[2,4-Dimethyl-3-(p-methoxyphenyl)benzo[f]dihydro-1-quinolylidene]-(5,6-benzo-2-quino]-ethane (V) [6]. A 0.07-g (0.1 mmole) sample of hydroxystyryl IV was dissolved by heating in 30 ml of ethanol, after which 10 ml of 10% aqueous KOH solution was added, and the mixture was heated on a water bath for 5 min. After 30 min, the resulting precipitate was removed by filtration, washed with water, dried, and crystallized from the ethanol—acetone (1:2) to give 0.03 g (62%) of shiny violet plates with mp 172-174°. UV spectrum: λ_{max} 668 nm (log ε 3.0); in acetone 696 (log ε 3.25); in chloroform 706 nm (log ε 4.60. Found: C 81.7; H 5.9%. $C_{34}H_{27}NO_2 \cdot H_2O$. Calculated: C 81.8; H 5.8%.

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MECHANISM OF NUCLEOPHILIC SUBSTITUTION OF HYDROGEN IN AZINES.

II.* KINETICS OF THE CONDENSATION OF N-METHYLACRIDINIUM IODIDE WITH AROMATIC AMINES

O. N. Chupakhin and V. L. Rusinov

UDC 547.835.9:541.127:542.953

A study of the kinetics of the reaction of N-methylacridinium iodide with arylamines shows that the reaction proceeds via a stepwise bimolecular mechanism with the formation of an intermediate.

The mechanism of reactions involving the nucleophilic substitution of hydrogen in the azine series has often been postulated as "addition—cleavage" [2-4]. However, data that show that even the well-studied nucleophilic substitution of halogen in aromatic nitro compounds cannot always be interpreted within the framework of this mechanism were recently obtained [5]. The mechanism of reactions involving nucleophilic substitution of aromatically bonded hydrogen in azines has been investigated kinetically only in one study [1] in the case of the reaction of the acridinium cation with active methyl-substituted heterocycles. This reaction evidently proceeds with the participation of the carbanion of the CH-active compound. The kinetics of the reactions of azinium cations with uncharged nucleophiles have not been investigated, although the absence of a charge on the nucleophile may superimpose peculiarities on the trend of the process.

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*See [1] for communication I.

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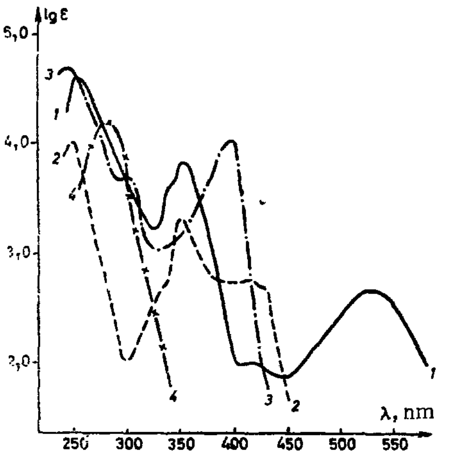


Fig. 1

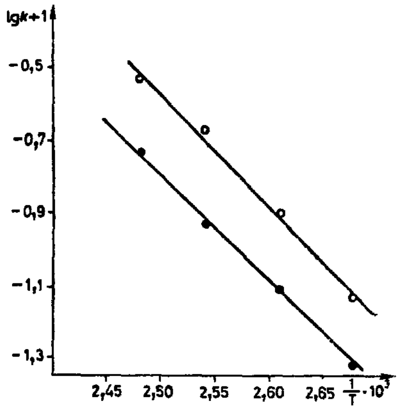
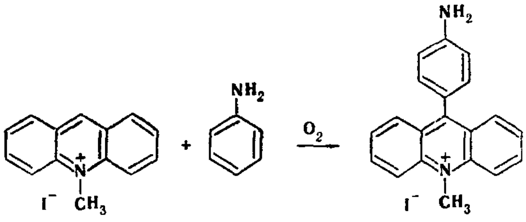


Fig. 2

Fig. 1. Electronic spectra in dimethylformamide: 1) 10-methyl-9-(4-aminophenyl)acridinium iodide (II); 2) N-methylacridinium iodide (I); 3) N-methylacridone (III); 4) 9-aminophenyl-9-benzylamino-10-methylacridan.

Fig. 2. Dependence of log k of 1/T for the reaction of I with aniline (●) and dimethylaniline (○).

In this connection, in the present research we made kinetic studies of the condensation of N-methylacridinium iodide (I) with a number of arylamines.



I II

The quaternary and protic salts of acridine react smoothly with aromatic amines in the presence of an oxidizing agent (sulfur [6] or air oxygen [7]). Owing to the high yield and deep colors of the products, this reaction can be used as a convenient model for the study of the mechanism of nucleophilic substitution of aromatically bonded hydrogen.

The reaction of I with aniline was investigated in greater detail. In addition to the primary condensation reaction, slow oxidation of I to N-methylacridone (III) also occurs. The condensation product — 10-methyl-9-(4-aminophenyl)acridinium iodide (II) — is not oxidized under the reaction conditions.

The process was monitored by spectrophotometry. The spectral region near 530 nm, which is free of the absorption of the starting and side compounds, was selected for the determination of the accumulation of II. The absorption of side product III is superimposed on the absorption of the starting cation I and product II (Fig. 1, and N-benzylamine was therefore added to the sample after measurement of the concentration of II. N-Benzylamine reacts instantaneously with I and II to give, respectively, 10-methyl-9-benzylaminoacridan and 10-methyl-9-aminophenyl-9-benzylaminoacridan [8], which do not absorb near 400 nm.

It was shown that the trend of the kinetic curve does not depend on the air-flow rate from 6 to 35 cm^3/min. This means that under selected conditions (flow rate 20 cm^3/min) the reaction proceeds in the kinetic region. The temperature dependence of the reaction rate constants obey the Arrhenius equation (Fig. 2), and this makes it possible to exclude a diffusion factor.

The kinetic curves of the reaction of N-methylacridinium iodide with aniline at 120° are presented in Fig. 3.

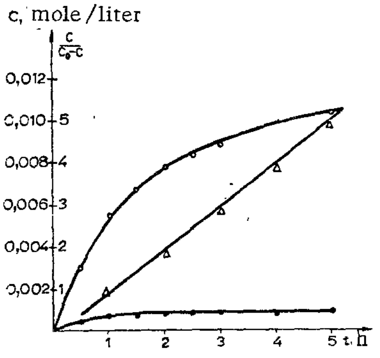


Fig. 3

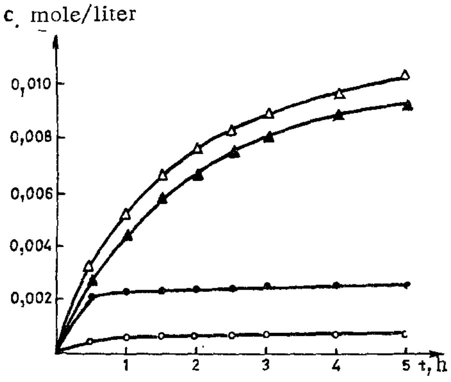


Fig. 4

Fig. 3. Kinetic curves of the reaction of N-methylacridinium iodide (I) with aniline: ○) 10-methyl-9-(4-aminophenyl)acridinium iodide (II) concentration; ●) N-methylacridone(III) concentration; Δ) dependence of $C/(C_0 - C)$ on time.

Fig. 4. Kinetic curves of the reaction of N-methylacridinium iodide (I) with aniline Δ) 10-methyl-9-(4-aminophenyl)acridinium iodide (II) concentration; ○) N-methylacridone (III) concentration in the case of the addition of neozon-D; ▲) and ●) N-methylacridone (III) concentrations in the case of the addition of azobisisobutyronitrile.

The rate of formation of acridone III is much lower than the rate of the principal reaction and its concentration changes only slightly during the reaction; the consumption of I in the case of its oxidation to III was therefore disregarded in the determination of the rate constants.

It was established that the partial reaction orders with respect to starting acridinium salt I and aniline, determined by the method of initial rates [9] are, respectively, 1.04 and 0.95.

The reaction rates at 100-130° were measured (Table 1). The kinetic curves treated by the integral method satisfy a second-order equation (Fig. 3).

A small kinetic isotope effect ($k_H/k_D = 2.28$) was observed when the reaction was carried out with 2,4,6-d_6-aniline.

The activation energies were determined for the reactions of methylacridinium ion I with aniline and dimethylaniline and were found to be, respectively, 13.1 and 13.0 kcal/mole. The difference in the rates of these reactions in the face of equal activation energies is due to entropy factors.

The presence of a free-radical inhibitor (neozon-D) and initiator (azobisisobutyronitrile) does not affect the rate of oxidative condensation. The absence of an effect by these additives cannot, however, exclude a process with the participation of radical particles in a cage. The additives do affect the rate of formation of N-methylacridone (Fig. 4), and this constitutes evidence for radical character of the oxidation of N-methylacridinium iodide.

The reaction is not catalyzed by base: the addition to the reaction mixture of N,N-dimethyl-m-xylidine, which is incapable of arylating the acridinium ion [6], does not change the reaction rate.

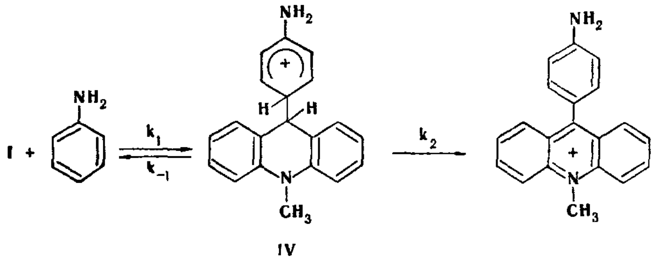
The condensation of the acridinium ion with aromatic amines involves interrelated processes of nucleophilic substitution of hydrogen in the I cation and electrophilic substitution of hydrogen in the nucleophilic agent. The results obtained in this study make it possible to express certain judgments regarding the mechanism of the reaction, particularly regarding that aspect which touches upon substitution of a proton in the arylamine.

According to the currently existing concepts regarding the dynamics of aromatic electrophilic substitution [10], the low value of the kinetic isotope effect (2 as against 6-8

TABLE 1. Rate Constants for the Reaction of N-Methylacridinium Iodide with Arylamines as a Function of Temperature (liter/mole sec)

Arylamine	Temp., °C			
	100	110	120	130
Aniline	0,0081±0,0002	0,0124±0,0002	0,0216±0,0002	0,0293±0,0003
N,N-Dimethylaniline	0,0047±0,0002	0,0077±0,0002	0,0118±0,0002	0,0180±0,0003
N-Methylaniline			0,0170±0,0002	
o-Toluidine			0,0198±0,0002	
2,4,6-d_3-Aniline			0,0095±0,0002	

in the case of a synchronous mechanism) and the absence of base catalysis constitutes evidence for reaction via a stepwise mechanism. The first step in the process consists in the addition of the arylamine to the acridinium cation to give σ complex IV. The hydrogen that is electrophilically replaced in the arylamine does not depart synchronously with addition but rather in the following non-rate-determining step:



In conformity with the above scheme the appearance of a small kinetic isotope effect can be explained by the considerable magnitude of the rate constant (k_{-1}) of the reverse reaction.

EXPERIMENTAL

The physical characteristics of the quaternary salts of 9-aminoarylacridines were presented in [7]. The starting acridine was purified by repeated crystallization from heptane to give a material with mp 110-111°.

N-Methylacridinium Iodide (I). A 4.4-g (14 mmole) sample of acridine was dissolved in 20 ml of dimethylformamide (DMF), after which 5.0 g (35 mmole) of methyl iodide was added, and the mixture was heated at 80° for 10 h. The precipitated crystals were removed by filtration and crystallized from alcohol to give a product with mp 225-229° (sublimation).

The primary and secondary amines were purified by fractionation over zinc, and the tertiary amines were treated with an equal volume of acetic anhydride and steam distilled, after which the amine was separated and fractionated. The boiling points and n_D^{20} values were in agreement with the data in [11].

The DMF was purified by the method in [12], refluxed with P_2O_5, and vacuum fractionated twice to give a product with n_D^{20} 1.4295 (literature value 1.4294 [11]).

Method Used for the Kinetic Experiments. A weighed sample of N-methylacridinium iodide was dissolved in 10 ml of DMF, and the solution was placed in a thermostat, the temperature in which was maintained with an accuracy of ±0.1°. The sample was maintained at the selected temperature for 10 min, after which a sample was withdrawn for determination of the initial concentration of I. The calculated amount of arylamine was then added with simultaneous bubbling in of air, the flow rate of which was maintained at 20 cm^3/min by means of a monostat-rheometer system.

The analysis was made by the sample-selection method: 0.1 ml of the reaction mixture was diluted with 10 ml of alcohol, and the optical density at 530-560 nm was measured with an SF-4A spectrophotometer. A 0.05-ml sample of benzylamine was added to the sample, and the optical density at 400 nm was measured in order to determine the concentration of acridone III.

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FORMATION OF A SPIRAN STRUCTURE IN THE CONDENSATION OF 2-AZAFLUORENE WITH ESTERS OF α, β-UNSATURATED ACIDS

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4'-Hydroxy-3-methyl-2',6'-diphenyl-3'ethoxycarbonylspiro(2-azafluorene-9,1'-cyclohex-3'-ene) was obtained by condensation of 3-methyl-2-azafluorene with ethyl cinnamate in the presence of potassium. The chemical mechanism of its formation and its three-dimensional structure are discussed.

Fluorene undergoes the Michael reaction with nitriles of α,β-unsaturated acids (for example, see [1]), but it does not react with their esters in the presence of alkaline catalysts [2]. We have established that the reaction of 3-methyl-2-azafluorene (I) with ethyl cinnamate in the presence of potassium leads to 4'-hydroxy-3-methyl-2',6'-diphenyl-3'-ethoxycarbonylspiro(2-azafluorene-9,1'-cyclohex-3'-ene) (II), the chelate structure of which is confirmed by the IR spectral data and also by the presence in the PMR spectrum of a singlet of an OH group at 12.65 ppm.

Keto ester II was converted to oxospiran V by hydrolysis and decarboxylation. Azafluorrene I evidently initially undergoes Michael condensation with ethyl cinnamate, and the resulting 3-methyl-9-bis(1-phenyl-2-ethoxycarbonylethyl)-2-azafluorene undergoes subsequent Dieckmann cyclization to give spiro compound II.

Ethyl acrylate and ethyl crotonate were subjected to a similar condensation with azafluorene I. Spirans III (previously obtained by a different method [3]) and IV were obtained. (See scheme on following page.)

It was shown by the double-resonance and INDOR methods that the signal at 5.62 ppm in the PMR spectrum of II (Table 1) is due to an aromatic proton that couples with two other protons with spin–spin coupling constants (SSCC) J = 8.0 and 1.5 Hz. Consequently, the

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