

## REACTION OF SUBSTITUTED 2-FURYL CYANIDES WITH AZIDES\*

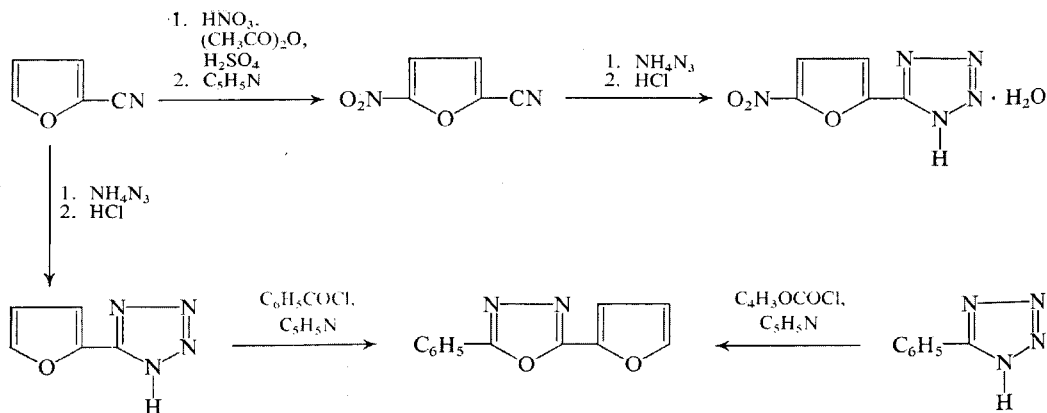
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Synthesis of 5-(5-X-2-furyl)tetrazoles by reaction of substituted 2-furyl cyanides with azides in dimethylformamide is studied.

During our investigation of furan compounds we studied the behaviour of the furan nucleus in an arylfuran system<sup>1-3</sup>. The examination of electron transfer across 2-furyl heterocyclic systems required a study of preparation of these systems. The hitherto known syntheses of 5-(2-furyl)tetrazoles are usually laborious or the yields are low. Pinner and Caro<sup>4</sup> described a synthesis of 5-(2-furyl)tetrazole by treatment of 2-furylhydrazoimide with nitrous acid. Similarly, Hirao and coworkers<sup>5</sup> prepared 5-(5-nitro-2-furyl)tetrazole in 80.2% yield. The starting hydrazoimides are prepared from cyanides *via* imino ethers in low yields by a difficult three-step synthesis<sup>6-8</sup>. Harry and Snyder<sup>9</sup> prepared 5-(5-nitro-2-furyl)tetrazole in 29% yield using Herbst and Wilson method<sup>10</sup>. Since we intended to use the Herbst-Wilson synthesis of tetra-



SCHEME 1

\* Part LXXI in the series Furan Derivatives; Part LXX: This Journal 41, 764 (1976).

zoles in the furan series we studied methods of preparation of furyl cyanides and reactions of these compounds with azides.

2-Furyl cyanide, as well as other substituted furyl cyanides, was prepared by dehydration of the corresponding oximes with acetic anhydride (Table I and II) using a modified method of Mndzhoyan and coworkers<sup>11</sup>. 5-Nitro-2-furyl cyanide was prepared by direct nitration of 2-furyl cyanide. Reaction of 2-furyl cyanide with a mixture of fuming nitric acid, acetic anhydride and sulphuric acid afforded an oily intermediate which upon decomposition with pyridine afforded 5-nitro-2-furyl cyanide in 50% yield (Scheme 1).

TABLE I  
Substituted 5-X-2-Furyl Cyanides

Compound X	Formula (m.w.)	Calculated/Found			M.p., °C (yield, %)
		% C	% H	% N	
<i>I</i> <sup>b</sup>	C <sub>5</sub> H <sub>2</sub> ClNO	47.11	1.57	10.97	52–54/5 <sup>a</sup>
Cl	(127.5)	46.95	1.69	10.82	(68)
<i>II</i>	C <sub>7</sub> H <sub>5</sub> NO <sub>3</sub>	55.64	3.33	9.26	95–96/3 <sup>a</sup>
COOCH <sub>3</sub>	(151.1)	55.47	3.42	9.29	(72.3)
<i>III</i>	C <sub>11</sub> H <sub>6</sub> B <sub>2</sub> O <sub>3</sub>	61.80	2.81	13.08	170
3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	(214.2)	61.95	2.88	13.19	(61)
<i>IV</i>	C <sub>11</sub> H <sub>6</sub> N <sub>2</sub> O <sub>3</sub>	61.80	2.81	13.08	98
2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	(214.2)	61.60	2.83	13.02	(79)
<i>V</i>	C <sub>12</sub> H <sub>7</sub> NO <sub>3</sub>	68.84	3.35	6.57	297
4-HOOC C <sub>6</sub> H <sub>4</sub>	(213.2)	68.65	3.47	6.69	(42)
<i>VI</i> <sup>c</sup>	C <sub>11</sub> H <sub>6</sub> ClNO	65.00	2.95	6.91	76
4-ClC <sub>6</sub> H <sub>4</sub>	(203.6)	64.73	2.79	7.03	(85.3)
<i>VII</i> <sup>d</sup>	C <sub>11</sub> H <sub>6</sub> BrNO	53.25	2.42	5.69	88
4-BrC <sub>6</sub> H <sub>4</sub>	(248.1)	53.10	2.31	5.60	(81.6)
<i>VIII</i>	C <sub>11</sub> H <sub>7</sub> NO	78.02	4.16	8.27	72
C <sub>6</sub> H <sub>5</sub>	(169.3)	77.94	4.02	8.13	(82.7)
<i>IX</i>	C <sub>12</sub> H <sub>9</sub> NO	78.75	4.95	7.65	87
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	(183.2)	78.92	4.75	7.62	(75)
<i>X</i>	C <sub>12</sub> H <sub>9</sub> NO <sub>2</sub>	72.41	4.53	7.08	86
4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	(189.2)	72.42	4.40	7.16	(77)

<sup>a</sup> Boiling point °C/Torr; % halogen calculated/found; <sup>b</sup> 27.81/27.93; <sup>c</sup> 17.43/17.45; <sup>d</sup> 32.26/32.29.

In order to reduce the amount of tars arising in the exothermic reaction of 5-nitro-2-furyl cyanide with sodium azide we carried out the reaction at lower temperature than described by Harry and Snyder<sup>9</sup>. We obtained 5-(5-nitro-2-furyl)tetrazole monohydrate which, in accord with the observation of Hirao and coworkers<sup>5</sup>, loses water on heating *in vacuo*. Heating 5-(5-nitro-2-furyl)tetrazole monohydrate with acetic anhydride afforded 5-methyl-2-(5-nitro-2-furyl)-1,3,4-oxadiazole.

The reaction of ammonium azide with 2-furyl cyanide and other substituted 2-furyl cyanides in dimethylformamide did not take place under the conditions described for 5-nitro-2-furyl cyanide. This reaction was accomplished at higher temperature and afforded substituted 5-(2-furyl)tetrazoles in 63.2–85.6% yield (Table III). The presence of the tetrazole ring in 5-(2-furyl)tetrazole was proved, besides by spectral methods, also by its transformation into 5-phenyl-2-(2-furyl)-1,3,4-oxadiazole. 5-(2-Furyl)tetrazole and substituted furyltetrazoles do not form hydrates, with the exception of 5-(5-nitro-2-furyl)tetrazole.

### EXPERIMENTAL

IR spectra were measured on a UR-20 (Zeiss) instrument, UV spectra on a UV-VIS Specord spectrophotometer and <sup>1</sup>H-NMR spectra on a BS 487C (80 Hz) spectrometer. Melting points were determined on a Kofler block and are uncorrected.

TABLE II  
Spectral Properties of Substituted 5-X-2-Furyl Cyanides

Compound	$\nu(\text{C}\equiv\text{N})^a$	$\lambda_{\text{max}}^b$	(log $\epsilon$ )	$\lambda_{\text{max}}^b$	(log $\epsilon$ )
I	2 237	215	(4.43)	254	(4.38)
II	2 243	214	(4.47)	268	(4.42)
III	2 232	214	(4.19)	290	(4.52)
IV	2 234	214	(4.54)	266	(4.31)
V	2 228 <sup>c</sup>	214	(4.44)	307	(4.61)
VI	2 229	215	(4.21)	300	(4.56)
VII	2 234	214	(4.19)	294	(4.59)
VIII	2 231	214	(4.10)	294	(4.47)
IX	2 228	214	(4.52)	296	(4.55)
X	2 227	214	(4.49)	304	(4.58)

<sup>a</sup> In chloroform; <sup>b</sup> in ethanol; <sup>c</sup> KBr technique.

## Nitration of 2-Furyl Cyanide

Fuming nitric acid (15 g) and concentrated sulphuric acid (10 drops) were added to acetic anhydride (30 ml) under stirring. Then 2-furyl cyanide (4.6 g; 0.05 mol) was added to this stirred mixture so as to keep the temperature below 25°C. The mixture was then stirred for 90 min at 25°C, poured on ice and the separated intermediate was taken into ether. The dried ethereal extract was concentrated *in vacuo*, the residue was treated with the same volume of pyridine and the solution was poured on ice. The separated 5-nitro-2-furyl cyanide was crystallised from a chloroform-cyclohexane mixture, m.p. 64–65°C (ref.<sup>12</sup>), yield 3.3 g (50%). IR spectrum (CCl<sub>4</sub>), cm<sup>-1</sup>: 1359, 1505 (NO<sub>2</sub>), 2244 (C≡N); UV spectrum (dioxane): λ<sub>max</sub> 291 nm (log ε 4.32); <sup>1</sup>H-NMR spectrum (CDCl<sub>3</sub>): 7.28 (d, *J* = 3.9 Hz, 1 H, C<sub>3</sub>—H furan), 7.38 (d, *J* = 3.9 Hz, 1 H, C<sub>(4)</sub>—H furan).

TABLE III

Substituted 5-(5-X-2-Furyl)tetrazoles

Compound X	Formula (m.w.)	Calculated/Found			M.p., °C (yield, %)
		% C	% H	% N	
<i>XI</i> CH <sub>3</sub> OOC	C <sub>7</sub> H <sub>6</sub> N <sub>4</sub> O <sub>3</sub> (194.2)	43.31 43.23	3.12 3.23	28.86 29.05	173 (82.7)
<i>XII</i> <sup>a</sup> Cl	C <sub>5</sub> H <sub>3</sub> ClN <sub>4</sub> O (170.6)	35.21 35.32	1.77 1.85	32.85 32.50	146 (74)
<i>XIII</i> CH <sub>3</sub>	C <sub>6</sub> H <sub>6</sub> N <sub>4</sub> O (150.1)	48.00 48.23	4.03 4.02	37.32 37.20	175 (63.2)
<i>XIV</i> 3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	C <sub>11</sub> H <sub>7</sub> N <sub>5</sub> O <sub>3</sub> (257.2)	51.37 51.40	2.74 2.65	27.23 27.26	276 (85)
<i>XV</i> 2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	C <sub>11</sub> H <sub>7</sub> N <sub>5</sub> O <sub>3</sub> (257.2)	51.37 51.30	2.74 2.61	27.23 27.20	242 (81.8)
<i>XVI</i> 4-HOOC C <sub>6</sub> H <sub>4</sub>	C <sub>12</sub> H <sub>8</sub> N <sub>4</sub> O <sub>3</sub> (256.2)	56.25 56.24	3.15 3.22	21.87 21.96	324 (82)
<i>XVII</i> <sup>b</sup> 4-ClC <sub>6</sub> H <sub>4</sub>	C <sub>11</sub> H <sub>7</sub> ClN <sub>4</sub> O (246.7)	53.57 53.47	2.86 2.73	22.71 22.88	248 (68)
<i>XVIII</i> <sup>c</sup> 4-BrC <sub>6</sub> H <sub>4</sub>	C <sub>11</sub> H <sub>7</sub> BrN <sub>4</sub> O (291.1)	45.39 45.32	2.42 2.28	19.25 19.33	263 (72)
<i>XIX</i> C <sub>6</sub> H <sub>5</sub>	C <sub>11</sub> H <sub>8</sub> N <sub>4</sub> O (212.2)	62.26 62.48	3.80 4.01	26.40 26.78	191–193 (65.7)
<i>XX</i> 4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	C <sub>12</sub> H <sub>10</sub> N <sub>4</sub> O (226.2)	63.71 63.60	4.46 4.65	24.76 24.83	199 (66.4)
<i>XXI</i> 4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	C <sub>12</sub> H <sub>10</sub> N <sub>4</sub> O <sub>2</sub> (242.2)	59.50 59.43	4.16 4.12	23.15 23.17	215 (82)

Halogen % calculated/ found: <sup>a</sup> 20.79/20.75, <sup>b</sup> 14.37/14.54, <sup>c</sup> 27.45/27.36.

## Reaction of 5-Nitro-2-furyl Cyanide with Ammonium Azide

A stirred mixture of 5-nitro-2-furyl cyanide (1.35 g; 0.01 mol), sodium azide (0.7 g; 0.012 mol) and ammonium chloride (0.6 g; 0.012 mol) in dimethylformamide (5 ml) was heated at 35–40°C for 4 hours. The reaction mixture was extracted with ether, the crystalline residue was dissolved in ethanol and the insoluble salts were filtered off. The filtrate was concentrated *in vacuo* and the salt of nitrofuryltetrazole was precipitated by addition of chloroform. The salt was dissolved in water and the solution was made acid (pH 3) by addition of hydrochloric acid. Crystallisation of the separated product afforded 1.16 g (58.4%) of 5-(5-nitro-2-furyl)tetrazole monohydrate, m.p. 71–72°C (ref.<sup>5</sup>). <sup>1</sup>H-NMR spectrum (hexadeuterioacetone): 6.30 (s, 3 H, H<sub>2</sub>O and NH in tetrazole), 7.41 (d,  $J = 3.5$  Hz, 1 H, C<sub>3</sub>—H furan), 7.61 (d,  $J = 3.5$  Hz, 1 H, C<sub>(4)</sub>—H furan). On crystallisation from acetonitrile or on heating at 60°C *in vacuo*, the monohydrate loses water and is transformed into the anhydrous compound, m.p. 121–123°C (ref.<sup>5</sup>). IR spectrum (KBr): 1355, 1520 cm<sup>-1</sup> (NO<sub>2</sub>); <sup>1</sup>H-NMR spectrum (hexadeuteriodimethyl sulphoxide): 7.43 (d,  $J = 4.0$  Hz, 1 H, C<sub>(3)</sub>—H furan), 7.73 (d,  $J = 4.0$  Hz, 1 H, C<sub>(4)</sub>—H furan), 9.55 (s, 1 H, broad, NH tetrazole).

## 5-(2-Furyl)tetrazole

A stirred mixture of 2-furyl cyanide (9.31 g; 0.1 mol), sodium azide (7.2 g; 0.12 mol), ammonium chloride (6.4 g; 0.12 mol) and dimethylformamide (30 ml) was heated at 100°C for 4 hours. The solvent was distilled off *in vacuo*, the residue was dissolved in water, the solution was acidified with hydrochloric acid and the precipitate was filtered and crystallised from hexane-acetone,

TABLE IV  
UV Spectral Data for 5-(5-X-2-Furyl)tetrazoles in Ethanol

Compound	$\lambda_{\max}$	(log $\epsilon$ )	$\lambda_{\max}$	(log $\epsilon$ )	$\lambda_{\max}$	(log $\epsilon$ )
XI	—	—	—	—	262	(4.25)
XII	204	(4.15)	—	—	278	(4.48)
XIII	—	—	—	—	265	(4.35)
XIV	203	(4.07)	212	(4.18)	308	(4.32)
XV	204	(4.29)	212	(4.25)	291	(4.28)
XVI	204	(4.06)	229	(4.03)	322	(4.48)
XVII	202	(4.11)	223	(4.00)	313	(4.42)
XVIII	204	(4.20)	224	(4.05)	314	(4.51)
XIX	203	(4.17)	217	(4.18)	308	(4.48)
XX	204	(4.27)	219	(4.18)	311	(4.46)
XI	204	(4.19)	222	(3.95)	314	(4.42)

affording 14.9 g (82%) of 5-(2-furyl)tetrazole, m.p. 203--204°C (ref.<sup>4</sup>). UV spectrum (ethanol):  $\lambda_{\max}$  259 nm (log  $\epsilon$  4.41); <sup>1</sup>H-NMR spectrum (hexadeuterioacetone): 6.53 (q,  $J = 3.5$  Hz,  $J = 1.5$  Hz, 1 H, C<sub>(4)</sub>-H furan), 6.72 (s, 1 H, broad, NH tetrazole), 7.08 (q,  $J = 3.5$  Hz,  $J = 0.5$  Hz, 1 H, C<sub>(3)</sub>-H furan), 7.66 (q,  $J = 1.5$  Hz,  $J = 0.5$  Hz, 1 H, C<sub>(5)</sub>-H furan).

5-(5-X-2-Furyl)tetrazoles were prepared by the same method. Their physical constants and analytical data are listed in Table III and IV.

#### 5-Methyl-2-(5-nitro-2-furyl)-1,3,4-oxadiazole

This compound was prepared according to Hirao and coworkers<sup>5</sup>. <sup>1</sup>H-NMR spectrum (hexadeuterioacetone): 2.56 (s, 3 H, CH<sub>3</sub>), 7.41 (d,  $J = 7$  Hz, 1 H, C<sub>(3)</sub>-H furan), 7.61 (d,  $J = 3.7$  Hz, 1 H, C<sub>(4)</sub>-H furan).

#### 5-Phenyl-2-(2-furyl)-1,3,4-oxadiazole

A) A mixture of 5-(2-furyl)tetrazole (2.72 g; 0.02 mol), pyridine (10 ml) and benzoyl chloride (2.8 g; 0.02 mol) was heated at 100°C till the evolution of nitrogen ceased. The solvent was distilled off and the residue was crystallised from tetrachloromethane, yielding 1.43 g (64.2%) of the product, m.p. 103°C.

B) A mixture of 5-phenyltetrazole (2.8 g; 0.02 mol), pyridine (10 ml) and 2-furoyl chloride (2.6 g, 0.02 mol) was heated to 100°C till the evolution of nitrogen ceased. The oxadiazole was isolated as described under A), yield 1.8 g (84.5%), m.p. 103°C (ref.<sup>13</sup>). <sup>1</sup>H-NMR spectrum (CCl<sub>4</sub>): 5.39 (q,  $J = 3.5$  Hz,  $J = 1.5$  Hz, 1 H, C<sub>(4)</sub>-H furan), 7.01 (q,  $J = 3.5$  Hz,  $J = 0.5$  Hz, 1 H, C<sub>(3)</sub>-H furan), 7.19--7.36 (m, 3 H, aromatic protons at C<sub>(3)</sub>, C<sub>(4)</sub> and C<sub>(5)</sub>), 7.44 (q,  $J = 1.5$  Hz,  $J = 0.5$  Hz, 1 H, C<sub>(5)</sub>-H furan), 7.81--7.99 (m, 2 H, aromatic protons at C<sub>(2)</sub> and C<sub>(6)</sub>).

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