# Furopyridines. XIII [1]. Reaction of 2-Methylfuro[2,3-*b*]-, -[3,2-*b*]-, -[2,3-*c*]- and -[3,2-*c*]pyridines with Lithium Diisopropylamide



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Lithiation of 2-methylfuro[2,3-*b*]- **1a**, -[2,3-*c*]- **1c** and -[3,2-*c*]pyridine **1d** with lithium diisopropylamide at −75° and subsequent treatment with deuterium chloride in deuterium oxide afforded 2-monodeuteriomethyl compounds **2a, 2c** and **2d**, while 2-methylfuro[3,2-*b*]pyridine **1b** gave a mixture of **1b, 2b**, 2-methyl-3-deuteriofuro[3,2-*b*]pyridine **2'b** and 2-(1-proynyl)pyridin-3-ol **5**. The same reaction of **1a** at −40° gave 3-(1,2-propadienyl)pyridin-2-ol **3** and 3-(2-propynyl)pyridin-2-ol **4**. Reaction of the lithio intermediates from **1a, 1c** and **1d** with benzaldehyde, propionaldehyde and acetone afforded the corresponding alcohol derivatives **6a, 6c, 6d, 7a, 7c, 7d, 8a, 8c** and **8d** in excellent yield; while the reaction of lithio intermediate from **1b** gave the expected alcohols **6b** and **8b** in lower yields accompanied by formation of 3-alkylated compounds **9, 11, 12** and compound **5**. While reaction of the intermediates from **1a, 1b** and **1d** with *N,N*-dimethylacetamide yielded the 2-acetonyl compounds **13a, 13b** and **13d** in good yield, the same reaction of **1c** did not give any acetylated product but recovery of the starting compound almost quantitatively.

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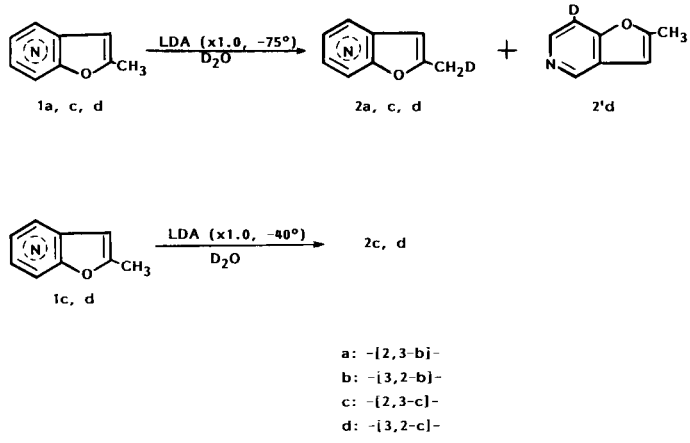
In continuation of our interest in the chemistry of furopyridines, in a previous investigation [1] we studied the reaction of 3-bromo, 2-phenylthio and 2-phenylthio-3-bromo derivatives of furopyridines with several alkyllithiums and found that the bromine atom of 3-bromo- and 2-phenylthio-3-bromofuropyridines and hydrogen at the 3-position of 2-phenylthiofuropyridines is replaced with lithium and the 1-2 bond of the furopyridines is cleaved subsequently to give *o*-ethynylpyridinols. In the meantime, the methyl group at the 2-position of furopyridines is expected to be easily lithiated with alkyllithium or lithium amides to form a lithio intermediate, through which *C*-alkyl, *C*-acyl and other *C*-substituted compounds can be derived; thus, we attempted to examine the behaviour of the 2-methyl derivatives of furo[2,3-*b*]- **1a** [2], furo[3,2-*b*]- **1b** [3], furo[2,3-*c*]- **1c** [4] and furo[3,2-*c*]pyridines **1d** [5] towards lithium diisopropylamide (LDA) and the subsequent reaction with an electrophile.

When 2-methylfuro[2,3-*b*]- **1a** and -[2,3-*c*]pyridine **1c** were reacted with 1.0 molar equivalent of LDA in tetrahydrofuran at −75° for 6 minutes and then treated with deuterium chloride in deuterium oxide, the corresponding 2-monodeuteriomethylfuropyridines **2a** and **2c** were obtained in about 85% from **1a** and 70% yield from **1c** accompanied by recovery of the starting compounds **1a** (about 15%) and **1c** (about 25%). The prolonged reaction time (1 hour) did not change the product but the yield of the monodeuterio compounds was increased (90% for both **2a** and **2c**).

While, the reaction of 2-methylfuro[3,2-*b*]pyridine **1b** with 1.0 molar equivalent of LDA at −75° for 6 minutes yielded a mixture of compound **1b**, 2-monodeuteriomethyl- **2b**, 2-methyl-3-deuteriofuro[3,2-*b*]pyridine **2'b** and 2-(1-propynyl)pyridin-3-ol **5** in the ratio of 10:40:25:25. The prolonged reaction time (1 hour) increased the yield of **2b**

Chart 1

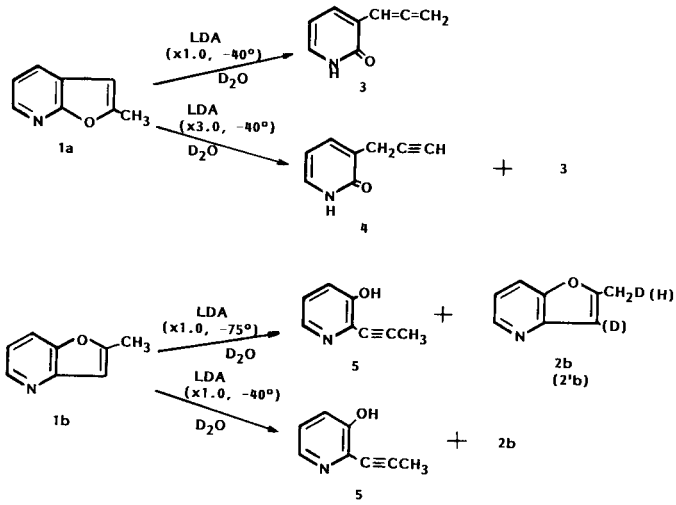



and **5** (**2b**:**2'b**:**5** = 50:10:40). Compound **5** was isolated from the crude product by chromatography on a silica gel column, and the structure was confirmed by its ir and pmr spectra and elemental analysis. The ir spectrum of **5** showed an absorption due to a triple bond at 2220 $cm^{-1}$, and the pmr spectrum signals of protons of the pyridine nucleus at δ 8.11 (H-6), 7.31 (H-4) and 7.10 (H-5) and that of the methyl group at δ 2.01. The reaction of 2-methylfuro[3,2-*c*]pyridine **1d** with 1.0 molar equivalent of LDA at −75° for 6 minutes gave a mixture of compound **1d**, 2-monodeuteriomethyl- **2d** and 2-methyl-7-deuteriofuro-[3,2-*c*]pyridine **2'd** (35:40:25). The same reaction with 2.0 molar equivalents of LDA for 2 hours yielded a mixture of **2d** and **2'd** in the ratio of 80:20.

Interestingly, the reaction of **1a** with 1.0 molar equivalent of LDA at −40° afforded 3-(1,2-propadienyl)pyridin-2-ol **3** in almost quantitative yield, and the reaction of **1a** with 3.0 molar equivalent of LDA at −40° gave a mixture of the allene compound **3** and 3-(2-propynyl)pyridin-2-ol **4**

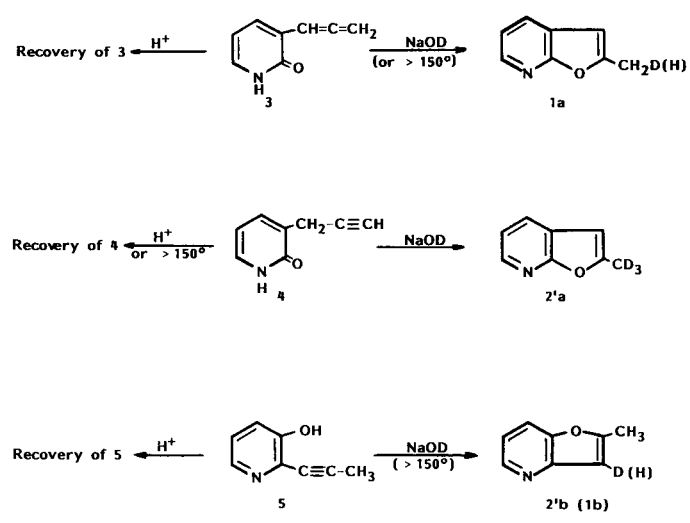
in the ratio of 1:1, which were isolated by chromatography on a silica gel column. The structures of **3** and **4** were confirmed by ir and nmr spectra and elemental analysis. The former showed an absorption of an allene structure at 1930 $cm^{-1}$ and the latter a terminal triple bond at 2100 $cm^{-1}$ in the ir spectra. The pmr spectrum of **3** exhibited signals assignable to the protons of the pyridine nucleus at $\delta$ 7.55 (H-6), 7.30 (H-4) and 6.31 (H-5) and the protons of the terminal methylene and methine groups at $\delta$ 5.16 and 6.53. The $^{13}C$-nmr spectrum exhibited signals of the terminal methylene, methine and quarternary carbon at $\delta$ 78.80, 87.45 and 210.41 and those of the pyridine nucleus at $\delta$ 107.46 (C-5), 125.00 (C-3), 132.71 (C-4), 137.07 (C-6) and 163.34 (C-2) respectively. Compound **4** showed signals of the protons of the pyridine nucleus at $\delta$ 7.77 (H-6), 7.35 (H-4) and 6.33 (H-5), proton of acetylene at $\delta$ 3.53. When 2-methylfuro[3,2-*b*]pyridine **1b** was reacted with 1.0 or 2.0 molar equivalents of LDA at $-40°$ for 2 to 6 hours and then treated with deuterium chloride in deuterium oxide, a mixture of compounds **2b** and **5** (*ca.* 1:1) was obtained. Whilst, the reaction of **1c** with the same reagent at $-40°$ afforded **2c** in almost quantitative yield, and **1d** gave **2d** (40% yield) and an unidentifiable resinous product.

Chart 2




It is worth noting that the allene and the methylacetylene compounds **3** and **5** were recyclized to the furopyridines **1a** and **1b** in almost quantitative yield by heating above 150°, while the terminal acetylene compound **4** could be distilled without any structural change at this temperature *in vacuo*; moreover, compound **3** was converted to the monodeuteriomethyl derivative **2a**, compound **4** to 2-trideuteriomethylfuro[2,3-*b*]pyridine **2'a** and compound **5** to 2-methyl-3-deuteriofuro[3,2-*b*]pyridine **2'b** by allowing the alkaline solution to stand in deuteriomethanol at 40° for 20 hours, while compounds **3**, **4** and **5** remained unchanged in the acidic solution by warming at 40° for 2-3 days.

Chart 3




In order to examine the reactivity with electrophiles, the lithio intermediates from 2-methylfuropyridines **1a**, **1b**, **1c** and **1d** in tetrahydrofuran were treated with benzaldehyde, propionaldehyde, acetone and *N,N*-dimethylacetamide (DMA). The reaction of compounds **1a**, **1c** and **1d** with the carbonyl compounds afforded the corresponding secondary alcohols **6a**, **6c**, **6d** and **7a**, **7c**, **7d** and the tertiary alcohols **8a**, **8c**, **8d** in excellent yields. However, reaction of the lithio intermediate from compound **1b** with benzaldehyde gave a mixture of several compounds, from which 2-(2-hydroxy-2-phenylethyl)furo[3,2-*b*]pyridine **6b**, 2-methyl-3-(1-hydroxy-1-phenylmethyl)furo[3,2-*b*]pyridine **9**, 2-(4-hydroxy-4-phenyl-1-butynyl)pyridin-3-ol **10**, **5** and **1b** were isolated by chromatography on a silica gel column; the reaction with propionaldehyde gave a mixture, from which 2-methyl-3-(hydroxypropyl)furo[3,2-*b*]pyridine **11**, **5** and **1b** could be isolated in fairly good yield, and the reaction with acetone gave a mixture, from which 2-(2-hydroxy-2-methylpropyl)furo[3,2-*b*]pyridine **8b**, 2-methyl-3-(1-hydroxy-1-methylethyl)furo[3,2-*b*]pyridine **12**, **5** and **1b** were isolated. The structures of these compounds were determined by ir, pmr, mass spectra and elemental analyses.

Chart 4

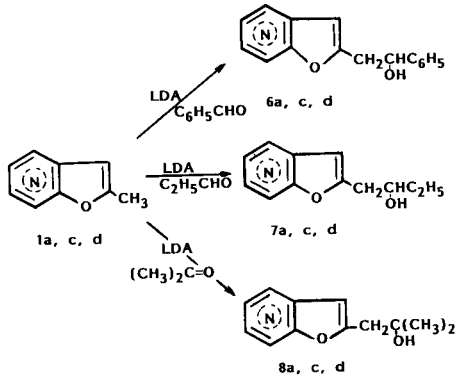
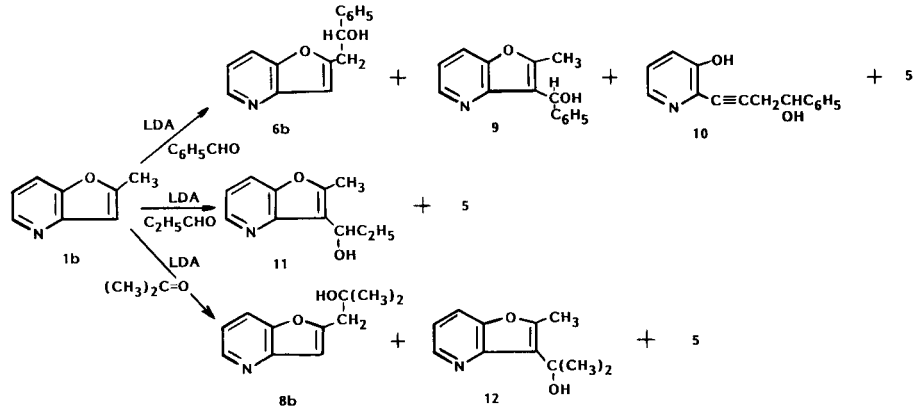


Chart 5



In contrast, the reaction of the lithio intermediates from 2-methylfuropyridines **1a, 1b, 1c** and **1d** with DMA gave results somewhat different from those with the carbonyl compounds. The intermediate from compounds **1a** and **1d** afforded the expected 2-acetonyl derivative **13a** and **13d** (50-60% from **1a** and 40-75% from **1d**) accompanied by recovery of the starting compound **1a** (35-50%) and **1d** (20-55%). The lithio intermediate from **1b** afforded a mixture of 2-acetonyl compounds **13b**, 2-methyl-3-acetylfuro-[3,2-*b*]pyridine **14**, **5** and **1b** by reaction with DMA at −75°. The lithio intermediate from **1c** did not give any reaction product, but recovery of **1c** in 90-95% yield by reaction with DMA at −75°.

These results suggest that exchange of the methyl hydrogen of 2-methylfuropyridines **1a, 1b, 1c** and **1d** with lithium from LDA proceeds rapidly, and the lithio intermediates from **1a, 1c** and **1d** are stable at −75° and react with carbonyl compounds to give the expected hydroxyl compound in excellent yield; while that from **1b** is less stable and isomerizes into the acetylene compound **5** through intramolecular exchange of the lithium with the hydrogen at the 3-position and fission of the 1-2 bond even at −75°. At −40°, the intermediates from both the quinoline isosteres **1a** and **1b** are unstable and are isomerized to the correpsonding allene or acetylene compounds **3**, **4** or **5**.

In a previous paper, we reported that the electronic effect of the pyridine ring of furopyridines upon C-2 is exerted mainly through the C-3–C-3a link by the comparison of $^{13}$C-nmr spectral data of 2- or 3-substituted furopyridines [6]. This postulation is supported by our results in this paper. Thus, the electron withdrawing effect of the ring nitrogen is efficiently exerted upon the 2-methyl group in furo[2,3-*c*]pyridine **1c**, and much less in furo[2,3-*b*]- **1a** and furo[3,2-*c*]pyridine **1d**; that is, the resonance form having a negative charge on the ring nitrogen is important for the intermediate **1c-Li** and not for the others. Accordingly, the negative charge on the lithiomethyl carbon of compound **1c** is widely distributed and the anion is stabilized, thus, the lithio intermediate from **1c** is much less reactive to a weak electrophile, DMA.

Chart 6

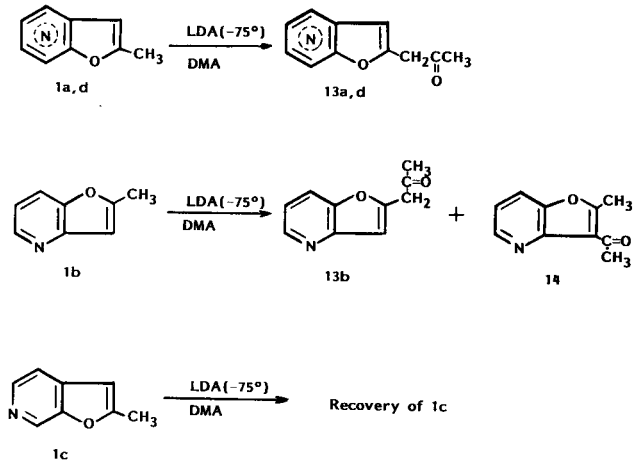
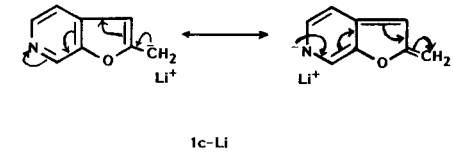


Chart 7



On the other hand, the inductive effect of the ring nitrogen of compound **1b** affects directly upon C-3, therefore the hydrogen at the 3-position becomes acidic and is exchanged intramolecularly with lithium at the methyl carbon to form the 3-lithio intermediate; moreover, the intermediate may be stabilized by forming a chelate ring between the lithium and the lone-pair electrons of the ring nitrogen. The acetylene compound **5** is afforded from this intermediate through fission of the 1-2 bond.

In the case of intermediate from **1a**, the sp$^2$ character of the orbital for one of the lone electron pairs and p character for another of the ring oxygen are much reduced because of the steric hindrance between the both lone-pair electrons of the oxygen and the nitrogen in the peri position; therefore, the conjugation of the lone-pair electrons

of the oxygen with the carbon double bonds would be much reduced. Thus, at −40°, the 1-2 bond is cleaved by the strong inductive effect of the oxygen and the allene compound **3** is formed. The allene compound isomerizes into the terminal acetylene compound **4** in the presence of excess LDA [7]. At −40°, the effect of the mode of annelation for compounds **1b**, **1c** and **1d** was essentially same with that at −75° respectively.

This research has demonstrated that the lithiation of 2-methylfuropyridines and the subsequent reaction of electrophiles are significantly affected by the mode of annelation of the furopyridines.

## EXPERIMENTAL

Melting points were determined by using a Yanagimoto micro melting point apparatus. All melting points are uncorrected. The ir spectra were recorded on a JASCO A-102 spectrometer. The pmr spectra were taken on a JEOL JNM-PMX 60 instrument with tetramethylsilane as an internal reference. The $^{13}$C-nmr spectra were taken JEOL GX-270 (68.7 MHz) spectrometer. Mass spectra were obtained by using JEOL JMS-D300 and JEOL JMS-OISG-2 spectometer.

Thin-layer chromatography (tlc) analyses were performed on silica gel (Kieselgel 60 F-254 on aluminium sheet, Merck). Visualization of spots was effected with uv light and iodine impregnated silica gel. Column chromatography was performed on silica gel (Kieselgel 60, 70-230 mesh, Merck).

Reaction of 2-Methylfuropyridines **1a**, **1b**, **1c** and **1d** with Lithium Diisopropylamide and Deuterium Chloride in Deuterium Oxide at −75°.

General Procedure.

A solution of 2-methylfuropyridine **1** (300 mg, 2.26 mmoles) in 5 ml of dry tetrahydrofuran was added by syringe over a period of 5 minutes to a stirred solution of lithium diisopropylamide prepared from diisopropylamine (230 mg, 2.27 mmoles) and *n*-butyllithium in hexane (1.42 ml, 1.6*M*, 2.27 mmoles) in 20 ml of dry tetrahydrofuran at −75° under a nitrogen atmosphere. After stirring at this temperature for 6 minutes, deuterium chloride in deuterium oxide (*ca.* 10%, 3 ml) was added at once and stirred at room temperature for 5 minutes. The mixture was basified with sodium bicarbonate and treated with chloroform and water, and the organic layer was separated. After drying over magnesium sulfate, the chloroform solution was evaporated *in vacuo* to give the crude deuterio compound **2**.

Distillation of the product from **1a**, **1c** and **1d** afforded a colorless oil of bp 140-150°/40 mm Hg in almost quantitative yield. The pmr spectra revealed that the distillates from **1a** and **1c** were composed of 2-monodeuteriomethyl-, **2a** and **2c**, and 2-methylfuropyridines, **1a** and **1c** in the ratio of 85:15 and 70:30; and that from **1d**, 2-monodeuteriomethyl- **2d**, 2-methyl-7-deuteriofuro[3,2-*c*]pyridine **2'd** and **1d** (40:25:35). The ratio of deuteriodeprotonation was determined by integration over the proton magnetic resonance of the 2-methyl protons (and the proton at 7-position of **2'd**) using the resonance of protons of the pyridine ring as the internal standard.

The crude deuterio product from **1b** was treated with ether, and from the ether solution the crystalline solid **5** separated (60 mg, 20%). The residue from the ether solution was distilled *in vacuo* to give an oil (230 mg) of bp 135-145°/40 mm Hg which was shown to be composed of **1b**, 2-monodeuteriomethyl- **2b** and 2-methyl-3-deuteriofuro[3,2-*b*]pyridine **2'b** (15:55:30) by its pmr spectrum.

2-(1-Propynyl)pyridin-3-ol **5**.

The crystalline solid **5** was recrystallized from acetone to give a pure sample of **5** as colorless cubes, mp 143-145°; ir (potassium bromide): 3200-2000 (broad), 2220 (-C≡C-), 1570, 1450, 1435, 1340, 1305, 1280, 1250, 1110, 1065, 990, 955, 905, 855, 845, 780, 745 cm$^{-1}$; pmr (deuteriochloroform): δ 8.11 (dd, J = 2.0, 4.4 Hz, 1H, H-6), 7.31 (dd, J = 2.0, 8.8 Hz, 1H, H-4), 7.10 (dd, J = 4.4, 8.8 Hz, 1H, H-5), 2.10 (s, 3H, -C$H_3$).

*Anal.* Calcd. for $C_8H_7NO$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.54; H, 5.31; N, 10.23.

When the reaction of the 2-methylfuropyridines **1a**, **1b**, **1c** or **1d** with 1.0 equivalent of lithium diisopropylamide was continued for 1 hour, the yield of the deuteriodeprotonation products was increased; 90:10 for **2a:1a** from **1a**, 50:10:40 for **2b:2'b:5** from **1b**, 90:10 for **2c:1c** from **1c** and 60:25:15 for **2d:2'd:1d** from **1d**, respectively.

The properties of the product (containing more than 90% of **2a**) from **1a** are: bp 130-135°/30 mm Hg (bath temperature); ir (liquid film): 3050, 2960, 2920, 2840, 2110, 2070, 1600, 1585, 1485, 1450, 1435, 1380, 1305, 1270, 1250, 1230, 1200, 1180, 1150, 1115, 1105, 1040, 1005, 940, 815, 790, 750 cm$^{-1}$; pmr (deuteriochloroform): δ 8.15 (dd, J = 1.6, 4.6 Hz, 1H, H-6), 7.69 (dd, J = 1.6, 7.2 Hz, 1H, H-4), 7.04 (dd, J = 4.6, 7.2 Hz, 1H, H-5), 6.28 (t, J = 0.8 Hz, 1H, H-3), 2.40 (almost s, 2.1H, -C$H_2$D and -C$H_3$ of **2a** and **1a**); ms: m/z 134.0573 (M$^+$, Calcd. for $C_8H_6NOD$: 134.0591).

The properties of the volatile component of the product from **1b** are: bp 130-140°/35 mm Hg (bath temperature); ir (liquid film): 3090, 3060, 3040, 2950, 2880, 2200, 2175, 1600, 1565, 1410, 1270, 1245, 1230, 1170, 1105, 1035, 960, 940, 795 cm$^{-1}$; pmr (deuteriochloroform): δ 8.43 (dd, J = 1.4, 4.6 Hz, 1H, H-5), 7.64 (ill splitted ddd, J = 1.0, 1.4, 8.2 Hz, 1H, H-7), 7.08 (dd, J = 4.6, 8.2 Hz, 1H, H-6), 6.58 (almost s, 0.6H, H-3 of **2b**), 2.42 (s, 2.4H, -C$H_2$D and C$H_3$ of **2b** and **2'b**); ms: m/z 134.0612 (M$^+$, Calcd. for $C_8H_6NOD$: 134.0591).

The properties of the product (containing more than 90% of **2c**) from **1c** are: bp 135-140°/35 mm Hg; ir (liquid film): 3100, 3070, 3045, 3010, 2930, 2850, 2180, 2140, 1590, 1460, 1420, 1255, 1180, 1150, 1025, 955, 935, 875, 820 cm$^{-1}$; pmr (deuteriochloroform): δ 8.67 (dd, J = 0.8, 1.0 Hz, 1H, H-7), 8.28 (d, J = 5.0 Hz, 1H, H-5), 7.29 (dd, J = 1.0, 5.0 Hz, 1H, H-4), 6.29 (almost s, 1H, H-3), 2.39 (almost s, 2.1H, -C$H_2$D and -C$H_3$ of **2c** and **1c**); ms: m/z 134.0591 (M$^+$, Calcd. for $C_8H_6NOD$: 134.0591).

The properties of volatile component of the product from **1d** are: ir (liquid film): 3100, 3040, 2920, 2850, 2180, 2130, 1600, 1570, 1455, 1425, 1320, 1260, 1175, 1155, 1130, 1020, 930, 895, 885, 810, 755 cm$^{-1}$; pmr (deuteriochloroform): δ 8.70 (d, J = 1.0 Hz, 1H, H-4), 8.33 (d, J = 5.6 Hz, H-6), 7.24 (dt, J = 1.0, 5.6 Hz, 0.8H, H-7 of **1d** and **2d**), 2.40 (almost s, 2.2H, -C$H_2$D and -C$H_3$ of **2d**, **2'd** and **1d**); ms: m/z 134.0568 (M$^+$, Calcd. for $C_8H_6NOD$: 134.0591).

The reaction of **1d** with 2.0 equivalent of lithium diisopropylamide for 2 hours afforded compound **2d** and **2'd** in yield of 60% and 15%.

Reaction of Compound **1a**, **1b**, **1c** and **1d** with Lithium Diisopro-

pylamide and Deuterium Chloride in Deuterium Oxide at −40°.

General Procedure.

To a solution of diisopropylamide prepared from diisopropylamine (230 mg, 2.27 mmoles) and *n*-butyllithium in hexane (1.42 ml, 1.6*M*, 2.27 mmoles) in 20 ml of dry tetrahydrofuran was added a solution of 2-methylfuropyridine **1** (300 mg, 2.26 mmoles) in 5 ml of dry tetrahydrofuran by syringe over a period of 5 minutes at −75° with stirring and under a nitrogen atmosphere, then the reaction flask was warmed to −40°. After stirring for 2 hours at this temperature, the reaction mixture was treated with deuterium chloride in deuterium oxide (*ca.* 10%, 3 ml), stirred at room temperature for 5 minutes, basified with sodium bicarbonate, and treated with chloroform and water. The chloroform layer was dried over magnesium sulfate and evaporated under reduced pressure.

In the case of **1a**, the residual crystalline mass (300 mg) was recrystallized from acetone to give 280 mg (93%) of colorless crystals **3** of mp 149-151°.

3-(1,2-Propadienyl)pyridin-2-ol **3**.

This compound had ir (potassium bromide): 3200-2300 (broad), 3140, 3070, 1930 (C=C=C), 1650, 1640, 1605, 1545, 1480, 1420, 1360, 1295, 1245, 1210, 1045, 975, 945, 880, 865, 840, 770 $cm^{-1}$; pmr (deuteriochloroform): δ 13.50 (br s, 1H, N*H*), 7.55 (dd, J = 6.6, 2.0 Hz, 1H, H-6), 7.30 (dd, J = 6.6, 2.0 Hz, 1H, H-4), 6.53 (t, J = 7.0 Hz, 1H, -C*H*=C=$CH_2$), 6.31 (t, J = 6.6 Hz, 1H, H-5), 5.16 (d, J = 7.0 Hz, 2H, -CH=C=C*H*$_2$); $^{13}$C-nmr (deuteriochloroform): δ 210.41 (s, -CH=*C*=$CH_2$), 163.34 (s, C=O), 137.07 (d, C-6), 132.71 (d, C-4), 125.00 (s, C-3), 107.46 (d, C-5), 87.45 (d, -*C*H=C=$CH_2$), 78.80 (t, -CH=C=*C*H$_2$).

*Anal.* Calcd. for $C_8H_7NO$: C, 72.17; H, 5.30; N, 10.52. Found: C, 71.98; H, 5.28; N, 10.27.

In the case of **1b**, the semi-solid residue (350 mg) was chromatographed on a silica gel (35 g) column. The first fraction eluted with chloroform-methanol (98:2) gave 130 mg (43%) of **1b** as a colorless oil, and the second fraction 150 mg (50%) of compound **5**, which were identified by ir and pmr spectra.

In the case of **1c** and **1d**, the residual oil (330 mg for **1c**, 140 mg of **1d**) was distilled under reduced pressure to give a colorless oil (290 mg (97%) from **1c**, 120 mg (40%) from **1d**) of bp 140-150°/40 mm Hg which was shown to be a sample of 2-monodeuteriomethyl derivatives, **2c** or **2d**, containing **1c** or **1d** less than 5% by the pmr spectrum.

Reaction of **1a** with 3 Molar Equivalents of Diisopropylamide at −40°.

A solution of compound **1a** (300 mg, 2.26 mmoles) in 5 ml of dry tetrahydrofuran was added by syringe to a solution of diisopropylamide prepared from diisopropylamine (690 mg, 7.0 mmoles) and *n*-butyllithium in hexane (4.23 ml, 1.6*M*, 6.77 mmoles) in 20 ml of dry tetrahydrofuran with stirring and under a nitrogen atmosphere at −75°, then the reaction flask was warmed to −40° and stirred for 2 hours. The reaction mixture was treated with 10% hydrochloric acid (3 ml), stirred at room temperature for 5 minutes, and treated with chloroform and water. The chloroform solution was dried (magnesium sulfate) and evaporated under reduced pressure to give 370 mg of a slightly brown crystalline mass. The residue was chromatographed on a silica gel (40 g) column using chloroform-methanol (99:1) as the eluant to give a band containing allene compound **3** and acetylene compound **4** (almost 1:1) followed by a band containing mainly **4**. The first band was chromatographed again on a silica gel (20 g) column using chloroform-methanol (98:2) as the eluant to give a band containing mainly **3** and a band consisting mainly of **4**. Recrystallization the both bands from acetone afforded pure samples of **3** and **4**, respectively.

3-(2-Propynyl)pyridin-2-ol **4**.

This compound had mp 187-189°; ir (potassium bromide): 3200, 3110, 3200-2000 (broad), 2100 (-C=CH), 1650, 1640, 1615, 1560, 1540, 1470, 1455, 1430, 1400, 1360, 1285, 1250, 1215, 1150, 1085, 1045, 950, 910, 875, 760, 750, 720 $cm^{-1}$; pmr (deuteriochloroform): δ 7.77 (ddt, J = 6.6, 1.6, 1.0 Hz, 1H, H-6), 7.35 (dd, J = 6.6, 1.6 Hz, 1H, H-4), 6.33 (t, J = 6.6 Hz, 1H, H-5), 3.53 (dd, J = 2.6, 1.0 Hz, 2H, -C*H*$_2$-C=CH), 2.26 (t, J = 2.6 Hz, 1H, $CH_2$-C=C*H*).

*Anal.* Calcd. for $C_8H_7NO$: C, 72.17; H, 5.30; N, 10.52. Found: C, 72.06; H, 5.34; N, 10.22.

Recyclization of 3-(1,2-Propadienyl)pyridin-2-ol **3**, 3-(2-Propynyl)-pyridin-2-ol **4** and 2-(1-Propynyl)pyridin-3-ol **5** to the Corresponding 2-Methylfuropyridines.

General Procedure.

a) A sample of **3** or **5** (50 mg, 0.38 mmole) in a glass tube was heated at 150-180° for 10 minutes. The completely melted product was distilled under reduced pressure to give compound **1a** or **1b** in almost quantitative yield respectively. Compound **4** was distilled at 190-200°/2.5 mm Hg without any change. The structures of these compounds were identified by comparison of the ir and pmr spectra with those of the authentic samples.

b) A solution of compound **3**, **4** or **5** (50 mg, 0.38 mmole) in deuteriomethanol (1 ml) and sodium deuterioxide in deuterium oxide (100 mg, 40%) was kept at 40°, and the reaction was followed by pmr techniques. After 20 hours, the reaction mixture was evaporated under reduced pressure to remove the solvent. The residual mass was treated with chloroform and a small amount of water, the chloroform layer was dried and evaporated to give a slightly yellow oil, which was distilled to give 2-monodeuteriomethylfuro[2,3-*b*]pyridine **2a** from **3**, 2-trideuteriomethylfuro[2,3-*b*]pyridine **2'a** from **4** and 2-methyl-3-deuteriofuro[3,2-*b*]pyridine **2'b** from **5** in almost quantitative yields. The structure of **2a** and **2'b** was identified by comparison of the ir and pmr spectra with those of the samples obtained by the reaction of **1a** and **1b** with LDA in the above.

2-Trideuteriomethylfuro[2,3-*b*]pyridine **2'a**.

This compound had bp 130-140°/35 mm Hg; ir (liquid film): 3100, 3060, 3020, 2930, 2200, 2140, 2050, 1595, 1585, 1465, 1400, 1335, 1320, 1270, 1250, 1240, 1170, 1110, 1035, 935, 900, 865, 800, 765 $cm^{-1}$; pmr (deuteriochloroform): δ 8.05 (dd, J = 1.6, 4.6 Hz, 1H, H-6), 7.60 (dd, J = 1.6, 7.4 Hz, 1H, H-4), 6.98 (dd, J = 4.6, 7.4 Hz, 1H, H-5), 6.23 (s, 1H, H-3); ms: m/z 136.0717 ($M^+$, Calcd. for $C_8H_4NOD_3$: 136.0716).

Reaction of Lithio Intermediates from 2-Methylfuro[2,3-*b*]- **1a**, -[3,2-*b*]- **1b**, -[2,3-*c*]- **1c** and -[3,2-*c*]pyridine **1d** with Benzaldehyde.

General Procedure.

To a solution of diisopropylamine (350 mg, 3.46 mmoles) in dry tetrahydrofuran (15 ml) was added a solution of *n*-butyllithium in hexane (2.1 ml, 1.6*M*, 3.36 mmoles) dropwise by syringe at −75° under a nitrogen atmosphere with stirring. After stirring at this

temperature for 20 minutes, a solution of compound **1** (300 mg, 2.26 mmoles) in dry tetrahydrofuran (5 ml) was added by syringe and stirred for 10-15 minutes at −75°. To this deep purple brown solution was added benzaldehyde (360 mg, 3.4 mmoles). Stirring was continued for 2 hours for **1a** and **1b**, 5 hours for **1c** and **1d** at −75°. The mixture was treated with 10% hydrochloric acid (3.5 ml) and water (10 ml), basified with sodium bicarbonate and extracted with chloroform. After evaporation of the chloroform, the residual syrup was dissolved in 10% hydrochloric acid, washed with benzene, basified with sodium bicarbonate, extracted with chloroform and dried (magnesium sulfate).

Further processing of the residue of the chloroform solution is indicated in a subsequent paragraph.

2-(2-Hydroxy-2-phenylethyl)furo[2,3-*b*]pyridine **6a**.

The crude solid residue (560 mg) from **1a** was recrystallized from ether to give a pure sample of compound **6a** (510 mg, 95%), mp 118-120°; ir (potassium bromide): 3230, 3080, 3010, 2910, 2850, 1585, 1490, 1395, 1355, 1310, 1260, 1230, 1200, 1180, 1140, 1110, 1075, 1040, 1030, 1015, 950, 935, 910, 840, 810, 770, 750 $cm^{-1}$; pmr (deuteriochloroform): δ 8.10 (dd, J = 1.8, 4.8 Hz, 1H, H-6), 7.69 (dd, J = 1.8, 7.6 Hz, 1H, H-4), 7.50-7.20 (m, 5H, $-C_6H_5$), 7.05 (dd, J = 4.8, 7.6 Hz, 1H, H-5), 6.38 (t, J = 0.6 Hz, 1H, H-3), 5.26 (t, J = 6.8 Hz, 1H, $-CH_2-CH(OH)-$), 3.46 (broad s, 1H, OH), 3.19 (dd, J = 0.6, 6.8 Hz, 2H, $-CH_2CH(OH)-$).

*Anal.* Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.70; H, 5.72; N, 5.99.

2-(2-Hydroxy-2-phenylethyl)- **6b**, 2-Methyl-3-(1-Hydroxy-1-phenylmethyl)furo[3,2-*b*]pyridine **9** and 2-(4-Hydroxy-4-phenyl-1-butynyl)pyridin-3-ol **10**.

The crude product (490 mg) from **1b** was chromatographed on a silica gel (51 g) column. The first fraction eluted with hexane-ethyl acetate (1:1) gave 154 mg (29%) of **9**, the second 90 mg of **9** and **1b**, the third 30 mg (10%) of **5** and the fourth 161 mg of a mixture of **6b** and **10**. The second fraction was treated with hexane to dissolve compound **1b**. The residue of the hexane solution was distilled under reduced pressure to give pure **1b** (25 mg, 8%). The third fraction was recrystallized from acetone to afford pure **5**. The structures of **1b** and **5** were identified by comparison of the ir and pmr spectra with those of the authentic samples. The fourth fraction was treated with ether to dissolve compound **6b** and to leave **10** as a crystalline solid.

Compound **6b**.

The residue (50 mg, 9%) of the ethereal solution was converted to the oxalate and recrystallized from methanol-acetone to give colorless crystals of mp 137-139°.

*Anal.* Calcd. for $C_{15}H_{13}NO_2 \cdot C_2H_2O_4$: C, 62.00; H, 4.59; N, 4.25. Found: C, 62.29; H, 4.73; N, 4.34.

The free base from the pure oxalate was a colorless viscous syrup and solidified on standing in a refrigerator for several days. Recrystallization of the solid from ether gave the pure sample of **6b**, mp 89-92; ir (liquid film): 3550-2600 (broad), 3060, 2900, 2860, 1590, 1565, 1490, 1475, 1450, 1410, 1330, 1260, 1245, 1200, 1180, 1140, 1080, 1050, 1030, 950, 930, 805, 785, 755, 700 $cm^{-1}$; pmr (deuteriochloroform): δ 8.34 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.57 (dt, J = 0.8, 8.0 Hz, 1H, H-7), 7.48-7.20 (m, 5H, $-C_6H_5$), 7.03 (dd, J = 4.6, 8.0 Hz, 1H, H-6), 6.61 (q, J = 0.8 Hz, 1H, H-3), 5.17 (t, J = 6.4 Hz, 1H, $-CH_2-CH(OH)-$), 3.21 (dd, J = 0.8, 6.4 Hz, 2H, $-CH_2-CH(OH)-$), 3.30 (broad s, 1H, OH); ms: m/z 239.0952 ($M^+$, Calcd. $C_{15}H_{13}NO_2$: 239.0946).

*Anal.* Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.53; H, 5.63; N, 5.45.

Compound **9**.

The first fraction (154 mg) and the hexane insoluble material (60 mg) were combined and recrystallized from ether to give pure sample of **9** (200 mg, 37%) of mp 84-85°; ir (potassium bromide): 3500-2550 (broad), 2910, 2830, 1610, 1560, 1480, 1420, 1310, 1295, 1270, 1235, 1165, 1140, 1110, 1075, 1035, 1025, 990, 960, 930, 860, 790, 770, 715, 700 $cm^{-1}$; pmr (deuteriochloroform): δ 8.35 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.56 (dd, J = 1.2, 8.0 Hz, 1H, H-7), 7.60-7.15 (m, 5H, $-C_6H_5$), 7.05 (dd, J = 4.6, 8.0 Hz, 1H, H-6), 6.13 (s, 1H, $-CH(OH)-$), 4.98 (broad s, 1H, OH), 2.26 (s, 3H, $2-CH_3$).

*Anal.* Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.43; H, 5.53; N, 5.81.

Compound **10**.

The ether insoluble material (110 mg) of the fourth fraction was recrystallized from methanol-acetone to give pure **10** (95 mg, 18%) of mp 140-142°; ir (potassium bromide): 3450-2450 (broad), 1565, 1445, 1340, 1300, 1250, 1230, 1170, 1110, 1060, 1045, 1015, 915, 795, 755 $cm^{-1}$; pmr (deuteriomethanol): δ 7.95 (dd, J = 2.5, 3.0 Hz, 1H, H-6), 7.60-7.17 (complex m, 7H, H-4, H-5 and $-C_6H_5$), 4.95 (t, J = 6.0 Hz, 1H, $-CH_2-CH(OH)-$), 2.90 (d, J = 6.0 Hz, $-CH_2-CH(OH)-$).

*Anal.* Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.70; H, 5.59; N, 6.00.

2-(2-Hydroxy-2-phenylethyl)furo[2,3-*c*]pyridine **6c**.

The crude residue (580 mg) from **1c** was recrystallized from acetone to afford pure sample of **6c** (505 mg, 94%), mp 104-107°; ir (potassium bromide): 3450-2550 (broad), 3060, 2890, 2810, 1585, 1420, 1260, 1175, 1140, 1055, 1025, 955, 935, 890, 820, 760 $cm^{-1}$; pmr (deuteriochloroform): δ 8.51 (d, J = 0.6 Hz, 1H, H-7), 8.15 (d, J = 5.2 Hz, 1H, H-5), 7.50-7.15 (complex m, 6H, H-4 and $-C_6H_5$), 6.42 (q, J = 0.6 Hz, 1H, H-3), 5.18 (t, J = 6.2 Hz, 1H, $-CH_2-CH(OH)-$), 4.02 (broad s, 1H, OH), 3.23 (dd, J = 0.6, 6.2 Hz, 2H, $-CH_2-CH(OH)-$).

*Anal.* Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.58; H, 5.57; N, 5.82.

2-(2-Hydroxy-2-phenylethyl)furo[3,2-*c*]pyridine **6d**.

The residue (540 mg) from **1d** was recrystallized from acetone to give 510 mg (95%) of pure sample of **6d**, mp 135-137°; ir (potassium bromide): 3450-2550 (broad), 3050, 3020, 2920, 2860, 1575, 1485, 1435, 1420, 1320, 1260, 1185, 1165, 1130, 1040, 1020, 930, 895, 850, 820, 805, 755 $cm^{-1}$; pmr (deuteriochloroform): δ 8.52 (d, J = 0.8 Hz, 1H, H-4), 8.19 (d, J = 5.6 Hz, 1H, H-6), 7.48-7.10 (complex m, 6H, H-7 and $-C_6H_5$), 6.40 (q, J = 0.6 Hz, 1H, H-3), 5.12 (t, J = 6.4 Hz, 1H, $-CH_2-CH(OH)-$), 3.96 (broad s, 1H, OH), 3.16 (dd, J = 0.6, 6.4 Hz, 2H, $-CH_2-CH(OH)-$).

*Anal.* Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.53; H, 5.49; N, 5.76.

Reaction of Lithio Intermediates from 2-Methylfuro[2,3-*b*]- **1a**, -[3,2-*b*]- **1b**, -[2,3-*c*]- **1c** and -[3,2-*c*]pyridine **1d** with Propionaldehyde.

General Procedure.

A solution of *n*-butyllithium in hexane (2.1 ml, 1.6*M*, 3.36 mmoles) was added to a solution of diisopropylamine (350 mg, 3.46 mmoles) in dry tetrahydrofuran (15 ml) by syringe at −75°

under a nitrogen atmosphere with stirring. After stirring at this temperature for 20 minutes, a solution of compound **1** (300 mg, 2.26 mmoles) in dry tetrahydrofuran (5 ml) was added by syringe and stirred for 10-15 minutes at −75°. Propionaldehyde (190 mg, 3.33 mmoles) was added to this dark purple brown solution by syringe. Stirring at −75° was continued for 2.5 hours for **1a**, 2 hours for **1b**, 6 hours for **1c** and **1d**. The mixture was treated with 10% hydrochloric acid (3.5 ml) and water (10 ml), basified with sodium bicarbonate, extracted with chloroform and dried over magnesium sulfate.

Further processing of the residue of the chloroform solution is described in a subsequent paragraph.

2-(2-Hydroxybutyl)furo[2,3-*b*]pyridine **7a**.

The residue from **1a** (410 mg) was purified by chromatography on a silica gel (45 g) column using hexane-ethyl acetate (1:1) as an eluent to give 321 mg (74%) of pure **7a** as a colorless syrup which showed a single spot in the tlc [$R_f$ 0.3 (hexane-ethyl acetate (1:2))]. Compound **7a** was characterized by the following data; ir (liquid film): 3600-2800 (broad), 3060, 2970, 2930, 2880, 1590, 1460, 1340, 1240, 1200, 1160, 1110, 1055, 1015, 980, 940, 900, 810, 770 $cm^{-1}$; pmr (deuteriochloroform): δ 8.15 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.76 (dd, J = 1.6, 7.4 Hz, 1H, H-4), 7.10 (dd, J = 4.8, 7.4 Hz, 1H, H-5), 6.51 (t, J = 0.8 Hz, 1H, H-3), 4.06 (dqn, J = 5.8, 6.0 Hz, 1H, $-CH_2CH(OH)-CH_2CH_3$), 2.93 (dd, J = 0.8, 6.0 Hz, 2H, $-CH_2CH(OH)-$), 2.90 (broad d, J = 5.8 Hz, 1H, O*H*), 1.60 (dq, J = 6.0, 6.8 Hz, 2H, $-CH(OH)CH_2CH_3$), 1.00 (t, J = 6.8 Hz, 3H, $-CH_3$); ms: m/z 191.0931 ($M^+$ Calcd. for $C_{11}H_{13}NO_2$: 191.0945).

2-Methyl-3-(1-hydroxypropyl)furo[3,2-*b*]pyridine **11**.

The residue from **1b** (450 mg) was chromatographed on a silica gel (45 g) column eluting with chloroform-methanol (99:1). The first fraction (43 mg, 14%) gave the starting compound **1b** (bp 130-140/30 mm Hg) which was identified by ir and pmr spectra. The second fraction (346 mg) was found to be a mixture of two components **5** and **11** (ratio: *ca.* 1:10) by tlc and pmr spectra.

The solid component **5** was isolated by dissolving the oily component **11** with ether. Recrystallization of the former from acetone gave pure sample of **5** (30 mg, 10%) which was identified by ir and pmr spectra.

The oily residue (300 mg) of the ethereal solution was again chromatographed on a silica gel (30 g) column eluting with chloroform-methanol (99:1), and collected the eluates (230 mg, 53%) which showed a single spot in the tlc [$R_f$ 0.38 (hexane-ethyl acetate (1:2))]. Compound **11** was characterized by the following data; ir (liquid film): 3600-2500 (broad), 3060, 3040, 2960, 2920, 2870, 1620, 1610, 1560, 1475, 1420, 1380, 1270, 1230, 1165, 1100, 1070, 1035, 1005, 965, 915, 890, 860, 770 $cm^{-1}$; pmr (deuteriochloroform): δ 8.32 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.53 (dd, J = 1.2, 7.8 Hz, 1H, H-7), 7.01 (dd, J = 4.6, 7.8 Hz, 1H, H-6), 4.85 (t, J = 6.6 Hz, 1H, $-CH(OH)CH_2-$), 2.42 (s, 3H, 2-$CH_3$), 2.03 (dq, J = 6.6, 7.0 Hz, 2H, $-CH(OH)CH_2CH_3$), 0.93 (t, J = 7.0 Hz, 3H, $-CH_2CH_3$); ms: m/z 191.0988 ($M^+$, Cald. for $C_{11}H_{13}NO_2$: 191.0945).

*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.99; H, 6.98; N, 7.01.

2-(2-Hydroxybutyl)furo[2,3-*c*]pyridine **7c**.

The crude residue (460 mg) from **1c** was dissolved in ether and treated with a slight excess of oxalic acid in ether. The oxalate which precipitated was recrystallized from methanol-acetone to give colorless fine needles (570 mg, 90%), mp 113-115°.

*Anal.* Calcd. for $C_{11}H_{13}NO_2 \cdot C_2H_2O_4$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.27; H, 5.37; N, 4.97.

The free base from the pure oxalate was a colorless syrup and decomposed by heating above 140°/0.1 mm Hg; ir (liquid film): 3550-2400 (broad), 3070, 2970, 2940, 2910, 2880, 1610, 1590, 1445, 1430, 1345, 1265, 1195, 1180, 1150, 1115, 1095, 1055, 1030, 1010, 985, 960, 910, 890, 825, 795 $cm^{-1}$; pmr (deuteriochloroform): δ 8.66 (dd, J = 0.8, 1.0 Hz, 1H, H-7), 8.26 (d, J = 5.2 Hz, 1H, H-5), 7.33 (dd, J = 1.0, 5.2 Hz, 1H, H-4), 4.07 (qn, J = 6.0 Hz, 1H, $-CH_2CH(OH)-CH_2-$), 2.97 (dd, J = 0.8, 6.0 Hz, 2H, $-CH_2CH(OH)-$), 2.90 (broad s, 1H, O*H*), 1.64 (dq, J = 6.0, 6.8 Hz, 2H, $-CH(OH)CH_2CH_3$), 1.06 (t, J = 6.8 Hz, 3H, $-CH_2CH_3$); ms: m/z 191.0921 ($M^+$, Calcd. for $C_{11}H_{13}NO_2$: 191.0945).

*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.22; H, 6.98; N, 7.15.

2-(2-Hydroxybutyl)furo[3,2-*c*]pyridine **7d**.

The oily residue (420 mg) from **1d** was converted to the oxalate and recrystallized from methanol-acetone to give colorless prisms (560 mg, 88%) of mp 134-137°.

*Anal.* Calcd. for $C_{11}H_{13}NO_2 \cdot C_2H_2O_4$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.58; H, 5.31; N, 5.03.

The free base from the oxalate was a colorless syrup; ir (liquid film): 3600-2500 (broad), 3060, 2980, 2940, 2890, 1600, 1580, 1460, 1440, 1330, 1265, 1175, 1155, 1115, 1060, 1025, 980, 935, 905, 890, 815, 755 $cm^{-1}$; pmr (deuteriochloroform): δ 8.68 (d, J = 0.8 Hz, 1H, H-4), 8.33 (d, J = 5.8 Hz, 1H, H-6), 7.28 (dt, J = 0.8, 5.8 Hz, 1H, H-7), 6.54 (q, J = 0.8 Hz, 1H, H-3), 4.03 (qn, J = 6.2 Hz, 1H, $-CH_2CH(OH)CH_2-$), 3.40 (broad s, 1H, O*H*), 2.93 (dd, J = 0.8, 6.2 Hz, 2H, $-CH_2CH(OH)-$), 1.62 (dq, J = 6.2, 7.2 Hz, 2H, $-CH(OH)CH_2CH_3$), 1.03 (t, J = 7.2 Hz, 3H, $-CH_2CH_3$); ms: m/z 191.0947 ($M^+$, Calcd. for $C_{11}H_{13}NO_2$: 191.0945).

*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.13; H, 7.01; N, 7.28.

Reaction of Lithio Intermediates from 2-Methylfuro[2,3-*b*]- **1a**, -[3,2-*b*]- **1b**, -[2,3-*c*]- **1c** and -[3,2-*c*]pyridine **1d** with Acetone.

General Procedure.

To a stirred solution of diisopropylamine (350 mg, 3.46 mmoles) in dry tetrahydrofuran (15 ml) was added a solution of *n*-butyllithium in hexane (2.1 ml, 1.6*M*, 3.36 mmoles) dropwise by syringe at −75° under a nitrogen atmosphere. After stirring at this temperature for 20 minutes, a solution of compound **1** (300 mg, 2.26 mmoles) in dry tetrahydrofuran (5 ml) was added by syringe and stirred for 10-15 minutes at −75°. To the deep colored solution was added acetone (200 mg, 3.45 mmoles). After stirring for 2 hours for **1a** and **1b**, 5 hours for **1c** and **1d** at −75°, the mixture was treated with 10% hydrochloric acid (3.5 ml) and water (10 ml), basified with sodium bicarbonate and extracted with chloroform.

Further processing the residue of the dried chloroform extract is indicated in the following paragraph.

2-(2-Hydroxy-2-methylpropyl)furo[2,3-*b*]pyridine **8a**.

The oily residue (420 mg) from **1a** was purified by chromatography on a silica gel (50 g) column eluting with hexane-ethyl acetate (1:1). The first fraction gave a small amount of **1a**, and the second gave 308 mg (71%) of pure **8a** which gave a single spot in tlc [$R_f$ 0.42 (hexane-ethyl acetate (1:2))]; ir (liquid film): 3550-3000 (broad), 3120, 3070, 2980, 2940, 1585, 1465, 1405, 1380, 1365, 1335, 1250, 1230, 1160, 1045, 980, 945, 910, 870, 835, 810, 775,

760, 720 $cm^{-1}$; pmr (deuteriochloroform): δ 8.26 (dd, J = 1.8, 4.8 Hz, 1H, H-6), 7.86 (dd, J = 1.8, 7.6 Hz, 1H, H-4), 7.18 (dd, J = 4.8, 7.6 Hz, 1H, H-5), 3.00 (d, J = 0.6 Hz, 2H, $-CH_2$), 2.10 (broad s, 1H, O*H*), 1.32 (s, 6H, $-C(OH)(CH_3)_2$); ms: m/z 191.0950 ($M^+$, Calcd. for $C_{11}H_{13}NO_2$: 191.0945).

2-(2-Hydroxy-2-methylpropyl)- **8b** and 2-Methyl-3-(1-hydroxy-1-methylethyl)furo[3,2-*b*]pyridine **12**.

The crude product (460 mg) from **1b** was chromatographed on a silica gel (50 g) column. The first fraction eluted with hexane-ethyl acetate (1:1) gave 160 mg (37%) of compound **12**, the second 63 mg (21%) of **1b**, the third 38 mg (13%) of **5**, and the fourth 89 mg (21%) of **8b**, which showed a single spot in tlc [$R_f$ 0.35 (hexane-ethyl acetate (1:2))]. The structures of **1b** and **5** were identified by ir and pmr spectra.

Compound **8b**.

This compound was a colorless viscous oil and decomposed by heating above 150° (0.1 mm Hg); ir (liquid film): 3550-2550 (broad), 3120, 3060, 2980, 2925, 2870, 1605, 1590, 1460, 1410, 1380, 1360, 1260, 1220, 1160, 1105, 975, 940, 905, 865, 825, 810, 790, 765, 720 $cm^{-1}$; pmr (deuteriochloroform): δ 8.33 (dd, J = 1.4, 4.4 Hz, 1H, H-5), 7.58 (ddd, J = 1.0, 1.4, 8.0 Hz, 1H, H-7), 6.71 (almost s, 1H, H-3), 3.00 (almost s, 2H, $-CH_2C(OH)(CH_3)_2$), 1.34 (s, 3H, $-C(OH)(CH_3)_2$), ms: m/z 191.0928 ($M^+$, Calcd. for $C_{11}H_{13}NO_2$: 191.0945).

*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.19; H, 7.10; N, 7.03.

Compound **12**.

The analytically pure sample of this compound was obtained by recrystallization from hexane, mp 52-53°; ir (potassium bromide): 3420, 3060, 3040, 2960, 2930, 2880, 1590, 1550, 1460, 1380, 1360, 1310, 1275, 1230, 1160, 1125, 1070, 980, 945, 920, 840, 795, 780 $cm^{-1}$; pmr (deuteriochloroform): δ 8.37 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.62 (dd, J = 1.2, 8.0 Hz, 1H, H-7), 7.11 (dd, J = 4.6, 9.0 Hz, 1H, H-6), 5.40 (broad s, 1H, O*H*), 2.54 (s, 3H, 2-$CH_3$), 1.77 (s, 6H, $-C(OH)(CH_3)_2$).

*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.71; H, 6.80; N, 7.14.

2-(2-Hydroxy-2-methylpropyl)furo[2,3-*c*]pyridine **8c**.

The crude product (450 mg) from **1c** was converted to the oxalate and recrystallized from methanol-acetone to give 600 mg (95%) of pure sample of **8c**-oxalate of mp 127-130.5°.

*Anal.* Calcd. for $C_{11}H_{13}NO_2 \cdot C_2H_2O_4$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.35; H, 5.38; N, 4.92.

The free base from the oxalate solidified on standing for several days at room temperature, and was recrystallized from ether-hexane to give colorless prisms of mp 67-69°; ir (potassium bromide): 3500-2400 (broad), 2960, 2920, 2850, 1600, 1580, 1420, 1370, 1355, 1310, 1260, 1205, 1165, 1145, 1030, 980, 940, 900, 870, 825 $cm^{-1}$; pmr (deuteriochloroform): δ 8.70 (t, J = 0.8 Hz, 1H, H-7), 8.27 (d, J = 4.8 Hz, 1H, H-5), 7.40 (dd, J = 0.8, 4.8 Hz, 1H, H-4), 6.54 (almost s, 1H, H-3), 3.94 (broad s, 1H, O*H*), 3.00 (almost s, 2H, $-CH_2C(OH)(CH_3)_2$), 1.35 (s, 6H, $-C(OH)(CH_3)_2$).

*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.20; H, 6.91; N, 7.13.

2-(2-Hydroxy-2-methylpropyl)furo[3,2-*c*]pyridine **8d**.

The crude product (440 mg) from **1d** was converted to the oxalate and recrystallized from methanol-acetone to give 605 mg (95%) of pure sample of **8d**-oxalate of mp 138-142°.

*Anal.* Calcd. for $C_{11}H_{13}NO_2 \cdot C_2H_2O_4$: C, 55.51; H, 5.38; N, 4.98. Found: C, 55.37; H, 5.33; N, 4.89.

The free base **8d** from the oxalate was a colorless viscous oil which gave a single spot in tlc [$R_f$ 0.45 (chloroform-methanol (95:5))], and was characterized by the following data: ir (liquid film): 3600-2500 (broad), 3040, 2970, 2920, 2870, 1575, 1455, 1435, 1375, 1360, 1330, 1265, 1180, 1160, 1020, 975, 940, 900, 860, 810, 755 $cm^{-1}$; pmr (deuteriochloroform): δ 8.80 (d, J = 0.8 Hz, 1H, H-4), 8.41 (d, J = 5.4 Hz, 1H, H-6), 7.36 (dt, J = 0.8, 5.4 Hz, 1H, H-7), 6.59 (q, J = 0.8 Hz, 1H, H-3), 3.00 (d, J = 0.8 Hz, 2H, $-CH_2C(OH)(CH_3)_2$), 2.37 (broad s, 1H, O*H*), 1.32 (s, 6H, $-C(OH)(CH_3)_2$); ms: m/z 191.0952 ($M^+$, Calcd. for $C_{11}H_{13}NO_2$: 191.0945).

*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.01; H, 7.12; N, 6.93.

Reaction of Lithio Intermediates from 2-Methylfuro[2,3-*b*]- **1a**, -[3,2-*b*]- **1b**, -[2,3-*c*]- **1c** and -[3,2-*c*]pyridine **1d** with *N,N*-Dimethylacetamide.

General Procedure.

To a solution of diisopropylamine (1.14 g, 11.3 mmoles) in dry tetrahydrofuran (35 ml) was added a solution of *n*-butyllithium in hexane (7.0 ml, 1.6*M*, 11.2 mmoles) by syringe at −75° under a nitrogen atmosphere with stirring. After stirring at this temperature for 20 minutes, a solution of compound **1** (600 mg, 4.5 mmoles) in dry tetrahydrofuran (5 ml) was added by syringe, stirred for 10 minutes, and *N,N*-dimethylacetamide (940 mg, 10.8 mmoles) was added. Stirring at −75° was continued for 24-26 hours. The mixture was treated with 10% hydrochloric acid (10 ml), basified with sodium bicarbonate and extracted with chloroform. After drying (magnesium sulfate), the chloroform solution was evaporated, and the residue was dissolved in ethyl acetate, washed with brine, dried (magnesium sulfate) and evaporated to afford a crude oily residue. In the case of **1c**, distillation of the crude residue yielded the starting compound **1c** (550 mg, 92%), which was identified by ir and pmr spectra.

Further processing of the residue from **1a**, **1b** and **1d** is indicated in subsequent paragraph.

2-Acetonylfuro[2,3-*b*]pyridine **13a**.

The oily residue (660 mg) from **1a** was chromatographed on a silica gel (66 g) column eluting with hexane-ethyl acetate (1.5:1). The first fraction gave 148 mg (25%) of **1a** which was identified by ir and pmr spectra. The second fraction yielded 448 mg of compound **13a** containing a small amount of contaminant, which was purified by chromatography on a silica gel (50 g) column eluting with hexane-ethyl acetate (1.5:1) to give pure sample of **13a** (410 mg, 52%) which showed a single spot in the tlc [$R_f$ 0.31 (chloroform)]; ir (liquid film): 3100, 3050, 3000, 2910, 1720, 1580, 1445, 1400, 1355, 1330, 1270, 1240, 1210, 1160, 1110, 1040, 1015, 940, 890, 830, 810, 770, $cm^{-1}$; pmr (deuteriochloroform): δ 8.18 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.80 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.12 (t, J = 0.8 Hz, 1H, H-3), 3.90 (d, J = 0.8 Hz, 2H, $-CH_2CO-$), 2.24 (s, 3H, $-CH_3$); ms: m/z 175.0635 ($M^+$, Calcd. for $C_{10}H_9NO_2$: 175.0633).

The ketone **13a** was converted to the oxime by the conventional method, which was recrystallized from ether to give analytically pure sample of mp 60-62°; ir (potassium bromide): 3550-2400 (broad), 1590, 1480, 1400, 1340, 1340, 1300, 1250, 1215, 1190,

1175, 1140, 1115, 1020, 980, 940, 915, 830, 815, 790, 770 $cm^{-1}$; pmr (deuteriochloroform): δ 9.45 (broad s, 1H, *OH*), 8.23 (dd, J = 1.8, 4.8 Hz, 1H, 7.82 (dd, J = 1.8, 7.6 Hz, 1H, H-4), 7.15 (dd, J = 4.8, 7.6 Hz, 1H, H-5), 6.50 (t, J = 0.8 Hz, 1H, H-3), 3.93 (d, J = 0.8 Hz, 0.3H, $-CH_2C(=NOH)-$ of syn or anti isomer), 3.70 (d, J = 0.8 Hz, 1.7H, $-CH_2(=NOH)-$ of anti or syn isomer), 1.96 (s, 3H, $-CH_3$).

*Anal.* Calcd. for $C_{10}H_{10}N_2O_2 \cdot 1/4H_2O$: C, 61.68; H, 5.43; N, 14.39. Found: C, 61.98; H, 5.58; N, 14.11.

2-Acetonylfuro[3,2-*b*]pyridine **13b** and 2-Methyl-3-acetylfuro[3,2-*b*]pyridine **14**.

The residue (750 mg) from **1b** was chromatographed on a silica gel (120 g) column. The first fraction eluted with hexane-ethyl acetate (1:1) yielded 58 mg (7%) of compound **14**, the second 114 mg (19%) of **1b**, the third 35 mg (6%) of **5**, and the fourth 247 mg (31%) of **13b**. Compound **1b** and **5** were identified by ir and pmr spectra.

Compound **13b**.

The fourth fraction was purified by chromatography on a silica gel (30 g) column eluting with hexane-ethyl acetate (1:1) to give a pure sample of **12b** which gave a single spot on tlc [$R_f$ 0.2 (hexane-ethyl acetate (1:2))]; ir (liquid film): 3120, 3030, 2960, 1920, 1720, 1635, 1590, 1410, 1355, 1260, 1245, 1160, 1100, 940, 785 $cm^{-1}$; pmr (deuteriochloroform): δ 8.35 (dd, J = 1.2, 4.8 Hz, 1H, H-5), 7.56 (ddd, J = 0.8, 1.2, 8.5 Hz, 1H, H-7), 7.02 (dd, J = 4.8, 8.6 Hz, 1H, H-6), 6.71 (dt, J = 0.6, 0.8 Hz, 1H, H-3), 3.82 (d, J = 0.6 Hz, 2H, $-CH_2C(=O)-$), 2.13 (s, 3H, $-CH_3$); ms: m/z 175.0628 ($M^+$, Calcd. for $C_{10}H_9NO_2$: 175.0633).

The oxime of **13b** had mp 145-149° (from methanol-ether); ir (potassium bromide): 3550-2400 (broad), 3080, 2830, 1595, 1570, 1555, 1495, 1405, 1365, 1260, 1245, 1195, 1150, 1130, 995, 940, 820, 780, 760 $cm^{-1}$; pmr (deuteriomethanol): δ 8.26 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.73 (ddd, J = 0.8, 1.2, 7.8 Hz, 1H, H-7), 7.15 (dd, J = 4.6, 7.8 Hz, 1H, H-6), 6.66 (d, J = 0.8 Hz, 1H, H-3), 3.67 (s, 2H, $-CH_2(=NOH)-$), 1.86 (s, 3H, $-CH_3$).

*Anal.* Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.93; H, 5.21; N, 14.45.

Compound **14**.

Recrystallization of the crude sample from hexane yielded an analytically pure sample of mp 96.5-97.5°; ir (potassium bromide); 3070, 3000, 2970, 2920, 2820, 1655, 1605, 1555, 1465, 1400, 1375, 1360, 1310, 1260, 1225, 1155, 1000, 910, 770 $cm^{-1}$; pmr (deuteriochloroform): δ 8.53 (dd, J = 1.4, 4.8 Hz, 1H, H-5), 7.66 (dd, J = 1.4, 8.4 Hz, 1H, H-7), 7.15 (dd, J = 4.8, 8.4 Hz, 1H, H-6), 2.87 (s, 3H, $-COCH_3$ or $2-CH_3$), 2.76 (s, 3H, $2-CH_3$ or $-COCH_3$).

*Anal.* Calcd. for $C_{10}H_9NO_2$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.86; H, 5.22; N, 7.96.

2-Acetonylfuro[3,2-*c*]pyridine **13d**.

The oily residue (700 mg) from **1d** was chromatographed on a silica gel (70 g) column eluting with hexane-ethyl acetate (45:55). The first fraction yielded 160 mg (27%) of **1d** which was identified by ir and pmr spectra. The second fraction gave 420 mg (53%) of **13d** as a viscous syrup which showed a single in tlc [$R_f$ 0.2 (hexane-ethyl acetate (1:2))]; ir (liquid film): 3110, 3050, 2960, 2910, 1715, 1600, 1575, 1460, 1355, 1260, 1160, 1020, 940, 890, 815, 760 $cm^{-1}$; pmr (deuteriochloroform): δ 8.83 (d, J = 0.8 Hz, 1H, H-4), 8.42 (d, J = 5.6 Hz, 1H, H-6), 7.35 (dt, J = 0.8, 5.6 Hz, 1H, H-7), 6.65 (q, J = 0.8 Hz, 1H, H-3), 3.86 (d, J = 0.8 Hz, 2H, $-CH_2C(=O)-$), 2.20 (s, 3H, $-CH_3$); ms: m/z 175.0623 ($M^+$, Calcd. for $C_{10}H_9NO_2$: 175.0633).

The ketone **13d** was converted to the oxime by the conventional method. Recrystallization from methanol afforded colorless cubes of mp 152-157°; ir (potassium bromide): 3550-2400 (broad), 3010, 2800, 1590, 1580, 1455, 1435, 1415, 1360, 1320, 1260, 1160, 1140, 1015, 945, 930, 905, 870, 820, 760 $cm^{-1}$; pmr (deuteriomethanol): δ 8.69 (d, J = 0.8 Hz, 1H, H-4), 8.26 (d, J = 5.6 Hz, 1H, H-6), 7.42 (dt, J = 0.8, 5.6 Hz, 1H, H-7), 6.66 (q, J = 0.8 Hz, 1H, H-3), 3.91 (d, J = 0.8 Hz, 0.6H, $-CH_2C(=NOH)-$ of syn or anti isomer), 3.67 (d, J = 0.8 Hz, 1.4H, $-CH_2C(=NOH)-$ of anti or syn isomer), 1.86 (s, 3H, $-CH_3$).

*Anal.* Calcd. for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 62.84; H, 5.13; N, 14.33.

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