NEW METHOD FOR THE SYNTHESIS OF SUBSTITUTED ANTHRANILS

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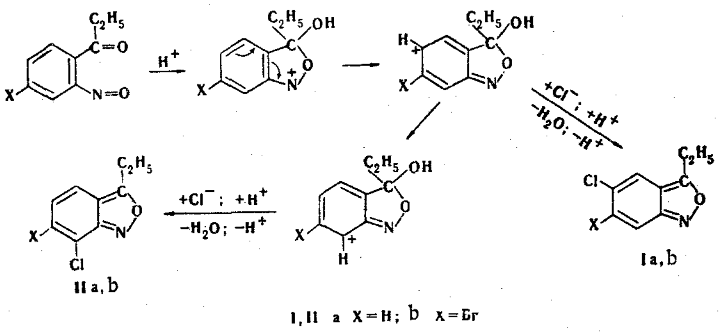
Substituted anthranils can be obtained by intramolecular cyclization of o-nitrosoacylbenzenes under the influence of dry hydrogen chloride in an inert solvent. Incorporation of a halogen atom into the 5 or 7 position occurs simultaneously with formation of the anthranil system. Reduction of the anthranils gives difficult-to-obtain o-acylanilines.

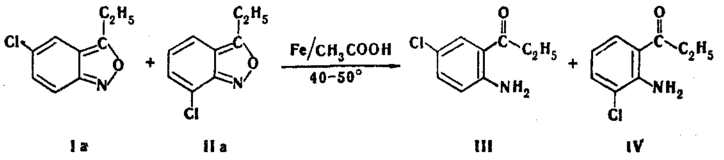
Despite the large number of studies devoted to anthranils, there is only one sufficiently general method for their preparation – reduction of aromatic o-nitro carbonyl compounds [1].

We propose a method for the synthesis of substituted anthranils by intramolecular cyclization of o-nitrosoacylbenzenes under the influence of hydrogen chloride. The accessibility of substituted o-nitrophenylcyclopropanes [2-4] and the simple and almost quantitative transition from them to o-nitrosoacylbenzenes [3-5]* open up a possibility for the preparation of diverse anthranils. In the present paper, the synthesis of anthranils is described for the two simplest cases. Incorporation of a halogen atom into the 5 or 7 position (in a ratio of 5 : 1) occurs simultaneously with the formation of the anthranil system. It can be assumed that the reaction proceeds via the following scheme:



The PMR spectra of Ia,b and IIa,b and the ratio of the integral intensities of the proton signals confirm the structures (see Table 1).

Reduction of a mixture of Ia and IIa with iron in glacial acetic acid gave the corresponding o-aminopropiophenones (III and IV). When hydrogen chloride was passed into a dry ether solution of a mixture of III and IV, amino ketone III gave the hydrochloride, while isomeric amino ketone IV did not. The IR spectra of III and IV contained bands of NH stretching vibrations (3380-3520 cm^{-1}) and, at 1540-1660 cm^{-1}, characteristic sets of bands of medium intensity due to the interaction of adjacent amino and carbonyl groups,



Ia IIa III IV

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* o-Nitrosoacylbenzenes are also readily obtained from o-nitrostyrenes [5].

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TABLE 1. PMR Spectra of Substituted 3-Ethylanthranils

Compound	Chemical shifts, δ, ppm *						J, Hz	
	CH_3	CH_2	H_4	H_5	H_6	H_7	J_{ortho}	J_{meta}
Ia	t 1,71	q 3,37	s 7,59	—	d 7,28	d 7,69	10	1,8
IIa	t 1,78	q 3,47	d 7,58	m 7,03	d 7,45	—	7; 9	1,2
Ib	t 1,82	q 3,48	s 7,86	—	—	s 8,11	—	—
IIb	t 1,91	q 3,57	d 7,55	d 7,27	—	—	9	—

*Abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

which form chelate bonds. The PMR spectra of III and IV recalled the corresponding spectra of 3-ethylanthranils, but the signals of the protons of the ethyl groups were shifted to strong field (triplet centered at 1.26 ppm and quartet centered at 2.88 ppm); this attests to weakening of the deshielding effect, which is apparently caused by disruption of the heterocyclic ring of the anthranil system.

EXPERIMENTAL

The IR spectra of mineral oil suspensions were recorded with a UR-20 spectrometer. The PMR spectra were recorded with a JNM H-60 spectrometer with an operating frequency of 60 MHz (CCl_4) and hexamethyldisiloxane (HMDS) as the internal standard.

5-Chloro-3-ethylanthranil (Ia) and 7-Chloro-3-ethylanthranil (IIa). A stream of hydrogen chloride was passed in the course of 45 min with stirring into a suspension of 10 g (0.06 mole) of o-nitrosopropiophenone [5] and 300 ml of dry benzene, after which the benzene solution was washed with water and dried with calcined magnesium sulfate. The solvent was removed by distillation, and the residue was chromatographed with a column filed with aluminum oxide with elution by ether–petroleum ether (1 : 3) to give 7.2 g (65%) of 5-chloro-3-ethylanthranil (Ia, n_D^{20} 1.5672) and 1.3 g (12%) of 7-chloro-3-ethylanthranil (IIa, n_D^{20} 1.5756). The products were light-yellow mobile liquids with a characteristic odor and were unstable on distillation. Found,% (for the mixture): C 59.5; H 4.5. C_9H_8ClNO. Calculated,%: C 59.5; H 4.4.

5-Chloro-6-bromo-3-ethylanthranil (Ib) and 7-Chloro-6-bromo-3-ethylanthranil (IIb). Similarly, 2.5 g (0.01 mole) of 4-bromo-2-nitrosopropiophenone [4] gave 2.02 g (74%) of a mixture of Ib and IIb. Found,% (for the mixture): C 41.6; H 2.8. $C_9H_7BrClNO$. Calculated,%: C 41.5; H 2.7. Chromatography with a column filled with aluminum oxide with elution by ether–petroleum ether (1 : 3) gave 5-chloro-6-bromo-3-ethylanthranil (Ib) with mp 51-52° and 7-chloro-6-bromo-3-ethylanthranil (IIb) with mp 41-42°.

2-Propionyl-4-chloroaniline (III) and 2-Propionyl-6-chloroaniline (IV). An 8.5 g (0.047 mole) sample of a mixture of Ia and IIa in 45 ml of alcohol was added with stirring to 18.4 g (0.33 mole) of reduced iron and 118 ml of glacial acetic acid, after which the mixture was heated to 40°, stirred for 2 h, and poured into 100 ml of water. The aqueous mixture was neutralized with saturated sodium carbonate solution and extracted with ether. The ether extract was washed with water, dried with magnesium sulfate, and saturated with hydrogen chloride. The resulting precipitate was removed by filtration and dried to give 7.5 g (73%) of 2-propionyl-4-chloroaniline. The mother liquor was evaporated, and the residue was chromatographed with a column filled with aluminum oxide with elution with ether–petroleum ether to give 1.3 g (15%) of 2-propionyl-6-chloroaniline (IV) with n_D^{20} 1.5948. Found,%: C 59.2; H 5.6. $C_9H_{10}ClNO$. Calculated,%: C 59.0; H 5.5. A 7.5 g sample of 2-propionyl-4-chloroaniline hydrochloride was dissolved in 100 ml of 2 N sodium hydroxide, and the amine was extracted with ether. The extract was washed with water and dried with magnesium sulfate, and the solvent was evaporated. The residue was recrystallized from aqueous alcohol to give 6 g (96%) of base III with mp 80°. Found,%: C 59.2; H 5.4. $C_9H_{10}ClNO$. Calculated,%: C 59.0; H 5.5.

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