REACTION OF ACRIDINE PROTON SALTS WITH ARYLAMINES IN THE PRESENCE OF SULFUR

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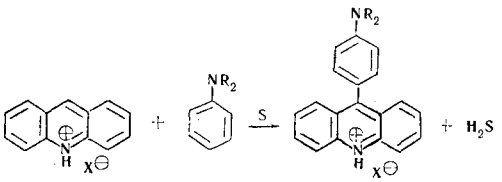
The reaction of acridine proton salts with arylamines in the presence of sulfur was studied. It is shown that various arylamines of the benzene and naphthalene series, both free and substituted, form the corresponding aminoarylacridines in high yields in this reaction.

In previous papers [1, 2] we reported a method for the aminoarylation of acridines which consisted of the reaction of quaternary acridinium salts with arylamines in the presence of sulfur.

In this paper we have investigated the possibility of the introduction of aromatic amine residues into acridine proton salts. The shift in the electron density toward the heterocyclic nitrogen makes it possible for nucleophilic reagents to attack acridine and particularly its quaternary salts at the 9 position. It might have been assumed that this shift would be even more significant in the proton salts, and that consequently nucleophilic attack would be appreciably facilitated.

We found that acridine proton salts actually readily react with arylamines in the presence of sulfur at 120-140°. Here, as in the case of quaternary salts, the aromatic amines react with the acridine ring at the para position rather than at the amino group to form salts of 9-(p-aminoaryl)acridines, which can be readily converted to the corresponding bases. The reaction is accompanied by hydrogen sulfide evolution.



An investigation of the applicability of this reaction indicated that it is characteristic for diverse acridine salts of both oxygen-containing and oxygen-free acids (nitrates, sulfates, and hydrohalides). As for the arylamine component, primary, secondary, and tertiary amines of the benzene series and naphthylamines enter into the reaction. The meta-substituted anilines (m-toluidine, m-phenylenediamines) that we investigated also form the corresponding aminoarylacridines in fair yields.

4-Aminobiphenyl also reacts with acridine proton salts. In the process, the reaction center, as might be assumed, is not transferred to the biphenyl system: the addition of the acridine residue occurs at the ortho position with respect to the amino group rather than at the p' position. In the case of N,N-dimethylaminobiphenyl, in which the ortho position is sterically hindered, the corresponding aminoarylacridine is not formed, and only thioacridone is isolated from the reaction mass. Thin-layer chromatography indicates the absence of any other products in the reaction mixture.

As seen from Table 2, all of the 9-aminoarylacridine salts are deeply colored, high-melting, crystalline substances which are quite soluble in water and most polar solvents. All of the salts are readily hy-

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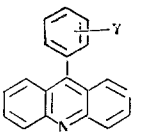
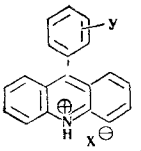
TABLE 1.



Y	Mp (°C)	Empirical formula	Found, %			Calculated, %			Yield, %
			C	H	N	C	H	N	
4-NH_2	269—270	$C_{19}H_{14}N_2$	84,5	5,3	10,3	84,4	5,2	10,3	95,0
4-NCH_3H	258—259	$C_{20}H_{16}N_2$	84,5	5,6	—	84,5	5,7	9,9	92,5
4-$N(CH_3)_2$	279	$C_{21}H_{18}N_2$	85,1	6,1	9,3	84,9	6,1	9,4	94,0
2-NH_2-5-C_6H_4	260	$C_{25}H_{18}N_2$	86,5	5,5	7,8	86,7	5,2	8,0	15,0
2,4-$(NH_2)_2$	—	$C_{19}H_{15}N_3$	80,3	5,8	—	80,0	5,3	14,7	91,5
2-NH_2-3,4-benzo*	300	$C_{23}H_{16}N_2$	86,0	5,3	9,2	86,2	5,0	8,7	85,5
2-CH_3-4-NH_2	229—230	$C_{20}H_{16}N_2$	84,5	5,9	10,0	84,5	5,7	9,9	70,5

*2-Aminonaphthyl.

TABLE 2.



X-	Y	Mp (°C)	Empirical formula	Found, %				Calculated, %				Yield, %
				C	H	N	Hal	C	H	N	Hal	
Cl	4-NH_2	295	$C_{19}H_{14}N_2 \cdot HCl$	74,2	5,0	—	11,2	74,4	4,9	9,1	11,6	95,1
Cl	4-$NHCH_3$	262	$C_{19}H_{16}N_2 \cdot HCl$	75,5	5,5	—	11,8	74,9	5,3	8,4	11,1	96,0
Cl	4-$N(CH_3)_2$	273	$C_{21}H_{18}N_2 \cdot HCl$	75,0	5,5	8,6	10,9	75,3	5,7	8,4	10,6	92,0
Cl	2-NH_2-3,4-benzo*	—	$C_{23}H_{16}N_2 \cdot HCl$	—	—	8,1	10,1	—	—	7,9	9,9	88,5
Br	2-NH_2	309—310	$C_{19}H_{14}N_2 \cdot HBr$	64,7	4,2	—	—	65,0	4,3	7,9	—	92,0
Br	4-$NHCH_3$	253—254	$C_{20}H_{16}N_2 \cdot HBr$	65,9	4,8	7,6	22,0	65,8	4,7	7,7	21,9	96,0
Br	4-$N(CH_3)_2$	270	$C_{21}H_{18}N_2 \cdot HBr$	66,5	5,2	7,7	20,9	66,5	5,0	7,4	21,1	94,0
I	4-NH_2	274	$C_{19}H_{14}N_2 \cdot HI$	57,4	4,1	7,0	—	57,3	3,8	7,0	31,9	91,6
I	4-$NHCH_3$	237—238	$C_{20}H_{16}N_2 \cdot HI$	58,2	4,2	—	—	58,3	4,1	6,8	30,9	96,0
I	4-$N(CH_3)_2$	227	$C_{21}H_{18}N_2 \cdot HI$	59,2	4,5	6,6	—	59,1	4,5	6,6	29,8	95,3
NO_3	4-NH_2	227—229	$C_{19}H_{14}N_2 \cdot HNO_3$	68,4	4,6	12,8	—	68,5	4,5	12,6	—	98,0
NO_3	4-$NHCH_3$	240—242	$C_{19}H_{16}N_2 \cdot HNO_3$	69,1	4,9	11,9	—	69,0	5,3	12,1	—	92,5
NO_3	4-$N(CH_3)_2$	—	$C_{21}H_{18}N_2 \cdot HNO_3$	69,4	5,3	11,9	—	69,8	5,3	11,6	—	94,5

*2-Aminonaphthyl.

drolyzed, so that their synthesis and purification must be accomplished in anhydrous solvent. Dilution with water of the alcohol solutions of the salts is sufficient to obtain the free bases. All of the 9-aminoaryl-acridines are yellow, crystalline substances which are moderately soluble in organic solvents.

In conclusion, it should be stated that the reaction described here makes it possible to obtain various 9-aminoarylacridines from various acridine salts; the synthesis of the 9-aminoarylacridines by closing of the acridine ring was previously inaccessible.

EXPERIMENTAL

9-(p-Aminoaryl)acridines and Their Salts (Tables 1 and 2). A mixture of 0.02 mole of anhydrous acridine salt, 0.03-0.04 mole of the appropriate arylamine, and 0.06 g-atom of powdered sulfur was heated at 120-140° for 1.5-2 h with constant stirring. The melt was thoroughly pulverized and repeatedly washed with hot heptane or benzene. The residue was recrystallized from absolute alcohol. To obtain the free base, the 9-aminoarylacridine salt was dissolved in ethanol, and the solution was diluted with water (1:2) and treated with sodium carbonate to pH 7.5-8.0. The resulting precipitate was washed with water, dried in a desiccator, and crystallized from a suitable solvent.

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2. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, Dokl. Akad. Nauk SSSR, 188, 376 (1969).