

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE STATE
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NITRATION OF ACYLANILINES

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Nitration of phenol and the cresols, except the para compound, gives isomeric mononitro derivatives. Zincke and collaborators¹ found that when an acetic acid solution of a brominated cresol is treated with sodium nitrite, the halogen atom, if it occupies a favorable position, may be replaced by the nitro group. In this way they obtained from the meta series a product in which the halogen atom para to hydroxyl was replaced, while in the ortho and para series the atom ortho to hydroxyl was substituted. In no case did they record the formation of isomeric nitro compounds in a single nitration.

Work in this Laboratory and elsewhere by Raiford and students² has proved that when halogenated phenols containing bromine or iodine as substituents are nitrated by this method they may exchange halogen in the ortho and para positions for the nitro group and thus give rise to isomeric mononitro derivatives.³ On this account it was desired to study halogen substitution products of benzene in which position 1 is occupied by some radical other than hydroxyl. Aniline derivatives suggested themselves.

When an acyl or alkyl aniline is subjected to bromination or nitration,⁴ the new substituent usually enters the anilide rather than the other radical, if either of the *o,o,p*-positions is available. Replacement of halogen by the nitro group in such products is extremely rare. Hübner⁵ obtained a monobromodinitro derivative by nitration of benzoyl-2,4-dibromoaniline with fuming nitric acid, but the structure of the product was not determined. Treatment of *p*-bromodimethylaniline with nitrous acid⁶ gave *p*-bromophenylmethylnitrosamine, and *p*-nitrodimethylaniline. When the starting material contained chlorine instead of bromine, no replacement of halogen was observed, but the products were *p*-chlorophenylmethylnitrosamine and 3-nitro-4-chlorodimethylaniline.

¹ Zincke, *J. prakt. Chem.*, [2] 61, 561 (1900).

² Raiford and collaborators, *THIS JOURNAL*, 44, 158 (1922). This paper contains important references to other work.

³ All attempts to replace chlorine in this way have been unsuccessful. Thus, when Raiford and Heyl [*Am. Chem. J.*, 43, 397 (1910)] and Raiford [*ibid.*, 46, 425 (1911)] subjected *sym.*-trichlorophenol and 2,4,6-trichloro-*m*-cresol, respectively, to the action of nitrous acid under the conditions indicated, only starting material could be recovered. More vigorous treatment of the cresol derivative with fuming nitric acid removed chlorine from the para position and gave a quinone instead of a nitro compound.

⁴ Remmers, *Ber.*, 7, 346 (1874); Hübner, *Ann.*, 208, 292 (1881).

⁵ Hübner, *Ber.*, 10, 1710 (1877).

⁶ Wurster and Scheibe, *ibid.*, 12, 1816 (1879); Koch, *ibid.*, 20, 2460 (1887).

Borrelli⁷ treated benzoyl-2,4,6-tribromoaniline with fuming nitric acid, and obtained two products that melted at 227 and 272–273°, respectively, and which were recorded on the basis of analyses⁸ for nitrogen and bromine as isomeric dinitrotribromobenzanilides. Since the structures of these compounds were not proved either by synthesis⁹ from the required amines and acid chlorides, or by the study of their possible hydrolysis products, it was of interest to consider them further.

In the present study Borrelli's work has been repeated by following his brief directions as closely as possible. The results obtained did not agree entirely with what he reported. The nitration product was a mixture of substances with different solubilities in benzene, as the previous author found. The two least soluble ones that melted at 242 and 266°, respectively, were isolated.¹⁰ Analyses indicated that they were mononitro derivatives, and hydrolysis gave, in each case, *sym.*-tribromoaniline, which showed that in the anilide the nitro group was attached to the benzoyl radical. The lower melting anilide was identified (see experimental part) as the *m*-nitrobenzoyl derivative, and the higher one as the ortho isomeride. Theory requires the existence of four mononitro and ten dinitro derivatives of benzoyl-2,4,6-tribromoaniline. To learn whether Borrelli's products might be included in that list all possible isomers were synthesized and examined. The identity of each was further established by study of its hydrolysis products. None of them corresponds in terms of physical constants with either of the compounds recorded by Borrelli.

When an acetanilide instead of a benzanilide substitution product was nitrated isomers were again obtained. Treatment of acetyl-2,4-dibromoaniline¹¹ with fuming nitric acid alone gave an 86% yield of the corresponding 2,4-dibromo-6-nitro compound.¹² When the starting material was first dissolved in concentrated sulfuric acid and fuming nitric acid was added to this solution, the reaction was much more rapid than before and required cooling to control it. Fractional crystallization of the product gave the 6-nitro compound mentioned above and the isomeric acetyl-2,4-dibromo-5-nitroaniline.¹³ This behavior is, in part, in accordance with the observation of others.¹⁴

⁷ Borrelli, *Gazz. chim. ital.*, **17**, 527 (1887).

⁸ The percentages reported do not indicate that the compounds were pure. The methods of analysis, the weights of materials used, the quantities of reagents, and the weights of final products are omitted. The results cannot, therefore, be checked by calculation.

⁹ Cf. Dacomo, *Ber.*, **18**, 1168 (1885).

¹⁰ Evaporation of the mother liquor left a brown residue that was not obtained in crystalline form.

¹¹ Chattaway and Clemo, *J. Chem. Soc.*, **109**, 90 (1916).

¹² Remmers, *Ber.*, **7**, 348 (1874).

¹³ Körner and Contardi, [*Atti Accad. Lincei*, [5] **17**, I, 465 (1908)] obtained this derivative in another way and proved its structure.

¹⁴ Hollemann, Hartogs and van der Linden, [*Ber.*, **44**, 727 (1911)] found that nitra-

Experimental Part

3,4-Dinitrobenzoyl Chloride.—A mixture of equal weights of phosphorus pentachloride and the required dinitrobenzoic acid¹⁶ was heated on a water-bath for thirty minutes, phosphorus oxychloride was distilled off and the residue allowed to cool and solidify. It melted at 45–47°.¹⁶

Anal. Subs., 0.1837: AgCl, 0.1128. Calcd. for C₇H₅O₅N₂Cl: Cl, 15.40. Found: Cl, 15.19.

Preparation of Benzoyl Derivatives.—With the exceptions indicated in the tables, the benzoyl derivatives were prepared in the following way. An intimate mixture of the required aniline and acid chloride in a suitable flask, set in an oil-bath and attached to an air condenser, was slowly raised to 120–130° and heated there until hydrogen chloride was no longer evolved, usually three to six hours.¹⁷ The powdered residue was then

TABLE I
MONONITROBENZOYL-2,4,6-TRIBROMOANILIDES (C₁₃H₇O₃N₂Br₃)¹⁸

Substituted benzoyl	Yield, %	M. p., °C.	Analysis			
			Subs., g.	AgX, g.	Calcd. Halogen, %	Found
2-Nitro-	81	265 ^a	0.2020	0.2389	50.10	50.33
3-Nitro- ^b	91	242 ^a	.2303	.2703	50.10	49.89
4-Nitro-	96	246–247 ^a	.2070	.2430	50.10	49.96

^a Nearly colorless needles by repeated crystallization from alcohol. ^b Composition checked by analysis for nitrogen. *Anal.* Subs., 0.2001: 9.8 cc. of N₂ at 22° and 746.9 mm. Calcd. for C₁₃H₇O₃N₂Br₃: N, 5.84. Found: N, 5.49. ^c Analyses were made by the Carius method.

TABLE II
DINITROBENZOYL-2,4,6-TRIBROMOANILIDES (C₁₃H₆O₃N₃Br₃)

Dinitrobenzoyl radical	Yield, %	M. p., °C.	Analyses			
			Subs., g.	AgX, g.	Calcd. Halogen, % ^a	Found
2,3-	53 ^f	282–283 ^b	0.2007	0.2166	45.80	45.93
2,4-	93	307–308 ^c	.2031	.2179	45.80	45.66
2,5-	66	286–287 ^c	.1660	.1777	45.80	45.56
2,6-	86	334–336 ^d	.1590	.1703	45.80	45.68
3,4-	94	263–264 ^c	.1856	.1991	45.80	45.65
3,5-	95	288 ^e	.1836	.1979	45.80	45.87

^a Halogen was determined by the Carius method. ^b Colorless leaflets after three crystallizations from alcohol. ^c Nearly colorless needles from alcohol. ^d Felted masses of colorless needles from alcohol. ^e Repeated crystallization from alcohol gave nearly colorless irregularly shaped masses. ^f Represents the amount of material after final crystallization.

tion of aniline in the presence of concentrated sulfuric acid gave a high percentage of meta derivative.

¹⁵ Obtained in 86% yield as directed by Sirks [*Rec trav. chim.*, **27**, 221 (1908)].

¹⁶ The acid chlorides of 2,3- and 2,5-dinitrobenzoic acids were obtained as oils by the method given above. Since the amounts available were small it was not feasible to attempt further purification. The identity of each was fixed by examination of the anilide obtained from it.

¹⁷ Limpricht, *Ann.*, **99**, 249 (1856); also Danckwortt, *Arch. Pharm.*, **223**, 581 (1890).

¹⁸ The 2- and 3-nitro derivatives are the ones obtained also by nitration of Borrelli's starting material.

TABLE III
 MONONITROBENZOYL-2,4,6-TRIBROMO-3-NITROANILIDES^a (C₁₃H₆O₅N₃Br₃)

Substituted benzoyl	Yield, %	M. p., °C.	Analyses			
			Subs., g.	0.1 N ^d AgNO ₃ , cc.	Halogen, %	
					Calcd.	Found
2-Nitro	88	269-270 ^b	0.1634	9.37	45.80	45.89
3-Nitro	93	236-237 ^c	.1971	11.23	45.80	45.59
4-Nitro	92	299-300 ^b	.1944	11.19	45.80	46.05

^a The nitrotribromoaniline used here was obtained in 93% yield by Wheeler's method [*Am. Chem. J.*, **17**, 701 (1895)]. ^b Small colorless needles from acetic acid. ^c Colorless, silky needles from alcohol. ^d Analyses made with the Parr bomb as directed by Brown and Beal [*THIS JOURNAL*, **45**, 1291 (1923)].

 TABLE IV
 BENZOYL DERIVATIVES OF OTHER SUBSTITUTED ANILINES

Substituted aniline	Formula	Yield, %	M. p., °C.	Analyses			
				Subs., g.	AgX, g.	Halogen, ^a %	
					Calcd.	Found	
2,5-Dibromo- ^c	C ₁₃ H ₈ ONBr ₂	96	152	0.1967	0.2070	45.07	44.78
2,6-Dibromo-4-nitro-	C ₁₃ H ₈ O ₃ N ₂ Br ₂	97	190-191 ^b	.1671	.1579	40.00	40.21
2-Methyl-4,6-dibromo- ^c	C ₁₄ H ₁₁ ONBr ₂	57	181-182 ^d	.2151	.2179	43.36	43.12
2,4,6-Tribromo-3-nitro-	C ₁₃ H ₇ O ₃ N ₂ Br ₃	94	234-235 ^d	.2067	.2449	50.10	50.37
2,4,6-Tribromo-3,5-dinitro- ^e	C ₁₃ H ₆ O ₅ N ₃ Br ₃	93	271-272 ^f	.1602	.1730	45.80	46.06

^a Halogen was determined by the Carius method. ^b Crystallized three times from alcohol. ^c Obtained by the Schotten-Baumann method. 2-Methyl-4,6-dibromoaniline was prepared in 77% yield as directed by Fries [*Ann.*, **346**, 165 (1906)]. ^d Colorless needles after repeated crystallization from alcohol. ^e Obtained from 2,4,6-tribromo-3,5-dinitroaniline that was prepared in 52% yield by Blanksma's method [*Rec. trav. chim.*, **21**, 255 (1902)]. ^f Colorless needles from alcohol.

extracted with sodium carbonate solution and finally crystallized from a suitable solvent. The composition of these products is shown by analytical data in the accompanying tables, and the structure of each was further established by hydrolysis and identification of the corresponding acid and amine.

Summary

1. Nitration of benzanilide or its halogen substitution products in the absence of sulfuric acid introduces the new substituent into one of the *o,o,p*-positions of the anilide residue if either of them is available. When the benzoyl derivative of *sym.*-tribromoaniline is used the substituent enters the acyl radical and gives a mixture of the isomeric 2-nitro- and 3-nitrobenzoyltribromoanilides.

2. When the acetyl derivative of 2,4-dibromoaniline was nitrated in the presence of concentrated sulfuric acid a mixture of the isomeric 5-nitro- and 6-nitrodibromo compounds was obtained.

3. In none of the aniline derivatives here studied was halogen replaced by the nitro group.

4. All mono- and dinitro substitution products of benzoyl-2,4,6-tri-

bromoaniline demanded by theory have been synthesized and their structures determined.

5. Further work is in progress in this Laboratory.

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BENZALPYRUVIC ACID DIBROMIDE

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The action of sunlight on β -bromobenzalpyruvic acid has been the subject of study in this Laboratory for several years.¹ The fact that large quantities of this unsaturated bromo compound have been required has led to improved methods of preparation of benzalpyruvic acid and of its dibromide from which the unsaturated bromo compound is prepared and to the observation that a marked characteristic of the dibromide is the ease with which it forms addition compounds with various solvents. In view of a recent paper by Musajo² in this same field it seems advisable to publish results already obtained.

The melting points of different samples of benzalpyruvic acid dibromide prepared in the early work varied from 125 to 142° and this variation was ascribed to contamination of the substance with the unsaturated bromo compound formed from it by loss of hydrogen bromide. It has now been found that the dibromide readily forms a hydrate in the presence of even traces of moisture and that the purest sample of the dibromide described previously contained enough of this hydrate to lower the melting point although not enough to affect the analytical results. In the present work, in which benzalpyruvic acid and the reagents used in the bromination reaction were thoroughly dried, the crude dibromide, obtained in 92 to 97% yield, has been found to melt at 148–150°; recrystallized from dried benzene, at 150–151°. The compound described by Musajo as melting at 147–150° is probably this substance and is certainly not a racemic isomer of the acid melting at 142° as he suggests. Under the conditions used in this Laboratory for the bromination no isomer is formed.

Experimental Part

Preparation of Benzalpyruvic Acid.—For the preparation of pure samples of the acid its methyl ester, obtained readily from crude acid and easily purified, was hydrolyzed in methyl alcoholic solution with potassium hydroxide. The marked insolubility of the potassium salt of the acid in methyl alcohol suggested the following procedure for the condensation reaction which is found to give better yields of pure product and in a much shorter time than the former method adapted from that of Erlenmeyer.

¹ Reimer, *THIS JOURNAL*, **48**, 2454 (1926).

² Musajo, *Gazz. chim. ital.*, **60**, 669 (1930).