REACTION OF ANTHRAPYRIDONES WITH NUCLEOPHILIC REAGENTS

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The reaction of anthrapyridone and its derivatives with aliphatic, aromatic, and heterocyclic amines, alkalis, and cyanides gives the corresponding 1-substituted anthrapyridones.

Anthrapyridone derivatives have long been used in the synthesis of dyes. However, the possibility of direct nucleophilic substitution in the anthrapyridone series has not been known until now. We have found that the reaction of anthrapyridones with aliphatic amines and alkalis leads to the formation of the corresponding 1-substituted anthrapyridones [1, 2].

Unsubstituted anthrapyridone and its N-methyl derivative (I) react with aliphatic amines in dimethylformamide or excess amine in the presence of a copper catalyst (copper metal or copper salts) to give 1-alkylamino derivatives (II) in yields of ~90% based on the amount of converted starting compound. The degree of conversion of anthrapyridones varies over considerable limits as a function of the amine used. Thus, for example, the yields in the reaction of I with cyclohexylamine, n-hexylamine, and piperidine, based on the amount of I introduced into the reaction, are 91, 63, and 10%, respectively. Increasing the reaction time leads to resinification and does not increase the yields. It is possible that the activity of the amines in this reaction is determined by the stability and reactivity of the intermediately formed complexes of copper with the amines. In the absence of copper, the reaction of anthrapyridones with aliphatic amines proceeds slowly to give extremely low yields.

Aromatic amines do not react with anthrapyridones under the conditions described above. The reaction can be realized in the presence of sodium amide. The increase in the activity of the aromatic amines when sodium amide is added can be explained by the formation of sodium arylamides, which have high nucleophilicity.

The structure of II was proved by the preparation of identical 1-alkylamino- or 1-arylamino derivatives by the action of the appropriate amines on 1-nitro-N-methylanthrapyridone (III) [3] and 1-chloro-N-methylanthrapyridone (IV) [4].

The reaction of 6-bromo-N-methylanthrapyridone (V) with aromatic amines in the presence of copper catalysts proceeds smoothly to give good yields of 6-arylamino derivatives, which makes it possible to use it extensively in industrial synthesis. In addition to substitution of the bromine atom by an alkylamino group (VI), the reaction of V with aromatic amines in the presence of copper also proceeds with the entry of an amine residue into the 1 position to give 1,6-di(alkylamino)-N-methylanthrapyridone (VII). In addition to VI and VII, traces of 1-alkylamino-N-methylanthrapyridone (II) are detected in the reaction products. The formation of the latter is caused by partial dehalogenation of starting compound V, which is rather frequently

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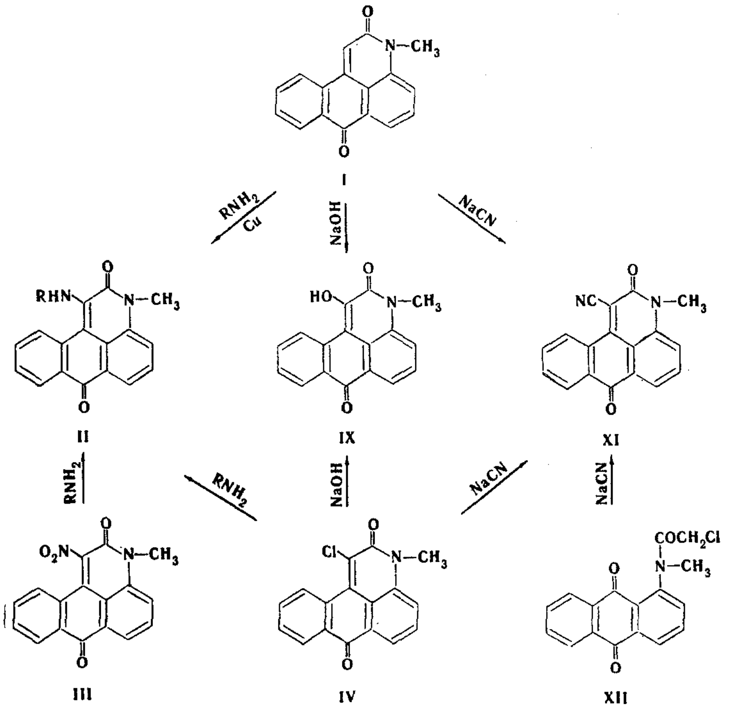
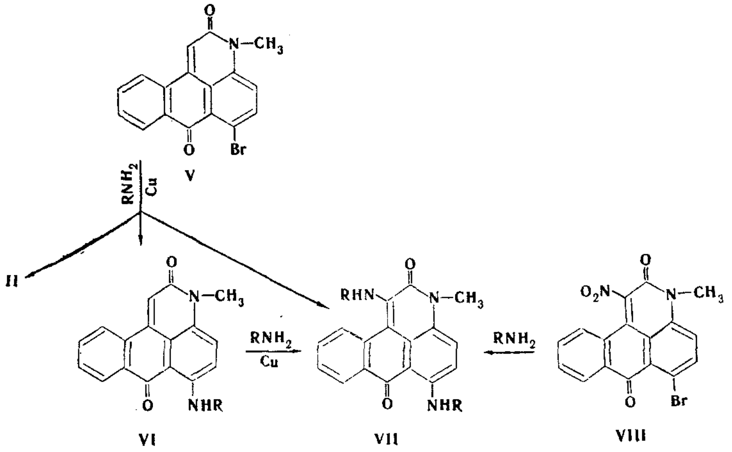


encountered when reactions are carried out under similar conditions. Compounds VII are identical to 1,6-di(alkylamino)-N-methylanthrapyridones obtained by the reaction of alkylamines on 1-nitro-6-bromo-N-methylanthrapyridone (VIII) [3].

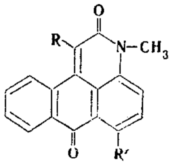


Dialkylamino derivatives VII can also be obtained by the action of alkylamines on 6-alkylamino-N-methylanthrapyridones (VI). The latter are obtained in high yields from V in the absence of copper. The combination of these two reactions makes it possible to obtain 1,6-diamino derivatives with various substituents in the amino groups, for example, VIIc. Compounds VI, which contain various amine residues, were obtained in order to find substances with high solubility in organic media, for example, in polymers.

The absorption spectra of 1-alkylamino- and 6-alkylaminoanthrapyridones (II, VI) each have two bands (for example, IIb, λ_{max} 340, 448 nm; VIb, λ_{max} 345, 545 nm). In the spectra of 1,6-di(alkylamino)anthrapyridones (VII), the band in the near-UV region does not change its position, while two bands, which are similar in character to the bands of II and VI but are shifted to short wavelengths (VIIb, λ_{max} 340, 425, 512 nm), appear in the visible region.

Alkylaminoanthrapyridones II, VI, and VII have bright luminescence in solutions (II has the maximum luminescence intensity) and are suitable for practical use as luminophores [5].

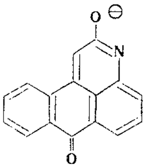
TABLE 1. Alkylamino Derivatives of N-Methylanthrapyridone



Compound	R	R′	Mp, °C (crystallization solvent)*	Empirical formula	Found, %			Calc., %		
					C	H	N	C	H	N
IIa	*n*-C_4H_9NH	H	122—123 (cyclohexane)	$C_{21}H_{20}N_2O_2$	—	—	8,5	—	—	8,4
IIb	*n*-$C_6H_{13}NH$	H	103—104 (cyclohexane)	$C_{23}H_{24}N_2O_2$	76,5	6,8	8,0	76,6	6,7	7,8
IIc	$C_6H_{11}NH$	H	182—183 (cyclohexane)	$C_{23}H_{22}N_2O_2$	77,1	6,3	7,8	77,1	6,2	7,8
IId	$(CH_2)_5N$	H	211—212 (cyclohexane)	$C_{22}H_{20}N_2O_2$	76,8	5,8	8,2	76,7	5,8	8,1
VIa	H	*n*-C_4H_9NH	211—212 (chloroform)	$C_{21}H_{20}N_2O_2$	75,9	6,1	8,5	75,9	6,1	8,4
VIb	H	*n*-$C_6H_{13}NH$	194—195 (white spirit)	$C_{23}H_{24}N_2O_2$	76,6	6,6	7,6	76,6	6,7	7,8
VIc	H	*n*-$C_{18}H_{37}NH$	165—166 (chlorobenzene)	$C_{35}H_{48}N_2O_2$	—	—	5,5	—	—	5,3
VId	H	$C_6H_{11}NH$	269—270 (nitrobenzene)	$C_{23}H_{22}N_2O_2$	—	—	7,8	—	—	7,8
VIe	H	$C_6H_5CH_2NH$	233—234 (white spirit)	$C_{24}H_{18}N_2O_2$	—	—	7,7	—	—	7,6
VIIa	*n*-C_4H_9NH	*n*-C_4H_9NH	141—142 (petroleum ether)	$C_{25}H_{29}N_3O_2$	74,3	7,3	10,4	74,4	7,2	10,4
VIIb	*n*-$C_6H_{13}NH$	*n*-$C_6H_{13}NH$	88—89 (petroleum ether)	$C_{29}H_{37}N_3O_2$	—	—	9,2	—	—	9,1
VIIc	$C_6H_{11}NH$	*n*-$C_6H_{13}NH$	147—148 (hexane)	$C_{29}H_{35}N_3O_2$	76,1	7,8	9,0	76,1	7,7	9,2

* The crystals of IIa,b and VIIa,b were cubic, while those of the remaining compounds were needles.

Heating a suspension of N-methylanthrapyridone (I) in an aqueous dioxane solution of sodium hydroxide gives 1-hydroxy-N-methylanthrapyridone (IX). However, this reaction cannot be accomplished for nitrogen-unsubstituted anthrapyridone. The latter, in contrast to I, which has a fixed pyridone structure, dissolves in aqueous dioxane solutions of alkali to give (probably) enol X, which cannot react with nucleophiles. Compound IX is identical to 1-hydroxy-N-methylanthrapyridone obtained by the action of alcoholic alkali on 1-chloro-N-methylanthrapyridone (IV) [6].



X

The patent literature [7] contains data on the possibility of the direct cyanation of I (without indications of the structure of the reaction product). On the basis of the information set forth above, it seemed most likely that the nitrile group enters the 1 position. This was confirmed by obtaining identical compounds XI by direct cyanation of I, by substitution of the chlorine atom in IV by a cyano group, and by the action of sodium cyanide on N-chloroacetyl-1-methylaminoanthraquinone (XII) [8].

EXPERIMENTAL

The absorption spectra of chloroform solutions were recorded with an SF-4 spectrophotometer. The compounds were identified from mixed-melting-point determinations and IR spectra. Anhydrous aluminum oxide was used for the chromatography.

1-Cyclohexylamino-N-methylanthrapyridone (IIc). A mixture of 1 g of I, 10 ml of cyclohexylamine, 15 ml of dimethylformamide, and 0.1 g of copper powder was refluxed for 4 h, and 60 ml of 8% hydrochloric acid was added. The resulting precipitate was removed by filtration, washed with water, dried, and chromatographed on Al_2O_3 (benzene) to give 1.21 g (91%) of IIc (Table 1).

1-n-Hexylamino-N-methylanthrapyridone (IIb). A) This compound was obtained under similar conditions: the precipitate was isolated and extracted with hot cyclohexane to dissolve IIb. (The residue from the extraction was unchanged I.) The yield after chromatographic purification was 87% based on the amount of converted I (63% based on the amount of I introduced into the reaction).

B) A mixture of 0.6 g of III and 5 ml of n-hexylamine was refluxed for 1 h and treated with 8% hydrochloric acid to give 91% IIb.

1-Piperidino-N-methylanthrapyridone (IId). This compound was obtained in 90% yield (based on converted I; 10% based on the amount of I used) by method A for the preparation of IIb.

1-n-Hexylaminoanthrapyridone. This compound was obtained from anthrapyridone by method A used for the preparation of IIb. Hot acetone was used for the extraction to give 92% (based on the converted anthrapyridone) of large, bright-yellow needles with mp 166-167° (from aqueous acetic acid). Found: C 76.0; H 6.3; N 8.2%. $C_{22}H_{22}N_2O_2$. Calculated: C 76.3; H 6.4; N 8.1%.

1-(p-Toluidino)-N-methylanthrapyridone. A mixture of 1 g of I, 10 g of p-toluidine, 15 ml of dimethylformamide, 0.5 g of sodium amide, and 0.25 g of cupric acetate was stirred at 155° for 4 h, cooled to 100°, and diluted with 8% hydrochloric acid. The precipitate was removed by filtration, washed with water, and dried. An orange zone (chloroform) was isolated from the mixture of products by chromatography on Al_2O_3. The eluate was evaporated, and the residue was dissolved in benzene. The benzene solution was diluted with petroleum ether, and the precipitated crystals (prisms, mp 238-239°) were removed by filtration to give 0.24 g (17%) of 1-(p-toluidino)-N-methylanthrapyridone, which was identical to the compound obtained from IV and p-toluidine and had a melting point in agreement with the reported value [3].

Reaction of V with Aliphatic Amines. A) In the Absence of Copper. A mixture of 1 g of V and 10 ml of n-hexylamine was refluxed for 6 h and diluted with 5-8% hydrochloric acid. The precipitate was removed by filtration, dried, and chromatographed on Al_2O_3 (chloroform) to give 0.94 g (89%) of VIb. Compounds VIa,d-e were similarly obtained in 75-95% yields by the action of n-butylamine, n-octadecylamine, and benzylamine on V at 120-130°. The reaction with n-butylamine was carried out in a sealed ampul. In the preparation of VIc, the reaction mass was diluted with benzene and transferred to a column filled with Al_2O_3; n-octadecylamine was eluted with benzene, while VIc was eluted with chloroform (Table 1).

B) In the Presence of Copper. A mixture of 10 g of V, 40 ml of n-butylamine, 0.5 g of cupric acetate, and 0.3 g of copper powder was refluxed for 10 h, diluted with 150 ml of 8% hydrochloric acid, and allowed to stand for the formation of a crystalline precipitate. The precipitate was removed by filtration, washed with 8% hydrochloric acid and water, and dried. The resulting mixture of products was separated by chromatography on Al_2O_3: the orange zone was eluted with chlorobenzene, while the reddish zone (1.8 g of VIa) was eluted with chloroform. According to paper chromatography (Whatman paper impregnated with a 10% solution of α-bromonaphthalene with elution with a saturated solution of α-bromonaphthalene in 75% acetic acid), the orange zone (3.3 g) was VIIa with IIa as an impurity (obtained from III in analogy with IIb). A mixture of products of the same composition was obtained by the reaction of V with n-hexylamine.

1,6-Di(n-butylamino)-N-methylanthrapyridone (VIIa). A mixture of 0.8 g of VIII [mp 346-347° (333-334° [3])] and 7 ml of n-butylamine was heated at 160° for 4 h in a sealed ampul and treated with 5% hydrochloric acid. The resulting mixture was extracted with chloroform and chromatographed on Al_2O_3 (chloroform). The eluate was evaporated, and the residue was dissolved in refluxing petroleum ether, from which 0.4 g (45%) of characteristic cubic crystals of VIIa precipitated. Compound VIIb was similarly obtained in 66% yield as orange-red cubes.

1-Cyclohexylamino-6-n-hexylamino-N-methylanthrapyridone (VIIb). A mixture of 0.7 g of VIb, 4 ml of cyclohexylamine, 10 ml of dimethylformamide, and 0.2 g of copper powder was refluxed for 4.5 h and diluted with 5% hydrochloric acid. The precipitate was removed by filtration and washed with water, dried, and chromatographed on Al_2O_3 (chloroform) to give 0.6 g (55%) of VIIc.

1-Hydroxy-N-methylanthrapyridone (IX). A total of 5 ml of a 40% solution of sodium hydroxide was added to a refluxing mixture of 1 g of I, 50 ml of dioxane, and 50 ml of water. Immediately after the addition of the alkali, the color of the reaction mixture changed from yellow to orange-red, which indicated the formation of the sodium salt of IX. The mixture was cooled and filtered, and the solid was extracted several times with warm 2% sodium hydroxide solution. The filtrates were combined and acidified with hydrochloric acid, and the precipitate was removed by filtration, washed, and dried to give 0.6 g (54%) of IX with mp 299-300° (dec., from acetic acid). The product was identical to IX obtained from IV via the method in [6]. According to [6], this compound has mp 280°.

1-Cyano-N-methylanthrapyridone (XI). A mixture of 0.5 g of IV, 0.25 g of sodium cyanide, and 10 ml of ethylene glycol was stirred at 100° for 2.5 h and diluted with water. The precipitate was removed by filtration, washed, and dried to give 0.5 g (97%) of XI with mp 315-316° (from dimethylformamide), which was identical to the substances obtained by the direct cyanation of I and by the action of sodium cyanide on XII via the methods in [7, 8].

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