

yellow oil, which was not analyzed but transformed into the anthocyanidin.

5,7,2',5'-Tetrahydroxy-2-phenylbenzopyrylium Chloride.—The benzoylchalcone was debenzoylated as described above. The hydroxychalcone was precipitated with hydrochloric acid and was separated from benzoic acid by extraction of the latter with cold dilute sodium bicarbonate solution. The residue was crystallized from 10% hydrochloric acid in which it was very soluble. The dark red crystal mass was extracted with ether, leaving less than a gram of anthocyanidin. It was a brownish-red crystalline powder, m. p. above 300°. *Anal.* Calcd. for $C_{16}H_{11}O_6Cl \cdot 2H_2O$: Cl, 10.4. Found: Cl, 10.3. It gave a red solution in acid and blue in sodium carbonate.

bis-(6,3,4'-Trihydroxy)-flavopinacol.—This flavopinacol, possessing the possible phlobatannin structure, was prepared by reduction of pure 6,3',4'-trihydroxyflavanone (1 g.) and also by reduction of a mixture (1 g.) of flavanone and 3,4,2',5'-tetrahydroxychalcone, consisting mostly of the latter. The flavanone (or mixture of chalcone and flavanone) was dissolved in alcohol (40 cc.) and zinc dust (5 g.) and concd. hydrochloric acid (12 cc.) were added. The solution was boiled for five minutes, during which time the color changed from dark orange (in the case of the mixture) to a pale yellow. The solution was filtered from unreacted zinc and nearly neutralized with sodium bicarbonate, a tan precipitate separating. The solution

was saturated with sodium chloride and extracted without filtering with two portions (75 cc. each) of ethyl acetate. The ethyl acetate was dried over sodium sulfate overnight and evaporated on the steam-bath. Most of the remaining solvent was removed in a vacuum desiccator over sodium hydroxide. The final product was a light red friable solid, retaining traces of solvent with great tenacity. It was readily soluble in acetone, alcohol, and ethyl acetate and partially soluble in water. The water-soluble portion was qualitatively indistinguishable from natural phlobatannins such as mimosa and hemlock tannins, as indicated in the table above. No analysis was attempted.

Summary

1. The production of a new flavopinacol from quinacetophenone and protocatechualdehyde is reported. This substance is qualitatively indistinguishable from such natural phlobatannins as hemlock and mimosa tannins.

2. New benzoyloxychalcones, hydroxychalcones, flavanones, and anthocyanidins derived from quinacetophenone are reported.

3. The peculiar sensitivity of 2',5'-hydroxychalcones to alkali is noted.

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Alkanolamines. VII. Condensation Products of Monoethanolamine and the Isomeric Dichloronitrobenzenes

BY CHESTER B. KREMER AND AARON BENDICH

The activation of a halogeno or nitro group on the benzene nucleus by the presence of other substituted groups is well known. The reactions among such molecules and the amino alcohols were originally investigated in these laboratories. This present paper records our findings with the isomeric dichloronitrobenzenes.

Quite recently, Waldkötter¹ has extended our findings dealing with the condensing ability of monoethanolamine. In general, however, he has dealt with benzene molecules which are quite heavily substituted in the nucleus and contain, usually, at least two nitro groups on the ring. Under such conditions, it is frequently an active nitro group that is split out on condensing with the amino alcohol rather than a halogeno group. Work carried out in our laboratories checks exactly with these results. Our investigations, however, have not been limited to reactions with the ethanolamines and we ex-

pect to publish these data in our next article.

The preparation of all six dichloronitrobenzenes is not an easy task. The 2,5- and 3,4-isomers are readily available, but the others are usually prepared through a number of intermediate syntheses. The fundamental researches dealing with the preparation of most of the isomers were carried out by Beilstein and Kurbatow² and improved and extended by Holleman and Reiding³ and Holleman and De Mooy.⁴ In preparing the 3,5- and the 2,6-dichloronitrobenzenes we followed their procedures with slight modifications. 2,4-Dichloronitrobenzene usually is prepared by the nitration of *m*-dichlorobenzene. We synthesized this material from a by-product formed in the synthesis of 2,6-dichloronitrobenzene. An outline of the complete synthesis of these three dichloronitrobenzenes is given in Chart I.

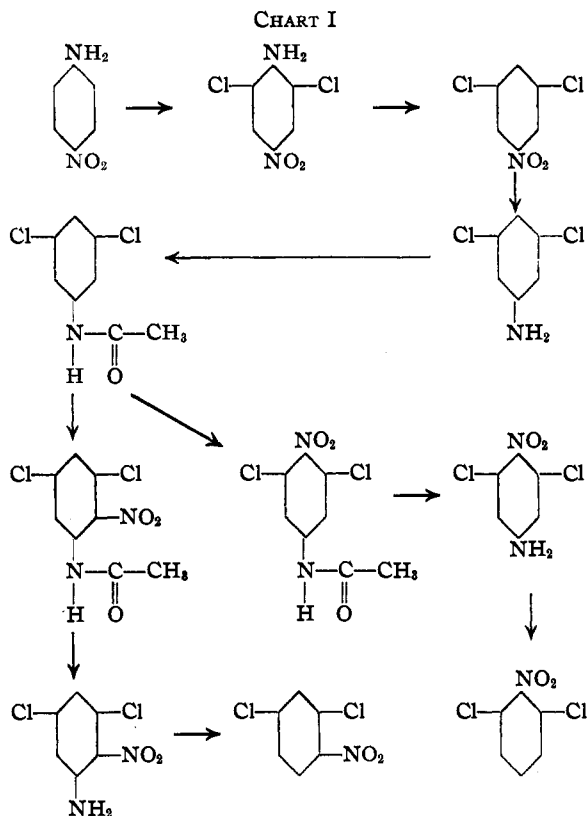
Theoretically, it should be possible to obtain

(2) Beilstein and Kurbatow, *Ann.*, **196**, 228 (1879).

(3) Holleman and Reiding, *Rec. trav. chim.*, **33**, 357-379 (1904).

(4) Holleman and De Mooy, *ibid.*, **35**, 1-66 (1916).

(1) Waldkötter, *Rec. trav. chim.*, **57**, 1294 (1938).

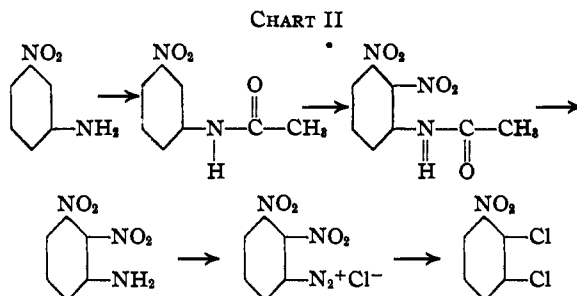


2,4- and 2,6-dichloronitrobenzenes by nitration in a suitable medium, followed by diazotization, of 2,4-dichloroaniline. Our preliminary results with this nitration were uniformly unsuccessful; but recently we have been able to obtain some very small yields of the desired products. We hope to be able to develop further this line of work.

2,3-Dichloronitrobenzene can be prepared by chlorinating *o*-chloronitrobenzene in the presence of antimony chloride. Holleman and Reiding³ used this method but it is not conducive to the preparation of large amounts of material. With this in mind, Holleman and De Mooy⁴ devised a synthesis of the compound by taking advantage of the fact that when 2,3-dinitroaniline is involved in a Sandmeyer reaction to replace the amine group with halogen, not only is the amine group replaced but also the ortho nitro group. In their synthesis of 2,3-dinitroaniline, they nitrated *m*-nitroacetanilide according to the procedure of Wender.⁵ It is claimed that a mixture of three isomers, with the desired product constituting about 50% of the whole, is obtained. We tried this nitration several times and found

(5) Wender, *Jahresber.*, **42**, 775 (1889).

that it gave most unsatisfactory results. We therefore devised a different method of nitration. By treating *m*-nitroacetanilide with fuming nitric acid (sp. gr. 1.50) at room temperature we were able to obtain a product which after one recrystallization from ethanol gave a melting point of 185–186°. With this method, 30 g. of the *m*-nitroacetanilide yielded 25 g. of the desired product and there could be recovered 6 g. of low melting isomers. The steps involved in the synthesis of 2,3-dichloronitrobenzene are given in Chart II.



The condensations between the amino alcohol and the dichloronitrobenzenes were carried out in the usual reflux apparatus, using propyl or butyl alcohol as solvent and magnesium oxide as an acid binding agent.

All of the nitro condensation products were highly colored solids varying from yellow to red with the exception of 2-(6-chloro-2-nitroanilino)-ethanol which was a red liquid. The reduced products were white solids with the exception of 2-(6-chloro-4-aminoanilino)-ethanol, which apparently is a liquid.

Experimental

Preparation of the Dichloronitrobenzenes.—The 2,5- and 3,4-dichloronitrobenzenes were obtained from the Eastman Kodak Co.

3,5-Dichloronitrobenzene.—One hundred and thirty-eight grams of *p*-nitroaniline is mixed with 2 liters of concentrated hydrochloric acid and 60 g. of potassium chlorate added slowly, care being taken to keep the temperature around 70°. When the reaction is complete, the whole is poured into 2 liters of water, the crude 2,6-dichloro-4-nitroaniline removed by filtration and washed free of acid. Varying amounts of 4-nitro-2-chloroaniline are usually found mixed with the desired dichlorinated product. The two can be separated by treatment with hot alcohol.

The 2,6-dichloro-4-nitroaniline is air dried and 105 g. is then added to a mixture of 375 cc. of ethanol and 100 g. of concentrated sulfuric acid in a flask equipped with reflux condenser and automatic stirrer. Thirty-six grams of sodium nitrite is added and the mixture heated on the water-bath for about one hour. This is followed by steam

distillation. Seventy grams of the 3,5-dichloronitrobenzene distil over, is filtered and recrystallized from ethanol; m. p. 65°.

2,6-Dichloronitrobenzene.—Ninety-six grams of 3,5-dichloronitrobenzene is added to 350 cc. of hydrochloric acid (sp. gr. 1.19) in 150 cc. of water and 180 g. of finely divided tin is added gradually until the reduction is complete. Two hundred grams of sodium hydroxide is then added and the whole steam distilled. About 70 g. of 3,5-dichloroaniline melting at 51° is obtained. The product is recrystallized from dilute ethanol.

The dichloroaniline is dissolved in 50 cc. of glacial acetic acid and 100 cc. of 45% acetic anhydride in glacial acetic acid is added. The acetanilide separates out instantly and forms a compact mass. After standing for four hours, it is diluted with water, filtered and air dried. The yield is quantitative and the product melts at 186°.

Fifty grams of the acetanilide is treated with 250 g. of fuming nitric acid (sp. gr. 1.51) until nitration is complete. The mixture is poured into water, whereupon a mixture of two isomers, 3,5-dichloro-4-nitroacetanilide and 3,5-dichloro-2-nitroacetanilide, precipitates out. These are separated by treatment with hot benzene, the former compound being quite insoluble in the hot solvent. The product is washed several times with hot benzene and finally recrystallized from dilute ethanol; m. p. 222°.

Ten grams of the 3,5-dichloro-4-nitroacetanilide is dissolved in 40 g. of concentrated sulfuric acid and warmed for a half hour around 110°. This solution is then poured into 150 cc. of ethanol; 3 g. of sodium nitrite is added and the mixture refluxed on the water-bath until evolution of nitrogen ceases. This is followed by steam distillation. There is obtained 6.5 g. of the 2,6-dichloronitrobenzene. This is recrystallized from ethanol and then vacuum distilled; b. p. 100–101°, 4–5 mm. pressure. Whereas the literature reports this compound as yellow, our product was pure white and melted at 70.5°.

2,4 - Dichloronitrobenzene.—3,5 - Dichloro - 2 - nitroacetanilide is prepared as described above. After separation from the 3,5-dichloro-4-nitroacetanilide, which is also produced at the same time, by means of hot benzene, the desired isomer is quite pure and melts at 138°. This compound is treated identically as described above for the other isomer and results in the same yield. A light yellow solid is obtained which melts at 34° and can be purified further by vacuum distillation; b. p. 105–107° at a pressure of 3–4 mm. and 132–133° at a pressure of 13–14 mm.

2,3-Dichloronitrobenzene.—One hundred and thirty-eight grams of *m*-nitroaniline was acetylated according to Kaufmann⁶ by mixing a concentrated solution of the aniline in benzene with 105 g. of acetic anhydride and refluxing for one hour. The mixture is cooled, the acetanilide filtered and air dried. It melts at 154–155°.

The acetanilide was nitrated as follows: 30 g. was treated with 60 cc. of fuming nitric acid (sp. gr. 1.50) at 20° for one hour. The resulting mixture was poured onto crushed ice and the resulting yellow product filtered and washed free of acid. Recrystallization from a relatively large volume of ethanol yielded 25 g. of a near white solid melting at 186–187°. Evaporation of the

mother liquor yielded 6–8 g. of isomers melting at 100°.

The dinitroacetanilide was treated with four times its volume of concentrated sulfuric acid and heated at 110° for half an hour. The mixture was poured onto crushed ice, the resulting orange solid filtered off and the 2,3-dinitroaniline recrystallized from a small volume of ethanol; m. p. 127°.

One hundred and eleven grams of the 2,3-dinitroaniline was treated with 128 cc. of concentrated hydrochloric acid and the mixture poured into an ice-cold concentrated solution containing 38 g. of sodium nitrite. To this solution was added dropwise a solution of cuprous chloride in hydrochloric acid prepared according to van der Linden.⁷ The mixture was stirred at room temperature for ten minutes and then refluxed over a free flame for half an hour. It was then cooled with ice and filtered. The filtered solid was steam distilled and the material coming over in the steam distillate recrystallized from ethanol. The 2,3-dichloronitrobenzene is white and melts at 61°. It can be purified further by vacuum distillation.

Condensation Reactions

These were run in a solvent, usually normal butyl alcohol, and in some cases magnesium oxide was employed as an acid binder.

Reactions Using Magnesium Oxide.—One-tenth of a mole of the dichloronitrobenzene was dissolved in 50 cc. of warm butanol and 0.1 mole of magnesium oxide was suspended in the solution. A reflux apparatus with mechanical stirrer and dropping funnel was employed. The suspension was heated until the alcohol refluxed gently and then slightly more than 0.1 mole of monoethanolamine was added dropwise and the mixture refluxed for several hours. The whole was filtered clear of any excess magnesium oxide and then steam distilled. On cooling the residue in the distillation flask, the condensed product separated out as a solid (with one exception) and was filtered off. It was then recrystallized from the appropriate solvent. The products obtained with the various dichloronitrobenzenes along with other data are given in Table I.

A somewhat modified procedure was followed in several cases with excellent results. Instead of butanol, propanol was employed as solvent in these runs. After refluxing the reaction mixture as described above and filtering off the magnesium oxide, the alcohol solution was cooled in ice, whereupon a goodly portion of the condensed product separated out. This was filtered off and the over-all yield materially increased by throwing the filtrate into water, whereupon further precipitation of the desired product occurred. This method obviates the use of steam distillation but requires a longer reaction period due to the lower boiling point of the propanol.

Reactions without Magnesium Oxide.—These were run practically the same as described above with the exception that the molar ratio of the monoethanolamine was two or three times that of the dichloronitrobenzene. When propanol was used as the solvent, the steam distillation was omitted as described above.

Reaction between 3,4-Dinitrochlorobenzene and Monoethanolamine.—This reaction was run to assist in proving the structure of the condensation product obtained

(6) Kaufmann, *Ber.*, **43**, 3480 (1909).

(7) Van der Linden, *Rec. trav. chim.*, **30**, 315 (1911).

TABLE I
SUBSTITUTED ANILINO ETHANOLS

Compound, ethanol	Yield, %	Cryst. from	M. p., °C. Corr.	Nitrogen, %	
				Calcd.	Found
2-(6-Chloro-2-nitroanilino)-	60		155-157/2 mm. (b. p.)	12.93	12.87
2-(5-Chloro-2-nitroanilino)-	88	Dil. EtOH	116	12.93	13.07
2-(4-Chloro-2-nitroanilino)-	70	<i>n</i> -BuOH	107.5	12.93	13.04
2-(3-Chloro-2-nitroanilino)-	13	Dil. EtOH	78.5	12.93	13.15
2-(6-Chloro-4-nitroanilino)-	64	Toluene	120	12.93	13.05
2-(6-Chloro-2-aminoanilino)-			135-137/2 mm. (b. p.)	15.01	15.06
2-(5-Chloro-2-aminoanilino)-	90	Toluene	104.5	15.01	15.00
2-(4-Chloro-2-aminoanilino)-	90	Benzene	122.5	15.01	15.17
2-(3-Chloro-2-aminoanilino)-	85	Toluene	74	15.01	14.88
2-(6-Chloro-4-aminoanilino)-			Oil, dec. at 185° (1 mm.)		

with 2,4-dichloronitrobenzene. The procedure was the same as just described. The product obtained is identical with that formed in condensing 2,4-dichloronitrobenzene with the amino alcohol.

Reductions

All reductions of the nitro compounds were carried out using sodium hydrosulfite in a weakly alkaline medium. Yields were practically quantitative in most cases. The properties of these reduced products are included in Table I.

Discussion

In certain of the dichloronitrobenzenes, two chloro groups are capable of replacement. This is the case with the 2,4- and the 2,6-isomers. In all of the other isomers only one chloro group is capable of replacement as the other is in the meta position to the activating nitro group and, as proved by work in these laboratories with amino alcohols, and in analogous work with ammonia, sodium methoxide and potassium sulfide as recorded in the literature,^{4,8} such a chloro group is inactive. In the case of 3,5-dichloronitrobenzene both of the chloro groups are in the meta position and no condensation whatsoever occurs here.

That only one of the two chlorine atoms is removed in condensing either 2,4- or 2,6-dichloronitrobenzene with monoethanolamine is shown by both quantitative and qualitative analyses. In the case of the 2,6-isomer it makes no difference which chlorine is removed; the resulting compound would be the same. It then only becomes a question of determining which of the two chlorine atoms in the 2,4-isomer reacts. It is

definitely established that the one ortho to the nitro group is mobile. This is proved by condensing 3,4-dinitrochlorobenzene in the same manner as described for the dichloronitrobenzenes. The product obtained is identical with that obtained in condensing 2,4-dichloronitrobenzene.

It is interesting to compare the ability of the dichloronitrobenzenes to condense with monoethanolamine, with those condensations involving ammonia, substituted amines and sodium methoxide. Much of this latter work has been carried out by Holleman and his co-workers.^{3,4} They find the most reactive isomer to be the 2,4. The remaining order is 3,4, 2,5, 2,3 and 2,6. Our results check fairly well with those presented in the literature. There can be no doubt that 2,6-dichloronitrobenzene is the least reactive, the yields seldom exceeding 15% even after long periods of refluxing. We find, however, that 2,5-dichloronitrobenzene appears to react more readily with monoethanolamine than the 3,4-compound, which is at variance with the findings of Holleman; but in general our order of reactivity follows closely his order of "speed of reaction."

Summary

1. A study of the preparation of the isomeric dichloronitrobenzenes has been made.
2. The reaction between the dichloronitrobenzenes and monoethanolamine in a neutral solvent has been studied.
3. A report is made upon the preparation and properties of several new chloronitroanilino and chloroaminoanilino ethanols.

(8) Kremer, *THIS JOURNAL*, **59**, 1681 (1937); Blanksma, *Rec. trav. chim.*, **28**, 105-112 (1909); Körner, *Gazz. chim. ital.*, **4**, 305-446 (1876); Beilstein and Kurbatow, *Ber.*, **11**, 2056-2057 (1879).