

**Furopyridines. X [1].**  
**Synthesis of Tricyclic Heterocycles, Furo[2,3-*b*:4,5-*c'*]-,**  
**Furo[3,2-*b*:4,5-*c'*]-, Furo[2,3-*c*:4,5-*c'*]- and Furo[3,2-*c*:4,5-*c'*]-dipyridine**

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This paper describes the synthesis of four tricyclic heterocycles, furo[2,3-*b*:4,5-*c'*]- (**5a**), furo[3,2-*b*:4,5-*c'*]- (**5b**), furo[2,3-*c*:4,5-*c'*]- (**5c**) and furo[3,2-*c*:4,5-*c'*]-dipyridine (**5d**). Starting with 2-formylfuropyridines (**1a-d**),  $\beta$ -(2-furopyridyl)acrylic acids **2a-d** were obtained by condensing with malonic acid. The acrylic acids were converted to the acid azides by reaction with ethyl chloroformate and the subsequent reaction with sodium azide. Heating of the acid azides at 230-240° with diphenylmethane and tributylamine gave tricyclic pyridinones **3a-d**, which were converted to the respective chloro derivatives **4a-d** by reaction with phosphorus oxychloride. Reduction of the chloro compounds over palladium-charcoal yielded compounds **5a-d** respectively. All the compounds **2** to **5** were characterized by elemental analysis and spectral data. The <sup>1</sup>H and <sup>13</sup>C nmr and electronic spectral features of the furodipyridines were discussed comparing with those of the parent furopyridines.

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In continuation of our research work on the chemistry of furopyridines, several 2- and/or 3-substituted derivatives have been synthesized and during the course of this investigation, the availability of 2-formyl derivatives **1a-d** [2] prompted us to synthesize four tricyclic heterocycles, furo[2,3-*b*:4,5-*c'*]- (**5a**), furo[3,2-*b*:4,5-*c'*]- (**5b**), furo[2,3-*c*:4,5-*c'*]- (**5c**) and furo[3,2-*c*:4,5-*c'*]-dipyridine (**5d**), which are expected to be new skeletal moieties of biologically active compounds, from compounds **1a-d** by the method of Eloy and Deryckere [3]. Three of these furodipyridines, **5a-c**, are new and the last one **5d** had been synthesized by diazotization of [3,3'-bipyridine]4,4'-diamine by Kaczmarek [4].

The 2-formyl compounds **1a-d** were converted to  $\beta$ -(2-furopyridyl)acrylic acids **2a-d** by heating with malonic acid in pyridine. The acrylic acids were treated with ethyl

chloroformate and triethylamine in tetrahydrofuran, followed by reaction with sodium azide to give the corresponding acid azides. The azides were heated at 230-240° with diphenylmethane and tributylamine to afford furodipyridinones **3a-d** whose structures were established on the basis of <sup>1</sup>H nmr, ir, spectral and elemental analytical data. In the <sup>1</sup>H nmr spectra of compounds **3a-d**, the signals for proton of the furan ring (3-position) shown in the spectra of **2a-d** disappeared. The smaller values (6.8-7.2 Hz) of the coupling constant of the typical AB-quartet at 7.59 and 6.80 ppm for **3a**, 7.58 and 6.74 ppm for **3b**, 7.67 and 6.80 ppm for **3c** and 7.58 and 6.78 ppm for **3d** which are assignable to the protons at the 7- and 8-positions for **3a**, 7- and 6-positions for **3b**, and 3- and 4-positions for **3c** and **3d** respectively, compared with those (15.2-15.6 Hz) of the olefinic protons of the acrylic acids **2a-d**, also support the newly formed pyridone structures of compounds **3a-d**.

Scheme 1

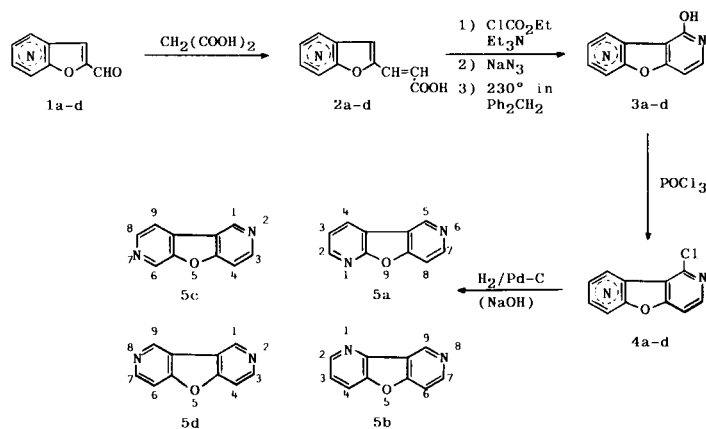


Table 1  
<sup>1</sup>H NMR Spectral Data of Furopyridines and Furodipyridines [a] [b] [c]

	H-2	H-3	H-4	H-5	H-6	–			
Furo[2,3- <i>b</i> ]pyridine	7.703 (d)	6.775 (d)	7.939 (dd)	7.222 (dd)	8.333 (ddd)				
	$J_{2,3} = 2.41$		$J_{4,5} = 7.67$		$J_{4,6} = 4.82$				
			$J_{4,6} = 1.76$						
<b>5a</b>	–	–	H-4	H-3	H-2	–	H-5	H-7	H-8
			8.332(dd)	7.400 (dd)	8.488(dd)		9.204 (d)	8.693 (d)	7.539 (dd)
			(0.393)	(0.178)	(0.155)		(0.266)	(0.203)	(0.119)
			$J_{4,2} = 1.75$		$J_{4,3} = 7.67$		$J_{5,8} = 0.88$		$J_{7,8} = 5.70$
			$J_{3,2} = 5.04$						
	H-2	H-3	–	H-5	H-6	H-7			
Furo[3,2- <i>b</i> ]pyridine	7.818 (d)	6.974 (dd)		8.540 (dd)	7.160 (dd)	7.715 (dt)			
	$J_{2,3} = 2.20$			$J_{5,6} = 4.82$		$J_{6,7} = 8.33$			
		$J_{3,7} = 1.10$		$J_{5,7} = 1.10$					
<b>5b</b>	–	–	–	H-2	H-3	H-4	H-9	H-7	H-6
				8.632 (dd)	7.383 (dd)	7.815 (dd)	9.439 (d)	8.706 (d)	7.490 (dd)
				(0.092)	(0.223)	(0.100)	(0.501)	(0.216)	(0.070)
				$J_{2,3} = 4.82$		$J_{3,4} = 8.33$		$J_{6,9} = 0.44$	
				$J_{2,4} = 1.09$					
	H-2	H-3	H-4	H-5	–	H-7			
Furo[2,3- <i>c</i> ]pyridine	7.715 (d)	6.759 (dd)	7.504 (dd)	8.410 (d)		8.886 (dd)			
	$J_{2,3} = 2.19$		$J_{4,5} = 0.88$						
				$J_{4,7} = 1.10$					
<b>5c</b>	–	–	H-9	H-8	–	H-6	H-1	H-3	H-4
			7.958 (dd)	8.690 (dd)		9.056 (dd)	9.346 (d)	8.792 (d)	7.606 (dd)
			(0.454)	(0.280)		(0.170)	(0.408)	(0.302)	(0.186)
			$J_{8,9} = 5.26$		$J_{6,8} = 0.44$		$J_{1,4} = 0.88$		$J_{3,4} = 5.92$
				$J_{6,9} = 1.10$					
	H-2	H-3	H-4	–	H-6	H-7			
Furo[3,2- <i>c</i> ]pyridine	7.625 (d)	6.819 (dd)	8.938 (d)		8.490 (d)	7.420 (ddd)			
	$J_{2,3} = 2.19$		$J_{4,7} = 0.88$		$J_{6,7} = 5.70$				
			$J_{3,7} = 1.09$						
<b>5d</b>	–	–	H-9		H-7	H-6	H-1	H-3	H-4
			(H-1)		(H-3)	9.345 (d)	9.345 (d)	8.743 (d)	7.580 (dd)
						(0.407)	(0.407)	(0.253)	(0.160)
						$J_{1,4} = 1.10$		$J_{2,4} = 5.90$	

[a] Spectra were taken in deuteriochloroform (ca. 15% solution) using JEOL FX 90Q instruments, and chemical shifts are presented in ppm from TMS as an internal standard and are given in units  $\delta$ , coupling constants (J) are in Hz. [b] The numerical data in the parentheses are differences between the chemical shifts of protons in furodipyridines and those of the corresponding protons in the parent furopyridines. [c] d: doublet, dd: double doublet, ddd: doublet of double doublet, dt: double triplet.

Table II  
<sup>13</sup>C NMR Spectral Data of Furopyridines and Furodipyridines [a] [b]

Furo[2,3- <i>b</i> ]pyridine	C-2	C-3	C-4	C-5	C-6	-	C-3a	C-7a			
	144.47	105.90	130.16	119.24	144.25	-	119.28	162.12			
<b>5a</b>	C-8a	C-4b	C-4	C-3	C-2	-	C-4a	C-9a	C-5	C-7	C-8
	159.22 (-0.07)	119.75 (-4.97)	130.22 (0.22)	120.11 (0.87)	147.51 (3.26)	-	114.19 (-5.09)	162.68 (0.56)	143.98 (-0.39)	148.47 (3.95)	107.61 (0.51)
Furo[3,3- <i>b</i> ]pyridine	C-2	C-3	-	C-5	C-6	C-7	C-3a [c]	C-7a [c]			
	148.76	108.19	-	145.98	118.82	118.09	147.61	147.69			
<b>5b</b>	C-5a	C-9a	-	C-2	C-3	C-4	C-9b	C-4a	C-9	C-7	C-6
	161.78 (2.56)	120.33 (-4.39)	-	146.30 (0.32)	122.16 (3.34)	118.82 (0.73)	141.88 (-5.73)	149.17 (1.48)	144.15 (-0.22)	148.95 (4.43)	107.73 (0.63)
Furo[2,3- <i>c</i> ]pyridine	C-2	C-3	C-4	C-5	-	C-7	C-3a	C-7a			
	147.93	105.97	116.02	142.42	-	133.98	133.74	152.24			
<b>5c</b>	C-4a	C-9b	C-9	C-8	-	C-6	C-9a	C-5a	C-1	C-3	C-4
	161.48 (2.19)	119.75 (-4.97)	115.48 (-0.54)	145.20 (2.78)	-	134.81 (0.83)	128.62 (-5.12)	152.41 (0.17)	144.20 (-0.17)	149.78 (5.26)	108.14 (1.04)
Furo[3,2- <i>c</i> ]pyridine	C-2	C-3	C-4	-	C-6	C-7	C-3a	C-7a			
	145.54	104.90	144.37	-	144.52	107.10	124.72	159.29			
<b>5d</b>	C-4a	C-9b	C-9	-	C-7	C-6	C-9a	C-5a	C-1	C-3	C-4
	160.75 (1.28)	119.09 (-4.82)	(C-1)	-	(C-3)	(C-4)	(C-9b)	(C-4a)	144.03 (-0.34)	148.61 (4.09)	107.68 (0.58)

[a] Spectra were taken in deuteriochloroform (*ca.* 15% solution) using JEOL FX 90Q instrument, and chemical shifts are presented in ppm from TMS as an internal standard and are given in units  $\delta$ . [b] The numerical data in the parentheses are differences between the chemical shifts of carbons in furodipyridines and those of the corresponding carbons in the parent furopyridines, the (-)-values indicate upfield shift. [c] Assignment may be interchanged.

Reaction of compounds **3a-d** with phosphorus oxychloride afforded the corresponding chloro derivatives **4a-d** of the furodipyridines. Catalytic reduction of the chloro derivatives **4a-d** over palladium charcoal in ethanol in the presence of sodium hydroxide [5] afforded furo[2,3-*b*:4,5-*c'*] (**5a**), furo[3,2-*b*:4,5-*c'*] (**5b**), furo[3,2-*c*:4,5-*c'*] (**5c**) and furo[3,2-*c*:4,5-*c'*]dipyridine (**5d**), respectively.

The <sup>1</sup>H nmr spectral data for these furodipyridines are presented in Table I [6]. All of the signals are clearly distinguishable and were easily assigned from their chemical

shift values, coupling patterns and constants comparing with those of the parent furopyridines. The signal of each proton appears at lower field than that of the corresponding proton in the parent furopyridine. This fact indicates the larger anisotropic effect by the ring-current of the tricyclic heteroaromatic than that in furopyridines. Signals for H-4 and H-5 of **5a**, H-9 of **5b**, and H-1 and H-9 of **5c** and **5d** fall especially far downfield because these protons occupy an angular position [7] in the phene-type structures. In compound **5b**, the H-9 proton shows an anisotropic effect by the lone pair electrons of the nitrogen atom at the 1-position [7].

The <sup>13</sup>C chemical shifts of the four furodipyridines and the parent furopyridines are listed in Table II [6]. The assignments of the carbon resonances were based on chemical shift correlations, and data reported for alkoxy derivatives of pyridine and furan derivatives [8]. The assignments of the chemical shifts of the hydrogen-bonded carbons were confirmed using the selected C-[H] spin decoupling method [9]. Overviewing the Table II, the signals of

Table III

Ionization Constants of Furodipyridines

Compounds	pKa <sub>1</sub> /20°	pKa <sub>2</sub> /20°
<b>5a</b>	4.75	-1.0
<b>5b</b>	4.60	0.1
<b>5c</b>	4.65	2.10
<b>5d</b>	4.90	2.57

hydrogen-bonded carbons and the  $\alpha$ -carbons of furanring, except C-5 of **5a**, C-9 of **5b**, C-1 and C-9 of **5c**, C-1 (C-9) of **5d** and C-8a of **5a**, in furodipyridines appear at lower field than those of the corresponding carbons in the parent furopyridines by 0.22-5.80 ppm. These facts suggest the lower electron density around these carbons: increase in delocalization of the  $\pi$ -electrons of these tricyclic heteroaromatics. It is noteworthy that the downfield shift (0.22 ppm) of the signal at C-4 of **5a** is much smaller and that the signals at C-5 of **5a**, C-9 of **5b**, C-1 and C-9 of **5c** and C-1 (C-9) of **5d** and the  $\beta$ -carbons of the furan-ring in furodipyridines appear at higher field than those of the corresponding carbons in the parent furopyridines. These facts may be interpreted by the steric compression effect [10].

The ionization constants of furodipyridines **5a-d** were measured by uv absorption methods and are presented in  $pK_a$  values in Table III. The  $pK_{a1}$  value of each furodipyridine is smaller than that of furo[3,2-*c*], ( $pK_a$  5.74 [11]) and of furo[2,3-*c*]pyridine ( $pK_a$  5.43 [11]). Such weaker basicities suggest that the  $\pi$ -electrons of these furodipyridines are highly delocalized.

The mass spectra of these furodipyridines are very similar to each other. Each compound exhibited the molecular ion at  $m/e$  170 as the base peak and intense peaks were observed at  $m/e$  144, 143, 142, 116, 115, 114, 89, 88, 87, 62 and 61.

The electronic spectrum of each furodipyridine shifts wholly toward longer wavelength (10-30 nm) compared

Table IV

Electronic Spectral Data of Furopyridines and Furodipyridines

Compounds	$\lambda$ max nm (log $\epsilon$ ) in methanol
Furo[2,3- <i>b</i> ]pyridine	207.0 (4.10), 2.49 (3.73), 277.3 (3.83), 279.7 (3.84), 286.0 (sh) (3.72)
<b>5a</b>	222.0 (4.28), 240.5 (4.00), 244.2 (4.00), 275.0 (sh) (4.04), 281.0 (4.11), 287.9 (4.15), 292.6 (4.16), 298.1 (4.20)
Furo[3,2- <i>b</i> ]pyridine	203.5 (4.05), 240.5 (3.65), 284.6 (3.94)
<b>5b</b>	230.0 (4.29), 293.5 (4.20), 297.8 (4.19), 304.4 (4.28)
Furo[2,3- <i>c</i> ]pyridine [a]	209.6 (3.89), 244.5 (3.90), 265.0 (3.63), 272.3 (3.63), 280.7 (3.47)
<b>5c</b>	245.9 (4.08), 265.0 (sh) (4.01), 270.0 (4.05), 287.7 (3.69), 299.0 (3.63)
Furo[3,2- <i>c</i> ]pyridine [a]	207.5 (4.13), 241.0 (3.95), 269.0 (3.30), 276.0 (3.08)
<b>5d</b>	242.0 (4.15), 266.8 (4.00), 269.5 (4.00), 272.5 (4.01) 278.1 (3.85)

[a] Reference [12a].

with that of the parent furopyridine owing to the extension of the  $\pi$ -electron system (Table IV).

Further investigations on the properties and chemical reactivities of furodipyridines are now in progress.

## EXPERIMENTAL

Melting points were determined by using a Yanagimoto micro melting point apparatus in open capillaries for all compounds, except **2a**, **3a**, **3b**, **3c** and **3d** which were determined in sealed capillaries because they sublime at higher temperatures, and are uncorrected. The ir spectra were recorded on a JASCO A-102 spectrometer. The  $^1H$  nmr spectra were taken on a JEOL JNM-PMX 60 and a JEOL FX 90Q instruments with tetramethylsilane as an internal reference. The  $^{13}C$  nmr spectra were taken on a JEOL FX 90Q instrument at 22.53 MHz with tetramethylsilane as an internal reference. Mass spectra were obtained by using JEOL JMS-300 spectrometer. Electronic spectra were determined on a JASCO UVIDEC-505 spectrometer.

General Procedure for the Synthesis of  $\beta$ -(2-Furopyridyl)-acrylic Acids **2a-d**.

A mixture of 2-formylfuropyridine (**1**) (1.0 g, 6.8 mmoles) and malonic acid (1.5 g, 14.4 mmoles) in pyridine (4 ml) was heated on a water bath for 2 hours. The mixture was diluted with cold water (50 ml) and adjusted to pH 4.5 with hydrochloric acid. After standing in a refrigerator overnight, the crystalline precipitates were filtered to give **2a**, **2b**, **2c** and **2d** in 96, 90, 68 and 70% yield, respectively.

$\beta$ -(2-Furo[2,3-*b*]pyridyl)acrylic Acid (**2a**).

This compound was recrystallized from methanol-water to give an analytical sample of mp 256-257°; ir (potassium bromide): 3100-2200, 1670, 1625, 1590, 1410, 1305, 1285  $cm^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.35 (dd,  $J_{5,6} = 4.8$ ,  $J_{4,6} = 1.8$  Hz, H-6), 8.15 (dd,  $J_{4,5} = 7.6$ ,  $J_{4,6} = 1.8$  Hz, H-4), 7.57 (d,  $J_{\alpha,\beta} = 15.6$  Hz, H- $\beta$ ), 7.36 (dd,  $J_{4,5} = 7.6$ ,  $J_{5,6} = 4.8$  Hz, H-5), 7.34 (s, H-3), 6.48 (d,  $J_{\alpha,\beta} = 15.6$  Hz, H- $\alpha$ ). *Anal.* Calcd. for  $C_{10}H_7NO_3$ : C, 63.49; H, 3.73; N, 7.40. Found: C, 63.25; H, 3.71; N, 7.36.

$\beta$ -(2-Furo[3,2-*b*]pyridyl)acrylic Acid (**2b**).

An analytically pure sample of this compound was obtained by recrystallization from ethanol-water, mp 260-263°; ir (potassium bromide): 3120, 3060, 3030, 2560-2200, 1695, 1635, 1610, 1570, 1410  $cm^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.55 (dd,  $J_{5,6} = 4.4$ ,  $J_{5,7} = 1.6$  Hz, H-5), 8.04 (dt,  $J_{6,7} = 8.2$ ,  $J_{3,7} = J_{5,7} = 1.6$  Hz, H-7), 7.64 (d,  $J_{\alpha,\beta} = 15.4$  Hz, H- $\beta$ ), 7.49 (d,  $J_{3,7} = 1.6$  Hz, H-3), 7.41 (dd,  $J_{5,6} = 4.4$ ,  $J_{6,7} = 8.2$  Hz, H-6), 6.56 (d,  $J_{\alpha,\beta} = 15.4$  Hz, H- $\alpha$ ).

*Anal.* Calcd. for  $C_{10}H_7NO_3$ : C, 63.49; H, 3.73; N, 7.40. Found: C, 63.18; H, 3.83; N, 7.13.

$\beta$ -(2-Furo[2,3-*c*]pyridyl)acrylic Acid (**2c**).

This compound was purified by recrystallization from ethanol-water, mp 285-289°; ir (potassium bromide): 3120, 3080, 3050, 2650-2150, 1690, 1635, 1610, 1535, 1420  $cm^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.83 (d,  $J_{4,7} = 0.8$  Hz, H-7), 8.31 (d,  $J_{4,5} = 4.8$  Hz, H-5), 7.62 (dd,  $J_{4,5} = 4.8$ ,  $J_{4,7} = 0.8$  Hz, H-4), 7.53 (d,  $J_{\alpha,\beta} = 15.2$  Hz, H- $\beta$ ), 7.30 (s, H-3), 6.50 (d,  $J_{\alpha,\beta} = 15.2$  Hz, H- $\alpha$ ).

*Anal.* Calcd. for  $C_{10}H_7NO_3$ : C, 63.49; H, 3.73; N, 7.40. Found: C, 63.38; H, 3.80; N, 7.44.

$\beta$ -(2-Furo[3,2-*c*]pyridyl)acrylic Acid (**2d**).

This compound was recrystallized from ethanol-water to give an analytically pure sample, mp 254-255°; ir (potassium bromide): 3150, 3100, 3060, 2600-2200, 1695, 1640, 1610, 1540, 1460  $\text{cm}^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.86 (s, H-4), 8.41 (d,  $J_{6,7} = 6.0$  Hz, H-6), 7.57 (dd,  $J_{6,7} = 6.0$ ,  $J_{3,7} = 1.0$  Hz, H-7), 7.49 (d,  $J_{\alpha,\beta} = 15.2$  Hz, H- $\beta$ ), 7.35 (d,  $J_{3,7} = 1.0$  Hz, H-3), 6.39 (d,  $J_{\alpha,\beta} = 15.2$  Hz, H- $\alpha$ ).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_7\text{NO}_3$ : C, 63.49; H, 3.73; N, 7.40. Found: C, 63.20; H, 3.65; N, 7.36.

#### General Procedure for the Synthesis of Furodipyridones **3a-3d**.

To a mixture of  $\beta$ -(2-furopyridyl)acrylic acid (**2**) (1.2 g, 6.35 mmoles) and triethylamine (2.0 g, 19.8 mmoles) in tetrahydrofuran (150 ml) was added dropwise ethyl chloroformate (2.0 g, 18.4 mmoles) at room temperature. After stirring for 1.5 hours, a solution of sodium azide (1.2 g, 18.5 mmoles) in water (5 ml) was added to the reaction mixture at room temperature, and stirred for 2 hours. After evaporation of the solvent, the residual solid mass was treated with benzene (50 ml) and water to extract the acid azide formed. After drying over magnesium sulfate, the benzene solution was added dropwise to a stirred mixture of diphenylmethane (70 ml) and tributylamine (7 ml) at 230°. During the addition, the temperature of the mixture was kept at 230-240° by controlling the addition of the azide solution, and the benzene evaporated was distilled off. After addition was completed, the diphenylmethane and tributylamine were evaporated under reduced pressure, the residue extracted with boiling water, filtered with charcoal, the filtrate concentrated to give furodipyridinones **3a**, **3b**, **3c** and **3d** in 62, 55, 46 and 47% yield, respectively.

#### Furo[2,3-*b*:4,5-*c'*]dipyridin-5(6*H*)-one (**3a**).

This compound was obtained as fine colorless needles by recrystallization from water, mp 307-308°; ir (potassium bromide): 3100-2500, 1635, 1600, 1550  $\text{cm}^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.38 (dd,  $J_{2,4} = 1.6$ ,  $J_{3,4} = 7.2$  Hz, H-4), 8.31 (dd,  $J_{2,3} = 5.0$ ,  $J_{2,4} = 1.6$  Hz, H-2), 7.59 (d,  $J_{7,8} = 7.0$  Hz, H-7), 7.44 (dd,  $J_{2,3} = 5.0$ ,  $J_{3,4} = 7.2$  Hz, H-3), 6.80 (d,  $J_{7,8} = 7.0$  Hz, H-8).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_6\text{N}_2\text{O}_2$ : C, 64.52; H, 3.25; N, 15.05. Found: C, 64.28; H, 3.28; N, 14.89.

#### Furo[3,2-*b*:4,5-*c'*]dipyridin-9(8*H*)-one (**3b**).

Recrystallization from water gave a pure sample, mp > 320°; ir (potassium bromide): 3100-2600, 1655, 1610, 1600, 1550  $\text{cm}^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.53 (dd,  $J_{2,3} = 4.4$ ,  $J_{2,4} = 1.2$  Hz, H-2), 8.01 (dd,  $J_{2,4} = 1.2$ ,  $J_{3,4} = 8.0$  Hz, H-4), 7.58 (d,  $J_{6,7} = 6.8$  Hz, H-7), 7.37 (dd,  $J_{2,3} = 4.4$ ,  $J_{3,4} = 8.0$  Hz, H-3), 6.74 (d,  $J_{6,7} = 6.8$  Hz, H-6).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_6\text{N}_2\text{O}_2$ : C, 64.52; H, 3.25; N, 15.05. Found: C, 64.53; H, 3.19; N, 14.98.

#### Furo[2,3-*c*:4,5-*c'*]dipyridin-1(2*H*)-one (**3c**).

This compound was purified by recrystallization from water to give fine needles of mp > 320°; ir (potassium bromide): 3150-2500, 1680, 1620, 1570  $\text{cm}^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  8.96 (d,  $J_{6,9} = 1.2$  Hz, H-6), 8.51 (d,  $J_{8,9} = 5.2$  Hz, H-8), 7.93 (dd,  $J_{6,9} = 1.2$ ,  $J_{8,9} = 5.2$  Hz, H-9), 7.67 (d,  $J_{3,4} = 7.2$  Hz, H-3), 6.80 (d,  $J_{3,4} = 7.2$  Hz, H-4).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_6\text{N}_2\text{O}_2$ : C, 64.52; H, 3.25; N, 15.05. Found: C, 64.44; H, 3.22; N, 14.84.

#### Furo[3,2-*c*:4,5-*c'*]dipyridin-1(2*H*)-one (**3d**).

This compound was obtained as fine needles by recrystalliza-

tion from water, mp > 320°; ir (potassium bromide): 3100-2600, 1670, 1610, 1565  $\text{cm}^{-1}$ ; pmr (DMSO- $d_6$ ):  $\delta$  9.13 (d,  $J_{6,9} = 0.8$  Hz, H-9), 8.53 (d,  $J_{6,7} = 5.6$  Hz, H-7), 7.68 (dd,  $J_{6,7} = 5.6$ ,  $J_{6,9} = 0.8$  Hz, H-6), 7.58 (d,  $J_{3,4} = 7.2$  Hz, H-3), 6.78 (d,  $J_{3,4} = 7.2$  Hz, H-4).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_6\text{N}_2\text{O}_2$ : C, 64.52; H, 3.25; N, 15.05. Found: C, 64.61; H, 3.00; N, 15.35.

#### General Procedure for the Chlorination of Furodipyridinones, **3a**, **3b**, **3c** and **3d**.

Furodipyridinone **3** (500 mg, 2.7 mmoles) was refluxed with phosphorus oxychloride (3 ml) for 2 hours. After cooling, the mixture was poured slowly onto ice, basified with concentrated ammonium hydroxide, extracted with chloroform, and dried over magnesium sulfate. Evaporation of the chloroform gave compounds **4a**, **4b**, **4c** and **4d** in 98, 99, 91 and 98% yield, respectively.

#### 5-Chlorofuro[2,3-*b*:4,5-*c'*]dipyridine (**4a**).

Recrystallization from ether gave an analytically pure sample, mp 140-142°; ir (potassium bromide): 3070, 3030, 2910, 1850, 1590, 1575, 1550, 1475, 1390  $\text{cm}^{-1}$ ; pmr (deuteriochloroform):  $\delta$  8.53 (dd,  $J_{2,4} = 1.8$ ,  $J_{3,4} = 7.6$  Hz, H-4), 8.45 (dd,  $J_{2,3} = 5.2$ ,  $J_{2,4} = 1.8$  Hz, H-2), 8.39 (d,  $J_{7,8} = 5.6$  Hz, H-7), 7.47 (d,  $J_{7,8} = 5.6$  Hz, H-8), 7.34 (dd,  $J_{2,3} = 5.2$ ,  $J_{3,4} = 7.6$  Hz, H-3).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_5\text{N}_2\text{OCl}$ : C, 58.70; H, 2.46; N, 13.69. Found: C, 58.84; H, 2.51; N, 13.58.

#### 9-Chlorofuro[3,2-*b*:4,5-*c'*]dipyridine (**4b**).

This compound was purified by recrystallization from acetone to afford a sample of mp 188-189°; ir (potassium bromide): 3060, 3040, 2950, 2850, 1620, 1585, 1560, 1440, 1420, 1390  $\text{cm}^{-1}$ ; pmr (deuteriochloroform):  $\delta$  8.81 (dd,  $J_{2,3} = 4.6$ ,  $J_{2,4} = 1.4$  Hz, H-2), 8.48 (d,  $J_{6,7} = 5.6$  Hz, H-7), 7.91 (dd,  $J_{2,4} = 1.4$ ,  $J_{3,4} = 8.4$  Hz, H-4), 7.49 (d,  $J_{6,7} = 5.6$  Hz, H-6), 7.44 (dd,  $J_{2,3} = 4.6$ ,  $J_{3,4} = 8.4$  Hz, H-3).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_5\text{N}_2\text{OCl}$ : C, 58.70; H, 2.46; N, 13.69. Found: C, 58.62; H, 2.52; N, 13.83.

#### 1-Chlorofuro[2,3-*c*:4,5-*c'*]dipyridine (**4c**).

An analytically pure sample was obtained by recrystallization from ether, mp 138-141°; ir (potassium bromide): 3100, 3070, 3050, 2930, 2850, 1625, 1585, 1565, 1555, 1410  $\text{cm}^{-1}$ ; pmr (deuteriochloroform):  $\delta$  9.01 (d,  $J_{6,9} = 1.0$  Hz, H-6), 8.68 (d,  $J_{8,9} = 5.0$  Hz, H-8), 8.49 (d,  $J_{3,4} = 5.8$  Hz, H-3), 8.11 (dd,  $J_{6,9} = 1.0$ ,  $J_{8,9} = 5.0$  Hz, H-9), 7.51 (d,  $J_{3,4} = 5.8$  Hz, H-4).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_5\text{N}_2\text{OCl}$ : C, 58.70; H, 2.46; N, 13.69. Found: C, 58.55; H, 2.50; N, 13.66.

#### 1-Chlorofuro[3,2-*c*:4,5-*c'*]dipyridine (**4d**).

This compound was purified by recrystallization from ether, mp 141-142°; ir (potassium bromide): 3060, 2930, 2850, 1590, 1585, 1560, 1430, 1420, 1395  $\text{cm}^{-1}$ ; pmr (deuteriochloroform):  $\delta$  9.36 (d,  $J_{6,9} = 0.8$  Hz, H-9), 8.63 (d,  $J_{6,7} = 5.2$  Hz, H-7), 8.36 (d,  $J_{3,4} = 5.2$  Hz, H-3), 7.44 (dd,  $J_{6,7} = 5.2$ ,  $J_{6,9} = 0.8$  Hz, H-6), 7.40 (d,  $J_{3,4} = 5.2$  Hz, H-4).

*Anal.* Calcd. for  $\text{C}_{10}\text{H}_5\text{N}_2\text{OCl}$ : C, 58.70; H, 2.46; N, 13.69. Found: C, 58.65; H, 2.36; N, 13.78.

#### General Procedure for the Dechlorination of the Chloro Compounds **4a**, **4b**, **4c** and **4d**.

A mixture of chlorofurodipyridine **4** (400 mg, 1.96 mmoles), 20% sodium hydroxide solution (1 ml) and palladium-charcoal

(5%, 200 mg) in methanol (20 ml) was stirred in a hydrogen atmosphere at room temperature. After the uptake of hydrogen (55-60 ml) had ceased, the catalyst was filtered off and the filtrate evaporated under reduced pressure. The residual solid mass was treated with water and ether. The ethereal solution was dried over potassium carbonate, and evaporated the solvent to afford crude furodipyridines **5a**, **5b**, **5c** and **5d** in 90, 97, 91 and 92% yield, respectively.

Furo[2,3-*b*:4,5-*c'*]dipyridine (**5a**).

Recrystallization of the crude sample from ether gave an analytically pure sample of mp 125-127°; ir (potassium bromide): 3040, 1590, 1580, 1565, 1550, 1480, 1440, 1385 cm<sup>-1</sup>; ms: (70 eV, electron impact) m/e 170 (M<sup>+</sup>), 144, 143, 142, 116, 115, 114, 102, 89, 88, 87, 71, 62.

*Anal.* Calcd. for C<sub>10</sub>H<sub>6</sub>N<sub>2</sub>O: C, 70.58; H, 3.55; N, 16.46. Found: C, 70.83; H, 3.57; N, 16.24.

Furo[3,2-*b*:4,5-*c'*]dipyridine (**5b**).

Recrystallization of the crude sample from acetone yielded an analytically pure sample, mp 115-116.5°; ir (potassium bromide): 3040, 1615, 1580, 1570, 1440, 1390 cm<sup>-1</sup>; ms: (70 eV, electron impact) m/e 170 (M<sup>+</sup>), 144, 143, 142, 116, 115, 114, 113, 89, 88, 87, 75, 62, 61.

*Anal.* Calcd. for C<sub>10</sub>H<sub>6</sub>N<sub>2</sub>O: C, 70.58; H, 3.55; N, 16.46. Found: C, 70.75; H, 3.53; N, 16.08.

Furo[2,3-*c*:4,5-*c'*]dipyridine (**5c**).

This compound was purified by recrystallization from hexane to give an analytically pure sample of mp 106-109°; ir (potassium bromide): 3030, 1625, 1570, 1560, 1475, 1460, 1420 cm<sup>-1</sup>; ms: (70 eV, electron impact) m/e 170 (M<sup>+</sup>), 144, 143, 142, 141, 116, 115, 114, 113, 89, 88, 87, 75, 74, 63, 62, 61.

*Anal.* Calcd. for C<sub>10</sub>H<sub>6</sub>N<sub>2</sub>O: C, 70.58; H, 3.55; N, 16.46. Found: C, 70.44; H, 3.48; N, 16.20.

Furo[3,2-*c*:4,5-*c'*]dipyridine (**5d**).

This compound was purified by recrystallization from ether to give an analytically pure sample, mp 178-179° (literature [4], mp 169-171°); ir (potassium bromide): 3050, 1585, 1565, 1470, 1430, 1405 cm<sup>-1</sup>; ms: (70 eV, electron impact) m/e 170 (M<sup>+</sup>), 144, 143, 142, 116, 115, 114, 88, 87, 75, 74, 62.

*Anal.* Calcd. for C<sub>10</sub>H<sub>6</sub>N<sub>2</sub>O: C, 70.58; H, 3.55; N, 16.46. Found: C, 70.31; H, 3.66; N, 16.13.

Determination of Ionization Constants.

Seven solutions of different pH values were prepared in acetate buffer, in phosphate buffer or in hydrochloric acid. The extinction coefficient (*E*) of the substance was measured at pH values corresponding to the range 15% to 85% ionization. The p*K*<sub>a1</sub> values were determined from the equation p*K*<sub>a1</sub> = pH - log (*E*<sub>BH<sup>+</sup></sub> - *E*) / (*E* - *E*<sub>B</sub>), and p*K*<sub>a2</sub> = pH - log (*E*<sub>BH<sup>2+</sup></sub> - *E*) / (*E* - *E*<sub>BH<sup>+</sup></sub>), where *E*<sub>B</sub>, *E*<sub>BH<sup>+</sup></sub> and *E*<sub>BH<sup>2+</sup></sub> are the extinction coefficient of the neutral molecule, mono-cation and di-cation, respectively.

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- [5] In the cases of **4a** and **4b**, the reduction without sodium hydroxide yielded a mixture of several products including compound **5**, compound assignable to the tetrahydro derivative and unidentifiable compounds.
- [6] Though <sup>1</sup>H nmr spectral data for the parent furodipyridines [**4**, **12a,b,c**] and furo[3,2-*c*:4,5-*c'*]dipyridine (**5d**) [4] and <sup>13</sup>C nmr spectral data of furo[3,2-*b*]pyridine [12d] had been reported separately, the data taken under the same condition with that for furodipyridines are also listed in Table I and II in order to compare the spectral data directly and accurately.
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