about half of the material to its mineral acid salt and the other half to a mixture of alkylated material and alkyl halide quaternary of the alkylated material. In the presence of potassium carbonate only the quaternary is obtained.

The following new ethylenediamines have been prepared and characterized: N-*n*-propyl, N,N'-di-*n*-propyl, N-*n*-butyl, N,N'-di-*n*-butyl, N-*n*-amyl and N,N'-di-*n*-amyl.

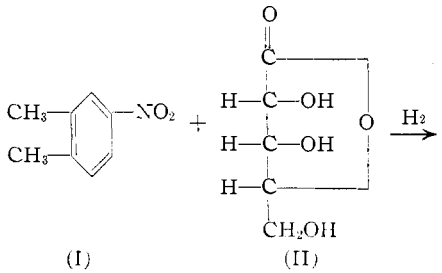
RENSSELAER, NEW YORK RECEIVED APRIL 24, 1946

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF HOFFMANN-LA ROCHE, INC.

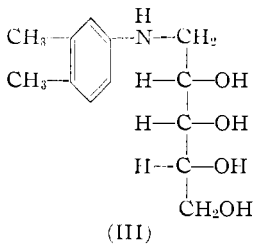
A Simplified Synthesis of N-Aryl-glycamines

BY L. M. JAMPOLSKY AND H. M. WUEST[1]

In the synthesis of riboflavin, N-(D-ribityl)-3,4-dimethylaniline (III) is an important intermediate. Some of the reported syntheses of this intermediate have been aimed chiefly at circumventing the use of D-ribose, a comparatively costly sugar. The readily available D-ribonolactone has been utilized for this purpose in procedures involving three to five steps to obtain the desired glycamine.[2] The synthesis described in this paper involves only one step, the reductive condensation of 3,4-dimethylaniline or 4-nitro-*o*-xylene (I) with D-ribonolactone (II) to yield N-(D-ribityl)-3,4-dimethylaniline (III).

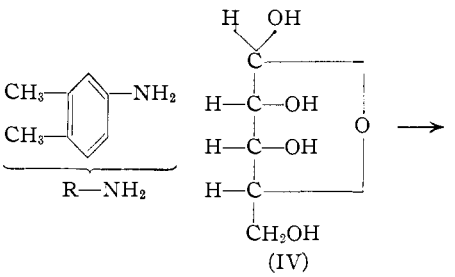


(I) (II)

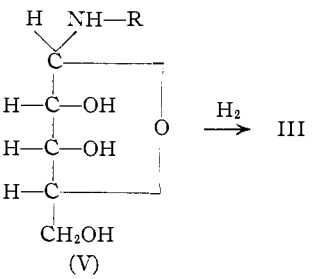


(III)

It is known that some lactones of aldonic acids (D-glucono-δ-lactone, L-rhamnono-δ-lactone, etc.) can be hydrogenated to the corresponding sugars.[3] It therefore seems probable that the 3,4-dimethylaniline used (or formed from 4-nitro-*o*-xylene by hydrogenation) immediately condenses with D-ribose (IV) (formed by hydrogenation of D-ribonolactone) to yield the easily reducible N-glycoside (V).[4]



(IV)



(V)

It is unlikely that 3,4-dimethyl-D-ribonylaniline is an intermediate because amide formation is negligible at the temperature used. Furthermore, we have confirmed the negative results of Tishler, Wendler, Ladenburg and Wellman,[2] who obtained no N-(D-ribityl)-3,4-dimethylaniline in attempting to catalytically reduce 3,4-dimethyl-D-ribonylaniline.

The reductive condensation appears to proceed favorably in ethanol in the presence of a small amount of potassium hydroxide. Although hydrogen adsorption takes place at atmospheric pressure, the reaction is very slow. Pressures of 100–200 atmospheres have been found to be convenient. Temperatures above 100° favor the irreversible formation of 3,4-dimethyl-D-ribonylaniline which, as has been stated, cannot be utilized.

Hydrogenation of D-ribonolactone alone under these conditions gives a 70% yield of adonitol. In order to test the general applicability of the method, N-(3,4-dimethylphenyl)-D-glucamine and N-(*p*-tolyl)-D-glucamine were prepared from D-glucono lactone plus 3,4-dimethylaniline and *p*-toluidine, respectively.

(1) Present address: William R. Warner & Co., New York, New York.

(2) Tishler, Wendler, Ladenburg and Wellman, THIS JOURNAL, **66**, 1328 (1944); Bergel, Cohen and Haworth, British Patent 550,169 (1942); Pasternack and Brown, U. S. Patent 2,237,263 (1941); Berger and Lee, *J. Org. Chem.*, **11**, 75 (1946).

(3) Glattfelt and Schimpff, THIS JOURNAL, **57**, 2204 (1935); Schmidt and Müller, *Ber.*, **76**, 344 (1943).

(4) Kuhn and Birkofer, *ibid.*, **71**, 621 (1938).

Experimental[5]

N-(D-Ribityl)-3,4-dimethylaniline (III). Method A. From 4-Nitro-*o*-xylene (I).—A mixture of 12 g. of D-ribonolactone, 10 g. of 4-nitro-*o*-xylene, and 3 cc. of *N* potassium hydroxide in 100 cc. of ethanol was hydrogenated at 60° and 100 atmospheres pressure with 1 g. of Adams platinum oxide catalyst. After twenty-four hours 50 cc. of ethanol was added and the mixture warmed to dissolve any precipitated product. The catalyst was separated by filtration and the solution cooled to 10°. After crystallization had taken place the product (3 g.) melting at 140–142° was filtered. Recrystallization from ethanol afforded further purification.

Method B. From 3,4-Dimethylaniline.—To a solution of ethanol (5000 cc.) containing 875 g. of D-ribonolactone and 730 g. of 3,4-dimethylaniline, was added 150 cc. of *N* potassium hydroxide. Fifty grams of Adams platinum oxide catalyst suspended in 290 cc. of distilled water was added and the mixture hydrogenated for thirty hours at 75° under a pressure of 2000 lb. per sq. in. The solution was then heated gently on a steam-bath until the material which crystallized was dissolved. The platinum black was filtered from the warm solution under a stream of carbon dioxide. After cooling the filtered solution, the crystals of N-(D-ribityl)-3,4-dimethylaniline (855 g.) were filtered off and washed with about 200 cc. of acetone. Recrystallized from ethanol, the product (792 g.) melted at 141–142°.

N-(3,4-Dimethylphenyl)-D-glucamine.—A mixture of 24 g. of D-glucono-δ-lactone, 20 g. 3,4-dimethylaniline, 4 cc. of 0.5 *N* potassium hydroxide and 2 g. of Adams platinum oxide catalyst in 160 cc. of ethanol was hydrogenated for seventy-two hours at 80° under a pressure of 2000 lb. per sq. in. The mixture was then warmed to dissolve the gel which had formed and filtered from the catalyst. The solution was evaporated to dryness *in vacuo* and the residue (30 g.) recrystallized four times from methanol. The needles melted at 134.5–135.5°. Kuhn and Birkofer[4] give the melting point as 131°.

Anal. Calcd. for $C_{14}H_{23}O_5N$: C, 58.91; H, 8.12; N, 4.91. Found: C, 58.94; H, 8.05; N, 5.00.

N-*p*-Tolyl-D-glucamine.—Forty-four grams of D-glucono-δ-lactone and 36.3 g. of *p*-toluidine were dissolved in 200 cc. of ethanol to which had been added 20 cc. of 0.5 *N* potassium hydroxide. Two and one-half grams of Adams platinum oxide catalyst was added and the mixture shaken with hydrogen under 2000 lb. pressure at 65° for seventy-two hours. The catalyst was filtered off and the filtrate evaporated to dryness *in vacuo*. The residue (weight *ca.* 35 g.) was shaken with ether and water. The aqueous layer was separated and evaporated to a small volume *in vacuo*. The crystals which formed were filtered off and recrystallized from methanol. The product, which had a tendency to form a gel in solution, melted at 123°.[4]

Anal. Calcd. for $C_{13}H_{21}O_5N$: C, 57.53; H, 7.80; N, 5.17. Found: C, 57.73; H, 7.90; N, 5.26.

(5) The analyses were carried out under the direction of Dr. Al Steyermark of these laboratories. All melting points were taken with an uncalibrated set of Anschütz thermometers.

Summary

1. A synthesis of N-aryl-glycamines is described which consists in the catalytic hydrogenation of aldonic acid lactones in the presence of arylamines.

2. The reaction described is of importance in the preparation of N-(D-ribityl)-3,4-dimethylaniline, an intermediate in the synthesis of riboflavin, from D-ribonolactone and 3,4-dimethylaniline.

NUTLEY, N. J. RECEIVED APRIL 30, 1946

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Structure and Activity of Sulfanilamides[1,2]

BY F. G. BORDWELL, AVIS B. COLBERT[3] AND BARRE ALAN

Fuson[4] has brought attention to the fact that the effect of a functional group is transmitted almost undiminished through a vinyl group (—CH=CH—). For this reason it would be expected that the amino group and sulfamyl group (SO_2NH_2) in 2-(*o*- and *p*-aminophenyl)-ethene-1-sulfonamide (VI and VII, R = H) would bear the same chemical relationship to one another as in sulfanilamide. It is therefore of interest to compare the bacteriostatic effect of compounds in these two series with that of sulfanilamide.

The synthesis outlined was used to prepare simple vinylogs of sulfanilamide. Nitration of 2-phenylethene-1-sulfonyl chloride (I) gave a

$$C_6H_5CH{=}CHSO_2Cl \longrightarrow \underset{\text{I}}{} \textit{o} \text{ and } \textit{p}\text{-}NO_2C_6H_4CH{=}CHSO_2Cl \longrightarrow \underset{\text{II and III}}{} \textit{o} \text{ and } \textit{p}\text{-}NO_2C_6H_4CH{=}CHSO_2NHR \longrightarrow \underset{\text{IV and V}}{} \textit{o} \text{ and } \underset{\text{VI and VII}}{\textit{p}\text{-}NH_2C_6H_4CH{=}CHSO_2NHR}$$

practically quantitative yield of a mixture of nitro sulfonyl chlorides, from which approximately 20% of II and 50% of III were separated by fractional crystallization. Condensation of II and III with ammonia gave the corresponding sulfonamides (IV and V) in good yield. Reduction of the nitro group in IV and V was readily accomplished using ferrous sulfate and ammonia. Acetylation of IV and V followed by reduction of the nitro group gave the corresponding vinylogs of sulfacetamide.

It is possible that the arrangement of groups around the olefinic double bond is important in determining the bacteriostatic effect of these vin-

(1) This investigation was supported in part by a grant from the Abbott Fund of Northwestern University.

(2) Presented at the One-Day Technical Conference of the Chicago Section of the American Chemical Society, Evanston, Illinois, November 16, 1945.

(3) Winthrop Chemical Company Fellow, 1944–1945. Part of the experimental work was abstracted from a thesis submitted by Miss Colbert as partial fulfillment of the degree of Master of Science, June 1945.

(4) Fuson, *Chem. Rev.*, **16**, 1 (1935).