 group in the same region as in chloroform (3.28 ppm). In conformity with this, only a monoacid salt (XI) could be formed from IVa, and two signals of N–CH_3 groups with a still greater difference in chemical shifts should have been observed in both CF_3COOH and chloroform.



XI

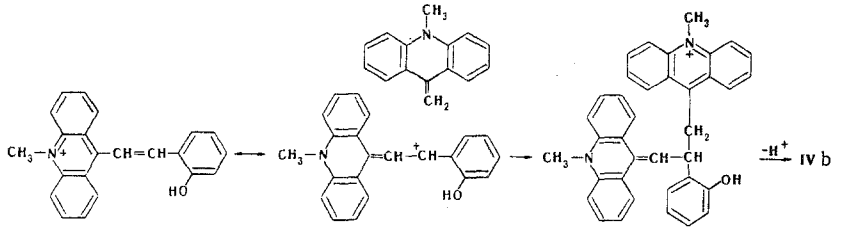


XII

The presence of a single signal of $N-CH_3$ groups in CF_3COOH is evidence for the equivalence of the acridine residues in salts of IV-X. This is possible only if there is not only the addition of a proton to the acridanylidene residue but also protonation of the chroman oxygen with cleavage of the C–O bond during the reaction with acid. As a result, a symmetrical dication (XII) should be formed. In fact, 2 moles of alkali per mole of perchlorate are consumed in the potentiometric titration of the perchlorate of IV, obtained by the addition of perchloric acid to an acetic acid solution of IV.

The 10-methyl-4'-(10-methyl-9-acridanylidenemethyl)spiro[acridan-9,2'-chroman] structure (IVb-Xb) should therefore be adopted for the products of the condensation of the 9,10-dimethylacridinium ion with salicylaldehyde and its derivatives. French chemists [8], in taking into account the erroneous formulas proposed earlier [3, 7], arrived at a similar conclusion regarding the structure of such products in the synthesis of spiropyrans of the indoline series.

Compounds IVb-Xb are apparently formed via a scheme similar to that recently established for the reaction of 1,1-diphenylethylene with salicylaldehyde [9]. The initially formed merocyanine form of compounds of the I-III type adds a proton and is converted to cation XIII. The latter reacts with a nucleophile – 9-methylene-10-methylacridan – which is obtained by reaction of piperidine with 9,10-dimethylacridinium methosulfate. Deprotonation of the adduct and closing of the ring give IVb-Xb.



XIII

EXPERIMENTAL

9,10-Dimethylacridinium Methosulfate. This compound was obtained by refluxing a solution of 6 g (31 mmole) of 9-methylacridine and 6 ml (62 mmole) of dimethyl sulfate in 120 ml of absolute toluene for 1 h. The resulting yellow-green crystals were removed by filtration [8.7 g (88%)] and crystallized from ethanol (1 :50) to give 7 g (71%) of 9,10-dimethylacridinium methosulfate with mp 233-234° (dec.). The product was quite soluble in water but insoluble in ether, benzene, and chloroform. UV spectrum in water, λ_{max}, nm (log ε): 258 (> 5.0), 342 (3.92), 358 (4.28), 400 (3.61), 419 (3.66). PMR spectrum in CF_3COOH, δ, ppm: 3.64 (9-CH_3, s), 3.98 ($CH_3SO_4^-$, s), 5.04 (10-CH_3, s).* Found: N 4.7; S 10.2%. $C_{16}H_{17}NO_4S$. Calculated: N 4.4; S 10.0%.

10-Methyl-4'-(10-methyl-9-acridanylidenemethyl)spiro[acridan-9,2'-chroman] (IVb). A 0.33-ml (3.13 mmole) sample of salicylaldehyde and 0.94 ml (9.4 mmole) of piperidine were added with stirring to a hot solution of 1.0 g (3.13 mmole) of 9,10-dimethylacridinium methosulfate in 40 ml of ethanol. The solution became dark brown, and a light-colored precipitate began to separate after a few minutes. The mixture was refluxed for 30 min and cooled, and the precipitate was removed by filtration and washed with ethanol and ether to give 0.68 g (84%) of IVb. The compound was dissolved in 8 ml of boiling benzene and filtered, and the filtrate was treated with 10 ml of ethanol to give 0.53 g (63%) of IVb with mp 195-196° (dec.). The product was soluble in chloroform, CCl_4, pyridine, and dioxane, only slightly soluble in ethanol, ether, and hexane, and insoluble in water.

Compounds Vb-Xb (Table 1) were similarly obtained in 85-99% yield. All of the substances are practically colorless in the crystallines state, except for the nitro derivative (VIIb), which is bright yellow. Compounds Vb and VIb were recrystallized from benzene (1 :7.5 and 1 :13, respectively), Xb was recrystallized from CCl_4 (1 :8), and VIIb was recrystallized from 50% benzene–ethanol (1 :30). For purification, VIIIb and IXb were dissolved in boiling benzene (1 :35 and 1 :5.5, respectively), the solutions were filtered, and the filtrates were treated with an equal volume of ethanol to precipitate the compounds. The yields of IVb-Xb after one recrystallization are presented in Table 1.

* The following abbreviations were used in describing the PMR spectra: s is singlet, d is doublet, t is triplet, q is quartet, and m is multiplet.

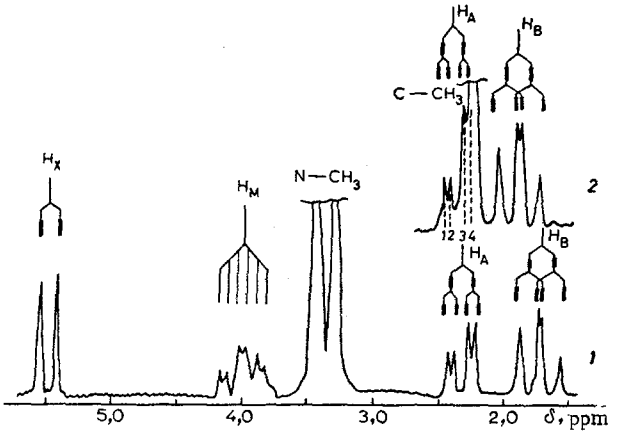


Fig. 3. PMR spectra of spiro derivatives of acridine (in $CDCl_3$): 1) IVb; 2) 6,10-dimethyl-4'-(10-methyl-9-acridanylidenemethyl)spiro[acridan-9,2'-chroman] (Vb).

9-Benzylidene-10-methylacridan. This compound [10] was obtained in 50% yield and had mp 140-141° (hexane). UV spectrum in dioxane, λ_{max}, nm (log ε): 235 (4.78), 300 (4.13), 394 (4.05); in CH_3COOH: 260 (> 5.0), 348 (3.93), 364 (4.22), 405 (3.70), 424 (3.74). PMR spectrum in CCl_4, δ, ppm: 3.35 (10-CH_3, s), 6.65 (=CH—, s), 6.95 (C_6H_5, s); in CF_3COOH: 4.66 (10-CH_3, s), 5.13 (9-CH_2, s), 6.96 (C_6H_5, s).

9-Methylene-10-methylacridan. This compound was obtained by the addition of 2 N NaOH to a solution of 1 mg of 9,10-dimethylacridinium iodide in 30 ml of water up to pH 10. The methylene base was extracted with 50 ml of dichloroethane, the extract was dried over Na_2SO_4, and the absorption spectrum was recorded: λ_{max} (D): 255, 285, 384 nm (0.55, 0.36, 0.20).

9,10-Dimethylacridan. This compound was obtained by the method in [11] in 84% yield and had mp 136-138° [from ethanol 1:30)]. UV spectrum in ethanol, λ_{max}, (log ε): 285 nm (4.24). PMR spectrum in $CHCl_3$, δ, ppm: 1.32 (9-CH_3, d), 3.28 (10-CH_3, s), 3.97 (9-H, q, J 7Hz); in CF_3COOH: 1.47 (9-CH_3, d), 3.23 (10-CH_3, s), 3.87 (9-H, q, J 7 Hz).

9-Benzyl-10-methylacridan. This compound was obtained by the method in [11] in 76% yield and had mp 106-107° [from ethanol (1:16)]. UV spectrum in ethanol: λ_{max} 287.5 nm, log ε 4.1. PMR spectrum in CCl_4 (25%), δ, ppm: 2.74 (9-CH_2, d), 3.12 (10-CH_3, s), 4.04 (9-H, t, J 6 Hz); in CF_3COOH: 1.95 (10-CH_3, s), 2.88 (9-CH_2, d), 4.03 (9-H, t, J 6 Hz).

9-Benzyl-10-methylacridinium Iodide. This compound was obtained by the method in [11] in 75% yield and had mp 224-227° [dec., from water (1:35)]. UV spectrum in water, λ_{max}, nm (log ε): 232.5 (4.33), 261 (4.90), 346 (3.87), 362 (4.16), 402 (3.63), 422 (3.68). The PMR spectrum in CF_3COOH was identical to the spectrum of 9-benzylidene-10-methylacridan in CF_3COOH.

The UV spectra of (1 to 5) $\cdot 10^{-5}$ M solutions of the compounds were recorded with an SF-8 spectrophotometer. The PMR spectra of IVb-VIIb and IXb were recorded with a Varian HA-100D spectrometer, those of VIIIb, Xb, and 9,10-dimethylacridinium methosulfate and 9-benzylidene-10-methylacridan were recorded with an RYa-2305 spectrometer (60 MHz), while those of the acridans and 9-benzyl-10-methylacridinium iodide were recorded with a JNM-3 spectrometer (40 MHz). The spectra of IVb-Xb were analyzed within the ABX approximation. The spectra of IVb-Xb were recorded with hexamethyldisiloxane (HMDS) as the internal standard; either HMDS or tetramethylsilane was used in the remaining cases.

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