# PRODUCTION OF 1-AZAFLUORENE FROM 2-METHYL-3-PHENYLPYRIDINE

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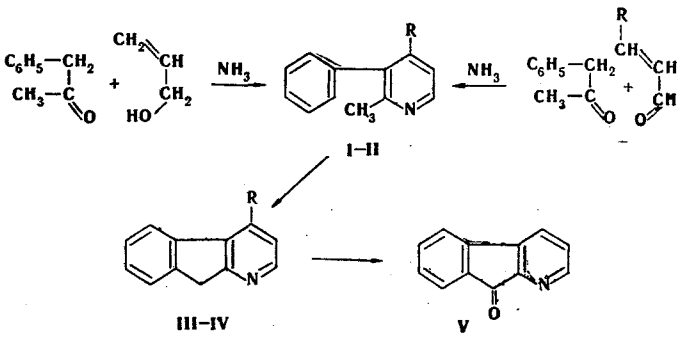
Among azafluorenes isomeric with respect to the position of the nitrogen atom 1-azafluorene remains inaccessible and least investigated. Only two examples of its production have been described, i.e., by pyrolysis of phenyl(3-pyridyl)diazomethane and by oxidation of benzo[f]quinoline with subsequent reduction of the 1-azafluorenone which forms [1]. In both cases the yield of 1-azafluorene is low. We have obtained 1-azafluorene by the catalytic dehydrocyclization of 2-methyl-3-phenylpyridine (I). This method has been used



I, III R=H; II, IV R=$CH_3$

successfully for the production of 2-, 3-, and 4-azafluorenes [2-4]. Earlier the pyridine base (I) was obtained with an 18% yield from allyl alcohol, methyl benzyl ketone, and ammonia at 475-500°C on cadmium phosphate [5]. We used an industrial catalyst (calcium phosphate with the addition of cadmium phosphate) in this condensation. At this catalyst the yield of phenylpyridine (I) amounts to 40%, and with acrolein instead of allyl alcohol the yield amounts to 46%. 2,4-Dimethyl-3-phenylpyridine (II) was obtained under analogous conditions from crotonaldehyde, methyl benzyl ketone, and ammonia.

During dehydrocyclization of 2-methyl-3-phenylpyridine (I) at the industrial K-16 catalyst at 520-540°C 1-azafluorene (III) is formed with a 24% yield. The isomeric 4-methyl-1-azafluorene (IV) and 4-methyl-3-azafluorene can form as a result of dehydrocyclization of the pyridine base (II). On the basis of the PMR spectra and TLC of the reaction products it can be supposed that both these isomers are formed, but it was possible to isolate azafluorene (IV) experimentally in the individual form.

Thus, the catalytic dehydrocyclization of phenylpyridines substituted by methyl at the ortho position of the pyridine ring is a general method for the synthesis of azafluorenes isomeric with respect to the position of the nitrogen atom.

During liquid-phase oxidation of 1-azafluorene (III) with oxygen in the presence of sodium hydroxide (this method was proposed earlier for the synthesis of fluorenone [6]) 1-azafluorenone (V) was obtained with a considerably higher yield than by oxidation with potassium permanganate.

## EXPERIMENTAL

The PMR spectra were recorded on a Tesla BS-478C spectrometer at 80 MHz in carbon tetrachloride with TMS as internal standard. The mass spectra were obtained on an MX-1303 instrument with a system for direct introduction of the sample into the ion source with an

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ionization potential of 70 V at 50°C.

2-Methyl-3-phenylpyridine (I). A. A mixture of 69 g (0.5 mole) of methyl benzyl ketone, 87 g (1.5 mole) of allyl alcohol, and ammonia (30 liters/h) was passed for 3 h at a constant rate through a quartz reactor containing 100 ml of catalyst (wt.%: CdO 10-13, CaO 41-45, $P_2O_5$ 41-45). The temperature in the catalyst zone was 375-390°C. The condensate was treated with 18% hydrochloric acid against Congo indicator. The neutral compounds were extracted with ether. The aqueous solution of the pyridinium salts was treated with sodium hydroxide. During distillation of the pyridine bases, extracted with ether, we isolated 20 g (40% calculated on the reacted amount of methyl benzyl ketone) of the pyridine base (I); bp 136-137°C (15 mm Hg). Found: $M^+$ 169. $C_{12}H_{11}N$. Calculated: Mol.wt. 169. Picrate of base (I); mp 135-136°C (from acetone). Published data [5]: mp 135-136.5°C.

B. A mixture of methyl benzyl ketone, acrolein, and ammonia (molar ratios 1:3:7) was passed through the reactor at the same temperature. After similar treatment we obtained a mixture of pyridine bases, from which we isolated phenylpyridine (I) with a 46% yield.

2,4-Dimethyl-3-phenylpyridine (II). Compound (II) was obtained similarly by the condensation of 0.25 mole of methyl benzyl ketone, 0.5 mole of crotonaldehyde, and ammonia. The yield was 44%. PMR spectrum: 1.96 (3H, s, 2-$CH_3$), 2.18 (3H, s, 4-$CH_3$), 6.82 (1H, d, 5-H), 6.95-7.32 (5H, m, H arom.), 8.15 ppm (1H, bd with weak splitting, 6-H). Found, %: C 85.1; H 7.2; N 7.9. $M^+$ 183. $C_{13}H_{13}N$. Calculated, %: C 85.3; H 7.1; N 7.7. Mol.wt. 183. Picrate of base (II), mp 173.5-174.5°C (from acetone). Found, %: N 13.7. $C_{19}H_{16}N_4O_7$. Calculated, %: N 13.6.

1-Azafluorene (III). A solution of 46.5 g (0.27 mole) of the pyridine base (I) in 100 ml of benzene was passed for 12 h through a steel reactor containing 100 ml of K-16 catalyst. The temperature in the catalyst zone was 520-540°C. From the catalysis product (34 g) after distillation of the benzene we isolated 6.5 g (24%) of 1-azafluorene (III); mp 83-84°C (from hexane). Published data [1]: mp 84-85°C. Found: $M^+$ 167. $C_{12}H_9N$. Calculated: Mol.wt. 167.

4-Methyl-1-azafluorene (IV). For the reaction we used 106 g (0.58 mole) of the pyridine (II) in 200 ml of benzene. The experiment was carried out similarly. The benzene was distilled from the product, and the remaining pyridine bases were distilled. The azafluorene fraction (22 g) was converted into picrates, which were boiled in 500 ml of acetone and rapidly filtered. The precipitate insoluble in acetone (7.7 g) was the picrate of the azafluorene (IV); mp 194-195°C. Found, %: N 13.6. $C_{19}H_{14}N_4O_7$. Calculated, %: N 13.7.

The picrate was decomposed with an aqueous solution of ammonia. The base was extracted with chloroform, and the chloroform solution was passed through a layer of aluminum oxide. After distillation of the chloroform we obtained 3.1 g (9%) of the azafluorene (IV); mp 70-71°C (from hexane). PMR spectrum: 2.52 (3H, s, 4-$CH_3$), 3.75 (2H, s, $CH_2$), 6.77 (1H, d, 3-H), 7.00-7.70 (4H, m, H arom.), 8.15 ppm (1H, d, 2-H). Found, %: C 86.1; H 6.2; N 7.8. $M^+$ 181. $C_{13}H_{11}N$. Calculated, %: C 86.2; H 6.1; N 7.7. Mol.wt. 181.

1-Azafluorenone (V). A. Oxygen was passed through a solution of 5 g (0.03 mole) of 1-azafluorene (III) in 20 ml of dimethyl sulfoxide at 30°C for 6 h (150 ml/min). At the beginning of the experiment and after every hour we added 0.1 ml of a 50% aqueous solution of sodium hydroxide. According to TLC, the degree of conversion of 1-azafluorene at the end of the experiment was 99%. The mixture was added to 300 ml of water. The precipitate (5.3 g) was separated and washed on the filter with cold acetone. After purification on a column of aluminum oxide with ether as eluent we obtained 3.5 g (65%) of 1-azafluorenone (V) in the form of yellow crystals; mp 127-128°C. Published data [1]: mp 128-129°C. Found: $M^+$ 181. $C_{12}H_7NO$. Calculated: Mol.wt. 181.

B. To a solution of 0.15 g (1 mmole) of azafluorene (III) in 35 ml of acetone at 40°C, while stirring, we added 0.25 g (1.5 mmole) of potassium permanganate over 5 h. The manganese dioxide was filtered off and washed with acetone. The residue (0.14 g) after distillation of the acetone was purified on a column of aluminum oxide and crystallized from hexane. We obtained 0.07 g (43%) of the 1-azafluorenone (V).

## LITERATURE CITED


1. C.Mayor and C. Wentrup, J. Am. Chem. Soc., 97, 7467 (1975).
2. N. S. Prostakov, K. D. Mat'yu, and V. A. Kurichev, Khim. Geterotsikl. Soedin., No. 5, 876 (1967).

3. N. S. Prostakov, V. O. Fedorov, and A. T. Soldatenkov, Khim. Geterotsikl. Soedin., No. 8, 1098 (1979).
4. N. S. Prostakov, G. A. Vasil'ev, V. P. Zvolinskii, A. V. Varlamov, A. A. Savina, O. I. Sorokin, and N. D. Lopatina, Khim. Geterotsikl. Soedin., No. 1, 112 (1975).
5. T. Ishiguro, J. Morita, and K. Ikhushima, J. Pharm. Soc. Jpn., 78, 220 (1958).
6. G. E. Niznik, U. S. Patent No. 3875237 (1975); Ref. Zh. Khim., No. 3, 3N150P (1976).

# EQUILIBRIUM NH ACIDITY OF NITROGEN HETEROCYCLES

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The equilibrium acidity of the NH bonds of compounds is of theoretical and practical significance but has been investigated little [1]. Nitrogen heterocycles have been investigated little in this respect, and the $pK_a$ values in water have only been obtained for a few of them [2, 3]. However, these values do not always correctly characterize the true acidity of the compounds (i.e., the acidity due to the internal structure) on account of the superimposition of the effects of specific solvation of the acids and the conjugate bases. A more reliable idea of the true acidity is given by the pK values determined in an aprotic polar solvent (DMSO). Scales of pK values as applied to many CH and OH acids with various structures in DMSO have already been established [4-8]. However, measurements of NH acidity in this solvent have been limited mainly to derivatives of aniline containing an electronegative group [COOR, C(O)R, etc.] at the nitrogen atom [9-11]. We therefore considered it expedient to determine the pK values in DMSO for a series of nitrogen heterocycles and some of their derivatives belonging to the NH-acid type, in which considerable variation in acidity can be achieved without the addition of acidifying groups at the nitrogen atom.

The equilibrium NH acidity of the heterocycles was studied by a transmetallation method [4], based on the spectrophotometric determination of the equilibrium constants ($K_{eq}$) for the reactions of the NH acids with potassium-substituted CH acids (indicators), the pK values of which are known. The investigated compounds, the employed CH indicators, the $K_{eq}$ values, and the pK values referred to 9-phenylfluorene as standard CH acid (pK 18.5) are given in Table 1.

From comparison of the obtained data with published $pK_a$ values (Table 2) it is seen that the equilibrium NH acidity of the heterocycles is higher in water than in DMSO. (This conclusion still holds if our results are referred to Bordwell's absolute scale [5], i.e., if the $pK_{DMSO}$ values are reduced by 0.6-1.2 logarithmic units). The increase in acidity differs and is more significant for pyrrole, pyrazole, and imidazole than for the corresponding benzo derivatives (cf. $\Delta pK_1$ in Table 2). This results in a tendency for the strength of the NH acids to level out in water compared with DMSO and, in some cases, even a reversal in the order of acidity (e.g., see carbazole and pyrazole).

The most likely reason for the differences in the $pK_a$ and $pK_{DMSO}$ values is stabilization of the N-anions in water on account of the formation of hydrogen bonds with the solvent. The degree of this specific solvation and its stabilizing effect must in all probability weaken with decrease in the true protophilicity of the N-anion, and for this reason replacement of the solvent has a more significant effect on the acidity of monocyclic NH acids than on the acidity of their benzo derivatives (cf. also indole and carbazole).

Other effects can make a specific contribution to the differentiation between the strength of the investigated NH acids. Thus, the formation of H bonds between the heterocycle and the solvent can lead to a decrease in the strength of the NH acids in DMSO, which is more protophilic than water [5]. The lower polarity of DMSO has a similar effect. On the

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