SUBSTITUTION REACTIONS OF PYRROLOANTHRONES

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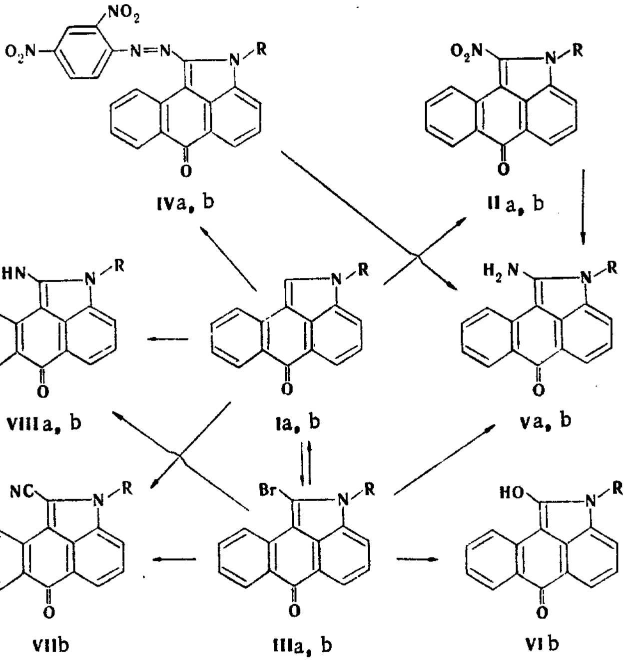
Pyrroloanthrone (6H-naphth[1,2,3-c,d]indol-6-one) and N-methylpyrroloanthrone, which was obtained from it by methylation in alkaline media, undergo electrophilic substitution (nitration, bromination, and diazo coupling) selectively in the 1 position. Nucleophilic substitution of 1-bromopyrroloanthrone is hindered by ionization at the nitrogen atom but takes place smoothly in the case of its N-methyl derivative. N-Methylpyrroloanthrone is capable of undergoing substitution of the hydrogen atom in the 1 position by a nucleophile residue.

We have previously found methods for the preparation [1] and decarboxylation [2] of pyrroloanthrone-1-carboxylic acid that make pyrroloanthrone (6H-naphth[1,2,3-c,d]indole-6-one) (Ia) accessible. The present paper is devoted to a study of its substitution reactions, information regarding which is not available in the literature.

Like pyrroles [3] and indoles [4], pyrroloanthrone Ia is converted by the action of alkalis to the anionic form, which is more deeply colored than the nonionized compound (λ_{max} 520 nm in the electronic spectrum of a solution in alcohol vis-à-vis λ_{max} 430 nm), which readily undergoes alkylation. For example, N-methylpyrroloanthrone (Ib) is formed in high yield in the reaction with methyl iodide or dimethyl sulfate at room temperature.



a R=H; b R=CH_3

Electrophilic substitution at the carbon atom proceeds under mild conditions and leads selectively to 1-substituted Ia, b. Thus 1-nitro derivatives IIa, b were obtained by the action of nitric acid in acetic acid at room temperature. Red products, which are not stable enough in the solid state for investigation and decompose on dissolving to give the starting compounds and 1-bromo derivatives IIIa, b, are formed in the reaction of Ia, b with bromine or with dioxane dibromide in organic solvents. Since the protonated forms of I and

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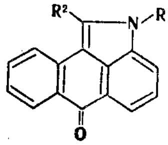
TABLE 1. Pyrroloanthrone Derivatives



Compound	R¹	R²	mp, °C[a]	Found, %			Empirical formula	Calc., %			Yield, %
				C	H	N		C	H	N	
IIa	H	NO_2	315—317	68,2	3,2	10,9	$C_{15}H_8N_2O_3$	68,2	3,0	10,6	65,4
IIb	CH_3	NO_2	250—252	69,2	3,6	9,8	$C_{16}H_{10}N_2O_3$	69,1	3,6	10,1	67,0
IIIa	H	Br	292	60,2	2,8[b]	4,5	$C_{15}H_8BrNO$	60,4	2,7	4,7	100
IIIb	CH_3	Br	230—231	61,4	3,1[c]	4,2	$C_{16}H_{10}BrNO$	61,5	3,2	4,5	94,0
IVa	H	$2,4\text{-}(NO_2)_2\text{-}C_6H_3N_2$	282—284	61,1	2,6	17,0	$C_{21}H_{11}N_5O_5$	61,0	2,7	17,0	69,0
IVb	CH_3	$2,4\text{-}(NO_2)_2\text{-}C_6H_3N_2$	290—293	61,7	3,3	16,3	$C_{22}H_{13}N_5O_5$	61,9	3,0	16,4	55,0
VIb	CH_3	OH	261—263	76,9	4,6	5,5	$C_{16}H_{11}NO_2$	77,0	4,4	5,6	80,0
VIIb	CH_3	CN	320—322	79,1	3,9	10,7	$C_{17}H_{10}N_2O$	79,0	3,9	10,8	75,0[d]
VIIIa	H	$n\text{-}C_4H_9NH$	235—236,5	78,4	6,2	9,4	$C_{19}H_{18}N_2O$	78,6	6,2	9,6	66,0
VIIIb	CH_3	$n\text{-}C_4H_9NH$	175—176	79,0	6,6	9,1	$C_{20}H_{20}N_2O$	79,0	6,6	9,2	99,0[d]

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[a] Compound IIIa was reprecipitated from N-methylpyrrolidone by the addition of water, IIIb was recrystallized from aqueous dioxane, VIIIb was recrystallized from benzene—hexane, and the remaining compounds were recrystallized from benzene. [b] Found: Br 26.8%. Calculated: Br 26.8%. [c] Found: Br 25.7%. Calculated: Br 25.7%. [d] The yields obtained by method A are indicated.

III, which are also red [electronic spectrum in a mixture of acetic and sulfuric acids (30:1), λ_{max} 510-520 nm], are not formed under these conditions, the red products are most likely molecular complexes. In addition, it was observed that 1-bromopyrroloanthrones IIIa, b, like halopyrroles [5], undergoes debromination on reaction with hydrogen bromide. The presence of alkaline agents prevents the indicated undesirable transformations, and bromination proceeds smoothly to give only 1-bromo derivatives IIIa, b. It is interesting that, despite the electron-acceptor effect of the condensed anthrone ring, pyrroloanthrones Ia, b retain the ability to undergo the diazo coupling that is characteristic of pyrroles [3]. However, the reaction can be accomplished only by the action of sufficiently active diazo compounds such as, for example, 2,4-dinitrobenzenediazonium salts, the reaction with which gave azo compounds IVa, b. The activity of pyrroloanthrone Ia as an azo component is not high enough for its reaction with benzenediazonium salts in the ionized form (in alkaline media).

The structures of 1-nitro- and 1-(2,4-dinitrophenylazo) derivatives IIa, b and IVa, b were proved by reduction, and the structure of 1-bromo derivatives IIIa, b was proved by ammonolysis, as a result of which 1-aminopyrroloanthrones (Va, b) identical to the compounds synthesized previously from pyrroloanthrone-1-carboxylic acid esters by the Curtis reaction [2] were obtained.

Nucleophilic substitution of pyrroloanthrones that do not contain substituents attached to the nitrogen atom is hindered markedly by ionization. Thus 1-bromopyrroloanthrone (IIIa) does not react with sodium hydroxide or sodium cyanide, whereas 1-bromo-N-methylpyrroloanthrone (IIIb) is converted smoothly to 1-hydroxy- and 1-cyano-N-methylpyrroloanthrones (VIb and VIIb). 1-n-Butylamino-N-methylpyrroloanthrone (VIIIb) is formed in the reaction of IIIb with n-butylamine whereas in the case of IIIa the reaction can be realized only in the presence of an acid (VIIIa).

It is interesting that unsubstituted N-methylpyrroloanthrone (Ib) also undergoes nucleophilic attack at the 1 position. For example, the reaction of Ib with n-butylamine in the presence of sodium amide and with sodium cyanide gave the corresponding 1-substituted compounds, which were identical to compounds VIIIb and VIIb. Reactions of this type are also characteristic for other peri-condensed anthrone derivatives, particularly anthrapyridone [6], and probably proceed as nucleophilic addition to the conjugation chain, which includes a carbonyl group, and subsequent oxidation. However, considering the data on electrophilic substitution presented above, this was hardly expected in the case of pyrroloanthrones.

Pyrroloanthrone is a peculiar system, the reactivity of which is determined by the mutual effect of the condensed pyrrole and anthrone rings. The possibility of direct substitution of the hydrogen atom by the nucleophile and electrophilic substitution at the same position is currently known for a number of compounds (for example, see [6]); however, insofar as we can judge, this is the first instance in which this sort of selective electrophilic reaction and diazo coupling are simultaneously possible. Most of the compounds synthesized in the present research and in earlier studies [1, 2] luminesce intensely in solution; this makes a study of the aspects of their practical application expedient.

EXPERIMENTAL

The yields and characteristics of the previously undescribed compounds are presented in Table 1.

N-Methylpyrroloanthrone (Ib). A) A 3.6-ml (56.8 mmole) sample of methyl iodide was added gradually at room temperature to a solution of 3 g (13.7 mmole) of pyrroloanthrone (Ia) in 50 ml of N-methylpyrrolidone and 2.4 ml of 40% sodium hydroxide solution (32.6 mmole), and the mixture was stirred for 1 h. It was then poured into 250 ml of water, and the precipitate was removed by filtration and dried to give 3.16 g (98.9%) of chromatographically pure Ib with mp 197.5-198.5°C (from benzene—hexane). With respect to its melting point and IR spectrum, the product was identical to the substance obtained by the method in [2].

B) Hydrogen bromide was bubbled at room temperature into 10 ml of acetic acid for 1 h, 0.1 g of 1-bromo-N-methylpyrroloanthrone (IIIb) was added, and the mixture was heated at 60-65°C in a slow stream of hydrogen bromide for 28 h. It was then poured into 50 ml of water, and the aqueous mixture was neutralized with ammonium hydroxide. The precipitate was removed by filtration, washed with water, dried, and chromatographed on Al_2O_3 (benzene) to give 0.038 g (51%) of Ib.

Pyrroloanthrone (Ia) was similarly obtained from 1-bromopyrroloanthrone IIIa.

1-Nitropyrroloanthrones (IIa, b). Fuming nitric acid (46 mmole) was added at room temperature to a solution of 4.6 mmole of pyrroloanthrone Ia or Ib in 100 ml of acetic acid, and the mixture was stirred for 3 h. It was then poured into 500 ml of water, and the precipitate was removed by filtration, washed with water, and dried to give 0.79 g of 1-nitropyrroloanthrone IIa. Chromatography on SiO_2 (40-100 mμ) (benzene) gave 0.8 g of 1-nitro-N-methylpyrroloanthrone IIb.

1-Bromopyrroloanthrone (IIIa). A solution of 1.1 ml (21.5 mmole) of bromine in 37 ml of dioxane and 1.1 ml of 40% sodium hydroxide solution (15 mmole) were added gradually at 45-50°C to a solution of 2 g (9.13 mmole) of pyrroloanthrone Ia in 200 ml of dioxane, and the mixture was stirred at this temperature for 30 min. The solvent was then removed by distillation to a volume of 50 ml, and the concentrate was cooled and diluted with 250 ml of water. The precipitate was removed by filtration, washed with water, and dried to give 2.62 g of chromatographically pure IIIa.

1-Bromo-N-methylpyrroloanthrone (IIIb). A solution of 0.9 ml (17.55 mmole) of bromine in 30 ml of dioxane was added gradually at 45-50°C to a solution of 1 g (4.3 mmole) of N-methylpyrroloanthrone (Ib) in 100 ml of dioxane and 3.1 ml of 40% sodium hydroxide solution (42 mmole). The mixture was worked up as in the synthesis of IIIa to give 1.26 g of IIIb.

1-(2,4-Dinitrophenylazo)pyrroloanthrones (IVa, b). A 4.6-mmole sample of 2,4-dinitrobenzenediazonium tetrafluoroborate was added at room temperature to a solution of 0.46 mmole of pyrroloanthrone Ia, b in 10 ml of glacial acetic acid, and the mixture was stirred for 20 h. It was then poured into 50 ml of water, and the resulting precipitate was removed by filtration, washed with water, dried, and chromatographed on SiO_2 (40-100 mμ) (chloroform) to give 0.13 g of IVa and 0.1 g of IVb.

1-Aminopyrroloanthrones (Va, b). A) A 0.5 g sample of bromo derivative IIIa or IIIb was heated in 30 ml of ammonium hydroxide at 170°C for 12-13 h, after which the mixture was cooled and neutralized with dilute hydrochloric acid. The precipitate was removed by filtration, washed with water, and reprecipitated from dimethylformamide (DMF) by the addition of water to give Va (36%) or Vb (53%), which were identical to the substances obtained by the method in [2].

B) A 0.1-g sample of Raney nickel was added to a solution of 0.1 g of dinitropyrroloanthrone IIa or IIb in 5 ml of DMF, and the mixture was stirred at room temperature for 7 h. The Raney nickel was removed by filtration, and the filtrate was poured into 25 ml of water. The precipitate was removed by filtration, washed with water, dried, and reprecipitated from butanol by the addition of hexane to give Va (79%) or Vb (67%).

C) A mixture of 0.1 g (0.235 mmole) of 1-(2,4-dinitrophenylazo)-N-methylpyrroloanthrone (IVb) and 0.2 g (3.08 mmole) of zinc dust in 10 ml of acetic acid was refluxed for 30 min, after which the zinc dust was removed by filtration, and the filtrate was diluted with water (50 ml). The precipitate was removed by filtration, washed with water, dried, and chromatographed on SiO_2 (100-250 mμ) (chloroform) to give 35 mg (60%) of IVb.

1-(2,4-Dinitrophenylazo)pyrroloanthrone (IVa) was similarly reduced to 1-aminopyrroloanthrone (Va).

1-Hydroxy-N-methylpyrroloanthrone (VIb). A 2-g sample of 1-bromo-N-methylpyrroloanthrone (IIIb) was heated in a sealed ampul with 100 ml of a 5% alcohol solution of potassium hydroxide at 170°C for 16 h, after which the mixture was cooled and neutralized with 0.1 N hydrochloric acid. The precipitate was removed by filtration, washed with water and alcohol, dried, and chromatographed on SiO_2 (40-100 mμ) (chloroform). The product was dried in vacuo over P_2O_5 (the product was hygroscopic) to give 0.64 g of VIb.

1-Cyano-N-methylpyrroloanthrone (VIIb). A) A 0.1-g (0.32 mmole) sample of 1-bromo-N-methylpyrroloanthrone IIIb and 0.1 g (0.86 mmole) of sodium cyanide were refluxed in 10 ml of alcohol, and the mixture was poured into 50 ml of water. The precipitate was removed by filtration, washed with water, and chromatographed on Al_2O_3 (benzene) to give 62 mg of VIIb.

B) A 0.1-g (0.43 mmole) sample of N-methylpyrroloanthrone Ib and 0.1 g (0.86 mmole) of sodium cyanide were refluxed in 10 ml of alcohol for 8 h, and the mixture was worked up as in method A to give 33 mg (30%) of VIIb.

1-n-Butylaminopyrroloanthrone (VIIIa). A mixture of 0.5 g (1.68 mmole) of 1-bromopyrroloanthrone (IIIa), 0.5 g (5.35 mmole) of n-butylamine hydrochloride, and 20 ml of n-butylamine was refluxed for 5 h, after which it was cooled and poured into 100 ml of 20% acetic acid. The precipitate was removed by filtration, washed with water, dried, and chromatographed on Al_2O_3 (with chloroform) to give 0.32 g of VIIIa.

1-n-Butylamino-N-methylpyrroloanthrone (VIIIb). A) A 0.1-g sample of 1-bromo-N-methylpyrroloanthrone IIIb was refluxed in 5 ml of n-butylamine for 5 h, after which the product was isolated as in the preparation of VIIIa to give 96 mg of VIIIb.

B) A mixture of 0.1 g (0.43 mmole) of N-methylpyrroloanthrone Ib, 0.1 g (2.56 mmole) of sodium amide, and 10 ml of n-butylamine was refluxed for 5 h, after which the product was isolated as in the preparation of VIIIa and chromatographed on Al_2O_3 (benzene) to give 39 mg (30%) of VIIIb.

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