MECHANISM OF THE REACTION OF ARYLAMINES WITH ACRIDINES IN THE PRESENCE OF SULFUR

O. N. Chupakhin, V. A. Trofimov,
and Z. V. Pushkareva

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The mechanism of the aminoarylation of acridines in the presence of sulfur was investigated. It was established that the process takes place in two steps: formation of an intermediate arylamine–acridine complex and oxidative dehydrogenation of the complex by sulfur. The second step probably is accomplished via an ionic mechanism.

We have previously reported a new reaction of acridine and its salts leading to the formation of 9-(p-aminoaryl)acridines in high yields [1,2]. In this paper we examine the mechanism of this reaction.

The process for the preparation of aminoarylacridines, carried out at 110-130 deg C in the presence of sulfur, is accompanied by hydrogen sulfide evolution, and in addition, a small amount of thioacridine (or N-alkylthioacridines when quaternary salts are used) is detected in the reaction mass in some cases.

It might be assumed that the formation of 9-(p-aminoaryl)acridines proceeds through a step involving intermediate 9-mercapto-substituted acridine. Experiments indicated that sulfur does not thionate acridine and its salts under the reaction conditions (110-130 deg). The formation in the reaction mixture of thioacridones can be explained by competitive sulfuration of the acridines at higher temperatures [3]. The appearance of thioacridine (or N-alkylthioacridones) in the reaction mixture at temperature up to 160 deg can be detected only by spectroscopy (Fig. 1), while thionation of the acridines becomes apparent at 180-190 deg, and appreciable amounts of sulfuration products can be isolated along with the major compounds.

As seen from Fig. 1, acridine methiodide (AM) is not sulfurated at 110-130 deg, as confirmed by the identical character of the absorption bands in the visible portion of the spectrum of the starting AM and a mixture of it with sulfur, held at 130 deg for 1 h. Appreciable amounts of N-methylthioacridone begin to form at 180-190 deg, as evidenced by the appearance of an absorption band similar to the absorption band of pure N-methylthioacridone.

Further study of the reaction of acridines with arylamines indicated that another type of reaction occurs in the absence of sulfur. It was established that acridine (as well as its salts) and aromatic amines undergo a rapid intermolecular reaction at room temperature to form unstable compounds which should be ascribed to charge-transfer complexes (CTC). The following experimental data are evidence for this.

1. When arylamine is added to alcohol or dimethylformamide solutions of acridine (or its salts), the color deepens. In the process, a new absorption band appears in the long-wave portion of the spectrum (Fig. 2). This band is not detected in the spectra of any of the starting components, and we have ascribed it to the absorption associated with charge transfer during the formation of a complex [4].

2. As seen from Fig. 3, the complex of AM with dimethylaniline (DMA) in dimethylformamide dissociates rapidly to the starting components when the solution is diluted, as evidenced by the decrease in the extinction and the shift in the absorption maximum to the short-wave side (i.e., starting compounds).

Solutions of these CTC are not subject to the fundamental law of light absorption. This means that the donor (arylamine) and acceptor (acridine or its salts) molecules in addition to the CTC are absorbing

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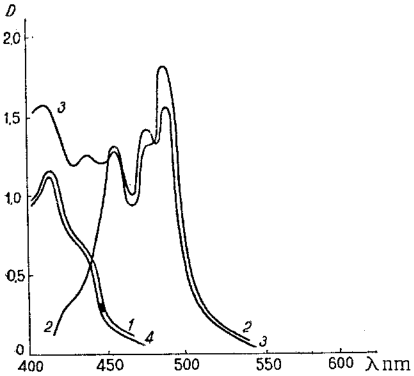

Fig. 1

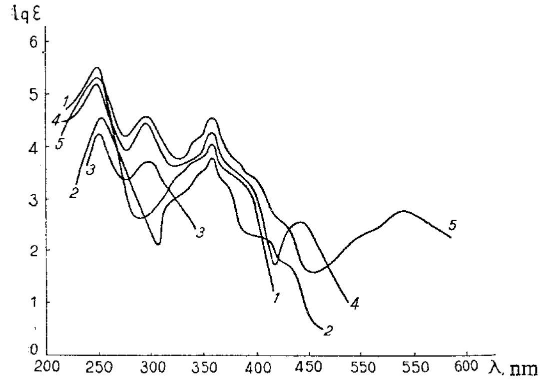

Fig. 2

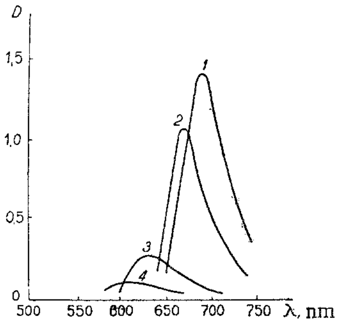

Fig. 3

Fig. 1. Absorption spectra in the visible region: 1) acridine methiodide; 2) mixture of acridine methiodide with sulfur, held at 130° for 1 h; 3) mixture of acridine methiodide with sulfur, held at 180° for 1 h; 4) methylthioacridone.

Fig. 2. Absorption spectra in the UV and visible regions (alcohol): 1) acridine; 2) acridine methiodide; 3) dimethylaniline; 4) equimolar mixture of acridine and dimethylaniline; 5) equimolar mixture of acridine methiodide and dimethylaniline.

Fig. 3. Absorption spectra in the visible region (dilution of the acridine methiodide–dimethylaniline complex in dimethylformamide): 1) 7% complex (0.185 mole/liter); 2) 5% complex (0.149 mole/liter); 3) 2.5% complex (0.0745 mole/liter); 4) 1.25% complex (0.0373 mole/liter) (the spectra were obtained immediately after mixing of solutions of the components at 0°.

particles. A consequence of this is the appearance of quasi-autonomic regions in the spectra of such solutions (Fig. 2).

3. Alcohol solutions of the acridine salts containing equimolar amounts or excess arylamine are decolorized by ether. In the process, the starting salt is precipitated, and the starting arylamine can be isolated from the solution.

All of these observations indicate the complex character of the compounds. Similar behavior of the CTC is noted in the studies of Andrews and Kiefer [5]. In an unpublished work, Mason [6] indicates the formation of a CTC between AM and DMA.

The structure of such complexes is of great interest. The assumption of the coordinating role of the quaternary nitrogen grouping in pyridine salts previously advanced by Emmert et al. [7] seems unlikely to us in this case since the complexes tend to give not only quaternary salts but also acridine itself. Data on the direct bending of the aromatic amine with the ring carbon atoms [8] seem more reliable.

We have noted that complexing is not observed when the 9 position of the acridine ring is blocked by bulky substituents; for example, 9-phenylacridine methiodide does not form complexes with arylamines.

On the basis of the above information, a structure corresponding to formula can be assigned to the complex formed between the acridine salt and arylamine.

Thus the reaction of acridine (and its salts) with arylamines in the presence of sulfur can be represented as a two-step process: 1) formation of an intermolecular complex between the starting acridine and arylamine; 2) conversion of complex I to aminoarylacridine under the influence of sulfur.

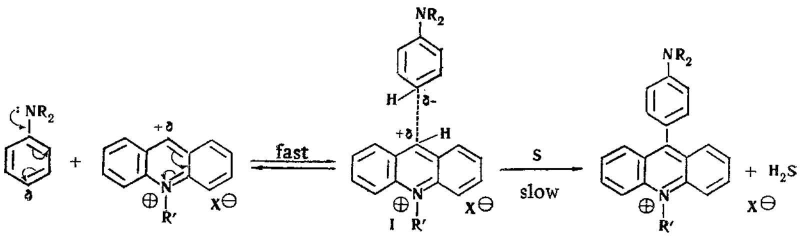

TABLE 1. Effect of Sulfur on the Reaction of Acridine and Its Salts with Arylamines

Starting acridine	Reaction temp.	Reaction time, h	Yield, %	
			in the absence of sulfur	in the presence of sulfur
Base	150—180	3—5	0	13
Methiodide	110—130	1,5—2	5	91
Hydrochloride	110—120	1,5—2	40	92

TABLE 2. Effect of Solvents on the Reaction of Acridine Hydriodide with Dimethylaniline in the Presence of Sulfur (reaction time 1.5 h, 100 deg)

Solvent	Solvent: dipole moment, D	Temperature at start of reaction	Yield, %
p-Xylene	0	No reaction	
Dioxane	0,45	No reaction	
Butanol	1,66	98—100	86
Dimethylformamide	3,82	87—88	93
Nitrobenzene	3,99	86—87	96

TABLE 3. Aminoarylation of Acridine and Its Salts with Dimethylaniline in the Presence of Sulfur

Starting acridine	Reaction temp.	Reaction time, h	Temperature at start of reaction*	Yield, %
Hydroiodide	120	1,5	102	98,7
Methiodide	120	1,5	104	91,0
Ethiodide	120	1,5	105	88,0
Base	180	5,5	170	13,5

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*The start of the reaction was fixed from the evolution of hydrogen sulfide, which was pumped off from the reaction vessel and passed through a lead nitrate solution.

Sulfur acts as a dehydrogenation agent in this reaction. If the process is carried out in the absence of sulfur, 9-(p-aminoaryl)acridines are formed in small yields or do not form at all (Table 1).

Considering its conversion to the reduced state (S^{-2}) in H_2S, sulfur,probably acts as an oxidant. Hydrogen sulfide can, of course, also form via a homolytic mechanism, but the following experimental facts are evidence in favor of the ionic character of the reaction.

First, the process takes place with higher yields in more polar solvents than in less polar solvents. The reaction is not observed in nonpolar solvents (Table 2).

Second, radical inhibitors, for example, phenyl-β-naphthylamine, do not affect the reaction of acridines with arylamines in the presence of sulfur.

Third, no EPR signals are observed in samples of the reaction mass taken at different times from the start of the reaction.

The literature also contains data which indicate that sulfur heterolytically attacks unsaturated systems at temperatures below 140 deg [9].

In order to study the reactivity of the various acridines we investigated the hydroiodide and several alkyl iodides. In agreement with the concepts set forth regarding the mechanism of the reaction, we observed a qualitative correlation between the electron-donor character of the residue attached to the heteroatom (i.e., a positive charge on the carbon atom in the 9-position) and the reactivity of the compound characterized by the temperature at the start of the reaction and the product yield (Table 3).

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