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SYNTHESIS OF 5-SUBSTITUTED CYANOFURANS AND THEIR REACTION WITH HYDRAZINE

P. A. Pavlov and V. G. Kul'nevich

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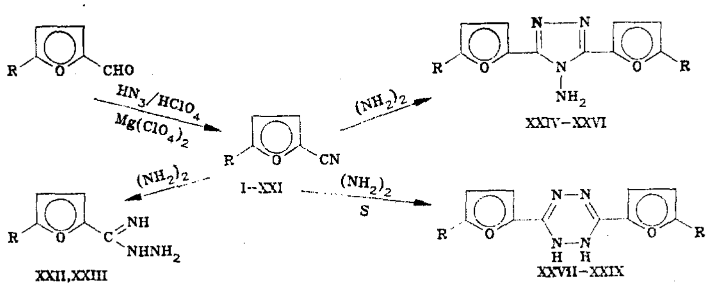
Based on the Schmidt reaction, a new method has been developed for the preparation of nitriles in furan series from the corresponding furfural derivatives. Depending on conditions, the reaction of 5-substituted cyanofurans with hydrazine leads to amidrazones, N-aminotriazoles, or 1,2,4,5-dihydrotetrazines.

The known methods for the preparation of cyanofurans from furancarboxaldehydes [1-6] have several disadvantages: multiplicity of stages, difficulties related to the regeneration of the reagents, limited number of suitable methods, because of scarcity of starting materials, as well as impossibility of their use for the preparation of individual compounds, for example, 5-nitro-2-cyanofuran [5].

For this purpose we used the Schmidt reaction [7], considered to be unsuitable for the preparation of nitriles of the furan series. Instead of sulfuric, phosphoric, hydrochloric and other mineral acids, and also Lewis acids [7], we used 72% perchloric acid, with which it was possible to avoid resinification of furancarboxaldehydes, but the yield of the nitrile did not exceed 50%. When anhydrous magnesium perchlorate was introduced, it was possible to reduce the amount of perchloric acid to catalytic quantities, and thus the yield of products I-XXI increased to 76-96%, while the time of the reaction was shortened.



I, XXIV, XXVII R = H, II, XXV, XXVII R = CH_3, III R = C_6H_5, IV R = $-C\equiv CC_6H_5$, V, XXII, XXVI, XXIX R = Br, VI R = I, VII, XXIII R = NO_2, VIII R = CH_2Cl, IX R = 4-$C_6H_4NO_2$, X R = 4-$OC_6H_4CH_3$, XI R = OC_6H_4Cl, XII R = SCH_3, XIII R = $SCH_2COOC_2H_5$, XIV R = 2,4-$SC_6H_3(NO_2)_2$, XV R = 5-thio-2-cyanofuran, XVI R = 5-thio-2-oxofuran, XVII R = $S{-}\underset{\substack{\| \\ O}}{C}{-}C_6H_5$, XVIII R = 3-$S{-}\underset{\substack{\| \\ O}}{C}{-}C_6H_4Br$, XIX R = thiofuro-5-yl, XX R = $SO_2C_6H_5$, XXI R = 4-$SO_2C_6H_4CH_3$

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In the preparation of compounds X and XI, the use of perchloric acid as the catalyst led to the resinification of the reaction mixture, but when $HClO_4$ was used in the form of dioxanium perchlorate, they could be obtained in a yield of 69-76%. The characteristics of the previously known compounds I-III, V, VII, IX, XX, XXI correspond to those described in [1-6], but their yields are 10-15% higher, and the yield of 5-nitro-2-cyanofuran even increased from 50 to 92%.

In the IR spectra of the compounds synthesized, the characteristic absorption bands of the stretching vibrations of the CN group are present in the region of 2244-2205 (I-XXI), C=O at 1780-1680 cm^{-1} (XIII-XIX) the COC grouping (X, XI) absorbs at 1260, 1230, and SO_2 at 1340, 1150, and 1130 cm^{-1} (XX, XXI). Compounds IV, VIII, X-XIX were synthesized for the first time, and their characteristics are given in Table 1.

The reaction of different nitriles with hydrazine with the formation of amidrazones, aminotriazoles, and tetrazines has been discussed fairly comprehensively in [8-10], but there is no information on the reaction of furan nitriles.

Our studies showed that the direction of the reaction depends on the conditions under which it is being carried out, while the stability of the desired end products depends on the nature of the substituent at the 5-position of the furan ring (Table 2). The reaction of 5-bromo- and 5-nitrocyanofurans with an alcoholic solution of hydrazine leads to the corresponding amidrazones, and that 2-cyanofuran and 5-methyl-2-cyanofuran, to unstable products, which could not be isolated.

Heating of 5-R-2-cyanofurans with an excess of hydrazine hydrate gave 4-amino-3,5-di(5-R-2-furyl)-1,2,4-triazoles (XXIV-XXVI) in a high yield. In boiling alcohol in the presence of sulfur, 3,6-di(5-R-2-furyl)-1,2-dihydro-1,2,4,5-tetrazines (XXVII-XXIX) are formed. 5-Nitro-2-cyanofuran, which resinifies under the above conditions, is an exception.

In the IR spectra of triazoles XXIV-XXVI there are two stretching vibration absorption bands at 3350-3325 and 3150 cm^{-1} of the primary amino group, and two deformational vibration bands at 1665-1645 and 1610 cm^{-1}. The IR spectra of dehydrotetrazines XXVII-XXIX are characterized by the presence of one single stretching vibration band of the secondary amino group in the 3320-3330 cm^{-1} region, and one deformational vibration band at 1740-1770 cm^{-1}.

In the PMR spectra of compounds XXIV-XXIX, the signals of the NH and NH_2 group protons are recorded as a broadened singlet, which disappears during deuteration.

When 3,6-di(2-furyl)-1,2-dihydro-1,2,4,5-tetrazine (XXVII) is heated in pyridine in the presence of copper sulfate, 3,6-di(2-furyl)-1,2,4,5-tetrazine (XXX) is formed in 81% yield, while the corresponding 4-amino-3,5-di(2-furyl)-1,2,4-triazole (XXIV) is isolated unchanged.

EXPERIMENTAL

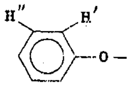
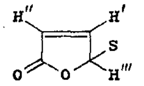
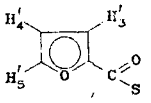
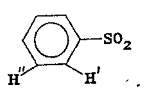
The IR spectra were run on a UR-20 spectrophotometer in mineral oil. The PMR spectra were recorded on a Tesla BS-467 spectrometer (60 MHz) for compounds I, II, V, VII, X, XI in $(CD_3)_2CO$; for III-VI, VIII, IX, XII-XXI in CCl_4, and for XXV and XXVIII in $CDCl_3$, using HMDS as internal standard. The spectra of the remaining compounds were recorded in DMSO-D_6, using t-BuOH as internal standard. The purity of the compounds synthesized was checked by chromatography of Silufol in a 3:20 ethanol—toluene system.

The benzene solution of hydrazoic acid was in all cases prepared by the method described in [7].

5-Substituted-2-cyanofurans (I-XXI). A 6.7 g (0.03 mole) portion of anhydrous magnesium perchlorate is added to a mixture of 0.1 mole of furancarboxaldehyde and 0.11 mmole of a benzene solution of hydrazoic acid, and then 1.4 ml (0.01 mole) of 72% perchloric acid is added dropwise, with stirring, at 35°C. The rate of addition is controlled by the current of liberated nitrogen, which should be rapid, but not violent. At the end of the evolution of nitrogen, the mixture is treated with water, the benzene layer is separated, washed once more with water, and dried over sodium sulfate. Benzene is removed under reduced pressure, and the residue is distilled *in vacuo* or recrystallized from alcohol. Compound XVI is recrystallized from CCl_4 and VII from a mixture of chloroform and cyclohexane.

Compounds X and XI are prepared in a similar way, but instead of perchloric acid, a previously prepared dioxaniumperchlorate is used [5 ml of 1,4-dioxane and 1.4 ml (0.01 mole) of 72% perchloric acid].

TABLE 1. Cyanofurans I-XXI

Compound	Mp [Bp], °C (mm)	n_4^{20}	d_4^{20}	PMR spectrum, ppm			SSCC, Hz		
				3-H	4-H	R	J_{R^3}	J_{R^4}	J_{34}
I	[47]	1,4797	1,0650	7,33 (d)	6,63 (dd)	7,82 d	0,75	1,8	3,7
II	[74—76] (33)	1,4849	1,0398	7,15 (d)	6,23 (d)	2,32 s	—	—	4,0
III	73	—	—	7,01 (d)	6,60 (d)	7,47 m.	—	—	4,0
IV	76	—	—	6,96 (d)	6,85 (d)	7,33 m	—	—	4,0
V	[78] (14)	1,5408	1,8976	7,28 (d)	7,65 (d)	—	—	—	4,0
VI	36—37	—	—	6,92 (d)	6,61 (d)	—	—	—	4,0
VII	64—65	—	—	7,60 (d)	7,71 (d)	—	—	—	3,0
VIII	[92—93]	1,5260	1,3614	6,99 (d)	6,45 (d)	4,48 s	—	—	4,0
IX	171	—	—	7,65 (d)	7,47 (d)	8,05 m	—	—	4,0 (J_{OM}) 9,0
X	[155]	1,5563	1,2851	6,80 (d)	5,25 (d)	 6,80 (d, H'); 7,03 (d, H'')	— $J_{H'H''}$ = 10,0	—	4,0
XI	43	—	—	6,93 (d)	5,49 (d)	6,97 (d, H'); 7,27 (d, H'')	— $J_{H'H''}$ = 9,0	—	4,0
XII	[111] (25)	1,5622	1,3644	6,98 (d)	6,28 (d)	2,45 (s)	—	—	4,0
XIII	[161] (8)	1,5178	1,3453	7,08 (d)	6,54 (d)	1,02 (t, CH_3); 4,08 (q, CH_2O); 3,51 (s, CH_2S)	— $J_{CH_2CH_3}$ = 7,0	—	4,0
XIV	126	—	—	7,00 (d)	6,72 (d)	7,60 (m)	—	—	4,0
XV	63	—	—	7,00	6,69.	—	—	—	4,0
XVI	81—82	—	—	7,38 (d)	6,88 (d)	 6,40 (t, H'''); 6,10 (dd, H''); 7,67 (dd, H')	— $J_{'H'''H}$ = 1,75 $J_{''H'''H}$ = 2,00 $J_{'H'''H}$ = 5,50	—	4,0
XVII	100	—	—	7,09 (d)	6,78 (d)	7,68 (m)	—	—	3,7
XVIII	113	—	—	6,55 (d)	6,01 (d)	6,60 (m)	—	—	4,0
XIX	75—76	—	—	7,10 (d)	6,79 (d	 7,44 (d, H_3'); 6,55 (q, H_4'); 7,58 (d, H_5')	— $J_{H_3'H_4'}$ = 3,8 $J_{H_4'H_5'}$ = 2,0 $J_{H_5'H_3'}$ = 0,75	—	3,85
XX	81	—	—	7,44, 7,55 (q. furan ring system protons)		7,85 (m) 	—	—	4,0
XXI	121	—	—	7,36, 7,51 (q, furan ring system protons)		2,38 (s, CH_3); 7,40 (d, H); 7,85 (d, H)	— $J_{H'H''}$ = 8,0	—	4,0

Amidrazones XXII, XXIII. A 0.5 ml (0.01 mole) portion of hydrazine hydrate is added to a mixture of 0.01 mole of cyanofuran V, VII in 10 ml of alcohol. The mixture is stirred, and left to stand overnight. The alcohol is distilled off under reduced pressure, and the residue is recrystallized from CCl_4 (XXII) and $CHCl_3$ (XXIII).

4-Amino-3,5-di(5-R-2-furyl)-1,2,4-triazole (XXIV-XXVI). A mixture of 0.1 mole of 5-R-2-cyanofuran and 40 ml (0.8 mole) of hydrazine hydrate is boiled for 3 h in a nitrogen current, then cooled, the crystals are filtered, washed with water and recrystallized from $CHCl_3$.

3-6-Di(5-R-2-furyl)-1,2-dihydro-1,2,4,5-tetrazines (XXVII-XXIX). A mixture of 0.1 mole of 5-R-2-cyanofuran, 30 ml of ethanol, 30 ml (0.6 mole) of hydrazine hydrate

Found, %				Empirical formula	Calculated, %				Yield, %
C	H	N	S (Hal)		C	H	N	S (Hal)	
64,5	0,3	15,0	—	C_5H_3NO	64,5	0,3	15,0	—	76
77,0	5,3	14,8	—	C_5H_5NO	77,0	5,2	14,8	—	82
70,0	41	8,3	—	$C_{11}H_7NO$	78,0	4,2	8,3	—	84
80,2	3,5	7,1	—	$C_{13}H_7NO$	80,2	3,6	7,8	—	94
34,8	1,2	8,4	(46,5)	C_5H_2BrNO	34,8	1,1	8,3	46,5	78
27,3	0,9	6,3	(57,7)	C_5H_2INO	27,4	0,9	6,4	57,7	85
43,5	1,4	20,3	—	$C_5H_2N_2O_3$	43,5	1,4	20,3	—	92
50,6	2,7	9,8	(25,2)	C_6H_4ClNO	50,7	2,8	9,8	25,3	96
52,8	2,8	13,3	—	$C_{11}H_6N_2O_3$	52,8	2,7	13,3	—	80
72,2	4,5			$C_{12}H_9NO_2$	72,4	4,5	7,0	—	69
60,0	2,6	6,4	(16,4)	$C_{11}H_6ClNO_2$	60,0	2,7	6,4	16,4	76
51,7	3,5	10,0	23,0	C_5H_5NOS	51,8	3,6	10,0	23,0	79
53,4	4,3	6,8	15,8	$C_9H_9NO_3S$	53,4	4,4	6,9	15,8	78
45,3	1,7	14,4	10,9	$C_{11}H_5N_3O_5S$	45,3	1,7	4,4	10,9	93
55,4	1,7	12,8	14,8	$C_{10}H_4N_2O_2S$	55,5	1,8	12,9	14,8	92
52,1	2,3	6,7	15,4	$C_9H_5NO_3S$	52,2	2,4	6,7	15,4	89
62,8	2,9	6,1	13,9	$C_{12}H_7NO_2S$	62,9	3,0	6,1	14,0	90
46,7	1,8	4,5	10,3 (25,9)	$C_{12}H_6BrNO_2S$	46,7	1,9	4,5	10,4 (26,0)	91
54,7	2,3	6,4	14,5	$C_{10}H_5NO_3S$	54,7	2,3	6,4	14,6	90
58,4	2,9	6,0	13,6	$C_{11}H_7NO_3S$	58,6	3,0	6,0	13,7	98
59,0	2,3	5,7	13,0	$C_{12}H_6NO_3S$	59,0	2,4	5,7	13,1	98

and 2 g of sulfur is boiled in a nitrogen current. After 2 h, crystals begin to separate. After heating for 1 more hour, the mixture is treated as described above. Compounds XXVII, XXVIII are recrystallized from chloroform, XXIX from toluene.

3,6-Di(2-furyl)-1,2,4,5-tetrazine (XXX). A mixture of 1.92 g (0.01 mole) of 1,2,dihydrotetrazine XXVII, 2.5 g (0.01 mole) of $CuSO_4$ and 10 ml of pyridine is heated with stirring for 5 h at 50°C. It is then cooled and filtered. The filtrate is poured into 100 ml of ice water, the crystals are filtered with suction, washed with cold alcohol, and recrystallized from $CHCl_3$. The yield of compound XXX is 1.54 g (81%).

TABLE 2. Characteristics of Compounds Synthesized

Compound	mp, °C	IR spectrum, cm^{-1}		PMR spectrum				SSCC, Hz			Found, %			Empirical formula	Calculated, %			Yield, %
		ν_{NH}	δ_{NH}	NH	R	H_3	H_4	$J_{2,3}$	$J_{3,4}$	$J_{2,4}$	C	H	N (Hal)		C	H	N (Hal)	
XXII	108	3500, 3300, 3200	1600	4,41 (br.s)	—	6,33 (d)	6,66 (d)	—	4,0	—	29,4	2,8	20,5 (39,1)	$C_5H_6BrN_3O$	29,4	2,9	20,6 (39,2)	92
XXIII	160*	3555, 3325, 3200	1600	4,57 (br.s), 3,39 (br.s)	—	5,80 (d)	6,50 (d)	—	4,0	—	35,3	3,4	32,9	$C_5H_6N_4O_3$	35,3	3,5	32,9	89
XXIV	240	3350	1645	5,10 (br.s)	6,70 (d)	5,55 (dd)	6,18 (d)	0,7	3,5	2,0	49,9	4,1	29,2	$C_8H_8N_4O_2$	50,0	4,2	29,2	87
XXV	242	3325, 3150	1665, 1610	5,05 (br.s)	2,35 (CH_3C)	6,08 (d)	7,03 (d)	—	3,9	—	54,4	5,4	25,4	$C_{10}H_{12}N_4O_2$	54,5	5,5	25,5	90
XXVI	244*	3325, 3180	1665, 1620	7,83 (br.s)	—	5,66 (d)	6,11 (d)	—	3,8	—	35,5	2,0	20,5 (29,5)	$C_8H_6BrN_4O_2$	35,5	2,2	20,7 (29,6)	85
XXVII	208	3330	1770	7,83 (br.s)	6,66 (d)	5,50 (dd)	6,03 (d)	0,7	3,5	2,0	50,0	4,0	29,0	$C_8H_8N_4O_2$	50,0	4,2	29,2	88
XXVIII	189*	3320	1740	7,05 (br.s)	2,26 (CH_3C)	6,00 (d)	6,55 (d)	—	4,0	—	54,5	5,3	25,5	$C_{10}H_{12}N_4O_2$	54,5	5,5	25,5	87
XXIX	255	3325	1760	7,91 (br.s)	—	5,60 (d)	6,04 (d)	—	4,0	—	35,3	2,1	20,6 (29,3)	$C_8H_6BrN_4O_2$	35,5	2,2	20,7 (29,6)	83
XXX	195	1600	—	—	6,95 (d)	5,88 (dd)	6,54 (d)	0,9	3,8	2,5	50,3	3,0	29,4	$C_8H_6N_4O_2$	50,5	3,1	29,5	81

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*With decomposition.

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CHLORINATION OF 1,3-DIOXOLAN-4-ONES

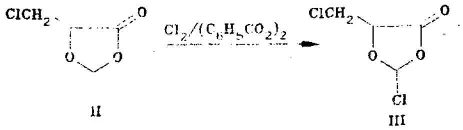
V. R. Likhterov and V. S. Étlis

UDC 547.729.7:542.944

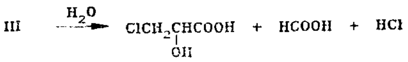
It is shown that the direction of chlorination of 1,3-dioxolan-4-ones in the presence of benzoyl peroxide is determined by the nature of the substituent at the 5-position of the ring. In this case a chloromethyl group, having a —I effect, promotes a selective replacement of hydrogen at the 2-position, while a methyl group mainly causes replacement of hydrogen at the 5-position.

The present work is devoted to the reaction of 1,3-dioxolan-4-ones with chlorine and aims to establish the effect of the substituent at the 5-position of the ring on the direction of chlorination.

5-Methyl- (I) and 5-chloromethyl-1,3-dioxolan-4-one (II) underwent chlorination. Replacement of hydrogen by chlorine proceeds only at an increased temperature (80-100°C) and in the presence of free-radical initiators. In the case of dioxolanone I on chlorination to an increase in weight equal to the replacement of one atom of hydrogen by chlorine, determination of the composition of the reaction mixture was not achieved. In the second case chlorination proceeds selectively and leads to 2-chloro-5-chloromethyl-1,3-dioxolan-4-one (III). This, evidently, can be accounted for by the influence of the substituent with a —I effect, which to a large extent lowers the reactivity of the C—H bond at the 5-position of the ring to attack by an electrophilic chlorine radical.



It was established (GLC) that the compound synthesized was a mixture of cis and trans isomers; it showed thermal stability and was readily distilled, but was unstable on hydrolysis. Among the products of hydrolysis were identified 3-chloro-2-hydroxypropionic, formic, and hydrochloric acids.



$$\text{III} \xrightarrow{H_2O} ClCH_2\underset{\displaystyle OH}{\underset{|}{C}}HCOOH + HCOOH + HCl$$

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