SYNTHESIS OF PYRIDONOANTHRAPYRIMIDINES

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The reaction of 6- and 8-chloroacetylaminopyrimidinoanthrones with pyridine in the case of the 8-isomer leads to the formation of a pyridone ring, while in the case of the 6-isomer it stops at the formation of the ω-pyridinium salt. The latter, like ω-pyridinium salts obtained from the 8-isomer and 1-chloroacetylaminoanthraquinone, is cyclized under the action of aniline. In this case aminopyridonoanthrapyrimidines and 1-aminoanthrapyridone are obtained. The cyclic salt, in turn, is converted to an amine, and by reductive elimination of a pyridinium group, to an unsubstituted pyridonoanthrapyrimidine. The acetylation of amines leads to the formation of an oxazole ring. Pyridonoanthrapyrimidines can also be produced from α-amino-derivatives of anthrapyridone by cyclization of dimethylformamidinium salts.

In the development of the method of synthesis of 1-aminoanthrapyridones by cyclization of α-chloroacetylamino-derivatives of anthraquinone or anthrone systems with the formation of pyridinium salts, followed by cleavage of the pyridinium group [1, 2], we attempted to carry out the analogous cyclization by the action of pyridine on 6- and 8-chloroacetylaminoanthrapyrimidines (I, II), in order to obtain amino-derivatives of isomeric pyridonoanthrapyrimidines – 8-amino-6H-benz[e]pyrido[4,3,2-g,h]perimidin-7-one (III) and 7-amino-9H-quino-[5,4,e,f]perimidin-8-one (IV). These bis-heterocyclic anthracene systems have received little study: for the former only the 2-phenyl-derivative is known [3], and there is no information on the latter at all.

The formation of two pyridone rings from 1,4- and 1,5-bis-chloroacetylaminoanthraquinones or from 6-chloroacetylaminoanthrapyridones [2] proceeds just as readily as that of one – from 1-chloroacetylaminoanthraquinones [1, 4]; moreover,the formation of intermediate ω-pyridinium (chain) salts cannot be observed. As was shown in [5], the reaction can be stopped at this stage by a small amount of hydrochloric acid, which, we should think, suppresses the influence of pyridine as the basic catalyst. At the same time, when the reaction was conducted with the compounds I and II it was found that in the case of the 6-isomer (I) it generally stopped at the formation of the ω-pyridinium salt (V), while in the case of the 8-isomer (II) it led to a cyclic pyridinium salt (VI), which, however, was formed rather slowly from the intermediate ω-pyridinium salt VII. The latter was also obtained in individual form when the reaction was conducted in the presence of hydrochloric acid. Cyclic (VI) and chain (V, VII) pyridinium salts may differ with respect to conc. H_2SO_4, in which VI is stable, while V and VII are hydrolyzed when heated to 6- and 8-aminopyrimidinoanthrones, as well as according to the IR spectra – the salt VI has one band of the pyridone carbonyl group at 1660 cm^{-1}, while in V and VII there are two: the anthrone CO group with ν 1640 cm^{-1} (low-frequency shift under the influence of an intramolecular hydrogen bond) and the acyl CO group with ν 1715-1720 cm^{-1}. The latter band is shifted 20 cm^{-1} in the high-frequency direction in comparison with chloroacetyl derivatives I and II as a result of the electron acceptor influence of the pyridinium group. The cyclic pyridinium salt VI was converted to the amine IV by heating in aniline.

Thus, peri-annelation of the pyrimidine ring greatly hinders cyclization of the ω-pyridinium salts in comparison with analogous derivatives of anthraquinone and anthrapyridone, making it impossible altogether in the case of the salt (V). Assuming that cyclization can be accomplished by using a more basic amine, we subjected the salt V to the influence of cyclohexylamine and N-methylaniline and immediately obtained the amino-derivative III sought. However, this same conversion also occurs quite unexpectedly under the action of aniline, which is less basic than pyridine (pK_a in nitromethane 9.07 and 11.95 [6]).

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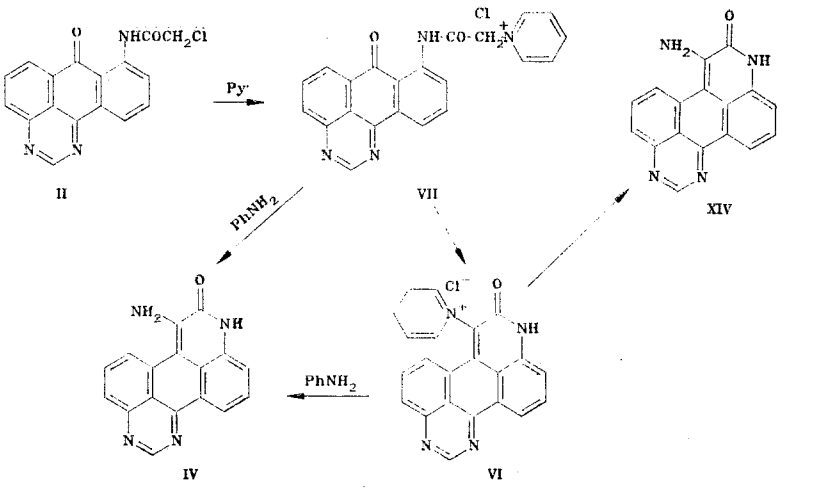
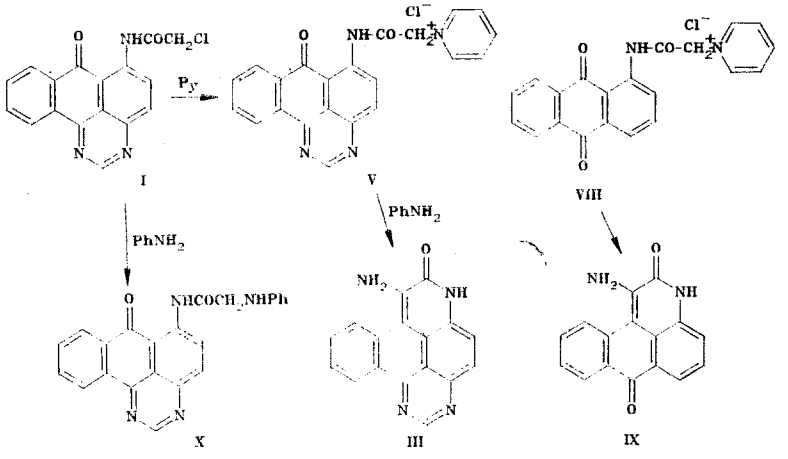


Analogously, the isomeric chain VII and nonchain salt VIII, produced from 1-chloroacetylaminoanthraquinone according to the method of [5], interacting with aniline, are converted to the amine IV and to 1-aminoanthrapyridone IX; moreover, in these cases also a substantial facilization of cyclization is noted. Thus, although cyclization in pyridine is conducted at its boiling point, in aniline the amines IV and IX are already detected in the cold, and when heating the reaction ends more rapidly than in pyridine. Consequently, a general method of conversion of ω-pyridinium salts of α-acylamino-derivatives of anthraquinone and anthrone systems to the corresponding 1-aminoanthrapyridone derivative has been found. It may be useful in cases when direct cyclization by pyridine is hindered. In addition to the case described above, we noted such hindrances, for example, in the interaction of sulfo-derivatives of 1-chloroacetylaminoanthraquinones with pyridine, since the sulfo groups like mineral acids, evidently may suppress basic catalysis.

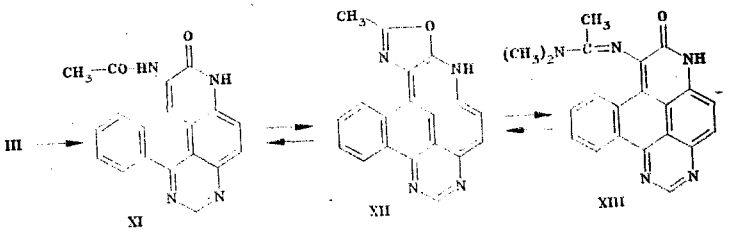


The reaction under discussion consists of two conversions — cyclization and cleavage of the pyridine ring; moreover, unquestionably the first step is the formation of cyclic pyridinium salts. This follows both from general concepts and from our experiments. In the first place, the appearance of an amino group in the side chain would passivate the methylene group and would eliminate cyclization. Actually, when 6-chloroacetylaminoanthrapyrimidine I is heated in aniline, only the formation of an ω-aniline derivative X occurs, although the electron donor influence of the phenylamino group is far less than that of the amino group. In the second place, it is known that pyridinium salts containing strongly electron acceptor N-substituents (of the type of 2,4-dinitrophenyl) are subjected to a complete Zincke cleavage [7]. The N-(anthraquinonyl-1)carbamoylaminomethylene group is not one of these substituents, and opening of the ring with the formation of a glutaconic aldehyde derivative [7] also cannot be assumed, since in this case the chain would contain a stronger electron donor alkylamino group. In all the cases under consideration, cyclization leads to extremely strong electron accep-

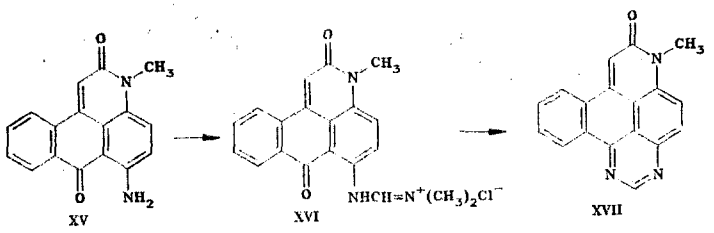
tor systems, as a result of which the pyridine ring is cleaved virtually at the moment of formation of intermediate cyclic salts, which therefore cannot be observed.

The main question is the specifics of the influence of aniline on cyclization, in which it can in no way be considered only as a basic catalyst. It is quite clear that the reaction proceeds according to a different mechanism. In our opinion, an initial interaction with the keto-group, forming a Schiff base, is the most probable, since some analogy to this can be seen in the fact that anils enter into alkali-catalyzed condensation with active alkyl groups far more readily than the carbonyl compounds that form them (so-called anil synthesis [8]). This hypothesis is supported by the disappearance of the band of the anthrone CO group in the IR spectrum of the chain salt IV in the case of dissolution in aniline (the spectrum was recorded on a two-beam instrument with deduction of the intrinsic absorption of aniline). The use of other methods in addition (electronic spectra, cryoscopy) did not lead to unambiguous conclusions.

The aminopyridonoanthrapyrimidines obtained, like 1-aminoanthrapyridones [9] and aminoanthradipyridones [2], are capable of forming oxazole rings in acylation. Thus, the amine III, when heated in acetic anhydride, is converted to a mixture of the acetyl derivative XI and the oxazole XII (2-methyloxazolo[4',5'-j]benz[e]pyridino[4,3,2-g,h]perimidine). In contrast to the cases studied previously [2, 9], in this reaction acid catalysis is essential (the amine III is unchanged in the absence of mineral acids), but the properties of the oxazole XII are similar to those described earlier [2, 9], which is manifested in the ease of opening of the oxazole ring during hydrolysis and interaction with nucleophiles, as well as reactions of recyclization. Thus, compound XII is converted by the action of dilute mineral acids to the acetyl-derivative XI, and in interaction with dimethylamine to the amidine XIII, which is returned to the initial compound upon heating.



Since pyridonoanthrapyrimidines, as was indicated, have not been studied, we considered it advisable to examine the possibilities of producing these systems, containing no functional groups, as well. Thus, by reductive elimination of the pyridinium group from the salt VI, by analogy with the similar conversions of pyridinium derivatives of anthrapyridones and anthradipyridones [2, 10], unsubstituted 9H-quino[5,4-e,f]pyrimidin-8-one (XIV) was produced (see the scheme on previous page). It was also found that these systems are readily produced on the basis of 6- and 8-aminoanthrapyridones and using the most rational method of construction of the pyrimidine ring — cyclization of dimethylformamidinium salts [11]. For example, using this approach — the action of DMFA and $POCl_3$ on 6-amino-N-methylanthrapyridone (XV), followed by treatment of the salt XVI with ammonium acetate — 6-methylbenz[e]pyrido[4,3,2-g,h]perimidin-7-one (XVII) was obtained in a high yield.



Cyclization of pyridinium derivatives of carbonyl compounds is a rather widespread method; consequently, the possibility discovered for conducting it under the action of aniline or other amines may prove useful for the synthesis of various systems; moreover, depending on the structure of the latter, the selection of the amine, and the conditions of the reaction, it probably can occur with conservation , opening, or complete cleavage of the pyridinium group.

TABLE 1. Yields, Constants, and Data of Elementary Analysis of the Synthesized Compounds

Compound	mp, °C*	Found, %			Gross formula	Calculated, %			Yield, %
		C	H	N (Cl)		C	H	N (Cl)	
I	248—249	63,29	3,00	12,97 (10,91)	$C_{17}H_{10}ClN_3O_2$	63,21	3,10	13,00 (10,95)	96
II	274—276	63,50	3,03	12,69 (10,83)	$C_{17}H_{10}ClN_3O_2$	63,21	3,10	13,00 (10,95)	91
III	>350	71,59	3,72	19,38	$C_{17}H_{10}N_4O$	71,32	3,52	19,57	96
IV	>350	71,61	3,53	19,73	$C_{17}H_{10}N_4O$	71,32	3,52	19,57	97
V	262,5—264	65,23	3,70	14,02 (8,95)	$C_{22}H_{15}ClN_4O_2$	65,57	3,75	13,92 (8,82)	95
VI	>350	67,64	4,67	14,30 (9,05)	$C_{22}H_{13}ClN_4O$	67,90	4,96	14,56 (9,26)	97
VII	259—261	65,27	3,51	13,46 (8,61)	$C_{22}H_{15}ClN_4O_2$	65,57	3,75	13,92 (8,82)	96
X	163—165	75,87	4,26	15,47	$C_{23}H_{16}N_4O_2$	75,61	4,38	15,43	86
XI	292—294	69,73	3,51	17,14	$C_{19}H_{12}N_4O_2$	69,51	3,66	17,20	90
XII	258,5—260,5	73,89	3,49	17,90	$C_{19}H_{10}N_4O$	73,50	3,21	17,57	73
XIII	—†	71,92	4,53	19,89	$C_{21}H_{17}N_5O$	70,90	4,82	19,65	87
XIV	>350	75,46	3,15	15,30	$C_{17}H_9N_3O$	75,26	3,34	15,49	94
XVII	>350	75,77	7,86	14,57	$C_{18}H_{11}N_3O$	78,78	7,89	14,73	83

*Solvent for crystallization: I, II, XII) chloroform; III) aqueous DMFA; IV, XIV, XVII) DMFA; X) methanol; XI) aqueous dioxane.
†It is recyclized upon heating to compound XII.

EXPERIMENTAL

The IR spectra were measured on a UR-20 spectrophotometer. The course of the reaction was monitored by the method of thin-layer chromatography on Silufol plates (eluent chloroform). The yields, constants, and results of elementary analysis of the synthesized compounds are cited in Table 1.

6- and 8-Chloroacetylaminobenz[e]perimidines (I, II). To a solution of 2.6 g (10.2 mmoles) of 6- or 8-aminobenz[e]perimidine in 100 ml chlorobenzene at 70°C, over a period of 20 min, 7.2 g (91 mmoles) of chloroacetyl chloride was added, mixed for 2 h at 120°C, cooled, the precipitate filtered off, washed with benzene and with ether.

6- and 8-Acetylaminobenz[e]perimidine-ω-pyridinium Chlorides (V, VII), 7-Pyridino-9H-quino[5,4-e]perimidin-8-one Chloride (VI). A solution of 1.0 g of compound I or II in 20 ml of pyridine was boiled for 1 h (in the case of II, 0.5 ml of 35% hydrochloric acid was added), cooled, the precipitate formed was removed, washed with ether, and the salt V or VII was obtained. To obtain the salt VI from the compound II, it was boiled for 3 h; the salt VII was initially formed.

8-Amino-6H-benz[e]pyrido[4,3,2-g,h]perimidin-7-one (III), 7-Amino-9H-quino[5,4-e,f]perimidin-8-one (IV), 1-Amino-7H-dibenz[f,i,j]isoquinoline-2,7-[3H]-dione (IX). A mixture of 2.6 mmoles of compound V-VIII and 10 ml of aniline was mixed for 2 h to 2 h 30 min at 100°C, cooled to 70°C, 10 ml of methanol was added, the precipitate formed was removed, and it was washed with methanol.

6-ω-Anilinoacetylaminobenz[e]perimidine (X). For 1 h at 150°C, 0.45 g 6-chloroacetylaminobenz[e]perimidine (I) and 6 ml of aniline were mixed, cooled to 30°C, 3 ml of methanol and 5 ml of ether were added, the precipitate formed was filtered off, and it was washed with methanol and with ether.

2-Methyloxazolo[4',5'-j]benz[e]pyrido[4,3,2-g,h]perimidine (XII). A mixture of 1.0 g of compound III, 15 ml of acetic anhydride, and 1 drop of conc. H_2SO_4 was mixed for 1 h at 140°C, cooled, poured out into water, the precipitate filtered off and washed with water. It was purified on a column with silica gel (chloroform), isolating a zone with violet fluorescence under UV irradiation.

8-Acetylamino-6H-benz[e]pyrido[4,3,2-g,h]perimidin-7-one (XI). A. A mixture of 0.4 g of compound II, 4 ml of acetic anhydride, 4 ml of acetic acid, and a drop of conc. H_2SO_4 was heated to boiling, mixed for 20 min, cooled, poured out into water, the precipitate formed removed and washed with water.

B. For 20 min 0.4 g of compound XII, 30 ml of 50% aqueous dioxane, and 0.5 ml of 30% hydrochloric acid was boiled; then it was cooled and the precipitate removed.

8-(N,N-Dimethylacetamidino)-6H-benz[e]pyrido[4,3,2-g,h]perimidin-7-one (XIII). To 0.4 g of compound XII in 20 ml of dioxane we added 2 ml of dimethylamine, mixed for 1 h 30 min at 20°C, filtered off the precipitate formed, washed with dioxane, dried, and obtained the amidine XIII, which is converted upon heating in a capillary to the oxazole XII.

9H-Quino[5,4-e,f]perimidin-8-one (XIV). To a solution of 0.5 g of compound VI in 100 ml of water we added 35 ml of an aqueous solution containing 0.7 g of the carbonate and 0.7 g sodium hydrosulfite, mixed for 1 h at 40°C, cooled, filtered off the precipitate formed, washed with water, and dried.

6-Methylbenz[e]pyrido[4,3,2-g,h]perimidine-7 (XVII). A mixture of 1 g of compound XV, 10 ml of dimethylformamide, and 1 ml of phosphorus oxychloride was mixed for 2 h at 50°C, cooled, the precipitate removed, washed with chloroform, with ether, and the dimethylformamidinium salt XVII obtained, which was introduced into 30 ml of methanol, 1 g of ammonium acetate was added, mixed for 30 min at 20°C, the precipitate filtered off, washed with water, and dried.

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INTERACTION OF 5-VINYLTETRAZOLE WITH TRIETHYLAMINE

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It was shown by the methods of UV spectrophotometry, conductometry, viscosimetry, and PMR spectroscopy that the interaction of 5-vinyltetrazole with triethylamine gives a polymeric salt of vinyltetrazole.

5-Substituted tetrazoles react with bases to form salts [1]. It is reported [2, 3] that polymeric salts are obtained by the reaction of hydrazine or triaminoguanidine with poly-5-vinyltetrazole.

We have suggested that 5-vinyltetrazole (VT), which exhibits the properties of a weak acid (pK_a 4.1), will also react with bases to form salts that can be used to synthesize water-soluble polymers.

The process of interaction of VT with bases was investigated in detail on the example of the reaction with triethylamine (TEA). The absorption band of VT in ethanol (λ_{max} 218 nm) is

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