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# HYDROGENATION OF THE SODIUM SALT OF 2-OXO-4-(3-PYRIDYL)BUTENOIC ACID ON PALLADIUM BLACK

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*We have studied the hydrogenation of the sodium salt of 2-oxo-4-(3-pyridyl)butenoic acid on palladium black in the temperature range 20-70°C in aqueous-alcohol medium. The products of the reaction are the sodium salts of 2-oxo-4-(3-pyridyl)butanoic acid and 2-hydroxy-4-(3-pyridyl)butanoic acid together with hydrogenolysis products. The reaction occurs via a series-parallel mechanism.*

**Keywords:** unsaturated and saturated 2-oxocarboxylic acids, palladium catalysts, hydrogenation.

Derivatives of 4-substituted 2-oxo- and 2-hydroxybutanoic acids are valuable synthons in the preparation of antihypertensive materials, homoamino acids, hydroxamic acids and other compounds [1, 2].

We have studied the hydrogenation of the sodium salts of 2-oxo-4-(2-furyl)-, 2-oxo-4-phenyl-, and 2-oxo-4-(2-thienyl)butenoic acids on nickel and palladium catalysts.

The hydrogenation of the sodium salt of 2-oxo-4-phenylbutenoic acid on nickel catalysts gives the corresponding 2-hydroxy-4-phenylbutanoic acid salt selectively [3].

The use of palladium black and 10% Pd/C catalyst causes the formation of the sodium salt of 2-oxo-4-phenylbutanoic acid as well. The hydrogenation of the sodium salt of 2-oxo-4-(2-furyl)butenoic acid on a skeletal nickel catalyst gives the corresponding salts of 2-oxo-4-(2-furyl)butanoic acid and 2-hydroxy-4-(2-furyl)butanoic acid and aliphatic compounds of the hydrogenolysis of the starting material molecule [4].

Hydrogenation of the sodium salt and the ethyl ester of 2-oxo-4-(2-thienyl)butenoic acid on skeletal nickel gives the corresponding derivatives of 2-oxo-4-(2-thienyl)butanoic acid and 2-hydroxy-4-(2-thienyl)butanoic acids [5]. In this case, the palladium catalysts produce a more selective formation of the corresponding oxo compound than does the skeletal nickel. The hydrogenation of the ethyl ester of 2-oxo-4-(2-thienyl)butenoic acid on palladium black gives both the mentioned compounds and also forms the ethyl ester of 2-oxo-4-(2-tetrahydrothienyl)butanoic acid.

In this communication we present the data for the hydrogenation of the sodium salt of 2-oxo-4-(3-pyridyl)butenoic acid (**1**) on palladium black. Information about this reaction is absent in the literature. The hydrogenation was carried out at 21-70°C with an initial concentration of the starting acid **1** of 0.174 M in aqueous alcohol and a starting material to palladium black ratio of 1:0.85 (see Table 1).

Similarly to the hydrogenation of the 4-substituted 2-oxobutenoic acids referred to, the hydrogenation of the sodium salt of 2-oxo-4-(3-pyridyl)butenoic acid gave the sodium salts of the 2-oxo- and 2-hydroxy-4-(3-pyridyl)butanoic acids (**2** and **3** respectively) and hydrogenolysis products. At a temperature of 21-30°C the yield of the sodium salt of the 2-oxo-4-(3-pyridyl)butanoic acid exceeds that of the corresponding hydroxy

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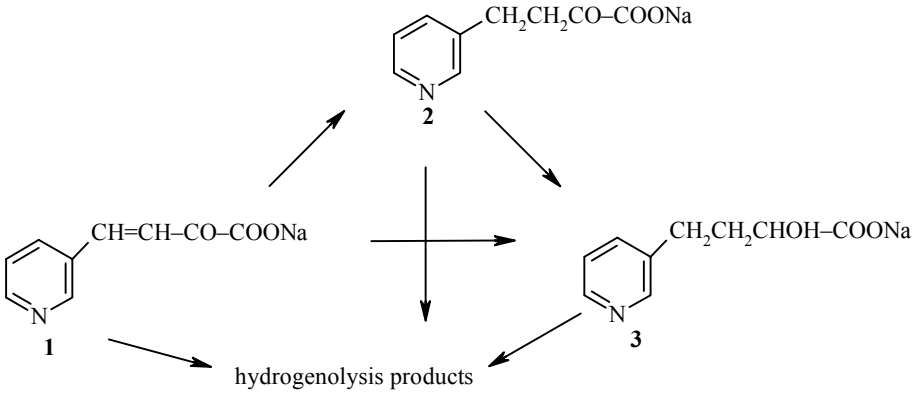
TABLE 1. Hydrogenation of the Sodium Salt of 2-Oxo-4-(3-pyridyl)butenoic Acid (**1**) in the Presence of Palladium Black*

| T, °C | Reaction time, h | Yield of sodium salt, mol % | | Unreacted acid **1**, % |
|---|---|---|---|---|
| | | 2-oxo-4-(3-pyridyl)-butanoic acid | 2-hydroxy-4-(3-pyridyl)-butanoic acid | |
| 21 | 0.75 | 17.5 | 10.5 | 49.6 |
| 21 | 1.5 | 41.4 | 26.2 | 24.0 |
| 21 | 2.0 | 43.2 | 24.3 | 7.9 |
| 21 | 3.0 | 62.2 | 32.1 | 1.5 |
| 21 | 4.0 | 67.5 | 33.1 | — |
| 60-70 | 1.0 | 14.8 | 58.2 | — |
| 60-70 | 1.5 | 15.4 | 53.7 | — |
| 60-70 | 2.5 | 17.5 | 47.6 | — |
| 60 | 1.0 | 12.5 | 57.8 | 0.9 |
| 60 | 2.5 | 19.0 | 53.3 | — |
| 60 | 3.5 | 17.1 | 50.3 | — |

* Ratio of the weight of starting material to Pd black = 1 : 0.88, $c_{init.}$ = 0.174 M.

compound by 2-3 times. With an increase in temperature the selectivity of the formation of this sodium salt **2** is decreased and that of the sodium salt of the acid **3** is increased. The curves for the consumption of **1** and the yield of **2** and **3** suggest a series-parallel type mechanism for the reaction course (see Fig. 1).




The hydrogenation of the sodium salt of 2-oxo-4-(4-pyridyl)butenoic acid was carried out in the temperature range 0-30°C. In this case the reaction occurs unselectively. The contribution of hydrogenolysis of the starting compound molecule is sharply increased. In contrast to the hydrogenation of the sodium salt of 2-oxo-4-(3-pyridyl)butenoic acid, the hydrogenation of 2-oxo-4-(4-pyridyl)butenoic acid is unpromising for the preparation of the corresponding oxo- and hydroxybutanoic acid derivatives.

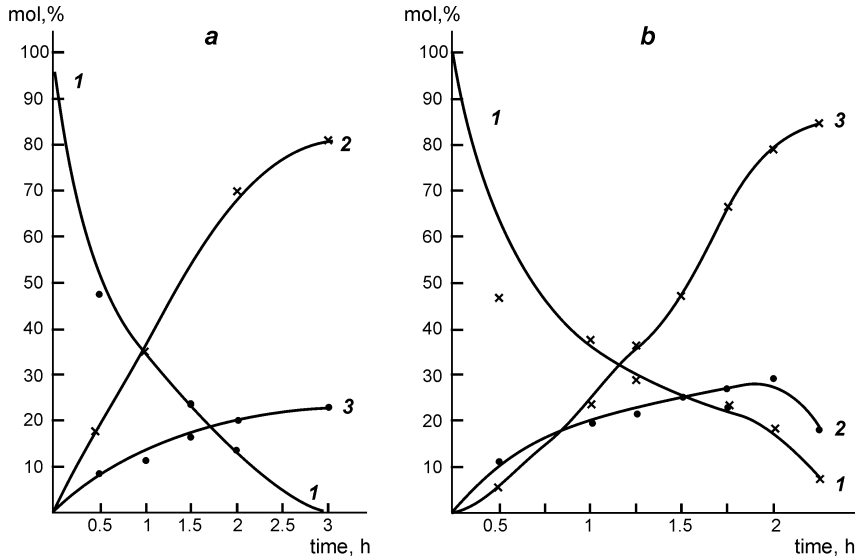



Fig. 1. Dependence of the conversion of 2-oxo-4-(3-pyridyl)butenoic acid sodium salt starting material (1) and of the yield of hydrogenation products on the reaction time using Pd black at a temperature of 30°C (a) and 60°C (b) (ratio of weight of starting material to catalyst = 1: 0.85, $c_{init}$ for **1** = 0.174 M). Curve 1 = unreacted starting material, 2 = sodium salt of 2-oxo-4-(3-pyridyl)butanoic acid (**2**), 3 = sodium salt of 2-hydroxy-4-(3-pyridyl)butanoic acid (**3**).

## EXPERIMENTAL

The starting material **1** was prepared by a method developed by us for the condensation of 3-pyridinecarbaldehyde with ethyl pyruvate. The content of the main product was 98%. The starting material and reaction products 2 and 3 were determined using HPLC on a Rainin chromatograph with a Dynamax-300A column (4.6 × 250 mm) using a reversed phase $C_8$ and λ = 262 nm. The eluent was 7% acetonitrile in 0.25 N triethylammonium phosphate (pH 6.0) [7].

The 2-hydroxy-4-(3-pyridyl)butanoic acid was separated chromatographically on a medium pressure Büchi apparatus. The Kontes preparative column (25 × 600 mm) was filled with Silasorb $C_{18}$ sorbent (particle size 30 microns) using 0.2% acetonitrile in 0.1% trifluoroacetic acid eluent.

$^1$H NMR spectra were taken on a Varian Mercury-200 BB spectrometer (200 MHz) using $CDCl_3$ solvent and TMS and DSS internal standards.

**Synthesis of the Na Salt of 2-Oxo-4-(3-pyridyl)butenoic Acid (1).** A solution of NaOH (3.5 M, 30 ml) was added over 0.5 h to a mixture of the 3-pyridinecarbaldehyde (25.7 g, 0.24 mol) and ethyl pyruvate (13.9 g, 0.12 mol) which was cooled to 5°C. The product was stirred for 1 h at 5°C and then for 2 h at room temperature. Ethanol (70 ml) was added to the reaction mixture. It was then allowed to stand for 24 h at room temperature. The precipitated yellow material was filtered off and washed on the filter with ethanol–ether (1:1; 3 × 50 ml) and ethanol–ether–chloroform (1:0.5:0.5; 2 × 50 ml). The precipitate was dried in air to give the target product (10.0 g) with 98% purity in 40% yield. $^1$H NMR spectrum (DMSO-$d_6$, TMS), δ, ppm, *J* (Hz): 6.93 and 7.49 (1H and 1H, dd, *J* = 16.5, CH=CH); 7.43 (1H, m, *J* = 7.8 and *J* = 4.8, 5-$H_{pyr}$); 8.10 (1H, m, *J* = 7.8, 4-$H_{pyr}$); 8.56 (1H, m, *J* = 4.8 and *J* = 1.5, 6-$H_{pyr}$); 8.79 (1H, m, *J* < 2, 2-$H_{pyr}$).

**Hydrogenation of the Sodium Salt of 2-Oxo-4-(3-pyridyl)butenoic Acid.** The sodium salt of 2-oxo-4-(3-pyridyl)butenoic acid (2.40 g, 12.0 mmol), water (47 ml), ethanol (23 ml), and damp palladium black (2.24 g) were added to a two necked flask fitted with a magnetic stirrer, reflux condenser, and tube for the passage of

hydrogen. The hydrogenation was carried out using molecular hydrogen for 3 h at 30°C. At the end of the reaction the catalyst was filtered off, washed with water–ethanol (2:1), and the catalyzate was evaporated to give a yellow oil (2.53 g). The product contained the sodium salt of acid **2** (1.91 g, yield 80.7%) and of acid **3** (0.54 g, yield 20%). For analytical purposes the hydrochloric salt of acid **3** was separated chromatographically. $^1$H NMR spectrum ($D_2O$), δ, ppm, *J* (Hz): 2.12 (2H, m, β-$CH_2$); 2.99 (2H, m, α-$CH_2$); 4.14 (1H, dd, *J* = 7.0, *J* = 4.6, CH(OH)); 8.00 (1H, dd, *J* = 8.0, *J* = 6.0, 5-$H_{pyr}$); 8.53 (1H, m, *J* = 8.0, 4-$H_{pyr}$); 8.65 (1H, m, *J* = 6.0, 6-$H_{pyr}$); 8.70 (1H, m, 2-$H_{pyr}$).

**2-Oxo-4-(3-pyridyl)butanoic Acid (2)** was separated as the corresponding 2,4-dinitrophenylhydrazone which was prepared by method [6]. The reaction product (2.00 g) was dissolved in HCl (2N, 25 ml), filtered, and a saturated solution of 2,4-dinitrophenylhydrazine hydrochloride (100 ml) was added. After 2 h the yellow precipitate was filtered off, washed with hydrochloric acid (2N, 20 ml) and distilled water to neutral pH, and dried for 5-6 h at 80°C. The product was the 2,4-dinitrophenylhydrazone hydrochloric salt of the acid **2** (purity 99%, yield 40%) with mp 245-246°C. $^1$H NMR spectrum (DMSO, TMS), δ, ppm, *J* (Hz): 3.05 and 3.21 (2H and 2H, mm, *J* = 6.8, $CH_2$–$CH_2$); 7.94 (1H, d, *J* = 9.4, 6-$H_{phen}$); 7.96 (1H, m, 5-$H_{pyr}$); 8.45 (1H, dd, *J* = 9.4, *J* = 2.6, 5-$H_{phen}$); 8.5 (1H, m, 4-$H_{pyr}$); 8.74 (1H, m, 6-$H_{pyr}$); 8.88 (1H, d, *J* = 2.6, 3-$H_{phen}$); 8.92 (1H, m, 2-$H_{pyr}$). Found, %: C 49.54; H 3.72; N 18.96. $C_{15}H_{13}N_5O_6$. Calculated, %: C 50.14; H 3.65; N 19.49.

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