

CONDENSATION REACTIONS OF FURYSULFONYLACETONITRILE WITH ALDEHYDES*

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Using the reaction of furylsulfonylacetonitrile with 4-X-substituted benzaldehydes (where X = NO₂, Cl, Br, I, F, CH₃, N(CH₃)₂, NHCOCH₃, H, CN, OCH₃ and OH), with 5-X-2-furaldehydes (X = NO₂, CH₃, H, N(CH₃)₂, I, Br, Cl, COOCH₃), with 5-(4-X-phenyl)-2-furaldehydes (X = NO₂, CH₃, H, NHCOCH₃, OCH₃, COOC₂H₅, Br, Cl) and with 5-(4-X-phenylthio)-2-furaldehydes (X = NO₂, Cl, Br, CH₃CONH, H, CH₃, CH₃O) corresponding α,β -unsaturated sulfones were prepared. The kinetics of this condensation reaction was investigated and the transfer effect of the influence of the substituent *via* the furan, phenylfuran, phenylthiofuran and benzene nucleus on the reaction centre is discussed on the basis of the correlation dependences of log *k'* on Hammett's σ_p constants.

Generally, for the preparation of α,β -unsaturated sulfones the condensation reaction of carbonyl compounds with compounds of general formula R—SO₂—CH₂—X is used, where R is alkyl, aryl, or heteroaryl and X is an electron accepting group such as COOH, COOR, CN, SO₂R, or a heterocyclic systems^{1,2}. Dressler and Graham³ investigated the course of the Knoevenagel condensation of arylsulfonylacetonitriles with aromatic aldehydes under various reaction conditions in detail. Best catalytic effect was found in piperidine and potassium tert-butoxide in benzene or toluene, as well as in ammonium acetate in glacial acetic acid.

For the preparation of α,β -unsaturated sulfones of the furan series the reaction of furylsulfonylacetonitrile with 4-substituted benzaldehydes, 5-substituted 2-furaldehydes, 5-(4-X-phenyl)-2-furaldehydes and 5-(4-X-phenylthio)-2-furaldehydes was made use of in this study. The reaction was carried out in ethanol in the presence of sodium ethoxide, or piperidine in acetic acid, using ammonium acetate and benzylamine as catalyst. Both methods afford corresponding sulfones in 70–85% yield (Table I). The so far undescribed furylsulfonylacetonitrile was prepared by alkylation of lithium 2-furysulfinate with chloroacetonitrile in dimethylformamide or dimethyl sulfoxide, by refluxing the mixture for 6 hours.

Furysulfonylacetonitrile displays in its electronic absorption spectrum four maxima, at 221 nm (log ϵ 3.99), 261 nm (2.88), 267 nm (3.04), and 274 nm (2.96),

* Part LXXX in the series Furan Derivatives; Part LXXIX: This Journal 42, 105 (1977).

TABLE I
Condensation Products of Furylsulfonylacetonitrile with Aldehydes

No X	Formula (m.w.)	M.p., °C yield, %	Calculated/Found				ν_{CN} , cm^{-1}
			% C	% H	% N	% S	
2-(2-Furylsulfonyl)-3-(4-X-phenyl)acrylonitriles							
H	1 $\text{C}_{13}\text{H}_9\text{NO}_3\text{S}$ (259.2)	124—125 ^a	60.24	3.50	5.40	12.33	2 221
		69	60.16	3.37	5.23	12.12	
CH ₃	2 $\text{C}_{14}\text{H}_{11}\text{NO}_3\text{S}$ (273.2)	138—140 ^a	61.55	4.06	5.13	11.72	2 220
		71	61.39	3.94	5.26	11.84	
OH	3 $\text{C}_{13}\text{H}_9\text{NO}_4\text{S}$ (275.2)	220—222 ^b	56.74	3.30	5.09	11.62	2 220
		80	56.55	3.23	5.14	11.48	
OCH ₃	4 $\text{C}_{14}\text{H}_{11}\text{NO}_4\text{S}$ (289.2)	113—115 ^b	58.14	3.83	4.89	11.06	2 220
		63	57.96	3.67	4.81	10.58	
N(CH ₃) ₂	5 $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_3\text{S}$ (302.2)	196—198 ^b	59.62	4.67	9.24	10.58	2 215
		89	59.48	4.55	9.30	10.49	
CH ₃ CONH	6 $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$ (316.2)	230—232 ^b	56.98	3.83	4.43	10.01	2 220
		90	56.77	3.68	4.56	9.84	
F	7 $\text{C}_{13}\text{H}_8\text{FNO}_3\text{S}$ (277.2)	128—130 ^a	56.33	2.91	5.06	11.53	2 222
		78	56.16	2.84	5.10	11.38	
Cl	8 $\text{C}_{13}\text{H}_8\text{ClNO}_3\text{S}$ (293.6)	141—143 ^a	53.18	2.75	4.78	10.93	2 220
		61	52.94	2.66	4.82	10.73	
Br	9 $\text{C}_{13}\text{H}_8\text{BrNO}_3\text{S}$ (338.1)	132—134 ^a	46.18	2.39	4.14	9.47	2 221
		70	45.88	2.24	4.26	9.29	
I	10 $\text{C}_{13}\text{H}_8\text{INO}_3\text{S}$ (385.1)	118—120 ^b	40.55	2.09	3.63	8.33	2 221
		73	40.31	1.98	3.64	8.35	
CN	11 $\text{C}_{14}\text{H}_8\text{N}_2\text{O}_3\text{S}$ (284.2)	188—190 ^b	59.17	2.84	9.86	11.30	2 230
		74	58.87	2.73	10.00	11.10	
NO ₂	12 $\text{C}_{13}\text{H}_8\text{N}_2\text{O}_5\text{S}$ (304.2)	158—160 ^b	51.33	2.65	9.22	10.52	2 220
		60	51.26	2.52	9.48	10.28	
2-(2-Furylsulfonyl)-3-(5-X-2-furyl)acrylonitriles							
H	13 $\text{C}_{11}\text{H}_7\text{NO}_4\text{S}$ (249.2)	78—79 ^a	53.02	2.83	5.62	12.87	2 222
		82	52.87	2.71	5.49	12.69	
CH ₃	14 $\text{C}_{12}\text{H}_9\text{NO}_4\text{S}$ (263.2)	129—130 ^a	54.76	3.45	5.32	12.18	2 222
		60	54.71	3.38	5.16	12.04	
N(CH ₃) ₂	15 $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$ (292.3)	200—201 ^a	53.42	4.14	9.58	10.97	2 210
		50	53.26	4.09	9.62	10.92	

TABLE I
(Continued)

No X	Formula (m.w.)	M.p., °C yield, %	Calculated/Found				ν_{CN} , cm^{-1}
			% C	% H	% N	% S	
2-(2-Furylsulfonyl)-3-(5-X-2-furyl)acrylonitriles							
Cl	$\text{C}_{11}\text{H}_6\text{ClNO}_4\text{S}$ (283.6)	130—132 ^a	46.59	2.13	4.94	11.31	2 222
		53.5	46.44	2.06	4.88	11.30	
Br	$\text{C}_{11}\text{H}_6\text{BrNO}_4\text{S}$ (328.1)	160—161 ^a	40.27	1.84	4.27	9.77	2 222
		69	40.25	1.90	4.16	9.62	
I	$\text{C}_{11}\text{H}_6\text{INO}_4\text{S}$ (375.1)	155—156 ^a	35.22	1.61	3.73	8.55	2 224
		66.6	35.26	1.71	3.68	8.41	
COOCH ₃	$\text{C}_{13}\text{H}_9\text{NO}_6\text{S}$ (307.2)	164—165 ^a	50.83	2.95	4.56	10.44	2 228
		83	50.65	2.91	4.48	10.37	
NO ₂	$\text{C}_{11}\text{H}_6\text{N}_2\text{O}_6\text{S}$ (294.2)	156—158 ^a	44.91	2.06	9.52	10.90	2 225
		73.5	44.82	2.02	9.47	10.80	
2-(2-Furylsulfonyl)-3-(5-(4-X-phenyl)-2-furyl)acrylonitriles							
H	$\text{C}_{17}\text{H}_{11}\text{NO}_4\text{S}$ (325.3)	162—163 ^a	62.77	3.41	4.31	9.86	2 216
		67	62.96	3.56	4.22	9.76	
CH ₃	$\text{C}_{18}\text{H}_{13}\text{NO}_4\text{S}$ (339.4)	173—175 ^b	63.70	3.86	4.13	9.45	2 216
		65	63.44	3.96	4.08	9.54	
CH ₃ O	$\text{C}_{18}\text{H}_{13}\text{NO}_5\text{S}$ (355.4)	171—173 ^b	60.83	3.69	3.94	9.02	2 216
		78	60.64	3.89	4.05	9.11	
CH ₃ CONH	$\text{C}_{19}\text{H}_{14}\text{N}_2\text{O}_5\text{S}$ (382.4)	262—264 ^b	59.68	3.69	7.33	8.39	2 215
		82	59.63	3.87	7.28	8.41	
Cl	$\text{C}_{17}\text{H}_{10}\text{ClNO}_4\text{S}$ (359.8)	210—211 ^a	56.75	2.80	3.89	8.91	2 220
		67	56.67	2.63	3.76	8.78	
Br	$\text{C}_{17}\text{H}_{10}\text{BrNO}_4\text{S}$ (404.4)	219—221 ^a	50.49	2.49	3.46	7.93	2 215
		63	50.17	2.56	3.52	7.90	
COOC ₂ H ₅	$\text{C}_{20}\text{H}_{15}\text{NO}_6\text{S}$ (397.4)	235—236 ^a	60.45	3.80	3.52	8.07	2 220
		84	60.23	4.00	3.48	8.16	
NO ₂	$\text{C}_{17}\text{H}_{10}\text{N}_2\text{O}_6\text{S}$ (370.3)	239—241 ^a	55.14	2.72	7.56	8.66	2 220
		79	55.21	3.00	7.62	8.75	
2-(2-Furylsulfonyl)-3-(5-(4-X-phenylthio)-2-furyl)arylonitriles							
H	$\text{C}_{17}\text{H}_{11}\text{NO}_4\text{S}_2$ (357.3)	74—75 ^a	57.15	3.10	3.92	17.95	2 220
		58	56.98	2.96	3.74	17.77	
CH ₃	$\text{C}_{18}\text{H}_{13}\text{NO}_4\text{S}_2$ (371.3)	144—145 ^a	58.23	3.53	3.77	17.27	2 222
		61	58.16	3.48	3.56	17.08	

TABLE I
 (Continued)

No X	Formula (m.w.)	M.p., °C yield, %	Calculated/Found				ν_{CN} , cm^{-1}
			% C	% H	% N	% S	
2-(2-Furylsulfonyl)-3-(5-(4-X-phenylthio)-2-furyl)acrylonitriles							
31 CH ₃ O	C ₁₈ H ₁₃ NO ₅ S ₂ (387.3)	105–106 ^a 53.5	55.82 55.65	3.38 3.21	3.62 3.48	16.56 16.48	2 220
32 CH ₃ CONH	C ₁₉ H ₁₄ N ₂ O ₅ S ₂ (414.3)	170–171 ^a 65.5	55.08 54.82	3.41 3.27	6.76 6.65	15.48 15.36	2 205
33 Cl	C ₁₇ H ₁₀ ClNO ₄ S ₂ (391.7)	147–148 ^a 63	52.13 52.11	2.57 2.46	3.58 3.44	16.37 16.05	2 220
34 Br	C ₁₇ H ₁₀ BrNO ₄ S ₂ (436.2)	168–169 ^a 69	46.81 46.72	2.31 2.22	3.21 3.08	14.70 14.50	2 222
35 NO ₂	C ₁₇ H ₁₀ N ₂ O ₆ S ₂ (402.3)	147–148 ^a 72.5	50.75 50.68	2.51 2.42	6.96 6.82	15.94 15.75	2 224

^a Crystallized from ethanol; ^b from chloroform.

which correspond to electronic transitions localized in the furan nucleus (or the CN group). In comparison with the UV spectrum of furan itself these bands are shifted bathochromically under the effect of the substituent in the position 2 of furan — similarly as in the case of the aldehyde group. In the UV spectra of the condensation products of furylsulfonylacetonitrile with various types of aldehydes mostly three or four absorption maxima appear. In the case of 1-furylsulfonyl-1-cyano-2-(4-X-phenyl)-ethylenes (Table II, compounds 1–12) the K-band appears in the 302–355 nm region. Its position is distinctly influenced by the substituents in the position 4 of benzene. The electron donating substituents shift it strongly bathochromically (for example OCH₃ by 43 nm, OH by 46 nm, NHCOCH₃ by 48 nm) as compared with the parent derivative. In the case of dimethyl derivative this band even reaches into the visible region, with λ_{max} 426 nm, owing to the presence of the dimethylamino group which enhances the strongly polar structure (Scheme 1). The exchange of the benzene ring in the condensation products for a furan ring (Table II, com-



SCHEME 1

TABLE II
UV Spectra of Derivatives and Rate Constants of Corresponding Condensation Reactions

No	λ_{\max} , nm (log ϵ)		$k' \cdot 10^4$, s ⁻¹	$t_{1/2}$, s	
1	206 (4.22)	224 (4.17)	307 (4.42)	1.83	3 786.8
2	206 (4.32)	232 (4.25)	320 (4.55)	1.50	4 620.0
3	207 (4.15)	242 (4.14)	353 (4.50)	1.24	2 851.8
4	208 (4.34)	240 (4.36)	350 (4.68)	1.27	5 456.7
5	205 (4.26)	268 (4.04)	426 (4.70)	0.30	23 100.0
6	207 (4.28)	242 (4.16)	355 (4.52)	1.09	6.357.8
7	205 (4.23)	228 (4.42)	310 (4.42)	1.52	4 559.2
8	208 (4.11)	228 (4.23)	310 (4.59)	1.57	4 414.0
9	206 (4.14)	230 (4.15)	318 (4.41)	1.91	3 628.2
10	204 (4.42)	236 (4.23)	330 (4.46)	2.43	2 851.8
11	203 (4.22)	228 (4.26)	303 (4.30)	3.30	2 100.0
12	205 (4.51)	218 (4.46)	308 (4.44)	4.34	1 596.7
13	206 (4.11)	238 (3.81)	341 (4.45)	10.98	631.1
14	206 (4.20)	240 (3.78)	360 (4.47)	8.20	845.1
15	208r (4.23)	230; 277r (4.30; 3.75)	465 (4.61)	3.09	2 242.7
16	206 (4.19)	234r (3.99)	349 (4.41)	16.72	414.7
17	207 (4.23)	239r (3.86)	354 (4.48)	10.28	674.1
18	207; 231r (4.20; 4.09)	273r (3.56)	365 (4.53)	10.12	684.7
19	207; 219 (4.24; 4.27)	—	341 (4.51)	18.95	365.7

TABLE II
 (Continued)

No	λ_{\max} , nm (log ϵ)		$k' \cdot 10^4$, s ⁻¹		$t_{1/2}$, s	
20	208 (4.09)	246 (4.06)	350—1 (4.32)		28.17	246.0
21	206 (4.30)	239 (4.23)	252 (4.30)	402 (4.47)	2.42	2 863.0
22	212 (4.30)	243 (4.23)	258 (4.29)	410 (4.49)	2.08	3 331.0
23	210 (4.30)	243 (4.15)	272 (4.23)	428 (4.43)	2.14	3 238.3
24	210 (4.49)	249 (4.23)	282 (4.41)	406 (4.57)	2.45	2 828.5
25	210 (4.33)	241 (4.28)	257 (4.36)	402 (4.56)	2.76	2 510.2
26	205 (4.40)	243 (4.26)	266 (4.38)	405 (4.56)	2.99	2 317.7
27	210 (4.36)	247 (4.28)	262 (4.39)	400 (4.60)	3.69	1 878.0
28	210 (3.99)	230 (3.92)	275 (3.71)	402 (4.21)	6.11	1 134.2
29	205 (4.39)	240 (4.14)	395 (4.32)		7.45	930.2
30	206 (4.39)	222; 242r (4.31; 4.15)	— —	405 (4.36)	8.37	827.9
31	204 (4.38)	233; 272r (4.34; 3.83)	— —	408 (4.39)	7.25	955.8
32	207 (4.26)	232; 275 (4.42; 3.76)	— —	407 (4.95)	9.8	707.1
33	206 (4.44)	226; 243 (4.30; 4.22)	391 (4.36)		10.52	658.7
34	204 (4.53)	231; 252r (4.40; 4.22)	390 (4.38)		13.52	512.5
35	210 (4.37)	238r (4.35)	303r; 357 (4.39; 4.41)		21.38	324.1

pounds 13–20) causes a substantial bathochromic shift of this band, equally as in the case of two other series of the condensation products (Table II, compounds 21–28, 29–35) in which the K-band also reaches into the visible region of the spectrum.

The above mentioned condensation reactions were also investigated by kinetic measurements with the aim of judging the influencing of the reaction rate on the carbonyl group by the substituent X in the position 4 of the benzene, phenylfuran, phenylthiofuran nucleus, or in the position 5 of the furan nucleus. The time dependence of this reaction was measured spectrophotometrically in the K-band region of the condensation product formed. The kinetic measurements were carried out in a methanolic solution of piperidine under the conditions of pseudomonomolecular reaction, using an excess of furylsulfonylacetonitrile which under the conditions of high concentrations of piperidine appears in a completely ionized form, while the formation of the carbanion of furylsulfonylacetonitrile itself is a very rapid reaction, in fact not measurable under our conditions. The pK_a value for the hydrogen atoms of the methylene group was also measured spectrophotometrically, and it was 12.75. From the correlation of $\log k'$ and the σ_p constants (Fig. 1)

$$\rho \text{ benzene series} = 0.61 \quad (r = 0.93, n = 12)$$

$$\rho \text{ furan series} = 0.58 \quad (r = 0.95, n = 8)$$

$$\rho \text{ arylfuran series} = 0.46 \quad (r = 0.96, n = 8)$$

$$\rho \text{ arylthiofuran series} = 0.43 \quad (r = 0.95, n = 7)$$

it follows that the greatest effect on the reaction centre — *i.e.* the carbonyl group — is displayed through the benzene, then the furan system, and the lowest effect — approximately equal — is displayed through the arylfuran or arylthiofuran system. However, as evident from the measured rate constants of the reaction of furylsulfonylacetonitrile with the aldehydes of individual series 5-X-2-furylaldehydes enter the

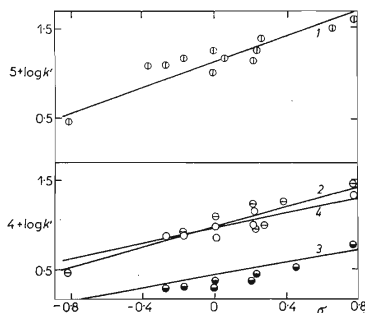


FIG. 1
Dependence of $\log k'$ on σ_p Values of the Reaction of Furylsulfonylacetonitrile with 4-X-Benzaldehydes (1), 5-X-2-Furaldehydes (2), 5-(4-X-Phenyl)-2-furaldehydes (3), and 5-(4-X-Phenylthio)-2-furaldehydes (4)

reaction most willingly. This can be explained by the fact that the reactivity of the carbonyl group of the aldehydes of the furan series is also influenced by the electron-accepting ability of the oxygen heteroatom in the furan nucleus.

EXPERIMENTAL

The 4-substituted benzaldehydes used in this investigation were substances of commercial origin, or they were prepared by known procedures. Among the aldehydes of the furan series only 2-furaldehyde was accessible. Other 5-substituted 2-furaldehydes were synthesized according to literature: 5-methyl- (ref.⁴), 5-bromo- (ref.⁵), 5-chloro- (ref.⁵), 5-iodo-, and 5-methoxycarbonyl- (ref.⁶), 5-nitro- (ref.⁷), 5-dimethylamino- (ref.⁸). Aldehydes of the phenylfuran series, used in our reactions, were prepared by arylation of 2-furaldehyde with appropriately substituted diazonium salts, under the conditions of Meerwein's reaction^{9,10}. 5-(4-X-Phenylthio)-2-furaldehydes were prepared by reacting the corresponding thiolates with 5-bromo- or 5-iodo-2-furaldehyde in ethanol or acetone, respectively.

Preparation of Furylsulfonylacetonitrile

A mixture of 7.5 g (0.1 mol) of chloroacetonitrile, 23 g (0.16 mol) of lithium furylsulfinate, and 50 ml of dimethylformamide was heated under stirring and refluxed at 90°C for 7–8 hours. The reaction mixture was then poured into water and the precipitated platelets were filtered off under suction and recrystallized from ethanol; m.p. 113–115°C, yield 8 g (46.9%). For C₆H₅·NO₃S (171.2) calculated: 42.10% C, 2.94% H, 8.18% N, 18.73% S; found: 42.25% C, 2.90% H, 8.05% N, 18.69% S.

Preparation of Unsaturated Sulfones

Method A: A mixture of 1.71 g (0.01 mol) of furylsulfonylacetonitrile, 0.01 mol of the corresponding aldehyde, 20 ml of ethanol and a catalytic amount of sodium ethoxide or piperidine was heated under stirring at 40°C for 2–3 hours, then poured into 100 g of crushed ice, the precipitated material was filtered off, dried and crystallized from a suitable solvent.

Method B: A mixture of 1.71 g (0.01 mol) of furylsulfonylacetonitrile, 0.01 mol of the corresponding aldehyde, 1.5 g (0.02 mol) of ammonium acetate, 0.1 ml of benzylamine (or piperidine), and 25–40 ml of glacial acetic acid was refluxed for 1–3 hours, then poured onto 100 g of crushed ice, the precipitated dark material was filtered off, dried and crystallized from a suitable solvent.

The synthesized α,β -unsaturated sulfones and their physico-chemical properties are listed in Table I.

Kinetic Measurements

The UV spectroscopic as well as kinetic measurements were carried out on a recording spectrophotometer Specord UV VIS in the 200–800 nm region, in 1 ml cells (temperated). The concentrations of the measured substances (UV spectra) ranged from 2 to 5 · 10⁻⁵ M in methanol. The kinetics of the condensation reaction was measured in reaction mixtures composed of 2 ml of furylsulfonylacetonitrile (resulting concentration in the mixture 2–5 · 10⁻³ M), 0.2–0.5 ml of aldehyde (resulting concentration 2–5 · 10⁻⁵ M), and 7.5 ml of a methanolic piperidine solu-

tion ($c = 5 \cdot 10^{-2} \text{ M}$). The reaction rate measurements were carried out in thermostated cells at $25^\circ \pm 0.2^\circ \text{C}$, at a wave-length corresponding to the K-band of the condensation product formed. The rate constants were calculated from the linear dependence of $\log \Delta E$ on time, using the 1st order kinetic equation.

The UV spectra values of the condensation products, the rate constant values k' (s^{-1}), and half-time values $t_{1/2}$ (s) of the condensation reactions are given in Table II.

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