Summary

1. The rate of thermal decomposition at 100° of the oxytocic principle of pituitary solution has been determined between *P*H 2.0 and 5.1.
2. The rate conforms to that calculated for a first order reaction.
3. A sharp reproducible maximum in stability occurs at *P*H 3.0–3.4.
4. Details of the simple extraction process have been worked out for the oxytocic principle only. Maximum coagulation occurs at *P*H 4.8–5.0. The zone is wide enough to allow routine and effective extraction at *P*H 4.2–4.5 under the conditions described.

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[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY OF TRINITY COLLEGE, CONNECTICUT, AND THE UNIVERSITY OF MISSISSIPPI]

THE REDUCTION OF MONONITROPYROCATECHOLS[1]

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The results presented in this communication represent an outgrowth of a project to prepare monohalogen derivatives of pyrocatechol by nitration, reduction, diazotization and substitution. The nitration of pyrocatechol results in two isomeric mononitro compounds

$$1,2\text{-}(OH)_2\text{-}C_6H_3\text{-}NO_2\text{-}3 \quad \text{and} \quad 1,2\text{-}(OH)_2\text{-}C_6H_3\text{-}NO_2\text{-}4$$

which upon reduction form the corresponding amines. It can be readily seen that this offers the possibility of obtaining certain pyrocatechols substituted in either the 3- or 4-position. Since 3-aminopyrocatechol had not been prepared, it seemed profitable to study it and some related compounds in detail.

In their work on aromatic amines, Jacobs and Heidelberger[2] prepared 4-aminopyrocatechol hydrobromide, 4-aminopyrocatechol, and several compounds derived from them. They arrived at the hydrobromide through sulfanilic acid, *p*-sulfophenylazoguaiacol, 4-aminoguaiacol, and finally 4-aminopyrocatechol hydrobromide by demethylation with hydrobromic acid.

Our work will show that the same results can be obtained easily and in good yield by the direct nitration of pyrocatechol, the separation of the isomers and subsequent reduction.

Nitration of Pyrocatechol.—Pyrocatechol was first nitrated by Benedikt[3] using a nitration mixture of potassium nitrate and sulfuric acid. It was not recognized that two isomers were formed and the melting point

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[1] Part of the material of this paper has been taken from a thesis submitted by I. L. Newell to the faculty of Trinity College (Connecticut), in partial fulfilment of the requirements for the degree of Master of Science.

[2] Jacobs and Heidelberger, THIS JOURNAL, **41**, 467 (1919).

[3] Benedikt, *Ber.*, **11**, 362 (1878).

indicates that the final product was a mixture. The method was improved by Weselsky and Benedikt,[4] using fuming nitric acid on pyrocatechol in ether solution. The isomers were separated by steam distillation, the 3-nitro compound being volatile, while the 4-nitro compound is not. Their conclusions as to the position of the nitro groups were based entirely on the analogous behavior of *o*- and *p*-nitrophenols under steam distillation. However, the constitution of these compounds has been determined by Cousin[5] and by Moureu.[6] Vermeulen[7] found that the 3-nitropyrocatechol could be dissolved out of the nitration mixture by means of petroleum ether, thus eliminating the long steam distillation.

In our work pyrocatechol was nitrated in ether solution as indicated above, and the residue prepared for extraction according to Vermeulen's method. However, we found that 3-nitropyrocatechol is only very slightly soluble in petroleum ether, but the extraction can be carried out with a petroleum distillate boiling at about 100°. Practical heptane from petroleum (Eastman) is well suited for this purpose. On cooling the boiling heptane solution in ice water, 3-nitropyrocatechol is deposited. Several extractions are necessary to remove the major portion. The crude 4-nitropyrocatechol is next subjected to steam distillation until the distillate is nearly colorless. The residual solution is then evaporated to dryness and the residue extracted with boiling xylene.[4] After recrystallization from 20% alcohol the melting points of the two isomers correspond to those recorded.

Several nitrations have shown that the yield is about 80% of the theoretical; 5–8% of this yield is 3-nitropyrocatechol.

Benedikt noticed that alkalies impart a purple color to a solution of nitropyrocatechols. The colorimetric properties of these compounds have proved interesting and are being further investigated in this Laboratory.

Experimental Part

The Reduction of Nitropyrocatechols.—Benedikt reduced nitropyrocatechols to the amino hydrochlorides, but was unable to obtain the free amines. If strong bases are used to form the free amine, the latter is destroyed by oxidation in the air. The reduction can be carried out in the usual manner with tin and hydrochloric or hydrobromic acid, tin precipitated with hydrogen sulfide, and the solution evaporated under reduced pressure.

3-Aminopyrocatechol Hydrochloride.—The almost colorless crystals resulting from the evaporation were recrystallized from 85% alcohol, to which a little hydrochloric acid had been added. On cooling in the ice box, the hydrochloride separated as slightly gray, flat needles or narrow plates. It darkened somewhat at 160° and melted at 196–202°. It is readily soluble in water, giving a faint violet tinge, readily soluble in alcohol

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[4] Weselsky and Benedikt, *Monatsh.*, **3**, 386 (1882).

[5] Cousin, *Ann. chim.*, [7] **13**, 498 (1898).

[6] Moureu, *Bull. soc. chim.*, [3] **15**, 649 (1896); *Compt. rend.*, **122**, 477 (1896).

[7] Vermeulen, *Rec. trav. chim.*, **25**, 23 (1903).

and ether, but less so in benzene or petroleum ether. Ferric chloride gives a deep violet color.

Anal. (Kjeldahl). Subs., 0.3872: 16.05 cc. of 0.1956 *N* HCl. Calcd. for $C_6H_7N\cdot HCl$: N, 8.67. Found: N, 8.78.

3-Aminopyrocatechol.—The free amine was prepared by treating a concentrated aqueous solution of the hydrochloride with a saturated solution of sodium bicarbonate from a dropping funnel. The entire operation, as well as the subsequent filtration and washing with ice water, was carried out in an atmosphere of carbon dioxide to prevent oxidation.[2] The base crystallizes in nearly colorless prisms which darken in the air. It is readily soluble in water and alcohol, but less so in benzene. After protracted drying in a vacuum desiccator over calcium chloride, it melted at 120–122° with decomposition.

Anal. (Kjeldahl). Subs., 0.4475: 18.36 cc. of 0.1956 *N* HCl. Calcd. for $C_6H_7O_2N$: N, 11.21. Found: N, 11.27.

4-Aminopyrocatechol hydrobromide and 4-aminopyrocatechol were prepared in an analogous manner and found to be identical with those prepared by Jacobs and Heidelberger.

Diacetyl-3-acetaminopyrocatechol.—Ten grams of 3-aminopyrocatechol hydrochloride was mixed with 5 g. of fused sodium acetate and boiled for one hour with an excess of acetic anhydride. The resulting mixture was poured into water and neutralized with dilute sodium carbonate solution. The crude triacetate was extracted with chloroform. After distillation of the chloroform, the residue was crystallized from boiling toluene, to which norit had been added to get rid of a pink color. It was recrystallized from 20% alcohol. The yield was 10 g. of glistening white, pointed blades melting sharply at 97°. It is readily soluble in alcohol and chloroform, slightly soluble in ether, cold water or toluene but readily soluble in the hot solvents.

Anal. (Kjeldahl). Subs., 0.5006: 9.68 cc. of 0.2035 *N* HCl. Calcd. for $C_{12}H_{13}NO_5$: N, 5.55. Found: N, 5.50.

The isomeric diacetyl-4-acetaminopyrocatechol has been prepared by Kehrmann and Hoehn[8] and the two compounds agree very closely in their properties.

Diacetyl 3-Aminopyrocatechol.—The methods used by Jacobs and Heidelberger[2] for the 4-amino isomer readily yielded this compound. Ten grams of 3-aminopyrocatechol hydrochloride was dissolved in 40 cc. of water and 46 cc. of saturated sodium acetate solution added. Eight cc. of acetic anhydride was added, and on shaking the compound was deposited. A further yield was obtained by saturating the filtrate with solid sodium acetate and adding 5 cc. more acetic anhydride. The yield was 10 g. of crude material. It was purified by crystallization from 50% alcohol after decolorization with norit and is slightly soluble in cold water or 50% alcohol, but readily soluble in the boiling reagents. It forms irregular hexagonal plates melting at 167–168° which are grayish white in color and glisten in the light. An aqueous suspension, when acidified with acetic acid and treated with sodium nitrite solution, forms a nitroso compound which crystallizes as golden yellow plates when the solution is chilled and agitated. The nitroso compound dissolves in alkalies with a brown to red color. The properties of the diacetyl 3-aminopyrocatechol thus agree very closely with the 4-amino isomer.

Anal. of the diacetate (Kjeldahl). Subs., 0.4856: 11.64 cc. of 0.2035 *N* HCl. Calcd. for $C_{10}H_{11}O_4N$: N, 6.70. Found: N, 6.83.

3-Acetaminopyrocatechol.—This compound can be prepared by treating 3-aminopyrocatechol hydrochloride in 50% acetic acid solution with 1.2 moles of acetic anhy-

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[8] Kehrmann and Hoehn, *Helv. Chim. Acta*, **8**, 218 (1925).

dride. The solution is warmed slightly and allowed to stand for twenty-four hours. It is then evaporated to dryness under reduced pressure and the residue extracted with ether. The ether is removed, the crude material dissolved in chloroform and precipitated by the addition of petroleum ether.

The acetamino compound can be more conveniently prepared from the triacetate by partial hydrolysis according to a method devised by Kehrmann and Hoehn.[8] The triacetate is added to 33% sodium hydroxide solution, and goes into solution with evolution of heat. In a few minutes the acetyl groups are hydrolyzed, after which the solution is cooled to 0° and neutralized with sulfuric acid. The acetamino compound is extracted with ether and purified as before. The yield is not good by either method of preparation. It is easily soluble in water, but slightly soluble in the hot solutions. It is insoluble in petroleum ether. From toluene or chloroform it forms white microscopic blades, melting at 124–125°. From water it forms regular tetrahedra, but crystallization is attended by gum formation. The 3-acetaminopyrocatechol forms a gray lead salt and gives an olive green color with ferric chloride. In contact with the air the aqueous solution assumes a red color which is probably due to quinone formation, since the color is discharged by sulfur dioxide.

Anal. (Kjeldahl). Subs., 0.2074: 5.96 cc. of 0.2035 *N* HCl. Calcd. for $C_8H_9O_3N$: N, 8.38. Found: 8.21.

The isomeric 4-acetaminopyrocatechol was prepared intermediately by Kehrmann and Hoehn but not isolated.

Summary

Pyrocatechol has been nitrated and the process for the separation of the isomers definitely established. The corresponding amines have been prepared by direct reduction, and 3-aminopyrocatechol and some compounds arising from it have been described. The procedure for the preparation of other pyrocatechols substituted in either the 3- or 4-position has thus been simplified. Further work along this line is in progress in this Laboratory.

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THE CHEMISTRY OF THE ACYL PARA-QUINONES. A CONTRIBUTION TO THE SOLUTION OF THE "PECHMANN DYES" PROBLEM[1]

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By the action of acetic anhydride upon β-benzoylacrylic acid, and some of its homologs, von Pechmann[3] obtained, in 1882, deeply colored products whose chemical constitution he did not ascertain. These products, which have been known since as "Pechmann Dyes," were studied twenty-four years later by Kozniewski and Marchlewski,[4] who assigned to them the

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[1] Presented in abstract before the Division of Organic Chemistry, at the St. Louis Meeting of the American Chemical Society, April, 1928.

[2] Recently Lydia C. Roberts Graduate Fellow at Columbia University.

[3] Von Pechmann, *Ber.*, **15**, 885 (1882).

[4] Kozniewski and Marchlewski, *Bull. acad. sci. Cracow*, 81 (1906).