INVESTIGATIONS IN THE FIELD OF ANTHRAPYRIDONE

IV. 2,6-Dichloroanthrapyridine and Its Reactions with Amines*

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6-Bromo-N-methylpyridone reacts with phosphorus pentachloride at 180° C to form, 2, 6-dichloroanthrapyridine. The latter reacts with amines at moderate temperatures forming 6-amino-2-chloro derivatives of anthrapyridine and at high temperatures forming 2, 6-diamino-substituted anthrapyridines.

We have previously shown that N-methylanthrapyridone forms with phosphorus pentachloride an addition product the thermal decomposition of which leads to 2-chloroanthrapyridine [1].

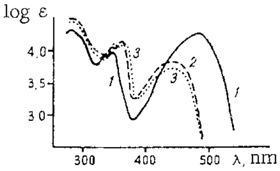
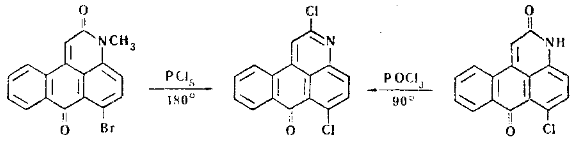


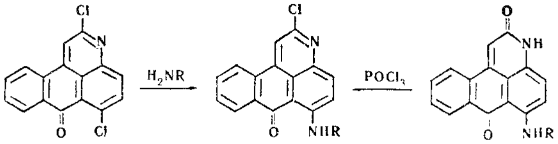
Fig. 1. Electronic spectra: 1) 6-anilino-2-chloroanthrapyridine; 2) 2-anilino-6-chloroanthrapyridine; 3) 2-anilinoanthrapyridine.

When 6-bromo-N-methylanthrapyridone (I) was heated with phosphorus pentachloride at 180° C in trichlorobenzene, 2,6-dichloroanthrapyridine (II) was formed with a yield of about 85%, i. e., in addition to the conversion of the N-methylpyridone ring into a chloropyridine ring observed previously, the bromine was replaced by chlorine. Structure II was shown by independent synthesis from 6-chloroanthrapyridone (III).



I II III

It was found that with an excess of an aliphatic or aromatic amine the dichloride II exchanges one halogen atom at temperatures of 50–80° C, forming a monoamino derivative with a yield close to quantitative. The brief heating of II with aniline at 140° C led to the formation of two other compounds besides a predominating amount (80%) of the same monoanilino derivative. One of them (about 10%) was 2,6-dianilinoanthrapyridine, and the other (8.5%) a monoanilino derivative isomeric but not identical with the main substance. The electronic spectra of the isomers obtained (see Fig. 1) differed considerably from one another but the absorption of the isomer isolated in smaller amount almost coincided with that of 2-anilinoanthrapyridine. It may be assumed that the main reaction product (and the only reaction product under mild conditions) is 6-anilino-2-chloroanthrapyridine. This conclusion also extends to the other amines and has been confirmed by the independent synthesis of, for example, 2-chloro-6-mesidinoanthrapyridine (IV).



II IV

The ready replacement of halogen in position 6 can be explained by the low electron density on the corresponding carbon atom because of the acceptor influence of the pyridine nitrogen atom and the anthraquinone carbonyl group.

The replacement of a second halogen atom after the replacement of the first requires more severe conditions. Because of this it is possible to obtain both symmetrical and unsymmetrical diamines with the intermediate isolation of the monochloro derivative.

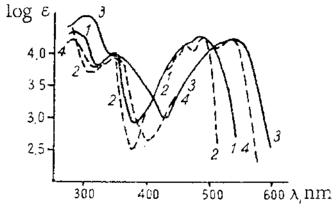
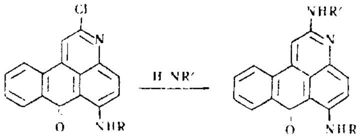


Fig. 2. Electronic spectra: 1) 6-anilino-2-chloroanthrapyridine; 2) 2-chloro-6-n-hexylaminoanthrapyridine; 3) 2,6-di-p-toluidinoanthrapyridine; 4) 2,6-di-n-hexylamino-anthrapyridine.

We carried out the secondary amination in the presence of a catalyst (copper acetate) and potassium acetate to bind the acid liberated.



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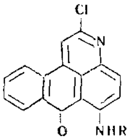
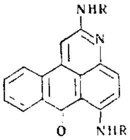
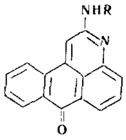
*For part III, see [1].

Amino-Substituted Anthrapyridines

Structural formula	R (R′)	Mp, °C	λmax, nm (log ε)	Empirical formula	Found, %			Calculated, %			Yield, %
					C	H	N	C	H	N	
	C_6H_5	223.6—225.0	280 (4.36) 345 (4.02) 480 (4.27)	$C_{22}H_{13}ClN_2O$	74.18 74.00	3.31 3.65	7.90 7.87	74.05	3.67	7.85	98.6
	2,4,6-$(CH_3)_3C_6H_2$	255.0—256.0	345 (4.07) 477 (4.30)	$C_{25}H_{19}ClN_2O$[a]	75.28 75.00	4.83 4.74	7.07 7.09	75.26	4.80	7.02	87
	p-$CH_3C_6H_4$	209.0—210.8	280 (4.24) 345 (3.97) 485 (4.30)	$C_{23}H_{15}ClN_2O$[b]	74.21 74.31	4.12 4.28	7.72 7.64	74.49	4.09	7.56	96
	n-C_6H_{13}	103.6—105.0		$C_{22}H_{21}ClN_2O$[c]	74.13 74.20	5.93 5.88	7.72 7.94	74.42	5.80	7.68	98
	*p*-$CH_3C_6H_4$ (*p*-$CH_3C_6H_4$)	215.4—216.0	297 (4.60) 535 (4.25)	$C_{30}H_{23}N_3O$	81.67 81.64	5.38 5.10	9.18 9.14	81.66	5.25	9.52	78
	p-$CH_3OC_6H_4$ (*p*-$CH_3OC_6H_4$)	210 —211	297 (4.55) 535 (4.21)	$C_{30}H_{23}N_3O_3$	76.51 76.32	5.20 5.18	8.90 8.99	76.14	4.90	8.88	81.6
	m-ClC_6H_4 (*m*-ClC_6H_4)	114.5—118.0	300 (4.64) 530 (4.23)	$C_{28}H_{17}Cl_2N_3O$	69.42 69.71	3.38 3.42	8.46 8.57	69.75	3.55	8.71	27
	n-C_6H_{13} (*n*-C_6H_{13})	79 — 80	280 (4.45) 345 (3.94) 533 (4.18)	$C_{28}H_{35}N_3O$	78.14 78.22	8.16 8.47	9.71 9.91	78.32	8.15	9.78	26[d]
	$HOCH_2CH_2$ ($HOCH_2CH_2$)	227.8—231.6	345 (3.96) 530 (4.16)	$C_{20}H_{19}N_3O_3$	68.91 68.94	5.55 5.27	11.60 11.48	68.75	5.48	12.03	47
	n-C_6H_{13} (C_6H_5)	129 —130	290 (4.64) 530 (4.21)	$C_{28}H_{27}N_3O$	80.06 80.31	6.72 6.51	9.97 9.92	79.78	6.46	9.97	30
	p-$CH_3C_6H_4$ (C_6H_5)	175 —178	295 (4.60) 535 (4.25)	$C_{29}H_{21}N_3O$	81.60 81.69	5.36 4.94	10.09 10.18	80.94	5.10	10.12	69
	C_6H_5	241 —242	280 (4.42) 345 (4.10) 365 (4.22) 450 (3.71)	$C_{22}H_{14}N_2O$	82.13 82.21	4.22 4.31	8.86 8.71	81.97	4.38	8.69	73
	p-$CH_3C_6H_4$	251 —252.5	280 (4.45) 345 (4.14) 365 (4.25) 440 (3.75)	$C_{23}H_{16}N_2O$	82.26 82.51	4.76 4.80	8.03 7.75	82.12	4.80	8.33	76
	n-C_6H_{13}	143.5—145.0	345 (4.04) 360 (4.22) 435 (3.67)	$C_{22}H_{22}N_2O$	80.06 80.11	6.66 6.78	8.52 8.60	79.96	6.71	8.48	50
	$HOCH_2CH_2$	213 — 214	—	$C_{18}H_{14}N_2O_2$	74.62 74.61	4.88 4.95	9.75 9.77	74.51	4.83	9.67	65

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[a] Found, %: Cl 8.87, 9.10. Calculated, %: Cl 8.89. [b] Found, %: Cl 9.48, 9.56. Calculated, %: Cl 9.56. [c] Found, %: Cl 9.38, 9.45. Calculated, %: Cl 9.72. [d] The reaction was carried out in a sealed tube at 160° C for 6 hr, and 57% of the monosubstituted derivative was isolated.

The color of the compounds obtained is of some interest. The dichloride II is an almost colorless substance, both its absorption maxima being located in the UV region. The introduction of an alkylamino or arylamino group into position 6 leads to an increase in the intensity of the absorption band in the 480 nm region. When the second halogen atom is replaced, there is a shift in the absorption band in the long-wave direction to 530 nm. It is interesting that the nature of the amine has almost no effect on the position of the maximum in both the monoamines and the diamines (Fig. 2). However, in the case of residues of aliphatic or sterically hindered amines (mesidine) there is a greater selectivity of absorption, particularly in the long-wave region. For this reason 2-chloro-6-hexyl- and 2-chloro-6-mesitylaminoanthrapyridines are yellow and the anilino derivative is orange. Analogously, 2,6-di(n-hexylamino)anthrapyridine is perceived by the eye as a red compound and its di-p-toluidine analog as a pink compound, in spite of the similar position of the absorption maxima.

EXPERIMENTAL*

2,6-Dichloroanthrapyridine (2,6-dichloro-7H-dibenz [f, ij] isoquinolin-7-one) (II). a) A mixture of 45.0 g (~0.1 mole) of technical 6-bromo-N-methylanthrapyridone (I), 52.0 g (0.25 mole) of phosphorus pentachloride, and 400 ml of dry trichlorobenzene was heated at 180° C for 8 hr, the phosphorus oxychloride and bromine vapors being distilled off during the reaction. After cooling, the precipitate that had deposited was filtered off, washed with chlorobenzene, and dried. Yield 28.0 g. From the filtrate, by distilling off the solvent followed by chromatic purification on alumina (elution with chloroform), an additional 6.2 g of II was obtained. The total yield was 34.2 g (85.8%), mp 260–261.5° C (from p-xylene), λ_{max} 355 and 385 nm, log ε 4.13 and 3.98. Found, %: C 64.30, 64.34; H 2.38, 2.23; Cl 23.03, 23.31. Calculated for $C_{16}H_7Cl_2NO$, %: C 64.02; H 2.35; Cl 23.63.

b) A mixture of 3.0 g of 1-amino-4-chloroanthraquinone, 6 g of anhydrous potassium acetate, and 30 ml of acetic anhydride was boiled for 3 hr and diluted with 50 ml of chlorobenzene, after which the precipitate was filtered off, washed with methanol, and recrystallized from dimethylformamide. The yield of 6-chloroanthrapyridone **(III)** was 2.0 g (60%), mp 405–406° C (after a second recrystallization from dimethylformamide). A mixture of 1.00 g of III and 12 ml of phosphorus oxychloride was stirred at 90–100° C for 1 hr 30 min. After the end of the reaction, the mixture was poured into ice water and the precipitate was filtered off, washed with hot water, dried, and recrystallized from p-xylene with the addition of carbon. The yield of II was 0.62 g (59%), mp 263–263.8° C. A mixture of the samples obtained by the two methods described melted at 261–261.6° C.

Reaction of the dichloroanthrapyridine II with aniline. a) A mixture of 3.00 g (0.01 mole) of II and 22 ml (0.22 mole) of aniline was stirred at 60° C for 4 hr and poured into 500 ml of hot water; the precipitate that deposited was filtered off, washed with water, and dried. The substance was dissolved in toluene and chromatographed on alumina. Three zones were formed: two yellow-orange and one pink. Toluene eluted the mobile orange zone, and partial evaporation of the solvent and the addition of petroleum ether yielded 3.60 g of 6-anilino-2-chloroanthrapyridine (for properties, see table). The elution of the less mobile pink and yellow zones with a mixture of chloroform and methanol (1 : 1) yielded less than 0.03 g of a mixture of two substances.

b) A mixture of 3.00 g of II and 20 ml of aniline was stirred at 140° C for 25 min. After a working up procedure similar to that described in (a), 2.84 g (80%) of 6-anilino-2-chloroanthrapyridine, 0.42 g (10.4%) of the pink 2,6-dianilinoanthrapyridine, and 0.30 g (8.4%) of 2-anilino-6-chloroanthrapyridine were obtained (both of the latter were eluted with chloroform). 2-Anilino-6-chloroanthrapyridine: mp 217.4–218° C. λ_{max} 285, 360, and 445 nm, log ε 4.50, 4.16, and 3.85. Found, %: C 74.32, 74.18; H 4.13, 4.12; Cl 9.83, 9.62; N 7.42, 7.61. Calculated for $C_{22}H_{13}ClN_2O$, %: C 74.05; H 3.67; Cl 9.94; N 7.85.

2-Chloro-6-mesidinoanthrapyridine (2-chloro-6-mesidino-7H-dibenz [f, ij] -isoquinolin-7-one). a) A mixture of 2.00 g (0.0066 mole) of II and 10 ml of mesidine was stirred at 90–100° C for 4 hr. The mass was treated with an excess of dilute hydrochloric acid and the precipitate was filtered off, washed with water, and dried. The substance was dissolved in benzene and chromatographed on alumina. First a yellow zone was eluted with benzene and then a red zone with chloroform. The eluates were concentrated to small bulk and diluted with petroleum ether. The yield of IV was 2.31 g (properties in the table). The yield of 2,6-dimesidinoanthrapyridine was 0.23 g (6.9%), mp 271.2–272.4° C (from benzene), λ_{max} 280, 340, and 527 nm, log ε 4.58, 4.00, and 4.25. Found, %: C 82.35, 81.24; H 6.19, 6.23; N 8.65, 8.22. Calculated for $C_{34}H_{31}N_3O$, %: C 82.06; H 6.23; N 8.45.

b) A mixture of 1.70 g of 6-mesidinoanthrapyridone and 17 ml of phosphorus oxychloride was heated at 90–100° C for 2 hr. Pouring the mixture into water and purifying the precipitate by chromatography on alumina (with chloroform as the eluant) gave 0.14 g of IV, mp 256.6–257.2° C (from butanol). A mixture of samples of the materials obtained by the different methods melted with no depression of the melting point.

The properties of the other monoamines obtained from the dichloride II are given in the table.

2,6-Diaryl(alkyl)aminoanthrapyridines. A mixture of 0.0066 mole of II or the monochloro derivative (for the unsymmetrical amines), 0.09–0.11 mole of aromatic amine, 0.0135 mole of potassium acetate, and 5–6 mmole of copper acetate was heated at 170–180° C until the orange zone of the monosubstituted derivative on a chromatogram had disappeared completely or was present only in traces (a drop of the reaction mixture dissolved in 2–3 ml of chloroform was chromatographed on an alumina plate and eluted with chloroform). At the end of the reaction, the mass was poured into an excess of 3–5% hydrochloric acid and the precipitate was filtered off, washed with water, dried, and chromatographed on alumina in chloroform. After evaporation of the solution, the compound was isolated by dilution with petroleum ether.

When aliphatic amines were used (ethanolamine and N-hexylamine), the reaction was carried out in the absence of a catalyst and potassium acetate. The properties of the compounds are given in the table.

2-Anilinoanthrapyridine (2-anilino-7H-dibenz[f, ij] isoquinolin-7-one). A mixture of 1.0 g of 2-chloroanthrapyridine [1] and 10 ml of aniline was stirred at 100–110° C for 8 hr. The mass was diluted with 300 ml of water and filtered, and the residue was washed with water and dissolved in 100 ml of propanol; to this solution was added 5 ml of 5 N caustic soda solution and it was diluted with water to 150 ml. The bright orange crystals were filtered off and washed with water to give 0.9 g (73%) of 2-anilinoanthrapyridine, after crystallization from chloroform and benzene, mp 241.0–242° C (given in the literature [2] 227–229° C). The other properties and also the properties of the other 2-aminoanthrapyridines, obtained similarly, are given in the table.

REFERENCES

1. S. I. Popov, T. N. Kurdyumova, and N. S. Dokunikhin, KhGS [Chemistry of Heterocyclic Compounds], 2, 254, 1966.

2. German patent no. 256297, Zbl., I, 758, 1913. 1913.

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*With the participation of L. D. Zil'berg.