HYDROGENATION OF 2,5-DIMETHYL-4-PHENYL(p-ALKYLBENZYL)PYRIDINES OVER METAL SULFIDES

M. A. Ryashentseva, Kh. M. Minachev,
V. V. Dorogov, and N. S. Prostakov

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The corresponding substituted piperidines were obtained in yields from 40 to 99.5% by the hydrogenation of 2,5-dimethyl-4-phenylpyridine and 2,5-dimethyl-4-[p-methyl(p-ethyl)-benzyl]pyridines in the presence of rhenium, platinum, and palladium sulfides.

The study of nickel catalysts for the hydrogenation of substituted pyridines to piperidines is important from a preparative point of view. Polysubstituted pyridines with aryl radicals as substituents are of special interest as objects of hydrogenation. Selective catalysts on which the pyridine ring is hydrogenated without involvement of the benzene ring are necessary for the hydrogenation of compounds of this type. This is again associated with the fact that more severe conditions than in the case of the hydrogenation of pyridine itself [1] are required in the case of substituted pyridines. The hydrogenation of 2- and 4-phenyl pyridines over a nickel catalyst has been accomplished previously. The yield of hydrogenation products did not exceed 60% [2]. Unfortunately, it was not indicated whether the benzene ring was involved during the hydrogenation in [2]. It follows from later studies that the benzene ring is also hydrogenated during the hydrogenation of 2- and 4-phenylpyridines and 2,6-diphenylpyridine over Raney nickel [3], 4-benzylpyridine over platinum [4], and 2-benzylpyridine over rhodium [5] or ruthenium dioxide [6].

In carrying out a systematic study of the sulfides of several metals as hydrogenation catalysts [7], we turned to an investigation of the hydrogenation of 2,5-dimethyl-4-phenylpyridine (I) [8], 2,5-dimethyl-4-(p-methylbenzyl)pyridine (II), and 2,5-dimethyl-4-(p-ethylbenzyl)pyridine (III) [9] in the presence of rhenium heptasulfide and platinum and palladium sulfides. The experimental results indicated that these sulfides can serve as catalysts for the selective hydrogenation of the pyridine ring without involving the aryl radical in the hydrogenation of substituted pyridines containing aryl radicals (I, II, and III). The optimum conditions for the hydrogenation of I-III were found; under these conditions, the corresponding 2,5-dimethyl-4-phenyl (IV), 4-(p-methylbenzyl)- (V), and 4-(p-ethylbenzyl)-2,5-dimethylpiperidines (VI) are formed in 85-99.5% yields in the presence of rhenium heptasulfide, in 93% yields in the presence of platinum sulfide, and in 40% yields in the presence of palladium sulfide.

In the case of the hydrogenation of III, the effect of the reaction time and temperature, the hydrogen pressure, and the amount of catalyst on the yield of VI was studied.* The optimum conditions for the hydrogenation of III over Re_2S_7 are as follows: a reaction time of 6 h, a temperature of 250°, a hydrogen pressure of 100-120 tech. atm, and 10% (of the weight of III) Re_2S_7. A change in the reaction temperature from 180 to 250° leads to an increase in the yield of VI from 68 to 99.5%. (The yield at 220° is 93.6%.) At 250°, changing the reaction time has only a slight effect on the yield of VI. (The yield of VI is 92.5% after 3 h, compared with 99.3% after 4 h.) An increase in the hydrogen pressure from 46 to 120 tech. atm increases the yield of VI by 11%. (The yield at 46 tech. atm is 88.6%.) The amount of catalyst has a substantial effect on the yield of VI (Table 1). The yield of VI decreases considerably (Table 1) when III is hydrogenated over Re_2S_7 in the presence of acetic acid.

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*The yield was determined by means of gas–liquid chromatography (GLC).

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR. Patrice Lumumba University, Moscow. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 88-90, January, 1972. Original article submitted October 2, 1970.

TABLE 1. Effect of the Nature and Amount of Catalyst on the Yield of 2,5-Dimethyl-4-(p-ethylbenzyl)piperidine (VI) (hydrogenation of III at 250°C and 120 tech. atm for 6 h)

Catalyst (% based on the weight of III)	Yield of VI, %
Re_2S_7 (1)	38,0
Re_2S_7 (3)	56,5
Re_2S_7 (6)	83,3
Re_2S_7 (8)	90,4
Re_2S_7 (10)	99,5
Re_2S_7 (10)	24,4*
PtS (1)	22,3
PtS (10)	92,6
PdS (10)	39,2

*In 12% acetic acid in alcohol.

The activity of platinum sulfide in the hydrogenation of III under the same conditions is inferior to that of rhenium heptasulfide, while palladium sulfide is considerably less active than rhenium and platinum sulfides under comparable conditions (Table 1).

The hydrogenation of I and II was carried out at 270° in the presence of Re_2S_7 (10% of the weights of I and II) at a hydrogen pressure of 95-102 tech. atm for 6 h. The hydrogenation products contain 92.8% IV and 95.8% V, respectively, according to GLC.

EXPERIMENTAL

Rhenium Heptasulfide. Hydrogen sulfide was purified successively with 10% HCl, I_2, H_2O, $CaCl_2$, and P_2O_5 and was passed for 4.5 h through a solution of 2 g of ammonium perrhenate in 30 ml of distilled water and 60 ml of 6 N HCl. After 24 h, the catalyst was removed by filtration and washed with distilled water until it no longer gave a reaction for chloride ions. It was then dried to constant weight (3-4 days) in a desiccator over calcium chloride. Found: Re 62.5 [11], S 38.1% [12]. Re_2S_7 Calculated: Re 62.5, S 37.9%.

Palladium Sulfide. A total of 120 ml of 6 N HCl was added to a solution of 1 g of $PdCl_2 \cdot 2H_2O$ in 30 ml of distilled water and 10 ml of concentrated hydrochloric acid, and purified hydrogen sulfide was then bubbled through the mixture for 3 h. The PdS was isolated as described in the preparation of Re_2S_7.

Platinum Sulfide. A stream of purified hydrogen sulfide was passed for 5 h through a solution of 1 g of $H_2PtCl_6 \cdot 6H_2O$ in 40 ml of distilled water, and the PtS was isolated as described in the preparation of Re_2S_7.

Hydrogenation of Pyridine Derivatives. A 70-ml glass ampul with a wide neck was charged with 0.01-0.10 g of catalyst and a solution of 1.0-1.6 g of I-III in 8-12 ml of absolute ethanol. The ampul was placed in a 120-ml stainless steel rotating autoclave equipped with a thermocouple. The autoclave was filled with hydrogen and was heated to the experimental temperature with stirring in 30 min. The mixture was cooled, and the catalyst was removed by filtration and washed with alcohol. The alcohol was removed by distillation, and the reaction products were vacuum distilled and chromatographed with a column (H 1.2 m, d 1.8 cm) packed with activity II Al_2O_3. Petroleum ether was initially used for the elution, followed by petroleum ether with the addition of 5, 10, 15, 20, and 25 ml of diethyl ether, respectively, for each 100 ml. The separation of piperidines IV-VI from starting I-III was monitored by thin-layer chromatography on activity II aluminum oxide with ether—petroleum ether (1:2) as the eluent; R_f 0.52-0.55 for IV-VI, and R_f 0.26-0.28 for I-III. The percentage of IV-VI in the reaction products was established by means of GLC with a 1.3-m-long column with a diameter of 4 mm packed with 12% polyethylene glycol adipate on Sferakhrom-1 and a gas (hydrogen) flow rate of 80-100 ml/min with a UKh-1 chromatograph with a thermal conductivity detector. Good separation of IV-VI from the corresponding starting I-III was observed during the chromatography and was checked with mixtures of pure samples.

2,5-Dimethyl-4-phenylpyridine (IV). The hydrogenation of 1.41 g (7.7 mmole) of I with 0.14 g of Re_2S_7 at 95 tech. atm and 270° for 6 h gave 1.40 g of bases, from which the fraction with R_f 0.56 was isolated by chromatography. Distillation of this product gave 1.02 g (70%) of IV with bp 90-93° (2 mm), n_D^{20} 1.5201, and d_4^{20} 0.9510. Found: C 82.4; H 10.2; N 7.4%; MR_D 60.51. $C_{13}H_{19}N$. Calculated: C 82.5, H 10.1, N 7.4%; MR_D 60.37. IR spectrum of IV (film) (cm^{-1}): 3095 medium (m), 3070 m, 3020 m, 1510 strong (s), 773 s, and 707 s.

2,5-Dimethyl-4-(p-methylbenzyl)piperidine (V). The hydrogenation of 1.63 g (7.7 mmole) of II with 0.16 g of Re_2S_7 at 102 tech. atm and 270° for 6 h gave 1.55 g of a fraction with bp 96-110° (2 mm), which was column chromatographed (R_f 0.57) and redistilled to give 1.14 g (69%) of V with bp 96-99° (2 mm), n_D^{20} 1.5161, and d_4^{20} 0.9391. Found: C 83.1; H 10.9; N 6.4%; MR_D 69.83. $C_{15}H_{23}N$. Calculated: C 83.0; H 10.7; N 6.4%; MR_D 70.23. IR spectrum of V (cm^{-1}): 3097 weak (w), 3051 w, 3019 w, 1521 s, 808 s, and 853 m.

2,5-Dimethyl-4-(p-ethylbenzyl)piperidine (VI). Hydrogenation of 1.01 g (4.5 mmole) of III with 0.1 g of Re_2S_7 at 120 tech. atm and 250° for 6 h gave after distillation of the reaction products, 0.89 g of a fraction with bp 95-131° (1 mm) which was column chromatographed (R_f 0.51) and redistilled to give 0.81 g (78%) of VI with bp 98-101° (2 mm), n_D^{20} 1.5102, and d_4^{20} 0.9275. Found: C 82.9; H 10.7; N 6.1%; MR_D 74.51. $C_{16}H_{25}N$. Calculated: C 83.1; H 10.8; N 6.1%; MR_D 74.23. IR spectrum of VI (cm^{-1}): 3093 s, 3054 m, 3012 w, 1522 s, 818 s, and 825 s.

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