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Note

Nickel-charcoal as a catalyst for the synthesis of *p*-aminophenyl α-D-mannopyranoside and α-L-fucopyranoside

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The *p*-aminophenyl glycosides have a variety of applications in the fields of protein, enzyme, and lectin purification[1–5]. A nickel–charcoal catalyst, prepared by reducing nickel(II) chloride hexahydrate with potassium borohydride in a solution of methanol containing activated charcoal, was used to reduce *p*-nitrophenyl glycosides to their corresponding *p*-aminophenyl glycosides. The catalyst is economical, highly efficient, and useful in a variety of reduction reactions.

RESULTS AND DISCUSSION

Nickel salts have been reduced with sodium and potassium borohydride to yield catalysts[6–9], and palladium chloride dihydrate was reduced with sodium borohydride by Tanaka and Pigman[10] to yield an effective catalyst. A support medium, which may be a solid as reported in this paper or a polymeric material that will maintain the catalyst in a collodial state[11], prevents the metallic catalyst from clumping and greatly improves its efficiency. One of the advantages of the activated charcoal as a support medium is that it removes impurities which are formed during the reduction reaction.

The catalyst was formed in methanol because the reduction of the nickel ion with either potassium or sodium borohydride proceeded at a modest rate. The nickel–charcoal was washed with methanol, then with water to remove borate, K^+, Cl^-, and OH^- ions, and then with methanol because the reduction of the *p*-nitrophenyl glycosides was carried out in methanol.

The nickel–charcoal catalyst prepared by the method described herein contains 7.3% of nickel. It appears to work as well as, or better than, the palladium-on-barium sulfate used by Westphal and Feier[12] for the same reductions. No attempt was made to establish the shelf life of the catalyst in either the wet or dry form, or the ideal percentage of nickel. The catalyst was prepared fresh for each experiment. The time required for complete reduction was a function of the amount of *p*-nitrophenyl glycoside. Higher temperature increased the rate of reduction, owing to greater solubility of the reactants, as well as the effectiveness of the catalyst.

EXPERIMENTAL

General. — *p*-Nitrophenyl α-D-mannopyranoside and *p*-nitrophenyl α-L-fucopyranoside were prepared by the method of Westphal and Feier[12]. A Parr pressure hydrogenation apparatus was used for hydrogenation. D-Mannose and L-fucose were obtained from Pfanstiehl Laboratories, Inc., Waukegan, IL 60085; neutral, decolorizing carbon (Norite) from Fisher Scientific Co., Fair Lawn, NJ 07410; $NiCl_2 \cdot 6 H_2O$ crystals from Mallinckrodt, St. Louis, MO 63118, and potassium borohydride from Sigma Chemical Co., St. Louis, MO 63118.

Preparation of nickel-on-activated charcoal. — Nickel(II) chloride hexahydrate (3 g) was dissolved in methanol (200 mL). To this solution were added activated charcoal (10 g) and, with constant stirring at room temperature, a total of 2 g of potassium borohydride in small portions over a period of 2 h. The solution was allowed to settle occasionally to check its color. A colorless supernatant indicated complete reduction of the nickel salt. When a faint green color was present, additional potassium borohydride (1 g) was added to complete the reduction. The solution was kept overnight in a covered container (not sealed). The next day, the alcohol was decanted and the nickel–charcoal precipitate was washed with methanol (2 × 200 mL) by stirring, settling, and decanting. After the methanol rinses, distilled water (300 mL) was added to the nickel–charcoal catalyst, and the suspension was stirred for a few min, allowed to settle, and the water decanted. The methanol treatment was repeated twice to remove the water. Immediately prior to use, the nickel–charcoal catalyst was filtered off in a suction funnel. As soon as the solvent had gone through, suction was stopped to limit the catalyst's contact with air. The entire catalyst was then quickly added to the 500-mL glass reduction-flask.

p-*Aminophenyl α-D-mannopyranoside.* — In a 500-mL, glass reduction-flask containing the freshly prepared nickel–charcoal (total amount as described in the preceding paragraph), methanol (200 mL) and *p*-nitrophenyl α-D-mannopyranoside (30 g) were added. The flask was warmed to ~60°, and hydrogen gas was added at a pressure of 4.5 bar. The flask was warmed continuously with a heating jacket and simultaneously shaken. Within 3 h, the theoretical amount of hydrogen was consumed. The reaction flask was kept for an additional hour under 4.5 bar to insure completeness of the reaction and to check for possible leaks in the system. After reduction, the flask was removed from the hydrogenator and warmed on a steam bath until the solution boiled. The suspension was then filtered under a vacuum through a hot Büchner funnel. The solid was washed with boiling methanol (150 mL). The clear, colorless filtrates were combined and flash evaporated at 35°. Ethanol was added to the crystalline mass and evaporated several times to remove most of the methanol. The residue was dissolved in ethanol, a small amount of activated charcoal was added, and the solution was filtered while hot. Colorless crystals formed upon cooling to room temperature. To increase the yield, ethyl ether was added to a final concentration of ~20%, and further crystallization was continued for 24 h at 4° (yield 19 g, 70%), m.p. 171°, $[\alpha]_D^{20}$ +128° (*c* 1.00, methanol); lit.[12] m.p. 164°, $[\alpha]_D^{20}$ +128° (methanol).

p-*Aminophenyl α-*L*-fucopyranoside.* — The same procedure was used to reduce *p*-nitrophenyl α-L-fucopyranoside as described for *p*-nitrophenyl α-D-mannopyranoside, except that 10 g of starting material was used, and in the crystallization step petroleum ether was substituted for ethyl ether (yield 5.7 g, 68%), m.p. 175°, $[\alpha]_D^{20}$ −204° (*c* 1.00, methanol); lit.[12] m.p. 175°, $[\alpha]_D^{20}$ −204° (methanol).

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