HYDRODEHALOGENATION OF BROMO- AND CHLOROPYRIDINES OVER PALLADIUM COMPLEX AND PALLADIUM METAL CATALYSTS

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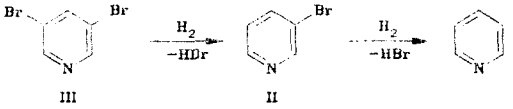
The hydrodehalogenation of 2-chloro-, 2-bromo-, 3-bromo, and 3,5-dibromopyridine has been studied in the presence of a palladium complex catalyst immobilized on silica gel, and a Pd/C catalyst. Cleavage of bromine from bromopyridines over the Pd complex is significantly faster than from the bromo-substituted furanes and thiophenes previously studied. Debromination over Pd/C is faster than over the complex catalyst. Over both catalysts 3-bromopyridine debrominates faster than the 2-isomer. When molecular deuterium is used, the respective deuterated pyridines can be obtained.

It is known [1, 2] that in the presence of a palladium chloride complex immobilized on silica gel that is modified with γ-aminopropyl groups (Pd-APS), vigorous hydrodehalogenation of bromo and chlorosubstituted thiophenes and furans takes place. In order to clarify the applicability of this reaction, the present work investigates the hydrodehalogenation of halopyridines in the presence of supported palladium complex and palladium metal catalysts.

Hydrodehalogenation of 2-bromopyridine (I) and 3-bromopyridine (II) takes place over the complex catalyst rapidly even at room temperature (250 and 700 mole/liter·min·mole Pd, respectively). Debromination of 3,5-dibromopyridine (III) goes in two steps: in the presence of Pd-APS the rate of monobromide II formation was 670, and of pyridine formation 270 mole/liter·min·mole Pd, while the concentration of 3-bromopyridine II in the reaction mixture reaches 40% (Fig. 1).



III II

It is of interest that the initial debromination rate of 2-bromopyridine (I) (calculated per mole of Pd) over metallic Pd/C is 3 times, and that of 3-bromopyridine (II) is 4.5 times higher than over the Pd-APS complex; they are 730 and 3330 mole/liter·min·mole Pd, respectively. Cleavage of bromine from dibromide III over the metallic catalyst also goes in steps (Fig. 1); the rates of formation of 3-bromopyridine (II) and pyridine are also substantially higher in the presence of Pd/C than over Pd-APS, viz., 2200 and 470 mole/liter·min·mole Pd, respectively.

Tests on the dehalogenation of an equimolar mixture of I and II showed that in the presence of Pd-APS or Pd/C the rate of bromine cleavage is close to the conversion rate of the less reactive compound I. Evidently this is due to the better adsorbability (coordination) of the 2-bromo derivative I,

In order to compare the reactivities of the heterocyclic and aromatic bromo derivatives, tests were carried out on the dehalogenation of equimolar mixtures of bromobenzene with the bromopyridine isomers. In the presence of Pd—APS bromine cleavage proceeds simultaneously from bromobenzene and both bromopyridines; the rates were ∿150 mole/liter·min·mole Pd for bromobenzene, and 300 mole/liter·min·mole Pd for the bromopyridines. Apparently bromobenzene competes with bromopyridine for coordination on the complex catalyst and thereby partially displaces bromopyridine, and lowers the rate of its conversion to pyridine.

Dechlorination of 2-chloropyridine, IV, proceeds over Pd-APS and Pd/C with similar initial rates (600 and 640 mole/liter. min·mole Pd); the reaction is finished after 50-60 min. When an equimolar amount of I or II is added to chloride IV, the reduction rate of IV over Pd-APS is sharply reduced to 40 or 150 mole/liter min mole Pd respectively, while reduction

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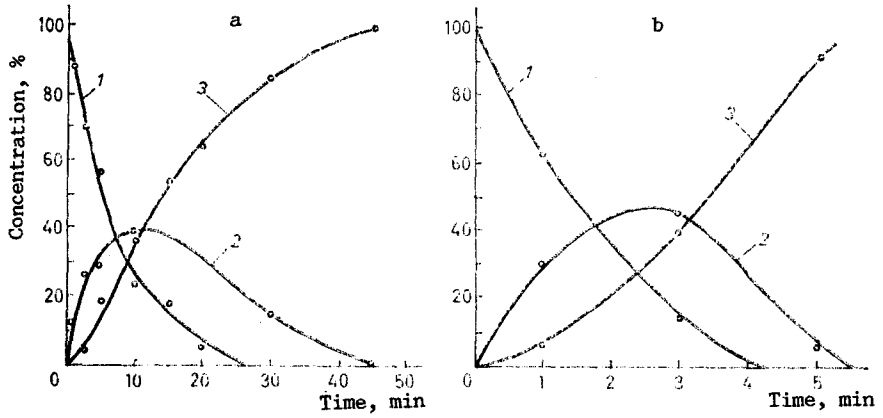
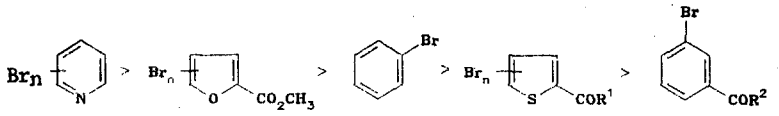


Fig. 1. Debromination of 3,5-dibromopyridine (1 mmole) in presence of Pd-APS (a) and Pd/C (b). 1) 3,5-dibromopyridine; 2) 3-bromopyridine; 3) pyridine.

of both chloro- and bromopyridines proceeds at the same time. In contrast, over Pd/C in the same mixtures dechlorination of IV begins only after ~80% of the bromopyridine has been converted, and its rate is close to the reduction rate of the compound by itself. The dechlorination of an equimolar mixture of IV and chlorobenzene proceeds similarly. In the presence of Pd–APS complex the two substrates are reduced at the same time, but over the metallic catalyst chlorobenzene begins to react only after ~80% of 2-chlorobenzene has been consumed.

Thus the catalytic hydrodehalogenation of halopyridines is characterized by the following features: 1) it is faster in the presence of metallic Pd than over the Pd complex; 2) in the presence of either catalyst, dehalogenation of 3-bromopyridine is 3-4.5 times faster than that of 2-bromopyridine.

On the basis of these results and the data of [1, 2] it can be said that over the Pd complex the rate of bromine cleavage is significantly higher from bromopyridines than from the previously studied bromosubstituted furan and thiophene carbonyl compounds. The bromo compounds that have been studied can be arranged in the following sequence:



n=1, 2; R^1=H, CH_3, C_6H_5; R^2=2-thienyl

It is difficult to interpret the observed features within the framework of the hydrodehalogenation mechanism previously discussed [3], and this problem evidently requires special study. It can only be presumed that the higher hydrodehalogenation rate of bromopyridines, as compared with the furan, thiophene, and benzene derivatives, is related to the presence in the pyridine of a strongly basic center, viz., the unshared electron pair on nitrogen, which insures efficient coordination (adsorption) of these compounds on the catalyst. In this case the very act of hydrodehalogenation may take place not on the center of adsorption or coordination, but on a neighboring reactive center. The higher debromination rate over Pd/C as compared with the complex may be the result of strong bonding of the pyridine compound as a ligand that displaces one of the γ-aminopropyl groups from the Pd complex. By the same reasons we can explain the smaller differences in the various competing dehalogenation rates observed on Pd-APS than on Pd/C. The reason for the easier cleavage of bromine from the 2 position than from the 3 position, observed on both catalysts, as it appears to us, can be that the coordination of the heteroatom with palladium sterically hinders the interaction of the carbon–halogen bond in the neighboring 2 position of the pyridine ring with a reactive center on the catalyst.

Hydrodebromination of bromopyridines can be used for preparative purposes. In particular, by analogy with selective deuterodehalogenation (replacement of halogen by deuterium in the same position) that we have previously proposed for thiophenes and furans [1], the method can be used to produce compounds containing deuterium in the pyridine ring. Thus, the deuterodebro-

mination of III over Pd/C we obtained (3,5-D_2)-pyridine. Chromatomass spectrometric analysis of the reaction mixture showed that the pyridine that is produced has the following distribution by weight: M 81 ($C_5H_3D_2N$), 79; M 80 (C_5H_4DN) 14; M 79 (C_5H_5N) 7%. When the metal complex Pd—APS was used, the product contained 84% dideuteropyridine, 15% monodeuteropyridine, and 1% untagged pyridine. The small amounts of pyridine and monodeuteropyridine apparently form because of the presence on the catalyst of hydrogen that was evolved in the decomposition of $NaBH_4$.

EXPERIMENTAL

Starting materials and reaction products were analyzed by GLC at 70-120° (programmed heating at 8°/min) on a LKhM-8MD chromatograph with flame ionization detector; stainless steel column 1 m × 3 mm, liquid phase SE-30 (10%) on Chromosorb W, nitrogen carrier gas. Internal standard, cymene or ethylbenzene.

The palladium complex (3% Pd) on silica gel modified with γ-aminopropyl groups was pre-reduced with $NaBH_4$ by the procedure of [4]. The 2% Pd/C catalyst was obtained by impregnation of BAU activated carbon with $PdCl_2$ solution, reduction with formaldehyde, and further reduction with $NaBH_4$.

Catalytic hydrodehalogenation was carried out with H_2 at 20° and atmospheric pressure by the procedure of [3]. In each experiment 0.05-0.075 g catalyst ($1.5 \cdot 10^{-2}$ mmole Pd), 0.01 g (∿ 0.3 mmole) $NaBH_4$, 1-2 mmole substrate, 2-4 mmol KOH, and 10 ml of solvent (ethanol, especially pure grade) were taken. 3,5-Dibromopyridine was used as a solution in 2 ml of benzene.

3-Bromopyridine and 3,5-dibromopyridine were obtained according to [5]. 2-Chloro- and 2-bromopyridine were commercial products, "pure" grade.

(3,5-D_2)-Pyridine. Into a "duck" type reaction vessel were introduced 0.16 g Pd/C ($3 \cdot 10^{-2}$ mmole Pd), 0.5 g (9 mmole) KOH, and 0.01 g (0.3 mmole) $NaBH_4$; the system was flushed with deuterium, and 10 ml of ethanol was added. The rocker was turned on. After decomposition of $NaBH_4$ and repeated flushing with deuterium, 0.781 g (3.3 mmole) of 3,5-dibromopyridine dissolved in 5 ml benzene was added. The reaction was finished after 45 min. According to GLC data the overall yield of (3,5-D_2)-pyridine, with traces of (3-D)-pyridine and pyridine, was ∿100%. The reaction mixture was filtered and the filtrate was analyzed by chromatomass spectrometry on a Varian MAT-111 instrument. When the complex catalyst was used, 0.4 g Pd—APS, 0.01 g $NaBH_4$, 0.4 g (7 mmole) KOH, and a solution of 0.56 g (2.36 mmole) 3,5-dibromopyridine in 4 ml benzene were taken. The yield of the deuterated pyridine mixture was ∿100%.

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