SYNTHESIS OF 2-AZAANTHRAQUINONE AND ITS DERIVATIVES

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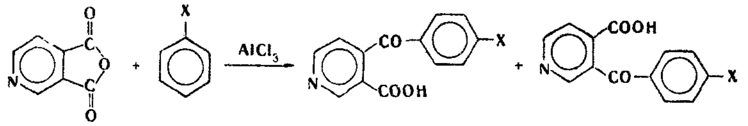
The acylation of benzene, toluene, and chlorobenzene with cinchomeronic acid anhydride in the presence of $AlCl_3$ has given in each case both possible isomers of the corresponding aroylpyridinecarboxylic acid. It was found that the yields of reaction products and their isomeric compositions depend on the conditions of performing the reaction. The intramolecular cyclization of the isomeric keto acids in the presence of 2% oleum has given 2-azaanthraquinone and chlorine derivatives of it.

Anthraquinone and its derivatives are important in the production of particularly fast varieties of dyes [1]. Although anthraquinone itself is produced mainly by the vapor-phase oxidation of anthracene, a number of its derivatives having technical importance are made by the acylation of aromatic hydrocarbons in the presence of aluminum chloride followed by the intramolecular cyclization of the benzoylbenzoic acids formed [2].

The aim of the present work was to investigate the acylation of benzene and its derivatives with cinchomeronic anhydride and the cyclization of the resulting aroylpyridinecarboxylic acids to 2-azaanthraquinone and its derivatives.

Cinchomeronic anhydride (I) has been studied in the Friedel-Crafts reaction only with benzene, and the results obtained by different workers [3-6] are somewhat contradictory. Phillips [3], who was the first to perform this reaction, reported that it formed γ-benzoylnicotinic acid (IIIa). In later investigations [4, 5], the reaction product formed was ascribed the structure of β-benzoylisonicotinic acid (IVa). Later, Kirpal [6] established that in this reaction both possible isomers (IIIa) and (IVa) are formed, and he separated and characterized them. In all the investigations the structures of the products formed were shown by decarboxylation to the corresponding phenyl pyridinyl ketones.

An experimental check of these results showed that the anhydride reacts with benzene, under more severe conditions than phthalic anhydride, to form two isomeric keto acids, and these were separated by virtue of their different solubilities:



I II a-c III a-c IV a-c

II-IV a X = H; b X = Cl; c X = CH_3

The yield of reaction products and the ratio of the isomers depends on the duration of the reaction. Thus, when the reaction mixture was boiled for 3-4 h, the yield of reaction products amounts to 35% and the predominating isomer was (IVa); on reaction for 6-8 h, 53% of a mixture of keto acids was formed and now (IIIa) predominated in it. Increasing the reaction time to 24 h led to an increase in yield to 73% with the exclusive formation of (IIIa). It is likely that during the reaction under the influence of the aluminum chloride (IVa) isomerizes into (IIIa), and this was the reason for the contradictory results obtained by various workers in the study of this reaction.

Toluene and chlorobenzene also react with the anhydride (I) under conditions more severe than those for the reactions with phthalic anhydride. When the reaction mixture was heated at 110-130°C for 4-8 h (until the evolution of hydrogen chloride ceased), acylation products were obtained with a yield of 40-52%, these containing, as in the case of benzene, two isomers with a predominance of the β-aroylpyridinecarboxylic acids (IVb and IVc). Toluene,

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TABLE 1. Characteristics of the Aroylpyridinecarboxylic Acids and Azaanthraquinones Synthesized

Compound	R_f	mp, °C	Found, %				Empirical formula	Calculated, %				Yield, %
			C	H	Cl	N		C	H	Cl	N	
IIIa	0,70	223—226[a]	—	—	—	—	—	—	—	—	—	39
IIIb	0,68	245—250	57,7	3,3	13,3	5,8	$C_{13}H_8ClNO_3$	59,8	3,1	13,4	5,3	8
IIIc	0,69	223—224	69,5	4,8	—	5,8	$C_{14}H_{11}NO_3$	69,7	4,6	—	5,8	13
IVa	0,55	277—279[b]	—	—	—	—	—	—	—	—	—	14
IVb	—	317	59,3	3,6	13,4	5,8	$C_{13}H_8ClNO_3$	59,8	3,1	13,4	5,3	32
IVc	0,57	299—299,5	69,5	4,8	—	5,7	$C_{14}H_{11}NO_3$	69,7	4,6	—	5,8	39
VIIIa	0,41	179[c]	—	—	—	—	—	—	—	—	—	36
IXa												
VIIIb	0,50	150—151	64,8	2,3	15,0	5,9	$C_{13}H_6ClNO_2$	64,6	2,5	14,7	5,8	67
IXb	0,42	125—127	64,7	2,7	15,1	5,8	$C_{13}H_6ClNO_2$	64,6	2,5	14,7	5,8	33

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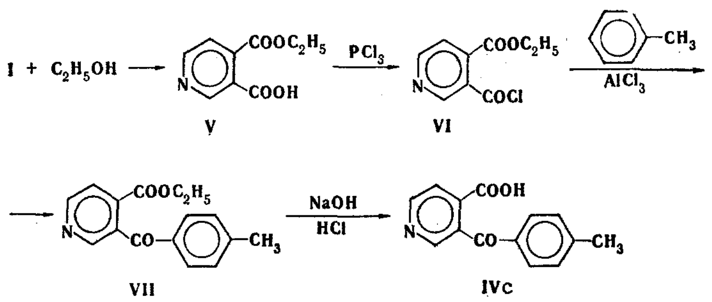
[a] According to the literature [6], mp 226°C. [b] According to the literature [6], mp 270°C. [c] According to the literature [3], mp 179°C.

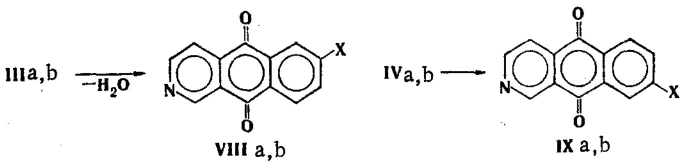
which is a more reactive aromatic compound, can be acylated even at room temperature, but the yield at a reaction time of 60 h does not exceed 25-30%.

Since the isomeric aroylbenzoic acids obtained in the acylation of toluene and chlorobenzene have similar physical properties to the known isomers of benzoylpyridinecarboxylic acids, for the compounds crystallizing from methanol and having lower melting points and greater mobilities on Silufol plates we have proposed the structure of the γ-aroylnicotinic acids, while the less soluble compounds are correspondingly, the β-aroylisonicontinic acids. To prove this hypothesis, one of them (IVc) was obtained by an independent method, as follows:



The reaction product proved to be identical with the acid (IVc) isolated from the mixture of keto acids formed in the acylation of toluene. The characteristics of the aroylpyridinecarboxylic acids synthesized are given in Table 1.

Compounds (IIIa-c) and (IVa-c) were investigated in the intramolecular cyclization reaction to give azaanthraquinone and derivatives of it, taking place in the following way:



VIII, IXa X=H; VIII, IX b X=Cl

The preparation of 1- and 2-azaanthraquinones by the intramolecular cyclization of β-benzoylpicolinic and γ-benzoylnicotinic acids in the presence of concentrated H_2SO_4 has been described in the literature with no indications of yield. We have investigated this reaction in detail for the case of compounds (IIIa-c) and (IVa-c) in the presence of concentrated H_2SO_4, oleum of various concentrations, and PPA. The cyclization of aroylpyridinecarboxylic acids takes place under more severe conditions than that of benzoylbenzoic acid. While the latter is converted into anthraquinone in the presence of PPA in quantitative yield [7], heating (IIIa) and (IVa) with PPA to 200°C did not give satisfactory results. At a higher temperature, the initial substance decomposed. When the reaction was performed in the presence of concentrated H_2SO_4, the yield of unpurified (Va) or (VIa) did not exceed 16%. Considerably better results were obtained when the reaction was performed in oleum. The maximum yield of reaction product, 34-36%, was achieved by heating a reaction mixture including 2% oleum at 220°C for 30 min, the isomeric acids (IIIa) and (IVa) giving approximately the same yield of reaction product. In 12% oleum we obtained only traces of compound (Va), which is probably due to the sulfonation of the (IIIa) under these conditions. A similar action of sulfuric acid has been reported in the cyclization of certain benzoylbenzoic acids where the addition of boric acid to the reaction mixture to suppress its sulfonating action was used sucessfully [8]. However, the performance of the cyclization of (IIIa) and (IVa) in the presence of H_3BO_3 did not change the yield of reaction product.

The reaction of (IIIb) took place similarly to those of (IIIa) and (IVa), compound (IXb) being formed with a yield of 31-33%. The cyclization of (IVb) took place considerably better. Heating in 2% oleum at 260°C for 30 min led to the formation of (VIIIb) with a yield of 67%. The introduction of a chlorine atom into the benzene ring probably opposes the sulfonation reaction, which permits cyclization to be carried out under more severe conditions. The lower yield of (IXb) obtained by the cyclization of (IIIb) is probably connected with the partial decomposition of the initial product under these conditions.

Attempts to convert (IIIc) and (IVc) into methylazaanthraquinones under various conditions were unsuccessful. In this case, probably, sulfonation was facilitated still further and became the dominating process, and moreover, under these conditions decomposition of the initial reactants was observed.

The 2-azaanthraquinone and its chlorine derivative that were obtained, like anthraquinone, give a qualitative reaction consisting in the appearance of a crimson coloration of alkaline solutions of the quinones in the presence of zinc dust which disappears after the removel of the zinc and vigorous shaking. The shape of the absorption curves of their electronic spectra does not differ from the spectrum of anthraquinone (λ_{max} 321-329 and 375-382 nm). The IR spectra show an absorption band in the 1685-1700 cm^{-1} region which is characteristic for quinones containing the two carbonyl groups in one ring.

EXPERIMENTAL

The isomeric compositions and individualities of the aroylpyridinecarboxylic acids were determined by chromatography on Silufol plates in the methanol—butanol—carbon tetrachloride (1 : 1 : 1) system. The spots were revealed with an ethanolic solution of copper acetate. The azaanthraquinones were chromatographed on Silufol plates in the ether—hexane (2 : 1) system, and the spots were revealed with iodine vapor. IR spectra were recorded on a UR-10 instrument in tablets with KBr, and UV spectra on a Specord UV-Vis instrument in chloroform solution.

Compounds (I) and (V) were obtained by methods described in the literature [9, 10].

γ-Benzoylnicotinic and β-Benzoylisonicotinic Acids (IIIa and IVa). With stirring, 18 g (0.13 mole) of $AlCl_3$ was added to a solution of 8 g (0.054 mole) of (I) in 60 ml of dry benzene. The mixture was kept at 100-105°C under a reflux condenser closed with a calcium chloride tube until the evolution of HCl had ceased (6-8 h). After cooling, the reaction mixture was treated with water and the benzene was distilled off with steam. The solid matter was removed from the hot residue and was dissolved in ammonia solution, the resulting solution then being boiled with activated carbon and acidified with concentrated HCl to pH 3-4. This yielded 1.7 g (15%) of compound (IVa). White precipitate, R_f 0.55, mp 277-279°C. According to the literature [6], mp 270°C.

The filtrate was made alkaline with ammonia solution and filtered and the precipitate of $Al(OH)_3$ was washed twice with hot water. The filtrate and the wash-waters were combined and acidified to pH 3-4. This gave 4.8 g (39%) of (IIIa). White precipitate with R_f 0.70, mp 223-225°C (from ethanol). According to the literature [6], mp 226°C.

γ-(p-Toluyl)nicotinic and β-(p-Toluyl)isonicotinic Acids (IIIb) and (IVb). Similarly, a mixture of 8.1 g (0.054 mole) of (I), 60 ml of toluene, and 18 g (0.13 mole) of $AlCl_3$ was kept for 4-5 h and was then treated with water; the resulting solution was made alkaline with ammonia, the toluene was distilled off with steam, and the $Al(OH)_3$ was separated off. The precipitate was boiled with small portions of water (a total of ~300 ml) until acidification of the filtrate no longer caused the appearance of a precipitate. The filtrate and the wash-waters were combined, evaporated to a volume of 200 ml, cooled, and acidified to pH 3-4. The resulting precipitate was separated off and crystallized from methanol. This gave 1.7 g (13%) of (IIIb) in the form of a white precipitate with mp 223-224°C, R_f 0.69. Found: C 69.5; H 4.8; N 5.8%. $C_{14}H_{11}NO_3$. Calculated: C 69.7; H 4.6; N 5.8%.

The solid matter that had not dissolved in the crystallization process was dissolved in ammonia, and the solution was boiled with carbon, filtered, and acidified. This gave 5.1 g (39%) of (IVb) in the form of a white precipitate with mp 299-299.6°C, R_f 0.57. Found: C 69.5; H 4.8; N 5.7%. $C_{14}H_{11}NO_3$. Calculated: C 69.7; H 4.6; N 5.7%.

β-(p-Toluyl)isonicotinic Acid (IVb). A solution of 3.4 g (0.017 mole) of (V) in 50 ml of toluene was treated with 1.52 ml (0.017 mole) of PCl_3. The reaction, which began at room temperature, was complete in a few minutes. The toluene solution of (VI) was separated off and was treated with 5.8 g (0.043 mole) of $AlCl_3$, and the mixture was kept at room temperature in a flask with a calcium chloride tube, with periodic stirring, for 1 h. The red oily product that had formed was decomposed with water, and the toluene was distilled off with steam. A low-melting substance (1.6 g) was separated off and it was boiled with NaOH solution for 2 h, after which the solution was cooled and was acidified to pH 3-4. The white precipitate that separated out was boiled in methanol, giving (IVb), identical in melting point and R_f value with the reaction product obtained by the acylation of toluene.

γ-(p-Chlorobenzoyl)nicotinic and β-(p-Chlorobenzoyl)isonicotinic Acids (IIIc and IVc). In a similar manner to (IIIa) and (IVa), 8.5 g (0.057 mole) of (I), 60 ml of dry chlorobenzene, and 20 g (0.15 mole) of $AlCl_3$ at 100-130°C gave 4.5 g (32%) of (IVc) in the form of a white precipitate with mp 317°C. When chromatographed on a Solufol plate, the spot was not shown up by an ethanolic solution of copper acetate. Found: C 59.3; H 3.6; Cl 13.4; N 5.8%. $C_{13}H_8ClNO_3$. Calculated: C 59.8; H 3.1; Cl 13.4; N 5.3%.

The filtrate yielded 1.1 g (8%) of the acid (IIIc) in the form of a white precipitate with mp 248-250°C (from methanol), R_f 0.68. Found: C 59.7; H 3.3; Cl 13.3; N 5.8%. $C_{13}H_8ClNO_3$. Calculated: C 59.8; H 3.1; Cl 13.4; N 5.3%.

2-Azaanthraquinone (VIIIa). A mixture of 0.23 g of (IIIa) and 1 ml of 2% oleum was heated at 220°C for 30 min. Then it was cooled and poured into 50 ml of water, and the mixture was made alkaline with KOH solution and extracted with toluene (3 × 20 ml). The solvent was evaporated off from the extract to give 0.075 g (36%) of (VIIIa) in the form of light yellow crystals with mp 179°C, which corresponds to the literature figure [3]. R_f 0.41. UV spectrum, λ_{max}, nm: 321 and 378. IR spectrum: 1700 cm^{-1} (C=O). Similarly, (IVa) gave (IXa) with a yield of 34%.

6-Chloro-2-azaanthraquinone (VIIIb). Similarly, 0.23 g of (IVb) in 1 ml of 2% oleum at 260°C for 30 min gave 0.14 g (67%) of (VIIIb) in the form of yellow-green crystals with mp 150-151°C (from cyclohexane), R_f 0.50. UV spectrum, λ_{max}, nm: 329 and 382. IR spectrum: 1685 cm^{-1} (C=O). Found: C 64.8; H 2.3; Cl 15.0; N 5.9%. $C_{13}H_6ClNO_2$. Calculated: C 64.6; H 2.5; Cl 14.7; N 5.8%.

7-Chloro-2-azaanthraquinone (IXb). Similarly, 0.23 g of (IIIb) and 1 ml of 2% oleum at 220°C for 30 min yielded 0.07 g (33%) of (IXb) in the form of yellow crystals with mp 125-127°C (from cyclohexane), R_f 0.42. UV spectrum, λ_{max}, nm: 327, 375 nm. Found: C 64.7; H 2.7; Cl 15.1; N 5.8%. $C_{13}H_6ClNO_2$. Calculated: C 64.6; H 2.5; Cl 14.7; N 5.8%.

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