İstanbul Ecz. Fak. Mec.
7, 96 (1971)

J. Fac. Pharm. İstanbul
7, 96 (1971)

The Reaction of o-, m- and p-Nitroanilines with Phthalic Anhydride

Nitro Anilinlerin Ftalik Anhidridle Reaksiyonu

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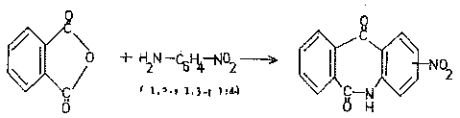
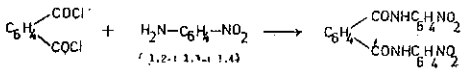
The use of phtalic anhydride and phthaloyl chloride as acylating agents in the Friedel-Crafts reaction has been previously mentioned (1). In the course of our studies, the condensation of the o-, m- and p- isomers of nitroanilines with the above mentioned substances under various conditions were investigated. Besides a probable amide formation, a Friedel-Crafts condensation due to the orientation of the nitro groups in the o- and p- positions was also expected. If this hypothesis was valid, then the condensation should have proceeded from the hydrogen of the ring as well as the amine group to afford a substituted morphanthridinedione nucleus.



When phthaloyl chloride was utilized instead of the anhydride, the reaction should have proceeded to give the diamide for all the isomers of nitroanilines.



In one of the previous studies on the reaction of nitroanilines with phthaloyl chloride, Dobreff (2) reported that the product was a mix-

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ture of nitrophthalanil, nitrophenylphthalamide and nitrophenylphhtalimide. Later Sherrill et al. (3) furthered the investigation on the same subject by trying various media such as ethyl acetate or chloroform. The reaction products were then characterized as the corresponding o-, m- and p-nitrophthalanilic acids which could be converted to nitrophenylphthalimides. In fact, formerly Meyer and Maier (4) had reported that phthalimides could be obtained by the fusion of phthalic anhydride with nitroanilines. Sherrill and co-workers (3) carried out their investigations by trying various media such as ether, chloroform and ethyl acetate as well as the fusion of the components, and reported the products as a mixture of the monoamides, diamides and the imides of the corresponding nitroanilines.

In his study of N-arylphthalimides, Grammaticakis (5) condensed the isomeric nitroanilines with phthalic anhydride and reported the formation of nitrophthalanilic acids in benzene, which could then be coverted to nitrophenylphthalimides by heating in ethanol.

It was of interest to point out the effect of the nitro group on the hydrogens of the ring as well as on the hydrogens of the amino group. Therefore, more energetic condensation agents were tried in various modified Friedel-Crafts reactions of phthalic anhydride with isomeric nitroanilines, and the reaction products were characterized.

EXPERIMENTAL

9.32 g (0.063 mole) phthalic anhydride, 10 g (0.072 mole) nitroaniline, 2 g (0.032 mole) nitromethane and 125 ml benzene were heated in a water bath under reflux. For comparison, the reaction was carried out several times in almost identical experiments, the only difference being the absence or presence of aluminium chloride.

In the course of the experiments, the formation of the crude product was observed to begin on the tenth minutes for the p- isomer, and on the twentieth minutes for the m- isomer. Investigations were done in order to increase the yield; various periods of heating, starting with half an hour up to six hours were tried.

Benzene was evaporated from the resultant mixture and the following experiments were done on the amorphous, yellowish crude product:

I. The unreacted nitroaniline was removed by several rapid extractions with hot water. The residue was then extracted with chloro-

form, dried over anhydrous Na_2SO_4, and the solvent was distilled off. It was observed that:

With the o- isomer, no residue remained after extraction with hot water; examination of the hot water extract indicated the presence of o-nitroaniline and phthalic acid.

The residue obtained by distilling the chloroform gave the mp. 240° and 260° for the m- and p- isomers respectively. In these isomers, a portion of the crude product which remained undissolved in hot water and chloroform was then crystallized from hot alcohol 96 % to give a substance with mp. 202° for the m- and mp. 190° for the p- isomer.

II. The crude product was extracted with ether (Solution A). The residue was then extracted with chloroform (Solution B); the still remaining portion of the product was finally dissolved in hot ethanol (Solution C).

The extracting solvents of Solutions A and B were distilled off and Solution C was allowed to stand for a probable crystallization. Characteristic data about the residues of Solutions A and B and the crystals collected from Solution C are given in Table I.

Table I. The reaction products of three isomeric nitroanilines.

	ortho- *17 g of crude substance*			*meta-* *19.7 g of crude susbtance*			*para-* *19.6 g of crude substance*		
	Yield	*Cryst. solvent*	*m.p. (C°)*	*Yield*	*Cryst. solvent*	*m.p. (C°)*	*Yield*	*Cryst. solvent*	*m.p. (C°)*
Sol. A	11.6 g	acetone	152°	2.8 g	water	103°	3.4 g	water	148-50°
Sol. B	3.0 g	ethanol	201°	3.1 g	acetic ac.	240°	0.5 g	ethanol	260°
Sol. C	no substance			14.1 g	ethanol	202°	1.8 g	ethanol	190°

III. The crude product which was dissolved in a 5 % solution of NaOH, was extracted with chloroform in a separatory funnel. The chloroform extracts were dried over anhydrous Na_2SO_4 and the solvent distilled to give Residue (B). To the alkaline solution, 12.5 % HCl was added in slight excess and the precipitate thus formed (A) was filtered and dried in a dessicator. The residues (A) and (B)

were subjected to further investigation of which the results are given in Table II.

Table II. The reaction products of three isomeric nitroanilines.

	ortho- 17 g of crude product			*meta-* 19.7 g of crude product			*para-* 19.6 g of crude product		
	Yield	*Cryst. solvent*	*m.p. (C°)*	*Yield*	*Cryst. solvent*	*m.p. (C°)*	*Yield*	*Cryst. solvent*	*m.p. (C°)*
A	1.4 g	acetone	149-51°	12.0 g	ethanol	202°	11.0 g	ethanol	190°
B*	0.2 g	—	64-69°	2.0 g	acetone	240°	2.84 g	ethanol	fract. I 260° fract. II 233-4°

The UV and IR characteristics of the condensation products of the isomeric nitroanilines with phthalic anhydride are given in Table III.

The IR characteristics of N,N′-bis(p-nitrophenyl)phthalamide are: 2.90 μ (NH-); 5.60 μ (CO); 5.75 μ (amide I band); 6.20 μ (NO_2 and aromatic CH); 6.52 μ (amide II band); 7.40 μ (NO_2); 7.78 μ (amide III band); 12.34 μ (p-disubstituted benzene); 13.50 μ (C-N-O of the nitro group).

CONCLUSION

In the reaction of phthalic anhydride with nitroanilines in the presence of activating agents, the condensation of the anhydride with the amine group of the nitroaniline was the only reaction, while no favorable results could be reported with the expected condensation of the hydrogen of the aromatic ring with the anhydride.

Investigations were done on the condensation products of the three isomers according to the variety of products and yields as well as their solubility. Three different methods of separation were utilized and the following results were observed:

* It was observed that in the procedure carried on the o- isomer, the chloroform extracts contained excessive amounts of the unreacted nitroaniline; therefore, the method was modified for this isomer by using ether in place of chloroform. The ethereal extracts were dried over anydrous Na_2SO_4 and the solvent removed by distillation to furnish a pale yellow residue with a yield of 2.90 g, m.p. 170-189°; this substance was crystallized from ethanol 96 % to give yellow crystals, m.p. 200-3°.

Table III. UV and IR characteristics of o-, m-, p-nitrophthalanilic acids and phthalimides.

	o-Nitro Phthalanilic acid	*o-Nitro Phthalimide*	*m-Nitro Phthalanilic acid*	*m-Nitro Phthalimide*	*p-Nitro Phthalanilic acid*	*p-Nitro Phthalimide*
UV	λ_{maks}^{EtOH} 349 mμ (ε 2812) λ_{maks}^{EtOH} 231 mμ (ε 24167)	λ_{maks}^{EtOH} 275 mμ (ε 1895) λ_{maks}^{EtOH} 223 mμ (ε 12209)	λ_{maks}^{EtOH} 239 mμ (ε 20020) Shoulder at 320 μ	λ_{maks}^{EtOH} 236 mμ (ε 4482)	λ_{maks}^{EtOH} 320 mμ (ε 15355) λ_{maks}^{EtOH} 221 mμ (ε 15730)	λ_{maks}^{EtOH} 288 mμ (ε 10783) λ_{maks}^{EtOH} 215 mμ (ε 67000)
IR	2.98 μ (NH and COOH) 5.93 μ CO and amide I band 6.20 μ NO_2 and aromatic CH 6.54 μ amide II band 7.46 μ NO_2 7.78 μ amide III band 13.40 μ C-N-O of NO_2 and o-disubst. benzene	5.85 μ CO 6.23 μ NO_2 and aromatic CH 7.10 μ NO_2 symm. stretching 13.47 μ C-N-O of No_2 and ortho subst. benzene	3.1 μ NH and COOH 5.80 μ CO 5.95 μ amide I band 6.20 μ NO_2 and aromatic CH 6.59 μ amide II band 7.40 μ NO_2 7.82 μ amide III band 11.80 μ C-N of NO_2 13.55 μ C-N-O (NO_2) 12.95 μ and 14.20 m-disubst. benzene	5.57 μ and 572. μ CO 7.15 μ NO_2 and aromatic CH 7.48 μ NO_2 13.50 μ C-N-O (NO_2) 12.35 μ and 14.05 μ m-disubst. benzene	3.05 μ NH and COOH 5.70 μ CO 6.03 μ CO and amide I band 6.19 μ NO_2 and aromatic CH 6.60 μ amide II band 7.40 μ NO_2 7.85 μ amide III band 13.30 μ C-N-O (NO_2) 12.02 μ p-disubst. benzene	5.70 μ CO 6.20 μ NO_2 and aromatic CH 6.51 μ NO_2 13.32 C-N-O (NO_2) 11.82 μ p-disubst. benzene

The characteristic bands of aromatic CH between 6 μ and 7 μ are also present.

Extraction of the unreacted nitroaniline with hot water yielded the best result with the p- isomer. In the case of the o- isomer, the reaction products which were o-nitrophthalanilic acid and o-nitrophtalimide were converted to o-nitroaniline and phthalic acid during the hot water extraction; therefore, the expected products could not be obtained. The decomposition of the corresponding reaction products of the m- and p- isomers with hot water is relatively slow, compared to the o-isomer; therefore, the removal of the unreacted m- and p- nitroanilines could be successfully accomplished by this first technique.

The second technique involved the removal of the nitroanilines from the reaction media by ether extraction. In the o- isomer, the ethereal extracts contained o-nitrophthalanilic acid as well as the unreacted o-nitroaniline. This fraction was then purified by dissolving it in hot acetone from which o-nitrophthalanilic acid crystallized as yellow prisms. The residue was secondly extracted with chloroform and was proved to contain the imide fraction of the product. It was also observed that all of the crude product could be extracted by ether and then chloroform, leaving no further residue. On the other hand, the ethereal extracts of m- and p- isomers afforded practically all of the unreacted nitroanilines, whereas the following chloroform extraction yielded relatively pure imide. Unlike the o- isomer, a residue remained after these extractions which was then crystallized from ethanol to give the corresponding pure nitrophthalanilic acids.

In the third method, the crude product was dissolved in NaOH and then acidified with HCl. The precipitate was characterized as the nitrophthalanilic acid which first formed the sodium salt and then the free acid as a result of acidification. The acidic filtrate was then subjected to chloroform extraction for the isolation of the imides. This technique afforded favorable yields for the p- isomer. In addition, another fraction of the crude product characterized as a diamide could also be obtained in fair yield. The second and third techniques were equally good for the separation of the m-nitro products; however, the former was more favorable for obtaining the imide fraction in higher yield. In the o- isomer, the imide and the phthalanilic acid were best separated if the third technique was modified to use ether instead of chloroform as the extracting solvent.

Attempts to utilize the Friedel-Crafts reaction between nitroanilines and phthalic anhydride for the preparation of the corresponding

substituted morphanthridinediones were unsuccessful, despite the use of various agents like aluminium chloride or hydrogen activators such as nitromethane. It can therefore be concluded that under above mentioned conditions, nitroanilines do not participate in the Friedel-Crafts condensation of the phthalic anhydride regardless of the use of activators.

SUMMARY

Investigations were done on the reaction of the three isomeric nitroanilines with phthalic anhydride in the presence of various energetic condensation agents. It was observed that under the specific conditions utilized, the Friedel-Crafts condensation was unsuccessful; therefore the expected morphanthridinedione derivatives could not be obtained, whereas the condensation between the hydrogens of the amine group and phthalic anhydride afforded the corresponding phthalanilic acids and imides. Various methods were developed for the separation of the admixed derivatives, and the UV and IR characteristics were given for these substances.

ÖZET

Bu çalışmada, üç izomer nitroanilinin enerjik kondansasyon ajanları karşısında ftalik anhidridle verdikleri reaksiyonlar incelendi. Denenen şartlar altında Friedel-Crafts kondansasyonunun yürümediği, dolayısıyla beklenen morphanthridinedion türevlerinin teşekkül etmediği, buna karşılık nitroanilinlerin amin grubu hidrojenleri ile ftalik anhidrid arasındaki kondansasyon neticesinde ftalanilik asid ve imidler husule geldiği tespit edildi. Elde edilen türev karışımlarının birbirlerinden ayrılmaları için metodlar geliştirildi ve bahsi geçen türevlere ait UV ve IR bulguları verildi.

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(Redaksiyona verildiği tarih : 7 Haziran 1971)