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A SIMPLE METHOD FOR THE SYNTHESIS OF 5-SUBSTITUTED 2-CYANOFURANS

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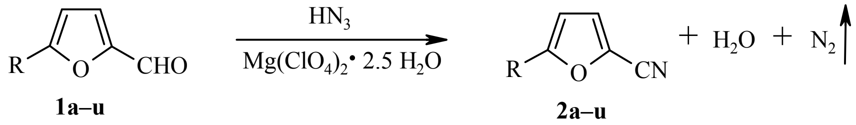
A new method based on the Schmidt reaction was developed for the production of 5-R-2-cyanofurans from 5-R-furfurals.

Keywords: hydrazoic acid, nitrile, furancarbaldehyde, cyanofuran, 2-cyanofurans.

The Schmidt reaction [1] differs favorably from other methods for the production of nitriles, since it is conducted in one stage using readily obtainable initial reagents and provides a simple method for treatment of the reaction mixture. However, with all its merits it has been considered unsuitable for the production of nitriles from aldehydes of the furan series on account of the need to use high concentrations of strong mineral acids or classical Lewis acids, which lead to resinification of the reaction mass as a result of the high sensitivity of furan compounds to acids.

In the methods we developed for the synthesis of 5-R-2-cyanofurans benzene solutions of hydrazoic acid and a catalytic system containing perchloric acid and anhydrous magnesium perchlorate in various ratios were used [2-5]. The procedure can be simplified by avoiding the presence of the strong mineral acid ($HClO_4$) and the poorly available magnesium perchlorate in the reaction mixture [6]. Here the yield of the targeted products is increased by 5-7% (in the case of 2-cyano-5-nitrofuran the yield is practically quantitative), the safety of the process is increased on account of the absence of the perchloric acid oxidizing agent and benzene, and the reaction becomes more controllable with uniform release of gaseous nitrogen. The effect is achieved by replacing the benzene solutions of hydrazoic acid by chloroform solutions and using the readily available hydrated magnesium perchlorate $Mg(ClO_4)_2{\cdot}(2\text{-}2.5)H_2O$ (anhydrone) as catalyst.



The identities of R and the physicochemical and spectral characteristics of compounds **2a-u** are given in Tables 1 and 2.

The use of anhydrone as catalyst is based on its strong dehydrating power and characteristics that are in the opinion of a series of authors typical of "soft" Lewis acids [6, 7]. It can be concluded on the basis of experimental data on the synthesis of 5-R-2-cyanofurans that anhydrone (hydrated magnesium perchlorate) is not inferior to the anhydrous salt in its catalytic characteristics.

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TABLE 1. The Physicochemical Characteristics of 5-R-2-Cyanofurans **2a-u**

Com-pound	Empirical formula	Found, % / Calculated, %			bp, °C (mm Hg)/mp, °C	R	n_D^{20}	d_4^{20}	Yield, %
		C	H	N					
1	2	3	4	5	6	7	8	9	10
2a	C_5H_3NO	64.44 64.52	3.16 3.25	14.91 15.05	147	H	1.4797	1.0850	84
2b	C_6H_5NO	67.36 67.28	4.58 4.71	13.00 13.08	74-76 (33)	Me	1.4849	1.0398	91
2c	$C_{11}H_7NO$	78.17 78.09	4.07 4.17	—	73	Ph	—	—	90
2d	$C_{13}H_7NO$	80.91 80.82	3.54 3.65	7.23 7.25	76	PhC≡C	—	—	94
2e	C_5H_2BrNO	35.03 34.92	1.20 1.17	8.17 8.14	78 (14)	Br	1.5408	1.8976	88
2f	C_5H_2INO	27.50 27.42	0.87 0.92	6.29 6.40	36-37	I	—	—	85
2g	$C_5H_2N_2O_3$	43.63 43.49	1.40 1.46	20.18 20.29	65	NO_2	—	—	96
2h	C_6H_4ClNO	51.15 50.91	2.85 2.85	9.79 9.89	93 (4)	$ClCH_2$	1.5260	1.3614	96
2i	$C_{11}H_6N_2O_3$	61.84 61.69	2.74 2.82	13.07 13.08	171	4-$O_2NC_6H_4$	—	—	85
2j	$C_{12}H_9NO_2$	72.49 72.35	4.51 4.55	6.92 7.03	155 (4)	4-MeC_6H_4O	1.5563	1.2851	79
2k	$C_{11}H_6ClNO_2$	60.37 60.16	2.69 2.75	6.30 6.38	43	4-ClC_6H_4O	—	—	81

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10
2l	C_6H_5NOS	$\frac{52.06}{51.78}$	$\frac{3.54}{3.62}$	$\frac{10.05}{10.06}$	111 (25)	MeS	1.5622	1.3644	79
2m	$C_9H_9NO_3S$	$\frac{51.42}{51.17}$	$\frac{4.19}{4.29}$	$\frac{6.65}{6.63}$	161 (8)	$EtOOCCH_2S$	1.5178	1.3453	78
2n	$C_{11}H_5N_3O_5S$	$\frac{45.51}{45.37}$	$\frac{1.68}{1.73}$	$\frac{14.32}{14.43}$	126	2,4-$(O_2N)_2C_6H_3S$	—	—	93
2o	$C_{10}H_4N_2O_2S$	$\frac{55.70}{55.55}$	$\frac{1.80}{1.86}$	$\frac{12.83}{12.96}$	63	5-Cyano-2-furylthio	—	—	92
2p	$C_9H_5NO_3S$	$\frac{52.68}{52.17}$	$\frac{1.98}{2.43}$	$\frac{6.71}{6.76}$	82	5-Oxo-2,5-dihydro-2-furylthio	—	—	89
2q	$C_{12}H_7NO_2S$	$\frac{63.01}{62.87}$	$\frac{3.00}{3.08}$	$\frac{6.12}{6.11}$	100	PhCOS	—	—	90
2r	$C_{12}H_6BrNO_2S$	$\frac{46.90}{46.77}$	$\frac{1.91}{1.96}$	$\frac{4.45}{4.55}$	113	3-BrC_6H_4COS	—	—	91
2s	$C_{10}H_5NO_3S$	$\frac{55.07}{54.79}$	$\frac{2.22}{2.30}$	$\frac{6.32}{6.39}$	76	2-Furoylthio	—	—	90
2t	$C_{11}H_7NO_3S$	$\frac{56.89}{56.65}$	$\frac{2.93}{3.03}$	$\frac{5.95}{6.01}$	81	$PhSO_2$	—	—	98
2u	$C_{12}H_9NO_3S$	$\frac{58.58}{58.29}$	$\frac{3.60}{3.67}$	$\frac{5.61}{5.66}$	121	4-$MeC_6H_4SO_2$	—	—	98

TABLE 2. The Spectral Characteristics of 5-Substituted 2-Cyanofurans **2a-u**

Compound	UV spectrum, λ_{max}, nm (log ε)	IR spectrum, cm^{-1}		^{1}H NMR spectrum				
				δ, ppm			SSCC, *J*, Hz	
		ν_{CN}	other bands	$H_{(3)}$ (d)	$H_{(4)}$ (d)	H_R	$J_{3,4}$	other SSCC
1	2	3	4	5	6	7	8	9
2a	240 (3.97)	2200	3110 (ν_{CH}); 1575 (ν_{cycl})	7.33	6.63 (dd)	7.82 (d)	3.7	0.75 ($J_{3,5}$); 1.8 ($J_{4,5}$)
2b	250 (4.17)	2200	3130 (ν_{CH}); 1580 (ν_{cycl})	7.15	6.23	2.32 (s)	4.0	—
2c	210 (4.27), 293 (4.37)	2210	3130 (ν_{CH}); 1575 (ν_{cycl})	7.01	6.60	7.47 (m)	4.0	—
2d	205 (4.36), 303 (4.83), 318 (4.75)	2200	3115 (ν_{CH}); 1573 (ν_{cycl})	6.96	6.85	7.33 (m)	4.0	—
2e	255 (4.13)	2205	3118 (ν_{CH}); 1575 (ν_{cycl})	7.28	7.65	—	4.0	—
2f	258 (4.48)	2200	3112 (ν_{CH}) 1580 (ν_{cycl})	6.92	6.61	—	4.0	—
2g	290 (4.32)	2244	1505 (ν_{NO2})	7.60	7.71	—	3.9	—
2h	248 (4.43)	2220	—	6.99	6.45		4.0	—
2i	205 (4.08), 333 (4.66)	2231	1515; 1345 (ν_{NO_2})	7.65	7.47	8.30 (d, *m*-H_{Ar}); 8.03 (d, *o*-H_{Ar})	4.0	9.0 ($J_{o,m}$)
2j	217 (4.12), 262 (4.52)	2205	1230; 1260 ($\nu_{C–O–C}$)	6.80	5.25	7.03 (d, *m*-H_{Ar}); 8.80 (d, *o*-H_{Ar})	4.0	10.0 ($J_{o,m}$)
2k	222 (4.09), 260 (4.55)	2205	1230; 1260 ($\nu_{C–O–C}$)	6.93	5.46	7.27 (d, *m*-H_{Ar}); 6.97 (d, *o*-H_{Ar})	4.0	9.0 ($J_{o,m}$)

TABLE 2 (continued)

1	2	3	4	5	6	7	8	9
2l	237 (3.94), 285 (4.46)	2220	—	6.98	6.28	2.45 (s)	4.0	—
2m	243 (4.09), 2.79 (4.24)	2205	—	7.08	6.54	1.02 (t, CH_3); (q, CH_2–CH_3); 3.51 (s, CH_2–S–)	4.0	7.0
2n	232 (3.87), 271 (4.41)	2205	1365, 1340, 1535 (ν_{NO_2})	7.00	6.72	7.60 (m)	4.0	—
2o	244 (4.40), 267 (4.53)	2220	—	7.00	6.69	—	4.0	—
2p	212 (4.13), 255 (4.19), 333 (3.83)	2205	1740, 1780 ($\nu_{C=O}$)	7.38	6.88	6.10 (dd, H-4'); 6.40 (t, H-2'); 7.67 (dd, H-3')	4.0	1.75 ($J_{2'3'}$), 2.00 ($J_{2'4'}$), 5.50 ($J_{3'4'}$)
2q	205 (4.12), 257 (4.39), 337 (3.75)	2220	1680 ($\nu_{C=O}$)	7.09	6.78	7.68 (m)	3.7	—
2r	205 (4.08), 256 (3.87), 333 (3.69)	2220	1700 ($\nu_{C=O}$)	6.55	6.01	6.60 (m)	4.0	—
2s	212 (4.19), 248 (4.41), 329 (3.73)	2220	1690 ($\nu_{C=O}$)	7.10	6.79	6.55 (q, H-4'); 7.44 (d, H-3'); 7.58 (d, H-5')	3.85	3.80 ($J_{3'4'}$), 2.0 ($J_{4'5'}$), 0.7 ($J_{3'5'}$)
2t	222 (4.35), 256 (4.60)	2205	1130, 1150, 1340 (ν_{SO_2})	7.44	7.55	7.85 (m)	4.0	—
2u	229 (4.39), 259 (4.55)	2205	1130, 1155, 1330 (ν_{SO_2})	7.36	7.51	2.38 (s, CH_3); 7.40 (d, *m*-H); 7.85 (d, *o*-H)	4.0	8.00 ($J_{o,m}$)

EXPERIMENTAL

The IR spectra of the synthesized compounds were recorded in Vaseline oil on a UR-20 spectrometer. The UV spectra were recorded in ethanol on a Specord UV-vis spectrometer. The ^{1}H NMR spectra were obtained on a Tesla BS-467 spectrometer (60 MHz) in hexadeuteroacetone for compounds **2a**,**b**,**e**,**g**,**j**,**k** and in carbon tetrachloride for compounds **2c**,**f**,**h**,**i**,**e**,**u** with HMDS as internal standard. The purity of the compounds was monitored by TLC (Silufol UV-254, ethanol–toluene, 3:20).

The solutions of hydrazoic acid in chloroform were prepared by the method described in [1]; the anhydrone was of pure grade supplied by the Altaikhimprom company.

2-Furonitrile (2a), 5-Methyl-2-furonitrile (2b), 5-Phenyl-2-furonitrile (2c), 5-Phenylethynyl-2-furonitrile (2d), 5-Bromo-2-furonitrile (2e), 5-Iodo-2-furonitrile (2f), 5-Nitro-2-furonitrile (2g), 5-Chloromethyl-2-furonitrile (2h), 5-(4-Nitrophenyl)-2-furonitrile (2i), 5-(4-Methylphenoxy)-2-furonitrile (2j), 5-(4-Chlorophenoxy)-2-furonitrile (2k), 5-Methylthio-2-furonitrile (2l), Ethyl S-(5-Cyano-2-furyl)thioglycolate (2m), 5-(2,4-Dinitrophenylthio)-2-furonitrile (2n), 5-(5-Cyano-2-furylthio)-2-furonitrile (2o), 5-(5-Oxo-2,5-dihydro-2-furylthio)-2-furonitrile (2p), S-(5-Cyano-2-furyl) Thiobenzoate (2q), S-(5-Cyano-2-furyl) 3-Bromothiobenzoate (2r), S-(5-Cyano-2-furyl) 2-Thiofuroate (2s), 5-Phenylsulfonyl-2-furonitrile (2t), 5-(4-Methylphenylsulfonyl)-2-furonitrile (2u) (General Procedure). In a three-necked flask with a mechanical stirrer and a reflux condenser to the initial furfural (0.1 mol) and a solution of hydrazoic acid in chloroform (0.11 mol) anhydrone (25.0 g, 0.1 mol) was added. The release of gaseous nitrogen began after 5 min. The flow of nitrogen became strongest after 10-15 min. When the release of nitrogen had stopped the reaction mixture was brought to boiling point and kept for 2 h. The contents of the flask were cooled to room temperature, water was added, and the mixture was filtered. The organic layer was washed twice with water, dried with anhydrous sodium sulfate, and evaporated. The residue was distilled under vacuum or recrystallized from ethanol. Compound **2g** was recrystallized from a mixture of chloroform and hexane, and compound **2p** from carbon tetrachloride.

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