Furopyridines. XII [1]. Reaction of 3-Bromo, 2-Phenylthio and 2-Phenylthio-3-bromo Derivatives of Furo[2,3-*b*]-, Furo[3,2-*b*]-, Furo[2,3-*c*]- and Furo[3,2-*c*]pyridine with Several Alkyllithiums

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This paper describes reactions of 3-bromo- **1a-d**, 2-phenylthio- **5a-d** and 2-phenylthio-3-bromofuropyridines **6a-d** with *n*-butyl-, *t*-butyl- and methyllithium and lithioacetonitrile. Lithiation of compounds **1a-d** with *n*-butyl- or methyllithium gave the parent furopyridines **2a-d** and *o*-ethynylpyridinols **3a-d**. Reaction of compounds **5a-d** with methyllithium afforded *o*-(phenylthioethynyl)pyridinols **7a-d**, which were also yielded by reaction of compounds **6a-d** with *t*-butyl- or methyllithium. The phenylthio group in compounds **7a-d** were substituted with *t*-butyl group by the reaction with excess *t*-butyllithium. In contrast, 2-phenylthio group in compounds **5a-d** and **6a-d** was substituted with cyanomethyl group by reaction with lithioacetonitrile to give compounds **11a-d** and **10b,c** respectively.

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We have been interested in the chemistry of furopyridines which are expected to be new moieties of biologically active compounds but hiterto have been little investigated by other research workers, and have reported the syntheses of the parent compounds and 2- and/or 3-substituted derivatives, and their chemical properties [2]. In the meantime, it had been reported that the bromine atom at 3-position of furan and thienopyridine can be replaced with a formyl group by the reaction with alkyllithium and *N,N*-dimethylformamide, through the 3-lithio intermediate [3,4], while 3-bromobenzofuran is converted into *o*-ethynylphenol by the reaction with *n*-butyllthium [5]. Thus, it becomes interesting to examine the reaction of 3-bromofuropyridines with alkyllithium.

When 3-bromofuropyridines **1a-d** [2b] were reacted with 1.2 equivalent moles of *n*-butyllithium in tetrahydrofuran at −75° and then treated with water, the corresponding parent furopyridines **2a-d** and *o*-ethynylpyridinols **3a-d** were obtained in 38% and 57% yield from **1a**, 56% and 36% from **1b**, 58% and 38% from **1c**, and 35% and 55% from **1d**, respectively. These results suggested that that bromine atom of 3-bromofuropyridines is easily exchanged with lithium to form 3-lithio intermediates, from which acetylene compounds are slowly afforded by fission of the 1-2 bond and the parent furopyridines are formed by replacement of the lithium atom of the remaining 3-lithio intermediate with a proton from water. Reaction of compounds **1a-d** with methylithium also gave the corresponding parent furopyridines **2a-d** and *o*-ethynylpyridinols **3a-d** in similar yield.

Thus, 3-bromofuropyridines **1a-d** were reacted with 3.6 equivalent moles of *n*-butyllithium and *N,N*-dimethylformamide. The products isolated, however, were acetylene compounds **3a-d** and 2-(2-formyl-1-pentenyl)furopyridines

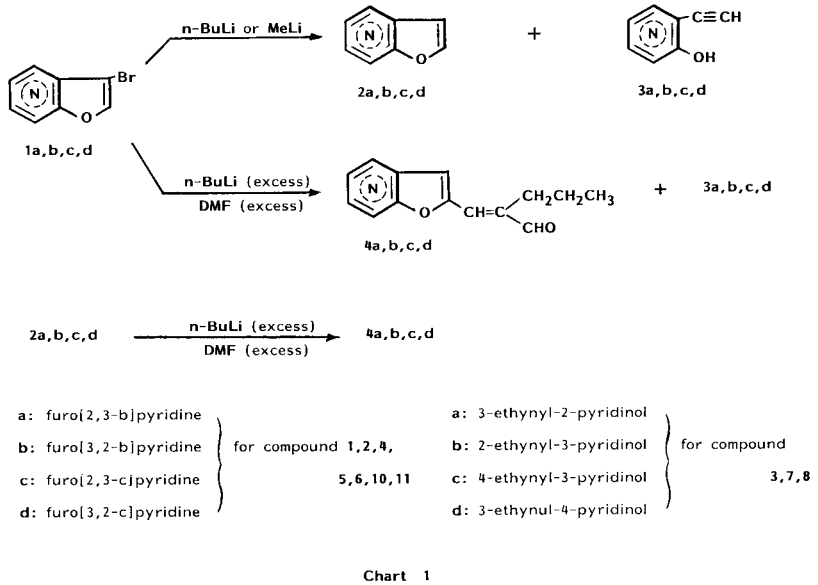
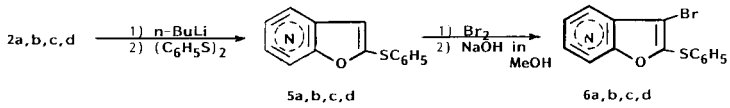


Chart 1



5a,b,c,d 6a,b,c,d

Chart 2

4a-d. The structures of the latter compounds **4a-d** were confirmed by ir and pmr spectra and elemental analysis, and identified with the compounds obtained by reaction of the corresponding parent furopyridines **2a-d** with excess *n*-butyllithium and *N,N*-dimethylformamide. The formation of the parent compound and the 2-(2-formyl-1-pentenyl) derivative from the corresponding 3-bromo derivative by the reaction with *n*-butyllithium and *N,N*-dimethylformamide could be interpreted as follows: substitution of the bromine or lithium atom at the 3-position with an hydrogen atom from the butyl group would give the parent compound **2**, which would be successively lithiated at the 2-position, in the presence of excess *n*-butyllithium, and then formylated with *N,N*-dimethylformamide to give the 2-formyl derivative. The latter compound would condense with 1-pentanal formed from *n*-butyllithium and *N,N*-dimethylformamide to give compound **4**.

Table I

Reaction Product(s) of 3-Bromofuropyridines **1a,b,c,d** with Several Alkyllithiums (at -75°)

Materials	Reactant(s)	Product(s)	(Yield, %)
1a	*n*-BuLi (1.2 eq)	**2a** (38)	**3a** (57)
1b	*n*-BuLi (1.2 eq)	**2b** (56)	**3b** (36)
1c	*n*-BuLi (1.2 eq)	**2c** (58)	**3c** (38)
1d	*n*-BuLi (1.2 eq)	**2d** (35)	**3d** (55)
1a	MeLi (3 eq)	**2a** (36)	**3a** (56)
1b	MeLi (3 eq)	**2b** (33)	**3b** (60)
1c	MeLi (3 eq)	**2c** (10)	**3c** (80)
1d	MeLi (3 eq)	**2d** (13)	**3d** (84)
1a	*n*-BuLi, DMF (excess)	**4a** (35)	**3a** (60)
1b	*n*-BuLi, DMF (excess)	**4b** (35)	**3b** (35)
1c	*n*-BuLi, DMF (excess)	**4c** (15)	**3c** (35)
1d	*n*-BuLi, DMF (excess)	**4d** (25)	**3d** (60)

Table II

Reaction Product(s) of 2-Phenylthio-3-bromofuropyridines **6a,b,c,d** with Several Alkyllithiums (at -75°)

Material	Base	Product(s)	(Yield, %)
6a	*t*-BuLi (1.2 eq)	**7a** (98)	
6b	*t*-BuLi (1.2 eq)	**7b** (96)	
6c	*t*-BuLi (1.2 eq)	**7c** (85) [a]	
6d	*t*-BuLi (1.2 eq)	–	
6a	MeLi (3 eq)	**7a** (90)	
6b	MeLi (3 eq)	**7b** (98)	
6c	MeLi (3 eq)	**7c** (45) [a]	**5c** (45)
6d	MeLi (3 eq)	**7d** (98)	
6a	*t*-BuLi (3 eq)	**8a** (36)	**9a** (30)
6b	*t*-BuLi (3 eq)	**8b** (80)	
6c	*t*-BuLi (3 eq)	**8c** (87)	
6d	*t*-BuLi (3 eq)	–	
6a	$LiCH_2CN$	–	
6b	$LiCH_2CN$	**10b** (53)	**11b** (14)
6c	$LiCH_2CN$	**10c** (60)	**11c** (23)
6d	$LiCH_2CN$	–	

[a] Yield of crude product.

Table III

Reaction Product(s) of 2-Phenylthiofuropyridines **5a,b,c,d** with Methyllithium and Lithioacetonitrile (at -75°)

Material	Base	Product(s)	(Yield, %)
5a	MeLi (3 eq)	**7a** (37)	**5a** (60)
5b	MeLi (3 eq)	**7b** (93)	
5c	MeLi (3 eq)	**7c** (75) [a]	**5c** (20)
5d	MeLi (3 eq)	**7d** (90)	
5a	$LiCH_2CN$	–	**5a** (95)
5b	$LiCH_2CN$	**11b** (90)	
5c	$LiCH_2CN$	**11c** (86)	
5d	$LiCH_2CN$	–	**5b** (99)
5a	$LiCH_2CN$ (at -20°)	**11a** (37)	
5d	$LiCH_2CN$ (at -20°)	**11d** (54)	

[a] Yield of crude product.

Nolan and Cohen reported that reaction of α-phenylthio-β-bromofuran derivatives with *t*-butyllithium and an electrophile afforded α-phenylthio-β-alkyl (or acyl) furans in good yield, and that the α-phenylthio group would activate the β-position to electrophilic attack [6]. Thus, we examined the reaction of 2-phenylthio-3-bromofuropyrridines **6a-d** with *t*-butyllithium in order to observe the stability of the 2-phenylthio-3-lithio intermediate.

Compounds **6a-d** were prepared from the parent compounds **2a-d** by lithiation with *n*-butyllithium and treatment with diphenyl disulfide affording 2-phenylthio compounds **5a-d**, bromination with molecular bromine, and the subsequent dehydrobromination with sodium hydroxide in methanol.

The reaction of compounds **6a-d** with 1.2 equivalent moles of *t*-butyllithium, however, yielded *o*-(2-phenylthioethynyl)pyridinols **7a-c** in 98% from **6a**, 96% from **6b** and 85% yield from **6c**. In the case of **6d**, only a colorless resinous product was obtained in almost quantitative yield. Interestingly, when the reactions were carried out

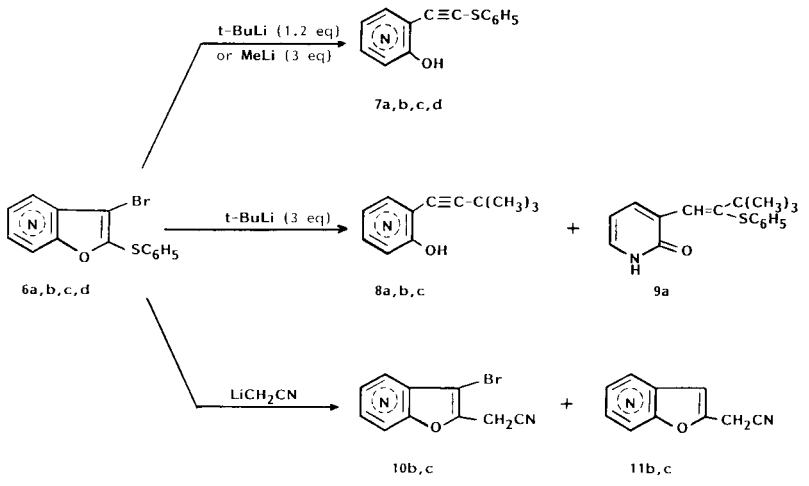


Chart 3

with 3 equivalent moles of *t*-butyllithium, *o*-(3,3-dimethyl-1-butynyl)pyridinols **8a-c** were obtained in 30% from **6a** (accompanying formation of 3-(2-phenylthio-3,3-dimethyl-1-butenyl)-2-pyridinol (**9a**) in 36%), 80% from **6b** and 87% from **6c**. In the case of **6d**, again a colorless resin was obtained. Whilst, reaction of **6a-d** with 3 equivalent moles of methyllithium afforded only the *o*-(phenylthioethynyl)-pyridinoles **7a-d** in good yield.

Reaction of 2-phenylthio-3-bromofuropyridines **6a-d** with lithioacetonitrile gave unexpected results: 2-cyanomethyl-3-bromo- **10b** and 2-cyanomethylfuro[3,2-*b*]pyridine (**11b**) were obtained in 53% and 14% from **6b**, and **10c** and **11c** in 60% and 23% yield from **6c**. In the case of **6a** and **6d**, no single compound could be isolated from the reaction mixture.

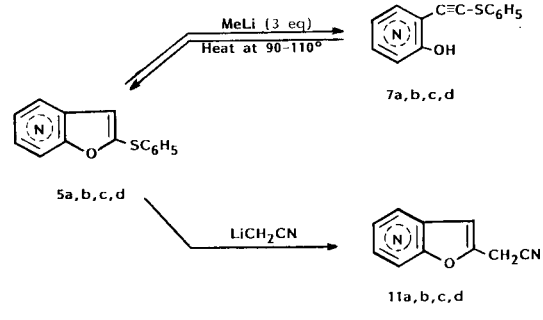


Chart 4

In order to compare the facile character in the nucleophilic substitution of the 2-phenylthio group, 2-phenylthiofuropyridines **5a-d** were reacted with lithioacetonitrile, and 2-cyanomethylfuropyridines **11** were obtained in 90% from **5b**, 86% from **5c** and 0% from **5a** and **5d** (complete recovery of the 2-phenylthio compound) at −75°. The reaction of **5a** and **5d** at −20° afforded 2-cyanomethyl derivative **11a** in 37% and **11d** in 54% yield. It is to be noted that 2-phenylthiobenzofuran (**5e**) did not undergo the substitution at all even at −20° and resulted in com-

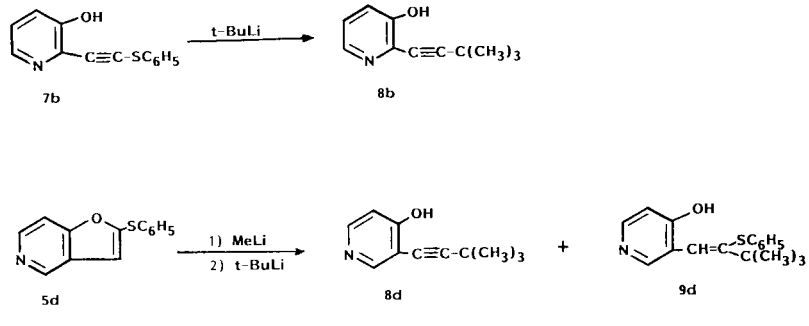


Chart 5

plete recovery of the starting material. In contrast, the reaction of the 2-phenylthio derivatives **5a-d** with 3 equivalent moles of methyllithium at −75° yielded the acetylene compound **7a** in 37% (accompanying recovery of **5a** in 60% yield) from **5a**, **7b** in 93% from **5b**, **7c** in 75% (accompanying recovery of **5c** in 20% yield) from **5c**, and **7d** in 90% yield from **5d**.

It is worth noting that the phenylthios group of 2-(2-phenylthioethynyl)-3-pyridinol **7b** was replaced with *t*-butyl group to give **8b** by the reaction with 2 equivalent moles of *t*-butyllithium in 80% yield. The reaction of 2-phenylthiofuro[3,2-*c*]pyridine **5d** with 3 equivalent moles of methyllithium and successive reaction with *t*-butyllithium afforded 3-(3,3-dimethyl-1-butynyl)-4-pyridinol (**8d**) and 3-(2-phenylthio-3,3-dimethyl-1-butenyl)-4-pyridinol (**9d**) in 29% and 51% yield. It is also interesting that *o*-(2-phenylthioethynyl)pyridinols **7a-d** were recyclized to give 2-phenylthiofuropyridines **5a-d** by heating at 90-110° in almost quantitative yield, while the *o*-(3,3-dimethyl-1-butynyl)pyridinols **8a-d** did not change at that temperature.

This research has demonstrated that the bromine atom of 3-bromo- and 2-phenylthio-3-bromofuropyridines or hydrogen at the 3-position of phenylthiofuropyridines is replaced with lithium by the reaction of methyl- or butyllithium and the 1-2 bond is cleaved subsequently to give *o*-ethynylpyridinols. These results are very similar to that of 3-bromobenzofuran. In contrast, lithioacetonitrile substitutes the phenylthio group of 2-phenylthio- and 2-phenylthio-3-bromofuropyridines to afford 2-cyanomethyl derivatives, while reaction of 2-phenylthiobenzofuran with lithioacetonitrile gave no 2-cyanomethyl compound but recovery of the starting compound. These results indicate the apparent activation by the pyridine nucleus in nucleophilic attack at the 2-position of furopyridines.

EXPERIMENTAL

Melting points were determined by using Yanagimoto micro melting point apparatus. All melting points are uncorrected. The ir spectra were recorded on a JASCO A-102 spectrometer. The pmr spectra were taken on a JEOL JNM-PMX 60 instrument with tetramethylsilane as an internal reference.

Reaction of 3-Bromofuropyridines **1a**, **1b**, **1c** and **1d** with *n*-Butyllithium.

General Procedure.

A solution of 3-bromo compound **1** (198 mg, 1 mmole) in 10 ml of dry tetrahydrofuran was stirred under a nitrogen atmosphere and cooled at −75°. To this solution was added a solution of *n*-butyllithium in hexane (0.75 ml, 1.6*M*, 1.2 mmoles) by syringe over a period of 5 minutes. After stirring at this temperature for 1 hour, the mixture was treated with 1 ml of water, and evaporated under reduced pressure at room temperature.

In the case of **1a** and **1b**, the residual mixture was diluted with 10 ml of water, acidified with 10% hydrochloric acid, then neutralized with sodium bicarbonate and extracted with chloroform. The extract was dried (magnesium sulfate) and evaporated the solvent. The residual syrup was treated with ether. The ether-soluble oil was distilled to give compound **2a** (45 mg, 38%), bp 140-145° (40 mm Hg) and **2b** (67 mg, 56%), bp 150-155° (45 mm Hg) which were identified by ir and pmr spectra. The ether insoluble crystalline solid was recrystallized from acetone to give **3a** (68 mg, 57%), mp 148-151° and **3b** (43 mg, 36%), mp 149-5-150.5°, respectively.

3-Ethynyl-2-pyridinol (**3a**).

This compound had ir: (potassium bromide): 3430 (broad), 3270, 3210, 3090, 3050, 2990, 2970, 2910, 2860, 2840, 2760, 2090, 1640, 1625, 1600, 1540, 1460, 1425, 1315, 1240 cm^{-1}; pmr (deuteriochloroform): δ 7.69 (dd, J = 2.9, 6.4 Hz, 1H, H-6), 7.50 (dd, J = 2.0, 6.4 Hz, 1H, H-4), 6.28 (t, J = 6.4 Hz, 1H, H-5), 3.37 (s, 1H, $-C\equiv CH$).

Anal. Calcd. for C_7H_5NO: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.84; H, 4.14; N, 11.73.

2-Ethynyl-3-pyridinol (**3b**).

This compound had ir: (potassium bromide): 3260, 3100-2200 (broad), 2100, 1950-1650 (broad), 1560, 1450, 1330, 1300, 1260, 1235, 1170, 1110 cm^{-1}; pmr (deuteriomethanol): δ 8.00 (t, J = 3.2 Hz, 1H, H-6), 7.26 (d, J = 3.2 Hz, 2H, H-4 and H-5), 3.84 (s, 1H, $-C\equiv CH$).

Anal. Calcd. for C_7H_5NO: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.63; H, 4.31; N, 11.52.

In the case of **1c** and **1d**, the strongly alkaline residual mixture was diluted with 10 ml of water and extracted with chloroform. Evaporation of the dried (magnesium sulfate) chloroform solution afforded crude **2c** and **2d** which were distilled to give pure samples (69 mg, 58% from **2c**, bp 120-125° (30 mm Hg) and 42 mg, 35% from **2d**, bp 125-130° (35 mm Hg)) and were identified by ir and pmr spectra. The aqueous layer after extraction with chloroform was passed through a column of 5 ml of Amberlite IRA-47. Evaporation of the eluate under reduced pressure yielded **3c** (45 mg, 38%), mp 135-138° dec (from acetone-ether) and **3d** (45 mg, 38%), mp 195-196°dec (from methanol).

4-Ethynyl-3-pyridinol (**3c**).

This compound had ir: (potassium bromide): 3240, 3100-2300 (broad), 2100, 1950-1650 (broad), 1590, 1565, 1435, 1370, 1320, 1310, 1255, 1240 cm^{-1}; pmr (deuteriomethanol): δ 8.06 (s, 1H, H-2), 7.87 (d, J = 4.8 Hz, 1H, H-6), 7.22 (d, J = 4.8 Hz, 1H, H-5), 3.75 (s, 1H, $C\equiv CH$).

Anal. Calcd. for C_7H_5NO: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.30; H, 4.08; N, 11.67.

3-Ethynyl-4-pyridinol (**3d**).

This compound had ir: (potassium bromide): 3150, 3010, 2960, 2900, 2850-2250 (broad), 2060, 1630, 1600, 1545, 1515, 1470, 1400, 1280, 1155 cm^{-1}; pmr (deuteriomethanol-deuterium oxide (2:1)): δ 8.00 (d, J = 1.6 Hz, 1H, H-2), 7.80 (dd, J = 1.6, 6.8 Hz, 1H, H-6), 6.52 (d, J = 6.8 Hz, 1H, H-5), 3.70 (s, 1H, $-C\equiv CH$).

Anal. Calcd. for C_7H_5NO: C, 70.58; H, 4.23; N, 11.76. Found: C, 70.53; H, 4.31; N, 11.55.

Reaction of 3-Bromofuropyridines **1a**, **1b**, **1c** and **1d** with Methyllithium.

General Procedure.

A solution of 3-bromo compound **1** (198 mg, 1 mmole) in 10 ml of tetrahydrofuran was cooled at −75° and stirred under a nitrogen atmosphere. To this solution was added a solution of methyllithium-lithium bromide complex in ether (2 ml, 1.5*M*, 3 mmoles) dropwise by syringe over a period of 10 minutes. After stirring at this temperature for 3 hours, the mixture was treated with 5 ml of water, and evaporated the solvent under reduced pressure at room temperature.

In the case of **1a** and **1b**, the residue was acidified with 10% hydrochloric acid, then basified with sodium bicarbonate, extracted with chloroform several times, and the extract dried (magnesium sulfate). Residue of the chloroform solution was treated with ether to give ether-soluble oil of **2a** (43 mg, 36%) and **2b** (39 mg, 33%) and the insoluble crystals of **3a** (67 mg, 56%) and **3b** 71 mg, 60%). The structure of these products were confirmed by comparison of the ir and pmr spectra with those of the samples obtained by the procedure described above.

In the case of **1c** and **1d**, the alkaline residue was diluted with 10 ml of water and extracted with chloroform to give compound **2c** (12 mg, 10%) and **2d** (15 mg, 13%) which were identified by comparison of the ir and pmr spectra with those of the authentic samples. The aqueous layer after chloroform extraction was passed through a column of Amberlite IRA-47, and the eluate evaporated to dryness under reduced pressure. The residual solid mass was extraced with hot chloroform several times to give compound **3c** (95 mg, 80%) and **3d** (100 mg, 84%). The ir and pmr spectra of these compounds were identical with those of the samples obtained by the procedure described above.

Reaction of 3-Bromofuropyridines **1a, 1b, 1c** and **1d** with *n*-Butyllithium and *N,N*-Dimethylformamide.

General Procedure.

A solution of compound **1** (198 mg, 1 mmole) in 5 ml of dry tetrahydrofuran was stirred under a nitrogen atmosphere and maintained at −75° while a solution of *n*-butyllithium in hexane (2 ml, 1.6*M*, 3.2 mmoles) was added dropwise by syringe over a period of 10 minutes. After stirring at this temperature for 30 minutes, the mixture was treated with *N,N*-dimethylformamide (150 mg, 2 mmoles). The reaction mixture was stirred at −75° for 1 hour, at −30° for 1 hour and at 0° for 1 hour. Then, the mixture was treated with 1 ml of water, evaporated the tetrahydrofuran under reduced pressure, diluted with 10 ml of water and extracted with ether. After drying (magnesium sulfate), the solvent was evaporated to give crude **4a, 4b, 4c** and **4d** which were purified by distillation or recrystallization.

2-(2-Formyl-1-pentenyl)furo[2,3-*b*]pyridine (**4a**).

This compound was purified by distillation under reduced pressure, bp 140-150° (bath temperature) (0.03 mm Hg) (mp 72.5-73°); ir (potassium bromide): 3090, 3040, 2940, 2910, 2850, 2810, 2750, 2710, 1660, 1620, 1580 cm^{-1}; pmr (deuteriochloroform): δ 9.48 (s, 1H, -C*H*O), 8.32 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.92 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.20 (dd, J = 4.8, 7.6 Hz, 1H, H-5), 6.98 (s, 2H, H-3 and -C*H*=C-), 2.79 (t, J = 7.0 Hz, 2H, =C-C*H*$_2$-C_2H_5), 1.57 (m, 2H, -CH_2-C*H*$_2$-CH_3), 1.01 (t, J = 6.2 Hz, 3H, -CH_2-CH_2-C*H*$_3$).

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.25; H, 6.02; N, 6.40.

2-(2-Formyl-1-pentenyl)furo[3,2-*b*]pyridine (**4b**).

This compound was recrystallized from ether to give an analytical sample of mp 71-71.5°; ir (potassium bromide): 3070, 3010, 2950, 2860, 2830, 2750, 1665, 1620, 1540, 1400 cm^{-1}; pmr (deuteriochloroform): δ 9.49 (s, 1H, -C*H*O), 8.52 (dd, J = 1.2, 4.8 Hz, 1H, H-5), 7.73 (dd, J = 1.2, 8.8 Hz, 1H, H-7), 7.21 (dd, J = 4.8, 8.8 Hz, 1H, H-6), 7.19 (s, 1H, H-3), 7.03 (s, 1H, -C*H*=C-), 2.74 (t, J = 6.4 Hz, 2H, =C-C*H*$_2$-CH_2-CH_3), 1.56 (m, 2H, -CH_2-C*H*$_2$-CH_3), 1.01 (t, J = 6.0 Hz, -CH_2-CH_2-C*H*$_3$).

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.39; H, 5.95; N, 6.21.

2-(2-Formyl-1-pentenyl)furo[2,3-*c*]pyridine (**4c**).

An analytically pure sample of this compound was obtained by recrystallization from ether, mp 116-117°; ir (potassium bromide): 3150, 3050, 2950, 2870, 2820, 2760, 2710, 1675, 1620, 1595 cm^{-1}; pmr (deuteriochloroform): δ 9.53 (s, 1H, -C*H*O), 8.86 (d, J = 1.2 Hz, 1H, H-7), 8.41 (d, J = 7.2 Hz, 1H, H-5), 7.48 (dd, J = 1.2, 7.2 Hz, 1H, H-4), 7.04 (s, 1H, -C*H*=C-), 6.99 (s, 1H, H-3), 2.77 (t, J = 6.8 Hz, 2H, =C-C*H*$_2$-C_2H_5), 1.56 (m, 2H, -CH_2-C*H*$_2$-CH_3), 1.02 (t, J = 6.4 Hz, 3H, -CH_2-CH_2-C*H*$_3$).

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.53; H, 6.12; N, 6.36.

2-(2-Formyl-1-pentenyl)furo[3,2-*c*]pyridine (**4d**).

This compound was purified by distillation under reduced pressure, bp 150-155° (bath temperature) (0.05 mm Hg) (mp 75-76°); ir (potassium bromide): 3100, 3120, 2940, 2910, 2850, 2800, 2740, 2700, 1665, 1620, 1600, 1565 cm^{-1}; pmr (deuteriochloroform): δ 9.50 (s, 1H, -C*H*O), 8.92 (s, 1H, H-4), 8.49 (d, J = 5.6 Hz, 1H, H-6), 7.38 (d, J = 5.6 Hz, 1H, H-7), 7.04 (s, 1H, -C*H*=C-), 7.01 (s, 1H, H-3), 2.75 (t, J = 6.8 Hz, 2H, =C-C*H*$_2$-C_2H_5), 1.56 (m, 2H, -CH_2-C*H*$_2$-CH_3), 1.02 (t, J = 6.4 Hz, 3H, -CH_2-CH_2-C*H*$_3$).

Anal. Calcd. for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.79; H, 6.07; N, 6.32.

The aqueous layer after ether extraction, in the cases of **1a, 1b** and **1c**, was acidified with 10% hydrochloric acid and then neutralized with sodium bicarbonate, and extracted with chloroform several times. The residue of the dried (magnesium sulfate) chloroform solution was recrystallized from acetone or acetone-ether to give compound **3a** (71 mg, 60%) **3b** (42 mg, 35%) and **3c** (42 mg, 35%). The aqueous layer for **1d** after ether extraction was passed through a column of Amberlite IRA-47 (5 ml). Evaporation of the eluate under reduced pressure afforded 90 mg of a solid mass, from which **3d** (71 mg, 60%) was obtained. The structure of compounds **3a, 3b, 3c** and **3d** were confirmed by ir and pmr spectra.

Compounds **4a, 4b, 4c** and **4d** from Furopyridines **2a, 2b, 2c** and **2d**.

General Procedure.

A solution of furopyridine **1** (220 mg, 2 mmoles) in 5 ml of dry tetrahydrofuran was stirred under a nitrogen atmosphere and cooled at −75°. To this solution was added a solution of *n*-butyllithium in hexane (3.8 ml, 1.6*M*, 6 mmoles) dropwise by syringe over a period of 5 minutes, the mixture was stirred for 1 hour at this temperature, and then treated with *N,N*-dimethylformamide (1.0 g, 14 mmoles). After stirring for 1 hour at the temperature, the mixture was stirred 10 hours at room temperature. The mixture was treated with 20 ml of brine and extracted with ethyl acetate 5 times. After drying (magnesium sulfate), the solvent was

evaporated to give 350-450 mg of the crude product which was chromatographed on a silica gel (Merck silica gel 60, 20 g) column. The fraction eluted with hexane-ethyl acetate (1:1) afforded compound **4a** (267 mg, 62%), **4b** (142 mg, 33%), **4c** (228 mg, 53%) and **4d** (176 mg, 41%), respectively. The ir and pmr spectra were identical with those of the samples obtained by the procedure described above.

General Procedure for the Preparation of 2-Phenylthiofuropyridines **5a**, **5b**, **5c** and **5d** and 2-Phenylthiobenzofuran **5e**.

A solution of furopyridine **2** (630 mg, 5.3 mmoles) or benzofuran (625 mg, 5.3 mmoles) in 20 ml of dry tetrahydrofuran was stirred under a nitrogen atmosphere and cooled at −75°. To this solution was added a solution of *n*-butyllithium in hexane (4 ml, 1.6*M*, 6.4 mmoles) dropwise by syringe over a period of 5 minutes at −75°. After stirring at this temperature for 40-60 minutes, to this mixture was added a solution of diphenyl disulfide (1.3 g, 6 mmoles) in dry tetrahydrofuran (10 ml). The mixture was stirred for 2 hours at −75°, treated with 5 ml of water and extracted with chloroform. The residual syrup of the dried (magnesium sulfate) chloroform solution was chromatographed on a column of silica gel (100 g). The second fraction eluted with chloroform gave the 2-phenylthio compounds **5** which were purified by distillation under reduced pressure or recrystallization to give pure samples of **5a**, **5b**, **5c**, **5d** and **5e** in yield of 70%, 90%, 91%, 75% and 85%, respectively.

2-Phenylthiofuro[2,3-*b*]pyridine (**5a**).

This compound had bp 150° (bath temperature) (0.2 mm Hg), colorless oil; ir (liquid film): 3110, 3040, 3000, 2900, 1590, 1580, 1520, 1470, 1455, 1435, 1385, 1320, 1300, 1250, 1210, 1155, 1105 cm^{-1}; pmr (deuteriochloroform): δ 8.27 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.83 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.56-7.05 (m, 6H, H-5 and S-C_6H_5), 6.84 (s, 1H, H3).

Anal. Calcd. for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 68.90; H, 4.09; N, 6.11.

2-Phenylthiofuro[3,2-*b*]pyridine (**5b**).

This compound had bp 140-150° (bath temperature) (0.1 mm Hg), colorless syrup; ir (liquid film): 3120, 3040, 3000, 2920, 1600, 1580, 1560, 1520, 1470, 1435, 1400, 1255, 1205, 1145, 1110 cm^{-1}; pmr (deuteriochloroform): δ 8.47 (dd, J = 1.4, 4.6 Hz, 1H, H-5), 7.60 (ddd, J = 0.8, 1.4, 8.4 Hz, 1H, H-7), 7.45-7.25 (m, 5H, S-C_6H_5), 7.10 (dd, J = 4.6, 8.4 Hz, 1H, H-7), 7.05 (d, J = 0.8 Hz, 1H, H-3).

Anal. Calcd. for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 68.87; H, 4.19; N, 6.19.

2-Phenylthiofuro[2,3-*c*]pyridine (**5c**).

This compound had bp 140-150° (bath temperature) (0.05 mm Hg), mp 75-76.5°; ir (potassium bromide): 3090, 3050, 3000, 1600, 1580, 1560, 1510, 1470, 1440, 1420, 1260, 1230, 1180, 1160 cm^{-1}; pmr (deuteriochloroform): δ 8.70 (s, 1H, H-7), 8.33 (d, J = 5.2 Hz, 1H, H-5), 7.53-7.16 (m, 6H, H-4 and S-C_6H_5), 6.72 (s, 1H, H-3).

Anal. Calcd. for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 69.01; H, 4.05; N, 6.13.

2-Phenylthiofuro[3,2-*c*]pyridine (**5d**).

This compound had mp 69-70° (from ether); ir (potassium bromide): 3100, 3050, 3000, 1600, 1570, 1530, 1470, 1450, 1430, 1325, 1265, 1140 cm^{-1}; pmr (deuteriochloroform): δ 8.84 (s, 1H, H-4), 8.47 (d, J = 5.6 Hz, 1H, H-7), 7.50-7.15 (m, 6H, H-6 and S-C_6H_5), 6.98 (d, J = 1.2 Hz, 1H, H-3).

Anal. Calcd. for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 69.03; H, 4.03; N, 6.20.

2-Phenylthiobenzofuran (**5e**).

This compound had bp 115° (bath temperature) (0.05 mm Hg), mp 54-55° (from hexane); ir (potassium bromide): 3030, 1565, 1520, 1460, 1430, 1410, 1290, 1240, 1220, 1150, 1135, 1100 cm^{-1}; pmr (deuteriochloroform): δ 7.60-7.12 (m, 9H, H-4,5,6,7 and S-C_6H_5), 6.97 (s, 1H, H-3).

Anal. Calcd. for $C_{14}H_{10}OS$: C, 74.31; H, 4.45. Found: C, 74.63; H, 4.49.

General Procedure for the Preparation of 2-Phenylthio-3-bromofuropyridines **6a**, **6b**, **6c** and **6d**.

A solution of bromine (600 mg, 3.8 mmoles) in dichloromethane was added dropwise to a solution of 2-phenylthio derivative **5** (710 mg, 3.1 mmoles) in dichloromethane (50 ml) at −15° with stirring. After stirring at −15° for 2 hours and at room temperature for 1 hour, the solvent was evaporated under reduced pressure. The residual light brown syrup was dissolved in methanol (30 ml), treated with 6 ml of 10% sodium hydroxide solution and stirred for 30 minutes at room temperature. After evaporation of the methanol, the residue was treated with chloroform and water. The chloroform layer was dried (magnesium sulfate) and evaporated the solvent to give the crude 2-phenylthio-3-bromo compounds **6** which were purified by distillation or recrystallization to give pure sample of **6a**, **6b**, **6c** and **6d** in yield of 95%, 90%, 87% and 74%, respectively.

2-Phenylthio-3-bromofuro[2,3-*b*]pyridine (**6a**).

This compound had bp 140-150° (bath temperature) (0.05 mm Hg), mp 52-52.5°; ir (potassium bromide): 3050, 1585, 1470, 1440, 1390, 1380, 1320, 1260, 1070, 990 cm^{-1}; pmr (deuteriochloroform): δ 8.33 (dd, J = 1.6, 4.8 Hz, 1H, H-6), 7.80 (dd, J = 1.6, 7.6 Hz, 1H, H-4), 7.50-7.10 (m, 6H, H-5 and S-C_6H_5).

Anal. Calcd. for $C_{13}H_8NOSBr$: C, 51.00; H, 2.63; N, 4.57. Found: C, 50.65; H, 2.73; N, 4.48.

2-Phenylthio-3-bromofuro[3,2-*b*]pyridine (**6b**).

This compound had bp 150-160° (bath temperature) (0.05 mm Hg); ir (liquid film): 3050, 1590, 1570, 1515, 1470, 1430, 1400, 1330, 1280, 1255, 1200, 1110, 1065, 1015, 1000, 995 cm^{-1}; pmr (deuteriochloroform): δ 8.55 (dd, J = 1.2, 4.4 Hz, 1H, H-5), 7.60 (dd, J = 1.6, 8.2 Hz, 1H, H-7), 7.43-7.08 (m, 6H, H-6 and S-C_6H_5).

Anal. Calcd. for $C_{13}H_8NOSBr$: C, 51.00; H, 2.63; N, 4.57. Found: C, 51.11; H, 2.94; N, 4.64.

2-Phenylthio-3-bromofuro[2,3-*c*]pyridine (**6c**).

This compound had bp 160-170° (bath temperature) (0.05 mm Hg); ir (liquid film): 3070, 3030, 1600, 1580, 1515, 1495, 1465, 1445, 1420, 1330, 1280, 1225, 1175, 1100, 1080, 1035, 1005, 900 cm^{-1}; pmr (deuteriochloroform): δ 8.78 (d, J = 0.8 Hz, 1H, H-7), 8.50 (d, J = 5.4 Hz, 1H, H-5), 7.57-7.20 (m, 6H, H-4 and S-C_6H_5).

Anal. Calcd. for $C_{13}H_8NOSBr$: C, 51.00; H, 2.63; N, 4.57. Found: C, 50.73; H, 2.79; N, 4.51.

2-Phenylthio-3-bromofur[3,2-*c*]pyridine (**6d**).

This compound had mp 82-83° (from hexane); ir (potassium bromide): 3050, 1600, 1575, 1530, 1480, 1440, 1315, 1270, 1230, 1170, 1155, 1085, 1070, 1020, 990 cm^{-1}; pmr (deuteriochloroform): δ 8.83 (d, J = 0.8 Hz, 1H, H-4), 8.57 (d, J = 5.8 Hz, 1H,

H-6), 7.50-7.17 (m, 6H, H-6 and S-C_6H_5).

Anal. Calcd. for $C_{13}H_8NOSBr$: C, 51.00; H, 2.63; N, 4.57. Found: C, 51.30; H, 2.87; N, 4.51.

Reaction of 2-Phenylthio-3-bromofuropyridines **6a**, **6b**, **6c** and **6d** with *t*-Butyllithium.

(A) With 1.2 Equivalent Moles.

General Procedure.

To a solution of 2-phenylthio-3-bromo compound **6** (506 mg, 1.65 mmoles) in 15 ml of tetrahydrofuran was added a solution of *t*-butyllithium in pentane (1.2 ml, 1.7*M*, 2 mmoles) by syringe under a nitrogen atmosphere and with cooling at −75° and stirring. After stirring for another hour at this temperature, the mixture was treated with 20 ml of water, acidified with 10% hydrochloric acid, basified with sodium bicarbonate, in the cases of **6a**, **6b** and **6c**, and extracted with chloroform. Evaporation of the dried (magnesium sulfate) chloroform solution yielded crude *o*-(phenylthioethynyl)pyridinols **7a**, **7b** and **7c**. Further processing of the crude product is indicated in subsequent paragraph. When the reaction mixture of **6d** was treated with water, a colorless solid mass was precipitated which was insoluble in common organic solvent and water, and showed no definite melting point.

3-(Phenylthioethynyl)-2-pyridinol (**7a**).

The crude product was recrystallized from ethyl acetate-hexane to give 356 mg (95%) of pure **7a**, mp 111-113°; ir (potassium bromide): 3150-2400 (broad), 2980, 2150, 1640, 1610, 1580, 1570, 1545, 1475, 1435, 1360, 1315, 1305, 1250 cm^{-1}; pmr (deuteriochloroform): δ 13.50 (broad s, 1H, -N*H*-CO-), 7.67 (dd, J = 2.2, 6.6 Hz, 1H, H-6), 7.55-7.13 (m, 6H, H-4 and S-C_6H_5), 6.27 (t, J = 6.6 Hz, 1H, H-5).

Anal. Calcd. for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 69.00; H, 4.14; N, 6.14.

2-(Phenylthioethynyl)-3-pyridinol (**7b**).

The crude product was recrystallized from methanol-acetone to afford 337 mg (90%) of **7b**, mp 112-114°; ir (potassium bromide): 3050, 3000-2250 (broad), 2150, 1950-1650 (broad), 1560, 1475, 1460, 1450, 1440, 1355, 1300, 1270, 1245 cm^{-1}; pmr (deuteriomethanol): δ 7.98 (dd, J = 2.4, 3.4 Hz, 1H, H-6), 7.70-7.20 (m, 7H, H-4,5 and S-C_6H_5).

Anal. Calcd. for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16. Found: C, 68.95; H, 4.14; N, 6.10.

4-(Phenylthioethynyl)-3-pyridinol (**7c**).

The oily crude product (610 mg) was chromatographed on a column of silica gel (70 g). The fraction eluted with chloroform-methanol (100:3) gave 312 mg (83%) of **7c** as a pale yellow oil which could not be purified for analytical sample, because this compound did not solidify and converted to compound **5c** by heating above 90°; ir (liquid film): 3100-2300 (broad), 3070, 2160, 1950-1700 (broad), 1600, 1585, 1560, 1480, 1440, 1420, 1305, 1265, 1225, 1205 cm^{-1}; pmr (deuteriochloroform): δ 10.67 (s, 1H, O*H*), 8.27 (s, 1H, H-2), 8.00 (d, J = 4.8 Hz, 1H, H-6), 7.62-7.10 (m, 6H, H-5 and S-C_6H_5).

(B) With 3 Equivalent Moles.

General Procedure.

A solution of 2-phenylthio-3-bromo compound **6** (430 mg, 1.4 mmoles) in 20 ml of tetrahydrofuran was stirred under a nitrogen atmosphere and cooled at −75°. To this solution was added a solution of *t*-butyllithium in pentane (2.5 ml, 1.7*M*, 4.2 mmoles) by syringe over a period of 10 minutes at −75°. After stirring at this temperature for 3 hours for **6b**, **6c** and **6d**, and 18 hours for **6a**, the mixture was treated with 10 ml of water, acidified with 10 hydrochloric acid, basified with sodium bicarbonate and extracted with chloroform.

Further processing of the residue of the dried (magnesium sulfate) chloroform solution is indicated in subsequent paragraph. Again, in the case of **6d**, only a colorless resinous solid was obtained which could not be processed further.

3-(3,3-Dimethyl-1-butynyl)-2-pyridinol (**8a**) and 3-(2-Phenylthio-3,3-dimethyl-1-butenyl)-2-pyridinol (**9a**).

The crude product (360 mg) was chromatographed on a silica gel (50 g) column. The first fraction eluted with hexane-ethyl acetate (6:4) yielded 148 mg (36%) of **9a** and the second fraction 73 mg (30%) of **8a**.

Compound **8a**.

This compound had mp 210-210° (in a sealed capillary) (from acetone); ir (potassium bromide): 3270, 3130, 3070, 2950, 2900, 2850, 3100-2400 (broad), 2200, 1620, 1605, 1545, 1380, 1360, 1325, 1290, 1260, 1230, 1210, 1180 cm^{-1}; pmr (deuteriochloroform): δ 13.35 (broad s, 1H, -N*H*-CO), 7.56 (dd, J = 2.0, 6.8 Hz, 1H, H-6), 7.38 (dd, J = 2.0,6.8 Hz, 1H, H-4), 6.20 (t, J = 6.8 Hz, 1H, H-5), 1.35 (s, 9H, -C(CH_3)$_3$).

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.70; H, 7.41; N, 7.98.

Compound **9a**.

This compound had mp 152-154° (from ethyl acetate); ir (potassium bromide): 3270, 3200-2500 (broad), 3130, 3060, 3000, 2960, 2910, 2860, 2830, 2770, 1635, 1620, 1580, 1555, 1480, 1460, 1440, 1390, 1360, 1330, 1310, 1250, 1220, 1165 cm^{-1}; pmr (deuteriochloroform): δ 12.90 (broad s, 1H, -NH-CO), 7.48-7.05 (m, 7H, H-4,6 and S-C_6H_5), 6.14 (t, J = 6.4 Hz, 1H, H-5), 6.05 (s, 1H, -C*H*=C-), 1.35 (s, 9H, -C(CH_3)$_3$).

Anal. Calcd. for $C_{17}H_{19}NOS$: C, 71.54; H, 6.71; N, 4.91. Found: C, 71.59; H, 6.73; N, 4.76.

2-(3,3-Dimethyl-1-butynyl)-3-pyridinol (**8b**).

The crude residue (360 mg) was chromatographed on a column of silica gel (50 g). The second fraction eluted with hexane-ethyl acetate (5:1) gave 197 mg (80%) of **8b** which was recrystallized from methanol-acetone to give analytically pure sample of mp 180-182°; ir (potassium bromide): 3060, 3000-2100 (broad), 1970, 2930, 2900, 2860, 2210, 1600, 1530, 1485, 1470, 1410, 1390, 1360, 1350, 1290, 1270, 1220, 1200, 1140 cm^{-1}; pmr (deuteriomethanol): δ 7.86 (dd, J = 2.4,3.6 Hz, 1H, H-6), 7.18 (dd, J = 2.4,8.0 Hz, 1H, H-4), 7.10 (dd, J = 3.6,8.0, 1H, H-5), 1.35 (s, 9H, -C(CH_3)$_3$).

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.41; H, 7.54; N, 7.85.

4-(3,3-Dimethyl-1-butynyl)-3-pyridinol (**8c**).

The crude residue (540 mg) was chromatographed on a column of silica gel (70 g). The second fraction eluted with chloroform-

methanol (100:2) yielded 214 mg (87%) of **8c** which was purified for analytical sample by recrystallization from acetone, mp 130-133; ir (potassium bromide): 3060, 3000-2100 (broad), 2970, 2930, 2900, 2860, 2210, 1600, 1530, 1485, 1470, 1410, 1360, 1350, 1290, 1270, 1220, 1200, 1140 cm^{-1}; pmr (deuteriochloroform): δ 9.20 (s, 1H, O*H*), 8.23 (s, 1H, H-2), 8.01 (d, J = 4.8 Hz, 1H, H-6), 7.20 (d, J = 4.8 Hz, 1H, H-5), 1.30 (s, 9H, $-C(CH_3)_3$).

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.61; H, 7.48; N, 7.84.

Reaction of 2-Phenylthio-3-bromofuropyridines **6a**, **6b**, **6c** and **6d** with Methyllithium.

General Procedure.

A solution of compound **6** (460 mg, 1.5 mmoles) in 10 ml of tetrahydrofuran was stirred under a nitrogen atmosphere and maintained at $-75°$ while a solution of methyllithium-lithium bromide complex in ether (3 ml, 1.5*M*, 4.5 mmoles) was added dropwise by syringe over a period of 10 minutes. After stirring at this temperature for 5 hours, the mixture was treated with 5 ml of water, acidified with 10% hydrochloric acid, basified with sodium bicarbonate and extracted with chloroform several times for the case of **6a**, **6b** and **6c**.

Further processing of the residue of the dried (magnesium sulfate) chloroform extract is described in following paragraph. In the case of **6d**, colorless crystalline precipitates formed were filtered.

Compound **7a**.

The crystalline residue (400 mg) was recrystallized from ethyl acetate to give 306 mg (90%) of **7a** which was identified by ir and pmr spectra.

Compound **7b**.

The crude residue (360 mg) was recrystallized from methanol-acetone to give 334 mg (98%) of **7b** which was identified by ir and nmr spectra.

Compound **7c**.

The crude residue (365 mg) was chromatographed on a silica gel column (40 g). The fraction eluted with chloroform-methanol (99:1) gave compound **5c** (153 mg, 45%) and the fraction eluted with chloroform-methanol (97:3) gave **7c** (154 mg, 45%) which were identified by ir and pmr spectra.

3-(2-Phenylthioethynyl)-4-pyridinol (**7d**).

The crude crystalline solid (356 mg) was recrystallized from methanol-acetone to give pure sample (333 mg, 98%) of mp 112-114°; ir (potassium bromide): 3350, 3070, 3020, 2970, 2900, 2850-2400 (broad), 1630, 1620, 1600, 1575, 1540, 1525, 1490, 1475, 1455, 1440, 1410, 1290, 1185, 1145 cm^{-1}; pmr (deuteriomethanol): δ 8.00 (d, J = 1.6 Hz, 1H, H-2), 7.70 (dd, J = 1.6,7.0 Hz, 1H, H-6), 7.57-7.13 (m, 5H, $S-C_6H_5$).

Anal. Calcd. for $C_{13}H_9NOS \cdot \frac{1}{2}H_2O$: C, 66.08; H, 4.27; N, 5.93. Found: C, 66.07; H, 4.31; N, 5.93.

Reaction of 2-Phenylthio-3-bromofuropyridines **6a**, **6b**, **6c** and **6d** with Lithioacetonitrile.

General Procedure.

To a stirred solution of acetonitrile (160 mg, 3.8 mmoles) in tetrahydrofuran (10 ml) was added a solution of *n*-butyllithium in hexane (2.0 ml, 1.6*M*, 3.4 mmoles) dropwise by syringe at $-75°$ under a nitrogen atmosphere. After stirring at this temperature for 1 hour, a solution of compound **6** (236 mg, 0.77 moles) in tetrahydrofuran (5 ml) was added and stirred for 3 hours at $-75°$. The mixture was treated with 15 ml of water, extracted with chloroform and dried (magnesium sulfate). Evaporation of the solvent afforded a viscous syrup. The residue for **6a** and **6d** showed linked spots in the thin-layer chromatogram on silica gel, and any single product could not be isolated from the syrup. The residue for **6b** was chromatographed on a column of silica gel eluting with hexaneethyl acetate (2:1) to give compounds **10b** and **11b** in 53% and 14% yields. The residue for **6c** was chromatographed on a column of silica gel eluting with chloroform-methanol (98:2) to give compounds **10c** (60%) and **11c** (23%).

2-Cyanomethyl-3-bromofuro[3,2-*b*]pyridine (**10b**).

Recrystallization of the crude sample from ether gave an analytical sample of mp 144-146°; ir (potassium bromide): 3070, 2950, 2890, 2770, 2240, 1590, 1570, 1560, 1470, 1405, 1350, 1330, 1280, 1265, 1245, 1215, 1200, 1155 cm^{-1}; pmr (deuteriochloroform): δ 8.62 (dd, J = 1.4,4.8 Hz, 1H, H-5), 7.77 (dd, J = 1.4,8.4 Hz, 1H, H-7), 7.30 (dd, J = 4.8,8.4 Hz, 1H, H-6), 4.01 (s, 2H, $-CH_2CN$).

Anal. Calcd. for $C_9H_5N_2OBr$; C, 45.60; H, 2.13; N, 11.82. Found: C, 45.93; H, 2.27; N, 11.73.

2-Cyanomethylfuro[3,2-*b*]pyridine (**11b**).

Recrystallization of the crude sample from ether yielded an analytically pure sample, mp 102-103°; ir (potassium bromide): 3110, 3060, 2930, 2870, 2790, 2250, 1605, 1560, 1475, 1410, 1350, 1315, 1260, 1245, 1205, 1190, 1165, 1135 cm^{-1}; pmr (deuteriochloroform): δ 8.53 (dd, J = 1.2,4.8 Hz, 1H, H-5), 7.75 (ddd, J = 0.8,1.2,8.4 Hz, 1H, H-7), 7.22 (dd, J = 4.8,8.4 Hz, 1H, H-6), 6.96 (q, J = 0.8 Hz, 1H, H-3), 3.97 (d, J = 0.8 Hz, 2H, $-CH_2CN$).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.70; H, 3.98; N, 17.64.

2-Cyanomethyl-3-bromofuro[2,3-*c*]pyridine (**10c**).

Analytically pure sample was obtained by recrystallization of the crude sample from ether, mp 112-115°; ir (potassium bromide): 3070, 3040, 2930, 2890, 2250, 1600, 1590, 1465, 1420, 1390, 1335, 1290, 1260, 1185, 1155 cm^{-1}; pmr (deuteriochloroform): δ 8.90 (d, J = 1.0 Hz, 1H, H-7), 8.56 (d, J = 5.2 Hz, 1H, H-5), 7.47 (dd, J = 1.0,5.2 Hz, 1H, H-4), 4.02 (s, 2H, $-CH_2CN$).

Anal. Calcd. for $C_9H_5N_2OBr$: C, 45.60; H, 2.13; N, 11.82. Found: C, 45.93; H, 2.27; N, 11.73.

2-Cyanomethylfuro[2,3-*c*]pyridine (**11c**).

This compound was purified by recrystallization from ether to give an analytically pure sample of mp 111-113°; ir (potassium bromide): 3120, 3050, 2940, 2880, 2800, 2250, 1600, 1465, 1430, 1405, 1340, 1310, 1260, 1200, 1185, 1150 cm^{-1}; pmr (deuteriochloroform): δ 8.83 (d, J = 0.8 Hz, 1H, H-7), 8.45 (d, J = 5.0 Hz, 1H, H-5), 7.52 (dd, J = 0.8,5.0 Hz, 1H, H-4), 6.82 (t, J = 0.8 Hz, 1H, H-3), 3.98 (d, J = 0.8 Hz, 2H, $-CH_2CN$).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.46; H, 3.92; N, 17.63.

Reaction of 2-Phenylthiofuropyridines **5a**, **5b**, **5c** and **5d** with Methyllithium.

General Procedure.

A solution of 2-phenylthio derivative **5** (250 mg, 1.1 mmoles) in 10 ml of dry tetrahydrofuran was stirred under a nitrogen atmos-

phere and maintained at −75° while a solution of methyllithium-lithium bromide complex in ether (2.2 ml, 1.5*M*, 3.3 mmoles) was added by syringe over a period of 10 minutes. After stirring for 17 hours for **5a** and **5c**, and 5 hours for **5b** and **5d**, the reaction mixture was treated with 10 ml of water, acidified with hydrochloric acid, basified with sodium bicarbonate. The crystalline precipitate from **5d** was filtered and recrystallized from methanol to give 225 mg (90%) of **7d**, which was identified by ir and pmr spectra. The reaction mixture from **5a, 5b** and **5c** was extracted with chloroform, dried (magnesium sulfate) and evaporated the solvent. Further processing of the residue is indicated in subsequent paragraph.

Compound **7a**.

The residue of the chloroform extract for **5a** was chromatographed on a silica gel (25 g) column. The first fraction eluted with hexane-ethyl acetate (3:1) gave 150 mg (60%) of **5a** and the second fraction 93 mg (37%) of **7a**, which were identified by ir and pmr spectra.

Compound **7b**.

The crystalline residue of the chloroform extract from **5b** was recrystallized from methanol-acetone to give 247 mg (99%) of pure sample of **7b** which was identified by ir and pmr spectra.

Compound **7c**.

The syrupy residue from **5c** was chromatographed on a column of silica gel (50 g). The first fraction eluted with chloroform-methanol (97:3) gave 50 mg (20%) of **5c** and the second fraction 175 mg (70%) of **7c**, which were identified by ir and pmr spectra.

Recyclization of *o*-(2-Phenylthioethynyl)pyridinols **7a, 7b, 7c** and **7d** to 2-Phenylthiofuropyridines **5a, 5b, 5c** and **5d**.

General Procedure.

A sample of **7** (114 mg, 0.5 mmoles) in a glass tube was heated at 90-110° for 30 minutes under a nitrogen atmosphere. The completely melted product was distilled under reduced pressure to afford compounds **5a, 5b, 5c** and **5d** in almost quantitative yield respectively. The structures of these compounds were identified by comparison of the ir and pmr spectra with those of the samples obtained by the procedure described above.

Reaction of 2-Phenylthiofuropyridines **5a, 5b, 5c** and **5d** and 2-Phenylthiobenzofuran **5e** with Lithioacetonitrile at −75°.

General Procedure.

To a stirred solution of acetonitrile (188 mg, 4.6 mmoles) in tetrahydrofuran (10 ml) was added a solution of *n*-butyllithium in hexane (2.5 ml, 1.6*M*, 4 mmoles) by syringe at −75° under a nitrogen atmosphere. After stirring 1 hour at this temperature, a solution of compound **5** (193 mg, 0.85 mmole) in tetrahydrofuran (5 ml) was added by syringe and stirred for 3 hours at −75°. The mixture was treated with 15 ml of water and extracted with chloroform. The chloroform extract was dried (magnesium sulfate) and evaporated to give a yellow to light brown syrup. The syrupy residue from **5b** and **5c** was chromatographed on a column of silica gel (30 g). The fraction eluted with chloroform-methanol (98:2) yielded **11b** (121 mg, 90%) and **11c** (114 mg, 86%), respectively. The structures of these compounds were identified by ir and pmr spectra. While, the residues from **5a, 5d** and **5e** were distilled under reduced pressure to recover the starting material in 95%, 99% and 95%, respectively, which were identified by ir and pmr spectra.

Reaction of 2-Phenylthio Compounds **5a, 5d** and **5e** with Lithioacetonitrile at −20°.

General Procedure.

To a solution of acetonitrile (156 mg, 3.8 mmoles) in tetrahydrofuran (10 ml) was added a solution of *n*-butyllithium in hexane (2.0 ml, 1.6*M*, 3.2 mmoles) dropwise by syringe at −75° under a nitrogen atmosphere with stirring. After stirring at this temperature for 1 hour, a solution of compounds **5** (160 mg, 0.7 mmole) in tetrahydrofuran (5 ml) was added, and the mixture was stirred at −75° for 1 hour and at −20° for 2 hours. The reaction mixture was treated with 15 ml of water and extracted with chloroform. The residue of the dried (magnesium sulfate) chloroform extract from **5a** and **5d** was chromatographed on a column of silica gel (20 g). The fraction eluted with chloroform-methanol (99:1) gave **11a** (41 mg, 37%) and **11d** (57 mg, 54%), respectively. The residue of the chloroform extract from **5e** was distilled under reduced pressure to give 145 mg (90%) of the starting material **5e** which was identified by ir and pmr spectra.

2-Cyanomethylfuro[2,3-*b*]pyridine (**11a**).

Recrystallization from ether gave an analytically pure sample, mp 89-90°; ir (potassium bromide): 3070, 2920, 2870, 2210, 1590, 1575, 1460, 1395, 1315, 1270, 1235, 1190, 1160, 1120, 1100 cm^{-1}; pmr (deuteriochloroform): δ 8.32 (dd, J = 1.6,4.8 Hz, 1H, H-6), 7.92 (dd, J = 1.6,7.8 Hz, 1H, H-4), 7.22 (dd, J = 4.8,7.8 Hz, 1H, H-5), 6.76 (t, J = 1.2 Hz, 1H, H-3), 3.93 (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, 68.43; H, 3.96; N, 17.52.

2-Cyanomethylfuro[3,2-*c*]pyridine (**11d**).

An analytically pure sample was obtained by recrystallization from ether, mp 61-62°; ir (potassium bromide): 3100, 3000, 2930, 2870, 2210, 1590, 1565, 1550, 1450, 1420, 1395, 1320, 1290, 1275, 1250, 1195, 1170, 1145, 1110 cm^{-1}; pmr (deuteriochloroform): δ 8.87 (d, J = 0.8 Hz, 1H, H-4), 8.50 (d, J = 5.6 Hz, 1H, H-6), 7.40 (dt, J = 0.8,5.6 Hz, 1H, H-7), 6.82 (q, J = 0.8 Hz, 1H, H-3), 3.93 (d, J = 0.8 Hz, 2H, $-CH_2CN$).

Anal. Calcd. for $C_9H_6N_2O$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.53; H, 3.91; N, 17.60.

Reaction of 2-(Phenylthioethynyl)-3-pyridinol (**7b**) with *t*-Butyllithium.

A solution of compound **7b** (147 mg, 0.65 mmole) in 15 ml of tetrahydrofuran was stirred under a nitrogen atmosphere and cooled at −75°. To this solution was added a solution of *t*-butyllithium in pentane (1.2 ml, 1.7*M*, 2.0 mmoles) dropwise by syringe over a period of 5 minutes. After stirring for 3 hours at this temperature, the mixture was treated with 15 ml of water, acidified with hydrochloric acid, neutralized with sodium bicarbonate and extracted with chloroform. The residue of the chloroform extract was treated with ether to leave 100 mg of ether-insoluble crystalline solid. Recrystallization of the solid from methanol-acetone gave 90 mg (80%) of compound **8b**, which was identified by ir and pmr spectra.

3-(3,3-Dimethyl-1-butynyl)-4-pyridinol (**8d**) and 3-(2-Phenylthio-3,3-dimethyl-1-butenyl)-4-pyridinol (**9d**) from 2-Phenylthiofuro-[3,2-*c*]pyridine (**5d**).

A solution of compound **5d** (187 mg, 0.82 mmole) in 10 ml of tetrahydrofuran was stirred under a nitrogen atmosphere and cooled at −75°. To this solution was added a solution of methyllithium-lithium bromide complex in ether (1.65 ml, 1.5*M*, 2.5 mmoles) dropwise by syringe. After stirring for 3 hours at this temperature, to this mixture was added a solution of *t*-butyllithium in pentane (1.5 ml, 1.7*M*, 2.6 mmoles) by syringe and stirred for 2 hours at −75°. The mixture was treated with 10 ml of water, evaporated the solvent under reduced pressure, acidified with hydrochloric acid, basified with sodium bicarbonate, and extracted with chloroform. The residue of the dried (magnesium sulfate) chloroform solution was chromatographed on a silica gel (25 g) column. The first fraction eluted with chloroform-methanol (100:7) gave 120 mg (51%) of **9d**, and the second fraction 42 mg (29%) of **8d**, which were identified by ir and pmr spectra.

3-(2,2-Dimethyl-1-butynyl)-4-pyridinol (**8d**).

This compound was purified by recrystallization from methanol-acetone, mp 179-180°; ir (potassium bromide): 3250, 3050, 2980, 2930, 2880, 3000-2200 (broad), 2220, 1630, 1545, 1530, 1510, 1500, 1480, 1460, 1400, 1350, 1300, 1280, 1235, 1165, 1130 cm^{-1}; pmr (deuteriochloroform): δ 7.90 (d, J = 1.4 Hz, 1H, H-2), 7.62 (dd, J = 1.4, 6.8 Hz, 1H, H-6), 6.45 (d, J = 6.8 Hz, 1H, H-5), 1.18 (s, 9H, $-C(CH_3)_3$).

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48; N, 7.99. Found: C, 75.44; H, 7.71; N, 7.87.

3-(2-Phenylthio-3,3-dimethyl-1-butenyl)-4-pyridinol (**9d**).

Recrystallization from acetone gave analytically pure sample, mp 201-202°; ir (potassium bromide): 3170, 3080, 2950, 2860, 2850-2300 (broad), 1620, 1580, 1545, 1480, 1390, 1360, 1315, 1265, 1220, 1165, 1125 cm^{-1}; pmr (deuteriochloroform): δ 7.53 (d, J = 6.6 Hz, 1H, H-6), 7.47 (s, 1H, H-2), 7.28-7.02 (m, 5H, $-C_6H_5$), 6.01 (s, 1H, $-CH=C=$), 1.27 (s, 9H, $-C(CH_3)_3$).

Anal. Calcd. for $C_{17}H_{19}NOS$: C, 71.54; H, 6.71; N, 4.91. Found: C, 71.67; H, 6.94; N, 4.85.

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