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COMMUNICATIONS

# Hydrogenation of Ethyl *p*-Nitrobenzoate on Carbon-Supported Palladium–Triphenylphosphine Catalyst

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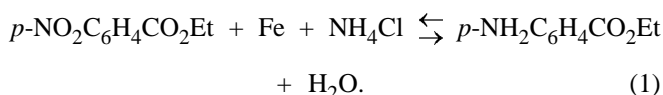
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**Abstract**—Hydrogenation of ethyl *p*-nitrobenzoate on carbon-supported palladium–triphenylphosphine catalyst at 40°C and atmospheric pressure of H<sub>2</sub> was studied.

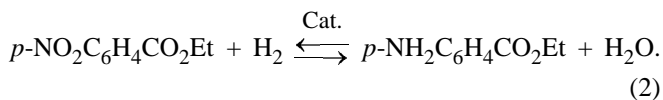
Hydrogenation of ethyl *p*-nitrobenzoate (ENB) attracts particular attention, since the reaction product is ethyl *p*-aminobenzoate (EAB), which is an anesthetic (medical name Anesthesin) and an intermediate in synthesis of novocaine.

Anesthesin is synthesized in industry by reduction of ENB in aqueous solution with the system iron powder–ammonium chloride [1–3]:



Reaction (1) is performed at 96–98°C; the yield of the target product does not exceed 90%, and it requires additional time-consuming purification. The synthesis is labor-consuming; it is performed under severe conditions, is accompanied by formation of colored by-products, and involves dilution of the reaction mixture with water, washing, and separation of the metallic slime, which gives rise to environmental problems.

The majority of the above problems can be avoided by performing catalytic hydrogenation of ENB with molecular hydrogen:



Some implementations of this process are reported in [4–8]. In some cases [4–6], classical heterogeneous hydrogenation catalysts based on platinum group metals were used. The reaction was performed at atmospheric or elevated [4] H<sub>2</sub> pressure; the reaction temperature was varied from 20 to 80°C. The yield of

Anesthesin did not exceed 90%. The drawbacks of these procedures are high consumption of Pd (5 wt%), its inefficient utilization, the necessity of the catalyst purification after every run, and severe reaction conditions (high pressure, elevated temperature, corrosive medium). In other works [7, 8], EAB was prepared on metal–polymer catalysts such as palladium-containing anion exchangers A-17-8-Pd and AN-1-Pd. The reaction was performed at 30–45°C and H<sub>2</sub> pressure of 1 atm; the yield was 98–100%. The major drawback of the process is relatively low reaction rate on such catalysts (by an order of magnitude lower than on Pd/C catalysts).

Thus, search for new, more effective catalysts of reaction (2) remains an urgent problem. In this connection, we studied hydrogenation of ENB on carbon-supported palladium–triphenylphosphine catalyst.

## EXPERIMENTAL

Carbon-supported palladium–triphenylphosphine catalyst was prepared as follows: 2.11 g of palladium acetate and 0.985 g of triphenylphosphine were dissolved in 200 ml of acetone in an inert atmosphere (N<sub>2</sub>, Ar), 50 g of a carbon support was added in an inert gas flow, and the mixture was stirred at room temperature until the solution became fully colorless. Then the reactor was purged with H<sub>2</sub> for 5 min, and the catalyst was reduced at 20–40°C for 4–6 h with vigorous stirring. The catalyst was filtered off, dried in a vacuum, and stored in an inert atmosphere. The resulting catalyst contained no more than 2 wt % Pd.

Reduction of ENB was performed in ethanol or 2-propanol at 40°C with H<sub>2</sub> at atmospheric pressure. The reactants were loaded in an inert gas atmosphere.

Hydrogenation of ENB was also performed at atmospheric pressure in a temperature-controlled reactor at 30–40°C. The components were also loaded in an inert gas atmosphere (N<sub>2</sub> or Ar) to prevent their oxidation with atmospheric oxygen and thus improve the product quality. After loading the catalyst prepared, ENB, and solvent, the whole system was kept at the required temperature for 3–5 min and purged with H<sub>2</sub> for 5 min, after which vigorous stirring was started. After the uptake of the theoretical amount of hydrogen, the reaction stops. The next portion of ENB is fully hydrogenated in the same time. The catalyst can effect hydrogenation of up to 50 portions of ENB without noticeable loss in the activity.

The total amount of converted ENB per gram of Pd is 29 250 g on the average. The yield of Anesthesin is quantitative (chromatographic analysis data).

The spent catalyst can be separated, regenerated, and then reused without noticeable loss in the activity.

The high activity and long life of the suggested catalyst are due to its structural features. As shown in [9], deposition of palladium on carbon supports followed by reduction with hydrogen results in formation of cluster complexes in which triphenylphosphine molecules stabilize palladium particles of definite size (optimal ratio PPh<sub>3</sub>/Pd ≈ 0.4), exhibiting the highest catalytic activity. This allows the hydrogenation rate and yield of the target product to be considerably increased; it also ensures long working life of the catalyst without noticeable loss in the activity.

The preservation of the catalyst activity is also favored by mild synthesis conditions (H<sub>2</sub> pressure 1 atm; temperature up to 40°C; anhydrous medium; single-component solvent readily removable by evaporation in isolation of the target product). It is also important that the solvents used are not involved in side reactions and are not so toxic as, e.g., toluene, benzene, or methanol used in alternative procedures [4, 8] (which is very important in preparation of pharmaceuticals); also, they do not require time-consuming washing of the finished product.

It should be noted that, with ultradispersed diamond used as catalyst support, the hydrogenation rate appreciably increases [10].

Thus, we have improved the hydrogenation process: the service life of the catalyst was increased

many-fold; the process was made simpler and shorter; the high pharmacopoeia quality of the finished product and its ~100% yield were attained.

## CONCLUSIONS

(1) A carbon-supported palladium–triphenylphosphine catalyst was suggested for preparation of Anesthesin of high pharmacopoeia quality in a quantitative yield.

(2) Anesthesin is prepared in one step under mild conditions without by-products. Fifty synthesis runs can be performed with one catalyst portion, after which it can be regenerated and reused.

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