

NEW METHOD FOR DEHYDROGENATION OF
1,4-DIHYDROPYRIDINES TO PYRIDINES USING
HOMOGENEOUS COMPLEX PALLADIUM CATALYSTS

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As is known, the dehydrogenation of 1,4-dihydropyridines to the corresponding pyridines is accomplished under the influence of an equimolar amount or excess of such reagents as HNO_3 , CrO_3 , H_2O_2 , N_2O_4 , chloranil, and *t*-amyl hydroperoxide [1-3].

In order to develop a method for the preparation of substituted pyridines from 1,4-dihydropyridines we studied the possibility of dehydrogenating the latter using complexes of the transition metals. As the hydrogen acceptor we used the $\text{Pd}(0)$ phosphine complex, which was obtained by the reduction of palladium acetylacetonate with triethylaluminum in the presence of stabilizing additives [$\text{P}(\text{C}_4\text{H}_9)_3$ and butadiene]. The deposition of Pd, which has a very low dehydrogenation activity under the conditions selected by us, is observed in the absence of tributylphosphine and butadiene.

The preliminary experiments disclosed that equimolar amounts of the complex do not have to be used to dehydrogenate 1,4-dihydropyridines, while the reaction is catalyzed by very small amounts of Pd catalyst. Besides this, the maximum activity of the Pd complexes in the dehydrogenation of dihydropyridines was obtained if $\text{CF}_3\text{CO}_2\text{H}$ was added to the catalytic system in an amount of 10 moles per mole of Pd.

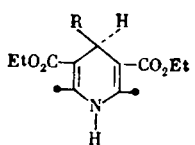
Other Brönsted acids ($\text{CH}_3\text{CO}_2\text{H}$, $\text{C}_6\text{H}_5\text{CO}_2\text{H}$, etc.) also exert a similar promoting effect, but when they are used the yields of the pyridines do not exceed 60%. In view of this, all of the experiments on the dehydrogenation of 1,4-dihydropyridines were run using a catalyst system composed of $\text{Pd}(\text{acac})_2$, $\text{P}(\text{C}_4\text{H}_9)_3$, $\text{Al}(\text{C}_2\text{H}_5)_3$, and $\text{CF}_3\text{CO}_2\text{H}$ in a mole ratio of 1:3:3:10. We studied 2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine (I) and its 4-alkyl- and aryl-substituted derivatives. Thus, 2,6-dimethyl-3,5-dicarbethoxypyridine (II) is formed in ~100% yield when (I) is heated on the mentioned catalyst in benzene solution (100°C , 10 h). Together with (II), the evolution of H_2 is observed in all of the experiments, the amount of which corresponds to the amount of the 1,4-dihydropyridine in the catalyze.

It was postulated that the intermediate hydride complexes of palladium formed in the dehydrogenation of dihydropyridines can convert olefins to saturated hydrocarbons. In view of this, all of the subsequent dehydrogenation experiments were run in the presence of 1,5-cyclooctadiene (COD) or its methyl derivatives, which were taken in a dihydropyridine-COD ratio equal to 1:0.5-1. It was established that the COD taken for reaction is hydrogenated in quantitative yield and with a high selectivity to cyclooctene (III), while the 1,4-dihydropyridine gives (II). The formation of cyclooctane is not observed even with a (I):COD ratio = 2:1. Cyclooctene is not hydrogenated on the mentioned catalyst and is recovered unchanged from the reaction. In the dehydrogenation of (I) the replacement of COD by the 1-methyl or 1,5-dimethyl-1,5-cyclooctadienes respectively gave 1-methyl-1-cyclooctene (IV) or 1,5-dimethyl-1-cyclooctene (V) in yields of 50 and 30%, although the yields of (II) in these experiments were at least 80-90%.

Apparently, the low yield of (IV) and (V) in our experiments can be explained by the steric hindrance created by the methyl groups during approach and activation of the methyl- and dimethyl-1,5-cyclooctadiene molecules on the central palladium ion. All of our attempts to involve conjugated 1,3-dienes (1,3-cyclooctadiene, butadiene, isoprene) in this reaction proved unsuccessful.

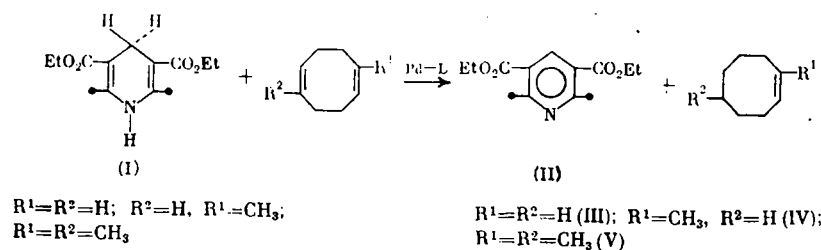
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TABLE 1



R	Yield, %*	
	pyridine derivative	cyclooctene
H	100 (V)	100
C ₆ H ₅	92 (VI)	86
<i>p</i> -C ₆ H ₄ -OCH ₃	80 (VII)	74
<i>o</i> -C ₆ H ₄ -OH	79 (VIII)	73
CH=CH-C ₆ H ₅	78 (IX)	72
CH ₃	52 (X)	46
C ₄ H ₉	25 (XI)	19

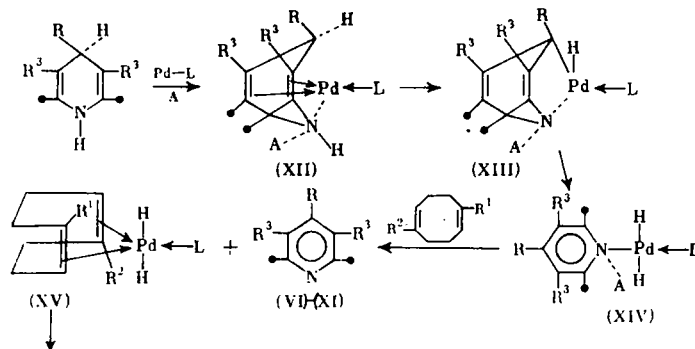
*The constants of the obtained pyridines and cyclooctenes coincide with the data given in [3-6].

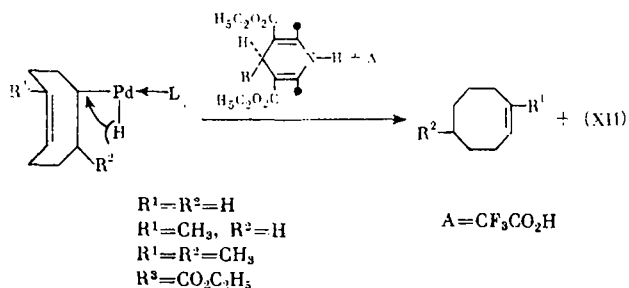


A study of the yield of the pyridines as a function of the structure of the C⁴ radical in the starting dihydro derivative revealed that the reaction proceeds most completely for the unsubstituted dihydropyridine (I). The dehydrogenation rate is slowest when alkyl substituents are present. Aromatic and unsaturated radicals facilitate an increase in the yield of the pyridines, which probably can be related to an increase in the lability of the C⁴ hydrogen atom. The results of the experiments in which COD served as the hydrogen acceptor are given in Table 1.

Concerning the mechanism of the promoting effect of CF₃CO₂H on the activity of the Pd catalyst it may be postulated that CF₃COOH forms molecular complexes with the dihydropyridines, in which the lability of the H atom on nitrogen is increased substantially and it is eliminated more easily, which leads to the hydride complex (XIII) in the case of (I). The subsequent decomposition of (XIII) proceeds to give the thermodynamically more stable pyridine and complex (XV).

On the basis of the obtained results the reaction for the dehydrogenation of 1,4-dihydropyridines by palladium complexes in the presence of COD can be depicted by the following scheme:





EXPERIMENTAL

The dihydropyridines were obtained as described in [7]. The mixture of products was analyzed on a Chrom-31 chromatograph. The column length was 2 m, the packing was silicone elastomer SE-30 deposited on Celite, and the carrier gas was helium.

General Procedure for Dehydrogenation of 1,4-Dihydropyridine Derivatives. a) To a solution of 0.5 mmole of $Pd(acac)_2$, 1.5 mmoles of $(C_4H_9)_3P$, and 2.0 mmoles of butadiene in 5 ml of benzene, in an argon atmosphere, at -5 to $0^\circ C$, was added 1.5 ml of $AlEt_3$ and the mixture was stirred for 0.5 h. Then the catalyst solution was transferred to a 100-ml steel autoclave, into which had previously been loaded 50 mmoles of the dihydropyridine, 50 mmoles of 1,5-cyclooctadiene, and 5 mmoles of CF_3CO_2H in 30 ml of benzene. The mixture was heated for 10 h at 100° , cooled, filtered through Al_2O_3 (III activity), washed with CH_2Cl_2 , and the combined eluates were evaporated. The residue was analyzed by GLC by comparing with authentic compounds. The results of the experiments are given in Table 1.

b) From 6.1 g of 1-methyl-1,5-cyclooctadiene and 12.65 g of 2,6-dimethyl-3,5-dicarbethoxydihydropyridine, on a catalyst composed of 0.5 mmole of $Pd(acac)_2$, 1.5 mmoles of $(C_4H_9)_3P$, 2 mmoles of butadiene, 1.5 mmoles of $AlEt_3$, and 5 mmoles of CF_3CO_2H , under the conditions of experiment a), we obtained 3.1 g of 1-methyl-1-cyclooctene and 11.3 g of 2,3-dimethyl-3,5-carbethoxypyridine.

Under similar conditions, from 6.8 g of 1,5-dimethyl-1,5-cyclooctadiene and 12.65 g of 2,6-dimethyl-3,5-dicarbethoxydihydropyridine we obtained 2.1 g of 1,5-dimethyl-1-cyclooctene and 10 g of 2,6-dimethyl-3,5-dicarbethoxypyridine.

CONCLUSIONS

1. We were the first to study the dehydrogenation of 1,4-dihydropyridines using catalytic amounts of homogeneous Pd catalysts and it was shown that 2,6-dimethyl-3,5-dicarbethoxy-1,4-dihydropyridine and its 4-substituted alkyl- ($CH_3-C_4H_9$) and aryl- (C_6H_5 , $o-C_6H_4OH$, $CH=CH-C_6H_5$, $p-C_6H_4-OCH_3$) derivatives are easily converted to the corresponding pyridines under the influence (10 h, 100°) of the catalyst: $Pd(acac)_2-P(C_4H_9)_3-Al(C_2H_5)_3-CF_3CO_2H$ (1:3:3:10).

2) When substituted 1,4-dihydropyridines are dehydrogenated in the presence of 1,5-cyclooctadienes the latter undergo simultaneous selective hydrogenation to the corresponding cyclooctenes.

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