NEW REACTION IN THE ACRIDINE SERIES

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A new reaction in the acridine series – reaction of its salt or the base with the salts or bases of N-heterocyclic compounds containing an active methyl group in the presence of sulfur – was investigated. It is shown that 9-acridinylheterylmethanes are formed as a result of this reaction.

Previously one of us observed that acridine and its quaternary and proton salts react with arylamines in the presence of sulfur to form 9-(p-aminoaryl)acridines [1, 2]. The reaction of the acridinium cation with arylamines leads to products which are similar to azo-coupling products.* Our observations [1, 2] and literature data [3] enable us to assume that N-heteroaromatic compounds with an active methyl group which are capable of coupling may react similarly with the acridinium anion in the presence of sulfur. The addition of substances with an active methylene group (acetylacetone, acetoacetic ester, etc.) to acridine to form adducts – acridane derivatives which can be oxidized to the corresponding 9-derivatives of acridine –was described in [5]. The formation of adducts or "coupling" products at the methyl group of heteroaromatic compounds is unknown.

We have found that acridine and its proton salts in the presence of sulfur smoothly react with N-heteroaromatic compounds containing an active methyl group. As a result of this study we have obtained acridinylheterylmethanes (Table 1). The reaction is carried out in the fused state or in dimethylformamide in the presence of sulfur at 125-130° for 2-3 h. The process is accompanied by hydrogen sulfide evolution.

The acridinylpyridylmethanes and 9-acridinyl-2-benzothiazolylmethane were obtained using the hydrochlorides of the starting compounds. The picolines do not condense with the acridine base, while 4-picoline gives I in low yield by reaction with acridine hydrochloride; appreciable amounts of thioacridone are formed in the process. On the other hand, acridinylquinolinylmethanes are formed only from the bases of the starting methylquinolines and acridine. If, however, one takes even one of the components of the reaction in the form of the hydrochloride, only thioacridone can be isolated. No acridinylheterylmethanes can be isolated by reaction with 2,6-lutidine and 2-methylbenzimidazole. This is apparently explained by the low lability of the hydrogen atoms of the methyl groups. The reaction mechanism is still not clear, but our observations enable us to assume that there is a certain optimum activity of the methyl group of the heterocycle which can enter into reaction with acridine.

The diheterylmethane structure of the compounds obtained was demonstrated in the case of the product from the reaction of acridine with 4-picoline (I). Oxidation of this product gives a diheteryl ketone which is identical to the ketone obtained by hydrolysis of the product of condensation of I with p-nitrosodimethylaniline. The condensation with p-nitrosodimethylaniline attests to the presence of a reactive methylene group joining the two heteroaromatic residues.†

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*A certain analogy in the reaction of the acridinium cation (positive charge in the 9 position) and the diazonium cation was indicated in one of Dimroth's papers; however, this position is disputed [4].

† Compare a similar reaction for 2,2'-diquinolylmethane [6].

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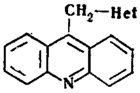
TABLE 1. 9-Acridinylheterylmethanes



Comp.	Het	Method	mp	Empirical formula	Found, %			Calc., %			Yield, %
					C	H	N	C	H	N	
I	4-Pyridyl	A	126—127	$C_{19}H_{14}N_2$	84,2	5,4	10,2	84,4	5,2	10,4	56
II	2-Pyridyl	A	133—134	$C_{19}H_{14}N_2$	84,2	5,3	10,4	84,4	5,2	10,4	32
III	2-Benzothiazolyl	A	198—199	$C_{21}H_{14}N_2S$**	77,7	4,3	8,8	77,3	4,3	8,5	18
IV	4-Quinolinyl	B	240—242	$C_{23}H_{16}N_2$	86,1	5,3	8,7	86,2	5,0	8,7	56
V	2-Quinolinyl	B	160—161	$C_{23}H_{16}N_2$	86,3	5,3	8,6	86,2	5,0	8,7	31

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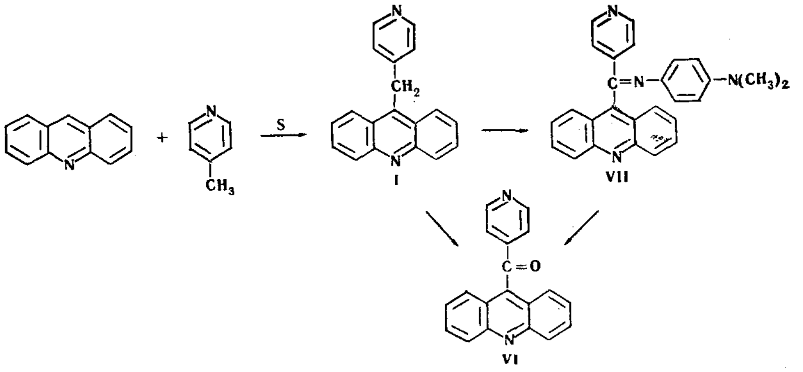
[*] Compounds I and II were crystallized from 60% ethanol, IV and V were crystallized from 80% ethanol, and III was crystallized from 95% ethanol.

[†] Found %: S 9.6. Calculated %: S 9.8.



The reaction described here makes it possible to obtain the previously unknown acridinylheterylmethanes which are of interest as model compounds for the study of cyanin dyes. The reaction may serve as a characteristic of the relative reactivity of the methyl groups of N-heteroaromatic compounds.

EXPERIMENTAL

Preparation of Acridinylheterylmethanes. A. A mixture of acridine hydrochloride, the hydrochloride of the methyl heterocycle, and sulfur in a molar ratio of 1 : 2 : 3 was stirred in the minimum amount of dimethylformamide at 130-135° until hydrogen sulfide evolution stopped (about 3 h). The reaction mass was dissolved in 1 N HCl or ethanol, and the base was isolated with 10% NaOH and crystallized (II was first chromatographed on aluminum oxide).

B. A mixture of acridine, the methyl heterocycle, and sulfur in a molar ratio of 1 : 1 : 3 was stirred for 2 h at no higher than 125°. The reaction mass was dissolved in 1 N HCl, and the solution was filtered. The base was isolated with 10% NaOH, and the precipitated resin was allowed to crystallize. The residue was reprecipitated several times, depending on the purity of the product, and then crystallized.

9-Acridinyl 4-Piperidyl Ketone (VI). A. A solution of 0.25 g (2.5 mmole) of chromic anhydride in acetic acid was gradually added to a solution of 0.5 g (1.9 mmole) of I in acetic acid and allowed to stand for 10 h at room temperature. The mixture was then neutralized with 20% NaOH, and the precipitate of VI was filtered and crystallized from alcohol to give 0.4 g (76%) of product with mp 216-217°. Found %: C 79.8; H 4.4; N 10.0. $C_{19}H_{12}N_2O$. Calculated %: C 80.3; H 4.2; N 9.9.

B. A mixture of 3 g of I (11.1 mmole) and 3.3 g (22 mmole) of p-nitrosodimethylaniline was refluxed in 20 ml of pyridine for 1.5 h. The mixture was then cooled and diluted with a large amount of water. The crystalline precipitate was filtered and dissolved in boiling alcohol. The crystals of a compound of unknown structure (0.5 g) which precipitated on cooling were filtered. The alcohol was then distilled from the filtrate until a volume of 30 ml was obtained, the solution was cooled, and the azomethine (VII) crystals were filtered and recrystallized from alcohol to give 1.8 g (40%) of a product with mp 255°. Compound VII (1 g) was refluxed with 20 ml of 30% H_2SO_4 for 1 h, neutralized with 30% NaOH, and the brown precipitate of VI was filtered and recrystallized from alcohol to give 0.5 g (75%) of product with mp 216-217°. No melting point depression was observed with a mixture of this sample and a sample obtained by method A. Found %: C 80.1; H 4.5; N 10.2. $C_{19}H_{12}N_2O$. Calculated %: C 80.3; H 4.2; N 9.9.

LITERATURE CITED

1. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, USSR Author's Certificate No. 215,999 (1967); Byull. Izobr., No. 28, 174 (1968).
2. O. N. Chupakhin, V. A. Trofimov, and Z. V. Pushkareva, Dokl. Akad. Nauk SSSR, 188, 376 (1969).
3. O. Dimroth and R. Griegee, Ber., 90, 2207 (1957).
4. F. Kröhnke and H. Honig, Ann., 624, 97 (1959).
5. F. Kröhnke and H. Honig, Ber., 90, 2215 (1957).
6. G. Scheibe and G. Schmidt, Ber., 55, 3157 (1922).