Substituted 5-phenoxy-2-furaldehydes and their derivatives

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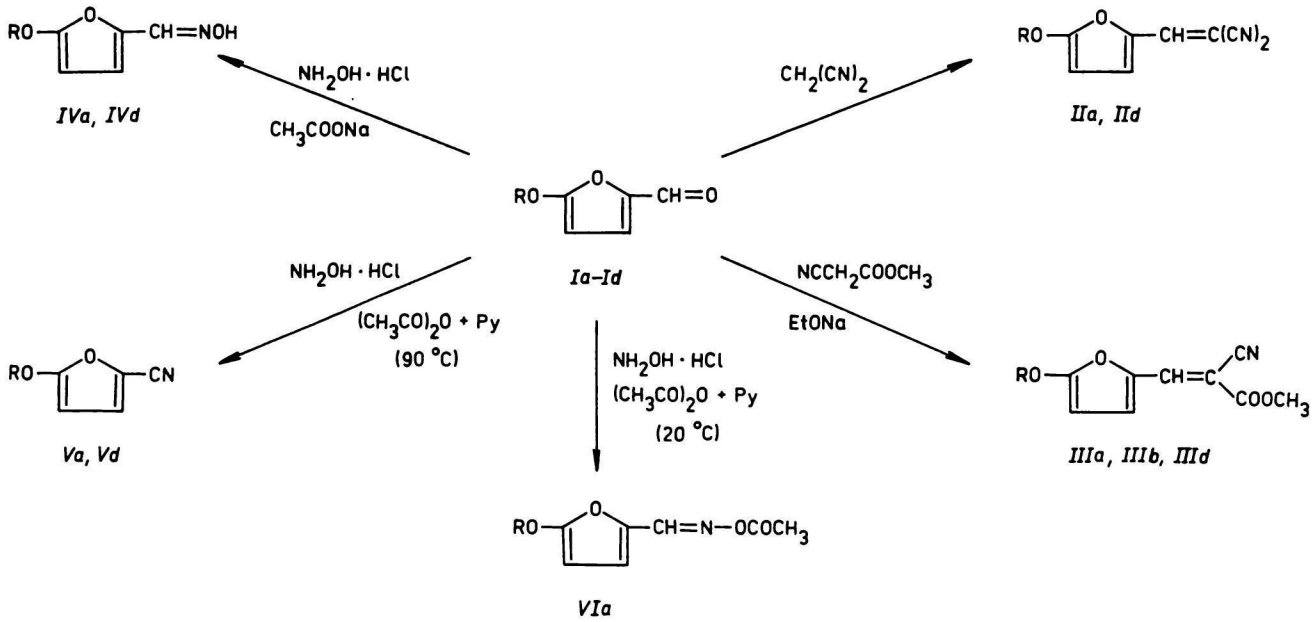
Dedicated to Associate Professor Dr. Ing. Š. Kováč, CSc., in honour of his 60th birthday

The preparation of substituted 5-phenoxy-2-furaldehydes (*I*) by the reaction of substituted sodium phenoxides with 5-bromo-2-furaldehyde is described. Reactions of *I* with malonic acid dinitrile afforded substituted 2-cyano-3-(5-phenoxy-2-furyl)acrylonitriles and with methyl cyanoacetate substituted methyl 2-cyano-3-(5-phenoxy-2-furyl)acrylates were obtained. By the reaction of compounds *I* with hydroxylammonium chloride different products were obtained in dependence on the reaction conditions.

Описано получение замещенных 5-фенокси-2-фуральдегидов (*I*), синтезированных путем реакции замещенных феноксидов натрия с 5-бром-2-фуральдегидом. Взаимодействие *I* с динитрилом малоновой кислоты вело к образованию замещенных 2-циано-3-(5-фенокси-2-фурил)акрилонитрилов, а с метилцианоацетатом к образованию замещенных метил-2-циано-3-(5-фенокси-2-фурил)акрилатов. При взаимодействии соединений *I* с солянокислым гидроксиламином образовывались в зависимости от реакционных условий различные продукты.

In the area of novel chemical means with herbicidal activity in the last few years, considerable attention has been drawn to the synthesis of diphenyl ethers. Recently few series of this type of compounds have been published [1—6]. This paper deals with the synthesis of heterocyclic analogues of diphenyl ethers having 5-substituted 2-furyl residue instead of the phenyl one (Scheme 1). The preparation of 5-(2-nitrophenoxy)-2-furaldehyde by the reaction of sodium 2-nitrophenoxide with 5-bromo-2-furaldehyde in dimethyl sulfoxide was described [7, 8]. In this communication we extended our study to di- to tetrasubstituted phenoxyfurans starting from the herbicidally active phenols.

The starting 5-bromo-2-furaldehyde in reaction with the substituted sodium phenoxides in dimethyl sulfoxide gave the substituted 5-phenoxy-2-furaldehydes. The yield of this reaction was influenced by features of substituents attached to the benzene ring. In case of the use of 3,4,6-trichloro-2-nitro-



For compounds *a* R = 2,4,5-trichlorophenyl
b R = 2-chloro-4-nitrophenyl
c R = 3,4,6-trichloro-2-nitrophenyl
d R = 4-chloro-2-methylphenyl

Scheme 1

phenoxide, 5-(3,4,6-trichloro-2-nitrophenoxy)-2-furaldehyde was obtained in 8 % yield. If pentasubstituted phenoxide with two nitro groups attached to the benzene ring, *i.e.* 2,3,5-trichloro-4,6-dinitrophenoxide, was used, yield of this reaction was very low (< 5 %) and the starting compounds were isolated. The reason of the unsuccessful reactions when using tetra- and pentasubstituted phenoxides lies in the low nucleophility of the corresponding phenoxide anions. The preparation of sodium phenoxides was realized in dimethyl sulfoxide, in the same conditions the second step of the reaction was realized as well. The best yield was obtained with 4-chloro-2-methylphenoxide.

The reaction of aldehydes *Ia—Id* with malonic acid dinitrile afforded substituted 2-cyano-3-(5-phenoxy-2-furyl)acrylonitriles (*IIa* and *IId*), with methyl cyanoacetate substituted methyl 2-cyano-3-(5-phenoxy-2-furyl)acrylates (*IIIa*, *IIIb*, *IIId*). By the reaction of compounds *I* with hydroxylammonium chloride corresponding oximes were prepared. If the reaction with hydroxylammonium chloride was realized in acetic anhydride in the presence of pyridine at 90 °C substituted 5-phenoxy-2-furyl cyanides were obtained. In the same conditions at room temperature *O*-acetylated oxime was isolated (*VIa*). The prepared substituted 5-phenoxy-2-furaldehydes and their derivatives are summarized in Table 1. The structure of all the studied compounds was proved by ^{1}H NMR data (Table 2).

Fungicidal activity of the prepared compounds was examined according to the previously published methods [9]. In laboratory conditions by the diffusive method *in vitro* on the model micromycetes, the antifungal activity of the compounds *Ia*, *Ib*, *Id*, *IIa*, *IIIa*, *IVd*, *Vd* was revealed. All active compounds were advanced to further screening. None of the prepared compounds in standard test methods [10] on herbicidal activity reached the activity of the used standards.

Experimental

The ^{1}H NMR spectra were recorded with a Tesla BS 487 C apparatus operating at 80 MHz. Tetramethylsilane was used as internal reference.

5-Bromo-2-furaldehyde was prepared according to [11].

Substituted 5-phenoxy-2-furaldehydes (Ia—Id)

To substituted sodium phenoxide, prepared by reaction of substituted phenol (0.1 mol) and sodium (2.3 g; 0.1 mol) in dimethyl sulfoxide (50 cm^3), melted 5-bromo-2--furaldehyde (17.5 g; 0.1 mol) was added under stirring at 90 °C. The reaction mixture was stirred at 90 °C for 7 h and poured into ice water. The separated precipitate was

Table 1

Characterization of the prepared compounds

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%				Yield	M.p.
			C	H	Cl	N	%	°C
Ia	$C_{11}H_5Cl_3O_3$	291.5	45.32	1.73	36.47		75	110—111
			45.42	1.75	36.35			
Ib	$C_{11}H_6ClNO_5$	267.6	49.37	2.26	13.25	5.23	30	100—105
			49.40	2.30	13.28	5.42		
Ic	$C_{11}H_4Cl_3NO_5$	336.5	39.26	1.20	31.61	4.16	8	125—127
			39.24	1.22	31.60	4.20		
Id	$C_{12}H_9ClO_3$	236.6	60.92	3.82	14.98	—	92	46—47
			60.88	3.80	14.86			
IIa	$C_{14}H_5Cl_3N_2O_2$	339.6	49.52	1.48	31.13	8.25	82	158—160
			49.54	1.50	31.12	8.33		
IId	$C_{15}H_9ClN_2O_2$	284.7	63.22	3.18	12.45	9.83	88	158—160
			63.28	3.24	12.40	9.85		
IIIa	$C_{15}H_8Cl_3NO_4$	372.6	48.35	2.16	28.54	3.76	92	182—185
			48.28	2.14	28.65	4.26		

Table 1 (Continued)

Compound	Formula	M_r	w_i(calc.)/% w_i(found)/%				Yield	M.p.
			C	H	Cl	N	%	°C
IIIb	$C_{15}H_9ClN_2O_6$	348.7	51.67	2.60	10.17	8.03	86	180—183
			51.57	2.62	10.00	8.09		
IIId	$C_{16}H_{12}ClNO_4$	317.5	60.47	3.80	11.16	4.40	94	116—117
			60.45	3.68	11.20	4.32		
IVa	$C_{11}H_6Cl_2NO_3$	306.5	43.10	1.97	34.69	4.57	90	164—167
			43.02	1.94	34.89	4.70		
IVd	$C_{12}H_{10}ClNO_3$	251.7	57.27	4.00	14.09	5.56	72	138—141
			57.20	3.99	14.03	5.46		
Va	$C_{11}H_4Cl_2NO_2$	288.5	45.79	1.40	36.86	4.85	78	55—56
			45.82	1.38	36.64	4.75		
Vd	$C_{12}H_8ClNO_2$	233.6	61.69	3.45	15.17	5.99	88	50—51
			61.70	3.52	15.10	6.02		
VIa	$C_{13}H_8Cl_3NO_4$	348.6	44.79	2.31	30.51	4.02	82	147—148
			44.80	2.27	30.61	4.26		

Table 2

^{1}H NMR spectral data (δ/ppm) of the synthesized compounds

Compound	H-3 (d)	H-4 (d)	CH= (s)	H_{ar}	Others
Ia	7.60	5.97	9.36	7.94 s, 8.10 s	—
Ic	7.59	6.08	9.40	8.49 s	—
Id	7.56	5.73	9.35	7.45 m, 7.10—7.42 m	2.12 (CH_3)
IIa	7.50	6.13	8.07	8.03 s, 8.07 s	—
IId	7.51	5.86	8.03	7.48 m, 7.23—7.48 m	2.12 (CH_3)
IIIa	7.56	6.06	8.00	8.03 s, 8.10 s	3.80 (CH_3)
IIIb	7.60	6.23	8.04	8.55 d, 8.30 dd, 7.75 d	3.80 (CH_3)
IIId	7.55	5.80	7.97	7.51—7.30 m	3.80 (CH_3) 2.22 (CH_3)
IVa	7.19	5.91	7.39	8.02 s, 7.62 s	11.75 (OH)
IVd	7.18	5.67	7.36	7.35 m, 6.96—7.33 m	2.22 (CH_3)
Va	7.63	6.02	—	8.02 s, 7.92 s	—
Vd	7.59	5.76	—	7.42 m, 7.10—7.42 m	2.22 (CH_3)
VIa	7.09	5.95	8.43	7.79 s, 8.08 s	2.12 (CH_3)

a) Measured in hexadeuteriodimethyl sulfoxide, $J_{3,4}$ = 3.8 Hz.

filtered off and distilled with water stream. After cooling the residue was filtered off and crystallized from ethanol. Similarly were prepared: 2-chloro-4-nitrophenoxy-2-furaldehyde (*Ib*), 3,4,6-trichloro-2-nitrophenoxy-2-furaldehyde (*Ic*), and 4-chloro-2-methylphenoxy-2-furaldehyde (*Id*).

Substituted 2-cyano-3-(5-phenoxy-2-furyl)acrylonitriles (IIa, IId)

To the substituted 5-phenoxy-2-furaldehyde (0.01 mol) in ethanol (20 cm^3) the malonic acid dinitrile (0.78 g; 0.01 mol) and 10 % sodium ethoxide (5 drops) were added. The reaction mixture was stirred for 1 h. The separated precipitate was filtered off and crystallized from ethanol.

Substituted methyl 2-cyano-3-(5-phenoxy-2-furyl)acrylates (IIIa, IIIb, IIId)

The selected compounds *I* (0.01 mol) in ethanol (20 cm^3), methyl cyanoacetate (0.5 g; 0.05 mol), and 10 % sodium ethoxide in ethanol (3 drops) were stirred for 1 h. The separated precipitate was filtered off and crystallized from ethanol.

Substituted 5-phenoxy-2-furaldehyde oximes (IVa, IVd)

I (0.01 mol) in ethanol (20 cm^3), hydroxylammonium chloride (1.12 g; 0.014 mol), and sodium acetate (0.55 g; 0.007 mol) in water (15 cm^3) were refluxed for 1 h. The reaction mixture was concentrated to a half-volume. The separated precipitate was filtered off and crystallized from ethanol.

Substituted 5-phenoxy-2-furyl cyanides (Va, Vb)

To the mixture of *I* (0.01 mol), pyridine (8 cm^3), and hydroxylammonium chloride (1.2 g; 0.017 mol) acetic anhydride (5.5 cm^3; 0.05 mol) was added under stirring at 95 °C. The reaction mixture was kept at 85—95 °C for 2 h, cooled and poured on ice. The separated precipitate was filtered off and crystallized from ethanol.

O-Acetyl-5-(2,4,5-trichlorophenoxy)-2-furaldehyde oxime (VIa)

To the mixture of *Ia* (2.9 g; 0.01 mol), pyridine (8 cm^3), and hydroxylammonium chloride (1.2 g; 0.017 mol) acetic anhydride (5.5 cm^3; 0.05 mol) was added under stirring at room temperature. After pouring into water the separated precipitate was filtered off and crystallized from ethanol.

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