Furopyridines. XV [1]. Synthesis and Properties of Ethyl 2-(3-Furo[2,3-*b*]-, -[3,2-*b*]-, -[2,3-*c*]- and -[3,2-*c*]pyridyl)acetate

Shunsaku Shiotani*, Masahiko Tsuno, Noriyasu Tanaka,
Miho Tsuiki and Makoto Itoh

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

Received June 28, 1994
Revised August 22, 1994

Ethyl 2-(3-furopyridyl)acetates **10a-d** were synthesized from furopyridin-3(2*H*)-ones **4a-d** by the Wittig-Horner reaction with diethyl cyanomethylphosphonate, hydrolysis and the subsequent esterification. Reaction of compounds **10a-d** with lithium diisopropylamide (LDA) gave the corresponding methylene-lithiated intermediate, and the subsequent reaction with benzaldehyde, acetone and iodomethane afforded the methylene-alkylated product respectively, while *N,N*-dimethylacetamide did not give any reaction product. The 2-position of **10a, b** and **d** is alkylated by the lithiation with excess of LDA and the successive reaction with an electrophile.

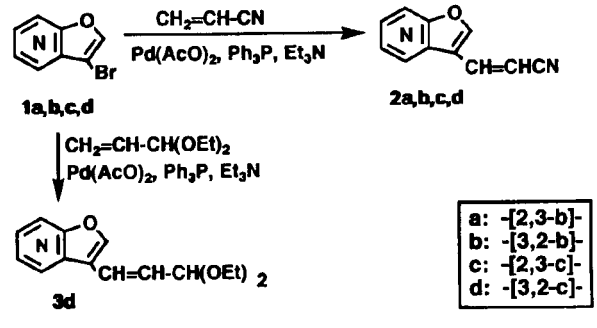
J. Heterocyclic Chem., **32**, 129 (1995).

In continuation of our interest in the chemistry of furopyridines, we reported the syntheses and chemical properties of furopyridines having methyl, cyano, formyl, carboxyl, ethoxycarbonyl, phenylthio, cyanomethyl or nitro group at the 2-position and bromo, methyl, cyano or ethoxy group at the 3-position [2]. In order to extend the chemistry of furopyridines, it was desired to synthesize derivatives having a carbon-containing function, such as formyl, carboxymethyl or aminomethyl, at the 3-position. Though 3-cyano derivatives of furopyridines had been prepared from the corresponding 3-bromo compounds, the cyano group could not be converted to a carboxyl group without cleavage of the O-C bond of the furan moiety by the alkaline or acidic hydrolysis [2d,e].

Thus, we first tried palladium-catalyzed vinylation [3] of 3-bromofuropyridines **1a, 1b, 1c** and **1d** with ethyl acrylate and acrolein diethylacetal in the presence of palladium(II) acetate, triphenylphosphine and triethylamine, which is commonly used as a method for the formation of carbon-carbon bonds from aromatic bromides and vinylic compounds. However, the yield of each entry was very poor: the reaction with ethyl acrylate yielded ethyl 3-(3-furo[2,3-*b*]pyridyl)acrylate (**2a**) (30%) from **1a**, complete recovery of the starting material from **1b**, ethyl 3-(3-furo[2,3-*c*]pyridyl)acrylate (**2c**) (65%) from **1c** and 3-(3-furo [3,2-*c*]pyridyl)acrylate (**2d**) (30%) from **1d**, and the reaction with acrolein acetal afforded the debrominated compound (furo[2,3-*b*]pyridine) from **1a** (42%), complete recovery of the starting material from **1b** and **1c**, and 3-(3-furo[3,2-*c*]pyridyl)acrolein acetal (**3d**) (10%) from **1d**. The low yields may be caused by the electron-donating effect of the furan-oxygen [3].

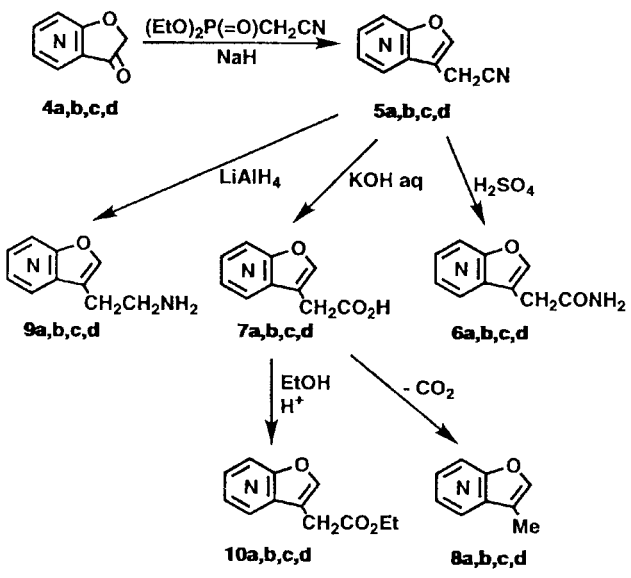
In the meantime, we previously reported the preparation of furopyridin-3(2*H*)-ones **4a, 4b, 4c** and **4d** which were expected to afford 3-cyanomethyl derivatives **5a, 5b, 5c** and **5d** by the Wittig-Horner reaction with diethyl cyanomethylphosphonate [4]. Thus, ketones **4a, 4b, 4c** and **4d** were reacted with diethyl cyanomethylphosphonate using sodium hydride as a base in tetrahydrofuran to give compounds **5a, 5b, 5c** and **5d** in excellent yield (80% from **4**, 96% from **4b**, 97% from **4c** and 97% from **4d**). Hydrolysis of nitriles **5a-d** with 95% sulfuric acid yielded the amides **6a, 6b, 6c** and **6d** in yield of 90% for **6a**, 78% for **6b**, 50% for **6c** and 63% for **6d**, while the hydrolysis with potassium hydroxide in aqueous ethanol afforded the corresponding carboxylic acid **7a** (96%), **7b** (95%), **7c** (98%) and **7d** (92%). Decarboxylation of the carboxymethyl compounds **7a-d** by heating with copper powder gave the 3-methyl derivatives **8a-d** in low yield. Reduction of the nitriles with lithium aluminum hydride afforded the aminoethyl derivatives **9a, 9b, 9c** and **9d**. Esterification of the carboxylic acids **7a-d** with ethanol by the conventional procedure yielded the corresponding ethyl esters **10a, 10b, 10c** and **10d** in fairly good yield.

Scheme 1

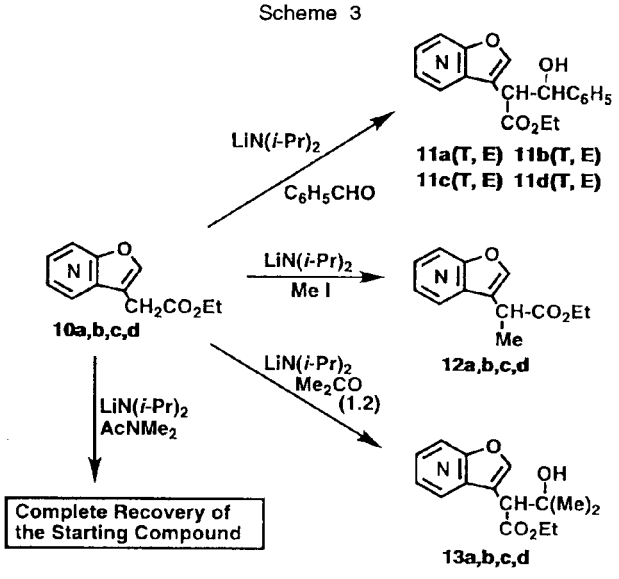


In order to examine the reactivity of the lithio intermediates of the esters **10a-d** with electrophiles, the esters were lithiated with lithium diisopropylamide (LDA) in tetrahydrofuran and then treated with benzaldehyde, acetone, iodomethane and *N,N*-dimethylacetamide (DMA).

Scheme 2



Scheme 3



Each reaction of compounds **10a, 10b, 10c** and **10d** with 1.2 molar equivalents of LDA and benzaldehyde at -75° afforded a mixture of the *threo* and *erythro* diasterioisomer (*ca.*1:1) of the corresponding 2-(3-furopyridyl)-3-hydroxy-3-phenylpropionate **11a-T, 11a-E; 11b-T, 11b-E; 11c-T, 11c-E** and **11d-T, 11d-E** in excellent yields.

Each pair of the diasterioisomers was separated by silica gel column chromatography. The configuration of each diasteromer was elucidated by analysis of the nmr spectral data and consideration with Dreiding model. For both the *threo* and *erythro* isomers, three staggered conformers respect to the C_α-C_β bond are possible respectively (Figure 1). On the other hand, it may be reasonable that the isomers showing similar coupling constant between the H_α and H_β may have the same configuration. The pmr data indicate that in every pair of the isomers the β-proton of the isomer eluted faster than another in column chromatography **11a-T, 11b-T, 11c-T** and **11d-T** couples with the α-proton by larger coupling constant (8.4-8.8 Hz), except **11b-T** (4.8 Hz). The β-proton of **11a-T, 11c-T** and **11d-T** couples also with the proton of the hydroxyl group by 3.2-4.4 Hz. These facts suggest that the **11-T** isomers are stabilized by intramolecular hydrogen bonding from the hydroxyl to the oxygen of the ethoxycarbonyl group. Thus, the conformer **T-1** (Figure 1) may correspond to the preferential conformation of the *threo* diasterisomers **11a-T, 11c-T** and **11d-T**. In the case of **11b-T**, the hydroxyl proton can be intramolecularly hydrogen bonded with both the oxygen of the ethoxycarbonyl group and the ring nitrogen at 4-position, and the position of the hydroxyl proton can not be fixed in the molecule; thus, the hydroxyl proton does not couple with the β-proton. From these considerations, the conformer **T-2** (Figure 1) may correspond to the preferential conformation the compound **11b-T**.

While, the β-proton of the isomer eluted slower in the column chromatography **11a-E, 11b-E, 11c-E** and **11d-E** couples with the α-proton by a smaller coupling constant (4.4-5.6 Hz). The β-proton of these isomers, except **11a-E**, does not couple with the hydroxyl proton. These facts

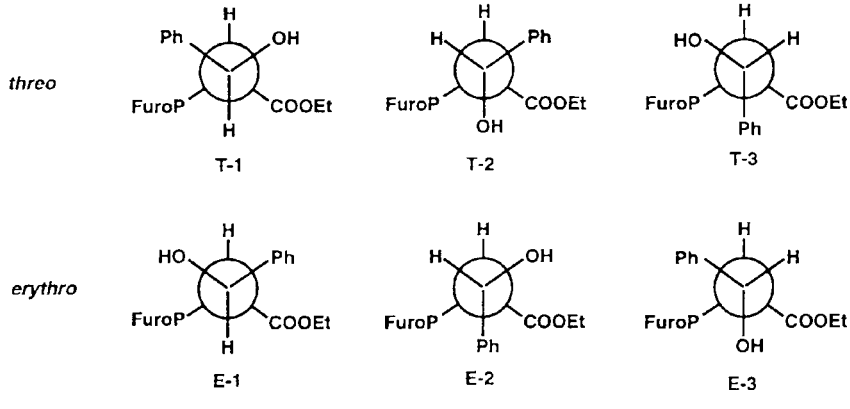


Figure 1. Possible Staggered Conformers of *threo* and *erythro* Diastereoisomers of Compounds **11a,b,c,d**.

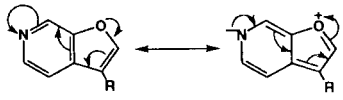


Figure 2

indicate that the hydroxyl protons of these isomers are intermolecularly hydrogen bonded with the ring nitrogen of the other furopyridine molecules; thus, the steric hindrance between the bulky furopyridyl group and the intermolecularly hydrogen bonded furopyridine molecules does not allow the conformation **E-1**. Therefore, the molecules of **11b-E, 11c-E** and **11d-E** may exist in the conformation **E-2** or **E-3**. In the case of **10a-E**, a derivative of furo[2,3-*b*]pyridine which is a very weak base (p*K*a 0.87) [2a], the intramolecular hydrogen bonding from the hydroxyl to the ethoxycarbonyl group may be preferred, and the molecule of **11a-E** may exist in the conformation **E-2** or **E-3**, again.

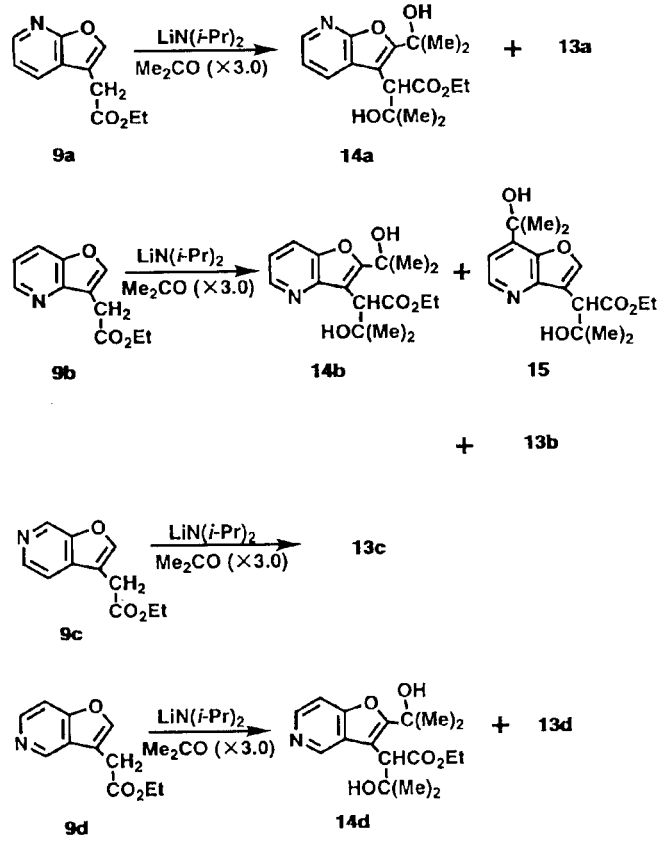
The reaction of the esters **10** with LDA and iodomethane at -40° yielded ethyl 2-(3-furopyridyl)propionates **12a** (97%), **12b** (94%), **12c** (94%) and **12d** (82%). In contrast, the reaction with DMA, a weak electrophile, at -20° gave no reaction product but the starting compound was recovered almost quantitatively.

The reaction of compounds **10** with 1.2 molar equivalents of LDA and acetone at -75° yielded the corresponding 2-(3-furopyridyl)-3-hydroxy-3-methylbutanoate **13a** (60%), **13b** (65%), **13c** (76%) and **13d** (70%). While, the reaction of **10a** with 3.0 molar equivalents of LDA and acetone at -75° gave compound **13a** (80%) and ethyl 2-{3-[2-(α-hydroxy-α-methylethyl)furo[2,3-*b*]pyrldyl]}-3-hydroxy-3-methylbutanoate (**14a**) (20%); **10b** gave compound **13b** (38%), ethyl 2-{3[2-(α-hydroxy-α-methylethyl)furo[3,2-*b*]pyridyl]}-3-hydroxy-3-methylbutanoate (**14b**) (45%) and ethyl 2-{3-[7-(α-hydroxy-α-methylethyl)furo[3,2-*b*]pyridyl]}-3-hydroxy-3-methylbutanoate (**15**) (17%); **10c** gave compound **13c** (almost 100%); **10d** yielded compound **13d** (60%) and ethyl 2-{3-[2(α-hydroxy-α-methylethyl)furo[3,2-*c*]pyridyl]}-3-hydroxy-3-methylbutanoate (**14d**).

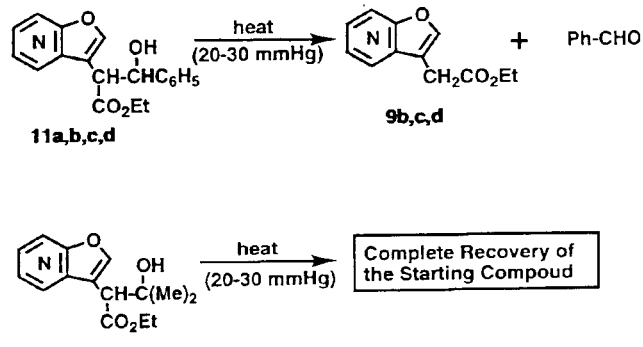
These results suggest that the hydrogen at the 2-position of the lithium salt of compounds **12a, 12b** and **12d** is still reactive to exchange with lithium from LDA, while that of compound **12c** is deactivated by the efficient electron withdrawing effect of the ring nitrogen through the C_{3a}-C_3 bond [2j, 5] (Figure 2).

It is worth noting that the compounds **11b, 11c** and **11d** were decomposed to the ethoxycarbonylmethyl compounds **10b, 10c** and **10d** and benzaldehyde by heating at 140-160° under reduced presure (20-30 mm Hg) in almost quantitative yield, while compounds **11a, 12a, b, c** and **d** were stable at this temperature and could be distilled without any decomposition; moreover, none of these compounds **11a-d** and **12a-d** yielded any dehydrated product by refluxing with hydrochloric acid in ethanol.

Scheme 4



Scheme 5



The reaction course for the decomposition of compounds **10b-d** at higher temperature can be interpreted as follows: The hydroxyl proton is drawn to the ring nitrogen of furopyridine, intermolecularly, and the electrons at the O-H bond are transfered to form the C=O double bond and subsequently the C-C bond is cleaved, which is assisted by the conjugation effect of the phenyl group as depicted in Figure 3. In the case of **10a**, the hydroxyl proton would be stabilized by the intra-

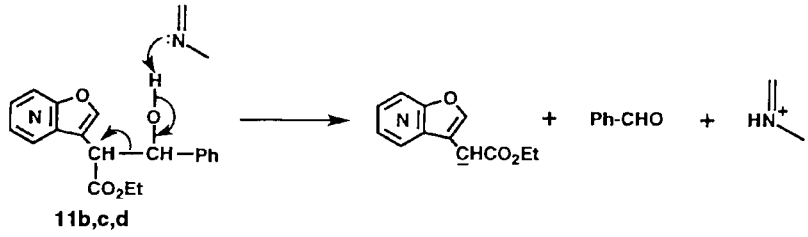


Figure 3

molecular hydrogen bonding and not drawn by the ring nitrogen of other furo[2,3-*b*]pyridines, a very weak base [2a], molecules. The inductive effect of the methyl group of compounds **11a-d** would prevent formation of the C=O double bond.

This research has demonstrated that the methylene proton of ethyl 2-(3-furopyridyl)acetates **10a-d** is more reactive than the proton at the 2-position for the lithiation with LDA, and that the proton at the 2-position is lithiated with excess of LDA, except compound **10c**.

EXPERIMENTAL

Melting points were determined by using Yanagimoto micro melting point apparatus. All melting points are uncorrected. The ir spectra were taken on a JASCO A-102 and a JASCO FT/IR 7300 spectrometer. The pmr spectra were taken on a JEOL JNM-PMX 60 instrument with tetramethylsilane as an internal reference. The mass spectra were obtained by using JEOL JMS-OISG-2 spectrometer.

General Procedure for the Preparation of Ethyl 3-(3-Furopyridyl)acrylates **2a, 2c** and **2d**.

A mixture of 3-bromofuropyridine **1a-d** (100 mg, 0.5 mmole), ethyl acrylate (60 mg, 0.6 mmole), palladium(II) acetate (5 mg, 0.02 mmole), triphenylphosphine (15 mg, 0.06 mmole) and triethylamine (1 ml) was heated at 110° in a sealed tube for 48 hours. After cooling, the mixture was treated with chloroform and water. The chloroform layer was dried (magnesium sulfate) and evaporated to give a brown paste. Further processing of the residue from **1a, 1c** and **1d** is indicated in the subsequent paragraph. In the case of **1b**, the cross-coupling product **2b** could not be isolated but the starting compound **1b** was recovered by silica gel column chromatography in 80% yield.

Ethyl 3-(3-Furo[2,3-*b*]pyridyl)acrylate **2a**.

The residue from **1a** (140 mg) was chromatographed on a silica gel (15 g) column, hexane-ethyl acetate (5:1), giving 33 mg (30%) of compound **2a** as colorless needles of mp 136-138.5° (from ether); ir (potassium bromide): 3100, 3050, 2970, 2930, 2900, 1710, 1635, 1580, 1540, 1480, 1400, 1385, 1360, 1310, 1245, 1190, 1170, 1135, 1110, 1030, 960, 875, 850, 795, 780 cm^{-1}; pmr (deuteriochloroform): δ 8.35 (dd, J = 2.0, 5.0 Hz, 1H, H-6), 8.13 (dd, J = 2.0, 8.0 Hz, 1H, H-4), 7.90 (s, 1H, H-2), 7.65 (d, J = 16.0 Hz, 1H, H-β), 7.27 (dd, J = 5.0, 8.0 Hz, 1H, H-5), 6.47 (d, J = 16.0 Hz, 1H, H-α), 4.27 (q, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 1.34 (t, J = 7.2 Hz, 3H, $-OCH_2CH_3$).

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.55; H, 5.14; N, 6.64.

Ethyl 3-(3-Furo[2,3-*c*]pyridyl)acrylate **2c**.

The residue from **1c** (130 mg) was chromatographed on a silica gel (15 g) column, hexane-ethyl acetate (5:1), to give 70 mg (64%) of **2c** as colorless needles, mp 109-110° (from ether); ir (potassium bromide): 3100, 3060, 3030, 2970, 2890, 1700, 1630, 1600, 1460, 1420, 1360, 1320, 1265, 1220, 1190, 1170, 1110, 1090, 1030, 960, 840, 820, 810 cm^{-1}; pmr (deuteriochloroform): δ 8.90 (s, 1H, H-7), 8.51 (d, J = 5.2 Hz, 1H, H-5), 7.95 (s, 1H, H-2), 7.75 (d, J = 16.0 Hz, 1H, H-β), 7.74 (d, J = 5.2 Hz, 1H, H-4), 6.51 (d, J = 16.0 Hz, 1H, H-α), 4.29 (q, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 1.36 (t, J = 7.2 Hz, 3H, $-OCH_2CH_3$).

Anal. Calcd. for $C_{12}H_{11}NO_3$: C, 66.35; H, 5.10; N, 6.45. Found: C, 66.56; H, 5.12; N, 6.30.

Ethyl 3-(3-Furo[3,2-*c*]pyridyl)acrylate **2d**.

The residue from **1d** (140 mg) was chromatographed on a silica gel (16 g) column, hexane-ethyl acetate (5:1), giving 34 mg (31%) of **2d** as colorless plates, mp 90-93° (from ether); ir (potassium bromide): 3120, 3050, 2980, 2930, 2890, 1700, 1630, 1570, 1460, 1450, 1360, 1315, 1270, 1250, 1200, 1175, 1090, 1030, 1000, 860, 825, 805 cm^{-1}; pmr (deuteriochloroform): δ 9.13 (s, 1H, H-4), 8.52 (d, J = 5.2 Hz, 1H, H-6), 7.82 (s, 1H, H-2), 7.72 (d, J = 16.0 Hz, 1H, H-β), 7.42 (d, J = 5.2 Hz, 1H, H-7), 6.53 (d, J = 16.0 Hz, 1H, H-α), 4.27 (d, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 1.36 (t, J = 7.2 Hz, 3H, $-OCH_2CH_3$).

Anal. Calcd. for $C_{12}H_{11}NO_3$ C, 66.35; H, 5.10; N, 6.45. Found: C, 66.72; H, 5.18; N, 6.38.

General Procedure for the Cross-coupling of 3-Bromofuropyridines **1a, 1b, 1c** and **1d** with Acrolein Diethyl Acetal.

A mixture of **1** (100 mg, 0.5 mmole), acrolein diethyl acetal (100 mg, 0.77 mmole), palladium(II) acetate (5 mg, 0.02 mmole), triphenylphosphine (16 mg, 0.06 mmole) in triethylamine (1.0 ml) was heated in a sealed tube for 48 hours. After cooling, the mixture was treated with chloroform and water. The chloroform layer was dried (magnesium sulfate) and evaporated to leave a brown syrup.

Chromatography of the residue (120-130 mg) from **1a, 1b** and **1c** (silica gel (15 g), hexane-ethyl acetate (5:1)) yielded furo[2,3-*b*]pyridine (26 mg, 42%), compound **1b** (65 mg, 65%) and **1c** (80 mg, 80%), respectively, and no cross-coupling product was isolated.

Further processing of the crude product from **1d** is described in the subsequent paragraph.

3-(3-Furo[3,2-*c*]pyridyl)acrolein Diethyl Acetal **3d**.

The residue (95 mg) from **1d** was chromatographed on a silica gel (12 g) column, hexane-ethyl acetate (5:1), to give 12 mg

(10%) of compound **3d** as a colorless syrup, bp 120°/0.01 mm Hg; ir (liquid film): 3120, 3070, 3030, 2960, 2910, 2860, 1605, 1590, 1455, 1435, 1370, 1350, 1330, 1295, 1240, 1160, 1135, 1100, 1090, 1050, 995, 960, 860, 810 cm^{-1}; pmr (deuteriochloroform): δ 9.11 (d, J = 0.8 Hz, 1H, H-4), 8.48 (d, J = 5.6 Hz, 1H, H-6), 7.68 (s, 1H, H-2), 7.37 (dd, J = 0.8, 5.6 Hz, 1H, H-7), 6.78 (d, J = 16.4 Hz, 1H, H-3'), 6.27 (dd, J = 4.4, 16.4 Hz, 1H, H-2'), 5.07 (d, J = 4.4 Hz, 1H, H-1'), 3.66 (q, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 3.60 (q, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 1.22 (t, J = 7.2 Hz, 6H, 2 x $-OCH_2CH_3$).

Anal. Calcd. for $C_{14}H_{17}NO_3$; C, 68.00; H, 6.93; N, 5.66. Found: C, 67.76; H, 6.94; N, 5.62.

General Procedure for the Preparation of 2-(3-Furopyridyl)-acetonitriles **5a, 5b, 5c** and **5d**.

To a stirred suspension of sodium hydride (1.72 g of 60% dispersion in mineral oil, 43 mmoles, washed with hexane) in dry tetrahydrofuran (40 ml) was added a solution of diethyl cyanomethylphosphonate (7.6 g, 43 mmoles) in tetrahydrofuran (20 ml) by syringe under a nitrogen atmosphere over 10 minutes. After an additional 20 minutes, the mixture was cooled to 0° and a solution of furopyridin-3(2*H*)-one **4** (5.25 g, 41 mmoles) in tetrahydrofuran (90 ml) was added by syringe over 20 minutes. The cooling bath was removed and stirring was continued at room temperature for 18 hours. After evaporation of the solvent, the residue was treated with chloroform and water. The chloroform layer was dried (magnesium sulfate) and evaporated to give a crystalline mass which was purified by recrystallization from ether-acetone to give **5a, 5b, 5c** and **5d** in yield of 80%, 96%, 97% and 97%, respectively.

2-(3-Furo[2,3-*b*]pyridyl)acetonitrile **5a**.

This compound was colorless plates of mp 97.5-98.5°; ir (potassium bromide): 3100, 3050, 3010, 2890, 2240, 1570, 1420, 1390, 1375, 1240, 1230, 1185, 1080, 1060, 965, 920, 820, 785, 770, 700 cm^{-1}; pmr (deuteriochloroform): δ 8.38 (dd, J = 1.6, 4.6 Hz, 1H, H-6), 8.00 (dd, J = 1.6, 7.4 Hz, 1H, H-4), 7.74 (t, J = 1.2 Hz, 1H, H-2), 7.29 (dd, J = 4.6, 7.4 Hz, 1H, H-5), 3.80 (d, J = 1.2 Hz, 2H, $-CH_2CN$).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.42; H, 3.99; N, 17.56.

2-(3-Furo[3,2-*b*]pyridyl)acetonitrile **5b**.

This compound had mp 124.5-126°, colorless needles; ir (potassium bromide): 3100, 3070, 3025, 2910, 2240, 1565, 1555, 1475, 1410, 1280, 1245, 1180, 1085, 830, 785, 765, 730 cm^{-1}; pmr (deuteriochloroform): δ 8.61 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.97 (t, J = 1.2 Hz, 1H, H-2), 7.83 (dd, J = 1.2, 8.4 Hz, 1H, H-7), 7.32 (dd, J = 4.6, 8.4 Hz, 1H, H-6), 3.90 (d, J = 1.2 Hz, 2H, $-CH_2CN$) .

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.65; H, 4.01; N, 17.39.

2-(3-Furo[2,3-*c*]pyridyl)acetonitrile **5c**.

This compound had mp 95-96°; colorless sandy crystals; ir (potassium bromide): 3110, 3050, 3020, 2930, 2900, 2830, 2240, 1610, 1580, 1570, 1460, 1420, 1360, 1280, 1270, 1175, 1095, 1085, 1025, 920, 905, 860, 830, 815, 780 cm^{-1}; pmr (deuteriochloroform): δ 8.88 (d, J = 0.8 Hz, 1H, H-7), 8.47 (d, J = 5.0 Hz, 1H, H-5), 7.76 (t, J = 1.2 Hz, 1H, H-2), 7.54 (dd, J = 0.8, 5.0 Hz, 1H, H-4), 3.77 (d, J = 1.2 Hz, 2H, $-CH_2CN$).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82;, N, 17.71. Found: C, 68.47; H, 3.96; N, 17.62.

2-(3-Furo[3,2-*c*]pyridyl)acetonitrile **5d**.

This compound had mp 103-104°, colorless needles; ir (potassium bromide): 3100, 3070, 3000, 2900, 2240, 1610, 1575, 1420, 1370, 1300, 1280, 1260, 1230, 1195, 1160, 1070, 1020, 860, 810, 765, 735 cm^{-1}; pmr (deuteriochloroform): δ 8.93 (d, J = 0.8 Hz, 1H, H-4), 8.54 (d, J = 5.6 Hz, 1H, H-6), 7.67 (t, J = 1.8 Hz, 1H, H-2), 7.43 (dd, J = 0.8, 5.6 Hz, 1H, H-7), 3.80 (d, J = 1.8 Hz, 2H, $-CH_2CN$) .

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.65; H, 3.97; N, 17.85.

General Procedure for the Preparation of 2-(3-Furopyridyl)-acetamides **6a, 6b, 6c** and **6d**.

A mixture of compound **5** (2.24 g, 14 mmoles), sulfuric acid (20.0 g, 205 mmoles) and water (2.5 g, 138 mmoles) was heated on a water bath for 30 minutes. After cooling, the mixture was diluted with ice-water, basified with sodium bicarbonate and extracted with ethyl acetate. The extract was dried (magnesium sulfate) and evaporated to give a crystalline mass which was recrystallized from methanol-acetone to give pure sample of **6a** (90%), **6b** (78%), **6c** (50%) and **6d** (63%), respectively.

2-(3-Furo[2,3-*b*]pyridyl)acetamide **6a**.

This compound had mp 197-198°; ir (potassium bromide): 3345, 3180, 3120, 2920, 1855, 1795, 1660, 1630, 1590, 1580, 1475, 1420, 1400, 1360, 1300, 1270, 1250, 1200, 1185, 1125, 1075, 865, 800, 790, 765 cm^{-1}; pmr (deuteriomethanol): δ 8.24 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 8.10 (dd, J = 1.6, 7.4 Hz, 1H, H-4), 7.79 (t, J = 1.0 Hz, 1H, H-2), 7.30 (dd, J = 4.8, 7.4 Hz, 1H, H-5), 3.36 (d, J = 1.0 Hz, 2H, $-CH_2CONH_2$).

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.61; H, 4.72; N, 15.69.

2-(3-Furo[3,2-*b*]pyridyl)acetamide **6b**.

This compound had mp 143-145°; ir (potassium bromide): 3260, 3100, 2860, 1670, 1620, 1600, 1540, 1395, 1275, 1265, 1235, 1175, 1165, 1065, 1050, 770, 760 cm^{-1}; pmr (deuteriochloroform): δ 8.38 (dd, J = 1.4, 4.6 Hz, 1H, H-5), 7.73 (t, J = 1.0 Hz, 1H, H-2), 7.63 (dd, J = 1.4, 8.2 Hz, 1H, H-7), 7.11 (dd, J = 4.6, 8.2 Hz, 1H, H-6), 6.13 (broad s, $-CONH_2$), 3.66 (d, J = 1.0 Hz, 2H, $-CH_2CONH_2$).

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.73; H, 4.67; N, 15.69.

2-(3-Furo[2,3-*c*]pyridyl)acetamide **6c**.

This compound had mp 198-199°; ir (potassium bromide): 3345, 3180, 3030, 3000, 2945, 2920, 2800, 1660, 1630, 1610, 1585, 1420, 1305, 1290, 1265, 1180, 1100, 1090, 865, 820 cm^{-1}; pmr (deuteriomethanol): δ 8.66 (d, J = 0.8 Hz, 1H, H-7), 8.25 (d, J = 5.0 Hz, 1H, H-5), 7.76 (t, J = 0.8 Hz, 1H, H-2), 7.23 (d, J = 5.0 Hz, 1H, H-4), 3.57 (d, J = 0.8 Hz, 2H, $-CH_2CONH_2$).

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.51; H, 4.62; N, 15.64.

2-(3-Furo[3,2-*c*]pyridyl)acetamide **6d**.

This compound had mp 209-211.5°; ir (potassium bromide): 3295, 3160, 3105, 3035, 2855, 2800, 1675, 1585, 1460, 1445, 1410, 1350, 1340, 1310, 1290, 1280, 1190, 1165, 1075, 1025, 870, 815 cm^{-1}; pmr (deuteriomethanol): δ 8.89 (d, J = 0.8 Hz, 1H, H-4), 8.39 (d, J = 6.0 Hz, 1H, H-6), 7.79 (t, J = 1.0 Hz, 1H,

H-2), 7.54 (dd, J = 0.8, 6.0 Hz, 1H, H-7), 3.68 (d, J = 1.0 Hz, 2H, -CH_2CONH_2).

Anal. Calcd. for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.64; H, 4.70; N, 15.70.

General Procedure for the Preparation of 2-(3-Furopyridyl)acetic Acids **7a, 7b, 7c** and **7d**.

A) A solution of the amide **6** (100 mg, 0.57 mmole), potassium hydroxide (100 mg, 1.8 mmoles) and water (1.0 ml) in ethanol (10 ml) was refluxed for 2 hours. After evaporation of the solvent, the slightly brown residue was dissolved in water (5 ml) and passed through a column of 10 ml of Amberlite IRC-50 to remove the potassium ion. Evaporation of the aqueous solution afforded a crystalline mass of crude **7a•2H_2O**, **7b•2H_2O**, **7c** and **7d** in yields of 83%, 90%, 95% and 90%, respectively.

B) A mixture of the cyano derivative **5** (1.84 g, 11.67 mmoles), potassium hydroxide (1.84 g, 33 mmoles), water (18.4 ml) and ethanol (43 ml) was refluxed for 2 hours. After evaporation of the solvent, the residual mass was processed in the same manner as described above. The carboxylic acid **7a, 7b, 7c** and **7d** were obtained in almost quantitative yields.

2-(3-Furo[2,3-*b*]pyridyl)acetic Acid **7a**.

The residue from **6a** was recrystallized from methanolacetone to give a pure sample of **7a•2H_2O** as colorless needles, mp 237-240°; ir (potassium bromide): 3435 (broad), 3070, 2930, 2900, 1730, 1610, 1590, 1575, 1405, 1280, 1260, 1230, 1100, 1060, 910, 870, 805, 775 cm^{-1}; pmr (deuteriomethanol): δ 8.18 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 9.03 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.75 (t, J = 2.0 Hz, 1H, H-2), 7.24 (dd, J = 4.8, 7.6 Hz, 1H, H-5), 3.72 (d, J = 2.0 Hz, 2H, -CH_2COOH).

Anal. Calcd. for $C_9H_7NO_3$•$2H_2O$: C, 50.71; H, 5.20; N, 6.57. Found: C, 50.91; H, 5.07; N, 6.65.

2-(3-Furo[3,2-*b*]pyridyl)acetic Acid **7b**.

Recrystallization of the crude **7b** from methanol-acetone afforded a pure sample of **7b•2H_2O** as colorless leaves, mp 156-158°; ir (potassium bromide): 3430 (broad), 3110, 3045, 2975, 2925, 1730, 1595, 1415, 1390, 1300, 1270, 1250, 1180, 1090, 1070, 945, 925, 795, 785, 770 cm^{-1}; pmr (deuteriomethanol): δ 8.40 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.92 (t, J = 1.2 Hz, 1H, H-2), 7.83 (dd, J = 1.2, 8.2 Hz, 1H, H-7), 7.26 (dd, J = 4.6, 8.2 Hz, 1H, H-6), 3.62 (d, J = 1.2 Hz, 2H, -CH_2COOH).

Anal. Calcd. for $C_9H_7NO_3$•$2H_2O$: C, 50.71; H, 5.20; N, 6.57. Found: C, 50.83; H, 4.85, N, 6.62.

2-(3-Furo[2,3-*c*]pyridyl)acetic Acid **7c**.

Recrystallization of the crude **7c** from methanol gave an analytically pure sample of **7c** as colorless needles, mp 233-236°; ir (potasslum bromide): 3460 (broad), 3165, 3125, 3065, 2920, 2855, 2790, 2465-2365 (broad), 1715, 1620, 1585, 1470, 1435, 1360, 1290, 1230, 1165, 1095, 1035, 940, 905, 875, 850, 825, 790, 775 cm^{-1}; pmr (deuteriomethanol): δ 8.77 (d, J = 0.8 Hz, 1H, H-7), 8.33 (d, J = 5.6 Hz, 1H, H-5), 7.96 (t, J = 1.0 Hz, 1H, H-2), 7.70 (dd, J = 0.8, 5.6 Hz, 1H, H-4), 3.76 (d, J = 1.0 Hz, 2H, -CH_2COOH) .

Anal. Calcd. for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.15; H, 4.11; N, 7.91.

2-(3-Furo[3,2-*c*]pyridyl)acetic Acid **7d**.

The crude **7d** was recrystallized from methanol to give an analytically pure sample as colorless needles, mp 202-204°; ir (potassium bromide): 3430 (broad), 3185, 3155, 3135, 3115, 3075, 3050, 3030, 2925, 2900, 2870, 1710, 1695, 1550, 1465, 1415, 1395, 1330, 1300, 1235, 1185, 1140, 1065, 1035, 930, 900, 820 cm^{-1}; pmr (deuteriomethanol): δ 8.85 (s, 1H, H-4), 8.37 (d, J = 5.6 Hz, 1H, H-6), 7.78 (t, J = 1.0 Hz, 1H, H-2), 7.53 (d, J = 5.6 Hz, 1H, H-7), 3.78 (d, J = 1.0 Hz, 2H, -CH_2COOH).

Anal. Calcd. for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 61.38, H, 4.10; N, 7.52.

Decarboxylation of 2-(3-Furopyridyl)acetic Acids **7a-d**.

The carboxylic acid **7** (300 mg, 1.7 mmoles) was mixed with copper powder (10 g) in a 5-ml flask equipped with an air condenser, and then heated to pyrolize using a soft flame. The distillate was redistilled *in vacuo* to give 3-methylfuropyridines **8a** (10%), **8b** (15%), **8c** (12%) and **8d** (14%).

The structures of **8a**, **8b** and **8c** were confirmed by comparison of the ir and pmr spectra with those of the authentic sample [2b, 2c, 2d].

3-Methylfuro[3,2-*c*]pyridine **8d**.

This compound was obtained as a slightly yellow oil of bp 130° (bath temperature) (25 mm Hg); ir (liquid film): 3090, 3040, 2910, 2850, 1625, 1575, 1445, 1380, 1340, 1285, 1195, 1155, 1060, 1015, 955, 860, 805, 760 cm^{-1}; pmr (carbon tetrachloride): δ 8.75 (d, J = 0.8 Hz, 1H, H-4), 8.38 (d, J = 5.6 Hz, 1H, H-6), 7.32 (q, J = 0.8 Hz, 1H, H-2), 7.27 (dd, J = 0.8, 5.6 Hz, 1H, H-7), 2.28 (d, J = 0.8 Hz, 3H, 3-Me); ms: m/z 133.0523 (M^+, Calcd. for C_8H_7NO: 133.0527).

General Procedure for the Preparation of 2-(3-Furopyridyl)-ethylamines **9a, 9b, 9c** and **9d**.

A mixture of the nitrile **5** (120 mg, 0.76 mmole) and lithium aluminum hydride (171 mg, 4.5 mmoles) in absolute ether (30 ml) was stirred and refluxed for 20 hours. The mixture was cooled, treated with aqueous Rochelle salt solution, and then extracted with chloroform. The residue from the dried (magnesium sulfate) chloroform solution was distilled to give **9a, 9b, 9c** and **9d** in 60%, 80%, 55% and 73% yield, respectively.

2-(3-Furo[2,3-*b*]pyridyl)ethylamine **9a**.

This compound had bp 105-115° (bath temperature) (0.25 mm Hg) (colorless oil); ir (liquid film): 3365 (broad), 2925, 2855, 1590, 1575, 1405, 1325, 1285, 1250, 1190, 1090, 935, 870, 805, 780 cm^{-1}; pmr (deuteriochloroform): δ 8.27 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.87 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.51 (t, J = 0.8 Hz, 1H, H-2), 7.17 (dd, J = 4.8, 7.6 Hz, 1H, H-5), 3.20-2.67 (complex m, 4H, -$CH_2CH_2NH_2$), 1.44 (s, 2H, -NH_2); ms: m/z 162.0793 (M^+, Calcd. for $C_9H_{10}N_2O$: 162.0792).

2-(3-Furo[3,2-*b*]pyridyl)ethylamine **9b**.

This compound had bp 100-110° (bath temperature) (0.25 mm Hg) (colorless oil); ir (liquid film): 3360 (broad), 3105, 2924, 2870, 1675, 1615, 1570, 1480, 1415, 1325, 1280, 1185, 1085, 1035, 775, 760 cm^{-1}; pmr (carbon tetrachloride): δ 8.38 (dd, J = 1.2, 4.8 Hz, 1H, H-5), 7.63 (t, J = 0.8 Hz, 1H, H-2), 7.58 (dd, J = 1.2, 8.4 Hz, 1H, H-7), 7.06 (dd, J = 4.8, 8.4 Hz, 1H, H-6), 3.20-2.68 (complex m, 4H, -$CH_2CH_2NH_2$), 1.14 (s, 2H, -NH_2); ms: m/z 162.0791 (M^+, Calcd. for $C_9H_{10}N_2O$: 162.0792).

2-(3-Furo[2,3-*c*]pyridyl)ethylamine **9c**.

This compound had bp 110-120° (bath temperature) (0.2 mm Hg) (colorless oil); ir (liquid film): 3360 (broad), 3105, 2925, 1870, 1675, 1615, 1570, 1480, 1415, 1325, 1280, 1185, 1085,

1035, 775, 760 cm^{-1}; pmr (carbon tetrachloride): δ 8.80 (d, J = 1.6 Hz, 1H, H-7), 8.38 (d, J = 5.6 Hz, 1H, H-5), 7.57 (t, J = 1.2 Hz, H-2), 7.47 (dd, J = 1.6, 5.6 Hz, 1H, H-4), 3.20-2.65 (complex m, 4H, $-CH_2CH_2NH_2$), 1.35 (s, 2H, $-NH_2$); ms: m/z 162.0799 (M^+, Calcd. for $C_9H_{10}N_2O$: 162.0792).

2-(3-Furo[3,2-*c*]pyridyl)ethylamine **9d**.

This compound had bp 110-120° (bath temperature) (0.2 mm Hg) (colorless oil); ir (liquid film): 3360 (broad), 3105, 2915, 2870, 1675, 1570, 1480, 1415, 1325, 1280, 1185, 1085, 1035, 775, 760 cm^{-1}; pmr (carbon tetrachloride): δ 8.94 (d, J = 0.8 Hz, 1H, H-4), 8.51 (d, J = 5.8 Hz, 1H, H-6), 7.45 (t, J = 0.8 Hz, 1H, H-2), 7.41 (dd, J = 0.8, 5.8 Hz, 1H, H-7), 3.27-2.73 (complex m, 4H, $-CH_2CH_2NH_2$), 1.53 (s, 2H, $-NH_2$); ms: m/z 162.0793 (M^+, Calcd. for $C_9H_{10}N_2O$: 162.0792).

General Procedure for the Preparation of Ethyl 2-(3-Furopyridyl)acetates **10a, 10b, 10c** and **10d**.

A solution of carboxylic acid **7** (1.9 g, 11 mmoles), sulfuric acid (2 ml) in ethanol (15 ml) was refluxed for 18 hours. After evaporation of the ethanol, the residual syrup was dissolved in water (20 ml), basified with sodium bicarbonate, extracted with chloroform and dried over magnesium sulfate.

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

Ethyl 2-(3-Furo[2,3-*b*]pyridyl)acetate **10a**.

The residue from **7a** was distilled to give the ester **10a** as a slightly yellow oil of bp 120-130° (bath temperature) (0.05 mm Hg) in 90% yield; ir (liquid film): 3115, 1065, 2985, 2940, 2905, 1735, 1590, 1575, 1405, 1370, 1285, 1250, 1175, 1100, 1030, 870, 775, 715 cm^{-1}; pmr (deuteriochloroform): δ 8.18 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.81 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.60 (t, J = 1.0 Hz, 1H, H-2), 7.08 (dd, J = 4.8, 7.6 Hz, 1H, H-5), 4.12 (q, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 3.56 (d, J = 1.0 Hz, 2H, $-CH_2COOEt$), 1.23 (t, J = 7.2 Hz, 3H, $-OCH_2CH_3$); ms: m/z: 205.0739 (M^+, Calcd. for $C_{11}H_{11}NO_3$: 205.0738).

Ethyl 2-(3-Furo[3,2-*b*]pyridyl)acetate **10b**.

Distillation of the residue from **7b** yielded the ester **10b** (87%) as a pale yellow oil of bp 110-120 (bath temperataure) (0.2 mm Hg); ir (liquid film): 3115, 3045, 2985, 2940, 2910, 1740, 1615, 1570, 1480, 1415, 1330, 1280, 1245, 1205, 1170, 1085, 1030, 940, 870, 785, 710 cm^{-1}; pmr (carbon tetrachloride): δ 8.42 (dd, J = 1.4, 4.6 Hz, 1H, H-5), 7.93 (t, J = 1.2 Hz, 1H, H-2), 7.62 (dd, J = 1.4, 8.4 Hz, 1H, H-7), 7.07 (dd, J = 1.2 Hz, 1H, H-6), 4.16 (q, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 3.56 (d, J = 1.0 Hz, 2H, $-CH_2COOEt$), 1.23 (t, J = 7.2 Hz, 3H, $-OCH_2CH_3$); ms: m/z 205.0739 (M^+, Calcd. for $C_{11}H_{11}NO_3$ 205.0738).

Ethyl 2-(3-Furo[2,3-*c*]pyridyl)acetate **10c**.

Distillation of the crude product from **7c** afforded the pure ester **10c** (97%) as an almost colorless oil, bp 110-120° (bath temperature) (0.1 mm Hg); ir (liquid film): 3120, 3065, 2985, 2940, 1735, 1615, 1465, 1430, 1370, 1260, 1180, 1160, 1100, 1030, 865, 825, 780 cm^{-1}; pmr (carbon tetrachloride): δ 8.70 (d, J = 1.0 Hz, 1H, H-7), 8.31 (d, J = 5.2 Hz, 1H, H-5), 7.63 (t, J = 1.2 Hz, 1H, H-2), 7.34 (dd, J = 1.0, 5.2 Hz, 1H, H-5), 4.10 (q, J = 7.0 Hz, 2H, $-OCH_2CH_3$), 3.54 (d, J = 1.2 Hz, 2H, $-CH_2COOEt$), 1.22 (t, J = 7.0 Hz, 3H, $-OCH_2CH_3$); ms: m/z 205.0739 (M^+, Calcd. for $C_{11}H_{11}NO_3$: 205.0738).

Ethyl 2-(3-Furo[3,2-*c*]pyridyl)acetate **10d**.

The residue from **7d** was distilled to give **10d** (75%) as a colorless oil of bp 120-130° (bath temperature) (0.6 mm Hg); ir (liquid film): 3125, 3040, 2985, 2940, 1735, 1615, 1580, 1460, 1370, 1295, 1260, 1180, 1160, 1080, 1030, 870, 815 cm^{-1}; pmr (carbon tetrachloride): δ 8.71 (d, J = 0.8 Hz, 1H, H-4), 8.31 (d, J = 5.6 Hz, 1H, H-6), 7.52 (t, J = 1.0 Hz, 1H, H-2), 7.22 (dd, J = 0.8, 5.6 Hz, 1H, H-7), 4.08 (q, J = 7.0 Hz, 2H, $-OCH_2CH_3$), 3.60 (d, J = 1.0 Hz, 2H, $-CH_2COOEt$), 1.20 (t, J = 7.0 Hz, 3H, $-OCH_2CH_3$); ms: m/z 205.0743 (M^+, Calcd. for $C_{11}H_{11}NO_3$: 205.0738).

Reaction of the Lithio Intermediates from Ethyl 2-(3-Furo pyridyl)acetates **10a, 10b, 10c** and **10d** with Benzaldehyde.

General Procedure.

To a stirred solution of diisopropylamine (123 mg, 1.22 mmoles) in dry tetrahydrofuran (15 ml) was added a solution of *n*-butyllithium in hexane (0.75 ml, 1.6 *M*, 1.2 mmoles) dropwise by syringe at -75° under nitrogen atmosphere. After stirring at this temperature for 20 minutes, a solution of compound **10** (205 mg, 1.0 mmole) in dry tetrahydrofuran (5 ml) was added by syringe and stirred for 20 minutes at -75°. Benzaldehyde (136 mg, 1.28 mmoles) was added to this cold mixture by syringe. After stirring at this temperature, the mixture was treated with 10% hydrochloric acid (2 ml) and water (10 ml), basified with sodium bicarbonate and extracted with chloroform. The chloroform solution was dried (magnesium sulfate) and evaporated to leave slightly brown syrupy residue. The pmr spectra of the crude products revealed that in every case the *threo*- and *erythro*-diasterioisomers are formed in the ratio of 1:1.

Further processing of the crude product is indicated in the following paragraph.

Ethyl *threo*-**11a-T** and ethyl *erythro*-2-(3-Furo[2,3-*b*]pyridyl)-3-hydroxy-3-phenylpropionate (**11a-E**).

The crude product (360 mg) from **10a** was chromatographed on a silica gel (40 g) column. The first fraction eluted with chloroform-methanol (99:1) gave 130 mg (35%) of **11a-T,** and the second fraction 130 mg (42%) of **11a-E**.

Compound **11a-T**.

The first fraction was recrystallized from ether to give **11a-T** as colorless sandy crystals, mp 122-125°; ir (potassium bromide): 3250, 3135, 3095, 3065, 3035, 3000, 2980, 2960, 2925, 2855, 1725, 1590, 1455, 1410, 1370, 1320, 1285, 1150, 1110, 1055, 800, 775, 760 cm^{-1}; pmr (deuteriochloroform): δ 8.25 (dd, J = 1.8, 4.8 Hz, 1H, H-6), 7.77 (dd, J = 1.8, 7.8 Hz, 1H, H-4), 7.65 (s, 1H, H-2), 7.15 (almost s, 5H, $-C_6H_5$), 7.10 (dd, J = 4.8, 7.8 Hz, 1H, H-5), 5.35 (dd, J = 4.4, 8.6 Hz, 1H, H-β), 4.22 (q, J = 7.2 Hz, 2H, $-OCH_2CH_3$), 4.09 (d, J = 8.6 Hz 1H, H-α), 3.18 (d, J = 4.4 Hz, 1H, -OH), 1.22 (t, J = 7.2 Hz, 3H, $-OCH_2CH_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: 69.71; 5.67; N, 4.37.

Compound **11a-E**.

Recrystallization of the second fraction from ether gave a pure sample of **11a-E** as colorless crystalline powder of mp 58-62°; ir (potassium bromide): 3435, 3140, 3095, 3065, 3035, 3000, 2980, 2960, 2925, 2855, 1725, 1590, 1455, 1410, 1370, 1320, 1285, 1150, 1110, 1055, 800, 775, 760 cm^{-1}; pmr (deuteriochloroform): δ 8.27 (dd, J = 1.8, 4.8 Hz, 1H, H-6), 7.82 (dd, J = 1.8, 7.8 Hz, 1H, H-4), 7.65 (s, 1H, H-2), 7.22 (almost s, 5H,

-C_6H_5), 7.14 (dd, J = 4.8, 7.8 Hz, 1H, H-5), 5.44 (dd, J = 3.2, 5.6 Hz, 1H, H-β), 4.12 (q, J = 7.2 Hz, 2H, -OC*H*$_2$CH$_3$), 4.05 (d, J = 5.6 Hz, 1H, H-α), 3.07 (d, J = 3.2 Hz, 1H, -OH), 1.12 (t, J = 7.2 Hz, 3H, -OCH$_2$C*H*$_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4 \cdot 1/2H_2O$: C, 67.49; H, 5.66; N, 4.37. Found: C, 67.77; H, 5.90; N, 4.39.

Ethyl *threo*-**11b-T** and Ethyl *erythro*-2-(3-Furo[3,2-*b*]pyridyl)-3-hydroxy-3-phenylpropionate (**11b-E**).

The residue (310 mg) of the dried chloroform solution from **10b** was chromatographed on a silica gel (35 g) column. The first fraction eluted with chloroform afforded 125 mg (40%) of **11ab-T**, and the second 140 mg (45%) of **11b-E**.

Compound **11b-T**.

Recrystallization of the crude **11b-T** from ether gave a pure sample of mp 104-106° as colorless cubes; ir (potassium bromide): 3165, 3030, 2985, 2905, 2870, 1740, 1620, 1445, 1415, 1325, 1310, 1280, 1240, 1180, 1085, 1050, 1025, 950, 785, 770, 705 cm^{-1}; pmr (deuteriochloroform): δ 8.52 (dd, J = 1.2, 4.8 Hz, 1H, H-5), 7.73 (dd, J = 1.2, 8.2 Hz, 1H, H-7), 7.64 (s, 1H, H-2), 7.23 (almost s, 5H, -C_6H_5), 7.16 (dd, J = 4.8, 8.2 Hz, 1H, H-6), 6.78 (broad s, 1H, -OH), 5.60 (d, J = 4.8 Hz, 1H, H-β), 4.42 (d, J = 4.8 Hz, 1H, H-α), 4.15 (q, J = 7.2 Hz, 2H, -OC*H*$_2$CH$_3$), 1.16 (t, J = 7.2 Hz, 3H, -OCH$_2$C*H*$_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.65; H, 5.59; N, 4.46.

Compound **11b-E**.

The second fraction was recrystallized from ether to give a pure sample of **11b-E** as colorless cubes of mp 91-93.5°; ir (potassium bromide): 3155, 3115, 3035, 2990, 2975, 2920, 2900, 2870, 1725, 1620, 1575, 1455, 1415, 1365, 1330, 1260, 1200, 1180, 1100, 1060, 780, 770 cm^{-1}; pmr (deuteriochloroform): δ 8.45 (dd, J = 1.4, 4.6 Hz, 1H, H-5), 7.75 (s, 1H, H-2), 7.67 (dd, J = 1.4, 8.2 Hz, 1H, H-7), 7.25 (almost s, 5H, C_6H_5), 7.16 (dd, J = 4.6, 8.2 Hz, 1H, H-6), 5.43 (d, J = 4.6 Hz, 1H, H-β), 5.39 (broad s, 1H, -OH), 4.43 (d, J = 4.6 Hz, 1H H-α) 4.12 (q, J = 7.0 Hz, 2H, -OC*H*$_2$CH$_3$), 1.11 (t, J = 7.0 Hz, 3H, -OCH$_2$C*H*$_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.50; H, 5.53; N, 4.45.

Ethyl *threo*-**11c-T** and Ethyl *erythro*-2-(3-Furo[2,3-*c*]pyridyl)-3-hydroxyl-3-phenylpropionate **11c-E**.

The crude product (350 mg) from **10c** was column-chromatographed (40 g of silica gel, chloroform-methanol (99:1)) to give 133 mg (43%) of **11c-T** (first fraction) and 150 mg of **11c-E** (second fraction).

Compound **11c-T**.

The first fraction was recrystallized from acetone-ether to give a pure sample of **11c-T**, mp 134-136° as colorless needles; ir (potassium bromide): 3155, 2905, 2860, 1720, 1615, 1495, 1470, 1450, 1430, 1380, 1325, 1305, 1290, 1280, 1200, 1180, 1095, 1050, 1030, 1010, 820, 765, 705 cm^{-1}; pmr (deuteriochloroform): δ 8.72 (d, J = 1.0 Hz, 1H, H-7), 8.27 (d, J = 5.6 Hz, 1H, H-5), 7.75 (s, 1H, H-2), 7.36 (dd, J = 1.0, 5.6 Hz, 1H, H-4), 7.14 (almost s, 5H, -C_6H_5), 5.29 (dd (changed to doublet by addition of deuterium oxide), J = 4.4, 8.8 Hz, 1H, H-β), 4.22 (q, J = 7.2 Hz, 2H, -OC*H*$_2$CH$_3$), 4.08 (d, J = 8.8 Hz, 1H, H-α), 3.65 (disappeared by addition of deuterium oxide), J = 4.4 Hz, 1H, -OH), 1.22 (t, J = 7.2 Hz, 3H, -OCH$_2$C*H*$_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.43; H, 5.54; N, 4.47.

Compound **11c-E**.

Recrystallization of the second fraction from ether yielded a pure sample of **11c-E**, colorless sandy crystals, mp 128-131°; ir (potassium bromide): 3185, 2975, 2935, 2900, 2865, 1725, 1615, 1435, 1370, 1320, 1290, 1250, 1180, 1150, 1105, 1050, 1030, 870, 830, 760, 700 cm^{-1}; pmr (deuteriochloroform): δ 8.71 (d, J = 1.0 Hz, 1H, H-7), 8.24 (d, J = 5.4 Hz, 1H, H-5), 7.75 (s, 1H, H-2), 7.36 (dd, J = 1.0, 5.4 Hz, 1H, H-4), 7.23 (almost s, 5H, -C_6H_5), 5.44 (d, J = 5.6 Hz, 1H, H-β), 4.10 (q, J = 7.2 Hz, 2H, -OC*H*$_2$CH$_3$), 4.08 (d, J = 5.6 Hz, 1H, H-α), 3.65 (broad s, 1H, -OH), 1.11 (t, J = 7.2 Hz, 3H, -OCH$_2$C*H*$_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.58; H, 5.56; N, 4.52.

Ethyl *threo*-**11d-T** and Ethyl *erythro*-2-(3-Furo[3,2-*c*]pyridyl)-3-hydroxy-3-phenylpropionate (**11d-E**).

The crude product (360 mg) from **10d** was chromatographed on a silica gel (40 g) column. The first fraction eluted with chloroform-methanol (99:1) gave 140 mg (45%) of **11d-T**, and the second 125 mg (40%) of **11d-E**.

Compound **11d-T**.

Recrystallization of the first fraction from acetone-ether yielded a pure sample of **11d-T** as colorless sandy crystals of mp 136-140°; ir (potassium bromide): 3185, 3110, 3005, 2990, 2960, 2900, 2845, 1725, 1575, 1455, 1435, 1370, 1325, 1290, 1270, 1175, 1080, 1060, 1020, 870, 820, 740 cm^{-1}; pmr (deuteriochloroform): δ 8.75 (d, J = 0.8 Hz, 1H, H-4), 8.40 (d, J = 5.6 Hz, 1H, H-6), 7.50 (d, 1H, H-2), 7.33 (dd, J = 0.8, 5.6 Hz, 1H, H-7), 7.17 (almost s, 5H, -C_6H_5), 5.34 (dd, J = 4.4, 8.4 Hz, 1H, H-β), 4.24 (q, J = 7.2 Hz, 2H, -OC*H*$_2$CH$_3$), 4.15 (d, J = 8.4 Hz, 1H, H-α), 3.67 (d, J = 4.4 Hz, 1H, -OH), 1.24 (t, J = 7.2 Hz, 3H, -OCH$_2$C*H*$_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.59; H, 5.60; N, 4.50.

Compound **11d-E**.

Recrystallization of the second fraction from ether gave a pure sample of **11d-E** as colorless needles, mp 138-140°; ir (potassium bromide): 3230, 3115, 3090, 3055, 3030, 1985, 2900, 1725, 1580, 1460, 1330, 1295, 1270, 1175, 1155, 1085, 1060, 1045, 1030, 870, 820, 760, 700 cm^{-1}; pmr (deuteriochloroform): δ 8.72 (d, J = 0.8 Hz, 1H, H-4), 8.34 (d, J = 5.6 Hz, 1H, H-6), 7.60 (s, 1H, H-2), 7.32 (dd, J = 0.8, 5.6 Hz, 1H, H-7), 7.21 (almost s, 5H, -C_6H_5), 5.28 (d, J = 5.2 Hz, 1H, H-β), 4.12 (d, J = 5.2 Hz, 1H, H-α), 4.10 (q, J = 7.0 Hz, 2H, -OC*H*$_2$CH$_3$), 3.48 (broad s, 1H, -OH), 1.13 (t, J = 7.2 Hz, -OCH$_2$C*H*$_3$).

Anal. Calcd. for $C_{18}H_{17}NO_4$: C, 69.44; H, 5.50; N, 4.50. Found: C, 69.37; H, 5.52; N, 4.45.

Reaction of the Lithio Intermediates from Compound **10a, 10b, 10c** and **10d** with Iodomethane.

General Procedure.

A solution of *n*-buyllithium in hexane (0.34 ml, 1.6 *M*, 0.54 mmole) was added to a solution of diisopropylamine (55 mg, 0.54 mmole) in dry tetrahydrofuran (10 ml) by syringe at -75° under a nitrogen atmosphere with stirring. After stirring at this temperature for 20 minutes, a solution of compound **10** (100 mg,

0.49 mmole) in dry tetrahydrofuran (5 ml) was added by syringe and stirred for 20 minutes at -75°. Iodomethane (78 mg, 0.55 mmole) was added to this mixture, and stirring was continuted for 5 hours. The mixture was treated with 10% hydrochloric acid (1.5 ml) and water (10 ml), basified with sodium bicarbonate and extracted with chloroform. The residue of the dried (magnesium sulfate) chloroform extract was chromatographed on a silica gel (15 g) column eluting with hexane-ethyl acetate (7:3) to give compounds **12a, 12b, 12c** and **12d** in 97%, 94%, 94% and 82% yield, respectively.

Ethyl 2-(3-Furo[2,3-*b*]pyridyl)propionate **12a**.

This compound was obtained as a colorless oil of bp 125-135° (bath temperature) (0.05 mm Hg); ir (liquid film): 3145, 3110, 3065, 2985, 2940, 2905, 2880, 1735, 1590, 1570, 1455, 1405, 1380, 1320, 1245, 1195, 1180, 1110, 1090, 1050, 1025, 980, 870, 800, 780 cm^{-1}; pmr (deuteriochloroform): δ 8.33 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 8.04 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.65 (d, J = 0.8 Hz, 1H, H-2), 7.22 (dd, J = 4.8 H, 7.6 Hz, 1H, H-5), 4.10 (q, J = 7.0 Hz, 2H, -OCH_2CH$_3$), 3.90 (dq, J = 0.8, 7.0 Hz, 1H, H-α), 1.69 (d, J = 7.0 Hz, 3H, -Me), 1.20 (t, J = 7.0 Hz, 3H, -OCH$_2$CH_3); ms: m/z 219.0888 (M$^+$, Calcd. for $C_{12}H_{13}NO_3$: 219.0895).

Ethyl 2-(3-Furo[3,2-*b*]pyridyl)propionate **12b**.

This compound was obtained as a colorless oil, bp 125-135° (bath temperature) (0.035 mm Hg); ir (liquid film): 3115, 3060, 3040, 3020, 2985, 2940, 1735, 1615, 1570, 1455, 1415, 1375, 1330, 1195, 1175, 1070, 870, 780 cm^{-1}; pmr (deuteriochloroform): δ 8.56 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.82 (d, J = 0.8 Hz, 1H, H-2), 7.73 (dd, J = 1.2, 8.0 Hz, 1H, H-7), 7.20 (dd, J = 4.6, 8.0 Hz, 1H, H-6), 4.20 (q, J = 7.0 Hz, 2H, -OCH_2CH$_3$), 4.18 (dq, J = 0.8, 7.0 Hz, 1H, H-α), 1.64 (d, J = 7.0 Hz, 3H, -Me), 1.23 (t, J = 7.0 Hz, 3H, -OCH$_2$CH_3); ms: m/z 219.0896 (M$^+$, Calcd. for $C_{12}H_{13}NO_3$: 219.0895)

Ethyl 2-(3-Furo[2,3-*c*]pyridyl)propionate **12c**.

This compound was obtained as a colorless oil, bp 120-130° (bath temperature) (0.05 mm Hg); ir (liquid film): 3150, 3110, 3075, 3040, 2985, 2940, 2910, 2880, 1735, 1610, 1580, 1470, 1430, 1380, 1325, 1290, 1255, 1180, 1100, 1030, 865, 825, 785 cm^{-1}; pmr (deuteriochloroform): δ 8.84 (d, J = 0.8 Hz, 1H, H-7), 8.41 (d, J = 5.0 Hz, 1H, H-5), 7.67 (d, J = 0.8 Hz, 1H, H-2), 7.58 (dd, J = 0.8, 5.0 Hz, 1H, H-4), 4.16 (q, J = 7.0 Hz, 2H, -OCH_2CH$_3$), 3.89 (dq, J = 0.8, 7.0 Hz, 1H, H-α), 1.61 (d, J = 7.0 Hz, 3H, -Me), 1.19 (t, J = 7.0 Hz, 3H, -OCH$_2$CH_3); ms: m/z 219.0893 (M$^+$, Calcd. for $C_{12}H_{13}NO_3$: 219.0895).

Ethyl 2-(3-Furo[3,2-*c*]pyridyl)propionate **12d**.

This compound was obtained as a colorless oil, bp 125-135° (bath temperature) (0.06 mm Hg); ir (liquid film): 3160, 3115, 3095, 3045, 2985, 2940, 2910, 2880, 1775, 1610, 1575, 1460, 1380, 1325, 1295, 1255, 1185, 1095, 1070, 1025, 870, 815 cm^{-1}; pmr (deuteriochloroform): δ 9.05 (d, J = 0.8 Hz, 1H, H-4), 8.53 (d, J = 5.8 Hz, 1H, H-6), 7.62 (d, J = 0.8 Hz, 1H, H-2), 7.42 (dd, J = 0.8, 5.8 Hz, 1H, H-7), 4.20 (q, J = 7.2 Hz, 2H, -OCH_2CH$_3$), 3.98 (dq, J = 0.8, 7.2 Hz, 1H, H-α), 1.64 (d, J = 7.2 Hz, 3H, -Me), 1.24 (t, J = 7.2 Hz, 3H, -OCH$_2$CH$_3$); ms: m/z 219.0892 (M$^+$, Calcd. for $C_{12}H_{13}NO_3$: 219.0895).

Reaction of Compounds **10a, 10b, 10c** and **10d** with 1.2 Molar Equivalents of Lithium Diisopropylamide and Acetone.

General Procedure.

To a stirred solution of lithium diisopropylamide prepared from diisopropylamine (123 mg, 1.22 mmoles) and *n*-butyllithium in hexane (0.75 ml, 1.6 *M*, 1.2 mmoles) in 15 ml of dry tetrahydrofuran was added a solution of compound **10** (205 mg, 1.0 mmole) in 5 ml of dry tetrahydrofuran by syringe over a period of 5 minutes at -75° under a nitrogen atmosphere. After stirring for 20 minutes, to the mixture was added acetone (70 mg, 1.2 mmoles) by syringe, and stirring was continued for 7 hours at this temperature. The cold reaction mixture was treated with 10% hydrochloric acid (2 ml), and the cold bath was removed. After evaporation of the solvent under reduced pressure, the mixture was diluted with water (20 ml), basified with sodium bicarbonate, extracted with chloroform, and dried (magnesium sulfate).

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

Ethyl 2-(3-Furo[2,3-*b*]pyridyl)-3-hydroxy-3-methylbutanoate **13a**.

The residue from **10a** (230 mg) was purified by chromatography on a silica gel (25 g) column using chloroform-methanol (99:1) as an eluent to give 150 mg (57%) of pure **13a** as a colorless syrup of bp 140-150° (bath temperature) (0.03 mm Hg); ir (liquid film): 3400, 3145, 3105, 3065, 2980, 2940, 2905, 2875, 1730, 1590, 1565, 1465, 1410, 1320, 1240, 1105, 1030, 950, 905, 870, 800, 775, 760 cm^{-1}; pmr (carbon tetrachloride): δ 8.18 (dd, J = 1.6, 4.6 Hz, 1H, H-6), 8.02 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.81 (s, 1H, H-2), 7.13 (dd, J = 4.5, 7.6 Hz, 1H, H-5), 4.15 (q, J = 7.0 Hz, 2H, -OCH_2CH$_3$), 3.77 (s, 1H, H-α), 3.48 (broad s, 1H, -OH), 1.31 and 1.17 (each s, 3H, -Me), 1.19 (t, J = 7.0 Hz, 3H, -OCH$_2$CH_3); ms: m/z 263.1151 (M$^+$, Calcd. for $C_{14}H_{17}NO_4$ 263.1157).

Ethyl 2-(3-Furo[3,2-*b*]pyridyl)-3-hydroxy-3-methylbutanoate **13b**.

Recrystallization of the crude product (210 mg) from ether-hexane yielded 170 mg (65%) of a pure sample of **13b** as colorless cubes of mp 63.5-65°; ir (potassium bromide): 3300 (broad), 3165, 3130, 3065, 2980, 2935, 1875, 1725, 1615, 1570, 1470, 1425, 1390, 1330, 1290, 1245, 1205, 1175, 1145, 1090, 1080, 1030, 780, 755 cm^{-1}; pmr (carbon tetrachloride): δ 8.41 (dd, J = 1.2, 4.6 Hz, 1H, H-5), 7.86 (s, 1H, H-2), 7.64 (dd, J = 1.2, 8.4 Hz, 1H, H-7), 7.11 (dd, J = 4.6, 8.4 Hz, 1H, H-6), 4.15 (q, J = 7.4 Hz, 2H, -OCH_2CH$_3$), 4.07 (s, 1H, H-α), 4.05 (s, 1H, -OH), 1.28 and 1.11 (each, s, 3H, -Me), 1.24 (t, J = 7.4 Hz, 3H, -OCH$_2$CH_3).

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.52. Found: C, 63.99; H, 6.55; N, 5.32.

Ethyl 2-(3-Furo[2,3-*c*]pyridyl)-3-hydroxy-3-methylbutanoate **13c**.

The crude product (240 mg) from **10c** was recrystallized from ether to give 200 mg (76%) of **13c** as colorless cubes, mp 88.5-91°; ir (potassium bromide): 3265 (broad), 3150, 2990, 2975, 2940, 2915, 2880, 1725, 1610, 1435, 1385, 1320, 1290, 1205, 1170, 1155, 1130, 1100, 1030, 910, 865, 835 cm^{-1}; pmr (carbon tetrachloride): δ 8.66 (d, J = 1.0 Hz, 1H, H-7), 8.22 (d, J = 5.2 Hz, 1H, H-5), 7.83 (s, 1H, H-2), 7.42 (dd, J = 1.0, 5.2 Hz, 1H, H-4), 4.13 (q, J = 7.2 Hz, 2H, -OCH_2CH$_3$), 3.70 (s, 1H, H-α), 3.37 (broad s, 1H, -OH), 1.33 and 1.14 (each s, 3H, -Me), 1.22

(t, J = 7.2 Hz, 3H, -OCH_2CH_3).

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.31. Found: C, 63.94; H, 6.55; N, 5.27.

Ethyl 2-(3-Furo[3,2-*c*]pyridyl)-3-hydroxy-3-methylbutanoate **13d**.

The crude product (280 mg) was purified by recrystallization from ether to afford **13d** as colorless needles of mp 118-119°; ir (potassium bromide): 3165 (broad), 2985, 2970, 2935, 2910, 1875, 1730, 1615, 1590, 1460, 1380, 1360, 1320, 1290, 1165, 1125, 1070, 1025, 900, 875, 820, 750 cm^{-1}; pmr (carbon tetrachloride): δ 8.78 (d, J = 1.0 Hz, 1H, H-4), 8.30 (d, J = 5.6 Hz, H-6), 7.72 (s, 1H, H-2), 7.26 (dd, J = 1.0, 5.6 Hz, 1H, H-7), 4.15 (q, J = 7.0 Hz, 2H, -OCH_2CH_3), 3.79 (s, 1H, H-α), 3.40 (broad s, 1H, -OH), 1.36 and 1.19 (each s, 3H, -Me), 1.24 (t, J = 7.0 Hz, 3H, -OCH_2CH_3).

Anal. Calcd. for $C_{14}H_{17}NO_4$: C, 63.87; H, 6.51; N, 5.32. Found: C, 63.98; H, 6.47; N, 5.26.

Reaction of Compounds **10a-d** with 3.0 Molar Equivalents of Lithium Diisopropylamide and Acetone.

General Procedure.

To a solution of diisopropylamine (305 mg, 3.0 mmoles) in dry tetrahydrofuran (15 ml) was added a solution of *n*-butyllithium in hexane (1.9 ml, 1.6 *M*, 3.0 mmoles) by syringe at -75° under a nitrogen atmosphere with stirring. After stirring at this temperature for 20 minutes, a solution of compound **10** (205 mg, 1.0 mmole) in dry teatrahydrofuran (5 ml) was added by syringe and stirred for 20 minutes. To this mixture was added acetone (175 mg, 3.0 mmoles). Stirring was continued for 7 hours at -75°. The mixture was treated with 10% hydrochloric acid (2 ml) and water (15 ml), basified with sodium bicarbonate, extracted with chloroform, dried over magnesium sulfate and evaporated to give a crude oily residue. In the case of **10c**, distillation of the crude product gave compound **13c** (bp 145-150° (bath temperature) (0.05 mm Hg)) in 90% yield, which was identified by ir and pmr spectra.

Further processing of the residue from **10a, 10b** and **10d** is indicated in the following paragraph.

Ethyl 2-{3-[2-(α-Hydroxy-α-methylethyl)furo[2,3-*b*]pyridyl]}-3-hydroxy-3-methylbutanoate **14a**.

Chromatography of the crude product (250 mg) from **10a** on a silica gel (30 g) using chloroform-methanol (99:1) as an eluent yielded 200 mg (76%) of **13a** (the first fraction, identified by ir and pmr spectra) and 60 mg (19%) of **14a** (the second fraction).

Compound **14a**.

Recrystallization of the second fraction from ether gave an analytically pure sample of mp 135.5-137.5° as colorless cubes; ir (potassium bromide): 3270 (broad), 2975, 2940, 2905, 1730, 1600, 1465, 1455, 1415, 1380, 1360, 1320, 1270, 1250, 1185, 1135, 1040, 980, 910, 865, 815, 785, 705 cm^{-1}; pmr (carbon tetrachloride): δ 8.15 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.98 (dd, J = 1.6, 8.2 Hz, 1H, H-4), 7.10 (dd, J = 4.8, 8.2 Hz, 1H, H-5), 4.77 (s, 1H, H-α), 4.14 (q, J = 7.2 Hz, 2H, -OCH_2CH_3), 3.93 and 3.40 (each broad s, 1H, -OH), 1.67 (s, 6H, 2 x -Me), 1.45 and 1.27 (each s, 3H, -Me), 1.18 (t, J = 7.2 Hz, 3H, -OCH_2CH_3).

Anal. Calcd. for $C_{17}H_{23}NO_5$: C, 63.54; H, 7.21; N, 4.36. Found: C, 63.79; H, 7.24; N, 4.32.

Ethyl 2-{3-[2-(α-Hydroxy-α-methylethyl)furo[3,2-*b*]pyridyl]}-3-hydroxy-3-methylbutanoate **14b** and Ethyl 2-{3-[7-(α-Hydroxy-α-methylethyl)furo[3,2-*b*]pyridyl]}-3-hydroxy-3-methylbutanoate **15**.

Chromatography of the crude product (275 mg) from **10b** on a silica gel (30 g) column using chloroform-methanol (99:1) as an eluent afforded 100 mg (38%) of **13b** (the first fraction, identified by ir and pmr spectra), 110 mg (34%) of **14b** (the second fraction) and 50 mg (15%) of **15** (the third fraction).

Compound **14b**.

Recrystallization of the second fraction from ether gave a pure sample of **14b** as colorless sandy crystals, mp 135-137°; ir (potassium bromide): 3500 (broad), 3280, 3100, 3080, 3050, 1980, 2935, 2870, 1725, 1615, 1430, 1370, 1315, 1275, 1240, 1210, 1165, 1140, 1030, 810 cm^{-1}; pmr (carbon tetrachloride): δ 8.36 (dd, J = 1.2, 4.8 Hz, 1H, H-5), 7.57 (dd, J = 1.2, 8.4 Hz, 1H, H-7), 7.07 (dd, J = 4.8, 8.4 Hz, 1H, H-6), 5.28 and 4.72 (each s, 1H, -OH), 46.3 (s, 1H, H-α), 4.11 (q, J = 7.4 Hz, 2H, -OCH_2CH_3), 1.58 (s, 6H, 2 x -Me), 1.52 and 0.93 (each s, 3H, -Me), 1.19 (t, J = 7.4 Hz, 3H, -OCH_2CH_3).

Anal. Calcd. for $C_{17}H_{23}NO_5$: C, 63.54; H, 7.21; N, 4.36. Found: C, 63.46; H, 7.24; N, 4.35.

Compound **15**.

This compound was obtained as a colorless oil; ir (liquid film): 3270 (broad), 2980, 2940, 2875, 1730, 1615, 1560, 1375, 1320, 1260, 1180, 1100, 1030, 965, 840, 790, 765 cm^{-1}; pmr (carbon tetrachloride): δ 8.33 (d, J = 5.0 Hz, 1H, H-5), 7.89 (s, 1H, H-2), 7.38 (d, J = 5.0 Hz, 1H, H-6), 4.20 (q, J = 7.0 Hz, 2H, -OCH_2CH_3), 4.14 (s, 1H, H-α), 3.70 (broad s, 2H, -OH), 1.72, 1.69, 1.30 and 1.14 (each s, 3H, -Me), 1.28 (t, J = 7.0 Hz, 3H, -OCH_2CH_3); ms: m/z 321.1590 (M^+, Calcd. for $C_{17}H_{23}NO_5$: 321.1575).

Ethyl 2-{3-[2-(α-Hydroxy-α-methylethyl)furo[3,2-*b*]pyridyl]}-3-hydroxy-3-methylbutanoate **14d**.

The crude product from **10d** (230 mg) was chromatographed on a silica gel (30 g) column eluting with chloroform-methanol (98:2). The first fraction gave 120 mg (45%) of **13d** (identified by ir and pmr spectra), and the second 110 mg (34%) of **14d**.

Compound **14d**.

The pure sample of **14d** was obtained by distillation of the crude product *in vacuo*, colorless oil of bp 140-150° (bath temperature) (0.06 mm Hg); ir (liquid film): 3230 (broad), 2980, 2940, 1735, 1580, 1465, 1370, 1270, 1215, 1135, 1105, 1035, 980, 920, 880, 815, 790, 760 cm^{-1}; pmr (carbon tetrachloride): δ 8.77 (s, 1H, H-4), 8.17 (d, J = 5.6 Hz, 1H, H-6), 7.23 (d, J = 5.6 Hz, 1H, H-7), 5.32 (broad s, 2H, 2 x -OH), 4.84 (s, 1H, H-α), 4.08 (q, J = 7.4 Hz, 2H, -OCH_2CH_3), 1.61 (s, 6H, 2 x -Me), 1.36 and 1.31 (each s, 3H, -Me), 1.12 (t, J = 7.4 Hz, 3H, -OCH_2CH_3); ms: m/z 321.1460 (M^+, Calcd. for $C_{17}H_{23}NO_5$: 321.1575).

Reaction of the Lithio Intermediate of Compounds **10a-d** with *N,N*-Dimethylacetamide.

General Procedure.

To a solution of diisopropylamide prepared from diisopropylamine (60 mg, 0.59 mmole) and *n*-butyllithium in hexane (0.37 ml, 1.6 *M*, 0.59 mmole) in 10 ml of dry tetrahydrofuran (5 ml) by syringe at -75° with stirring and under a nitrogen atmosphere, then the reaction flask was warmed to -20°. After stirring for 20

minutes, to the reaction mixture was added *N,N*-dimethylacetamide (53 mg, 0.6 mmole). Stirring was continued for 3 hours at this temperature. The mixture was treated with 10% hydrochloric acid (1.5 ml) and water (10 ml), basified with sodium bicarbonate and extracted with chloroform. Distillation of the residue of the dried (magnesium sulfate) chloroform extract under reduced pressure gave the starting compound **10** (identified by ir and pmr spectra) in 90-95% yield.

Pyrolysis of Compounds **11a-d** and **13a-d**.

A sample (100-150 mg) of compound **11a-d** (mixture of the diasteromers) or **13a-d** in a glass tube was heated at 140-160° (20-30 mm Hg) for 15-20 minutes. The slightly yellow syrupy residue was distilled under reduced pressure to give compounds **10b** from **11b, 10c** from **11c** and **10d** from **11d**, almost quantitatively, which were identified by the ir and pmr spectra. In the cases of **11a** and **13a-d,** the starting compound was recovered quantitatively.

REFERENCES AND NOTES

[1] Part **XIV**: S. Shiotani, *J. Heterocylic Chem.*, **30**, 1035 (1993).

[2a] S. Shiotani, H. Morita, M. Inoue, T. Ishida and A. Itai, *J. Heterocyclic Chem.*, **21**, 725 (1984); [b] S. Shiotani and H. Morita, *J. Heterocyclic Chem.*, **23**, 665 (1986); [c] H. Morita and S. Shiotani, *J. Heterocyclic Chem.*, **23**, 549 (1986); [d] H. Morita and S. Shiotani, *J. Heterocyclic Chem.*, **23**, 1465 (1986); [e] H. Morita and S. Shiotani, *J. Heterocyclic Chem.*, **24**, 373 (1987); [f] S. Shiotani, H. Morita, T. Ishida and Y. In, *J. Heterocyclic Chem.*, **25**, 1205 (1988); [g] S. Shiotani and H. Morita, *J. Heterocyclic Chem.*, **27**, 637 (1990); [h] S. Shiotani and H. Morita, *J. Heterocyclic Chem.*, **29**, 413 (1992); [j] S. Shiotani, *J. Heterocyclic Chem.*, **30**, 1025 (1993).

[3] R. F. Heck, in Organic Reactions, Vol **27**, W. G. Douben, ed, John Wiley & Sons, Inc., New York, NY, 1982, p 345.

[4a] J. Boutagg and R. Thomas, *Chem. Rev.*, **74**, 87 (1974); [b] J. W. Ellingboe, T. R. Alessi, T. M. Dolak, T. Nguyen, J. D. Tomer, F. Guzzo, J. F. Bagli and M. L. McCaleb, *J. Med. Chem.*, **35**, 1176 (1992).

[5] S. Shiotani and H. Morita, *J. Heterocyclic Chem.*, **28**, 1469 (1991).