Electrophilic Benzylation of 2-Aminopyridine Ring

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In the reaction of 2-aminopyridine and its 3- or 5-methyl derivatives with benzyl chloride used in a molar ratio of 1:2, benzylation of 2-aminopyridine ring has been stated that 2-amino-3- or 5-benzylpyridines **c** as the major products were obtained. Formation of **c** type compounds took place in the decomposition of 2-benzylamino-3- or 5-benzylpyridines **b** obtained in the reaction of the 2-benzylaminopyridines **a**, excess benzyl chloride was used. Production of the **b** and **c** compounds, where the benzyl substituent occupied position 3 or 5 in 2-aminopyridine supported the electrophilic mechanism of the reaction (radical reaction was excluded). In the case of 2-aminopyridine and its 3-methyl derivative bis-(2-amino-5-pyridyl)phenylmethanes **d** were formed as the by-products.

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Electrophilic alkylation of azaaromatic compounds are very scarce [1]. An interesting example in the pyridine series is the thermal reaction of triphenylchloromethane with pyridone-2 yielding 5-triphenylmethylpyridone-2 [2]. During studies carried out in our laboratory the selectively electrophilic benzylation and pyridylmethylation of the 2,6-diaminopyridine ring at the 3 and the 3,5 positions was found to occur during rearrangement reaction of *N*-mono and *N,N'*-disubstituted 2,6-diaminopyridines. The rearrangement was controlled either thermally [3] or by Lewis acid {*e.g.* hydrogen chloride (Hofmann-Martius reaction [4] or aluminum chloride (Reilly-Hickinbottom [5])}.

In contrast to *N*-benzyl and *N*-picolyl-2,6-diaminopyridines, 2-benzyl and 2-(2-picolyl)aminopyridine did not rearrange. Thermal reactions of 2-benzylaminopyridine hydrochloride and 2-(2-picolyl)aminopyridine hydrochloride led only to 2-aminopyridine and unidentifiable tarry products [4].

This paper presents the results of the reaction of 2-aminopyridine (**1**), 2-amino-3-methylpyridine (**2**), and 2-amino-5-methylpyridine (**3**) with benzyl chloride (**4**), where benzylation of the 2-aminopyridine ring takes place. The yield of the reactions were mentioned at an IUPAC Conference in Moscow [6] and in the Letter to the Editor [7].

The reaction of **1**, **2** or **3** with **4** used in a molar ratio of 1:2, respectively, was carried out at 250° ±5°, that is generally illustrated in Scheme 1. The quantitative and qualitative compositions of the reaction mixtures depended on the heating time (see Table 1).

Table 1

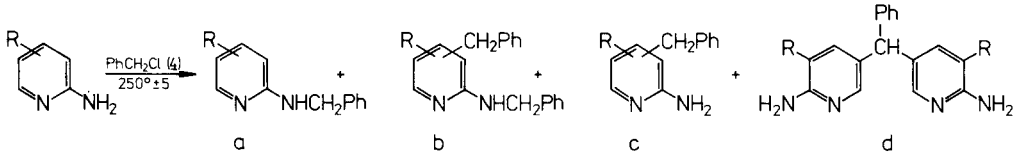
Reaction of 2-Aminopyridines **1-3** (0.05 mole) with Benzyl Chloride (**4**) used in a Molar Ratio of 1:2. Carried out at 250° ±5°

Reaction No	2-Aminopyridines	Reaction time, hours	Products yield, g (%) [a]
I	2-Aminopyridine (**1**)	0.5	**1a**, 1.8 (20)
			1b, 5.6 (41)
II	2-Aminopyridine (**1**)	3.0	**1b**, 2.6 (19)
			1c, 4.4 (48)
			1d, 0.3 (2.2)
III	2-Amino-3-methylpyridine (**2**)	1.0	**2b**, 6.8 (47)
			2c, 1.9 (19)
			2d, 0.8 (5.3)
IV	2-Amino-3-methylpyridine (**2**)	3.0	**2b**, 3.0 (21)
			2c, 4.2 (42)
			2d, 1.1 (7.2)
V	2-Amino-3-methylpyridine (**3**)	3.0	**3a**, 2.4 (24)
			3b, 4.1 (28)
			3c, 2.5 (25)

[a] The yields of the products are related to the aminopyridine used.

When the reaction mixture of **1** and **4** was heated for 0.5 hour the reaction products consisted of **1a** and **1b**. After 3 hours heating, **1a** was not isolated from the reaction mixture; **1b**, **1c** and **1d** were the only products. The longer the heating time the larger quantities of **c** were generated with simultaneously decreasing amounts of **a** and **b**.

Scheme 1



1 ; R=H	1a ; R=H	1b and 1c ; R=H, 5-CH_2Ph
2 ; R=3-CH_3	–	2b and 2c ; R=3-CH_3, 5-CH_2Ph
3 ; R=5-CH_3	3a ; R=5-CH_3	3b and 3c ; R=5-CH_3, 3-CH_2Ph

1d ; R=H	
2d ; R=CH_3	
–	

In the compounds of structures **b** and **c** the benzyl substituent occupied position 3 or 5 in 2-aminopyridines **1-3** susceptible to the electrophilic substitution, that indicated that benzylation of the 2-aminopyridine ring occurred according to an electrophilic mechanism. In order to prove that the reaction does not have a radical sequence it was performed in the presence of a catalytic amount of benzoyl peroxide and hydroquinone. These radical reaction accelerating and inhibiting compounds did not influence the rate and the yield of the reaction. The reaction of 2-benzylaminopyridine (**1a**) with a benzyl radical generated from the oxidation of the phenylacetic acid [8] was also examined, but in this case only bibenzyl and the starting material were isolated. It should be noticed, that in the products of the reactions of **1**, **2** or **3** with **4**, bibenzyl was not detected, which was additional evidence of the non radical character of the reaction.

The experimental results indicate that in the first step of the reaction 2-benzylaminopyridines **a** were formed. The absence of 2-benzylamino-3-methylpyridine in the reaction mixture of **2** with **4** should not be surprising. Comparable yields of the compounds **2b** and **2c** (reaction of **2** with **4**) and **1b** and **1c** (reaction of **1** with **4**) after 3 hours heating (Table 1) suggest that in this case the reaction should occur in the same manner. The formation of the **b** structure compounds took place in the second step as a result of the reaction of **a** with used in excess benzyl chloride (**4**). In the third step of the reaction the decomposition of the aminomethylene bond in the **b** structure compounds led to **c** formation.

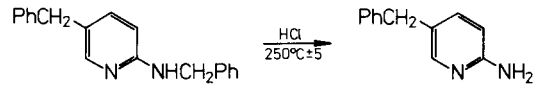
In order to prove the formation of the **b** structure compounds in the reaction of **a** with **4**, **1a** with **4** was subjected to heating. In the previously used conditions, *i.e.*, heating at 250° ±5°, when **1a** with **4** used in molar ratio 1:1, **1b** was produced in 39% yield along with the small amounts of **1c**, while in the reaction of **1a** hydrochloride with **4** (molar ratio 1:1), **1b**, **1c**, **1d** and 2-aminopyridine (**1**) were obtained.

The above presented experimental results indicate the important influence of hydrochloride on the yield and the ratio of the compounds obtained. In more polar medium, at the same time and using heating conditions, the total reaction yield increased. The total yield of **b** and **c** structure compounds in the products of reaction **1a** hydrochloride with **4** increased to 56% in comparison with the reaction **1a** with **4**, prove conclusively, that in this case the production of the benzyl cation should increased too. This assumption is clear, because the highly polar reaction medium allows for benzyl cation formation.

The benzyl cation can be formed in the heterolytic decomposition of the benzyl chloride or the aminomethylene bond in the **a** and **b** compounds. Quantum chemical calculations, using MNDO methods, carried out for benzyl chloride pointed out the charge of 0.18 e on the methylene carbon and -0.22 e on the chloride atom, while for 2-benzylaminopyridine (**1a**) 0.21 e on methylene carbon and -0.31 e on the amino nitrogen atom. This data indicated that the benzyl cation formation should be easier as a result of the aminomethylene bond decomposition in **a** or **b** compounds than from benzyl chloride.

The decomposition of the aminomethylene bond in the **a** compounds as well as in the literature data [4] accounted for the presence of 2-aminopyridine (**1**) in the reaction products of **1a** hydrochloride with **4**. The same decomposition in the **b** compounds resulted in **c** structure compounds, which was proved by the thermal reaction of the **1b** hydrochloride, producing **1c** in good yield (Scheme 2).

Scheme 2



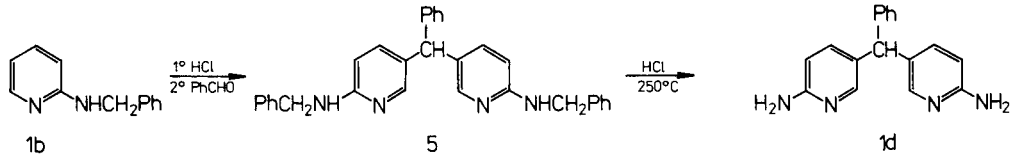
1b 1c

The data obtained confirm that in the reaction of 2-aminopyridines **1**, **2** or **3** with benzyl chloride (**4**), used in molar ratio 1:2, respectively, electrophilic benzylation of the 2-aminopyridine ring takes place, which is supported by the following facts: i) formation of the products **b** and **c**, where the benzyl substituent occupied position 3 or 5 in 2-aminopyridines **1-3** susceptible to electrophilic substitution, ii) absence the bibenzyl in the reaction mixture, iii) absence of the benzoyl peroxide and hydroquinone influence of the reaction rate and yield, iv) absence of the benzylation products in the reaction **1a** with benzyl radical.

In the reaction of **1**, **2** or **1a** hydrochloride with **4** the **d** structure compounds were formed as the by-products. Here it should be noted, that all the reactions were carried out in an open flask. Under these conditions partial oxidation of benzyl chloride into benzaldehyde might have occurred. To confirm the fact that benzaldehyde effects the formation of compounds **d**, the reaction of benzaldehyde and **1a** hydrochloride was carried out as well. As a result of this process bis-(2-benzylamino-5-pyridyl)phenylmethane (**5**) was obtained. Heating of **5** hydrochloride leads to decomposition of **5** to bis-(2-amino-5-pyridyl)phenylmethane (**1d**) (Scheme 3).

In the reaction of **3** with **4** bis-(2-amino-5-methyl-3-pyridyl)phenylmethane was not obtained. It my be due to the fact, that in this case the amino groups in the 2,2'-positions reacted together into triazaantracene derivatives. This assumption was proved by the magnificent fluorescence of the aqueous reaction solution, the same as was observed in triazaanthracene syntheses [9]. However I did not isolate such derivatives from the reaction mixture.

Scheme 3



The structures of all the compounds obtained were determined on the basis of elemental analyses and of pmr and mass spectra.

For example: the structural differences of **a** and **c**, despite their indentical quantitative and qualitative compositions, and identical molecular ions are visible in fragmentations observed in mass spectra. In the spectra of **a** an intensive peak at m/e 106 is observed, which indicates the presence of the benzylamino grouping in the molecule [3,10]. Lack of m/e 106 ion in the mass spectrum of **c** excludes the presence of the benzylamino grouping in its molecule and proves the assumed structure for **c**.

In the pmr spectra of **a** compounds a doublet at δ 4.40-4.44 ppm corresponding to the couplet methylene protons of the aminomethylene group (-NH-CH_2-) is present. In the **c** compounds a singlet signal at δ 3.75-3.79 ppm was attributed to the protons of an isolated methylene group. The signals, however, corresponding to β protons of the 2-aminopyridines **1-3** (in the case of **1** proton at 5 position) were not observed.

EXPERIMENTAL

Elemental analyses were performed on a Perkin-Elmer 240 analyzer, mass spectra were recorded on LKB 9000S spectrometer at 70 eV. Melting points, measured on a Boetius apparatus, are uncorrected. Pmr spectra were recorded in deuteriochloroform with a Tesla 487C spectrometer, TMS being using as the internal standard; the chemical shifts are expressed in δ values downfield from TMS. The reactions were monitored by means of tlc.

General Procedure for the Reaction of 2-Aminopyridines **1-3** with Benzyl Chloride (**4**).

Into a round-bottom flask fitted with an air refluxing condenser and a thermometer 0.05 mole of 2-aminopyridine (4.7 g of **1** and 5.4 of **2** or **3**) and 0.10 mole (12.7 g) of freshly distilled benzyl chloride (**4**) was added. The flask was placed on an air bath and the temperature of the reaction mixture increased to 180° until the mixture began to boil. Next, the temperature was gradually raised during 3 hours to 250°C $\pm$5° and the reaction mixture was allowed to stand at that temperature for additional period of time (Table 1). After cooling, the reaction mixture was washed out from the flask with 20 ml of methanol and treated with 10% aqueous ammonium hydroxide to *p*H 9. After addition of 100 ml of water, the resulting oil was extracted with chloroform. The organic layer was dried over anhydrous sodium sulfate, and them the solvent was distilled off. The residue was separated by distillation under reduced pressure, using distillation column 5 cm length.

I. After 0.5 hours the reaction of **1** with **4**, **1a** and **1b** were obtained in 20 and 41% yield, respectively (Table 1).

2-Benzylaminopyridine (**1a**).

This compound was collected at 135-145°/1 mm Hg. After crystallization from isopropyl alcohol colorless needles were obtain, mp 95-96°, lit [11] mp 96-97°; pmr: δ 4.44 (d, 2H, CH_2, J = 6 Hz), 5.32 (br, 1H, NH), 6.28 (d, 1H, 3-H, J = 8 Hz), 6.52, 6.44 (2d, each, 1H, 5-H, J = 8 Hz), 7.12-7.42 (m, 6H, 5 phenyl protons and 4-H), 8.00 ppm (d, 1H, 6-H, J = 4 Hz); ms: m/e (I%); M, 184 (96), M-H, 183 (44), 106 (100), 91 (67).

Anal. Calcd. for $C_{12}H_{12}N_2$ (184.24): C, 78.22; H, 6.57; N, 15.21. Found: C, 78.34; H, 6.66; N, 15.01.

2-Benzylamino-5-benzylpyridine (**1b**).

This compound was collected at 230-235°/1 mm Hg. After crystallization from 1-butanol colorless prisms were obtained, mp 103-104.5°; pmr: δ 3.74 (s, 2H, $PyCH_2Ph$), 4.40 (d, 2H, CH_2NH, J = 6 Hz), 5.04 (br, 1H, NH), 6.21 (d, 1H, 3-H, J = 8 Hz), 7.06-7.30 (m, 11H, 10 phenyl protons and 4-H), 7.88 ppm (s, 1H, 6-H); ms: m/e (I%), M, 274 (100), M-H, 273 (38), M-Ph, 197 (14), 106 (90), 91 (68), 77 (5).

Anal. Calcd. for $C_{19}H_{18}N_2$ (274.35): C, 83.18; H, 6.61; N, 10.21. Found: C, 83.25; H, 6.55; N, 10.38.

II. After 3 hours reaction of **1** with **4**, **1b**, **1c** and **1d** were obtained in 19, 48 and 2.2% yield, respectively (Table 1).

2-Benzylamino-5-benzylpyridine (**1b**) had identical mp, mass and pmr spectra with those obtained in earlier reaction.

2-Amino-5-benzylpyridine (**1c**).

This compound was collected at 130-135°/1 mm Hg. After crystallization from 1-butanol colorless plates were obtained, mp 78-80°; pmr: δ 3.79 (s, 2H, CH_2), 4.49 (br s, 2H, NH_2), 6.35 (d, 1H, 3-H, J = 8 Hz), 7.09-7.25 (m, 6H, 5 phenyl protons and 4-H), 7.94 ppm (s, 1H, 6-H); ms: m/e (I%); M, 184 (100), M-H, 183 (67), M-Ph, 107 (43), 91 (10), 77 (7).

Anal. Calcd. for $C_{12}H_{12}N_2$ (184.24): C, 78.22; H, 6.57; N, 15.21. Found: C, 78.28; H, 6.62; N, 15.18.

Bis-(2-amino-5-pyridyl)phenylmethane (**1d**).

This compound was collected at 290-300°/1 mm Hg. After crystallization from isopropyl alcohol light-yellow needles were obtained, mp 164-166°; pmr: δ 4.48 (br s, 4H, NH_2), 5.24 (s, 1H, CH), 6.35 (d, 2H, 3-H, J = 8 Hz), 7.06-7.30 (m, 7H, 5 phenyl protons and 4-H) 7.81 ppm (s, 2H, 6-H); ms: m/e (I%), M, 276 (100), M-H, 275 (26), M-Ph, 199 (77), 183 (33).

Anal. Calcd. for $C_{17}H_{16}N_4$ (276.33): C, 73.88; H, 5.84; N, 20.28. Found: C, 73.75; H, 5.67; N, 20.10.

III. After 1 hour reaction of **2** with **4**, **2b**, **2c** and **2d** were obtained in 47, 19 and 5.3% yield, respectively (Table 1).

2-Benzylamino-3-methyl-5-benzylpyridine (**2b**).

This compound was collected at 220-225°/1 mm Hg. The oil was purified in a silica gel column (2 x 40 cm), using ethyl acetate as eluent; pmr: δ 1.98 (s, 3H, CH_3), 3.78 (s, 2H, $PyCH_2Ph$), 4.26 (br, 1H, NH), 4.65 (d, 2H, CH_2NH, J = 6 Hz), 7.00 (s, 1H, 4-H), 7.12-7.32 (m, 10H, phenyl protons), 7.91 ppm (s, 1H, 6-H); ms: m/e (I%), M, 288 (100), M-H, 287 (32), M-Ph, 211 (11), 106 (76), 91 (73), 77 (8).

Anal. Calcd. for $C_{20}H_{20}H_2$ (288.38): C, 83.29; H, 6.99; N, 9.72. Found: C, 83.33; H, 7.20; N, 9.61.

2-Amino-3-methyl-5-benzylpyridine (**2c**).

This compound was collected at 160-165°/1 mm Hg. After crystallization from benzene:hexane 1:1, colorless plates were obtained, mp 100-102.5°; pmr: δ 2.00 (s, 3H, CH_3), 3.76 (s, 2H, CH_2), 4.49 (br s, 2H, NH_2), 7.00 (s, 1H, 4-H), 7.19-7.25 (m, 5H, phenyl protons), 7.81 ppm (s, 1H, 6-H); ms: m/e (I%), M, 198 (100), M-H, 197 (42), M-Ph, 121 (32), 91 (11), 77 (6).

Anal. Calcd. for $C_{13}H_{14}N_2$ (198.26): C, 78.75; H, 7.12; N, 14.13. Found: C, 78.48; H, 6.92; N, 14.15.

Bis-(2-amino-3-methyl-5-pyridyl)phenylmethane (**2d**).

This compound was collected at 290-300°/1 mm Hg. After crystallization from isopropyl alcohol:hexane 2:1, light-yellow prisms were obtained, mp 237-241°; pmr: δ 2.06 (s, 6H, CH_3), 4.34 (br s, 4H, NH_2), 5.24 (s, 1H, CH), 7.01 (s, 2H, 4-H), 7.14-7.32 (m, 5H, phenyl protons), 7.73 ppm (s, 2H, 6-H); ms: m/e (I%), M, 304 (100), M-H, 303 (26), M-Ph, 227 (84), 197 (40).

Anal. Calcd. for $C_{19}H_{20}N_4$ (304.38): C, 74.97; H, 6.62; N, 18.41. Found C, 74.75; H, 6.89; N, 18.25.

IV. After 3 hours reaction of **2** with **4**, **2b**, **2c** and **2d** were obtained in 21, 42 and 7.2% yield, respectively (Table 1).

2-Benzylamino-3-methyl-5-benzylpyridine (**2b**), 2-amino-3-methyl-5-benzylpyridine (**2c**) and bis-(2-amino-3-methyl-5-pyridyl)phenylmethane (**2d**) had identical mp, mass and pmr spectra with those of the same compounds obtained in earlier reaction.

V. After 3 hours reaction of **3** with **4**, **3a**, **3b** and **3c** were obtained in 24, 28 and 25% yield, respectively (Table 1).

2-Benzylamino-5-methylpyridine (**3a**).

This compound was collected at 155-160°/1 mm Hg. After crystallization from isopropyl alcohol colorless prisms were obtained, mp 110-112°; pmr: δ 2.10 (s, 3H, CH_3), 4.40 (d, 2H, CH_2, J = 6 Hz), 5.21 (br, 1H, NH), 6.21 (d, 1H, 3-H, J = 8 Hz), 7.08-7.35 (m, 6H, 5 phenyl protons and 4-H), 7.80 ppm (s, 1H, 6-H); ms: m/e (I%), M, 198 (100), M-H, 197 (30), 106 (92), 91 (56).

Anal. Calcd. for $C_{13}H_{14}N_2$ (198.26): C, 78.75; H, 7.12; N, 14.13. Found: C, 78.82; H, 7.10; N, 14.05.

2-Benzylamino-3-benzyl-5-methylpyridine (**3b**).

This compounds was collected at 235-240°/1 mm Hg. The oil was purified in a silica gel column (2 x 40 cm), using ethyl acetate as eluent; pmr: δ 2.14 (s, 3H, CH_3), 3.71 (s, 2H, $PyCH_2Ph$), 4.22 (br, 1H, NH), 4.54 (d, 2H, CH_2NH, J = 6 Hz), 7.00-7.25 (m, 11H, 10 phenyl protons and 4-H), 7.89 ppm (s, 1H, 6-H); ms: m/e (I%), M, 288 (100), M-H, 287 (31), M-Ph, 211 (12), 106 (69), 91 (75), 77 (7).

Anal. Calcd. for $C_{20}H_{20}N_2$ (288.38): C, 83.29; H, 6.99; N, 9.72. Found: C, 83.53; H, 7.20; N, 9.53.

2-Amino-3-benzyl-5-methylpyridine (**3c**).

This compound was collected at 145-155°/1 mm Hg. After crystallization from isopropyl alcohol:hexane 1:1, colorless plates were obtained, mp 145-146°; pmr: δ 2.02 (s, 3H, CH_3), 3.75 (s, 2H, CH_2), 4.19 (br s, 2H, NH_2), 7.04 (s, 1H, 4-H), 7.10-7.30 (m, 5H, phenyl protons), 7.76 ppm (s, 1H, 6-H); ms: m/e (I%), M, 198 (100), M-H, 197 (38), M-Ph, 121 (27), 91 (12), 77 (7).

Anal. Calcd. for $C_{13}H_{14}N_2$ (198.26): C, 78.75; H, 7.12; N, 14.13. Found: C, 78.75; H, 7.32; N, 13.90.

Investigation of the Influence of Hydroquinone on the Reaction of 2-Aminopyridine (**1**) with Benzyl Chloride (**4**).

To the reaction mixture containing 4.7 g (0.05 mole) of 2-aminopyridine (**1**) and 12.7 g (0.10 mole) of benzyl chloride (**4**), 1.6 g (0.015 mole) of hydroquinone was added and then the reaction was carried out according to the general procedure for the reaction of 2-aminopyridines **1-3** with benzyl chloride (**4**). After 3 hours heating at 250° ±5° 2-benzylamino-5-benzylpyridine (**1b**), 2-amino-5-benzylpyridine (**1c**) and bis-(2-amino-5-pyridyl)phenylmethane (**1d**) were obtained in 18, 40 and 2% yield, respectively. The compounds obtained were in all respects identical with those of the same prepared earlier.

Investigation of the Influence of Benzoyl Peroxide on the Reaction of 2-Aminopyridine (**1**) with Benzyl Chloride (**4**).

The amount of reagents and the conditions used were identical with those employed in the reaction effected in the presence of hydroquinone, but instead of the latter, benzyl peroxide (3.6 g, 0.015 mole) was added to the mixture. The products **1b**, **1c** and **1d** obtained in 20, 45 and 2% yield, respectively, were in all respects identical with those of the same prepared earlier.

Examination of the Ability of the Benzyl Radical to React with 2-Benzylaminopyridine (**1a**).

Into a flask containing a bar magnet was introduced 3.7 g (0.02 mole) of 2-benzylaminopyridine (**1a**), 2.72 g, (0.02 mole) of phenylacetic acid and 5.3 ml of concentrated sulfuric acid in 15 ml of water. The mixture was vigorously stirred and heated up to 90°, then a solution of 4.7 g (0.02 mole) of sodium peroxydisulphate in 10 ml of water was added dropwise during 30 minutes. Stirring and heating was continued for an additional 1 hour, cooled, made alkaline with sodium hydroxide solution and extracted with chloroform. The residue from evaporation of the solvent was separated by distillation under reduced pressure. From the reaction, 0.7 g of bibenzyl and 3.3 g of **1a** were obtained. Bibenzyl was collected at 100-105°/1 mm Hg (lit [12] bp 140-150°/13 mm Hg) and after crystallization from ethanol colorless needles were obtained, mp 51-52° (lit [12] mp 52°, on the basis of pmr spectra, the substance corresponded in all respects with the compound described in ref [13].

Reaction of 2-Benzylaminopyridine (**1a**) with Benzyl Chloride (**4**).

A mixture 2.8 g (0.015 mole) of 2-benzylaminopyridine (**1a**) and 1.9 g (0.015 mole) of benzyl chloride (**4**) was subjected to heating. The heating mixture began to boil at 210°. Then, the temperature was gradually raised during 3 hours to 250° ±5° and the mixture was kept at these temperature for another 3 hours. After cooling the reaction mixture was worked-up in the manner described in general procedure for reaction of **1-3** with **4**. In this process 1.6 g (39% yield) of 2-benzylamino-5-benzylpyridine (**1b**), 0.1

g (3.6% yield) of 2-amino-5-benzylpyridine (**1c**) and 0.8 g of starting substance **1a** were obtained. All the compounds obtained were in all respects identical with those prepared earlier.

Reaction of 2-Benzylaminopyridine (**1a**) Hydrochloride with Benzyl Chloride (**4**).

A sample of 9.2 g (0.05 mole) of 2-benzylaminopyridine (**1a**) was placed in a distilling flask and then 4.4 ml of concentrated hydrochloric acid was added. Therefore the formation of hydrochloride is possible. The flask was placed on an air bath, and in order to distill off water the temperature was gradually raised to 160°. Next, 6.3 g (0.05 mole) of benzyl chloride (**4**) was added. The mixture began to boil at 180°. During 3 hours heating the temperature gradually increased to 250° ±5°. After 3 hours heating at 250° ±5°, the reaction mixture was worked-up in the manner described in the general procedure for the reaction of **1-3** with **4**. From the reaction, 3.5 g (26% yield) of 2-benzylamino-5-benzylpyridine (**1b**), 2.8 g (30% yield) of 2-amino-5-benzylpyridine (**1c**), 0.8 g (5.8% yield) of bis-(2-amino-5-pyridyl)-phenylmethane (**1d**), and 0.2 g (4.3% yield) of 2-aminopyridine (**1**) were obtained. All of the compounds obtained had the identical mp, mass and pmr spectra with those obtained earlier.

Decomposition of 2-Benzylamino-5-benzylpyridine (**1b**) Hydrochloride.

A sample of 2.7 g (0.01 mole) of 2-benzylamino-5-benzylpyridine (**1b**) was placed in a distilling flask and then 0.9 ml of concentrated hydrochloric acid was added. Therefore the formation of the hydrochloride is possible. The flask was placed on an air bath, and in order to distill water the temperature was raised to 250°. The reaction mixture was heated at 250° ±5° for 2 hours, cooled and next was worked-up in the manner described in the general procedure for the reaction of **1-3** with **4**. From the reaction, 0.8 g (44% yield) of 2-amino-5-benzylpyridine (**1c**) (collected at 130-140°/1 mm Hg, mp 78-80° from 1-butanol) was obtained in all respects identical with those prepared earlier.

Bis-(2-benzylamino-5-pyridyl)phenylmethane (**5**).

2-Benzylaminopyridine (**1a**) (4.6 g, 0.025 mole) was placed in a distilling flask and an ethanol solution of hydrochloric acid to *p*H 3 was added. Ethanol was evaporated under reduced pressure at temperature below 100°. Next, 2.1 g (0.020 mole) of benzaldehyde was added, and during heating at 180-200° water and partially benzaldehyde were distilled off. The reaction mixture was heated at 200° for 1 hour, cooled, dissolved in 20 ml of methanol and treated with a 5% solution of sodium hydroxide to *p*H 9. After addition of water, the resulting oil was extracted with toluene. The residue after evaporation of the solvent was crystallized from ethylene chloride-cyclohexane and yielded 2.3 g (40% yield) of bis-(2-benzylamino-5-pyridyl)-phenylmethane (**5**) as light-yellow needles, mp 184-186°; pmr: δ 4.46 (d, 4H, CH_2, J = 6 Hz), 4.81 (br, 2H, NH), 5.52 (s, 1H, CH), 6.29 (d, 2H, 3-H, J = 8 Hz), 7.09-7.30 (m, 17H, 15 phenyl protons and 4-H), 7.85 ppm (s, 2H, 6-H); ms: m/e (I%), M, 456 (54), M-H, 455 (12), M-Ph, 379 (15), 106 (23), 91 (100).

Anal. Calcd. for $C_{31}H_{28}N_4$ (456.56): C, 81.55; H, 6.18; N, 12.27. Found: C, 81.31; H, 6.24; N, 12.48.

Bis-(2-amino-5-pyridyl)phenylmethane (**1d**).

Bis-(2-benzylamino-5-pyridyl)phenylmethane (**5**) (1.4 g 0.003 mole) was placed in a distilling flask and an ethanol solution of hydrochloric acid was added until *p*H 3 was reached. After evaporation of the ethanol the reaction mixture was heated at 250° ±5° during 1 hour, cooled, dissolved in 10 ml of methanol and alkalized with 5% sodium hydroxide solution to *p*H 9. After addition of 50 ml of water, the resulting oil was extracted with chloroform. The residue after evaporation of the solvent was separated by distillation under reduced pressure and the fraction of bp 290-300°/1 mm Hg was collected. Crystallization from isopropyl alcohol gave light-yellow needles, 0.3 g (33% yield) of bis-(2-amino-5-pyridyl)phenylmethane (**1d**), mp 164-166°, on the basis of pmr and mass spectra, the substance corresponded in all respects with those prepared earlier.

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