Furopyridines. XXVII [1]. Reactions of 2-Methyl and 2-Cyano Derivatives of Furo[2,3-*b*]-, -[3,2-*b*]-, - [2,3-*c*]- and -[3,2-*c*]pyridine

Seiji Yamaguchi, Masahide Kurosaki, Keiko Orito, Hajime Yokayama, Yoshiro Hirai and Shunsaku Shiotani*

Department of Chemistry, Faculty of Science, Toyama University, Gofuku 3190, Toyama 930, Japan

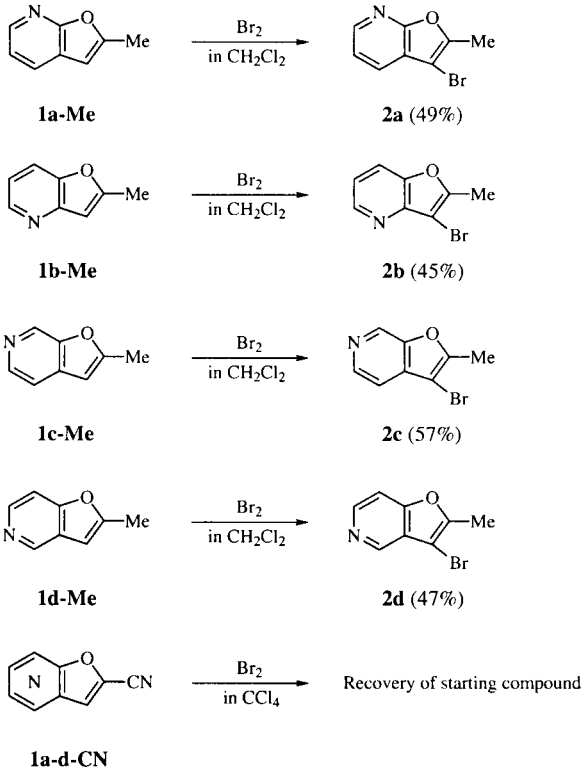
Received June 3, 1998

Bromination of 2-methylfuropyridines **1a-d-Me** gave the 3-bromo derivatives **2a-d,** while the 2-cyano compounds **1a-d-CN** resulted in the recovery of the starting compounds. Nitration of **1a-d-Me** and **1a-d-CN** did not yield the corresponding nitro derivative, except for **1-c-CN** giving 3-nitro derivative **3c** in 7% yield. *N*-Oxidation of **1a-d-Me** and **1b-d-CN** with *m*-chloroperbenzoic acid yielded the *N*-oxides **4a-d-Me** and **4b-d-CN,** whereas **1a-CN** did not afford the *N*-oxide. Cyanation of *N*-oxides **4a-d-Me** and **4b-d-CN** with trimethylsilyl cyanide gave the corresponding α-cyanopyridine compounds **5a-d-Me** and **5b-d-CN.** Chlorination of **4a-d-Me** and **4b-d-CN** with phosphorus oxychloride also gave the α-chloropyridine compounds **6b-d-Me** and **6b-d-CN,** accompanying formation of γ-chloropyridine **6a-Me, 6'b-Me** and **6'b-CN,** β-chloropyridine **6"b-CN,** and α'-chloropyridine derivatives **6'c-Me** and **6'c-CN.** Acetoxylation of **4a-d-Me** and **4b-d-CN** with acetic anhydride yielded α-acetoxypyridine compounds **7a-Me** and **7b-CN,** pyridone compounds **11d-Me, 11c-CN** and **11d-CN,** 3-acetoxy compounds **8, 9b, 9c,** and 2-acetoxymethyl derivatives **10b** and **10c.**

J. Heterocyclic Chem., **35**, 1237 (1998).

In continuation of our studies on the chemistry of furopyridines, we recently reported the reactions of cyanopyridine derivatives of furo[2,3-*b*]-, -[3,2-*b*]-, -[2,3-*c*]- and -[3,2-*c*]pyridine and their *N*-oxides to see the effects of a functional group at the furan or the pyridine ring upon the reactivity of the monosubstituted furopyridines for the second electrophilic and/or nucleophilic reaction [1]. In this paper we describe the bromination and nitration of 2-methyl- and 2-cyanofuropyridines, and the cyanation, chlorination and acetoxylation of their *N*-oxides.

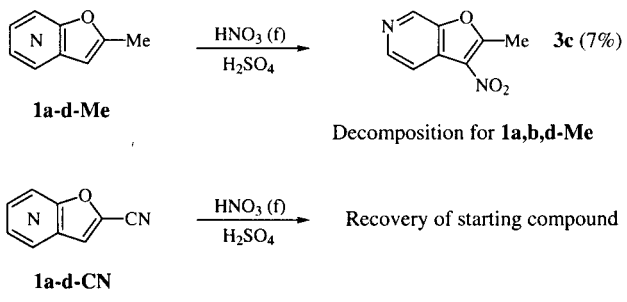
Scheme 1



Bromination of 2-methylfuro[2,3-*b*]- (**1a-Me**) [2], -[3,2-*b*]- (**1b-Me**) [3], -[2,3-*c*]- (**1c-Me**) [4] and -[3,2-*c*]pyridine (**1d-Me**) [5] with molecular bromine in dichloromethane afforded the corresponding 3-bromo derivative **2a-d** in yield of 49% for **2a**, 45% for **2b**, 57% for **2c** and 47% for **2d** accompanying recovery of the starting compound. While, bromination of 2-cyanofuropyridines **1a-d-CN** gave no brominated product but resulted in recovery of the starting compound (88% for **1a-CN**, 84% for **1b-CN**, 80% for **1c-CN** and 80% for **1d-CN**). Nitration of **1a-d-Me** with a mixture of fuming nitric acid and sulfuric acid resulted in decomposition of the furopyridines and no compound could be isolated from the reaction mixture, except for **1c-Me** which yielded the 3-nitrated compound **3c** in 7% yield. Nitration of **1a-d-CN** again resulted in decomposition of the furopyridines accompanying recovery of the starting compound (33% for **1a-CN**, 56% for **1b-CN**, 63% for **1c-CN** and 39% for **1d-CN**). Structures of the 3-bromo compounds **2a-d** and the 3-nitro derivative **3c** were confirmed from their ^{1}H-nmr spectra showing disappearance of the signal of the 3-proton and the presence of three pyridine protons in each compound.

N-Oxidation of 2-methylfuropyridines **1a-d-Me** and 2-cyanofuropyridines **1b-d-CN** with *m*-chloroperbenzoic acid yielded the *N*-oxides **4a-d-Me** and **4b-d-CN** in excellent yield (81% for **4a-Me**, 98% for **4b-Me**, 98% for **4c-Me**, 94% for **4d-Me,** 92% for **4b-CN**, 86% for **4c-CN** and 39% for **4d-CN**). Compound **1a-CN,** however, did not

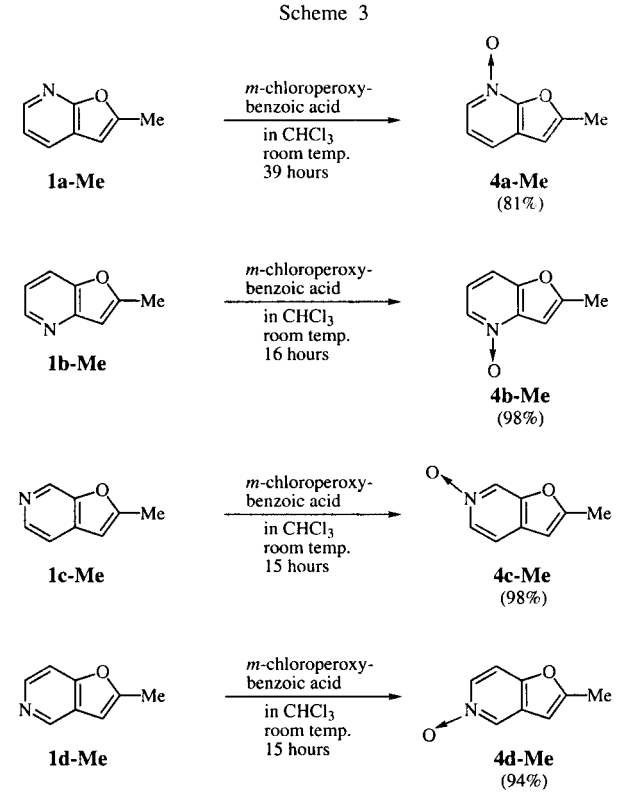
Scheme 2



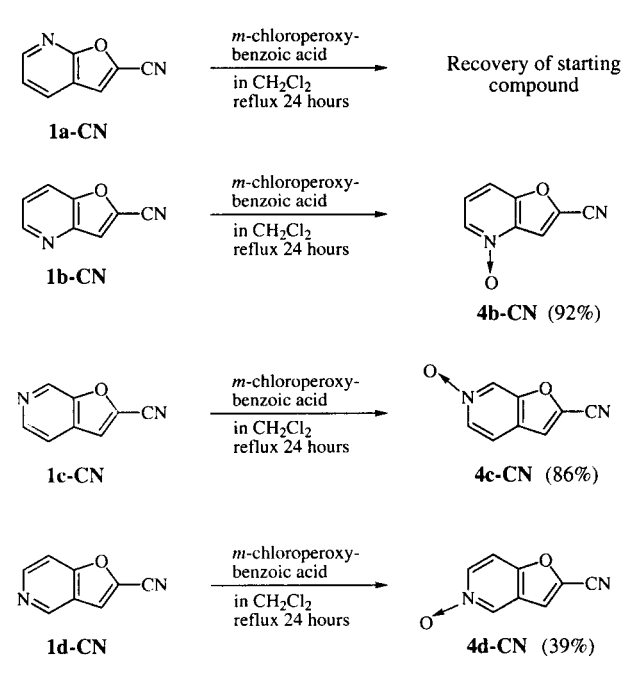
give the *N*-oxide but recovered the starting compound (80%). These results suggested that the electronic effects of methyl and cyano groups at the 2-position do not have an affect upon the basicity of the ring nitrogen of furopyridines, except for the *N*-oxidation of **1a-CN.** In this case, the electron withdrawing inductive effect of the ring oxygen would be enhanced by the cyano group at the 2-position, therefore, the electrons at the ring nitrogen would be strongly attracted by the ring oxygen through the C_{7a}-O bond.

Cyanation of the *N*-oxides **4a-d-Me** and **4b-d-CN** with trimethylsilyl cyanide in the presence of triethylamine in acetonitrile yielded the compound having a second cyano group at the α-position to the ring nitrogen, 6-cyano-2-methylfuro[2,3-*b*]- (**5a-Me**, 36%), 5-cyano-2-methylfuro[3,2-*b*]- (**5b-Me**, 84%), 7-cyano-2-methylfuro[2,3-*c*]- (**5c-Me**, 87%) and 4-cyano-2-methylfuro[3,2-*c*]- (**5d-Me,** 91%), 2,5-dicyanofuro[3,2-*b*]- (**5b-CN**, 68%), 2,7-dicyanofuro[2,3-*c*]- (**5c-CN**, 99%) and 2,4-dicyanofuro[3,2-*c*]pyridine (**5d-CN,** 99%). These compounds showed signals of the pyridine protons as a pair of doublets (J = 7.9 Hz for **5a-Me**, 8.0 Hz for **5b-Me** and **5b-CN**, 5.0 Hz for **5c-Me**, 5.3 Hz for **5c-CN** and 5.6 Hz for **5d-Me** and **5d-CN**) in their ^{1}H-nmr spectra. These facts suggested the position of the second cyano group of **5a-Me** at C-6, **5b-Me** and **5b-CN** at C-5, **5c-Me** and **5c-CN** at C-7, and **5d-Me** and **5d-CN** at C-4. In the case of **4a-Me**, a strange compound **5'a** was isolated, which had mp 143-147°, showed signals of three pyridine protons, of methylene protons and of protons of four methyl groups in its ^{1}H-nmr spectrum, exhibited three aromatic methine, two aromatic quarternary, one methine, one aliphatic methine, two cyano, one C-methyl cabon and three carbons of trimethylsilyl in the ^{13}C-nmr spectrum, and exhibited absorption of cyano group at 2239 cm^{-1} in the ir spectrum. The elemental analysis indicated the molecular formula $C_{13}H_{17}N_3O_2Si$. Thus, the structure of **5'a** was assigned as 2-cyano-2-methyl-2,3-dihydro-7-trimethylsiloxyfuro-[2,3-*b*]pyridinium cyanide.

Scheme 3

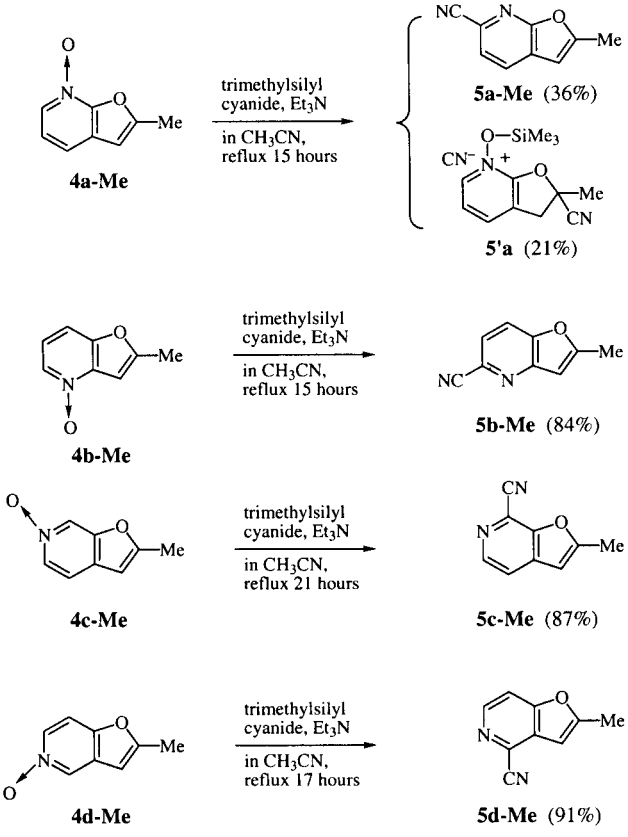


Scheme 4



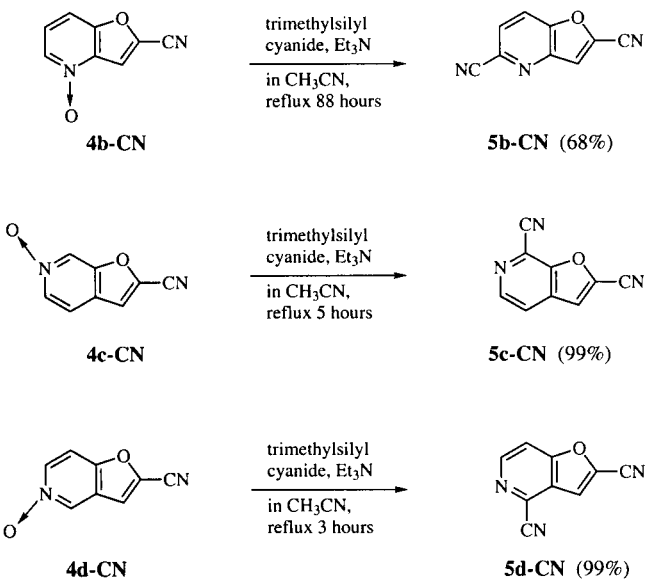
Chlorination of compounds **4a-d-Me** and **4b-d-CN** with phosphorus oxychloride gave 4-chloro-2-methylfuro[2,3-*b*]- (**6a-Me**, 71%) from **4a-Me**, 5-chloro-2-methylfuro[3,2-*b*]- (**6'b-Me**, 4%) and 7-chloro-2-methylfuro[3,2-*b*]- (**6b-Me**, 79%) from **4b-Me**, 5-chloro-2-methylfuro[2,3-*c*]- (**6'c-Me**, 3%) and 7-chloro-2-methylfuro[2,3-*c*]- (**6c-Me**, 60%) from **4c-Me**, 4-chloro-2-methylfuro[3,2-*c*]- (**6d-Me**, 61%) from **4d-Me**, 5-chloro-

Scheme 5



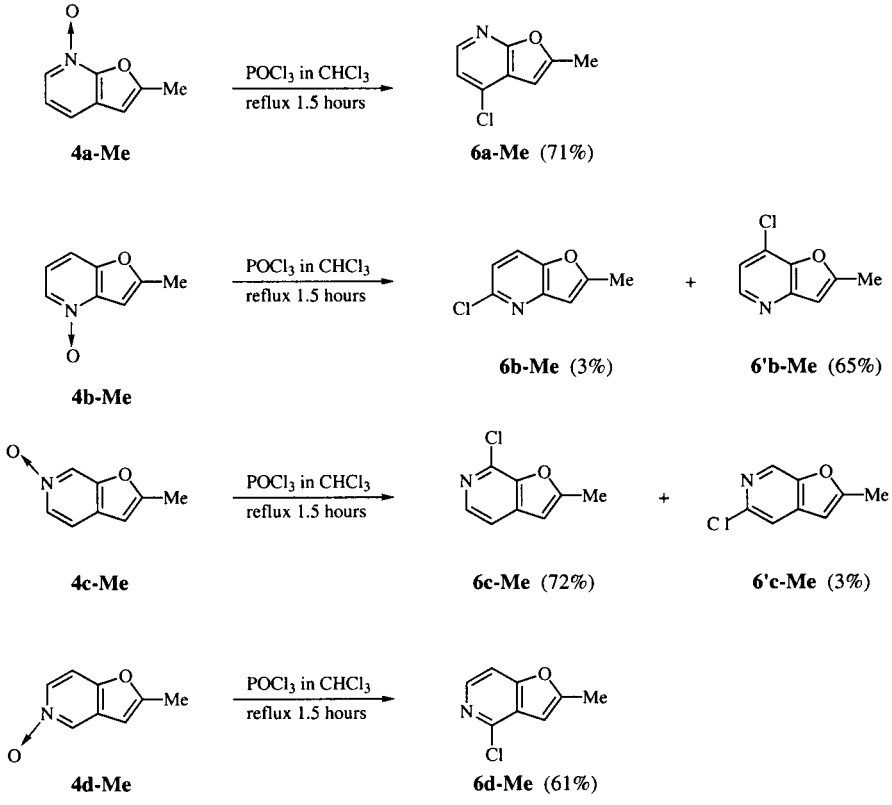
2-cyanofuro[3,2-*b*]- (**6b-CN**, 53%), 6-chloro-2-cyanofuro[3,2-*b*]- (**6"b-CN**, 3%) and 7-chloro-2-cyanofuro[3,2-*b*]- (**6'b-CN**, 14%) from **4b-CN**, 7-chloro-2-cyanofuro[2,3-*c*]- (**6c-CN**, 60%), 5-chloro-2-cyanofuro[2,3-*c*]- (**6'c-CN**, 5%) and 4-chloro-2-cyanofuro[2,3-*c*]- (**6"c-CN**, 2%) from **4c-CN**, and 4-chloro-2-cyanofuro[3,2-*c*]pyridine (**6d-CN**, 67%) from **4d-CN**. Compounds **6a-Me**, **6b-Me**, **6'b-Me**, **6c-Me**, **6d-Me**, **6b-CN**, **6'b-CN**, **6c-CN** and **6d-CN** showed, in the ^{1}H-nmr spectra, signals of a furan proton, methyl protons and pyridine protons as a pair of doublets (J = 4.6 Hz for **6d-Me**, 5.2 Hz for **6'b-CN**, 5.3 Hz for **6a-Me**, **6'b-Me**, **6c-Me** and **6c-CN**, 5.9 Hz for **6d-CN**, 8.5 Hz for **6b-Me** and 8.8 Hz for **6b-CN**). From these facts, the position of the chlorine atom in each compound was determined. Compound **6'c-Me**, **6"b-CN**, **6'c-CN** and **6"c-CN** showed signals of the pyridine protons as two singlets, and the position of the chlorine atom in **6'c-Me** and **6'c-CN** was determined as the 5-position, that in **6"b-CN** as the 6-position, and that in **6"c-CN** as the 4-position.

Scheme 6



Acetoxylation of the *N*-oxides **4a-d-Me** and **4b-d-CN** afforded somewhat complex results; **4a-Me** yielded 6-acetoxy-2-methylfuro[2,3-*b*]- (**7a-Me**, 70%) and 2,3-diacetoxy-2-methyl-2,3-dihydrofuro[2,3-*b*]pyridine (**8**, 10%), **4b-Me** gave 3-acetoxy-2-methylfuro[3,2-*b*] (**9b**, 64%) and 2-acetoxymethylfuro[3,2-*b*]pyridine (**10b**, 34%), **4c-Me** gave 3-acetoxy-2-methylfuro[2,3-*c*]- (**9c**, 55%) and 2-acetoxymethylfuro[2,3-*c*]pyridine (**10c**, 28%), **4d-Me** gave 2-methylfuro[3,2-*c*]pyridin-4(5*H*)-one (**11d-Me**, 52%) [5], **4b-CN** gave 5-acetoxy-2-cyanofuro[3,2-*b*]- (**7b-CN**, 25%) and 6-acetoxy-2-cyanofuro[3,2-*b*]pyridine (**7'b**, 4%), **4c-CN** gave 2-cyanofuro[2,3-*c*]pyridin-7(6*H*)-one (**11c-CN**, 72%), and **4d-CN** gave 2-cyanofuro[3,2-*c*]-pyridin-4(5*H*)-one (**11d-CN**, 64%). The position of the acetoxyl group in **7a-Me** (C-6) and **7b-CN** (C-5) was confirmed by the ^{1}H-nmr spectra showing signals of a furan proton as a singlet and the pyridine protons as a pair of doublets (J = 8.0 Hz for **7a-Me**, 9.1 Hz for **7b-CN**). Compound **7'b** showed in its ^{1}H-nmr spectrum signals of a furan proton and two pyridine protons with small coupling constants (H-3; d, J = 0.9 Hz, H-5; d, J = 2.1 Hz, H-7; dd, J = 0.9, 2.1 Hz). The structure of **8** was determined from the elemental analysis and the ^{1}H-nmr spectrum exhibiting signals of three pyridine protons at δ 8.20 (dd), 7.73 (dd) and 6.95 (dd), two acetoxy methyls at δ 2.14 and 2.04, singlet of an aliphatic methylene at δ 6.35, and a singlet of C-methyl protons at δ 1.88. The ^{1}H-nmr spectra of **9b** and **9c** showed signals of three pyridine protons (δ 8.50 (dd), 7.64 (dd) and 7.17 (dd) for **9b**, and 8.75 (s), 8.31 (d) and 7.29 (d) for **9c**), an acetoxy methyl (δ 2.43 for **9b**, and 2.41 for **9c**) and a singlet of C-methyl (δ 2.43 for **9b**, and 2.39 for **9c**). The structures of compound **10b** and **10c** were determined from the ^{1}H-nmr spectra, in which signals of an acetoxy methyl (δ 2.15 for **10b** and **10c**), a methylene (δ 5.25 for **10b** and **10c**), three pyridine protons (δ 8.55 (dd), 7.75 (ddd) and 7.24 (dd) for **10b**, and 8.88 (s), 8.43 (d) and 7.52 (d) for **10c**) and a furan proton (δ 6.98 for **10b**, and 6.80 for **10c**) were exhibited. The lactam structure of com-

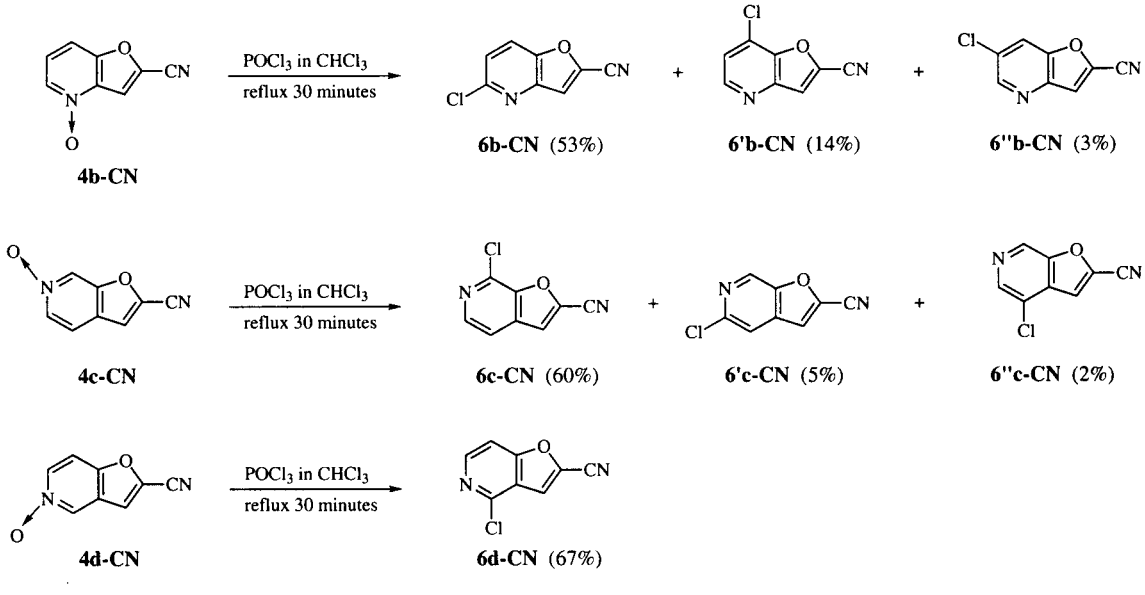
Scheme 7



pound **11c-CN** and **11d-CN** was confirmed from the ir spectrum of each compound showing absorption of lactam carbonyl at 1683 cm^{-1} for **11c-CN** and 1696 cm^{-1} for **11d-CN**, and the ^{1}H-nmr spectrum showing signals of two pyridine protons as a pair of doublet (δ 7.43 and 6.70 for **11c-CN**, and 7.54 and 6.76 for **11d-CN**) and a furan proton as a singlet (δ 7.68 for **11c-CN**, and 7.80 for **11d-CN**) respectively.

Formation of compounds having a cyano, a chloro or an acetoxy substituent at the pyridine carbon and furopyridones **11d-Me**, **11c-CN** and **11d-CN** is interpreted by the well known mechanism for the cyanation, chlorination and

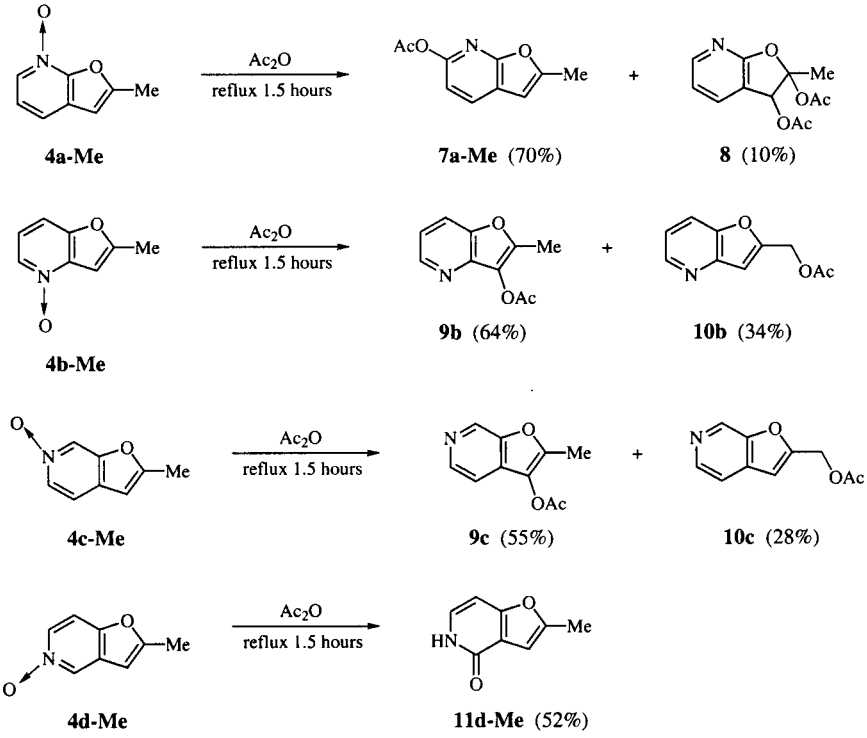
Scheme 8



acetoxylation of the *N*-oxides of pyridine, quinoline and isoquinoline [6]. Formation of the compounds acetoxylated at the furan ring or the C-methyl group at 2-position **9b**, **9c**, **10b** and **10c** can be interpreted by the mechanism previouly postulated by us [7].

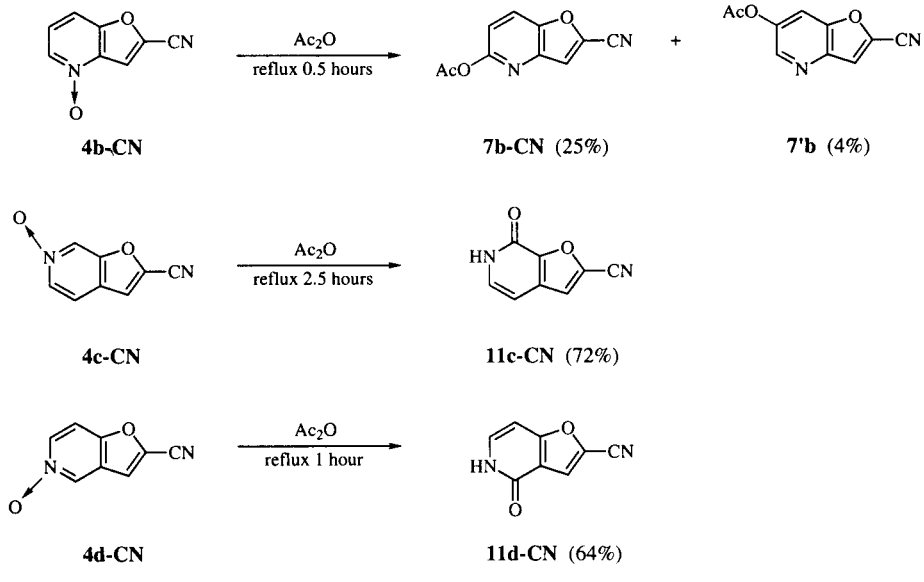
the 2-position is much decreased by its electron withdrawing effect, and the cyanation, chlorination and acetoxylation of the *N*-oxides of 2-methylfuropyridines are virtually not affected by the substituent, while, the 2-cyano group of the *N*-oxides of 2-cyanofuropyridines

Scheme 9



Thus, this research has demonstrated that the reaction of an electrophile (bromination and nitration) at the furan moiety in furopyridines having a cyano group at inhibits the attack of chloride or acetate anion at the 2-position, in comparison with those of unsubstituted furopyridines [8].

Scheme 10



EXPERIMENTAL

Melting points were determined by using a Yanagimoto micro melting point apparatus and are uncorrected. The ir spectra were taken on a JASCO FT/IR 7300 spectrometer. The nmr spectra were recorded on a JEOL A-400 or MAC-FX (90 MHz) instrument with tetramethylsilane as an internal reference in deuteriochloroform. The mass spectra were obtained by using JEOL JMS-OISG-2 spectrometer.

General Procedure for Bromination of 2-Methylfuropyridines **1a-d-Me.**

To a solution of 2-methylfuropyridine **1a-Me**, **1b-Me**, **1c-Me** or **1d-Me** (124 mg, 0.93 mmole) in dichloromethane (3 ml) at -15° was added 520 mg (3.3 mmoles) of bromine in 2 ml of dichloromethane dropwise with stirring. After the addition was complete, the mixture was stirred for 7 hours for **1a-Me** (5 hours for **1b-Me,** 20 hours for **1d-Me**) at room temperature. In the case of **1c-Me** the reaction mixture was refluxed for 20 hours. The solvent was removed under reduced pressure to give an orange mass, which was treated with 10% sodium hydroxide solution (10 ml) and extracted with ether three times. The ether extracts were combined, dried (magnesium sulfate) and evaporated to give a solid mass. The residue was purified by chromatography on a silica gel column eluting with hexane-ethyl acetate (9:1) to give 3-bromo-2-methylfuro[2,3-*b*]- **2a** (97 mg, 49%) from **1a-Me**, -[3,2-*b*]- **2b** (86 mg, 45%) and **1b-Me** (5 mg, 4%) from **1b-Me**, -[2,3-*c*]- **2c** (113 mg, 57%) and **1c-Me** (46 mg, 37%) from **1c-Me,** and -[3,2-*c*]- pyridine **2d** (92 mg, 47%) from **1d-Me.**

Compound **2a**.

This compound had bp 90-110° (bath temperature)/25 mm Hg, colorless oil; ir (neat): 3069, 2920, 2850, 1643, 1603, 1550, 1463, 1399, 1378, 1233, 1049, 977, 772, 748 cm^{-1}; ^{1}H-nmr: δ 8.16 (dd, J = 5.0, 1.6 Hz, 1H, H-6), 7.62 (dd, J = 7.5, 1.6 Hz, 1H, H-4), 7.12 (dd, J = 7.5, 5.0 Hz, 1H, H-5), 2.39 (s, 3H, 2-Me); ms: m/z (relative intensity) 213 (M^++2, 96), 212 (39), 211 (M^+, 100), 210 (32), 132 (48), 104 (51); hrms: 210.9620; M^+, Calcd. for C_8H_6NOBr: 210.9632.

Anal. Calcd. for C_8H_6NOBr: C, 45.31; H, 2.85; N, 6.61. Found: C, 45.75; H, 2.84; N, 6.34.

Compound **2b**.

This compound had mp 42-46° (from ether, colorless crystals); ir (potassium bromide): 3069, 3056, 3035, 3019, 2982, 2922, 2848, 1610, 1572, 1558, 1415, 1265, 1235, 1226, 1170, 1055, 982, 917, 800, 772 cm^{-1}; ^{1}H-nmr: δ 8.54 (dd, J = 4.7, 1.1 Hz, 1H, H-5), 7.65 (dd, J = 8.2, 1.1 Hz, 1H, H-7), 7.19 (dd, J = 8.2, 4.7 Hz, 1H, H-6), 2.53 (s, 3H, 2-Me).

Anal. Calcd. for C_8H_6NOBr: C, 45.31; H, 2.85; N, 6.61. Found: C, 45.31; H, 2.90; N, 6.53.

Compound **2c**.

This compound had mp 60-63° (from ether, colorless crystals); ir (potassium bromide): 2925, 2854, 1637, 1601, 1467, 1426, 1253, 1182, 1159, 1056, 911, 820 cm^{-1}; ^{1}H-nmr: δ 8.75 (d, J = 0.8, 1H, H-7), 8.45 (d, J = 5.2 Hz, 1H, H-5), 7.38 (dd, J = 5.2, 0.8 Hz, 1H, H-4), 2.52 (s, 3H, 2-Me).

Anal. Calcd. for C_8H_6NOBr: C, 45.31; H, 2.85; N, 6.61. Found: C, 45.61; H, 2.98; N, 6.35.

Compound **2d**.

This compound had mp 35-38° (from ether, colorless crystals); ir (neat): 3059, 2963, 2923, 2854, 1634, 1607, 1585, 1457, 1446, 1436, 1285, 1259, 1184, 1157, 1050, 1029, 970, 866, 824, 815 cm^{-1}; ^{1}H-nmr: δ 8.75 (d, J = 0.8 Hz, 1H, H-4), 8.50 (d, J = 5.6 Hz, 1H, H-6), 7.33 (dd, J = 5.6, 0.8 Hz, 1H, H-7), 2.49 (s, 3H, 2-Me); ms: m/z (relative intensity) 213 (M^++2, 91), 212 (49), 211 (M^+, 100), 210 (37), 132 (97); hrms: 210.9637; M^+, Calcd. for C_8H_6NOBr: 210.9632.

Anal. Calcd. for C_8H_6NOBr: C, 45.31; H, 2.85; N, 6.61. Found: C, 45.47; H, 3.03; N, 6.25.

General Procedure for Bromination of 2-Cyanofuropyridines **1a-d-CN.**

To a stirred solution of **1a-CN**, **1b-CN**, **1c-CN** or **1d-CN** (50 mg, 0.35 mmole) in carbon tetrachloride (5 ml) at -15° was added a solution of bromine (168 mg, 1.05 mmoles) in carbon tetrachloride (1.7 ml) during 10 minutes. After being stirred for 16 hours at room temperature, the mixture was refluxed for 2.5 hours. The mixture was cooled, evaporated, treated with 10% sodium hydroxide solution and extracted with chloroform. Evaporation of the dried chloroform extract afforded the starting compound (**1a-CN**, 45 mg, 88%; **1b-CN**, 42 mg, 84%; **1c-CN**, 40 mg, 80%; **1d-CN**, 40 mg, 80%), which was identified by the ir and ^{1}H-nmr spectra.

General Procedure for Nitration of 2-Methylfuropyridines **1a-d-Me** and 2-Cyanofuropyridines **1a-d-CN.**

Sulfuric acid (0.4 ml) was added to the 2-methyl- **1a-d-Me** or 2-cyanofuropyridines **1a-d-CN** (105 mg, 0.79 mmole) at -15° during 5 minutes. To this solution was added a mixture of 0.3 ml of sulfuric acid and 1.0 ml of fuming nitric acid (d, 1.50) at 0-5°. After being stirred for 30 minutes at room temperature, the mixture was treated with ice, basified with sodium bicarbonate, extracted with ethyl acetate (5 times). Evaporation of the dried extract from 2-methylfuropyridines **1a-Me**, **1b-Me** and **1d-Me** afforded almost a negligible amount of residue. The residue from **1c-Me** was recrystallized from ether-acetone to give 10 mg (7%) of 3-nitro-2-methylfuro[2,3-*c*]pyridine **3c**. Evaporation of the dried extract from **1a-CN**, **1b-CN**, **1c-CN** and **1d-CN** afforded the starting compound in 33%, 56%, 63% and 39%, respectivly, which were identified by comparison of the ir and ^{1}H-nmr spectra.

Compound **3c**.

This compound had mp 97-102° (colorless crystals); ir (potassium bromide): 2925, 2854, 1608, 1596, 1509, 1419, 1389, 1332, 1254, 1178, 1161, 941, 839, 825 cm^{-1}; ^{1}H-nmr: δ 8.90 (d, J = 0.9 Hz, 1H, H-7), 8.63 (d, J = 5.3 Hz, 1H, H-5), 8.05 (dd, J = 5.3, 0.9 Hz, 1H, H-4), 3.00 (s, 3H, 2-Me).

Anal. Calcd. for $C_8H_6N_2O_3$: C, 53.94; H, 3.39; N, 15.72. Found: C, 54.03; H, 3.50; N, 15.68.

General Procedure for the Preparation of the *N*-oxide of 2-Methylfuro[2,3-*b*]- **4a-Me**, -[3,2-*b*]- **4b-Me**, -[2,3-*c*]- **4c-Me** and -[3,2-*c*]pyridines **4d-Me.**

A mixture of **1a-Me**, **1b-Me**, **1c-Me** or **1d-Me** (1.11 g, 8.3 mmoles) and *m*-chloroperbenzoic acid (75% purity, 2.5 g, 10.0 mmoles) in chloroform (20 ml) was stirred at room temperature for 16 hours (40 hours for **1a-Me**). The reaction mixture was filtered slowly with an alumina (basic, 100 g) pad to remove the acidic compounds. The filtrate was evaporated to give a solid mass which was purified by distillation or sublimation under

reduced pressure to afford **4a-Me** (1.01 g, 81%) from **1a-Me**, **4b-Me** (1.21 g, 98%) from **1b-Me**, **4c-Me** (1.21 g, 98%) from **1c-Me** and **4d-Me** (1.16 g, 94%) from **1d-Me.**

Compound **4a-Me.**

This compound had mp 140-145° (colorless crystals, bp 145-150°((bath temperature)/0.1 mm Hg); ir (potassium bromide): 3119, 3098, 3083, 2968, 2925, 2853, 1611, 1469, 1456, 1440, 1251, 1204, 1056, 918, 820, 728 cm^{-1}; ^{1}H-nmr: δ 8.07 (dd, J = 6.2, 1.2 Hz, 1H, H-6), 7.36 (dd, J = 7.9, 1.2 Hz, 1H, H-4), 7.05 (dd, J = 7.9, 6.2 Hz, 1H, H-6), 6.42 (q, J = 1.2 Hz, 1H, H-3), 2.48 (d, J = 1.2 Hz, 3H, 2-Me).

Anal. Calcd. for $C_8H_7NO_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.42; H, 4.66; N, 9.45.

Compound **4b-Me.**

This compound had mp 107-111° (colorless crystals, bp 130-140° (bath temperature)/0.1 mm Hg); ir (potassium bromide): 3134, 2961, 2923, 2853, 1619, 1593, 1467, 1439, 1269, 1246, 1209, 1049, 937, 867, 783, 765 cm^{-1}; ^{1}H-nmr: δ 8.15 (dd, J = 6.5, 0.8 Hz, 1H, H-5), 7.36 (dd, J = 8.2, 0.8 Hz, 1H, H-7), 7.08 (dd, J = 8.2, 6.5 Hz, 1H, H-6), 6.87 (q, J = 0.9 Hz, 1H, H-3), 2.53 (d, J = 0.9 Hz, 3H, 2-Me).

Anal. Calcd. for $C_8H_7NO_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 63.97; H, 4.85; N, 9.30.

Compound **4c-Me.**

This compound had mp 143-147° (colorless crystals, sublimed at 130-140° (bath temperature)/0.1 mm Hg); ir (potassium bromide): 3119, 3097, 2924, 2854, 1671, 1599, 1459, 1293, 1159, 1126, 988, 919, 857, 843, 782 cm^{-1}; ^{1}H-nmr: δ 8.50 (d, J = 1.5 Hz, 1H, H-7), 8.10 (dd, J = 6.7, 1.5 Hz, 1H, H-5), 7.31 (d, J = 6.7 Hz, 1H, H-4), 6.45 (q, J = 1.1 Hz, 1H, H-3), 2.50 (d, J = 1.1 Hz, 3H, 2-Me).

Anal. Calcd. for $C_8H_7NO_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.64; H, 4.86; N, 9.42.

Compound **4d-Me.**

This compound had mp 166-171° (colorless crystals, sublimed at 140-150° (bath temperature)/0.1 mm Hg); ir (potassium bromide): 3118, 3096, 2925, 2854, 1603, 1453, 1198, 1164, 1129, 927, 848, 786 cm^{-1}; ^{1}H-nmr: δ 8.45 (d, J = 2.1 Hz, 1H, H-4), 8.12 (dd, J = 7.0, 2.1 Hz, 1H, H-6), 7.29 (d, J = 7.0 Hz, 1H, H-7), 6.38 (q, J = 0.9 Hz, 1H, H-3), 2.49 (d, J = 0.9 Hz, 3H, 2-Me).

Anal. Calcd. for $C_8H_7NO_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.47; H, 4.82; N, 9.43.

General Procedure for the *N*-Oxidation of 2-Cyanofuro[2,3-*b*]- **1a-CN**, -[3,2-*b*]- **1b-CN**, -[2,3-*c*]- **1c-CN** and -[3,2-*c*]pyridines **1d-CN.**

A mixture of **1a-CN**, **1b-CN**, **1c-CN** or **1d-CN** (410 mg, 2.8 mmoles) and *m*-chloroperbenzoic acid (75% purity, 1.75 g, 7.0 mmoles) in dichloromethane (20 ml) was stirred at room temperature for 18 hours (in the case of **1a-CN**, the reaction mixture was refluxed for 18 hours after being stirred at room temperature for 20 hours). The reaction mixture was filtered slowly with an alumina (basic, 50 g) pad to remove the acidic compounds. The filtrate was evaporated to give a solid mass which was purified by recrystallization from ether-acetone for **4b-CN** (418 mg, 92%) and **4c-CN•1/2H$_2$O** (412 mg, 86%) and from ether-methanol for **4d-CN** (177 mg, 39%). The residue (330 mg, 80%) from the reaction of **1a-CN** was identified as the starting compound by comparison of the ir spectrum.

Compound **4b-CN.**

This compound had mp 188-191° (colorless crystals); ir (potassium bromide): 3124, 3099, 3030, 2238, 1610, 1576, 1461, 1431, 1361, 1270, 1250, 1216, 1152, 1060, 1047, 947, 892, 782 cm^{-1}; ^{1}H-nmr: δ 8.29 (dd, J = 6.3, 0.7 Hz, 1H, H-5), 7.85 (d, J = 1.0 Hz, 1H, H-3), 7.50 (ddd, J = 8.8, 1.0, 0.7 Hz, 1H, H-7), 7.40 (dd, J = 8.8, 6.3 Hz, 1H, H-6).

Anal. Calcd. for $C_8H_4N_2O$: C, 60.01; H, 2.52; N, 17.49. Found: C, 59.61; H, 2.39; N, 17.16.

Compound **4c-CN.**

This compound had mp 185-189° (colorless crystals); ir (potassium bromide): 3142, 3111, 3076, 3041, 2231, 1637, 1567, 1481, 1445, 1308, 1177, 1134, 933, 880, 861, 821 cm^{-1}; ^{1}H-nmr: δ 8.62 (dd, J = 1.5, 1.2 Hz, 1H, H-7), 8.20 (dd, J = 6.8, 1.5 Hz, 1H, H-5), 7.54 (d, J = 6.8 Hz, 1H, H-4), 7.45 (d, J = 1.2 Hz, 1H, H-3).

Anal. Calcd. for $C_8H_4N_2O•1/2H_2O$: C, 56.81; H, 2.98; N, 16.56. Found: C, 56.87; H, 2.59; N, 16.31.

Compound **4d-CN.**

This compound had mp 164-167° (colorless crystals); ir (potassium bromide): 3136, 3118, 3106, 3070, 3039, 2242, 1630, 1437, 1209, 1166, 1135, 1119, 948, 896, 851, 828, 785 cm^{-1}; ^{1}H-nmr: δ 8.65 (dd, J = 1.8, 0.6 Hz, 1H, H-4), 8.32 (dd, J = 7.3, 1.8 Hz, 1H, H-6), 7.51 (ddd, J = 7.3, 0.9, 0.6 Hz, 1H, H-7), 7.43 (d, J = 0.9 Hz, 1H, H-3).

Anal. Calcd. for $C_8H_4N_2O$: C, 60.01; H, 2.52; N, 17.49. Found: C, 59.71; H, 2.53; N, 17.17.

General Procedure for Cyanation of **4a-Me**, **4b-Me**, **4c-Me** and **4d-Me** with Trimethylsilyl Cyanide.

A mixture of *N*-oxide **4a-d-Me** (120 mg, 0.8 mmole), trimethylsilyl cyanide (0.17 ml, 1.2 mmoles) and triethylamine (0.26 ml, 2.0 mmoles) in acetonitrile (3 ml) was stirred and refluxed for 15 hours (21 hours for **4c-Me**). After evaporation of the solvent, the reaction mixture was dissolved in chloroform, washed with water and dried over magnesium sulfate. The residue of the chloroform solution from **4b-Me**, **4c-Me** and **4d-Me** was recrystallized from acetone-ether to give 5-cyano-2-methylfuro[3,2-*b*]- **5b-Me** (106 mg, 84%), 7-cyano-2-methylfuro[2,3-*c*]- **5c-Me** (112 mg, 87%) and 4-cyano-2-methylfuro[3,2-*c*]pyridine **5d-Me** (117 mg, 91%) respectively. The residue from **4a-Me** was chromatographed on a silica gel column eluting with hexane-ethyl acetate (9:1) to give 46 mg (36%) of 6-cyano-2-methylfuro[2,3-*b*]pyridine **5a-Me** and 58 mg (21%) of 2-cyano-2-methyl-2,3-dihydro-7-trimethylsilylfuro[2,3-*b*]pyridinium cyanide **5'a**.

Compound **5a-Me.**

This compound had mp 126-130° (from acetone, colorless crystals); ir (potassium bromide): 3107, 2923, 2853, 2231, 1608, 1590, 1581, 1398, 1387, 1358, 1290, 1272, 1220, 1157, 1106, 969, 912, 852, 775 cm^{-1}; ^{1}H-nmr: δ 7.90 (d, J = 7.9 Hz, 1H, H-4), 7.58 (d, J = 7.9 Hz, 1H, H-5), 7.53 (q, J = 0.9 Hz, 1H, H-3), 2.56 (d, J = 0.9 Hz, 3H, 2-Me).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.33; H, 3.91; N, 17.76.

Compound **5'a.**

This compound had mp 143-147° (from acetone-ether, colorless crystals); ir (potassium bromide): 3128, 3106, 3061, 3027,

2995, 2962, 2901, 2239, 1639, 1589, 1428, 1290, 1250, 1194, 1178, 1127, 1105, 1035, 991, 854, 761 cm^{-1}; ^{1}H-nmr: δ 8.22 (d, J = 6.3 Hz, 1H, H-6), 7.42 (dd, J = 7.8, 6.3 Hz, 1H, H-5), 7.37 (d, J = 7.8 Hz, 1H, H-4), 3.23 and 3.13 (AB-q, J = 14.0 Hz, 2H, H-3 and H-3'), 1.74 (s, 3H, 2-Me), 0.150 (s, 9H, $SiMe_3$); ^{13}C-nmr: δ 139.2 (s, C-7a), 138.8 (d, C-6), 128.2 (s, Si-CN), 127.6 (d, C-5), 126.9 (d, C-4), 120.3 (s, C-3a), 111.2 (s, 2-CN), 69.1 (s, C-2), 45.7 (t, C-3), 29.2 (q, 2-Me), 0.92 (q, 3 x C, $SiMe_3$).

Anal. Calcd. for $C_{13}H_{17}N_3O_2Si$: C, 56.70; H, 6.22; N, 15.26. Found: C, 56.95; H, 6.15; N, 15.13.

Compound **5b-Me**.

This compound had mp 130-133° (colorless crystals); ir (potassium bromide): 3115, 3072, 3048, 3000, 2965, 2925, 2853, 2231, 1605, 1419, 1268, 1223, 1162, 1155, 946, 925, 845, 817 cm^{-1}; ^{1}H-nmr: δ 7.74 and 7.65 (AB-q, J = 8.5 Hz, 2H, H-6 and H-7), 6.67 (s, 1H, H-3), 2.57 (s, 3H, 2-Me).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.51; H, 3.91; N, 17.69.

Compound **5c-Me.**

This compound had mp 124-128° (colorless crystals); ir (potassium bromide): 3137, 3082, 3009, 2961, 2922, 2855, 2234, 1606, 1442, 1423, 1262, 1182, 1144, 1064, 992, 925, 861 cm^{-1}; ^{1}H-nmr: δ 8.44 (d, J = 5.0 Hz, 1H, H-5), 7.65 (d, J = 5.0 Hz, 1H, H-4), 6.57 (q, J = 1.1 Hz, 1H, H-3), 2.60 (d, J = 1.2 Hz, 3H, 2-Me).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.57; H, 3.93; N, 17.77.

Compound **5d-Me.**

This compound had 115-119° (colorless crystals); ir (potassium bromide): 3185, 3145, 3104, 3086, 3002, 2963, 2927, 2854, 2236, 1600, 1572, 1434, 1385, 1274, 1239, 1187, 1058, 992, 923, 830 cm^{-1}; ^{1}H-nmr: δ 8.51 (d, J = 5.6 Hz, 1H, H-6), 7.54 (dd, J = 5.6, 0.9 Hz, 1H, H-7), 6.66 (qn, J = 0.9 Hz, 1H, H-3), 2.57 (d, J = 0.9 Hz, 3H, 2-Me).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17 71. Found: C, 68.32; H, 4.16; N, 17.63.

General Procedure for Cyanation of **4b-CN**, **4c-CN** and **4d-CN** with Trimethylsilyl Cyanide.

A mixture of *N*-oxide **4b-d-CN** (500 mg, 3.1 mmoles), trimethylsilyl cyanide (1.12 g, 11.3 mmoles) and triethylamine (440 mg, 4.3 mmoles) in acetonitrile (50 ml) was stirred and refluxed for 5 hours (88 hours for **4b-CN**). After evaporation of the solvent, the reaction mixture was dissolved in chloroform, washed with water and dried over magnesium sulfate. The residue of the chloroform solution was recrystallized from ether to give 2,5-dicyanofuro[3,2-*b*] **5b-CN** (361 mg, 68%), 2,7-dicyanofuro[2,3-*c*]- **5c-CN** (520 mg, 99%) and 2,4-dicyanofuro[3,2-*c*]pyridine **5d-Me** (522 mg, 99%) respectively.

Compound **5b-CN.**

This compound had mp 165-168° (colorless crystals); ir (potassium bromide): 3147, 3094, 2241, 1600, 1571, 1448, 1407, 1308, 1257, 1215, 1155, 1132, 946, 935, 853 cm^{-1}; ^{1}H-nmr: δ 8.06 (dd, 8.5, 0.9 Hz, 1H, H-7), 7.88 (d, J = 8.5 Hz, 1H, H-6), 7.74 (d, J = 0.9 Hz, 1H, H-3).

Anal. Calcd. for $C_9H_3N_3O$: C, 63.91; H, 1.78; N, 24.84. Found: C, 64.00; H, 1.91; N, 24.66.

Compound **5c-CN.**

This compound had mp 119-123° (colorless crystals); ir (potassium bromide): 3139, 3115, 3084, 2240, 1609, 1448, 1409, 1325, 1266, 1196, 1069, 936, 884 cm^{-1}; ^{1}H-nmr: δ 8.71 (d, J = 5.3 Hz, 1H, H-5), 7.91 (d, J = 5.3 Hz, 1H, H-4), 7.60 (s, 1H, H-3).

Anal. Calcd. for $C_9H_3N_3O$: C, 63.91; H, 1.78; N, 24.84. Found: C, 63.98; H, 1.97; N, 24.81.

Compound **5d-CN.**

This compound had mp 126-128° (colorless crystals); ir (potassium bromide): 3137, 3116, 3085, 2237, 1603, 1581, 1557, 1446, 1426, 1311, 1286, 1270, 1208, 1164, 1055, 1007, 945, 871, 849 cm^{-1}; ^{1}H nmr: δ 8.82 (d, J = 5.6 Hz, 1H, H-6), 7.84 (d, J = 5.6 Hz, 1H, H-7), 7.75 (s, 1H, H-3).

Anal. Calcd. for $C_9H_3N_3O$: C, 63.91; H, 1.78; N, 24.84. Found: C, 63.76; H, 1.80; N, 24.66.

General Procedure for Chlorination of **4a-Me**, **4b-Me**, **4c-Me**, **4d-Me**, **4b-CN**, **4c-CN** and **4d-CN** with Phosphorus Oxychloride.

A mixture of **4a-d-Me** (112 mg, 0.75 mmole) or **4b-d-CN** (119.5 mg, 0.75 mmole), phosphorus oxychloride (1 ml, 11.3 mmoles) and absolute chloroform (0.5 ml, ethanol in commercial chloroform was removed by treatment with sulfuric acid, phosphorus pentoxide and potassium carbonate and distillation) was refluxed for 1.5 hours for **4a-d-Me** (0.5 hours for **4b-d-CN**). After being cooled, the mixture was treated with ice-water and chloroform, basified with sodium bicarbonate and separated the layers. The chloroform layer was dried over magnesium sulfate and evaporated. Further processing of the residue is indicated in a subsequent paragraph.

4-Chloro-2-methylfuro[2,3-*b*]pyridine **6a-Me**.

The residue (100 mg) from **4a-Me** was distilled under reduced pressure to give 90 mg (71%) of **6a-Me** as a colorless oil of bp 120-140° (bath temperature)/20 mm Hg; ir (neat): 3184, 3120, 3084, 3019, 2968, 2925, 2853, 1602, 1578, 1468, 1440, 1371, 1358, 1241, 1169, 1148, 1012, 945, 935, 858, 815, 803, 765, 716 cm^{-1}; ^{1}H-nmr: δ 8.12 (d, J = 5.3 Hz, 1H, H-6), 7.18 (d, J = 5.3 Hz, 1H, H-5), 6.48 (q, J = 1.3 Hz, 1H, H-3), 2.51 (d, J = 1.3 Hz, 3H, 2-Me); ms: m/z (relative intensity) 169 (M^++2, 39), 168 (M^++1, 36), 167 (M^+, 100), 166 (84), 131 (21), 104 (31); hrms: 167.0136; M^+, Calcd. for C_8H_6NOCl: 167.0138.

Anal. Calcd. for C_8H_6NOCl: C, 57.33; H, 3.61; N, 8.36. Found: C, 57.15; H, 3.54; N, 8.67.

5-Chloro-2-methyl- **6b-Me** and 7-Chloro-2-methylfuro[3,2-*b*]-pyridine **6'b-Me.**

The residue (105 mg) from **4b-Me** was chromatographed on a silica gel column eluting with hexane-ethyl acetate (95:5) to afford compound **6b-Me** (4 mg, 3%) and **6'b-Me** (82 mg, 65%).

Compound **6b-Me.**

This compound had mp 90-92° (from ether, colorless crystals); ir (potassium bromide): 3119, 3074, 2964, 2919, 2854, 1598, 1561, 1413, 1290, 1265, 1198, 1186, 1151, 1093, 937, 907, 828, 802, 695 cm^{-1}; ^{1}H-nmr: δ 7.60 (dd, J = 8.5, 0.9 Hz, 1H, H-7), 7.13 (d, J = 8.5 Hz, 1H, H-6), 6.54 (qn, J = 0.9 Hz, 1H, H-3), 2.51 (d, J = 0.9 Hz, 3H, 2-Me); ms: m/z (relative intensity) 169 (M^++2,30), 168 (M^++1, 23), 167 (M^+, 100), 166 (46), 104 (50); hrms: 167.0141; M^+, Calcd. for C_8H_6NOCl: 167.0138.

Anal. Calcd. for C_8H_6NOCl: C, 57.33; H, 3.61; N, 8.36. Found: C, 56.95; H, 3.58; N, 8.09.

Compound **6'b-Me.**

This compound had bp 105-115° (bath temperture)/18 mm Hg (colorless oil); ir (neat): 3117, 3049, 3009, 2958, 2923, 2854, 1607, 1557, 1439, 1393, 1348, 1241, 1226, 1169, 967, 926, 956, 817, 762, 719 cm^{-1}; ^{1}H-nmr: δ 8.34 (d, J = 5.3 Hz, 1H, H-5), 7.14 (d, J = 5.3 Hz, 1H, H-6), 6.64 (q, J = 0.9 Hz, 1H, H-3), 2.54 (d, J = 0.9 Hz, 3H, 2-Me); ms: m/z (relative intensity) 169 (M^++2, 33), 168 (M^++1, 23), 167 (M^+, 100), 166 (47), 138 (16), 132 (15), 104 (62); hrms: 167.0136; M^+, Calcd. for C_8H_6NOCl: 167.0138.

Anal. Calcd. for C_8H_6NOCl: C, 57.33; H, 3.61; N, 8.36. Found: C, 57.90; H, 3.54; N, 8.49.

7-Chloro-2-methyl- **6c-Me** and 5-chloro-2-methylfuro[2,3-*c*]-pyridine **6'c-Me.**

The residue (120 mg) from **4c-Me** was chromatographed on a silica gel column eluting with hexane-ethyl acetate (97:3) to afford compound **6'c-Me** (4 mg, 3%) and **6c-Me** (91 mg, 72%).

Compound **6c-Me.**

This compound had mp 88-90° (from ether, colorless crystals); ir (potassium bromide): 3115, 3068, 2957, 2918, 2853, 1610, 1600, 1560, 1439, 1424, 1280, 1209, 1200, 1170, 1068, 969, 929, 839, 726 cm^{-1}; ^{1}H-nmr: δ 8.13 (d, J = 5.3 Hz, 1H, H-5), 7.35 (d, J = 5.3 Hz, 1H, H-7), 6.47 (q, J = 0.9 Hz, 1H, H-3), 2.55 (d, J = 0.9 Hz, 3H, 2-Me).

Anal. Calcd. for C_8H_6NOCl: C, 57.33; H, 3.61; N, 8.36. Found: C,57.55; H, 3.89; N, 8.36.

Compound **6'c-Me.**

This compound had bp 100-120° (bath temperature)/30 mm Hg (colorless oil); ^{1}H-nmr: δ 8.49 (s, 1H, H-7), 7.41 (s, 1H, H-4), 6.39 (q, J = 0.9 Hz, 1H, H-3), 2.52 (d, J = 0.9 Hz, 1H, 2-Me); ms: m/z (relative intensity) 169 (M^++2, 37), 168 (M^++1, 25), 167 (M^+, 100), 166 (39), 149 (34), 138 (16), 132 (15), 104 (11); hrms: 167.0145; M^+, Calcd. for C_8H_6NOCl: 167.0138.

Anal. Calcd. for C_8H_6NOCl: C, 57.33; H, 3.61; N, 8.36. Found: C, 56.98; H, 3.47; N, 8.56.

4-Chloro-2-methylfuro[3,2-*c*]pyridine **6d-Me.**

The residue (120 mg) from **4d-Me** was distilled under reduced pressure to give compound **6d-Me** (78 mg, 61%), colorless oil of bp 115-125° (bath temperature)/20 mm Hg; ir (neat): 3121, 3059, 2963, 2923, 2854, 1603, 1569, 1431, 1282, 1271, 1179, 1003, 952, 932, 816, 800, 757, 721 cm^{-1}; ^{1}H-nmr: δ 8.18 (d, J = 4.6 Hz, 1H, H-6), 7.29 (dd, J = 4.6, 0.9 Hz, 1H, H-7), 6.48 (qn, J = 0.9 Hz, 1H, H-3), 2.50 (d, J = 0.9 Hz, 1H, 2-Me); ms: m/z (relative intensity) 169 (M^++2, 32), 168 (M^++1, 32), 167 (M+, 100), 166 (68), 132 (33); hrms 167.0140; M^+, Calcd. for C_8H_6NOCl: 167.0138.

Anal. Calcd. for C_8H_6NOCl: C, 57.33; H, 3.61; N, 8.36. Found: C, 57.34; H, 3.56; N, 7.98.

5-Chloro-2-cyano- **6b-CN**, 7-Chloro-2-cyano- **6'b-CN** and 6-Chloro-2-cyanofuro[3,2-*b*]pyridine **6"b-CN.**

The residue (105 mg) was chromatographed on a silica gel column eluting with chloroform to give 70 mg (53%) of **6b-CN**, 19 mg (14%) of **6'b-CN** and 4 mg (3%) of **6"b-CN.**

Compound **6b-CN.**

This compound had mp 175-177° (from acetone-ether, colorless crystals); ir (potassium bromide): 3135, 3074, 2235, 1579, 1548, 1407, 1265, 1195, 1139, 1104, 944, 851, 833, 705 cm^{-1}; ^{1}H-nmr: δ 7.89 (dd, J = 8.8, 0.9 Hz, 1H, H-7), 7.60 (d, J = 0.9 Hz, 1H, H-3), 7.47 (d, J = 8.8 Hz, 1H, H-6).

Anal. Calcd. for $C_8H_3N_2OCl$: C, 53.81; H, 1.69; N, 15.69. Found: C, 53.85; H, 1.83; N, 15.74.

Compound **6'b-CN.**

This compound had mp 105-108° (from ether-hexane, colorless crystals); ir (potassium bromide): 3138, 3087, 2238, 1600, 1564, 1544, 1479, 1380, 1243, 1234, 1130, 971, 937, 860, 844, 824, 693 cm^{-1}; ^{1}H-nmr: δ 8.62 (d, J = 5.2 Hz, 1H, H-5), 7.71 (s, 1H, H-3), 7.49 (d, J = 5.2 Hz, 1H, H-6).

Anal. Calcd. for $C_8H_3N_2OCl$: C, 53.81; H, 1.69; N, 15.69. Found: C, 53.81; H, 1.77; N, 15.58.

Compound **6"b-CN.**

This compound had mp 98-102° (from hexane, colorless crystals); ir (potassium bromide): 3139, 3032, 2235, 1599, 1568, 1461, 1409, 1382, 1254, 1179, 1082, 1052, 954, 847, 802, 771 cm^{-1}; ^{1}H-nmr: δ 8.70 (d, J = 2.0 Hz, 1H, H-5), 7.91 (dd, J = 2.0, 0.9 Hz, 1H, H-7), 7.87 (d, J = 0.9 Hz, 1H, H-3); ms: m/z (relative intensity) 180 (M^++2, 34), 179 (M^++1, 12), 178 (M^++, 100), 150 (20), 135 (12), 132 (10); hrms 177.9928; M^+, Calcd. for $C_8H_3N_2OCl$: 177.9934.

Anal. Calcd. for $C_8H_3N_2OCl$: C, 53.81; H, 1.69; N, 15.69. Found: C, 53.91; H, 1.85; N, 15.48.

7-Chloro-2-cyano- **6c-CN**, 5-Chloro-2-cyano- **6'c-CN** and 4-Chloro-2-cyanofuro[2,3-*c*]pyridine **6"c-CN.**

The residue (100 mg) from **4c-CN** was chromatographed on a silica gel column eluting with chloroform to give **6c-CN** (80 mg, 60%), **6'c-CN** (7 mg, 5%) and **6"c-CN** (3 mg, 2%).

Compound **6c-CN.**

This compound had mp 131-134° (from hexane-ether, colorless needles); ir (potassium bromide): 3122, 3104, 3071, 2239, 1603, 1575, 1448, 1404, 1184, 1069, 974, 939, 865, 823 cm^{-1}; ^{1}H-nmr: δ 8.35 (d, J = 5.3 Hz, 1H, H-5), 7.61 (d, J = 5.3 Hz, 1H, H-4), 7.55 (s, 1H, H-3).

Anal. Calcd. for $C_8H_3N_2OCl$: C, 53.81; H, 1.69; N, 15.69. Found: C, 53.68; H, 1.70; N, 15.59.

Compound **6'c-CN.**

This compound had mp 144-147° (from acetone-ether, colorless needles); ir (potassium bromide): 3126, 3102, 3079, 3024, 2241, 1603, 1578, 1551, 1445, 1388, 1273, 1251, 1184, 1171, 1069, 943, 921, 883, 723 cm^{-1}; ^{1}H-nmr: δ 8.78 (dd, J = 0.8, 0.6 Hz, 1H, H-7), 7.67 (d, J = 0.8 Hz, 1H, H-3), 7.44 (d, J = 0.6 Hz, 1H, H-4).

Anal. Calcd. for $C_8H_3N_2OCl$: C, 53.81; H, 1.69; N, 15.69. Found: C, 53.70; H, 1.80; N, 15.51.

Compound **6"c-CN.**

This compound had mp 112-117° (from ether, colorless crystals); ir (potassium bromide): 3114, 3089, 2243, 1579, 1556, 1456, 1403, 1259, 1176, 1109, 957, 947, 882, 835 cm^{-1}; ^{1}H-nmr: δ 8.91 (d, J = 0.6 Hz, 1H, H-7), 8.56 (s, 1H, H-5), 7.58 (d, J = 0.6 Hz, 1H, H-3); ms: m/z (relative intensity) 180 (M^++2, 33), 179 (M^++1, 12), 178 (M^+, 100), 143 (35), 123 (15), 115 (16), 88 (47); hrms: 177.9925; M^+, Calcd. for $C_8H_3N_2OCl$: 177.9934.

4-Chloro-2-cyanofuro[3,2-*c*]pyridine **6d-CN.**

The residue (103 mg) from **4d-CN** was recrystallized from ether to afford 89 mg (67%) of compound **6d-CN,** colorless

needles of mp 115-116°; ir (potassium bromide): 3140, 3105, 3086, 3071, 2236, 1601, 1576, 1437, 1419, 1301, 1263, 1188, 961, 939, 836, 817 cm^{-1}; ^{1}H-nmr: δ 8.47 (d, J = 5.9 Hz, 1H, H-6), 7.58 (d, J = 1.2 Hz, 1H, H-3), 7.49 (dd, J = 5.9, 1.2 Hz, 1H, H-7).

Anal. Calcd. for $C_8H_3N_2OCl$: C, 53.81; H, 1.69; N, 15.69. Found: C, 53.57; H, 1.73; N, 15.50.

General Procedure for Acetoxylation of **4a-Me**, **4b-Me**, **4c-Me**, **4d-Me**, **4b-CN**, **4c-CN** and **4d-CN** with Acetic Anhydride.

A mixture of **4a-d-Me** (112 mg, 0.75 mmole) or **4b-d-CN** (119.5 mg, 0.75 mmole) in acetic anhydride (2 ml) was refluxed for 1.5 hours (2.5 hours for **4b-CN**, 1 hour for **4c-CN** and **4d-CN**). After removal of the excess of acetic anhydride under reduced pressure, the reaction mixture was treated with water, basified with sodium bicarbonate and extracted with chloroform. The chloroform extract was dried over magnesium sulfate and evaporated. Further processing of the residue is indicated in a subsequent paragraph.

6-Acetoxy-2-methyl- **7a-Me** and *trans*-2,3-Diacetyl-2-methyl-2,3-dihydrofuro[2,3-*b*]pyridine **8**.

The residue (145 mg) from **4a-Me** was chromatographed on a silica gel column eluting with hexane-ethyl acetate (97:3) to give 102 mg (70%) of **7a-Me** and 25 mg (10%) of **8**.

Compound **7a-Me.**

This compound had bp 105-125° (bath temperature)/0.1 mm Hg (colorless oil); ir (neat): 3115, 2924, 2855, 1770, 1593, 1459, 1401, 1371, 1294, 1272, 1194, 1162, 1110, 1021, 984, 899, 830, 765 cm^{-1}; ^{1}H-nmr: δ 7.84 (d, J = 8.0 Hz, 1H, H-4), 6.94 (d, J = 8.0 Hz, 1H, H-5), 6.38 (q, J = 0.9 Hz, 1H, H-3), 2.48 (d, J = 0.9 Hz, 3H, 2Me), 2.35 (s, 3H, -Ac).

Anal. Calcd. for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.78; H, 4.77; N, 7.21.

Compound **8**.

This compound had mp 137-142° (sublimated at 110-120°(bath temperature)/0.1 mm Hg, colorless crystals); ir (potassium bromide): 3068, 3035, 3010, 2923, 2858, 1742, 1605, 1426, 1386, 1302, 1248, 1234, 1197, 1111, 1090, 1036, 947, 896, 802 cm^{-1}; ^{1}H-nmr: δ 8.20 (dd, J = 5.3, 1.8 Hz, 1H, H-6), 7.73 (dd, J = 7.3, 1.8 Hz, 1H, H-4), 6.95 (dd, J = 7.3, 5.3 Hz, 1H, H-5), 6.35 (s, 1H, H-3), 2.14 (s, 3H, -Ac), 2.04 (s, 3H, -Ac), 1.88 (s, 3H, 2-Me).

Anal. Calcd. for $C_{12}H_{13}NO_5$: C, 57.37; H, 5.10; N, 5.58. Found: C, 57.60; H, 5.10; N, 5.45.

3-Acetoxy-2-methyl- **9b** and 2-Acetoxymethylfuro[3,2-*b*]pyridine **10b**.

The residue (165 mg) from **4b-Me** was chromatographed on a silica gel column eluting with hexane-ethyl acetate (95:5) to yield **9b** (92 mg, 64%) and **10b** (48 mg, 34%).

Compound **9b**.

This compound had bp 130-140° (bath temperature)/0.01 mm Hg (colorless oil); ir (neat): 3122, 3072, 2926, 2851, 1741, 1587, 1482, 1431, 1372, 1272, 1201, 1154, 935, 805 cm^{-1}; ^{1}H-nmr: δ 8.50 (dd, J = 5.0, 1.2 Hz, 1H, H-5), 7.64 (dd, J = 8.5, 1.2 Hz, 1H, H-7), 7.17 (dd, J = 8.5, 5.0 Hz, 1H, H-6), 2.43 (s, 6H, -Ac and 2-Me); ms: m/z (relative intensity) 191 (M^+, 1), 165 (64), 149 (61), 147 (35), 122 (71), 95 (85), 94 (100), 79 (29), 77 (29); hrms: 191.0583. M^+, Calcd. for $C_{10}H_9NO_3$: 191.0582.

Anal. Calcd. for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.48; H, 4.71; N, 7.01.

Compound **10b**.

This compound had bp 135-140° (bath temperature)/0.1 mm Hg (colorless oil); ir (neat): 3120, 3024, 2926, 2851, 1747, 1604, 1414, 1378, 1365, 1236, 1172, 1143, 1030, 938, 818, 794 cm^{-1}; ^{1}H-nmr: δ 8.55 (dd, J = 4.7, 1.5 Hz, 1H, H-5), 7.75 (ddd, 8.5, 1.5, 0.5 Hz, 1H, H-7), 7.24 (dd, J = 8.5, 4.7 Hz, 1H, H-6), 6.98 (d, J = 0.5 Hz, 1H, H-3), 5.25 (s, 2H, 2-CH_2OAc), 2.15 (s, 3H, -Ac); ms: m/z (relative intensity) 191 (M^+, 18), 149 (46), 132 (35), 120 (19), 103 (19); hrms: 191.0578; M^+, Calcd. for $C_{10}H_9NO_3$: 191.0582.

Anal. Calcd. for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.49; H, 4.68; N, 6.98.

3-Acetoxy-2-methyl- **9c** and 2-Acetoxymethylfuro[2,3-*c*]pyridine **10c**.

The residue (150 mg) from **4c-Me** was chromatographed on a silica gel column eluting with hexane-ethyl acetate (95:5) to give **9c** (80 mg, 55%) and **10c** (40 mg, 28%).

Compound **9c**.

This compound had bp 145-155° (bath temperature)/0.1 mm Hg (colorless oil); ir (neat): 3036, 2996, 2925, 2854, 1756, 1606, 1584, 1434, 1374, 1224, 1200, 1155, 1040, 959, 946, 888, 801 cm^{-1}; ^{1}H-nmr: δ 8.75 (s, 1H, H-7), 8.31 (d, 5.0 Hz, 1H, H-5), 7.29 (d, J = 5.0 Hz, 1H, H-4), 2.42 (s, 3H, -Ac), 2.39 (s, 3H, 2-Me); ms: m/z (relative intensity) 191 (M^+, 13), 149 (52), 148 (17), 132 (11), 120 (9), 103 (6); hrms: 191.0587; M^+, Calcd. for $C_{10}H_9NO_3$: 191.0582.

Anal. Calcd. for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.50; H, 4.61; N, 7.52.

Compound **10c**.

This compound had bp 140-150°(bath temperature)/0.1 mm Hg (colorless oil); ir (neat): 3054, 2926, 1749, 1608, 1472, 1428, 1367, 1189, 1143, 1032, 830 cm^{-1}; ^{1}H-nmr: δ 8.88 (s, 1H, H-7), 8.43 (d, J = 5.3 Hz, 1H, H-5), 7.52 (d, J = 5.3 Hz, 1H, H-4), 6.80 (s, 1H, H-3), 5.25 (s, 2H, 2-CH_2OAc), 2.15 (s, 3H, -Ac).

Anal. Calcd. for $C_{10}H_9NO_3$: C, 62.82; H, 4.74; N, 7.33. Found: C, 62.87; H, 4.68; N, 7.22.

2-Methylfuro[3,2-*c*]pyridin-4(5*H*)-one **11d-Me.**

The residue (100 mg) from **4d-Me** was recrystallized from acetone to give 58 mg (52%) of compound **11d-Me** which was identified by comparison of the ir and ^{1}H-nmr spectra with those of authentic sample [5].

5-Acetoxy-2-cyano- **7b-CN** and 6-Acetoxy-2-cyanofuro[3,2-*b*]-pyridine **7'b**.

The residue (90 mg) from **4b-CN** was chromatographed on a silica gel column eluting with chloroform to give 37 mg (25%) of **7b-CN** and 6 mg (4%) of **7'b**.

Compound **7b-CN.**

This compound had mp 147-151° (from ether-hexane, colorless crystals); 3113, 3105, 3083, 2923, 2853, 2234, 1762, 1553, 1415, 1369, 1210, 1114, 941, 906, 863, 839 cm^{-1}; ^{1}H-nmr: δ 7.96 (dd, J = 9.1, 0.9 Hz, 1H, H-7), 7.59 (d, J = 0.9 Hz, 1H, H-3), 7.21 (d, J = 9.1 Hz, 1H, H-6). 2.39 (s, 3H, Ac).

Anal. Calcd. for $C_{10}H_6N_2O_3$: C, 59.41; H, 2.99; N, 13.86. Found: C, 59.30; H, 3.15; N, 13.64.

Compound **7'b**.

This compound had mp 88-92° (from hexane, colorless crystals); ir (potassium bromide): 3066, 2924, 2854, 2238, 1774, 1606, 1579, 1485, 1373, 1274, 1202, 1137, 1015, 935, 905, 877 cm^{-1}; ^{1}H-nmr: δ 8.54 (d, J = 2.1 Hz, 1H, H-5), 7.76 (dd, J = 2.1, 0.9 Hz, 1H, H-7), 7.66 (d, J = 0.9 Hz, 1H, H-3), 2.40 (s, 3H, -Ac); ms: m/z (relative intensity) 202 (M^+, 20), 161 (15), 160 (100), 120 (17), 118 (18), 117 (8), 87 (45), 85 (100), 83 (100); hrms: 202.0368; M^+, Calcd. for $C_{10}H_6N_2O_3$: 202.0378.

2-Cyanofuro[2,3-*c*]pyridin-7(6*H*)-one **11c-CN**.

The residue (100 mg) from **4c-CN** was recrystallized from acetone to give compound **11c-CN** (86 mg, 72%), mp 295-298° (colorless crystals); ir (potassium bromide): 3114, 3055, 3009, 2965, 2898, 2237, 1683, 1616, 1519, 1483, 1369, 1293, 1264, 1200, 1132, 955, 856, 779 cm^{-1}; ^{1}H-nmr (deuteriomethanol): δ 7.68 (s, 1H, H-3), 7.30 (d, J = 6.7 Hz, 1H, H-4), 6.70 (d, J = 6.7 Hz, 1H, H-5).

Anal. Calcd. for $C_8H_4N_2O_2$: C, 60.01; H, 2.52; N, 17.49. Found: C, 59.89; H, 2.82; N, 17.12.

2-Cyanofuro[3,2-*c*]pyridin-4(5*H*)-one **11d-CN**.

The residue (95 mg) from **4d-CN** was recrystallized from acetone to give 76 mg (64%) of **11d-CN**, colorless crystals of mp 251-255°; ir (potassium bromide): 3300-2755 (broad), 2236, 1696, 1581, 1428, 1220, 1163, 1066, 952, 859, 785 cm^{-1}; ^{1}H-nmr (deuteriomethanol): δ 7.80 (d, J = 0.9 Hz, 1H, H-3), 7.54 (d, J = 7.3 Hz, 1H, H-6), 6.76 (dd, J = 7.3, 0.9 Hz, 1H, H-7).

Anal. Calcd. for $C_8H_4N_2O_2$: C, 60.01; H, 2.52; N, 17.49. Found: C, 59.60; H, 2.70; N, 17.09.

REFERENCES AND NOTES

[1] Part **XXVI**. S. Yamaguchi, H. Saitoh, M. Kurosaki, H. Yokoyama, Y. Hirai and S. Shiotani, *J. Heterocyclic Chem.*, submitted.

[2] H. Morita and S. Shiotani, *J. Heterocyclic Chem.*, **23**, 1465 (1986).

[3] S. Shiotani and H. Morita, *J. Heterocyclic Chem.*, **23**, 665 (1986).

[4] H. Morita and S. Shiotani, *J. Heterocyclic Chem.*, **23**, 549 (1986).

[5] F. Eloy and A. Deryckere, *J. Heterocyclic Chem.*, **8**, 57 (1971).

[6a] R. A. Abramovitch and G. M. Singer, *Chem. Heterocyclic Compound,* **14**, Suppl. 1, 1 (1974); [b] R. A. Abramovitch and B. M. Smith, *Chem. Heterocyclic Compound,* **14**, Suppl. 2, 1 (1974); [c] S. Oae and R. Ogino, *Heterocycles,* **6**, 583 (1976).

[7] S. Shiotani, K. Taniguchi, T. Ishida and Y. In, *J. Heterocyclic Chem.*, **33**, 647 (1996).

[8a] S. Shiotani and K. Taniguchi, *J. Heterocyclic Chem.*, **33**, 1051 (1996); [b] S. Shiotani and K. Taniguchi, *J. Heterocyclic Chem.*, **34**, 925 (1997).