SUBSTITUTED PYRIDINES, 2,5-DIMETHYL-4-p-NITROBENZYL PYRIDINE AND ITS REACTIONS

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2,5-Dimethyl-4-p-nitrobenzylpyridine has been prepared. Its nitro group has been reduced and its methylene group oxidized.

2,5-Dimethyl-4-benzylpyridine (I) [1], a representative of the γ-pyridylarylmethane series, is readily nitrated to the mono- and dinitro derivatives. 2,5-Dimethyl-4-o, p-dinitrobenzylpyridine (II) predominates when the reaction is carried out at 25-70°C, the amount increasing with time. The principal reaction product at 10 to 0°C is 2,5-dimethyl-4-p-nitrobenzylpyridine (III). In every case, a difficulty-separable mixture of II and III was formed, the absence of I being shown by thin layer chromatography. The nitro group enters in the p-position of the benzene ring, i.e., these pyridylarylmethanes nitrate in a similar manner to alkyl-benzenes.

The IR spectrum of crystalline III shows a band at 840 cm⁻¹ assigned to the out-of-plane stretching of the two adjacent aromatic C–H bonds. On this band is superimposed a more intense band at 860 cm⁻¹, caused by stretching vibration of the C–N bonds of the nitro group, which hinders the assignment of the bands in this region [2].

The nitro group in III was reduced to the amino group. In the IR spectrum of 4-p-aminobenzylpyridine (IV), out-of-plane vibration of the two adjacent C–H bonds appears more clearly as an intense band at 835 cm⁻¹, thus confirming the orientation of the nitro group in the p-position of the benzene ring.

In order to obtain 2,5-dimethyl-4-p-nitrobenzoylpyridine (V), which is a new γ-pyridyl aryl ketone, the substituted pyridine III was oxidized with potassium permanganate in presence of magnesium nitrate at 60°C. Oxidation of the arylpyridylmethane III was not fully selective, partial oxidation of the methyl groups in the pyridine ring taking place. Oxidation of III to V was confirmed by IR and NMR spectroscopy. The IR spectrum of V showed a very intense band at 1684 cm⁻¹, corresponding to carbonyl group stretching. An increase in the frequency of vibration of the carbonyl group in V in comparison with that in diaryl ketones (1665 cm⁻¹), and its closeness to the value for alkyl aryl ketones (1690 cm⁻¹) is apparently due to reduced conjugation of the carbonyl group with the aromatic rings as a result of the distortion of the planarity of the system. This is caused by the effect of the methyl group at C₅ of the pyridine ring. Comparison of the


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NMR spectra (for which the authors thank L. Petrovskaya) of III and V confirms the oxidation of the CH₂ group to CO. In the NMR spectrum of III, signals are observed which are due to the methylene and methyl groups at C5 and C2 of the pyridine ring. The chemical shifts of these protons, on the δ-scale, are equal to 2.15, 2.43, and 4.02 ppm relative to TMS, respectively. The relative integral intensities of one of the CH₂ group signals to the corresponding value for the CH₃ group is 3:2. In the NMR spectrum of V, only the signals due to the CH₃ group protons are observed.

**EXPERIMENTAL**

Nitration of 2,5-Dimethyl-4-benzylpyridine. a) To a nitrating mixture prepared from 52 g (0.5 mole) of nitric acid (d 1.37) and 103.5 g (1.0 mole) of sulfuric acid (d 1.83) was added 10 g (0.051 mole) of I. The mixture was stirred for 2 h at 65-70°, then poured on to ice and neutralized with sodium carbonate. The ethereal extract of the organic bases afforded 8.5 g of crystalline residue. Thin layer chromatography (grade II alumina, 1:3 ethyl acetate-heptane) showed the presence of two components, with RF 0.322 and 0.228. Repeated recrystallization gave II (RF 0.226), mp 109-111° (from ethyl acetate-heptane). Found: N 14.61, 14.58%, C₁₄H₁₃N₃O₄. Calculated: N 14.63%.

Nitration of I at room temperature gave the same results.

b) To a nitrating mixture of 156 g (1.5 mole) of nitric acid and 308 g (3.0 mole) of sulfuric acid was added gradually with stirring at 0° 29 g (0.147 mole) of I. The mixture was stirred for 2 h at a temperature not greater than 10°. Chromatography of a sample of the reaction mixture (grade II alumina, 1:2 ethyl acetate-heptane) taken at half-hour intervals (after working up) showed that starting material I (RF 0.50) had already disappeared in the first sample, this sample showing the presence of III (RF 0.302) and traces of II (RF 0.206). In subsequent samples, the amount of II increased. The reaction mixture was poured on to 400 g of ice, diluted with 1.5 liters of water, and neutralized with sodium carbonate. The organic bases were extracted with chloroform, giving 34.4 g of crystals, from which were isolated 19 g (53%) of bright yellow crystals of III, mp 96-98° (from benzene). Found: C 69.19, 69.07; H 5.74, 5.93; N 11.31, 11.66%. C₁₄H₁₄N₂O₂. Calculated: C 69.42; H 5.78; N 11.57%. IR spectrum, ν, cm⁻¹: 3115 very weak, 3075 very weak, 1603 very strong, 1560 weak, 1530 very strong (νs NO₂), 1500 weak, 1360 very strong (νs NO₂), 1195 weak, 1183 medium, 1170 weak, 1130 strong, 1040 weak, 987 strong (single aromatic C-H bond), 887 strong (C-N-O), 860 strong (C-N), 840 strong (two adjacent aromatic C-H bonds), 808 medium, 743 strong (C-N-O), 697 strong.

Pierate of III, mp 157-158° (from alcohol). Found: N 14.57, 14.79%. C₁₄H₁₄N₂O₂ • C₆H₅N₃OT. Calculated: N 14.86%.

2,5-Dimethyl-4-p-aminobenzylpyridine (IV). To a solution of 10 g (0.0415 mole) of III in 20 ml of concentrated hydrochloric acid was added 9.4 g (0.079 mole) of granulated tin. The mixture was heated to 70°, then 10 ml of acid was added during 1 h 30 min, followed by heating for 1 h at 100°. The mixture was neutralized with sodium hydroxide solution, and the organic bases were extracted with chloroform to give 8.3 g of crystals from which were isolated 3 g (34%) of rose-colored crystals of IV, mp 96-98° (from benzene). Found: C 79.14, 79.36; H 7.51, 7.30; N 13.26, 13.19%. C₁₄H₁₄N₂. Calculated: C 79.25; H 7.55; N 13.20%. IR spectrum, ν, cm⁻¹: 3440 strong, 3330 strong, 3220 strong (pNH₂), 1635 v. strong (SNH₂), 1615 v. strong, 1570 v. strong, 1550 v. weak, 1520 v. strong (SNH₂), 1502 weak, 1283 v. strong (C-N), 1250 weak, 1185 weak, 1170 v. weak, 1130 v. weak, 1070 v. weak, 1045 v. weak, 1025 v. weak, 1000 v. weak, 891 strong (single aromatic C-H bond), 835 v. strong (two adjacent aromatic C-H bonds), 795 weak, and 745 v. weak.

Dipierate of IV, mp 180-181°. Found: N 17.04, 17.02%. C₁₄H₁₆N₂ • 2C₆H₅N₃OT. Calculated: N 16.72%.

Acetate of IV. 0.5 g (0.0021 mole) of IV, 0.3 ml of acetic anhydride, and 10 ml of benzene were heated for 5 min. From the resulting precipitate (0.52 g) there was isolated 2,5-dimethyl-4-p-acetylaminobenzylpyridine, as colorless crystals, mp 196-198° (from 1% acetic acid in benzene). Found: C 75.80, 75.87; H 7.48, 7.12; N 11.15, 11.23%. C₁₆H₁₈N₂O. Calculated: C 75.59; H 7.08; N 11.02%.

2,5-Dimethyl-4-p-nitrobenzoylpyridine (V). To a mixture of 8.9 g (0.0368 mole) of III, 17.26 g (0.088 mole) of magnesium nitrate hexahydrate, and 90 ml of water during 5 h at 60° was added slowly 8.81 g (0.0557 mole) of potassium permanganate. The manganese dioxide was filtered off and washed with 100 ml of water. The filtrate and the manganese dioxide were washed with ether, and from the ether extract there was obtained 7.12 g of crystals. From these crystals there was isolated 4.6 g (49%) of yellow crystals of V,