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Synthesis of 1-Ethylpyrrolidone-2 by Hydrogenation of 1-Vinylpyrrolidone-2 over a Pd/C Catalyst

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Abstract—A selective catalytic system for the hydrogenation of 1-vinylpyrrolidone-2 (VP) to 1-ethylpyrrolidone-2 (EP) is found. The factors responsible for the formation of by-products in the conversion of VP are studied. The presence of acid sites or radical species in a catalytic system results in the fast polymerization of VP. The resulting by-product, polyvinylpyrrolidone, may deactivate the hydrogenation catalyst by surface blocking. VP can be hydrogenated to EP under mild conditions and with a high selectivity using a palladium catalyst supported on a porous carbon material Sibunit. The kinetics of VP hydrogenation over the Pd/C catalyst is studied.

INTRODUCTION

The use of catalysis opens new avenues for the preparation of organic fine chemicals [1]. Complex processes of the preparation of biologically active compounds and medicines are of most interest. 1-Ethyl-pyrrolidone-2 (EP) is one of the key intermediates for the synthesis of various heterocyclic compounds that exhibit pharmacological activity [2]. In particular, EP is the initial compound in the new catalytic synthesis of the medicinal preparation Sulpirid proposed earlier by us [3–5].

Syntheses of EP are based on the following reactions, which are complicated from the preparative viewpoint: the intramolecular cyclization of corresponding aliphatic amides and amines [6, 7], the ethylation of pyrrolidone-2 [8, 9], and the alkylation of 1,4-diaza-1,3-butadiene with an organozinc compound [10]. The catalytic hydrogenation of 1-vinylpyrrolidone-2 (VP) may be the most elegant method for the preparation of EP. EP was catalytically synthesized by the hydrogenation of VP in dilute solutions at a low temperature and at very high concentrations of the Raney nickel catalyst [11]. However, the hydrogenation of VP is accompanied by side reactions of VP conversion caused by the high reactivity of VP molecules containing the conjugated system of π-electrons of the C=C bond, the lone pair of electrons in the nitrogen atom, and π-electrons of the carbonyl group. In particular, VP is readily polymerized via a vinyl group in the presence of radical initiators, acid–base catalysts [12], and transition metal compounds [13]. Additionally, the hydrolysis of VP may result in lactam ring opening [12] followed by the formation of polyamides. These side processes drastically decrease the yield of the target product and may rapidly deactivate the catalyst.

This paper is devoted to the study of both the hydrogenation and side reactions of VP and to the search for a highly efficient catalytic system for the synthesis of EP.

EXPERIMENTAL

The initial VP was purified by distillation in a vacuum at 65–67°C (2 torr) prior to experiments. The hydrogenation of VP was carried out in a stainless-steel autoclave (150 ml) equipped with an electromagnetic stirrer (800–1000 rpm) and an automatic system for the measurement of the rates of hydrogen consumption. The loading of VP was 25 ml (0. 234 mol). The reaction was performed on a powdered catalyst: 4% Pd supported on a carbon material Sibunit of a 5–50 μm fraction. The specific surface area of the support (measured by argon adsorption) was 480 m^2/g; the total pore volume (measured by incipient wetness technique) was 0.7 cm^3/g; and the predominant diameter of transport pores was 30–35 nm. The average size of the supported palladium particles determined by electron microscopy was 3.5 nm.

The content of the products in the reaction mixture was analyzed by GLC (flame-ionization detector, 2 m × 3 mm column packed with 15% PEG-20M + 2.5% KOH on Chromaton N (0.16- to 0.20-mm fraction)).

RESULTS AND DISCUSSION

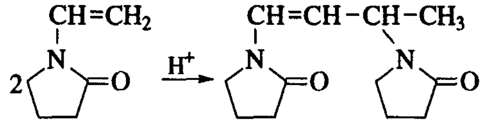
Search for a Selective Catalytic System

In the catalytic conversion of highly reactive molecules, the selectivity to a target product may largely be determined by the contribution of side routes of noncatalytic conversions of such molecules rather than by the selectivity of a catalyst used. Under the conditions of liquid-phase catalytic hydrogenation, VP can be subjected to a number of side transformations that are caused by its thermal lability and tendency to polymerize. We carried out a set of experiments to studying VP conversions in the absence of a catalyst for the hydrogenation to search for the parameters that will allow the suppression of such side reactions.

Thermal stability. The thermal stability of VP was studied in the temperature range from 25 to 90°C (Fig. 1). The concentration of freshly distilled VP remained virtually constant in an inert atmosphere for 5 h, which is in agreement with the literature data [12]. This points to the fact that pure VP is thermally stable in the temperature range studied, and the contribution of this route to the formation of by-products can be neglected.

Radical polymerization. On heating VP in air, a monotonic decrease in the VP concentration was observed in the kinetic curve (Fig. 1), and the solution rapidly transformed to a viscous mass. Evidently, in the presence of oxygen, peroxy compounds that initiate the polymerization of VP by the free-radical mechanism [12] can be formed. Thus, this route can significantly contribute to the formation of by-products before the contact of VP with the catalyst and before the hydrogenation. It is important to note that, in the presence of an alkali (NaOH), the heating of VP in both an inert atmosphere and air did not markedly change the concentration of VP (Fig. 1). This points to the fact that the radical polymerization of VP was suppressed in the alkaline medium. Unfortunately, we failed to accomplish the catalytic hydrogenation of VP in the presence of the alkali.

Acid dimerization. Even when trace amounts of an aqueous solution of a strong acid (~10^{-7} moles of $HClO_4$ per mole of VP) were added, the concentration of VP decreased and the viscosity of the solution increased (Fig. 1). Taking into account the data on the polymerization of VP in the presence of dilute acids [12], the main product (T_b = 118–122°C/2 torr) isolated from the reaction mixture was identified as a VP dimer. The formation of this dimer can be the reaction



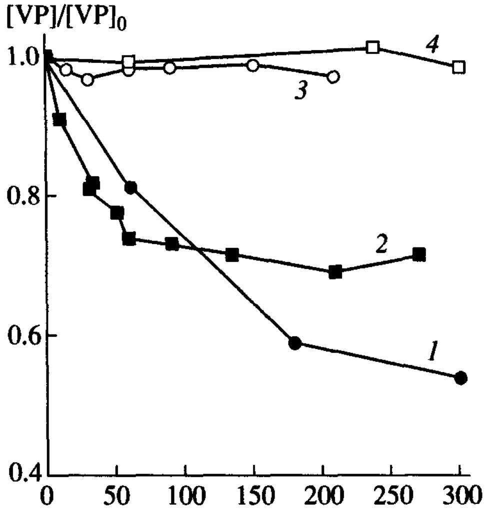
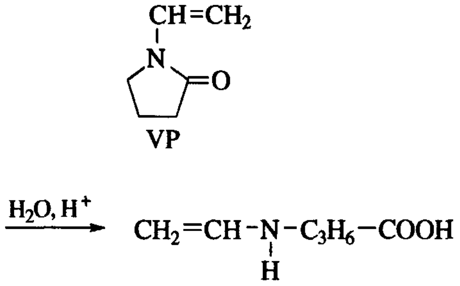


Fig. 1. $[VP]/[VP]_0$ as a function of the heating time (τ) (*1*) in air, (*2*) in the presence of acid ($HClO_4$), (*3*) in argon, and (*4*) in the presence of alkali (NaOH) (the loads of VP, $HClO_4$ (80%), and NaOH (5%) are 0.234 mole, 1.5 μl, and 30 μl, respectively; T = 80°C).

The kinetic curve of VP concentration versus time had two segments (Fig. 1). The first segment corresponded to the beginning of VP conversion when its concentration rapidly decreased. An increase in the amount of the added acid initially resulted in a more pronounced decrease of [VP]. Thus, the steeper initial segment of the kinetic curve corresponded to the fast polymerization of VP in the presence of a strong acid. The subsequent deceleration VP dimerization may point to a decrease in the concentration of a free acid in the solution. It seems likely that, along with the acid dimerization of VP, the acid hydrolysis of the amide bond occurred and resulted in the opening of the pyrrolidone cycle [12] by the following reaction:



$$\xrightarrow{H_2O,\,H^+} CH_2{=}CH{-}\underset{H}{N}{-}C_3H_6{-}COOH$$

γ-vinylaminobutyric acid

The resulting γ-vinylaminobutyric acid acted as a buffer binding protons of the strong acid.

Thus, the above experiments showed that the main factor that caused the formation of by-products was the presence of oxygen (in peroxy initiators of radical processes) and compounds of the acid nature in the system. Trace impurities in the initial VP and on the reactor walls may be a source of acidic compounds, but acid sites at the surface of the catalyst used for hydrogenation may be of the greatest importance. Evidently, this is the reason why the selective hydrogenation of VP over metallic catalysts supported on oxides of the acid nature (Al_2O_3, SiO_2) failed.

It might be expected that the catalysts supported on porous materials with weak acid–base properties, for example, active carbons, whose surface contains carboxyl groups possessing weak acidic properties (K_a ~ 4.2 × 10^{-5}) [14], will be the most selective catalysts. One such material is the composite carbon support Sibunit [15], which differs from active carbons in the extremely low concentration of mineral impurities (SiO_2, Al_2O_3, and Fe_3O_4) at its surface that are capable of initiating side reactions of VP hydrogenation. It will be shown below that EP can be obtained with a high yield over a palladium catalyst supported on Sibunit.

VP Hydrogenation over a Pd/C Catalyst

Figure 2 presents the effect of some parameters (concentrations of the catalyst and VP, hydrogen pressure, and reaction temperature) on the rate of VP hydrogenation.

Catalyst concentration. For the ranges of temperature and hydrogen pressure under study, the curves of the initial rate of VP hydrogenation as a function of the concentration of the loaded catalyst had two typical segments (Fig. 2). The initial segments of the curves are characterized by a linear increase in the reaction rate with an increase in the catalyst concentration. The other portion is characterized by an approximately constant reaction rate at high concentrations of the catalyst when the observed hydrogenation rate was probably determined by the rate of hydrogen dissolution. In the transition region between these two portions, the rate of hydrogenation was comparable to the rate of hydrogen dissolution. This allowed the evaluation of the rate of hydrogen dissolution under the experimental conditions. It turned out that, for the ranges of temperature and pressure under study, the rate of hydrogen dissolution per a unit pressure varied from 21 to 27 mmol H_2 l^{-1} atm^{-1} min^{-1}. In all subsequent experiments, the load of the catalysts was chosen so that the rate of the catalytic reaction was no higher than half the rate found for hydrogen dissolution.

Under the chosen conditions (P_{H_2} = 10 atm, T = 70°C), the yield of EP was close to 100% over the entire range of the catalyst concentrations (Fig. 2). At the same time, a weak trend toward a decrease in the selectivity to EP with a decrease in the catalyst concentration can be noted. The reason is the prolonged overall time of hydrogenation, i.e., the residence time of EP under the reaction conditions extended resulting in an increase in the amounts of by-products formed by the noncatalytic conversion of VP. A more significant decrease in the selectivity to EP was observed in the hydrogenation of VP at higher temperatures (Fig. 2).

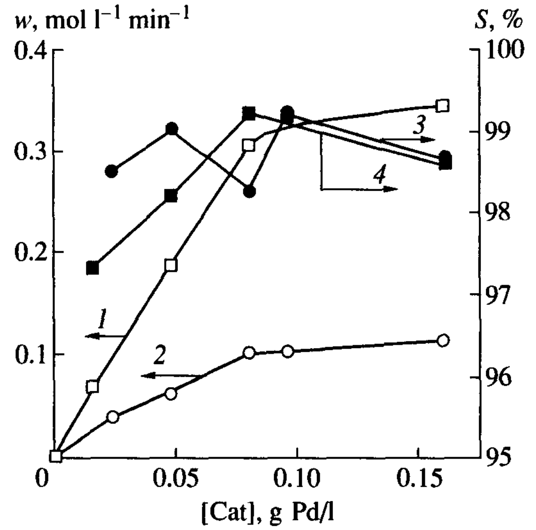


Fig. 2. Dependence of (*1*, *2*) the apparent rate of VP hydrogenation (w) and (*3*, *4*) the selectivity to EP (S) on the catalyst concentration ([Cat]) (the load of VP is 0.234 mole; (*2*, *3*) T = 50°C, P_{H_2} = 4 atm; (*1*, *4*) T = 70°C, P_{H_2} = 10 atm).

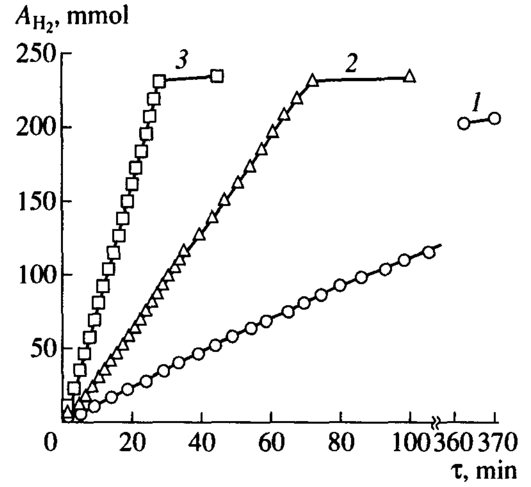


Fig. 3. Dependence of the amount of consumed H_2 (A_{H_2}) on the time of VP hydrogenation (τ). P_{H_2}, atm: (*1*) 2; (*2*) 4.5; (*3*) 10 (the loads of VP and 4% Pd/C are 0.234 mole and 0.05 g, respectively, T = 70°C).

Concentration of VP. In the temperature range from 20 to 100°C and at hydrogen pressures varying from 4 to 10 atm, the curves for the dependence of amounts of consumed hydrogen on the reaction time were similar and had linear portions up to 95% conversion of VP (Fig. 3). This points to the zero order of the reaction rate with respect to VP concentration in the ranges of temperatures and pressures under study. The existence of such a dependence was evidently due to a high value of the equilibrium constant of VP adsorption on the surface of Pd that resulted from the strong coordination of the conjugated π-system formed by C=O and C=C groups and the lone pair of electrons of the nitrogen atom of the VP molecule to the surface Pd atoms. As a result, the concentration of surface Pd atoms occupied by adsorbed VP molecules remained virtually constant when the VP concentration in the solution changed considerably. The concentration of such Pd atoms determined the rate of hydrogenation.

However, at a low hydrogen pressure (Fig. 3), a gradual decrease in the rate of VP hydrogenation was observed with time. The initial linear portion of the curve for amounts of consumed hydrogen as a function of the reaction time flattened out at the amount of consumed hydrogen approximating to a steady-state value. At low concentrations of the catalyst and at 70°C, the

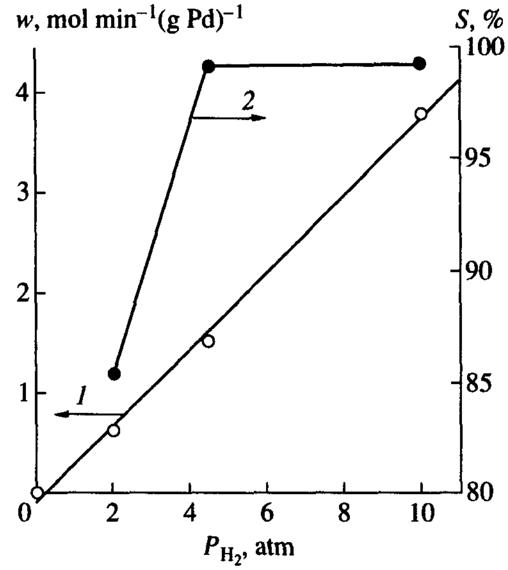


Fig. 4. Dependence of (*1*) the apparent rate of VP hydrogenation (*w*) and (*2*) the selectivity to EP (*S*) on the hydrogen pressure (the loads of VP and 4% Pd/C are 0.234 mole and 0.05 g, respectively, $T = 70$°C).

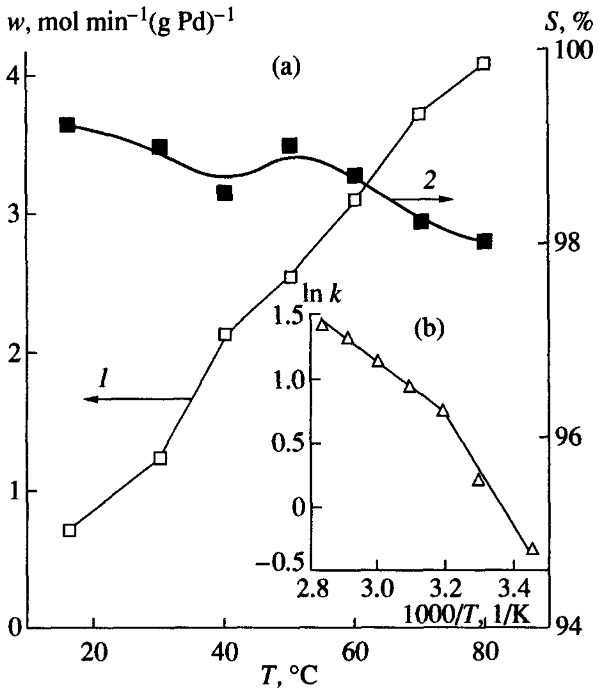


Fig. 5. (a) Dependence of (*1*) the apparent rate of VP hydrogenation (*w*) and (*2*) the selectivity to EP (*S*) on temperature (the loads of VP and 4% Pd/C are 0.234 mole and 0.05 g, respectively, $P_{H_2} = 6$ atm) and (b) the Arrhenius plot of the apparent rate constant (*k*) of VP hydrogenation (the loads of VP and 4% Pd/C are 0.234 mole and 0.05 g, respectively, $P_{H_2} = 6$ atm).

steady-state value corresponded to the incomplete hydrogenation of VP. These results are indicative of the deactivation of the catalyst with by-products formed during the long residence of VP under the hydrogenation conditions.

Hydrogen pressure. For the temperature range studied (20–100°C), the rate of VP hydrogenation was firstorder with respect to hydrogen pressure (Fig. 4). This points to the fact that the rate of VP hydrogenation was determined by the stage of hydrogen activation on Pd.

It is important to note that, as the hydrogen pressure (P_{H_2}) decreased from 10 to 2 atm (Fig. 4), the selectivity to EP decreased from 99.2 to 85.4%. We compared the GLC data for the reaction products of VP hydrogenation and for the sample obtained by the catalytic hydrogenation of a dimer fraction until hydrogen consumption stopped (the stoichiometry of the reaction is 1 mole of H_2 per 1 mole of dimer). The hydrogenated dimer of VP was predominantly formed as a by-product. It seems likely that, at a low hydrogen pressure and high temperatures, the rate of the side conversion of the initial VP becomes comparable with the rate of VP hydrogenation.

Reaction temperature. The curve of the temperature dependence of the initial rate of VP hydrogenation per unit catalyst concentration had a complex shape (Fig. 5a). As the reaction temperature increased from 15 to 40°C, the initial rate of VP hydrogenation per unit catalyst concentration steeply increased (the slope almost tripled). At higher temperatures (40–80°C), the slope of this curve became smaller. For the chosen optimal conditions ($P_{H_2} = 6$ atm and $T = 15$–80°C) (Fig. 5), the selectivity to EP insignificantly decreased with an increase in the temperature and remained in the range from 99.2 to 98.0%. However, at a low hydrogen pressure (2 atm), the selectivity to EP markedly decreased to 85.4% already at 70°C and we failed to complete hydrogenation at a higher temperature (≥80°C) because of catalyst deactivation. Obviously, the appearance of the observed by-product (hydrogenated dimer of VP) is due to the stronger temperature dependence of the rate of VP dimerization as compared to the temperature dependence of the rate of its hydrogenation.

The temperature dependence of the apparent rate constant for hydrogenation plotted in the Arrhenius coordinates (Fig. 5b) is a two-portion curve with the observed activation energy of 8.2 kcal/mol for the low-temperature portion and of 3.7 kcal/mol, for $T = 40$–70°C. An almost 200% decrease in the apparent activation energy may point to the effect of mass transfer processes inside the catalyst grain, i.e., to the occurrence of the process under the conditions controlled by the internal diffusion. This may be explained by the appearance of trace amounts of the product of VP polymerization, polyvinylpyrrolidone, which is adsorbed on the carbon surface and hindered the mass transfer inside the catalyst micrograins. Such an explanation seems quite plausible because only 0.035 g of polyvinylpyrrolidone (its density is ~1.0 g/cm^3), which correspond to ~0.1% of the weight of the initial VP, would be enough to completely fill the pore space of 0.05 g of the catalyst with a pore volume of 0.7 cm^3/g used in the experiment. The limiting case of this phenomenon is the accumulation of high-molecular polyvinylpyrrolidone in substantial amounts in the system that may result in the encapsulation of particles and entire deactivation of the catalyst (Fig. 3).

Thus, having studied the hydrogenation of VP over the Sibunit-supported palladium catalyst, we found the highly efficient system for the preparation of EP, a valuable intermediate for the synthesis of biologically active substances.

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