

# Furan derivatives. LIX.

## 1,1,2-Trisubstituted ethylenes of 5-nitrofuran series

<sup>a</sup>M. HRDINA, <sup>b</sup>A. JURÁŠEK, and <sup>a</sup>R. FRIMM

<sup>a</sup>Research Institute of Drugs,  
920 01 Hlohovec

<sup>b</sup>Department of Organic Chemistry, Slovak Technical University,  
880 37 Bratislava

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Synthesis of 1-(5-nitro-2-furyl)-1-(4-acetamidophenylsulfonyl)-2-(5-X-furyl)-ethylenes (X = H, CH<sub>3</sub>, Br, I, Cl, NO<sub>2</sub>, SCH<sub>3</sub>, and COOCH<sub>3</sub>) by direct condensation of 5-nitrofurfuryl 4-acetamidophenyl sulfone with 5-substituted furaldehydes is described. Acid hydrolysis of the product afforded 1-(5-nitro-2-furyl)-1-(4-aminophenylsulfonyl)-2-(5-X-furyl)ethylenes which gave 1-(5-nitro-2-furyl)-1-(4-isothiocyanatophenylsulfonyl)-2-(5-X-furyl)-ethylenes by reaction with thiophosgene.

In our previous works we dealt with the preparation and structural study of  $\alpha,\beta$ -unsaturated sulfones of 5-nitrofuran series with phenyl [1, 2] and methyl residues [3], respectively on the SO<sub>2</sub> group.

In this work described derivatives were synthesized with the purpose to find out their biological activities. Molecules of these compounds contain such structural groups which are often present in biologically active compounds, *i.e.* 5-nitrofuran ring bound to ethylene, sulfo, and isothiocyanate groups [4–7].

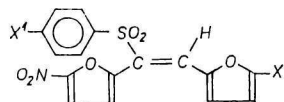
Acetamido derivatives I–VIII were prepared by one-step condensation of 5-nitrofurfuryl 4-acetamidophenyl sulfone with the appropriate 5-substituted furaldehydes in acetic acid or its esters under the catalytic action of acetate salts and amines. Their acid hydrolysis afforded the appropriate amino derivatives which gave the isothiocyanates IX–XVI by reaction with thiophosgene in water–chloroform medium and inert atmosphere.

Physical constants and data of elemental analysis of the prepared compounds are in Table 1. Some compounds showed wide range of melting points, namely compounds IV, VI, and IX. These derivatives were probably mixtures of geometrical isomers *E* and *Z* similarly as was the case with other 1,1,2-trisubstituted ethylene derivatives [1].

Infrared and ultraviolet spectral data are summarized in Table 2. The asymmetric and symmetric vibrations of –NO<sub>2</sub> and –SO<sub>2</sub> groups in the i.r. spectra are most significant for the characterization of these compounds. Bands of  $\nu_{as}(\text{NO}_2)$  appeared as a complex band at 1530–1510 cm<sup>-1</sup> with compounds I–VIII, while with IX–XVI, they were split into a band of medium intensity with a constant position at 1545 cm<sup>-1</sup> and a sharp one of high intensity at 1515–1510 cm<sup>-1</sup>. The band positions of –NO<sub>2</sub> and –SO<sub>2</sub> vibrations were not influenced by the nature of substituents. Compounds IX–XVI showed a broad complex band of high intensity in the region of 2117–2102 cm<sup>-1</sup> with a shoulder at 2200 cm<sup>-1</sup> that was characteristic of –NCS group. All the other bands

Table 1

Characterization of 1-(5-nitro-2-furyl)-1-(4-acetamidophenylsulfonyl)-2-(5-X-furyl)ethylenes *I–VIII* and 1-(5-nitro-2-furyl)-1-(4-isothiocyanatophenylsulfonyl)-2-(5-X-furyl)ethylenes *IX–XVI*



No.	X	X <sup>1</sup>	Formula	M	Calculated/found				Yield [%]	M.p. [°C]
					% C	% H	% N	% S		
<i>I</i>	H	NHCOCH <sub>3</sub>	C <sub>18</sub> H <sub>14</sub> N <sub>2</sub> O <sub>7</sub> S	402.38	53.73 53.87	3.50 3.63	6.96 6.92	7.96 7.92	46	173–176
<i>II</i>	CH <sub>3</sub>	NHCOCH <sub>3</sub>	C <sub>19</sub> H <sub>16</sub> N <sub>2</sub> O <sub>7</sub> S	416.32	54.81 54.79	3.87 3.94	6.72 6.74	7.70 7.63	51	140–142
<i>III</i>	Br	NHCOCH <sub>3</sub>	C <sub>18</sub> H <sub>13</sub> N <sub>2</sub> O <sub>7</sub> SBr	481.29	44.91 45.20	2.72 2.80	5.82 5.90	6.66 6.72	42	167–170
<i>IV</i>	I	NHCOCH <sub>3</sub>	C <sub>18</sub> H <sub>13</sub> N <sub>2</sub> O <sub>7</sub> SI	528.28	40.92 40.63	2.48 2.61	5.30 5.41	6.06 5.96	34	148–158
<i>V</i>	Cl	NHCOCH <sub>3</sub>	C <sub>18</sub> H <sub>13</sub> N <sub>2</sub> O <sub>7</sub> SCl	436.82	49.50 49.34	2.80 2.83	6.41 6.33	7.34 7.43	42	167–169
<i>VI</i>	NO <sub>2</sub>	NHCOCH <sub>3</sub>	C <sub>18</sub> H <sub>13</sub> N <sub>3</sub> O <sub>9</sub> S	447.38	48.32 48.45	2.93 2.99	9.39 9.43	7.16 7.30	37	148–160
<i>VII</i>	SCH <sub>3</sub>	NHCOCH <sub>3</sub>	C <sub>19</sub> H <sub>16</sub> N <sub>2</sub> O <sub>7</sub> S <sub>2</sub>	448.38	50.89 50.71	3.59 3.56	6.24 6.34	14.30 14.25	34	149–155
<i>VIII</i>	COOCH <sub>3</sub>	NHCOCH <sub>3</sub>	C <sub>20</sub> H <sub>16</sub> N <sub>2</sub> O <sub>9</sub> S	460.42	52.17 52.19	3.50 3.57	6.08 6.30	6.96 7.20	56	164–168
<i>IX</i>	H	NCS	C <sub>17</sub> H <sub>10</sub> N <sub>2</sub> O <sub>6</sub> S <sub>2</sub>	402.40	50.74 50.66	2.50 2.42	6.96 6.86	15.93 15.75	28	86–92

Table 1 (Continued)

No.	X	X <sup>1</sup>	Formula	M	Calculated/found				Yield [%]	M.p. [°C]
					% C	% H	% N	% S		
X	CH <sub>3</sub>	NCS	C <sub>18</sub> H <sub>12</sub> N <sub>2</sub> O <sub>6</sub> S <sub>2</sub>	416.43	51.91	2.90	6.72	15.40	30	177–182
					51.80	2.93	6.77	15.31		
XI	Br	NCS	C <sub>17</sub> H <sub>9</sub> N <sub>2</sub> O <sub>6</sub> S <sub>2</sub> Br	481.30	42.42	1.88	5.82	13.32	27	165–172
					42.36	1.97	5.71	13.43		
XII	I	NCS	C <sub>17</sub> H <sub>9</sub> N <sub>2</sub> O <sub>6</sub> S <sub>2</sub> I	528.30	38.64	1.71	5.30	12.31	31	170–175
					38.71	1.78	5.20	12.22		
XIII	Cl	NCS	C <sub>17</sub> H <sub>9</sub> N <sub>2</sub> O <sub>6</sub> S <sub>2</sub> Cl	436.85	46.75	2.08	6.42	14.70	29	175–177
					46.70	2.14	6.53	14.75		
XIV	NO <sub>2</sub>	NCS	C <sub>17</sub> H <sub>9</sub> N <sub>3</sub> O <sub>8</sub> S <sub>2</sub>	447.40	45.64	2.02	9.39	14.33	28	105–110
					45.69	2.10	9.26	14.37		
XV	SCH <sub>3</sub>	NCS	C <sub>18</sub> H <sub>12</sub> N <sub>2</sub> O <sub>6</sub> S <sub>3</sub>	448.49	48.20	2.69	6.24	21.44	30	183–185
					48.13	2.61	6.16	21.52		
XVI	COOCH <sub>3</sub>	NCS	C <sub>19</sub> H <sub>12</sub> N <sub>2</sub> O <sub>8</sub> S <sub>2</sub>	460.44	49.56	2.62	6.08	13.92	28	160–165
					49.51	2.57	6.16	13.79		

Table 2

Ultraviolet and infrared spectral data of the synthesized compounds

No.	$\lambda_{\max}$ [nm]				$\nu_{\text{as}}(\text{NO}_2)$	$\nu_{\text{s}}(\text{NO}_2)$	$\nu_{\text{as}}(\text{SO}_2)$	$\nu_{\text{s}}(\text{SO}_2)$	$\nu(\text{C}-\text{O}-\text{C})$	$\nu_{\text{def}}(\text{C}-\text{H})$
	log $\epsilon$									
I	208	275	313	392 i	1510	1360	1335	1158	1030	900
	4.56	4.51	4.67	3.94						
II	209	274	321	412 i	1530	1360	1332	1158	1040	900
	4.42	4.38	4.53	3.80						
III	211	271	316	405 i	1520	1360	1336	1158	1030	900
	4.59	4.55	4.50	3.68						
IV	210	270	319	407 i	1520	1559	1334	1158	1030	897
	4.57	4.48	4.60	3.92						
V	209	270	315	407 i	1510	1361	1330	1157	1030	892
	4.49	4.38	4.38	3.52						
VI	210	265	317 sh	382 i	1512	1359	1335	1159	1030	900
	4.54	4.48	4.42	4.14						
VII	208	269	323	412 i	1512	1360	1330	1158	1032	896
	4.57	4.50	4.43	3.92						
VIII	208	268	313	368 i	1520	1360	1334	1157	1033	900
	4.51	4.41	4.54	4.07						

Table 2 (Continued)

No.	$\lambda_{\max}$ [nm]			$\nu_{\text{as}}(\text{NO}_2)$	$\nu_{\text{s}}(\text{NO}_2)$	$\nu_{\text{as}}(\text{SO}_2)$	$\nu_{\text{s}}(\text{SO}_2)$	$\nu(\text{C}-\text{O}-\text{C})$	$\nu_{\text{def}}(\text{C}-\text{H})$	$\nu(\text{NCS})$
	log $\epsilon$									
IX	232	290	—	1515	1365	1320	1159	1031	892	2115
	4.44	4.53		1545						
X	232	289	323 i	1515	1369	1320	1159	1032	899	2112
	4.34	4.40	4.20	1545						
XI	231	295	322 sh	1512	1368	1320	1160	1031	900	2115
	4.39	4.49	4.45	1545						
XII	230	301	—	1510	1365	1315	1157	1032	899	2115
	4.32	4.48		1545						
XIII	234	292	325 i	1510	1367	1315	1157	1031	900	2114
	4.41	4.43	4.23	1545						
XIV	231	294	389 i	1511	1364	1319	1158	1031	898	2113
	4.47	4.54	3.47	1545						
XV	232	288	324 i	1510	1364	1318	1158	1031	900	2117
	4.32	4.35	4.19	1545						
XVI	230	313	—	1510	1362	1317	1158	1030	900	2102
	4.30	4.45		1545						

i — inflex; sh — shoulder.

belonged to aliphatic C=C vibrations, vibrations of the furan ring, and  $\nu_{\text{def}}(\text{C-H})$  vibrations, respectively. A characteristic band for furan ring was observed at 900–892  $\text{cm}^{-1}$  with all compounds. The last absorption band in the u.v. spectra appeared in most cases as an inflex or shoulder at 368–412 nm but with compounds IX–XVI (except XIV) at 322–325 nm. The position of this band indicated that the investigated 1,1,2-trisubstituted ethylenes represented in-plane systems [1–3].

### Experimental

5-Nitrofurfuryl 4-acetamidophenyl sulfone was prepared from sodium 4-acetamidobenzenesulfinate and 5-nitrofurfuryl nitrate [8, 9]. Sodium 4-acetamidobenzenesulfinate was obtained from acetanilide [10–12] and 5-nitrofurfuryl nitrate by nitration of furfuryl alcohol [13–15]. 5-Substituted aldehydes of the furan series were synthesized according to [16–22].

Infrared spectra were measured on a UR-20 (Zeiss, Jena) spectrophotometer in NaCl cells of 0.02 mm thickness. The apparatus was calibrated with polystyrene foil. Saturated chloroform solutions of compounds were measured; however, KBr technique was applied to take the spectra of NCS derivatives.

Ultraviolet spectra of compounds I–VIII (ethanol) and compounds IX–XVI (dimethylcellosolve) were measured on a recording Specord UV-VIS (Zeiss, Jena) spectrophotometer in 10-mm cells. The concentration of compounds varied from  $2.5 \times 10^{-5}$  –  $5.0 \times 10^{-5}$  M. The measurement accuracy was  $\pm 1$  nm.

#### *1-(5-Nitro-2-furyl)-1-(4-acetamidophenylsulfonyl)-2-(5-X-furyl)ethylenes* (I–VIII)

To 5-nitrofurfuryl 4-acetamidophenyl sulfone (3.24 g; 0.01 mole) and the appropriate 5-substituted furaldehyde (0.011 mole) in glacial acetic acid (25 ml), ammonium acetate (1.5 g; 0.02 mole) and benzylamine (0.25 ml) were added. This mixture was refluxed for 3 hrs, cooled, and poured onto small pieces of ice (100 g) under vigorous stirring. The formed precipitate was sucked off, washed with water, and dried. The crude product was extracted with chloroform or acetone. After boiling the extract with charcoal, filtration, and addition of ether, petroleum ether, or water, the product was precipitated and purified on a chromatographic column of alumina (Brockmann) in the solvent system ethyl acetate–benzene (2 : 1).

#### *1-(5-Nitro-2-furyl)-1-(4-aminophenylsulfonyl)-2-(5-X-furyl)ethylenes*

Acetamido derivative I–VIII (0.01 mole) in 6 N hydrochloric acid (150 ml) was refluxed for 2 hrs. Charcoal was added to the solution, boiled, and filtered. After cooling the filtrate, the appropriate amines were liberated by addition of ammonium hydroxide to pH 7–8. The precipitate was sucked off, washed with water, dried, and used for preparation of compounds IX–XVI.

#### *1-(5-Nitro-2-furyl)-1-(4-isothiocyanatophenylsulfonyl)-2-(5-X-furyl)ethylenes* (IX–XVI)

Water (250 ml) and chloroform (250 ml) were poured into a 1000-ml three-necked flask provided with a stirrer and a nitrogen inlet. Thiophosgene (2.28 g; 0.02 mole) and calcium carbonate (10 g) were added into the solution under stirring. Then the previously

prepared solution of amino derivative (0.018 mole) in chloroform (150 ml) was added dropwise from a separation funnel. The flask content was stirred for 2 hrs. Charcoal was added to the separated chloroform layer, boiled, and filtered. The filtrate was dried with calcium chloride and after filtration chloroform was distilled off. The solid residue was crystallized from acetone and purified chromatographically as compounds I—VIII.

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