Furopyridines. XX [1]. Wittig-Horner Reaction of a Phosphonate of Reissert Analogues of Furo[3,2-*c*]-, -[2,3-*c*]- and -[3,2-*b*]pyridines

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Furo[3,2-*c*]- (**1a**), -[2,3-*c*]- (**1b**) and -[3,2-*b*]pyridine (**1c**) were reacted with isopropyl chloroformate and trimethyl phosphite to give dimethyl 5-isopropoxycarbonyl-4,5-dihydrofuro[3,2-*c*]pyridine-4-phosphonate (**2a**), dimethyl 6-isopropoxycarbonyl-6,7-dihydrofuro[2,3-*c*]pyridine-7-phosphonate (**2b**) and dimethyl 4-isopropoxycarbonyl-4,7-dihydrofuro[3,2-*b*]pyridine-7-phosphonate (**2c**) as unstable syrups. Reaction of **2b** and **2c** with *n*-butyllithium and then with benzaldehyde, *p*-methoxybenzaldehyde, *p*-cyanobenzaldehyde or propionaldehyde afforded the normal Wittig reaction products **5b-H**, **5b-OMe**, **5b-CN**, **5b-Et**, **5c-H**, **5c-H**, **5c-OMe** and **5c-CN**, except for **2b** with propionaldehyde. While, the same reactions of compound **2a** and the reaction of **2b** with propionaldehyde afforded the unexpected products, 5-isopropoxycarbonylfuro[3,2-*c*]pyridinio-4-aryl-(or ethyl)methoxides **3a-H**, **3a-OMe**, **3a-CN** and **3a-Et**, 4-(1'-aryl(or ethyl)-1'-hydroxymethyl)furo[3,2-*c*]pyridines **4a-H**, **4a-OMe**, **4a-CN** and **4a-Et** accompanying formation of the normal products. Treatment of the normal Wittig reaction products with lithium diisopropylamide and then with acetone gave the derivatives alkylated at the 2- or the benzylic positions.

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In continuation of our studies on the chemistry of furopyridines, we recently reported the Reissert-Henze reaction of furo[3,2-*b*]pyridine *N*-oxide to give the 5-cyano derivative [2]. In order to extend the chemistry of furopyridines, we wished to develop additional methods for introducing a carbon functional group at the pyridine carbon of furopyridines. Inamoto *et al.* [3] had reported the Wittig-Horner reaction of dimethyl 2-isopropoxycarbonyl-1,2-dihydroisoquinoline-1-phosphonate and the quinoline analogue with several aldehydes to give 1-alkyl(or aralkyl)-isoquinolines and 2-alkyl(or aralkyl)quinolines as the final product. In this paper we report the application of this reaction to the syntheses of furopyridines having a benzyl or propyl group at the α- or γ-position of the ring nitrogen.

Furo[3,2-*c*]- (**1a**), -[2,3-*c*]- (**1b**) and -[3,2-*b*]pyridines (**1c**) were treated with isopropyl chloroformate and successively with trimethyl phosphite to give the corresponding dimethyl *N*-isopropoxycarbonyl-*N*,α-dihydrofuropyridine-α-phosphonates **2a** and **2b** from **1a** and **1b** and -4,7-dihydrofuro[3,2-*b*]pyridine-7-phosphonate (**2c**) from **1c** as an unstable viscous syrup. The same reaction of furo[2,3-*b*]pyridine (**1d**) resulted in complete recovery of the starting furopyridine, which would be interpreted by the extremely low reactivity of **1d** to form the acyl ammonium salt caused by its low basicity (p*K*a 0.87 [4]). The *N*-isopropoxycarbonylphosphonate structures of **2a**, **2b** and **2c** were supported by their pmr spectra showing the signals of isopropyl protons at δ 1.28 (d, J = 6.5 Hz, 6H) and 4.93 (septet, J = 6.5 Hz, 1H) for **2a**, at δ 1.34 (d, J = 6.5 Hz, 6H) and 5.08 (septet, J = 6.5 Hz, 1H) for **2b**, and at δ 1.32 (d, J = 6.5 Hz, 6H) and 5.00 (septet, J = 6.5 Hz, 1H) for **2c**, and the signals of methyl protons in the phosphonate moiety at δ 3.45 (d, J = 10.5 Hz, 3H) and 3.59 (d, J = 10.5 Hz, 3H) for **2a**, at δ 3.67 (d, J = 10.5 Hz, 6H) for **2b**, and at δ 3.67 (d, J = 10.5 Hz, 6H) for **2c**. The position of the phosphonate group in compound **2c** (γ-position) was deduced from the chemical shift in the pmr spectra of the pyridine protons of arylmethyl- **5c-H**,

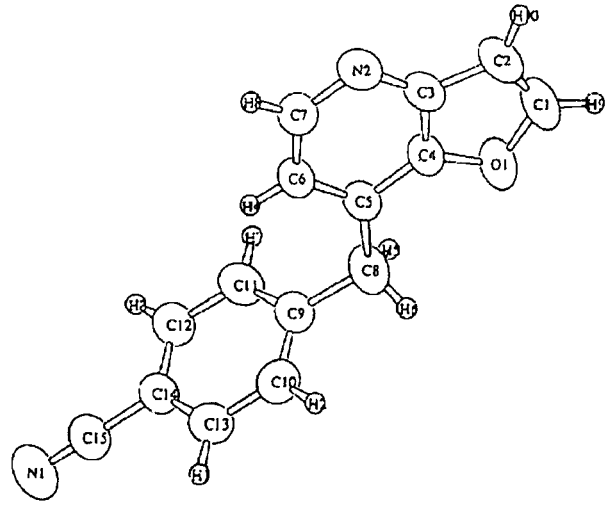


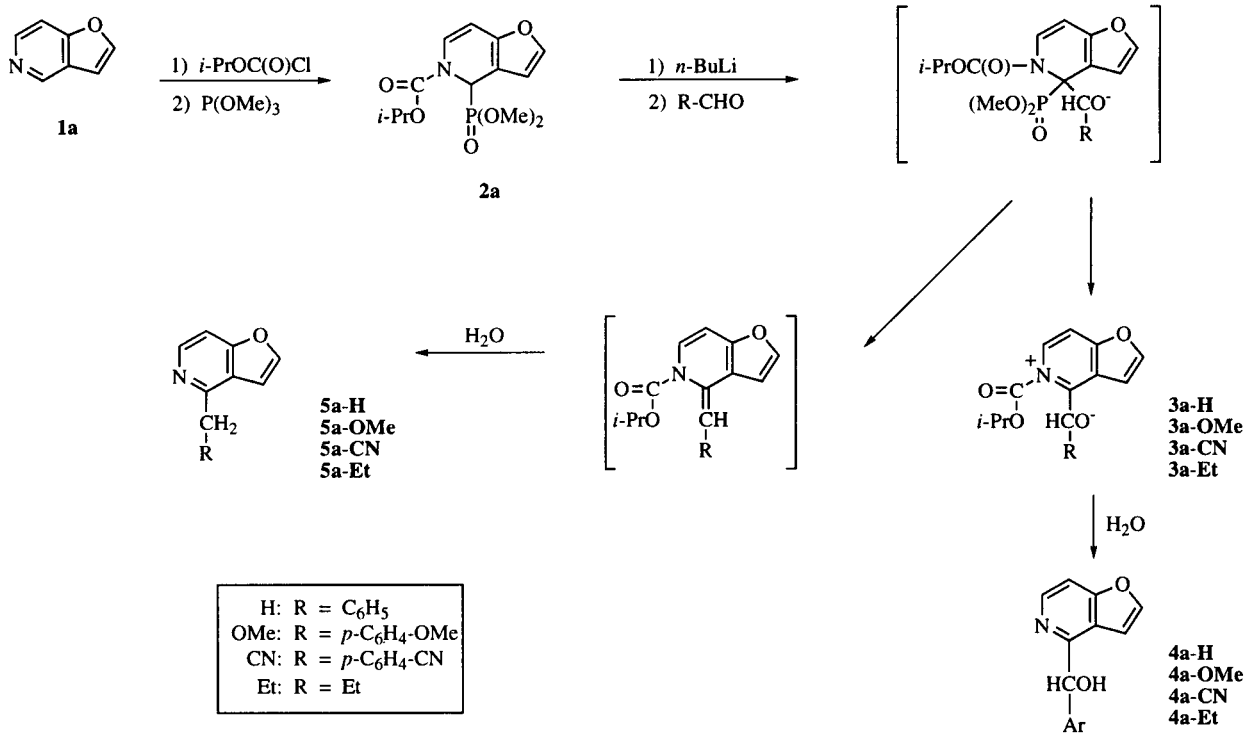
Figure 1. ORTEP drawing of Compound **5c-CN**.

5c-OMe, **5c-CN** and propylfuro[3,2-*b*]pyridine **5c-Et** obtained from **2c**, and confirmed by the X-ray structural analysis of 7-(*p*-cyanobenzyl)furo[3,2-*b*]pyridine (**5c-CN**).

Dimethyl 5-isopropoxycarbonyl-4,5-dihydrofuro-[3,2-*c*]pyridine-4-phosphonate (**2a**) was reacted with *n*-butyllithium in tetrahydrofuran at -78°, and then with benzaldehyde, *p*-methoxybenzaldehyde, *p*-cyanobenzaldehyde or propionaldehyde. The pmr spectrum of each crude reaction product indicated that the product is a mixture of several compounds.

Chromatography of the reaction products of **2a** with benzaldehyde, *p*-methoxybenzaldehyde and propionaldehyde on a silica gel column yielded the unexpected compounds, 5-isopropoxycarbonylfuro[3,2-*c*]pyridinio-4-phenylmethoxide (**3a-H**) (36%) and 4-(1'-hydroxy-1'-phenylmethyl)furo[3,2-*c*]pyridine (**4a-H**) (18%), accompanying the normal product, 4-benzylfuro[3,2-*c*]pyridine (**5a-H**) (5.3%) from benzaldehyde, 5-isopropoxycarbonylfuro[3,2-*c*]pyridinio-4-(*p*-methoxyphenyl)methoxide (**3a-OMe**) (23%), 4-(1'-hydroxy-1'-*p*-methoxyphenylmethyl)furo[3,2-*c*]pyridine (**4a-OMe**) (28%) and 4-*p*-methoxybenzylfuro[3,2-*c*]pyridine (**5a-OMe**) (11%) from *p*-methoxybenzaldehyde, and 4-isopropoxycarbonylfuro[3,2-*c*]pyridinio-4-(1'-propoxide) (**3a-Et**) (38%), 4-(1'-hydroxypropyl)furo[3,2-*c*]pyridine (**4a-Et**) (34%) and 4-propylfuro[3,2-*c*]pyridine (**5a-Et**) (5%) from propionaldehyde, respectively. Refluxing of compounds **3a-H**, **3a-OMe** and **3a-Et** with hydrochloric acid afforded **4a-H**, **4a-OMe** and **4a-Et** in 86%, 76% and 65% yield. Though the reaction product of **2a** with *p*-cyanobenzaldehyde was so complex that any single compound could not be isolated by chromatography on silica gel, hydrolysis of the crude product with hydrochloric acid gave 4-(1'-*p*-cyanophenyl-1'-hydroxymethyl)furo[3,2-*c*]pyridine (**4a-CN**) (28%) and 4-*p*-cyanobenzylfuro[3,2-*c*]pyridine (**5a-CN**) (44%). The betaine structure of compounds **3a-H**, **3a-OMe** and **3a-Et** was supported by pmr and mass spectra. In the pmr spectrum, **3a-H** exhibited the signal of the isopropyl protons at δ 1.24 and 1.25 (d, J = 6.0 Hz, 6H) and 4.74 (septet, J = 6.0 Hz, 1H), the methine proton at the benzyl position at δ 6.80 (s, 1H) and the phenyl protons at δ 7.23 (m, 5H); **3a-OMe** the isopropyl at δ 1.26 (d, J = 6.5 Hz, 6H) and 4.86 (septet, J = 6.5 Hz, 1H), the methine at the benzyl position at δ 6.88 (s, 1H) and the methoxy at δ 3.74 (s, 3H); **3a-Et** the isopropyl at δ 1.21 and 1.29 (d, J = 6.5 Hz, 6H) and 4.83 (septet, J = 6.5 Hz, 1H), the methine at the 1'-position at δ 5.86 (t, J = 7.0 Hz, 1H) and the ethyl at δ 0.98 (t, J = 7.0 Hz, 3H) and 2.10 (qn, J = 7.0 Hz 2H). The mass spectra of **3a-H**, **3a-OMe** and **3a-Et** exhibited the molecular ion peak at m/z 311 (hrms: 311.1162 for $C_{18}H_{17}NO_4$ (Calcd: 311.1156)), m/z 341 (hrms: 341.1243 for $C_{19}H_{19}NO_5$ (Calcd: 341.1262)) and m/z 263 (hrms: 263.1156 for $C_{14}H_{17}NO_4$ (Calcd:

Scheme 1



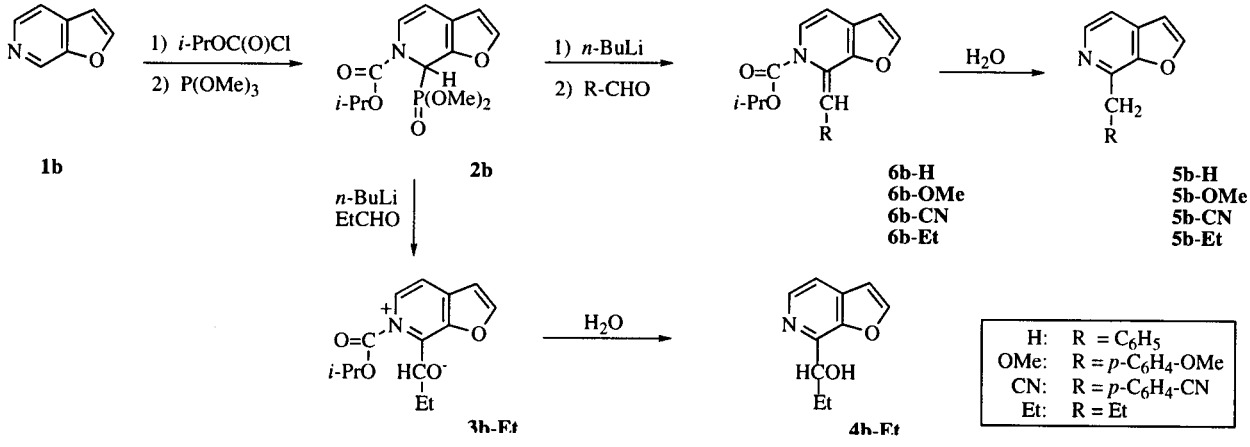
263.1156)), respectively.

The structures of the 4-(1'-aryl-1'-hydroxymethyl) derivatives **4a-H**, **4a-OMe**, **4a-CN** and **4a-Et** were confirmed by elemental analyses, and the ir and pmr spectra. The elemental analysis of each compound suggested the molecular formula $C_{14}H_{11}NO_2$ for **4a-H**, $C_{15}H_{13}NO_3$ for **4a-OMe**, $C_{15}H_{10}N_2O_2$ for **4a-CN** and $C_{10}H_{11}NO_2$ for **4a-Et**. In the ir spectra compounds **4a-H**, **4a-OMe**, **4a-CN** and **4a-Et** exhibited the absorption of hydroxyl group at 3204 cm^{-1} (broad), 3357 cm^{-1} (broad), 3435 cm^{-1} (broad) and 3243 cm^{-1} (broad), respectively. The pmr spectrum of **4a-H** showed the signal of the methine proton of the benzyl position at δ 5.87 (s, 1H), the phenyl protons at δ 7.20 (m, 5H) and the hydroxyl proton at δ 5.15 (broad s, 1H); **4a-OMe** the methine at δ 5.90 (s, 1H), the benzene aromatic protons at δ 6.77 and 7.22 (AB-q, J = 9.0 Hz, 4H) and the hydroxyl proton at δ 4.73 (broad s, 1H); **4a-CN** the methine at δ 5.96 (s, 1H), the hydroxyl at δ 5.08 (broad s, 1H); **4a-Et** the methine at δ 4.98 (t, J = 6.0 Hz, 1H), the ethyl at δ 0.93 (t, J = 7.0 Hz, 3H) and 1.90 (m, 2H) and the hydroxyl at δ 4.86 (broad s, 1H).

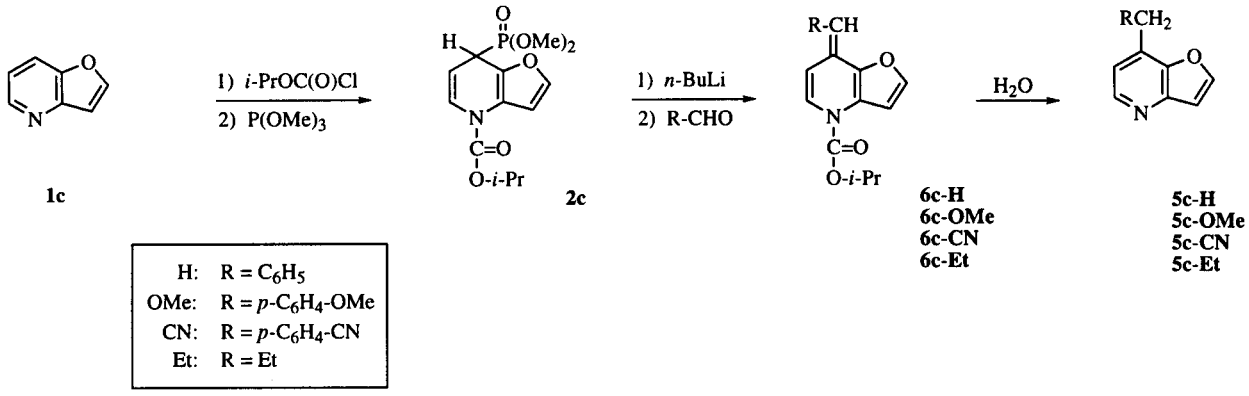
The reaction of dimethyl 6-isopropoxycarbonyl-6,7-dihydrofuro[2,3-*c*]pyridine-7-phosphonate (**2b**) with benzaldebyde and *p*-methoxybenzaldehyde gave the exo-methylene compounds **6b-H** and **6b-OMe** as viscous oils, which were unstable and could not be isolated by chromatography on silica gel. Treatment of **6b-H** with silica gel, hydrochloric acid or sodium hydroxide in aqueous ethanol afforded 7-benzylfuro[2,3-*c*]pyridine (**5b-H**) in 73% (silica gel), 84% (hydrochloric acid) and 67% (sodium hydroxide), and **6b-OMe** gave 7-*p*-methoxybenzylfuro-[2,3-*c*]pyridine (**5b-OMe**) (79%, 67% and 98%) respectively. The same reaction with *p*-cyanobenzaldehyde gave the exo-methylene compound **6b-CN** as colorless crystals of mp 146.5-150°, which was converted to the 7-*p*-cyanobenzyl derivative **5b-CN** by treatment with silica gel, hydrochloric acid or sodium hydroxide in 58%, 70% and 90% yield, respectively. The reaction of **2b** with propionaldehyde afforded a mixture of the betaine compound **3b-Et**, 7-(1'-hydroxypropyl)furo[2,3-*c*]pyridine (**4b-Et**) and 7-propylfuro[2,3-*c*]pyridine (**5b-Et**), which were isolated by column chromatography in 20%, 11% and 34%, respectively. Hydrolysis of **3b-Et** with hydrochloric acid gave **4b-Et** in 65% yield.

The reaction of dimethyl 4-isopropoxycarbonyl-4,7-dihydrofuro[3,2-*b*]pyridine-7-phosphonate (**2c**) with benzaldehyde, *p*-methoxybenzaldehyde and propionaldehyde yielded the unstable γ-exomethylene compounds **6c-H**, **6c-OMe** and **6c-Et** and with *p*-cyanobenzaldehyde the γ-exo-methylene compound **6c-CN** as pale yellow crystals of mp 166-170°, from which compounds **5c-H**, **5c-OMe**, **5c-CN** and **5c-Et** were produced by chromatography on silica gel in 58% (**5c-H**), 17% (**5c-OMe**) and 77% (**5c-CN**) yield, by treatment with hydrochloric acid in 73% (**5c-H**), 73% (**5c-OMe**), 99% (**5c-CN**) and 74% (**5c-Et**), and by refluxing with sodium hydroxide in 47% (**5c-H**), 59% (**5c-OMe**) and 90% (**5c-CN**), respectively (Scheme 3). The doublet of the pyridine proton of **5c-H** appeared at δ 8.32, of compound **5c-OMe** at δ 8.23, of **5c-CN** at δ 8.47 and of **5c-Et** at δ 8.44 are assigned to H-5 (α to the ring nitrogen) by comparison with the spectrum of furo[3,2-*b*]pyridine which shows the signal of H-5 at δ 8.46 and H-7 at δ 7.64 [5]. The zig-zag coupling occurring between H-3 and H-7 of furo[3,2-*b*]pyridine was not observed in the pmr spectra of these compounds. Moreover, the ^{13}C-^{1}H cosy spectrum of **5c-CN** revealed that the carbon at δ 146.3 (C-5) [6] connects to the proton at δ 8.47, and that of **5c-Et** the carbon at δ 146.0 (C-5) to the proton at δ 8.44. These nmr spectral data strongly suggested the position of the substituents of the **5c**'s to be at the 7-position. In order to confirm the assignment reached by use of the nmr spectral informations, the X-ray struc-

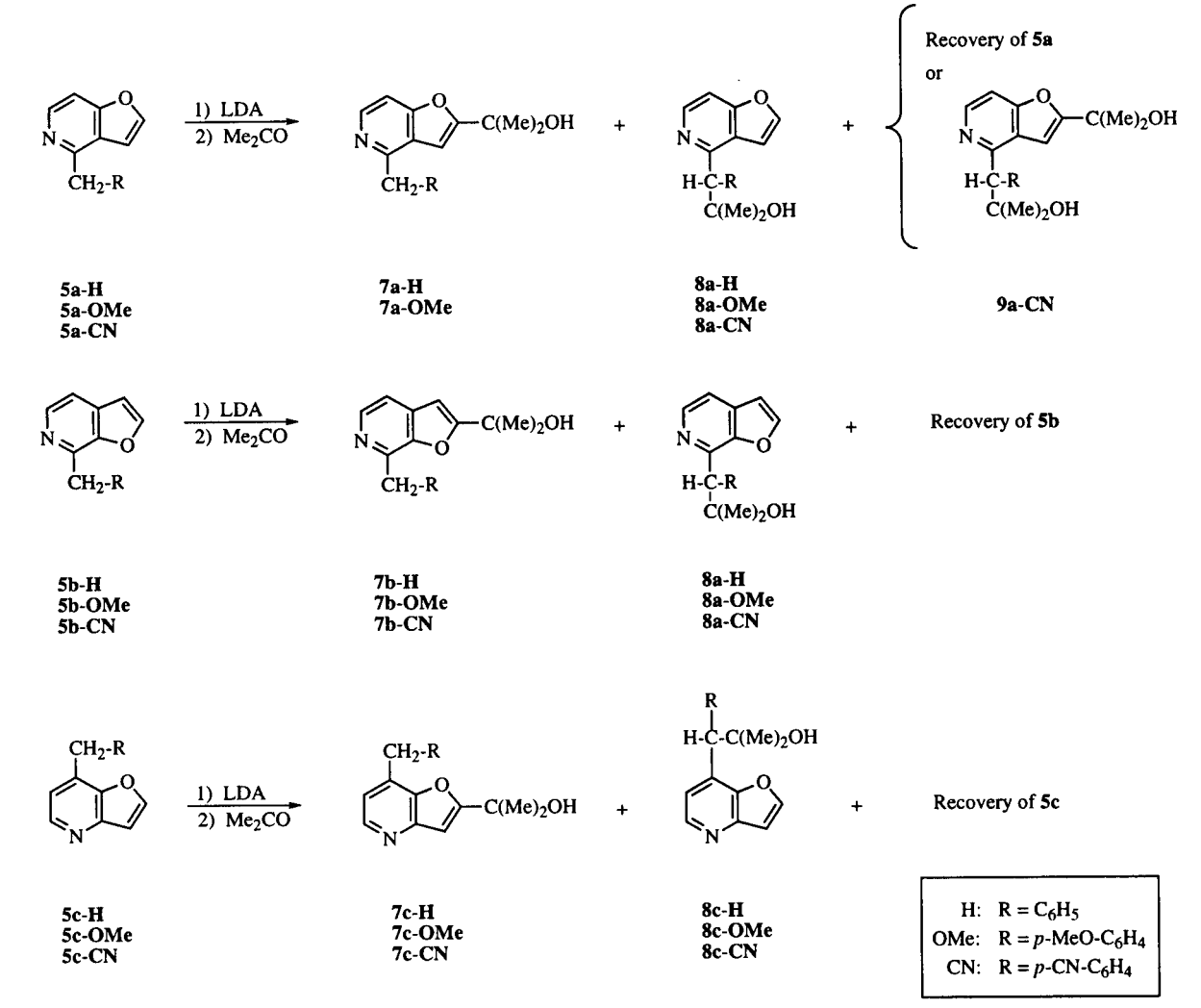
Scheme 2



Scheme 3



Scheme 4



tural determination of compound **5c-CN** was performed by the Osaka group of authors (Figure 1).

The results described above revealed that the Wittig-Horner type reaction of furo[2,3-*c*]- (**1b**) and

Table I

Crystal Data and Data Collection of **5c-CN**

Empirical Formula	$C_{15}H_{10}N_2O$
Formula Weight	234.26
Crystal Color, Habit	colorless, platelike
Crystal Dimensions	0.50 x 0.40 x 0.25
Crystal System	triclinic
Lattice Type	Primitive
No. of Reflections Used for Unit Cell Determination (2θ range)	20 (40.0 - 62.0°)
Omega Scan Peak Width at Half-height	0.12°
Lattice Parameters	a = 8.898(2)A b = 10.282(2)A c = 7.415(2)A α = 108.96(2)° β = 113.07(2)° γ = 90.28(2)° V = 583.5(3)A^3
Space Group	P1(#2)
Z value	2
D_{calc}	1.333 g/cm^3
F_{000}	244.00
μ(CuKα)	6.88 cm^{-1}
Diffractometer	Rigaku AFC5R
Radiation	CuKα (l = 1.54178 A)
Temperature	20.0°
Scan Type	ω
Scan Rate	4.0°/min(in ω) - up to 3 scans
Scan Width	(1.52 + 0.15 tan θ)°
$2\theta_{max}$	120.0°
No. of Reflections Measured	Total 1771 Unique: 1660 (R_{int} = 0.029)
Goodness of Fit Indicator	2.79
Residuals: R; Rw	0.049; 0.059

Table III

Bond Length in **5c-CN**

O(1) - C(1)	1.383(3)	O(1) - C(4)	1.375(3)
N(1) - C(15)	1.142(3)	N(2) - C(3)	1.347(3)
N(2) - C(7)	1.333(3)	C(1) - C(2)	1.312(4)
C(1) - H(9)	1.05	C(2) - C(3)	1.434(3)
C(2) - H(10)	1.02	C(3) - C(4)	1.379(3)
C(4) - C(5)	1.373(3)	C(5) - C(6)	1.385(3)
C(5) - C(8)	1.517(3)	C(6) - C(7)	1.393(3)
C(6) - H(4)	1.01	C(7) - H(8)	1.07
C(8) - C(9)	1.502(3)	C(8) - H(5)	0.99
C(8) - H(6)	1.02	C(9) - C(10)	1.389(3)
C(9) - C(11)	1.380(3)	C(10) - C(13)	1.380(3)
C(10) - H(2)	1.06	C(11) - C(12)	1.387(3)
C(11) - H(7)	1.10	C(12) - C(14)	1.380(3)
C(12) - H(3)	1.09	C(13) - C(14)	1.383(3)
C(13) - H(1)	0.99	C(14) - C(15)	1.436(3)
C(1) - H(9)	1.05	C(2) - H(10)	1.02
C(6) - H(4)	1.01	C(7) - H(8)	1.07
C(8) - H(5)	0.99	C(8) - H(6)	1.02
C(10) - H(2)	1.06	C(11) - H(7)	1.10
C(12) - H(3)	1.09	C(13) - H(1)	0.99

Table IV

Bond Angles (°) in **5c-CN**

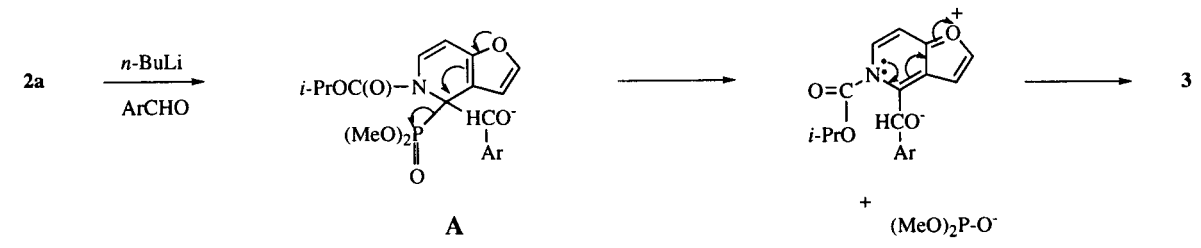
O(1) - C(1) - H(9)	113.1	C(2) - C(1) - H(9)	133.4
C(1) - C(2) - H(10)	124.6	C(3) - C(2) - H(10)	128.5
C(5) - C(6) - H(4)	114.0	C(7) - C(6) - H(4)	125.0
N(2) - C(7) - H(8)	114.9	C(6) - C(7) - H(8)	119.6
C(5) - C(8) - H(5)	112.3	C(5) - C(8) - H(6)	106.4
C(9) - C(8) - H(5)	108.9	C(9) - C(8) - H(6)	111.3
H(5) - C(8) - H(6)	101.2	C(9) - C(10) - H(2)	120.5
C(13) - C(10) - H(2)	118.4	C(9) - C(11) - H(7)	123.5
C(12) - C(11) - H(7)	113.9	C(11) - C(12) - H(3)	119.8
C(14) - C(12) - H(3)	120.9	C(10) - C(13) - H(1)	115.2
C(14) - C(13) - H(1)	125.4		

Table II

Atomic Coordinates and B_{iso}/B_{eq} for **5c-CN**

Atom	x	y	z	B_{eq}
O(1)	0.6823(2)	0.4790(2)	0.1680(2)	4.99(4)
N(1)	0.7098(3)	-0.0805(3)	1.0246(4)	7.20(7)
N(2)	0.9282(2)	0.7199(2)	0.6762(3)	5.11(5)
C(1)	0.7100(3)	0.5966(3)	0.1272(4)	5.24(6)
C(2)	0.8010(3)	0.7023(3)	0.2970(4)	4.98(6)
C(3)	0.8393(2)	0.6546(2)	0.4692(3)	4.04(5)
C(4)	0.7632(2)	0.5180(2)	0.3819(3)	3.78(4)
C(5)	0.7690(2)	0.4355(2)	0.4970(3)	3.78(4)
C(6)	0.8606(3)	0.5036(2)	0.7104(3)	4.23(5)
C(7)	0.9353(3)	0.6408(2)	0.7893(4)	4.93(6)
C(8)	0.6856(4)	0.2856(3)	0.3911(4)	5.49(6)
C(9)	0.6934(3)	0.2088(2)	0.5353(3)	4.13(5)
C(10)	0.8049(3)	0.1163(2)	0.5676(4)	4.63(5)
C(11)	0.5897(3)	0.2269(2)	0.6368(4)	4.86(6)
C(12)	0.5943(3)	0.2537(2)	0.7651(4)	4.67(5)
C(13)	0.8132(3)	0.0435(2)	0.6971(3)	4.62(5)
C(14)	0.7066(3)	0.0623(2)	0.7951(3)	4.06(5)
C(15)	0.7095(3)	-0.0168(2)	0.9241(4)	5.11(6)
H(1)	0.898(3)	-0.22(2)	0.723(3)	5.7(5)
H(2)	0.878(3)	0.101(3)	0.496(4)	6.1(6)
H(3)	0.517(3)	0.165(3)	0.835(4)	6.8(6)
H(4)	0.873(3)	0.457(2)	0.803(3)	5.0(5)
H(5)	0.567(3)	0.286(3)	0.307(4)	6.6(6)
H(6)	0.734(3)	0.231(3)	0.294(5)	7.3(7)
H(7)	0.508(3)	0.289(2)	0.611(3)	5.3(5)
H(8)	1.000(3)	0.681(3)	0.939(4)	6.2(6)
H(9)	0.658(3)	0.584(3)	-0.021(4)	6.4(6)
H(10)	0.830(3)	0.793(3)	0.301(4)	6.2(6)

Chart 1



furo[3,2-*b*]pyridine (**1c**) gave normal reaction products, except for **1b** with propionaldehyde. In contrast, furo-[3,2-*c*]pyridine gave unexpected results, formation of betaine compounds **3a-H**, **3a-OMe**, **3a-Et** and compounds having a hydroxyl group at the 1'-position, **4a-H**, **4a-OMe**, **4a-CN** and **4a-Et** accompanying formation of the normal products **5a-H**, **5a-OMe**, **5a-CN** and **5a-Et**. The similar reaction of furo[2,3-*b*]pyridine (**1d**) resulted in complete recovery of the starting compound.

The formation of arylmethyl and alkyl derivatives **5** as the final products is interpreted by the normal Wittig-Horner reaction mechanism [7]. While, the formation of 1'-aryl-1'-hydroxymethyl and 1'-hydroxypropyl derivatives **4**, the formation of abnormal products, would be suggested as follows: the dimethyl phosphite anion would be eliminated from the intermediate adduct **A**, which is affected by the electron donating effect of the ring oxygen as shown in Chart 1, to give the betaine compound, and the subsequent hydrolysis of the betaine.

In order to examine the reactivity for lithiation at the C-2 and/or the benzylic carbon, the arylmethyl derivatives **5a-H**, **5a-OMe**, **5a-CN**, **5b-H**, **5b-OMe**, **5b-CN**, **5c-H**, **5c-OMe** and **5c-CN** were lithiated with 1.5 equivalents of lithium diisopropylamide, and the lithio intermediates were treated with acetone. The reaction of benzyl derivatives **5a-H**, **5b-H** and **5c-H** afforded the products alkylated at C-2 (**7-H**) and at the benzylic carbon (**8-H**) in the ratio of *ca.* 1:1 to 1:2 accompanying recovery of the starting compound: **7a-H** 33%, **8a-H** 42% and recovery of **5a-H** 12%; **7b-H** 28%, **8b-H** 48% and **5b-H** 11%; **7c-H** 33%, **8c-H** 42% and **5c-H** 29%. The *p*-methoxybenzyl compounds **5a-OMe**, **5b-OMe** and **5c-OMe** gave the C-2 alkylated derivatives **7a-OMe** 15%, **7b-OMe** 38% and **7c-OMe** 0%), and the derivatives alkylated at the benzylic position, **8a-OMe** 0%, **8b-OMe** 33% and **8c-OMe** 0% accompanying recovery of the starting compounds, **5a-OMe** 56%, **5b-OMe** 10% and **5c-OMe** 11%. The *p*-cyanobenzyl compounds **5a-CN**, **5b-CN** and **5c-CN** were significantly less reactive, and yielded the C-2 alkylated derivative **7c-CN** in 7% yield and the derivatives alkylated at the benzylic position, **8a-CN** 5% and **8b-CN** 19% with recovery of 5% (**5a-CN**), 36% (**5b-CN**) and 77% (**5c-CN**). In the case of **5a-CN**, the compound was alkylated at both C-2 and the benzylic position, **9a-CN** in 36% yield.

Thus, this research demonstrated that the Wittig-Horner type reaction of furopyridines yields the normal products and/or the unexpected products, and is significantly affected by the mode of annelation of furopyridines.

EXPERIMENTAL

All melting points were determined by using Yanagimoto micro melting point apparatus and are uncorrected. Infrared spectra were taken on a JASCO FT/IR 7300 spectrometer. The pmr spectra were recorded on a JEOL JNM-PMX 60 instrument with tetramethylsilane as an internal reference in deuteriochloroform unless otherwise stated. The ^{13}C-nmr spectra were recorded on a JEOL A-400 instrument at 100 MHz. Mass spectra were obtained by using a JEOL JMS-OISG-2 spectrometer.

General Procedure for the Preparation of Dimethyl 5-Isopropoxycarbonyl-4,5-dihydrofuro[3,2-*c*]pyridine-4-phosphonate (**2a**), Dimethyl 6-Isopropoxycarbonyl-6,7-dihydrofuro[2,3-*c*]pyridine-7-phosphonate (**2b**) and Dimethyl 4-Isopropoxycarbonyl-4,7-dihydrofuro[3,2-*b*]pyridine-7-phosphonate (**2c**).

To a solution of the furopyridines **1a-1d** (1.35 g, 11.3 mmoles) in acetonitrile (150 ml) was added isopropyl chloroformate (1.4 g, 11.4 mmoles) with stirring and ice cooling under nitrogen. After being stirred for 10 minutes, to the mixture was added a solution of sodium iodide (2.53 g, 16.9 mmoles) in acetonitrile (100 ml) and then trimethyl phosphite (1.4 g, 11.3 mmoles). After being stirred for 10 minutes at 50°, the solvent was evaporated under reduced pressure. The residual syrup was treated with water and chloroform. The chloroform layer was dried (magnesium sulfate) and evaporated to leave 2.85 g (80%) of the phosphonate **2a**, **2b** and **2c** as a reddish syrup, which was used for the next step without purification. In the case of furo[2,3-*b*]pyridine **1d**, the starting compound was recovered in 95% yield from the chloroform extract.

Compound **2a** had pmr: δ 1.28 (d, J = 6.5 Hz, 6H), 3.45 (d, J = 10.5 Hz, 3H), 3.59 (d, J = 10.5 Hz, 3H), 4.93 (septet, J = 6.5 Hz, 1H), 5.54 (d, J = 9.0 Hz, 1H), 5.73 (d, J = 12.0 Hz, 1H), 6.28 (d, J = 1.0 Hz, 1H), 6.58 (d, J = 9.0 Hz, 1H), 7.18 (d, J = 1.0 Hz, 1H); ir (neat) 1713, 1371, 1340, 1261, 1033 cm^{-1}; ms: m/z (relative intensity) 315 (2), 234 (15), 233 (22), 206 (32), 164 (26), 120 (18), 119 (100); hrms: 315.0887. (M^+, Calcd. for $C_{13}H_{18}NO_6P$: 315.0871.

Compound **2b** had pmr: δ 1.34 (d, J = 6.5 Hz, 6H), 3.67 (d, J = 10.5 Hz, 6H), 5.08 (septet, J = 6.5 Hz, 1H), 5.68 (d, J = 7.5 Hz, 1H), 6.09 (d, J = 12.0 Hz, 1H), 6.30 (d, J = 1.0 Hz, 1H), 6.78

(d, J = 7.5 Hz, 1H), 7.38 (d, J = 1.0 Hz, 1H); ir (neat) 1714, 1372, 1320, 1259, 1030 cm^{-1}; ms: m/z (relative intensity) 315 (1), 273 (1), 233 (3), 207 (5), 206 (42), 165 (4), 164 (33), 120 (28), 119 (100); hrms: 315.0855. M^+, Calcd. for $C_{13}H_{18}NO_6P$: 315.0871.

Compound **2c** had pmr: δ 7.25-6.75 (m, 4H), 5.02 (m, 1H), 5.00 (septet, J = 6.5 Hz, 1H), 3.67 (d, J = 10.5 Hz, 6H), 1.32 (d, J = 6.5 Hz, 6H); ir (neat): 1721, 1383, 1313, 1284, 1055 cm^{-1}; ms: m/z (relative intensity) 315 (2), 227 (11), 207 (14), 206 (99), 165 (8), 164 (83), 121 (9), 120 (100); hrms: 315.0875. M^+, Calcd. for $C_{13}H_{18}NO_6P$: 315.0871.

Reaction of Dimethyl 5-Isopropoxycarbonyl-4,5-dihydrofuro-[3,2-*c*]pyridine-4-phosphonate (**2a**) with Benzaldehyde, *p*-Methoxybenzaldehyde, *p*-Cyanobenzaldehyde and Propionaldehyde.

General Procedure.

To a solution of the phosphonate **2a** (285 mg, 0.905 mmole) in tetrahydrofuran (15 ml) was added dropwise a solution of *n*-butyllithium in hexane (1.6 *M*, 0.7 ml, 1.12 mmoles) with stirring at -78° under nitrogen. After being stirred for 30 minutes at this temperature, to the reaction mixture was added benzaldehyde, *p*-methoxybenzaldehyde, *p*-cyanobenzaldehyde or propionaldehyde (1.5 mmoles), and then the cold bath was removed. After being stirred for 4 hours at room temperature, the reaction mixture was evaporated under reduced pressure, and treated with chloroform and water. The chloroform layer was dried over magnesium sulfate, and evaporated to give a brown viscous oil (295 mg from benzaldehyde, 328 mg from *p*-methoxybenzaldehyde, 258 mg from *p*-cyanobenzaldehyde and 203 mg from propionaldehyde). The pmr spectrum of each crude reaction product indicated that the product is a mixture of several compounds.

Further processing of the residue is described in the subsequent paragraphs.

5-Isopropoxycarbonylfuro[3,2-*c*]pyridinio-4-phenylmethoxide (**3a-H**), 4-(1'-Hydroxybenzyl)furo[3,2-*c*]pyridine (**4a-H**) and 4-Benzylfuro[3,2-*c*]pyridine (**5a-H**).

The crude product (295 mg) from the reaction of **2a** with benzaldehyde was chromatographed on a silica gel (30 g) column, hexane-ethyl acetate (2:1), giving 93 mg (33%) of compound **3a-H** as a yellow oil, 36 mg (18%) of compound **4a-H** as colorless crystals and 10 mg (5%) of compound **5a-H** as a colorless oil.

Compound **3a-H**.

This compound was somewhat unstable to heat and decomposed on distillation even under reduced pressure, and could not be obtained as a sample. The structure was characterized by the following spectral data; pmr: δ 8.23 (d, J = 6.0 Hz, 1H, H-6), 7.41 (d, J = 2.0 Hz, 1H, H-2), 7.33-6.83 (m, 7H, H-3, H-7 and -C_6H_5), 6.80 (s, 1H, H-1'), 4.74 (septet, J = 6.0 Hz, 1H, -C*H*$(CH_3)_2$), 1.25, 1.24 (d, J = 6.0 Hz, 6H, -CH(CH_3)$_2$); ir (neat): 3050, 3025, 2975, 2950, 2920, 2850, 1748, 1454, 1258, 1092 cm^{-1}; ms: m/z (relative intensity) 312 (13), 311 (M^+, 60), 225 (22), 224 (100), 209 (12), 208 (44), 207 (26); hrms: 311.1162. M^+, Calcd. for $C_{18}H_{17}NO_4$: 311.1156.

Compound **4a-H**.

This compound had mp 97-102° (from ether); pmr: δ 8.28 (d, J = 6.0 Hz, 1H, H-6), 7.36 (d, J = 2.0 Hz, 1H, H-2), 7.30-7.07 (m, 6H, H-7 and -C_6H_5), 6.43 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 5.87 (s, 1H, H-1'), 5.15 (broad s, 1H, OH); ir (potassium bromide): 3330 (br), 3204 (br), 3145, 3123, 3091, 3060, 3030, 2924, 1602, 1584,1450, 1425, 1270, 1136, 1028 cm^{-1}.

Anal. Calcd. for $C_{14}H_{11}NO_2$: C, 74.65; H, 4.92; N, 6.22. Found: C, 74.88; H, 5.04; N, 6.10.

Compound **5a-H**.

This compound had bp (130°, bath temperature, 0.1 mm Hg); pmr: δ 8.27 (d, J = 6.0 Hz, 1H, H-6), 7.39 (d, J = 2.0 Hz, 1H, H-2), 7.23-7.10 (m, 6H, H-7 and -C_6H_5), 6.53 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 4.37 (s, 2H, H-1'); ir (neat): 3085, 3063, 3029, 2923, 2848, 1611, 1579, 1495, 1418, 1192, 1167, 1127, 704 cm^{-1}; ms: m/z (relative intensity) 210 (6), 209 (M^+, 43), 208 (100), 181 (4), 180 (7); hrms: 209.0829. M^+, Calcd. for $C_{14}H_{11}NO$: 209.0840.

Anal. Calcd. for $C_{14}H_{11}NO$: C. 80.36; H. 5.30; N. 6.69. Found: C, 80.06; H. 5.48; N. 6.42.

Hydrolysis of **3a-H** with Hydrochloric Acid.

A mixture of compound **3a-H** (66 mg, 0.21 mmole) and hydrochloric acid (10%, 10 ml) in ethanol (10 ml) was refluxed for 43 hours. The mixture was evaporated, and the residue was dissolved in water, made alkaline with sodium bicarbonate and extracted with chloroform. Evaporation of the dried chloroform layer gave 41 mg (86%) of compound **4a-H**.

5-Isopropoxycarbonylfuro[3,2-*c*]pyridinio-4-(*p*-methoxyphenyl)methoxide (**3a-OMe**), 4-(1'-Hydroxy-1'-*p*-methoxyphenyl)-methylfuro[3,2-*c*]pyridine (**4a-OMe**) and 4-*p*-Methoxybenzylfuro[3,2-*c*]pyridine (**5a-OMe**).

The residue (328 mg) from the reaction of **2a** with *p*-methoxybenzaldehyde was chromatographed on a silica gel (30 g) column eluting with hexane-ethyl acetate (2:1) to give 70.5 mg (23%) of **3a-OMe** as a yellow syrup, 65 mg (28%) of **4a-OMe** as colorless crystals and 22 mg (10%) of **5a-OMe** as a colorless oil.

Compound **3a-OMe**.

This compound could not be purified because of its instability to heat. The structure was characterized by the following spectral data; pmr: δ 8.44 (d, J = 5.5 Hz, 1H, H-6), 7.61 (d, J = 2.0 Hz, 1H, H-2), 7.39 and 6.82 (AB-q, J = 9.0 Hz, 4H, -C_6H_4OMe), 7.30 (dd, J = 5.5, 0.8 Hz, 1H, H-7), 7.03 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 6.88 (s, 1H, H-1'), 4.86 (septet, J = 6.5 Hz, 1H, -C*H*$(Me)_2$), 3.74 (s, 3H, -C_6H_4OMe), 1.26 (d, J = 6.5 Hz, 6H, -CH(Me)$_2$); ir (neat): 3130, 3051, 2983, 2937, 2839, 1744, 1612, 1514, 1251, 1177, 1091, 914, 832 cm^{-1}; ms: m/z (relative intensity) 341 (M^+, 4), 271 (4), 254 (24), 238 (18), 237 (29), 223 (11), 222 (58); hrms: 341.1251. M^+, Calcd. for $C_{19}H_{19}NO_5$: 341.1262.

Compound **4a-OMe**.

This compound had mp 110-112° (from ether-hexane), colorless crystals; pmr: δ 8.35 (d, J = 6.0 Hz, 1H, H-6), 7.50 (d, J = 2.2 Hz, 1H, H-2), 7.33 (dd, J = 6.0, 0.8 Hz, 1H, H-7), 7.22 and 6.77 (AB-q, J = 9.0 Hz, 4H, -C_6H_4OMe), 6.45 (dd, J = 2.2, 0.8 Hz, 1H, H-3), 3.70 (s, 3H, -C_6H_4O*Me*); ir (potassium bromide): 3357 (br), 3130, 3004, 2957, 2933, 2837, 1611, 1585, 1511, 1430, 1273, 1249, 1175, 1032, 832 cm^{-1}.

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.49. Found: C, 70.34; H, 5.16; N, 5.36.

Compound **5a-OMe**.

This compound had bp 145-165° (bath temperature, 0.2 mm Hg), colorless oil; pmr: δ 8.44 (d, J = 6.0 Hz, 1H, H-6), 7.53 (d, J = 2.0 Hz, 1H, H-2), 7.32 (dd, J = 6.0, 0.8 Hz, 1H, H-7), 7.20 and 6.80 (AB-q, J = 9.0 Hz, 4H, -C_6H_4OMe), 6.64 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 4.34 (s, 2H, H-1'), 3.77 (s, 3H, -C_6H_4O*Me*); ir (neat): 3149, 3002, 2931, 2836, 1606, 1585, 1511, 1454, 1248, 1178, 1132, 1038, 818 cm^{-1}; ms: m/z (relative intensity) 239 (M^+, 93), 238 (100), 224 (32); hrms: 239.0944. M^+, Calcd. for $C_{15}H_{13}NO_2$: 239.0955.

Anal. Calcd. for $C_{15}H_{13}NO_2$:C, 75.30; H, 5.48; N, 5.85. Found: C, 75.19; H, 5.82; N, 5.87.

Hydrolysis of **3a-OMe** with Hydrochloric Acid.

A mixture of compound **3a-OMe** (62 mg, 0.18 mmole) and hydrochloric acid (10%, 10 ml) in ethanol (10 ml) was refluxed for 38 hours. The reaction mixture was evaporated, and the residue was dissolved in water, basified with sodium bicarbonate and extracted with chloroform. The residue of the chloroform extract was chromatographed to give 16 mg (28%) of **4a-OMe** and 28 mg (47%) of 4-(1'-ethoxy-1'-*p*-methoxyphenylmethyl)-furo[3,2-*c*]pyridine (**4'a-OMe**).

Compound **4'a-OMe**.

This compound had bp 150-165° (bath temperature, 0.1 mm Hg), colorless oil; pmr: δ 8.25 (d, J = 5.5 Hz, 1H, H-6), 7.46 (d, J = 2.0 Hz, 1H, H-2), 7.24 and 6.69 (AB-q, J = 8.5 Hz, 4H, -C_6H_4OMe), 7.18 (dd, J = 5.5, 0.8 Hz, 1H, H-7), 7.02 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 5.60 (s, 1H, H-1'), 3.63 (s, 3H, -C_6H_4O*Me*), 3.52 (q, J = 7.0 Hz, 2H, -O$CH_2$$CH_3$), 1.23 (t, J = 7.0 Hz, 3H, -OCH_2CH_3); ir (neat): 3130, 3058, 2974, 2931, 2873, 2837, 1611, 1580, 1511, 1453, 1270, 1248, 1174, 1098, 1037, 828 cm^{-1}; ms: m/z (relative intensity) 283 (M^+, 3), 254 (9), 239 (23), 238 (20), 237 (100), 223 (10), 222 (63); hrms: 283.1199. M^+, Calcd. for $C_{17}H_{17}NO_3$: 283.1207.

Anal. Calcd. for $C_{17}H_{17}NO_3$: C, 72.07; H, 6.05; N, 4.94. Found: C, 72.46; H, 6.33; N, 5.31.

4-(1'-*p*-Cyanophenyl-1'-hydroxymethyl)furo[3,2-*c*]pyridine (**4a-CN**) and 4-*p*-Cyanobenzylfuro[3,2-*c*]pyridine (**5a-CN**).

The reaction product (258 mg) of **2a** with *p*-cyanobenzaldehyde was refluxed with hydrochloric acid (10%, 10 ml) in ethanol (10 ml) for 23 hours. After evaporation of the solvent, the residue was dissolved in water, basified with sodium bicarbonate extracted with chloroform. The residue (120 mg) of the chloroform extract was chromatographed on a silica gel (12 g) eluting with chloroform-methanol (99:1) to give 46 mg (21%) of **4a-CN** and 62 mg (29%) of **5a-CN**.

Compound **4a-CN**.

This compound had mp 122.5-125° (from acetone-ether), colorless crystals; pmr: δ 8.33 (d, J = 6.0 Hz, 1H, H-6), 7.52-7.32 (m, 5H, H-2 and -C_6H_4CN), 7.23 (dd, J = 6.0, 0.8 Hz, 1H, H-7), 6.54 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 5.96 (s, 1H, H-1'), 5.08 (broad s, 1H, -OH); ir (potassium bromide): 3435 (br), 3131 (br), 2228, 1603, 1584, 1433, 1276, 1219, 1133, 1082, 1064, 858, 823 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2O_2$: C, 71.99; H, 4.03; N, 11.19. Found: C, 72.25; H, 4.19; N, 11.17.

Compound **5a-CN**.

This compound had mp 87-90.5° (from ether), colorless crystals; pmr: δ 8.36 (d, J = 6.0 Hz, 1H, H-6), 7.56-7.26 (m, 5H, H-2 and -C_6H_4CN), 7.28 (dd, J = 6.0, 0.8 Hz, 1H, H-7), 6.62 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 4.38 (s, 2H, H-1'); ir (potassium bromide): 3149, 3045, 2931, 2228, 1605, 1583, 1533, 1452, 1428, 1270, 1133, 1038, 817 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2O$: C, 76.91; H, 4.30; N, 11.96. Found: C, 77.02; H, 4.36; N, 11.90.

5-Isopropoxycarbonylfuro[3,2-*c*]pyridinio-4-(1'-propoxide) (**3a-Et**), 4-(1'-Hydroxypropyl)furo[3,2-*c*]pyridine (**4a-Et**) and 4-Propylfuro[3,2-*c*]pyridine (**5a-Et**).

The crude reaction product (203 mg) of **2a** with propionaldehyde was chromatographed on a silica gel (25 g), hexane-ethyl acetate (2:1), to give 89.5 mg (38%) of **3a-Et**, 54 mg (34%) of **4a-Et** and 7 mg (5%) of **5a-Et**.

Compound **3a-Et**.

This compound was a slightly yellow viscous syrup and decomposed on heating above 100°. The structure was characterized by the following spectral data; pmr: δ 8.40 (d, J = 6.0 Hz, 1H, H-6), 7.53 (d, J = 2.0 Hz, 1H, H-2), 7.32 (dd, J = 6.0, 0.8 Hz, 1H, H-7), 7.05 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 5.87 (t, J = 7.0 Hz, 1H, -C*H*CH_2CH_3), 4.84 (septet, J = 6.5 Hz, 1H, -C*H*$(Me)_2$), 2.11 (qn, J = 7.0 Hz, 2H, -CHCH_2CH_3), 1.28 and 1.20 (d, J = 6.5 Hz, 6H, -CH(*Me*)$_2$), 0.98 (t, J = 7.0 Hz, 3H, -$CHCH_2CH_3$); ir (neat): 3122, 2980, 2935, 2884, 1742, 1610, 1582, 1465, 1420, 1375, 1265, 1181, 1097, 830, 793 cm^{-1}; ms: m/z (relative intensity) 263 (M^+, 2), 236 (6), 235 (44), 176 (17), 160 (41), 159 (17), 149 (19), 148 (100); hrms: 263.1156. M^+, Calcd. for $C_{14}H_{17}NO_4$: 263.1156.

Compound **4a-Et**.

This compound had mp 56-57° (from ether), colorless crystals; pmr: δ 8.33 (d, J = 5.5 Hz, 1H, H-6), 7.63 (d, J = 2.0 Hz, 1H, H-2), 7.32 (dd, J = 5.5, 0.8 Hz, 1H, H-7), 6.96 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 4.98 (t, J = 6.0 Hz, 1H, -C*H*CH_2CH_3), 4.86 (broad s, 1H, OH), 2.16-1.66 (m, 2H, -CHCH_2CH_3), 0.93 (t, J = 7.0 Hz, 3H, -$CHCH_2CH_3$); ir (potassium bromide): 3180 (br), 3143, 3105, 3038, 2976, 2961, 2928, 2916, 2873, 2848, 1602, 1589, 1529, 1461 1432, 1279, 1140, 1116, 1071, 1032, 1005, 975, 854, 803, 774 cm^{-1}; ms: m/z (relative intensity) 177 (M^+, 1), 176 (1), 175 (2), 160 (12), 159 (6), 150 (11), 149 (100), 148 (70), 133 (16); hrms: 177.0779. M^+, Calcd. for $C_{10}H_{11}NO_2$: 177. 0789.

Anal. Calcd. for $C_{10}H_{11}NO_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 68.12; H, 6.38; N, 7.88.

Compound **5a-Et**.

This compound had bp 130-140° (bath temperature, 20 mm Hg), colorless oil; pmr: δ 8.34 (d, J = 5.5 Hz, 1H, H-6), 7.55 (d, J = 2.0 Hz, 1H, H-2), 7.23 (dd, J = 5.5, 0.8 Hz, 1H, H-7), 6.78 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 3.00 (t, J = 8.0 Hz, 2H, -C$H_2CH_2CH_3$), 2.16-1.55 (m, 2H, -$CH_2CH_2CH_3$), 0.98 (t, 3H, J = 7.0 Hz, -$CH_2CH_2CH_3$); ir (neat): 3111, 2963, 2933, 2873, 1604, 1587, 1534, 1457, 1427, 1271, 1139, 1030, 847, 815, 747 cm^{-1}; ms: m/z (relative intensity) 161 (M^+, 6), 160 (4), 146 (17), 134 (9), 133 (100); hrms: 161.0842. M^+, Calcd. for $C_{10}H_{11}NO$: 161.0840.

Reaction of Dimethyl 6-Isopropoxycarbonyl-6,7-dihydrofuro-

[2,3-*c*]pyridine-7-phosphonate (**2b**) with Benzaldehyde, *p*-Methoxybenzaldehyde, *p*-Cyanobenzaldehyde and Propionaldehyde.

General Procedure.

To a solution of phosphonate **2b** (741 mg, 2.35 mmoles) in tetrahydrofuran (150 ml) was added dropwise a solution of *n*-butyllithium in hexane (1. 6 *M*, 1.8 ml, 2.88 mmoles) with stirring at -78° under nitrogen. After being stirred for 30 minutes at this temperature, to the reaction mixture was added benzaldehyde, *p*-methoxybenzaldehyde, *p*-cyanobenzaldehyde or propionaldehyde (3.7 mmoles), and then the cold bath was removed. After being stirred for 4 hours at room temperature, the reaction mixture was evaporated under reduced pressure, treated with chloroform and water. The chloroform layer was dried over magnesium sulfate, and evaporated to give a brown viscous oil (701 mg from benzaldehyde, 888 mg from *p*-methoxybenzaldehyde and 556 mg from propionaldehyde) or a brown solid mass from *p*-cyanobenzaldehyde (727 mg). Each pmr spectrum of the crude reaction product of **2b** with benzaldehyde, *p*-methoxybenzaldehyde and *p*-cyanobenzaldehyde suggested the product is mainly composed of the exo-olefinic compounds **6b-H**, **6b-OMe** and **6b-CN**.

Compound **6b-H** had isopropyl protons at δ 0.92 (d, J = 5.5 Hz, 6H) and 4.70 (septet, J = 5.5 Hz, 1H) and an olefinic proton at δ 6.30 (s, 1H).

Compound **6b-OMe** had isopropyl protons at δ 0.95 (d, J = 5.5 Hz, 6H) and 4.66 (septet, J = 5.5 Hz, 1H) and an olefinic proton at δ 6.20 (s, 1H).

Compound **6b-CN** had isopropyl protons at δ 1.02 (d, J = 5.5 Hz, 6H) and 4.75 (septet, J = 5.5 Hz, 1H) and an olefinic proton at δ 6.26 (s, 1H).

Further processing of the residue is described in the subsequent paragraphs.

7-Benzylfuro[2,3-*c*]pyridine (**5b-H**).

(A) The crude product (701 mg) from the reaction of **2b** with benzaldehyde was chromatographed on a silica gel (70 g) column eluting with hexane-ethyl acetate (2:1) to give 359 mg (73%) of **5b-H** as a colorless oil of bp 130° (bath temperature, 0.1 mm Hg); pmr δ 8.23 (d, J = 5.5 Hz, 1H, H-5), 7.58 (d, J = 1.8 Hz, 1H, H- 2), 7.43-7.05 (m, 6H, H-4 and -C_6H_5), 6.63 (d, J = 1.8 Hz, 1H, H-3), 4.36 (s, 2H, H-1'); ir (neat): 3085, 3063, 3029, 2923, 2848, 1611, 1578, 1495, 1418, 1192, 1167, 1127, 879, 836, 819 cm^{-1}; ms: m/z (relative intensity) 210 (4), 209 (M^+, 34), 208 (100), 180 (3); hrms: 209.0827. M^+, Calcd. for $C_{14}H_{11}NO$: 209.0840.

Anal. Calcd. for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.17; H, 5.50; N, 6.49.

(B) The residue (435 mg) from **2b** and benzaldehyde was stirred with hydrochloric acid (10%, 9 ml) in ethanol (10 ml) at 40° for 1 hour. After evaporation of the solvent, the residual syrup was dissolved in water, basified with sodium bicarbonate and extracted with chloroform. The extract was dried (magnesium sulfate) and evaporated to give 255 mg (84%) of compound **5b-H**.

(C) The residue (383 mg) from **2b** and benzaldehyde was refluxed with sodium hydroxide (10% aqueous solution, 10 ml) in ethanol (10 ml) for 2 hours. After evaporation of the solvent, the residue was treated with chloroform and water. Evaporation of the dried chloroform layer yielded 178 mg (67%) of compound **5b-H**.

7-*p*-Methoxybenzyl[2,3-*c*]pyridine (**5b-OMe**).

(A) The residue (888 mg) from **2b** and *p*-methoxybenzaldehyde was chromatographed on a silica gel (20 g) column, hexane-ethyl acetate (2:1), to give 428 mg (76%) of **5b-OMe** as colorless crystals of mp 78-80° (from ether); pmr δ 8.18 (d, J = 5.5 Hz, 1H, H-5), 7.55 (d, J = 2.0 Hz, 1H, H-2), 7.23 (d, J = 5.5 Hz, 1H, H-4), 7.21 and 6.68 (AB-q, J = 9.0 Hz, 4H, -C_6H_4OMe), 6.62 (d, J = 2.0 Hz, 1H, H-3), 4.30 (s, 2H, H-1'), 3.65 (s, 3H, -C_6H_4OMe); ir (potassium bromide): 3121, 3071, 3002, 2955, 2933, 2837, 1613, 1511, 1416, 1248, 1178, 1038, 821 cm^{-1}; ms: m/z (relative intensity) 239 (M^+, 100), 238 (98), 224 (38); hrms: 239.0946. M^+, Calcd. for $C_{15}H_{13}NO_2$: 239.0946.

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.52; H, 5.52; N, 5.78.

(B) The residue (311 mg) from **2b** and *p*-methoxybenzaldehyde was stirred with hydrochloric acid (10%, 10 ml) in ethanol (10 ml) at 40° for 4 hours. After evaporation of the solvent, the residue was dissolved in water, basified with sodium bicarbonate and extracted with chloroform. The extract was dried (magnesium sulfate) and evaporated to give 140 mg (71%) of compound **5b-OMe**.

(C) The residue (391 mg) from **2b** and *p*-methoxybenzaldehyde was refluxed with sodium hydroxide (10% aqueous solution, 10 ml) in ethanol (10 ml) for 4 hours. After evaporation of the solvent, the residue was treated with chloroform and water. Evaporation of the dried chloroform layer gave 235 mg (98%) of compound **5b-OMe**.

6-Isopropoxycarbonyl-7-*p*-cyanobenzal-6,7-dihydrofuro[2,3-*c*]-pyridine (**6b-CN**).

The solid residue (727 mg) from **2b** and *p*-cyanobenzaldehyde was recrystallized from ether to give 650 mg (86%) of **6b-CN** as yellow crystals of mp 146.5-150°; pmr: δ 7.82 (d, J = 2.0 Hz, 1H, H-2), 7.50-7.13 (m, 5H, H-5 and -C_6H_4CN), 6.33 (d, J = 2.0 Hz, 1H, H-3), 5.26 (s, 1H, H-1'), 6.96 (d, 7.5 Hz, 1H, H-4), 4.75 (septet, J = 5.5 Hz, 1H, -C*H*(Me)$_2$), 1.02 (d, J = 5.5 Hz, 6H, -CH(*Me*)$_2$); ir (potassium bromide): 2985, 2927, 2230, 1746, 1631, 1606, 1417, 1376, 1262, 1100, 1023 cm^{-1}.

Anal. Calcd. for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 71.00; H, 5.34; N, 8.87.

7-*p*-Cyanobenzylfuro[2,3-*c*]pyridine (**5b-CN**).

(A) Compound **6b-CN** (50 mg, 0.16 mmole) was heated at 40° with hydrochloric acid (10%, 10 ml) in ethanol (10 ml). After evaporation of the solvent, residual mass was dissolved in water, made alkaline with sodium bicarbonate and extracted with chloroform. The chloroform extract was dried (magnesium sulfate) and evaporated to give 26 mg (70%) of **5b-CN** as colorless crystals of mp 102-105° (from ether); pmr δ 8.25 (d, J = 5.5 Hz, 1H, H-5), 7.66 (d, J = 2.0 Hz, 1H, H-2), 7.40 (almost s, 4H, -C_6H_4CN), 7.33 (d, J = 5.5 Hz, 1H, H-4), 6.74 (d, J = 2.0 Hz, 1H, H-3), 4.23 (s, 2H, H-1'); ir (potassium bromide): 3042, 2932, 2230, 1612, 1579, 1416, 1189, 1158, 1123, 1036, 1023, 880, 823, 765 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2O$: C, 76.91; H, 4.30; N, 11.96. Found: C, 76.89; H, 4.34; N, 11.97.

(B) Compound **6b-CN** (41 mg, 0.13 mmole) was refluxed with sodium hydroxide (10% aqueous solution, 0.5 ml) in ethanol (10 ml) for 4 hours. After evaporation of the solvent, the residue was treated with chloroform and water. Evaporation of the dried chloroform layer gave 27 mg (90%) of compound **5b-**

CN.

6-Isopropoxycarbonylfuro[2,3-*c*]pyridinio-7-(1'-propoxide) (**3b-Et**), 7-(1'-Hydroxypropyl)furo[2,3-*c*]pyridine (**4b-Et**) and 7-Propylfuro[2,3-*c*]pyridine (**5b-Et**).

The crude reaction product (556 mg) from **2b** and propionaldehyde was chromatographed on a silica gel (60 g), hexane-ethyl acetate (1:1), to give 121 mg (20%) of **3b-Et**, 47 mg (11%) of **4b-Et** and 139 mg (34%) of **5b-Et**.

Compound **3b-Et**.

This compound was a slightly yellow viscous syrup and decomposed on heating above 100°. The structure was characterized by the following spectral data; pmr: δ 8.23 (d, J = 5.5 Hz, 1H, H-5), 7.60 (d, J = 2.0 Hz, 1H, H-2), 7.33 (d, J = 5.5 Hz, 1H, H-4), 6.67 (d, J = 2.0 Hz, 1H, H-3), 5.92 (t, J = 7.0 Hz, 1H, -C*H*CH_2CH_3), 4.75 (septet, J = 6.5 Hz, 1H, -C*H*$(Me)_2$), 2.15 (qn, J = 7.0 Hz, 2H, -CHC*H*$_2CH_3$), 1.27 and 1.20 (d, J = 6.5 Hz, 6H, -CH(*Me*)$_2$), 0.96 (t, J = 7.0 Hz, 3H, -$CHCH_2CH_3$); ir (neat): 3122, 2980, 2935, 2884, 1742, 1610, 1582, 1465, 1420, 1375, 1265, 1181, 1097, 905, 830, 792 cm^{-1}; ms: m/z (relative intensity) 264 (1), 263 (M^+,1), 236 (7), 235 (46), 176 (17), 160 (39), 159 (17), 149 (19), 148 (100); hrms: 263.1152. M^+, Calcd. for $C_{14}H_{17}NO_4$: 263.1156.

Compound **4b-Et**.

This compound had bp 140-160°(bath temperature, 20 mm Hg), colorless oil (solidified on standing in a refrigerator); pmr: δ 8.23 (d, J = 5.5 Hz, 1H, H-5), 7.63 (d, J = 2.0 Hz, 1H, H-2), 7.37 (d, J = 5.5 Hz, 1H, H-4), 6.77 (d, J = 2.0 Hz, 1H, H-3), 5.13 (dd, J = 4.5, 7.0 Hz, 1H, -C*H*CH_2CH_3), 4.47 (broad s, 1H, OH), 2.36-1.60 (m, 2H, -CHC*H*$_2CH_3$), 0.94 (t, J = 7.0 Hz, 3H, -$CHCH_2CH_3$); ir (neat): 3407 (br), 3120, 3031, 2967, 2935, 2873, 2877, 1613, 1580, 1463, 1271, 1181, 1127, 1035, 974, 871, 830 cm^{-1}.

Anal. Calcd. for $C_{10}H_{11}NO_2 \cdot 1/4H_2O$: C, 66.10; H, 6.38; N, 7.71. Found: C, 66.32; H, 6.26; N, 7.51.

Compound **5b-Et**.

This compound had bp 130-140° (bath temperature, 20 mm Hg), colorless oil; pmr: δ 8.19 (d, J = 5.5 Hz, 1H, H-5), 7.58 (d, J = 2.0 Hz, 1H, H-2), 7.24 (d, J = 5.5 Hz, 1H, H-4), 6.65 (dd, J = 2.0 Hz, 1H, H-3), 3.04 (t, J = 7.5 Hz, 2H, -C*H*$_2CH_2CH_3$), 2.18-1.58 (m, 2H, -CH_2C*H*$_2CH_3$), 0.98 (t, J = 7.0 Hz, 3H, -$CH_2CH_2CH_3$); ir (neat): 3101, 3025, 2963, 2933, 2873, 1611, 1580, 1464, 1417, 1269, 1178, 1129, 1035, 824 cm^{-1}; ms: m/z (relative intensity) 161 (M^+, 3), 160 (3), 146 (15), 134 (9), 133 (100); hrms: 161.0836. M^+, Calcd. for $C_{10}H_{11}NO$: 161.0840.

Hydrolysis of **3b-Et** with Hydrochloric Acid.

A mixture of **3b-Et** (32 mg, 0.12 mmole) and hydrochloric acid (10%, 10 ml) in ethanol (10 ml) was refluxed for 50 hours. After evaporation of the solvent, the residue was dissolved in water, basified with sodium bicarbonate and extracted with chloroform. Evaporation of the chloroform extract yielded 14 mg (65%) of **5b-Et**.

Reaction of Dimethyl 4-Isopropoxycarbonyl-4,7-dihydrofuro[3,2-*b*]pyridine-7-phosphonate (**2c**) with Benzaldehyde, *p*-Methoxybenzaldehyde, *p*-Cyanobenzaldehyde and Propionaldehyde.

General Procedure.

To a solution of phosphonate **2c** (819 mg, 2.6 mmoles) in tetrahydrofuran (150 ml) was added dropwise a solution of *n*-butyllithium in hexane (1. 6 *M*, 2.0 ml, 3.2 mmoles) with stirring at -78° under nitrogen. After being stirred for 30 minutes at this temperature, to the reaction mixture was added benzaldehyde, *p*-methoxybenzaldehyde, *p*-cyanobenzaldehyde or propionaldehyde (4.1 mmoles), and then the cold bath was removed. After being stirred for 4 hours at room temperature, the reaction mixture was evaporated under reduced pressure, treated with chloroform and water. The chloroform layer was dried over magnesium sulfate, and evaporated to give a brown viscous oil (812 mg from benzaldehyde, 993 mg from *p*-methoxybenzaldehyde and 586 mg from propionaldehyde) or a solid mass from *p*-cyanobenzaldehyde (927 mg). Each pmr spectrum of the crude reaction product of **2c** with benzaldehyde, *p*-methoxybenzaldehyde and *p*-cyanobenzaldehyde suggested the product is mainly composed of the exo-olefinic compounds **6c-H**, **6c-OMe** and **6c-CN**).

Compound **6c-H** had isopropyl protons at δ 1.32 (d, J = 5.5 Hz, 6H) and 5.08 (septet, J = 5.5 Hz, 1H) and an olefinic proton at δ 6.24 (s, 1H).

Compound **6c-OMe** had isopropyl protons at δ 1.35 (d, J = 5.5 Hz, 6H) and 5.03 (septet, J = 5.5 Hz, 1H) and an olefinic proton at δ 6.10 (s, 1H).

Compound **6c-CN** had isopropyl protons at δ 1.40 (d, J = 5.5 Hz, 6H) and 5.10 (septet, J = 5.5 Hz, 1H) and an olefinic proton at δ 6.13 s, 1H. Further processing of the residue is described in the subsequent paragraphs.

7-Benzylfuro[3,2-*b*]pyridine (**5c-H**).

(A) The residue (812 mg) from **2c** and benzaldehyde was chromatographed on a silica gel (25 g) column, hexane ethyl acetate (2:1), to give 316 mg (58%) of **5c-H**, colorless oil, bp 130° (bath temperature, 0.1 mm Hg); pmr: δ 8.32 (d, J = 5.0 Hz, 1H, H-5), 7.72 (d, J = 2.0 Hz, 1H, H-2), 7.13 (almost s, 5H), 6.90 (dd, J = 5.0, 0.8 Hz, 1H, H-6), 6.85 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 4.16 (s, 2H, H-1'); ir (neat): 3087, 3061, 3029, 2924, 2857, 1619, 1567, 1496, 1454, 1386, 1127, 1019, 869, 790, 749, 704 cm^{-1}; ms: m/z (relative intensity) 210 (17), 209 (M^+, 100), 208 (15); hrms: 209.0838. M^+, Calcd. for $C_{14}H_{11}NO$: 209.0840.

Anal. Calcd. for $C_{14}H_{11}NO$: C, 80.36; H, 5.30; N, 6.69. Found: C, 80.09; H, 5.57; N, 6.55.

(B) The residue (214 mg) from **2c** and benzaldehyde was warmed at 40° with hydrochloric acid (10%, 10 ml) in ethanol (10 ml) for 1 hour. After evaporation of the solvent, the residue was dissolved in water, basified with sodium bicarbonate and extracted with chloroform. The dried chloroform extract was evaporated to give 105 mg (73%) of **5c-H**.

(C) Treatment of the residue (334 mg) from **2c** and benzaldehyde with sodium hydroxide as in the case of **2b** afforded **5c-H** (68 mg, 47%).

7-*p*-Methoxybenzylfuro[3,2-*b*]pyridine (**5c-OMe**).

(A) The residue (993 mg) from **2c** and *p*-methoxybenzaldehyde was chromatographed on a silica gel (30 g) column, hexane-ethyl acetate (1:1), to give 94 mg (17%) of compound **5c-OMe** as a colorless oil of bp 130° (bath temperature, 0.12 mm Hg); pmr: δ 8.28 (d, J = 4.5 Hz, 1H, H-5), 7.67 (d, J = 2.0 Hz, 1H, H-2), 7.06 and 6.79 (AB-q, J = 8.5 Hz, 4H, -C_6H_4OMe),

6.82 (d, J = 4.5 Hz, 1H, H-6), 6.80 (d, J = 2.0 Hz, 1H, H-3), 4.12 (s, 2H, H-1'), 3.70 (s, 3H, -C_6H_4OMe); ir (neat): 3123, 3031, 3002, 2955, 2934, 2836, 1619, 1512, 1387, 1248, 1179, 1035, 818, 762 cm^{-1}; ms: m/z (relative intensity) 240 (18), 239 (M^+, 100), 224 (14); hrms: 239.0942. M^+, Calcd. for $C_{15}H_{13}NO_2$: 239.0946.

Anal. Calcd. for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 74.93; H, 5.61; N, 5.86.

(B) Refluxing of the residue (347 mg) from **2c** and *p*-methoxybenzaldehyde with hydrochloric acid (10%, 10 ml) in ethanol (10 ml) afforded 158 mg (73%) of compound **5c-OMe**.

(C) Refluxing of the residue (387 mg) from **2c** and *p*-methoxybenzaldehyde with sodium hydroxide (10% aqueous solution, 10 ml) in ethanol (10 ml) gave 144 mg (59%) of compound **5c-OMe**.

4-Isopropoxycarbonyl-7-*p*-cyanobenzal-6,7-dihydrofuro[3,2-*b*]pyridine (**6c-CN**).

The solid residue (927 mg) from **2c** and *p*-cyanobenzaldehyde was recrystallized from chloroform-ether to give 749 mg (90%) of **6c-CN** as yellow crystals of mp 167.5-170°; pmr: δ 7.60-7.13 (m, 6H, H-5, H-2 and -C_6H_4CN), 6.95 (d, J = 2.0 Hz, 1H, H-3), 6.45 (d, J = 8.0 Hz, 1H, H-6), 6.13 (s, 1H, H-1'), 5.13 (septet, J = 5.5 Hz, 1H, -C*H*$(Me)_2$), 1.40 (d, J = 5.5 Hz, 6H, -CH($Me)_2$); ir (potassium bromide): 2984, 2937, 2214, 1726, 1643, 1593, 1364, 1292, 1278, 1175, 1106 cm^{-1}.

Anal. Calcd. for $C_{19}H_{16}N_2O_3$: C, 71.24; H, 5.03; N, 8.74. Found: C, 70.94; H, 5.09; N, 8.64.

7-*p*-Cyanobenzylfuro[3,2-*b*]pyridine (**5c-CN**).

(A) Compound **6c-CN** (50 mg, 0.16 mmole) was chromatographed on a silica gel (6 g) eluting with hexane-ethyl acetate (1:1) to give compound **5c-CN** (28 mg, 77%) as colorless crystals of mp 118-122° (from acetone-ether); pmr (400 MHz): δ 8.47 (d, J = 4.8 Hz, 1H, H-5), 7.84 (d, J = 2.0 Hz, 1H, H-2), 7.58 and 7.38 (AB-q. J = 8.4 Hz, 4H, -C_6H_4CN), 6.99 (d, J = 2.0 Hz, 1H, H-3), 6.98 (d, J = 4.8 Hz, 1H, H-6), 4.30 (s, 2H, H-1'); ^{13}C-nmr: 148.5 (d, C-2), 147.3 (s, C-3a), 146.32 (s, C-7a), 146.27 (d, C-5), 143.4 (s, C- 1"), 132.2 (d, 2 x C, C-2" and C-6"), 130.8 (s, C-4"), 129.5 (d, 2 x C, C-3" and C-5"), 119.2 (d, C-6), 118.5 (s, C-7), 110.5 (s, CN), 108.2 (d, C-2), 35.2 (t, C-1'): ir (potassium bromide): 3140, 3049, 2229, 1616, 1567, 1508, 1426, 1387, 1178, 1123, 1031, 863, 851 cm^{-1}.

Anal. Calcd. for $C_{15}H_{10}N_2O$: C, 76.91, H, 4.30; N, 11.96. Found: C, 76.92; H, 4.38; N, 11.86.

(B) Treatment of compound **6c-CN** (51 mg, 0.16 mmole) with hydrochloric acid (10%, 10 ml) in ethanol (10 ml) at 40° for 4 hours afforded 37 mg (99%) of **5c-CN**.

(C) Refluxing of compound **6c-CN** (49 mg, 0.15 mmole) with sodium hydroxide (10% aqueous solution, 0.5 ml) in ethanol (10 ml) for 4 hours gave 32 mg (90%) of compound **5c-CN**.

7-Propylfuro[3,2-*b*]pyridine (**5c-Et**).

Crude **6c-Et** (586 mg) was refluxed with hydrochloric acid (10%, 10 ml) in ethanol (10 ml). After evaporation of the solvent, the residual syrup was dissolved in water, basified with sodium bicarbonate, extracted with chloroform. Evaporation of the chloroform extract yielded 311 mg (74%) of **5c-Et** as a colorless oil of bp 130-140° (bath temperature, 20 mm Hg); pmr (400 MHz): δ 8.44 (d, J = 4.6 Hz, 1H, H-5), 7.81 (d, J = 2.0 Hz, 1H, H-2), 7.03 (d, J = 4.6 Hz, 1H, H-6), 6.96 (d, J = 2.0 Hz, 1H, H-3), 2.88 (t, J = 7.0 Hz, 2H, -$CH_2CH_2CH_3$), 1.79 (sextet, J = 7.0 Hz, 2H, -$CH_2CH_2CH_3$), 0.99 (t, J = 7.0 Hz, 3H, -$CH_2CH_2CH_3$); ^{13}C-nmr: 148.0 (d, C-2), 147.1 (s, C-3a), 147.8 (s, C-3a), 156.0 (d, C-S), 134.4 (s, C-7), 119.2 (d, C-6), 108.2 (d, C-3), 31.2 (t, C-1'), 22.3 (t, C-2'), 13.8 (q, C-3'); ir (neat): 3115, 3105, 3070, 2963, 2938, 2874, 1619, 1567, 1539, 1389, 1190, 1128, 1022, 869, 824, 750 cm^{-1}; ms: m/z (relative intensity) 162 (12), 161 (M^+,100), 146 (14), 134 (8), 133 (89), 132 (21); hrms: 161.0838. M^+, Calcd. for $C_{10}H_{11}NO$: 161.0840.

Reaction of Lithio Intermediates from 4-Benzyl- (**5a-H**), 4-*p*-Methoxybenzyl- (**5a-OMe**), 4-*p*-Cyanobenzylfuro[3,2-*c*]pyridine (**5a-CN**), 7-Benzyl- (**5b-H**), 7-*p*-Methoxybenzyl-(**5b-OMe**), 7-*p*-Cyanobenzylfuro[2,3-*c*]pyridine (**5b-CN**), 7-Benzyl- (**5c-H**), 7-*p*-Methoxybenzyl- (**5c-OMe**) and 7-*p*-Cyanofuro[3,2-*b*]pyridine (**5c-CN**) with Acetone.

General Procedure.

To a solution of diisopropylamine (0.14 ml, 1.0 mmole) in dry tetrahydrofuran (20 ml) was added a solution of *n*-butyllithium in hexane (1.6 *M*, 0.63 ml, 1.0 mmole) by syringe at -75° under a nitrogen atmosphere with stirring. After being stirred at this temperature for 20 minutes, a solution of arylmethylfuropyridine **5** (0.66 mmole) in dry tetrahydrofuran (10 ml) was added by syringe, stirred for 20 minutes, and acetone (0.07 ml, 1.0 mmole) was added. Stirring at -40° was continued for 4 hours. The mixture was treated with 10% hydrochloric acid (1 ml). After evaporation of the solvent, the residue was dissolved in water, basified with sodium bicarbonate and extracted with chloroform. After drying (magnesium sulfate), the chloroform solution was evaporated to give a brown oily residue (150-250 mg).

Further processing of the residue is described in the following paragraph.

2-(α-Hydroxy-α-methylethyl)-4-benzylfuro[3,2-*c*]pyridine (**7a-H**) and 4-{1'-(α-Hydroxy-α-methylethyl)-1'-phenylmethyl}furo-[3,2-*c*]pyridine (**8a-H**).

The residue (190 mg) from **5a-H** was chromatographed on a silica gel (20 g) column using chloroform-methanol (99.5:0.5) as an eluent to give 58 mg (33%) of **7a-H** as a slightly yellow oil, 74 mg (42%) of **8a-H** as a colorless oil and the starting compound (18 mg, 12%).

Compound **7a-H** had pmr: δ 8.32 (d, J = 6.0 Hz, 1H, H-6), 7.19 (almost s, 5H, -C_6H_5), 7.05 (d, J = 6.0 Hz, 1H, H-7), 6.43 (s, 1H, H-3), 4.32 (s, 2H, H-1'), 2.60 (s, 1H, OH), 1.61 (s, 6H, 2 x Me); ir (neat): 3374 (broad), 3029, 2979, 2931, 1582, 1454, 1433, 1378, 1274, 1254, 1155, 1030, 937, 814, 757 721, 699 cm^{-1}; ms: m/z (relative intensity) 267 (M^+, 48), 266 (99), 252 (44), 250 (29), 249 (45), 248 (100), 208 (22), 180 (14), 174 (17); hrms: 267.1269. M^+, Calcd. for $C_{17}H_{17}NO_2$: 267 1258.

Compound **8a-H** had pmr: δ 8.40 (d, J = 5.6 Hz, 1H, H-6), 7.51-7.24 (m, 7H, H-2, H-7 and -C_6H_5), 6.68 (dd, J = 2.4, 0.8 Hz, 1H, H-3), 4.21 (s, 1H, H-1'), 1.29 (s, 3H, Me), 1.13 (s, 3H, Me); ir (neat): 3317 (broad), 3108, 3062, 3026, 2974, 2929, 1601, 1586, 1534, 1495, 1452, 1429, 1378, 1361, 1269, 1153, 1133, 1039, 958, 859, 816, 737, 700 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.05; H, 6.69; N, 5.14.

2-(α-Hydroxy-α-methylethyl)-4-*p*-methoxybenzylfuro[3,2-*c*]pyridine (**7a-OMe**).

The residue (205 mg) from **5a-OMe** was chromatographed on a silica gel (20 g) column eluting with hexane-ethyl acetate (1:1) to give 30 mg (15%) of **7a-OMe** and 89 mg (56%) of the starting compound (**5a-OMe**).

Compound **7a-OMe** had pmr: δ 8.37 (d, J = 5.5 Hz, 1H, H-6), 7.26 (d, J = 5.5 Hz, 1H, H-7), 7.18 and 6.78 (AB-q, J = 8.0 Hz, 4H, -C_6H_4OMe), 6.47 (s, 1H, H-3), 4.28 (s, 2H, H-1'), 3.67 (s, 3H, -C_6H_4OMe), 1.62 (s, 6H, 2 x Me); ir (neat): 3331 (broad), 2964, 2926, 1611, 1580, 1510, 1458, 1261, 1091, 1031, 802 cm^{-1}; ms; m/z (relative intensity) 297 (M^+, 13), 296 (11), 280 (20), 279 (100), 278 (86), 264 (22); hrms: 297.1379. M^+, Calcd. for $C_{18}H_{19}NO_3$: 297.1364.

4-{1'-(α-Hydroxy-α-methylethyl)-1'-(*p*-cyanophenyl)methyl}-furo[3,2-*c*]pyridine (**8a-CN**), 2-(α-Hydroxy-α-methylethyl)-4-{1'-(α-hydroxy-α-methylethyl)-1'-(*p*-cyanophenyl)methyl}furo-[3,2-*c*]pyridine (**9a-CN**).

The residue (160 mg) from **5a-CN** was chromatographed on a silica gel (18 g) column using hexane-ethyl acetate (1:1) as an eluent to give 10 mg (5%) of **8a-CN** as colorless crystals of mp 126-130°, 84 mg (36%) of **9a-CN** as a colorless oil and 8 mg (5%) of the starting compound.

Compound **8a-CN** had pmr: δ 8.40 (d, J = 5.5 Hz, 1H, H-6), 7.56 (almost s, 5H, H-2 and -C_6H_4CN), 7.31 (dd, J = 5.5, 0.8 Hz, 1H, H-7), 6.73 (dd, J = 2.0, 0.8 Hz, 1H, H-3), 4.27 (s, 1H, H-1'), 1.31 and 1.12 (s, 6H, 2 x Me); ir (neat): 3432 (broad), 3150, 3115, 3103, 3045, 2982, 2925, 2228, 1603, 1587, 1535, 1505, 1429, 1267, 1154, 1039, 958, 851, 777, 745 cm^{-1}.

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.96; H, 5.52; N, 9.58. Found: C, 74.02; H, 5.41; N, 9.47.

Compound **9a-CN** had pmr: δ 8.35 (d, J = 5.5 Hz, 1H, H-6), 7.58 and 7.43 (AB-q, J = 8.5 Hz, 4H, -C_6H_4CN), 7.26 (d, J = 5.5 Hz, 1H, H-7), 6.55 (s, 1H, H-3), 4.22 (s, 1H, H-1'), 1.61 (s, 6H, 2 x Me), 1.22 (s, 3H, Me), 1.03 (s, 3H, Me); ir (neat): 3329 (broad), 2977, 2935, 2229, 1605, 1583, 1505, 1435, 1238, 1155, 1092, 1018, 958, 936, 849, 816, 762 cm^{-1}.

Anal. Calcd. for $C_{21}H_{22}N_2O_3$: C, 71.98; H, 6.33; N, 7.99. Found: C, 71.65; H, 6.46; N, 7.71.

2-(α-Hydroxy-α-methylethyl)-7-benzylfuro[2,3-*c*]pyridine (**7b-H**) and 7-{1'-(α-Hydroxy-α-methylethyl)-1'-phenylmethyl}furo-[2,3-*c*]pyridine (**8b-H**).

The residue (180 mg) from **5b-H** was chromatographed on a silica gel (20 g) column using hexane-ethyl acetate (2:1) as an eluent to give 49 mg (28%) of **7b-H** as a colorless oil, 85 mg (48%) of **8b-H** as colorless crystals of mp 119-122° (from ether) and the starting compound (15 mg, 11%).

Compound **7b-H** had pmr: δ 8.14 (d, 5.5 Hz, 1H, H-5), 7.40-7.10 (m, 6H, H-4 and -C_6H_5), 6.12 (s, 1H, H-3), 4.31 (s, 2H, H-1'), 2.75 (broad s, 1H, OH), 1.60 (s, 6H, 2 x Me); ms: m/z (relative intensity) 268 (5), 267 (M^+, 29), 266 (67), 252 (11), 251 (7), 250 (11), 249 (40), 248 (100), 247 (11), 208 (37); hrms: 267.1250. M^+, Calcd. for $C_{17}H_{17}NO_2$: 267.1258.

Compound **8b-H** had pmr: δ 8.20 (d, J = 4.8 Hz, 1H, H-5), 7.50 (d, J = 2.0 Hz, 1H, H-2), 7.46-7.00 (m, 5H, -C_6H_5), 7.22 (d, J = 4.8 Hz, 1H, H-4), 6.58 (d, J = 2.0 Hz, H-3), 4.43 (s, 1H, H-1'), 1.22 (s, 3H, Me), 1.09 (s, 3H, Me); ir (neat): 3379 (br), 3153, 3125, 3079, 3026, 2983, 2973, 2931, 1612, 1579, 1454, 1420, 1406, 1268, 1176, 1121, 1037, 956, 825, 739 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.42; H, 6.40; N, 5.31.

2-(α-Hydroxy-α-methylethyl)-7-*p*-methoxybenzylfuro[2,3-*c*]pyridine (**7b-OMe**) and 7-{1'-(α-Hydroxy-α-methylethyl)-1'-*p*-methoxyphenylmethyl}furo[2,3-*c*]pyridine (**8b-OMe**).

The residue (170 mg) from **5b-OMe** was chromatographed on a silica gel (20 g) column using hexane-ethyl acetate (2:1) as an eluent to give 74 mg (38%) of **7b-OMe** as colorless crystals of mp 60-63.5° (from ether), 65 mg (33%) of **8b-OMe** as a colorless oil and the starting **5b-OMe** (15 mg, 10%).

Compound **7b-OMe** had pmr: δ 8.16 (d, J = 5.0 Hz, 1H, H-5), 7.28 (d, J = 5.0 Hz, 1H, H-4), 7.25 and 6.71 (AB-q, J = 8.5 Hz, 4H, -C_6H_4OMe), 6.51 (s, 1H, H-3), 4.27 (s, 2H, H-1'), 3.67 (s, 3H, OMe), 3.00 (broad s, 1H, OH), 1.63 (s, 6H, 2 x Me); ir (potassium bromide): 3447 (br). 2926, 2853, 1619, 1587, 1512, 1467, 1275, 1377, 1177, 1161, 1040, 939, 835 cm^{-1}; ms: m/z (relative intensity) 297 (M^+, 14), 296 (13), 280 (20), 279 (100), 278 (95), 264 (24); hrms: 297.1364. M^+, Calcd. for $C_{18}H_{19}NO_3$: 297.1364.

Compound **8b-OMe** had pmr: δ 8.26 (d, J = 5.2 Hz, 1H, H-5), 7.61 (d, J = 2.0 Hz, 1H, H-2), 7.47 and 6.74 (AB-q, J = 8.6 Hz, 4H, -C_6H_4OMe), 7.34 (d, J = 5.1 Hz, 1H, H-4), 6.68 (d, J = 2.0 Hz, 1H, H-3), 4.47 (s, 1H, H-1'), 3.71 (s, 3H, OMe), 1.28 and 1.16 (s, 6H, 2 x Me); ir (neat): 3335 (br), 3122, 3080, 3037, 2973, 2935, 2836, 1612, 1580, 1510, 1463, 1420, 1267, 1248, 1179, 1127, 1038, 957, 829, 754 cm^{-1}.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.66; H, 6.78; N, 4.54.

7-{1'-(α-Hydroxy-α-methylethyl)-1'-*p*-cyanophenylmethyl}-furo[2,3-*c*]pyridine (**8b-CN**).

The residue (150 mg) from **5b-CN** was chromatographed on a silica gel (20 g) column using hexane-ethyl acetate (2:1) as an eluent to give 38 mg (19%) of **8b-CN** as colorless crystals of mp 113.5-116° (from ether) and the starting **5b-CN** (55 mg, 36%).

Compound **8b-CN** had pmr: δ 8.28 (d, J = 5.5 Hz, 1H, H-5), 7.63 and 7.45 (AB-q, J = 8.5 Hz, 4H, -C_6H_4CN), 7.60 (d, J = 2.0 Hz, 1H, H-2), 7.38 (d, J = 5.5 Hz, 1H, H-4), 6.71 (d, J = 2.0 Hz, 1H, H-3), 4.53 (s, 1H, H-1'), 1.62 (broad s, 1H, OH), 1.26 and 1.10 (s, 6H, 2 x Me).

Anal. Calcd. for $C_{18}H_{16}N_2O_2$: C, 73.96; H, 5.52; N, 9.58. Found: C, 73.61; H, 5.58; N, 9.59.

2-(α-Hydroxy-α-methylethyl)-7-benzylfuro[3,2-*b*]pyridine (**7c-H**) and 7-{1'-(α-Hydroxy-α-methylethyl)-1'-phenylmethyl}furo-[3,2-*b*]pyridine (**8c-H**).

The residue (190 mg) from **5c-H** was chromatographed on a silica gel (20 g) column using chloroform-methanol (99.5:0.5) as an eluent to give 27 mg (15%) of **7c-H** as colorless crystals of mp 102-105° (from ether), 85 mg (48%) of **8c-H** as a colorless oil and the starting **5c-H** (40 mg, 29%).

Compound **7c-H** had pmr: δ 8.28 (d, J = 5.5 Hz, 1H, H-5), 7.21 (almost s, 5H, -C_6H_5), 6.86 (d, J = 5.5 Hz, 1H, H-6), 6.70 (s, 1H, H-3), 4.16 (s, 2H, H-1'), 3.15 (broad s, 1H, OH), 1.63 (s, 6H, 2 x Me); ir (potassium bromide): 3464 (br), 3025, 2976, 2932, 1625, 1585, 1491, 1453, 1396, 1253, 1181, 1146, 964, 929, 853, 809, 720 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.61; H, 6.58; N. 5.16.

Compound **8c-H** had pmr: δ 8.37 (d, J = 5.2 Hz, 1H, H-5), 7.71 (d, J = 2.2 Hz, 1H, H-2), 7.68-7.07 (m, 5H, -C_6H_5), 7.14 (d, J = 5.2 Hz, 1H, H-6), 6.87 (d, J = 2.2 Hz, 1H, H-3), 4.51 (s, 1H, H-1'), 2.68 (broad s, 1H, OH), 1.25 (s, 6H, 2 x Me); ir (neat):

3282 (br), 3029, 2975, 2932, 1616, 1566, 1494, 1454, 1387, 1182, 1129, 1084, 1019, 960, 973, 797, 758 cm^{-1}.

Anal. Calcd. for $C_{17}H_{17}NO_2$: C, 76.38; H, 6.41; N, 5.24. Found: C, 76.46; H, 6.31; N, 5.38.

7-{1'-(α-Hydroxy-α-methylethyl)-1'-*p*-methoxyphenylmethyl}-furo[3,2-*b*]pyridine (**8c-OMe**).

The residue (175 mg) from **5c-OMe** was chromatographed on a silica gel (20 g) column using hexane-ethyl acetate (1:1) as an eluent to give 131 mg (67%) of **8c-OMe** as a slightly yellow oil and the starting **5c-OMe** (17 mg, 11%).

Compound **8c-OMe** had pmr: δ 8.40 (d, J = 5.2 Hz, 1H, H-5), 7.72 (d, J = 2.2 Hz, 1H, H-2), 7.70 (d, J = 5.2 Hz, 1H, H-6), 7.44 and 6.85 (AB-q, J = 8.8 Hz, 4H, -C_6H_4OMe), 6.87 (d, J = 2.2 Hz, 1H, H-3), 4.50 (s, 1H, H-1'), 3.70 (s, 3H, OMe), 2.23 (broad s, 1H, OH), 1.63 (s, 6H, 2 x Me); ir (neat): 3267 (br), 3032, 2972, 2933, 2837, 1614, 1565, 1510, 1464, 1383, 1247, 1180, 1129, 1036, 872, 762 cm^{-1}; ms: m/z (relative intensity) 297 (M^+, 1), 280 (7), 279 (30), 241 (9), 240 (82), 239 (100), 238 (41), 225 (16), 224 (99); hrms: 297.1349. (M^+, Calcd. for $C_{18}H_{19}NO_3$: 297.1364.

7-{1'-(α-Hydroxy-α-methylethyl)-1'-*p*-cyanophenylmethyl}-furo[3,2-*b*]pyridine (**7-CN**).

The residue (175 mg) from **5c-CN** was chromatographed on a silica gel (20 g) column using hexane-ethyl acetate (1:1) as an eluent to give 14 mg (7%) of **7c-CN** as a slightly yellow oil and the starting **5c-CN** (118 mg, 77%).

Compound **7c-CN** had pmr: δ 8.28 (d, J = 5.0 Hz, 1H, H-5), 7.50-7.27 (AB-q, J = 7.5 Hz, 4H, -C_6H_4CN), 6.77 (d, J = 5.0 Hz, 1H, H-6), 6.68 (s, 1H, H-3), 4.22 (s, 2H, H-1'), 1.92 (broad s, 1H, OH), 1.60 (s, 6H, 2 x Me); ir (neat): 3379 (br), 2982, 2933, 2229, 1625, 1608, 1508, 1395, 1250, 1174, 1093, 962, 935, 821 cm^{-1}; ms: m/z (relative intensity) 293 (2), 292 (M^+, 1), 278 (2), 277 (8), 275 (23), 274 (100); hrms: 292.1208. M^+, Calcd. for $C_{18}H_{16}N_2O_2$: 292.1211.

X-Ray Structural Determination of Compound **5c-CN.**

The structure was solved by direct methods [8] and expanded using Fourier techniques [9]. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically. The final cycle of full-matrix least-squares refinement [10] was based on 1460 observed reflections ($I>3.00\sigma(I)$) and 203 variable parameters and converged (largest parameter was 0.01 times its esd) with unweighted and weighted agreement factors of:

$$R = \Sigma \| F_O | - | F_C \| / \Sigma | F_O | = 0.049$$
$$R_w = [(\Sigma_w(| F_O | - | F_C |)^2 / \Sigma_w F_O^2)]^{1/2} = 0.059$$

The standard deviation of an observation of unit weight [11] was 2.79. The weighting scheme was based on counting statistics and included a factor (p = 0. 015) to downweight the intense reflections. Plots of $\Sigma_w(| F_O | - | F_C |)^2$ versus $| F_O |$, reflection order in data collection, sin θ/λ and various classes of indices showed no unusual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.17 and -0.33 e^-/A^3, respectively.

Neutral atom scattering factors were taken from Cromer and Waber [12]. Anomalous dispersion effects were included in Fcalc [13]; the values for Δf' and Δf'' were those of Creagh and McAuley [14]. The values for the mass attenuation coefficients are those of Creagh and Hubbel [15]. All calculations were performed using the teXsan [16] crystallographic software package of Molecular Structure Corporation.

REFERENCES AND NOTES

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

[2] S. Shiotani and K. Taniguchi, *J. Heterocyclic Chem.*, in press.

[3a] K. Akiba, Y. Negishi and N. Inamoto, *Synthesis*, 55 (1979); [b] K. Akiba, Y. Negishi, K. Kurumaya and N. Inamoto, *Tetrahedron Letters*, **22**, 4977 (1981).

[4] S. Shiotani, H. Morita, M. Inoue, T. Ishida, Y. Iitaka and A. Itai, *J. Heterocyclic Chem.*, **21**, 725 (1984).

[5] S. Gronowitz, C. Westerlund and A.-B. Hörnfeldt, *Acta Chem. Scand., Ser.* **B 29**,. 233 (1975).

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

[7] A. Maeroker in Organic Reactions, Vol **14**, C. Cope, ed, John-Wiley & Sons Inc., New York, 1965, pp 270-490.

[8] SHELXS86: G. M. Sheldrick in Crystallographic Computing 3, G.M. Sheldrick, C. Kruger and R. Goddard, ed, Oxford University Press, 1985, pp 175-189.

[9] DIRDIF92: P. T. Beurskens, G. Admiraal, G. Beurskens, W. P.Bosman, S. Garica-Granda, R. O. Gould, J. M. M. Smits and C. Smykalla (1992). The DIRDIF program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands.

[10] Least-Squares: Function minimized: $\Sigma_w(| F_O | - | F_C |)^2$, where $w = 1/\sigma^2(F_O) = 4F_O^2/\sigma^2(F_O^2)$, $\sigma^2(F_O^2) = [S^2(C+R^2B)+(pF_O^2)^2]/Lp^2$ {S = Scan rate; C = Total Integrated Peak Count; R = Ratio of Scan Time to background counting time; B = Total Background Count; Lp = Lorentz-polarization factor; p = p-factor}.

[11] Standard deviation of an observation of unit weight: $[\Sigma_w(| F_O | - | F_C |)^2/(No - Nv)]^{1/2}$, where: No = number of observations, Nv = number of variables.

[12] D. T. Cromer and J. T. Waber, International Tables for X-ray Crystallography, Vol **IV**, The Kynoch Press, Birmingham, England, 1974, Table 2.2 A.

[13] J. A. Ibers and W. C. Hamilton, *Acta Crystallogr.*, **17**, 781 (1964).

[14] D. C. Creagh and W. J. McAuley, International Tables for Crystallography, Vol **C**, A. J. C. Wilson, ed, Kluwer Academic Publishers, Boston, 1992, Table 4.2.6.8, pp 219-222.

[15] D. C. Creagh and J. H. Hubbell, International Tables for Crystallography, Vol **C**, A. J. C. Wilson, ed, Kluwer Academic Publishers, Boston, 1992, Table 4.2.4.3. pp. 200-206.

[16] teXsan: Crystal Structure Analysis Package, Molecular Structure Corporation (1985 and 1992).