Novel Trisubstituted Ethylenes and Their Reactions with Nucleophiles

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The preparation of a β-keto sulfone, in particular (phenylsulfonyl)-(2-thienylcarbonyl)methane which was further utilized in condensation reactions with 5-X-2-furancarbaldehydes is described. Reactions of 1-(5-X-2-furyl)-2-(phenylsulfonyl)-2-(thienylcarbonyl)ethylenes formed with nucleophiles were studied. The structure of the prepared derivatives was confirmed by IR, UV, ^{1}H NMR and in some instances also by ^{13}C NMR spectra.

This is a part in the series of papers dealing with furylethylene derivatives which carry three substituents at the ethylene bond [1—5]. We concentrated here on the sulfur-containing 5-X-2-furfurylidene derivatives and their reactions with nucleophiles.

As the starting compound in the synthesis of trisubstituted ethylenes served a β-keto sulfone — (phenylsulfonyl)-(2-thienylcarbonyl)methane — prepared from thiophene by acylation and subsequent bromination, leading to 2-bromoacetylthiophene. The latter, in turn, was treated with sodium benzenesulfinate to give the above β-keto sulfone. This compound contains an active methylene group which makes it, in principle, capable of undergoing a condensation reaction with 5-X-2-furancarbaldehydes affording thereby the 1-(5-X-2-furyl)-2-(phenylsulfonyl)-2-(thienylcarbonyl)ethylenes *I—IV* (Table 1). However, under conditions described for 5-X-2-furfurylsulfones [6—8] the β-keto sulfone failed to undergo a condensation with aldehydes; successful condensation could be achieved under by *Lehnert* [9] modified conditions of the Knoevenagel condensation, namely using $TiCl_4$ and pyridine in tetrahydrofuran. This method furnished the requisite α,β-unsaturated sulfones in fair yields.

Sharp melting points, TLC check and ^{1}H NMR spectral data of condensation products indicate a stereospecific reaction, leading to the formation of a single geometrical isomer. The measured coupling constant $^3J_{CO,H_\alpha}$ = 8.7 Hz suggests a *trans* position of the carbonyl group and the alkene H_α proton, hence all condensation products are *E* isomers [10—14].

The synthesized 1-(5-X-2-furyl)-2-(phenylsulfonyl)-2-(thienylcarbonyl)ethylenes *I—IV* constitute in nucleophilic substitution reactions a substrate with several possible reaction sites. Accordingly, their reactions with nucleophilic reagents were studied under several sets of reaction conditions. Thus treatment with sulfur nucleophiles at laboratory temperature, or with oxygen nucleophiles at boiling point of the solvent gave products *V—XI* of nucleophilic substitution in position 5 of the furan ring in about 50 % yields.

A different behaviour was observed, when compounds *I—IV* were treated with secondary amines. Thus in the reaction with *N*-phenylpiperazine at laboratory temperature derivative *I* was converted within 30 min into 2-bis(*N*-phenylpiperazinyl)methyl-5-bromofuran. In similar reactions with piperidine and diethylamine reactions times up to 3 h were required. A treatment with morpholine and pyrrolidine of the derivative *I* produced after 3 h reaction time tary products from which the corresponding aminals could be isolated by column chromatography, albeit in lower yields.

Derivatives *II—IV* gave aminals only with *N*-phenylpiperazine. In other solvents, such as ethanol, dimethylformamide, dimethyl sulfoxide, the treatment of derivatives *I—IV* at various temperatures and reactions times with nitrogen nucleophiles gave the expected aminals *XII—XV* (Table 4). Apart from aminals the reaction mixtures contained the unreacted substrate and the β-keto sulfone.

The identical results were obtained also by the analysis of the reaction mixture of substitution products *V—XI*; no other products of nucleophilic substitution were discovered.

Reactions of derivatives *II—IV* with other secondary amines were unsuccessful, *i.e.* either starting compounds or intractable tars were isolated.

The structures of the synthesized compounds were elucidated on the basis of spectral data. In infrared spectra (Table 1) vibrations of conjugated carbonyl groups ν(CO) were, as expected, shifted to lower values ($\tilde{\nu}$ = 1650 cm^{-1}). Also typical were the stretching antisymmetric and symmetric vibra-

Table 1. Characterization and IR Spectral Data of 1-(5-X-2-Furyl)-2-(phenylsulfonyl)-2-(thienylcarbonyl)ethylenes

Compound	X	Formula	w_i(calc.)/%	Yield/%	M.p./°C	$\tilde{\nu}$/cm^{-1}		
		M_r	w_i(found)/% S			ν(C=O)	$\nu_{as}(SO_2)$	$\nu_s(SO_2)$
I	Br	$C_{17}H_{11}BrO_4S_2$	15.15	59	158—159	1640	1328	1160
		423.31	15.91					
II	NO_2	$C_{17}H_{11}NO_6S_2$	16.47	38	186—187	1639	1329	1163
		389.41	16.53					
III	Ph—S	$C_{23}H_{16}O_4S_3$	21.25	51	165—166	1650	1310	1156
		452.57	21.60					
IV	Ph—SO_2	$C_{23}H_{16}O_6S_3$	19.85	49	190—191	1652	1338[a]	1172[a]
		484.57	19.97				1322[b]	1152[b]
V	4-Cl—Ph—S	$C_{23}H_{15}ClO_4S_3$	19.75	53	172—173	1645	1320	1148
		489.02	19.93					
VI	4-CH_3CONH—Ph—S	$C_{25}H_{19}NO_5S_3$	18.87	56	180—181	1642[c]	1325	1150
		509.69	19.25			1652[d]		
VII	CH_3—S	$C_{18}H_{14}O_4S_3$	24.63	60	160—161	1650	1330	1160
		390.50	24.69					
VIII	Ph—O	$C_{23}H_{15}O_5S_2$	14.73	59	102—103	1650	1312	1156
		435.50	14.88					
IX	2-NO_2—Ph—O	$C_{23}H_{14}NO_7S_2$	13.35	46	150—151	1650	1324	1160
		480.50	13.64					
X	3-NO_2—Ph—O	$C_{23}H_{14}NO_7S_2$	13.35	42	169—170	1648	1336	1162
		480.50	13.89					
XI	4-NO_2—Ph—O	$C_{23}H_{14}NO_7S_2$	13.35	59	175—177	1652	1335	1160
		480.50	13.41					

a) $PhSO_2$ on ethylene, *b*) $PhSO_2$ on furan, *c*) carbonyl on thiophene, *d*) carbonyl of —$NHCOCH_3$.

tions of the sulfo group at $\tilde{\nu}$ = 1310—1338 and 1148—1172 cm^{-1}, respectively.

The UV spectra (Table 2) display three complex bands at λ = 215—225 nm, 240—275 nm and at 285—310 nm, corresponding to electron transitions in furan, thiophene and the phenylsulfonyl moiety, respectively. In the derivative *II* the longest wavelength maximum at λ = 340 nm belongs to the electron transition from the π-orbitals delocalized over the entire molecule.

The ^{1}H NMR spectra of condensation and substitution products *I*—*XI* (Table 3) show a typical singlet of the ethylene proton at δ = 7.60—7.95. Doublets of the furan protons are found at δ = 6.28—7.50 with $J_{3,4}$ = 4 Hz. Signals of thiophene protons are upfield-shifted due to the presence of a longer conjugated system. In ^{1}H NMR spectra of aminals (Table 4) there are characteristic singlets of alkene protons at δ = 3.6—4.1 and two multiplets of methylene groups of cyclic secondary amines at δ = 1.38—3.32.

^{13}C NMR spectra (Table 5) confirmed in condensation products the presence of a carbonyl group (signals shifted to δ = 181); signals of furan carbons are found at δ = 110—120 and 139—153, respectively. Owing to the effect of the carbonyl group, signals of thiophene carbons are downfield-shifted to δ = 125—140. Similarly, signals of ethylene carbons are found shifted to δ = 134—150.

Table 2. UV Spectral Data of the Compounds *I*—*XI*

Compound	λ_{max}/nm (log (ε/(m^2 mol^{-1})))
I	233 (3.06), 289 (3.35), 305 (3.46)
II	217 (3.21), 245 (3.23), 269 (3.28), 309 (3.29), 340 (3.33)
III	242 (3.38), 273 (3.29), 299 (3.45)
IV	223 (3.26), 234 (3.19), 283 (3.39), 307 (3.52)
V	229 (3.06), 278 (3.26), 303 (3.42)
VI	265 (3.50), 300 (3.35)
VII	216 (3.28), 248 (3.09), 279 (3.35), 300 (3.37)
VIII	241 (3.11), 285 (3.20), 299 (3.41)
IX	235 (3.01), 276 (3.25), 301 (3.42)
X	233 (2.93), 281 (3.15), 303 (3.29)
XI	229 (3.05), 278 (3.24), 303 (3.41)

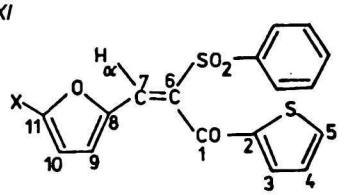
EXPERIMENTAL

^{1}H and ^{13}C NMR spectra of $CDCl_3$ solutions were taken with the spectrometer FX-100 (Jeol) using tetramethylsilane as internal standard. Infrared spectra (KBr discs, 0.8 mg in 300 mg of KBr) were measured with a Specord M 80 (Zeiss, Jena) calibrated with a 25 μm thick polystyrene film. Ultraviolet spectra of methanolic solutions (10^{-4} mol dm^{-3} concentration in a 0.2 cm cell) were taken with a Specord M 40 (Zeiss, Jena).

(Phenylsulfonyl)-(2-thienylcarbonyl)methane

2-Bromoacetylthiophene [15, 16] (0.1 mol in 50 cm^3 of absolute methanol) was added to the

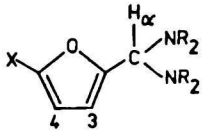
Table 3. ^{1}H NMR Data (δ) of the Compounds *I*—*XI*



Compound	H_α	H-9	H-10	H-3	H-4	H-5	Phenyl	H_X
	s	d	d	d	t	d	m	
I	7.78	7.05	6.58	7.88	7.10	7.58	7.55—7.66 7.90—7.97	
II	7.95	7.26	7.50	7.90	7.13	7.64	7.61—7.70 7.93—7.99	
III	7.79	7.09	6.78	7.85	7.10	7.58	7.53—7.60 7.88—7.93	7.15—7.30 m
IV	7.85	7.31	7.18	7.87	7.12	7.55	7.53—7.61 7.88—7.97	7.55—8.08 m
V	7.62	6.67	6.33	7.73	7.08	7.64	7.51—7.56 7.91—7.95	7.15—7.24 m
VI	7.60	6.72	6.46	7.55	6.99	7.49	7.50—7.54 7.91—7.96	2.11 s, 7.46 m, 7.03—7.35 m
VII	7.70	6.93	6.48	7.79	7.10	7.69	7.50—7.54 7.91—7.95	2.92 s
VIII	7.61	6.37	6.89	7.80	7.08	7.54	7.49—7.62 7.80—7.93	6.92—7.21 m
IX	7.60	6.28	6.64	7.73	7.03	7.47	7.50—7.60 7.92—7.95	7.36—8.11 m
X	7.62	6.65	6.42	7.71	7.08	7.64	7.52—7.60 7.91—7.99	7.33—7.93 m
XI	7.68	6.50	6.91	7.82	7.11	7.64	7.92—7.96 7.51—7.59	7.25—8.14 m

vigorously stirred suspension of sodium benzenesulfinate (0.1 mol in 100 cm^3 of absolute methanol). The reaction mixture was refluxed for 3 h, purified with charcoal, filtered and concentrated *in vacuo* to one third of the original volume. The crystallized solid was filtered off, washed with water and dried. M.p. = 82—83 °C, yield 82 %. For $C_{12}H_{10}O_3S_2$ (M_r = 266.34) w_i(calc.): 24.08 % S; w_i(found): 24.10 % S. IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 1650 ν(CO), 1320 $\nu_{as}(SO_2)$, 1160 $\nu_s(SO_2)$. UV spectrum, λ_{max}/nm (log {ε}): 216 (3.4), 265 (3.4), 272 (3.44), 296 (3.57). ^{1}H NMR spectrum (DMSO-d_6), δ: 5.17 (s, 2H, CH_2), 7.92 (d, 1H, H-3), 7.17 (dd, 1H, H-4), 7.83 (d, 1H, H-5).

Table 4. Characterization of the Aminals



Compound	X	Formula	w_i(calc.)/%	w_i(found)/%	Yield/%	M.p./°C	UV data		^{1}H NMR data (δ)			
							λ_{max}/nm		H_α	H-3	H-4	$H_{heterocycle}$
	NR_2	M_r	N				log (ε/(m^2 mol^{-1}))		s	d	d	m
XII[a]	NO_2	$C_{25}H_{29}N_5O_3$	15.64	54	120—121		217	244	4.10	6.38	6.74	2.52—2.78
	b	447.54	16.08				3.32	3.28				3.24—3.32
XIII	Br	$C_{13}H_{19}BrN_2O_3$	8.46	20	189—190		214	242	3.75	6.37	6.41	2.84—2.95
	c	331.21	8.91				3.11	3.62				3.03—3.18
XIV	Br	$C_{15}H_{23}BrN_2O$	8.56	48	94—95		216	239	3.70	6.25	6.40	1.38—1.60
	d	327.26	9.04				3.15	3.53				2.33—2.50
XV	Br	$C_{13}H_{19}BrN_2O$	9.36	33	117—118		201	244	3.66	6.20	6.47	1.42—1.60
	e	299.21	9.55				3.83	3.59				

a) Ph (6.84—6.94 m, 7.20—7.35 m), $J_{3,4}$ = 3.66—4.11 Hz. *b*) *N*-Phenylpiperazinyl, *c*) morpholinyl, *d*) piperidinyl, *e*) pyrrolidinyl.

Table 5. ^{13}C NMR Data of the Compounds *I—IV*

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11	C_{phenyl}
I	181.20	139.52	136.13	135.97	126.15	149.14	133.76	109.55	121.19	114.86	143.78	138.12, 129.15, 127.56, 128.54
II	181.43	138.33	136.97	135.87	124.73	148.42	136.44	142.73	112.34	118.76	143.00	138.42, 129.88, 127.00, 128.35
III	181.23	139.54	136.48	136.01	126.55	150.92	134.34	143.62	120.63	119.23	149.87	137.92, 129.98, 128.54, 129.17
IV	181.24	140.45	136.49	136.12	125.37	150.98	134.16	142.75	118.43	118.46	152.94	138.56, 129.11, 126.94, 128.66

1-(5-X-2-Furyl)-2-(phenylsulfonyl)-2-(thienylcarbonyl)ethylenes *I—XI*

Condensation Products I—IV

To tetrahydrofuran (THF) (200 cm^3), stirred and cooled to 0 °C, $TiCl_4$ (0.1 mol in 25 cm^3 CCl_4) was added first and then 5-X-2-furancarbaldehyde (0.05 mol) dissolved in THF (25 cm^3) and β-keto sulfone (0.05 mol). The temperature of the reaction mixture was maintained at 0 to −5 °C and within 2 h pyridine (16 cm^3; 0.2 mol) in THF (30 cm^3) was added. The mixture was stirred for another 24 h at 0 °C and poured to 50 cm^3 of water. The aqueous layer was extracted with ether, extracts combined, dried with $MgSO_4$, concentrated until crystallization commenced. The crude product was purified by crystallization from ethanol.

Substitution Products V—XI

5-X-2-Furfurylidene *I—IV* (0.03 mol), dissolved in acetone (20 cm^3), was treated at laboratory temperature with a nucleophilic reagent (0.09 mol). The progress of the reaction was monitored by thin-layer chromatography. After completion (10—72 h) the reaction product was isolated by column chromatography on silica gel, eluted with a benzene—ethyl acetate mixture (φ_r = 2 : 1).

Aminals *XII—XV*

5-X-2-Furfurylidene *I—IV* (0.003 mol) and the nitrogen nucleophile (0.009 mol) were stirred in acetonitrile (ethanol or dimethylformamide, 20 cm^3) at laboratory temperature until a precipitate was formed. The crude product was separated by suction and purified by crystallization from ethanol.

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