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Dedicated to Full Member of the Russian Academy of Sciences N.S. Zefirov on His 70th Anniversary

Cyanopyridines. Synthesis and Recyclization of Their Quaternary Salts

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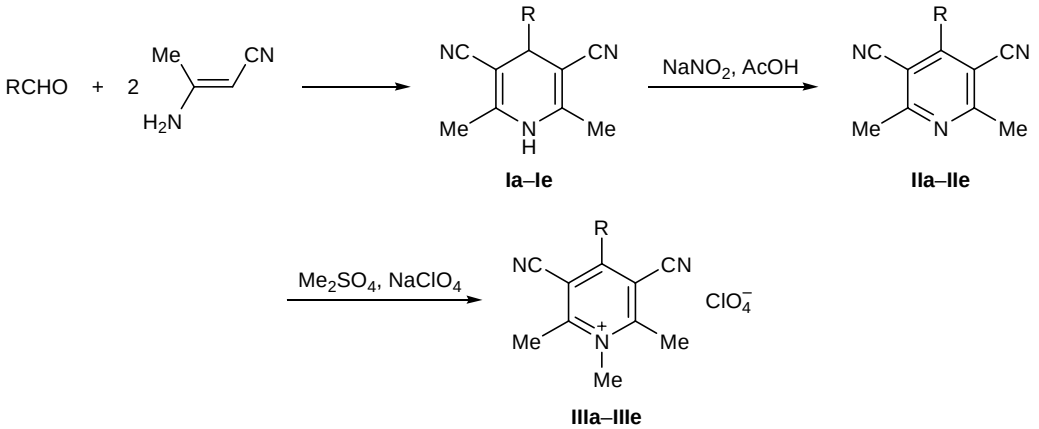
Abstract—3-Cyanopyridines containing an acetyl, ester, nitro, or cyano group in the 5-position were synthesized via various versions of the Hantzsch reaction. Recyclization of quaternary pyridinium salts by the action of aqueous–alcoholic alkali afforded 2-methylaminopyridine derivatives and 6-methylamino-3-nitro-2,4-diphenylbenzonitrile.

In continuation of our studies on recyclization of pyridinium salts having a cyano group in position *3* [1–3] we synthesized previously unknown cyanopyridines **IIa**–**IIg** with a view to examine the effect of structural and electronic factors on the direction of recyclization of quaternary salts derived therefrom. Symmetrically substituted 3,5-dicyanopyridines **IIa**–**IIe** were obtained by cyclocondensation of 3-amino-2-butenenitrile with various aldehydes (Hantzsch–Meyer–Mohr reaction), by analogy with the synthesis of 3,5-dicyanopyridines reported previously [4–6]. 1,4-Dihydropyridines **Ia**–**Ie** were oxidized with sodium nitrite in acetic acid. Both stages in the synthesis of pyridines **IIa**–**IIe** (Scheme 1) were characterized by fairly high yields.

5-Acetyl-6-methyl-2-phenylpyridine-3-carbonitrile (**IIf**) was prepared by three-component condensation of benzoylacetonitrile, triethyl orthoformate, and 4-amino-3-penten-2-one at a ratio of 1:3:1 at 70°C. Under these conditions, addition of the β-carbon atom in the enamine fragment of 4-amino-3-penten-2-one to ethoxymethylene derivative of benzoylacetonitrile gave rise to a new carbon–carbon bond and closure of pyridine ring [7, 8] (Scheme 2). The synthesis of ethyl 5-cyano-2-methyl-4-phenylpyridine-3-carboxylate (**IIg**) included structural modification of previously described ethyl 5-cyano-2-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylate [9] via nucleophilic replacement of the hydroxy group by chlorine and subsequent reductive dechlorination (Scheme 3). Nitro-

Scheme 1.



R = 4-ClC_6H_4 (**a**), 4-$MeOC_6H_4$ (**b**), 2,4-$(MeO)_2C_6H_3$ (**c**), 2-furyl (**d**), Me (**e**).

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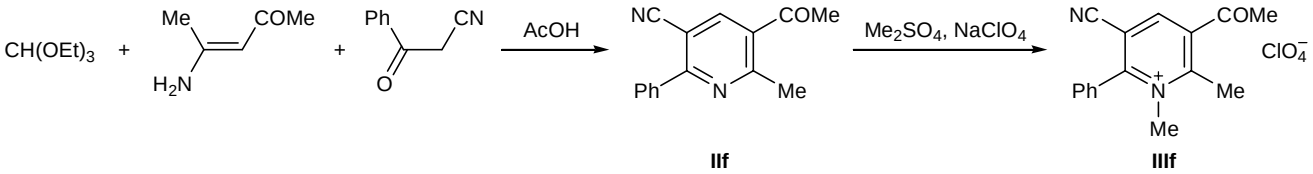
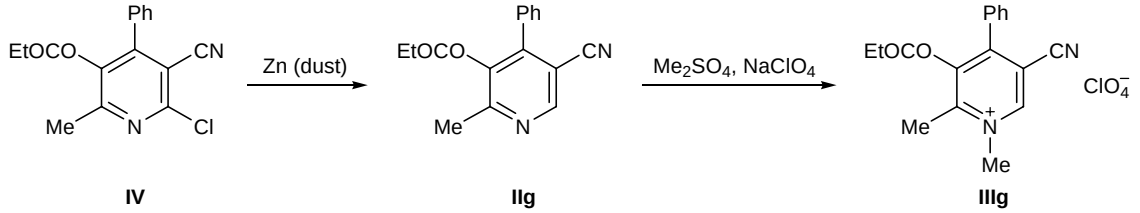
Scheme 2.



Scheme 3.

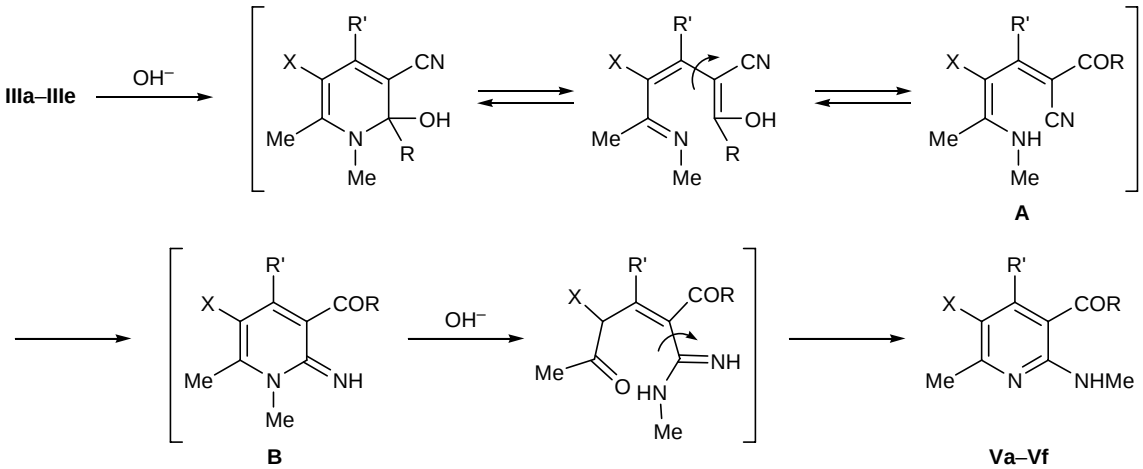


pyridine **IIh** was obtained by us previously [10]. The alkylation of weakly basic pyridines **IIa**–**IIh** was effected with the aid of dimethyl sulfate. Quaternary pyridinium salts were isolated as the corresponding perchlorates which were prepared by anion exchange reaction.

Recyclization of pyridinium salts **IIIa**–**IIIg** by the action of aqueous–alcoholic alkali followed the double rearrangement scheme described in [1] and afforded 6-methylaminopyridine derivatives **Va**–**Vf** as shown in Scheme 4. Attack by hydroxide ion on symmetrically substituted salts **IIIa**–**IIIe** is directed at the α-carbon atom of the pyridine ring to give a pseudobase which may be considered to be a neutral analog of anionic σ-complex. Heterocyclization of open-chain tautomer **A** involves attack by the secondary amino group on the electron-deficient carbon atom of the cyano group, leading to cyclic amidine **B**. Recyclization of the latter follows a Dimroth-type reaction to produce 5-acetyl-6-methylaminopyridines **Va**–**Ve**. Likewise, recyclization of unsymmetrically substituted salt **IIIf** via double rearrangement yields 3-acetyl-5-benzoyl-2-methyl-6-methylaminopyridine (**Vf**). The recyclization direction is determined by the site of addition of hydroxide ion which attacks the most electron-deficient C^6 atom in salt **IIIf**. The recyclization of pyridinium salt **IIIg** having both cyano and ester groups may involve both these (Scheme 5). The major product is methylaminopyridine **Vg** which is formed from open-chain precursor **A**. The regioselectivity of this reaction originates from predominant attack by hydroxide ion on the least sterically shielded C^6 atom in pyridinium salt **IIIg**. Intramolecular acylation by the ester group of the secondary amino group in open-chain structure **B** gives pyridinone **VI**.

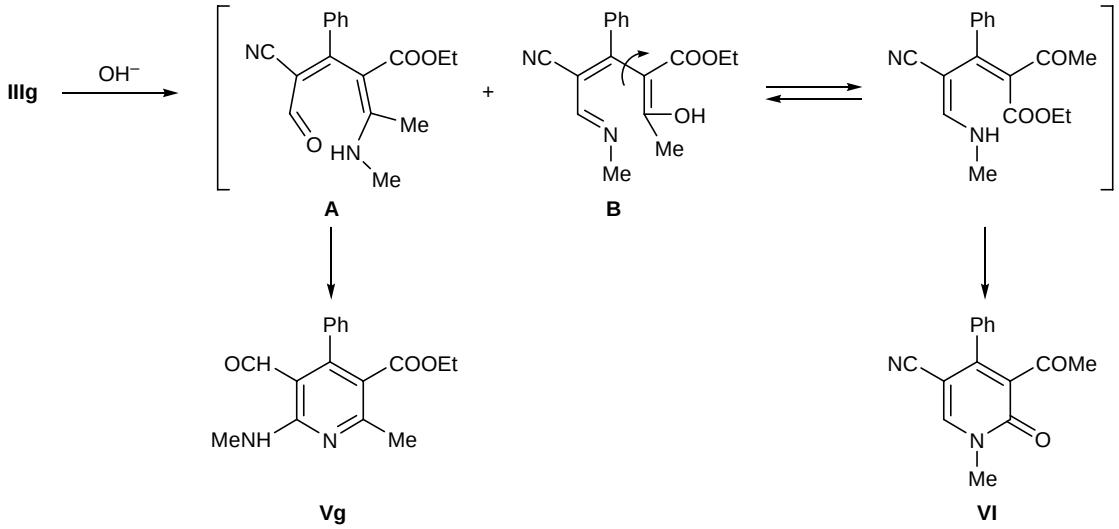
As shown in [3], recyclization of 3-cyano-5-ethoxycarbonyl-1,2,6-trimethyl-4-phenylpyridinium perchlorate under analogous conditions leads to formation

Scheme 4.



R = Me, X = CN, R' = 4-ClC_6H_4 (**a**), 4-$MeOC_6H_4$ (**b**), 2,4-$(MeO)_2C_6H_3$ (**c**), 2-furyl (**d**), Me (**e**); R = Ph, R' = H, X = COMe (**f**).

Scheme 5.



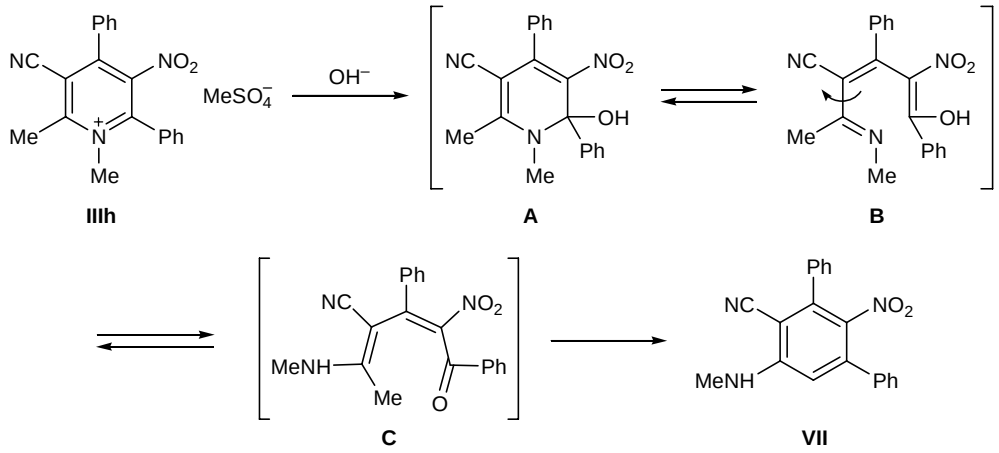
of 5-acetyl-1,2-dimethyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carbonitrile as the only product. From unsymmetrically substituted 5-cyano-3-nitropyridinium salt **IIIh** we obtained substituted terphenyl **VII** (Scheme 6). Here, attack by hydroxide ion is directed at the most π-deficient 2-position of the pyridine ring (at the *ortho* position with respect to the nitro group) to give pseudobase **A**. Closure of benzene ring involves intramolecular aldol-type condensation of the emerging benzoyl group with the methyl group of open-chain intermediate **C**. The recyclization yields difficultly accessible terphenyl derivative **VII** with a high regioselectivity.

Our results led us to draw the following conclusions. Recyclization of 3-cyanopyridinium salts by the action of alkali can occur with participation of the cyano group in the formation of new pyridine ring or without it. When hydroxide ion is covalently bound to the α-carbon atom of the pyridine ring in the *ortho* position with respect to the cyano group, the latter is involved in the recyclization. When hydroxide ion adds at the *para* position with respect to the cyano group, the recyclization occurs without its participation but involves ester moiety to afford the corresponding pyridinone or gives carbocycle provided that a nitro group is present in the pyridine ring.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker AC-200 spectrometer operating at 200 MHz; the chemical shifts were measured relative to tetramethylsilane as internal reference. The IR spectra were obtained from solutions in chloroform on a Specord IR-75 instrument. The mass spectra (electron impact, 70 eV) were run on a Finnigan MAT-8200 mass spec-

Scheme 5.



trometer with direct sample admission into the ion source. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using chloroform or chloroform–ethyl acetate (9:1 or 1:1) as eluent. The melting points were determined on a Boetius apparatus.

Commercial 3-amino-2-butenenitrile (from Fluka) was used. Compounds **Ib**–**IIIb** were synthesized as described in [4], 1,4-dihydropyridine **Ie** was prepared by the procedure reported in [6], and benzoylacetonitrile was obtained according to [11]. The synthesis of cyanopyridine **IIe** was described in [12], and of pyridinium methyl sulfate **IIIh**, in [10].

4-(4-Chlorophenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile (Ia). A solution of 0.82 g (10 mmol) of 3-amino-2-butenenitrile and 0.70 g (5 mmol) of *p*-chlorobenzaldehyde (the aldehyde was added in 3 portions) in 10 ml of glacial acetic acid was heated for 2 h at 100°C. After 12 h, the precipitate was filtered off and washed with cold ethanol. Yield 0.99 g (74%), mp 237–238°C (from ethanol). IR spectrum, ν, cm^{-1}: 2210 (CN), 3450 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.04 s (6H, CH_3), 4.47 s (1H, 4-H), 7.32 d (2H, 3'-H, 5'-H, J = 8.5 Hz), 7.52 d (2H, 2'-H, 6'-H, J = 8.5 Hz), 9.57 s (1H, NH). Found, %: C 66.73; H 4.50. $C_{15}H_{12}ClN_3$. Calculated, %: C 66.79; H 4.48.

4-(2,4-Dimethoxyphenyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile (Ic) was synthesized in a similar way. The product was purified by flash chromatography on a dry column charged with Silicagel L (5/40 μm); gradient elution with hexane, chloroform, and chloroform–ethyl acetate (1:1). Yield 85%, mp 225–227°C (from ethanol). IR spectrum, ν, cm^{-1}: 2205 (CN), 3450 (NH). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.01 s (6H, CH_3), 3.77 s (6H, CH_3O), 4.65 s (1H, 4-H); *ABX*: 6.57 (1H, 5'-H), 6.59 (1H, 3'-H), 7.08 (1H, 6'-H), $J_{5',3'}$ = 2.4, $J_{6',3'}$ = 0, $J_{5',6'}$ = 8.0 Hz; 9.41 s (1H, NH). Found, %: C 69.15; H 5.67. $C_{17}H_{17}N_3O_2$. Calculated, %: C 69.14; H 5.80.

4-(2-Furyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarbonitrile (Id) was synthesized in a similar way. Yield 62%, mp 174–175°C (from ethanol) [5].

4-(4-Chlorophenyl)-2,6-dimethylpyridine-3,5-dicarbonitrile (IIa). Sodium nitrite, 1.04 g (15 mmol), was added in portions to a suspension of 2.70 g (10 mmol) of dihydropyridine **Ia** in 30 ml of glacial acetic acid under stirring at 60–70°C. The mixture was stirred for 1 h at that temperature, diluted with a 4-fold volume of an ice–water mixture, and neutralized with ammonia. The precipitate was filtered off and washed with water. Yield 2.43 g (90%), mp 232–234°C (from ethanol). IR spectrum: ν(CN) 2230 cm^{-1}. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.87 s (6H, CH_3), 7.47 d (2H, 3'-H, 5'-H, J = 8.8 Hz), 7.57 d (2H, 2'-H, 6'-H, J = 8.8 Hz). Found, %: C 67.39; H 3.74. $C_{15}H_{10}ClN_3$. Calculated, %: C 67.30; H 3.77.

4-(2,4-Dimethoxyphenyl)-2,6-dimethylpyridine-3,5-dicarbonitrile (IIc) was synthesized in a similar way. Yield 87%, mp 134–135°C (from ethanol). IR spectrum: ν(CN) 2230 cm^{-1}. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.84 s (6H, CH_3), 3.85 s (3H, CH_3O), 3.88 s (3H, CH_3O); *ABX*: 6.61 (1H, 5'-H), 6.65 (1H, 3'-H), 7.23 (1H, 6'-H), $J_{5',3'}$ = 2.3, $J_{6',3'}$ = 0, $J_{5',6'}$ = 8.8 Hz). Found, %: C 69.40; H 5.31. $C_{17}H_{15}N_3O_2$. Calculated, %: C 69.61; H 5.15.

4-(2-Furyl)-2,6-dimethylpyridine-3,5-dicarbonitrile (IId) was synthesized in a similar way. Yield 85%, mp 143–145°C (from ethanol). IR spectrum: ν(CN) 2235 cm^{-1}. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.85 s (6H, CH_3), 6.70 d.d (1H, 4'-H, $J_{4',3'}$ = 3.8, $J_{4',5'}$ = 1.8 Hz), 7.67 d.d (1H, 3'-H, $J_{3',4'}$ = 3.8, $J_{3',5'}$ = 0.6 Hz), 7.80 d.d (1H, 5'-H, $J_{5',4'}$ = 1.8, $J_{5',3'}$ = 0.6 Hz). Found, %: C 69.99; H 3.94. $C_{13}H_9N_3O$. Calculated, %: C 69.95; H 4.06.

5-Acetyl-6-methyl-2-phenylpyridine-3-carbonitrile (IIf). Triethyl orthoformate, 5 ml (30 mmol), and 4-amino-3-penten-2-one, 0.99 g (10 mmol), were added to a solution of 1.45 g (10 mmol) of benzoylacetonitrile in 5 ml of glacial acetic acid. The mixture was stirred for 4 h at 70°C, cooled, diluted with water, and left overnight. The precipitate was filtered off and washed with water. The product was purified by column chromatography on Silicagel L (100/160 μm) using benzene–ethyl acetate (9:1) as eluent. Yield 1.42 g (60%), mp 132–133°C (from 2-propanol). IR spectrum, ν, cm^{-1}: 2230 (CH), 1690 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.66 s (3H, CH_3), 2.89 s (3H, $COCH_3$), 7.53–7.56 (3H, Ph), 7.95–8.02 m (2H, Ph), 8.35 s (1H, 4-H). Found, %: C 76.39; H 5.12. $C_{15}H_{12}N_2O$. Calculated, %: C 76.25; H 5.12.

Ethyl 6-chloro-5-cyano-2-methyl-4-phenylpyridine-3-carboxylate (IV). Anhydrous dimethylformamide, 0.1 ml, was added to a suspension of 2.70 g (10 mmol) of ethyl 5-cyano-2-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carboxylate [9] in 8 ml of $POCl_3$. The mixture was heated for 2.5 h under reflux, cooled, and poured onto ~30 g of ice under vigorous

stirring. The precipitate was filtered off and washed with water. Yield 2.44 g (84%), mp 107–108°C (from ethanol). IR spectrum, ν, cm^{-1}: 1720 (C=O), 2230 (CN). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 t (3H, CH_2CH_3, J = 7.2 Hz), 2.67 s (3H, CH_3), 4.05 q (2H, CH_2CH_3, J = 7.2 Hz), 7.34–7.39 m (5H, Ph). Found, %: C 63.54; H 4.25. $C_{16}H_{13}ClN_2O_2$. Calculated, %: C 63.90; H 4.36.

Ethyl 5-cyano-2-methyl-4-phenylpyridine-3-carboxylate (IIg). A solution of 1.98 g (6.6 mmol) of chloropyridine **IV** in a mixture of 14 ml of acetic acid, 14 ml of ethanol, and 4 ml of water was heated on a water bath to the boiling point, and 2.10 g (26.4 mmol) of zinc dust was added in portions over a period of 1 h. The mixture was cooled and filtered, the filtrate was diluted with water, and the precipitate was filtered off. Yield 1.33 g (76%), mp 113–114°C (from ethanol). IR spectrum, ν, cm^{-1}: 1720 (C=O), 2230 (CN). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.94 t (3H, CH_2CH_3, J = 7.2 Hz), 2.70 s (3H, CH_3), 4.08 q (2H, CH_2CH_3, J = 7.2 Hz), 7.38–7.51 m (5H, Ph), 8.87 s (1H, 6-H). Found, %: C 72.24; H 5.25. $C_{16}H_{14}N_2O_2$. Calculated, %: C 72.16; H 5.30.

General procedure for the synthesis of quaternary cyanopyridinum salts IIIa–IIIg. A mixture of 5 mmol of pyridine **IIa**–**IIg** and 1.4 ml (15 mmol) of freshly distilled dimethyl sulfate was heated under the conditions given below. The mixture was washed with diethyl ether (3×10 ml), and the ether extracts were separated by decanting. The residue was dissolved in a minimal amount of water, and a saturated aqueous solution of 0.64 g (5.3 mmol) of $NaClO_4$ was added. The precipitate was filtered off, dried, and purified by recrystallization.

4-(4-Chlorophenyl)-3,5-dicyano-1,2,6-trimethylpyridinium perchlorate (IIIa). The reaction mixture was heated for 55 h at 90–95°C. Yield 92%, mp 232–234°C (decomp., from ethanol). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.18 s (6H, CH_3), 4.30 s (3H, CH_3), 7.75 d (2H, 3'-H, 5'-H, J = 8.8 Hz), 7.86 d (2H, 2'-H, 6'-H, J = 8.8 Hz). Found, %: C 50.35; H 3.58. $C_{16}H_{13}Cl_2N_3O_4$. Calculated, %: C 50.28; H 3.43.

3,5-Dicyano-4-(2,4-dimethoxyphenyl)-1,2,6-trimethylpyridinium perchlorate (IIIc). The reaction mixture was heated for 48 h at 80–85°C. Yield 65%, mp 115–116°C (from ethanol). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.13 s (6H, CH_3), 3.89 s (3H, CH_3O), 3.92 s (3H, CH_3O), 4.22 s (3H, CH_3); *ABX*: 6.68 (1H, 5'-H), 6.70 (1H, 3'-H), 7.50 (1H, 6'-H), $J_{5',6'}$ = 8.0, $J_{3',6'}$ = 0, $J_{5',3'}$ = 2.1 Hz). Found, %: C 52.71; H 4.44. $C_{18}H_{18}ClN_3O_6$. Calculated, %: C 53.01; H 4.45.

3,5-Dicyano-4-(2-furyl)-1,2,6-trimethylpyridinium perchlorate (IIId). The reaction mixture was heated for 30 h at 65–70°C. Yield 96%, mp 189–191°C (decomp., from EtOH). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.13 s (6H, CH_3), 4.19 s (3H, CH_3), 7.14 d.d (1H, 4'-H, $J_{4',3'}$ = 3.9, $J_{4',5'}$ = 1.7 Hz), 8.11 d (1H, 3'-H, $J_{3',4'}$ = 3.9 Hz), 8.53 d (1H, 5'-H, $J_{5',3'}$ = 1.4 Hz). Found, %: C 49.76; H 3.38. $C_{14}H_{12}ClN_3O_5$. Calculated, %: C 49.79; H 3.58.

3,5-Dicyano-1,2,4,6-tetramethylpyridinium perchlorate (IIIe). The reaction mixture was heated for 50 h at 80–85°C. Yield 64%, mp 151–152°C (from ethanol). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.93 s (3H, CH_3), 3.10 s (6H, CH_3), 4.19 s (3H, CH_3). Found, %: C 46.41; H 4.25. $C_{11}H_{12}ClN_3O_4$. Calculated, %: C 46.25; H 4.23.

3-Acetyl-5-cyano-1,2-dimethyl-6-phenylpyridinium perchlorate (IIIf). The reaction mixture was heated for 48 h at 80–85°C. Yield 66%, mp 222–224°C (from water). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 2.77 s (3H, CH_3), 2.92 s (3H, $COCH_3$), 3.95 s (3H, CH_3), 7.65–7.86 m (5H, Ph), 9.46 s (1H, 4-H). Found, %: C 54.98; H 4.21; N 7.77. $C_{16}H_{15}ClN_2O_5$. Calculated, %: C 54.79; H 4.31; N 7.99.

5-Cyano-3-ethoxycarbonyl-1,2-dimethyl-4-phenylpyridinium perchlorate (IIIg). The reaction mixture was heated for 4 h at 75–80°C. Yield 76%, mp 169–171°C (from 50% ethanol). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 0.91 t (3H, CH_2CH_3, J = 7.1 Hz), 2.87 s (3H, CH_3), 4.15 q (2H, CH_2CH_3, J = 7.1 Hz), 4.35 s (3H, CH_3), 7.49–7.71 m (5H, Ph), 9.96 s (1H, 6-H). Found, %: C 53.65; H 4.62. $C_{17}H_{17}ClN_2O_6$. Calculated, %: C 53.62; H 4.50.

General procedure for the synthesis of α-methylaminopyridines Va–Vf. Pyridinium perchlorate **IIIa**–**IIIg**, 1 mmol, was dispersed in 4 ml of ethanol, and 1.8 ml (5 mmol) of 10% aqueous sodium hydroxide was added. The mixture immediately turned brightly colored, and the color disappeared after heating for a short time (10–20 min) on a water bath. The mixture was cooled, and the precipitate was filtered off. The product was purified from tarry impurities by filtering through a thin layer of silica gel using chloroform as eluent.

5-Acetyl-4-(4-chlorophenyl)-2-methyl-6-methylaminopyridine-3-carbonitrile (Va). Yield 77%, mp 173–174°C (from ethanol). IR spectrum, ν, cm^{-1}:

1650 (C=O), 2220 (CN), 3370 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.70 s (3H, CH_3), 2.67 s (3H, $COCH_3$), 3.09 d (3H, NCH_3, J = 4.9 Hz), 7.33 d (2H, 3'-H, 5'-H, J = 8.6 Hz), 7.50 d (2H, 2'-H, 6'-H, J = 8.6 Hz), 8.23 br.s (1H, N**H**CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 301 (25.4), 300 (23.5), 299 (74.2) $[M]^+$, 298 (36.1), 286 (32.9), 285 (17.8), 284 (100), 282 (21.9), 249 (14.7), 43 (20.0), 30 (12.4). Found, %: C 64.47; H 4.78. $C_{16}H_{14}ClN_3O$. Calculated, %: C 64.11; H 4.71.

3-Acetyl-4-(4-methoxyphenyl)-2-methyl-6-methylaminopyridine-3-carbonitrile (Vb). Yield 92%, mp 176–177°C (from ethanol). IR spectrum, ν, cm^{-1}: 1650 (C=O), 2220 (CN), 3360 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.68 s (3H, CH_3), 2.66 s (3H, $COCH_3$), 3.08 d (3H, NCH_3, J = 4.9 Hz), 3.87 s (3H, CH_3O), 7.01 d (2H, 3'-H, 5'-H, J = 8.8 Hz), 7.31 d (2H, 2'-H, 6'-H, J = 8.8 Hz), 8.11 br.s (1H, N**H**CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 296 (14.3), 295 (74.4) $[M]^+$, 294 (35.0), 281 (18.8), 280 (100), 278 (19.3), 265 (12.4), 252 (11.4), 237 (11.8), 43 (17.8). Found, %: C 69.01; H 5.68. $C_{17}H_{17}N_3O_2$. Calculated, %: C 69.14; H 5.80.

3-Acetyl-4-(2,4-dimethoxyphenyl)-2-methyl-6-methylaminopyridine-3-carbonitrile (Vc). Yield 79%, mp 155–156°C (from ethanol). IR spectrum, ν, cm^{-1}: 1650 (C=O), 2220 (CN), 3360 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.77 s (3H, CH_3), 2.64 s (3H, $COCH_3$), 3.07 d (3H, NCH_3, J = 4.9 Hz), 3.83 s (3H, CH_3O), 3.86 s (3H, CH_3O); *ABX*: 6.57 (1H, 5'-H), 6.58 (1H, 3'-H), 7.00 (1H, 6'-H), $J_{5',3'}$ = 2.3, $J_{6',3'}$ = 0, $J_{5',6'}$ = 8.3 Hz; 8.35 br.s (1H, N**H**CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 325 (78.5) $[M]^+$, 311 (13.3), 310 (68.7), 308 (13.2), 295 (27.9), 294 (100), 282 (22.6), 266 (8.7), 43 (14.3), 28 (13.6). Found, %: C 66.82; H 5.78. $C_{18}H_{19}N_3O_3$. Calculated, %: C 66.45; H 5.89.

3-Acetyl-4-(2-furyl)-2-methyl-6-methylaminopyridine-3-carbonitrile (Vd). Yield 73%, mp 140–141°C (from ethanol). IR spectrum, ν, cm^{-1}: 1650 (C=O), 2210 (CN), 3370 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.78 s (3H, CH_3), 2.67 s (3H, $COCH_3$), 3.06 d (3H, NCH_3, J = 4.9 Hz), 6.67 d.d (1H, 4'-H, $J_{4',3'}$ = 3.5, $J_{4',5'}$ = 1.8 Hz), 7.17 d.d (1H, 3'-H, $J_{3',4'}$ = 3.5, $J_{3',5'}$ = 0.7 Hz), 7.64 d.d (1H, 5'-H, $J_{5',4'}$ = 1.8, $J_{5',3'}$ = 0.7 Hz), 7.83 br.s (1H, N**H**CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 256 (15.8), 255 (100) $[M]^+$, 240 (54.4), 226 (11.8), 213 (46.0), 212 (22.7), 201 (10.1), 198 (10.1), 197 (10.0), 196 (25.1), 185 (21.0), 184 (26.3), 169 (8.0), 156 (8.6), 43 (41.1). Found, %: C 66.10; H 5.23. $C_{14}H_{13}N_3O_2$. Calculated, %: C 65.87; H 5.13.

3-Acetyl-2,4-dimethyl-6-methylaminopyridine-3-carbonitrile (Ve). Yield 66%, mp 137–138°C (from ethanol). IR spectrum, ν, cm^{-1}: 1650 (C=O), 2220 (CN), 3370 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.53 s (3H, CH_3), 2.59 s (6H, CH_3), 3.02 d (3H, NCH_3, J = 4.9 Hz), 7.84 br.s (1H, N**H**CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 203 (51.2) $[M]^+$, 202 (14.8), 189 (12.0), 188 (100), 186 (20.1), 161 (12.4), 160 (13.8), 132 (13.8), 131 (9.3), 43 (14.7). Found, %: C 65.32; H 6.42. $C_{11}H_{13}N_3O$. Calculated, %: C 65.01; H 6.45.

3-Acetyl-5-benzoyl-2-methyl-6-methylaminopyridine (Vf). Yield 70%, mp 144–145°C (from ethanol). IR spectrum, ν, cm^{-1}: 1660 (C=O), 3330 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.33 s (3H, CH_3), 2.77 s (3H, $COCH_3$), 3.20 d (3H, NCH_3, J = 4.8 Hz), 7.46–7.62 m (5H, Ph), 8.20 s (1H, 4-H), 9.16 br.s (1H, N**H**CH_3). Found, %: C 76.56; H 6.33; N 5.10. $C_{17}H_{17}NO_2$. Calculated, %: C 76.38; H 6.41; N 5.24.

Recyclization of 5-cyano-3-ethoxycarbonyl-1,2-dimethyl-4-phenylpyridinium perchlorate (IIIg). The reactant ratio was the same as in the general procedure for the synthesis of α-methylaminopyridines. The reaction mixture was stirred for 1 h at room temperature, diluted with an equal volume of water, acidified with 50% acetic acid on cooling, and treated with chloroform. The extract was dried over magnesium sulfate and evaporated, and the products, α-methylaminopyridine **Vg** and pyridinone **VI**, were separated by column chromatography on Silicagel L (100/160 μm) using chloroform as eluent.

Ethyl 5-formyl-6-methyl-2-methylamino-4-phenylpyridine-3-carboxylate (Vg). Yield 43%, mp 81–82°C (from ethanol). IR spectrum, ν, cm^{-1}: 1715, 1645 (C=O); 3330 (NH). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.84 t (3H, $CH_2C\mathbf{H}_3$, J = 7.1 Hz), 2.54 s (3H, CH_3), 3.15 d (3H, NCH_3, J = 5.0 Hz), 3.89 q (2H, $C\mathbf{H}_2CH_3$, J = 7.2 Hz), 7.23–7.42 m (5H, C_6H_5), 9.06 br.s (1H, N**H**CH_3), 9.53 s (1H, CHO). Mass spectrum, *m*/*z* (I_{rel}, %): 299 (19.7), 298 (100) $[M]^+$, 297 (12.9), 270 (19.9), 269 (41.7), 253 (24.2), 242 (25.5), 241 (56.2), 225 (40.3). Found, %: C 68.08; H 6.14. $C_{17}H_{18}N_2O_3$. Calculated, %: C 68.44; H 6.08.

5-Acetyl-1-methyl-6-oxo-4-phenyl-1,6-dihydropyridine-3-carbonitrile (VI). Yield 7%, mp 173–173.5°C (from ethanol). IR spectrum, ν, cm^{-1}: 2220 (CN); 1710, 1660 (C=O). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.19 s (3H, $COCH_3$), 3.65 s (3H, NCH_3), 7.30–7.49 m (5H, Ph), 7.95 s (1H, 6-H). Mass spectrum, *m*/*z*

(I_{rel}, %): 253 (12.3), 252 (67.7) $[M]^+$, 251 (100), 238 (17.8), 237 (95.9), 210 (9.2), 196 (42.4), 140 (18.8), 127 (10.1), 43 (21.9), 42 (44.6), 31 (11.7). Found, %: C 71.30; H 4.68. $C_{15}H_{12}N_2O_2$. Calculated, %: C 71.42; H 4.79.

6-Methylamino-3-nitro-2,4-diphenylbenzonitrile (VII). Pyridinium perchlorate **IIIh**, 0.44 g (1 mmol), was dispersed in 4 ml of ethanol, and 1.8 ml (5 mmol) of 10% aqueous sodium hydroxide was added. The mixture was stirred for 6 h at room temperature and diluted with water, and the precipitate was filtered off and recrystallized from ethanol. Yield 0.21 g (62%), yellow crystals, mp 194–195°C. IR spectrum, ν, cm^{-1}: 3430 (NH); 2215 (CN); 1530, 1360 (NO_2). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.99 d (3H, NCH_3, J = 4.8 Hz), 5.20 br.s (1H, N**H**CH_3), 6.58 s (1H, 6-H), 7.30–7.54 m (10H, H_{arom}). Mass spectrum, m/z (I_{rel}, %): 330 (23.8), 329 $[M]^+$ (100), 312 (8.2), 300 (18.8), 299 (14.5), 297 (12.1), 284 (24.3), 283 (10.8), 282 (12.1), 281 (14.8), 272 (20.6), 255 (11.8), 254 (13.2), 253 (11.0), 240 (14.2), 220 (11.2), 28 (10.7). Found, %: C 72.86; H 4.59. $C_{20}H_{15}N_3O_2$. Calculated, %: C 72.94; H 4.59.

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