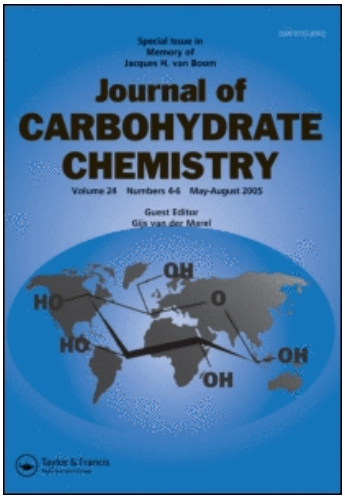

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Catalytic Synthesis of D-Glucosaminic Acid from D-Glucosamine on Active Charcoal-Supported Pd-Bi Catalysts

Gu Wen-xiu[a]; Xia Wen-shui[b]
[a] The School of Chemical & Material Engineering, Southern Yangtze University, Wuxi, Jiangsu, China
[b] The School of Food, Southern Yangtze University, Wuxi, Jiangsu, China

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Gu Wen-xiu

The School of Chemical & Material Engineering, Southern Yangtze University, Wuxi, Jiangsu, China

Xia Wen-shui

The School of Food, Southern Yangtze University, Wuxi, Jiangsu, China

D-Glucosaminic acid (2-amino-2-deoxy-D-gluconic acid), is a component of bacterial lipopolysaccharides, sweetener, condiments, and a chiral synthon. A catalytic oxidation of D-glucosamine to D-glucosaminic acid by molecular oxygen on active charcoal-supported Pd-Bi catalysts is described in good yield.

Keywords D-Glucosaminic acid, D-Glucosamine, Pd-Bi/C catalyst, Oxidation

In recent years, research on D-glucosaminic acid has increased because of its industrial, agricultural, food, and medical applications.[1] D-Glucosaminic acid has recently been identified as a promising sweetener and condiment.[2] It is also a member of the "chiral pool" and has been used as a starting material for the asymmetric synthesis of various amino acids and several glycosidase inhibitors.[3,4] In addition, D-glucosaminic acid has recently been investigated as an unusual component of *Rhizobuim leguminosarum* lipopolysaccharide,[5] and its use as a cation coordinating agent has also been widely

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Address correspondence to Gu Wen-xiu, The School of Chemical & Material Engineering, Southern Yangtze University, Wuxi, Jiangsu 214036, China. E-mail: guwenxiu@yahoo.com.cn

studied.[6] D-Glucosaminic acid has also been investigated for potential use in the chromatographic separation of charged biomolecules[3] and as a complex with platinum for cancer therapy.[7] The platinum(IV)/D-glucosaminic acid complex has received considerable attention because of lower toxicity and the possibility of oral administration.

There were a few reports in the literature describing the synthesis of D-glucosaminic acid. The classical synthesis of D-glucosaminic acid from D-glucosamine involves the use of yellow mercuric oxide as an oxidant,[8] followed by treatment with hydrogen sulfide. The yields of the procedure were not consistent and the resulting mercuric sulfide was difficult to separate from the products, which limited applications of D-glucosaminic acid in the food and pharmaceutical industries. The other strategy for synthesis of D-glucosaminic acid is achieved through enzymatic processes.[9,10] Thereinto, D-glucosaminic acid was prepared by air oxidation of D-glucosamine catalyzed by glucose oxidase, whereas glucose oxidase accepted D-glucosamine only as a poor substrate, with a maximal catalytic efficiency of 2% as compared to that on D-glucose. Thus, a better yield of D-glucosaminic acid was dependent on larger amounts of enzyme and prolonged reaction times (72 h).

We propose here a new, facile, and environmentally safe preparation of D-glucosaminic acid by use of molecular oxygen as an oxidant and Pd-Bi/C as a catalyst. The catalytic oxidation presents some additional advantages, namely (i) high selectivities and mild reaction conditions (oxidation with molecular oxygen at atmospheric pressure near room temperature); (ii) the possibility of conducting the oxidation in one step in a single reaction vessel; (iii) a higher site-time yield per catalyst mass; and (iv) much shorter reaction time (3 h). Moreover, the catalytic process is environmentally clean since it is conducted on recyclable catalysts and gives no noxious effluents nor side products.

CATALYST PREPARATION

The Pd-Bi/C catalysts were prepared by a traditional impregnation and reduction method. The cylindrical active charcoal (MCA-210, 1500 m^2/g, coconut shell activated carbon, Ningde Xinsen Chemical Industry Co., Ltd, China) support was treated with 10% nitric acid, heated on the boiling water bath with frequent agitation for 2 to 3 h, filtered, washed with distilled water, and dried for 5 h at 120°C. The dried active charcoal (10.0 g) was then suspended in distilled water (100 mL) and kept in a water bath at 80°C with stirring; a solution of $PdCl_2$ (0.83 g) in 35% hydrochloric acid was added dropwise; and the mixture stirred for 2 h at 80°C. After addition of 35% aqueous formaldehyde solution (1 mL), $PdCl_2$ was reduced by the slow addition of 30% sodium hydroxide aqueous solution to weak alkalinity with stirring overnight. The suspension was filtered,

resuspended in distilled water (100 mL), and held at 40°C with nitrogen flow bubbled through for 20 min, and glucose (5.0 g) was then added with stirring. Subsequently, a solution of $BiCl_3$ (0.74 g) in 35% hydrochloric acid was added dropwise at 40°C with a continuous supply of nitrogen. After addition, the suspension was stirred for another 2 h, laid overnight, filtered, washed with water until neutral, and air-dried. The contents of Pd and Bi of the catalyst obtained herein were 3.04% and 1.74%, respectively.

OXIDATIVE PROCEDURE

A typical procedure is as follows: D-glucosamine hydrochloride (5.0 g) was dissolved in water (200 mL), and the pH was adjusted to 7.0 with 1.00 mol/L NaOH. Then $KHCO_3$ (2.3 g) and Pd-Bi/C (2.0 g) catalyst were added. A strong oxygen current was bubbled into the mixture with vigorous agitation at 30°C, and after 6 h, the pH rose to 7.8. The catalyst was separated by filtration, and the filtrate was adjusted to pH 4.0 with 1.00 mol/L HCl and concentrated under reduced pressure to about 20 mL. Absolute ethyl alcohol was then added to the above concentrated solution until crystallization was

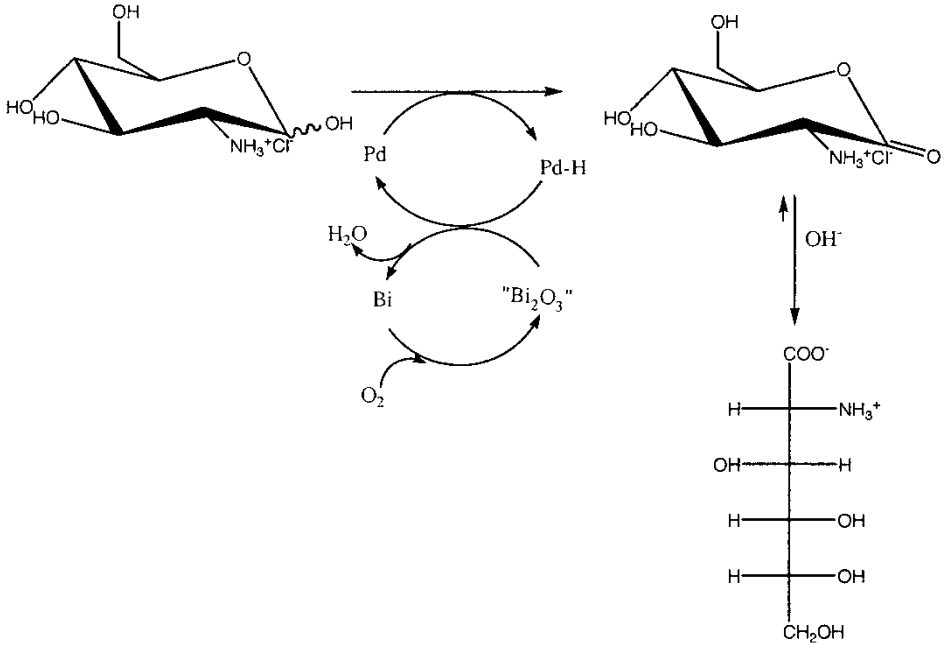

Figure 1: Tentative scheme for the mechanism of D-glucosamine hydrochloride oxidation on Pd-Bi/C catalyst.

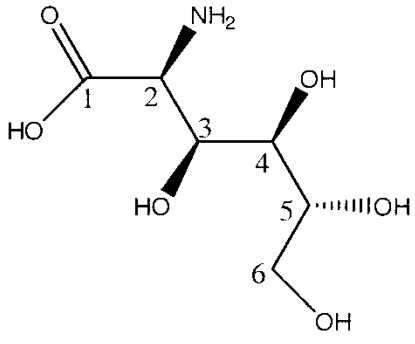

Figure 2: D-Glucosaminic acid.

complete. After the material stood in a refrigerator for several hours, the crystals were removed by filtration and washed first with cold 85% alcohol and then with absolute alcohol. The mother liquor and washings were concentrated under reduced pressure to about 20 mL and from this concentrate another crop of crystals was obtained. The product was recrystallized five times by dissolving in a small amount of water and then adding absolute ethyl alcohol. This gave pure D-glucosaminic acid as white needle crystals. Yield: 70%; m.p. 260°C (dec), $[\alpha]_D$-15 (*c* 4, 2.5% aq HCl); lit: $[\alpha]_D$-14 (*c* 1.64, 2.5% aq HCl). ^{1}H NMR (500 MHz, D_2O) 4.56 (d, 1H, $J = 4$ Hz, H-2), 4.02 (d, $J = 4$ Hz, H-3), 3.97 (dd, 1H, $J = 3$ Hz, 12 Hz, H-6b), 3.90 (s, 1H, H-6a), 3.89 (br, 1H, H-5), 3.80 (dd, 1H, $J = 6$ Hz,12 Hz, H-4). ^{13}C NMR (500 MHz, D_2O) 172.2(C-1), 72.5 (C-3), 70.6 (C-5), 67.1 (C-4), 62.5 (C-6), 58.0 (C-2). ^{135}Dept 65.4 (C-6). ν (cm^{-1}, KBr) 3299, 2964, 1622, 1583, 1406, 1325, 1112, 1035, 933. FAB-MS: m/z 196.0 (M + 1). Anal. Calcd. for $C_6H_{13}NO_6$: C, 36.92; H, 6.71; N, 7.18. Found: C, 36.60; H, 6.71; N, 7.03.

We propose that D-glucosamine oxidation on Pd-Bi/C catalyst proceeds according to the oxidative dehydrogenation mechanism given in Figure 1, where bismuth acts as an assistant catalyst, avoiding the overoxidation of the palladium surface.

^{1}H NMR, ^{13}C NMR, IR, and FAB-MS confirmed the product D-glucosaminic acid (Fig. 2).

The catalyst Pd-Bi/C was recycled for eight times, and the catalytic activity and the conversion yield did not apparently change. The conclusion can be made that the Pd-Bi/C is a highly active catalyst for the oxidation of D-glucosamine with molecular oxygen under atmospheric pressure at near room temperature in near neutral medium. Therefore, the present procedure may be considered as a more practical procedure for the preparation of D-glucosaminic acid.

The further study of Pd-Bi/C catalyst is under way.

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