Furan Derivatives. XXIII. Synthesis and Absorption Spectra of 5-(Nitrophenyl)-2-furaldehyde Derivatives

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By condensation of 5-(4-nitrophenyl)-, 5-(3-nitrophenyl)- and 5-(2-nitrophenyl)-2-furaldehydes with various nitrogen bases sixteen furfurylidene derivatives were prepared, eleven of which are newly synthesized compounds. Their infrared and ultraviolet spectra are interpreted.

Following our previous studies on the synthesis and properties of the condensation products of 5-(nitrophenyl)-2-furaldehydes with benzene carboxylic and pyridine carboxylic acid hydrazides [1—6] a series of related compounds was prepared. Many of the synthesized 5-(nitrophenyl)-2-furfurylidene hydrazones [1—4] exhibit a relatively high tuberculostatic activity, even against some strains of *Mycobacterium tuberculosis*, resistant to common antibiotics and tuberculostatics, respectively. It was found that this tuberculostatic activity can be significantly increased by introducing suitable substituents in position 2- of the furan ring (the nitrophenyl group remaining in position 5-) [1, 6].

Experimental

A. Preparation of 5-(nitrophenyl)-2-furfurylidene thiosemicarbazones (I, VI and XI)

5-(4-Nitrophenyl)-2-furaldehyde, 5-(3-nitrophenyl)-2-furaldehyde and 5-(2-nitrophenyl)-2-furaldehyde (0.65 g, 0.003 mole) were dissolved in boiling ethanol (140, 80 and 40 ml), respectively.

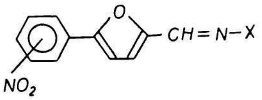
Thiosemicarbazide (0.28 g, 0.003 mole), dissolved in water (6 ml) was added to these solutions. The reaction mixture was allowed to stand for 2 hours at room temperature. The crystalline precipitate of thiosemicarbazide was filtered off, washed with water (50 ml) and ethanol (20 ml) and recrystallized from a suitable solvent (Table 1) and dried at 100—105°C.

B. Preparation of 5-(nitrophenyl)-2-furfurylidene cyanoacetylhydrazones (II, VII and XII)

5-Cyanoacetylhydrazide (0.302 g, 0.003 mole) was dissolved in hot water (5 ml) and added to a boiling ethanol solution of the appropriate aldehyde, prepared according to *A*.

Table 1

A survey of the prepared derivatives of 5-(4-nitrophenyl), 5-(3-nitrophenyl) and 5-(2-nitrophenyl)-2-furaldehyde



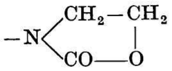
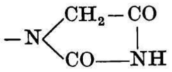
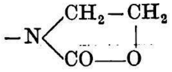
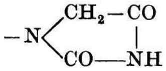
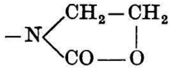
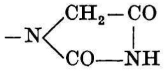
No.	Position of $-NO_2$	X	Molecular formula	*M*	Calculated/found				Yield [%]	M.p. °C (Boetius)
					% C	% H	% N	% S		
I	4-	$-NH-CS-NH_2$	$C_{12}H_{10}N_4O_3S$	290.3	49.7 50.03	3.47 3.43	19.3 19.52	11.0 10.74	89	236—237
II	4-	$-NH-CO-CH_2-CN$	$C_{14}H_{10}N_4O_4$	298.3	56.3 56.29	3.38 3.53	18.75 18.01		80	207—208
III	4-	$-OH$	$C_{11}H_8N_2I_4$	232.2	56.9 56.7	3.47 3.25	12.05 12.09		93	175—176
IV	4-		$C_{14}H_{11}N_3O_5$	301.2	55.8 55.55	3.68 3.88	13.98 14.21		92	312—313
V	4-		$C_{14}H_{10}N_4O_5$	314.3	53.45 53.70	3.44 3.56	17.82 18.03		81	279—280
VI	3-	$-NH-CS-NH_2$	$C_{12}H_{10}N_4O_3S$	290.3	49.7 49.57	3.47 3.70	19.3 19.22	11.0 10.81	80	207—208
VII	3-	$-NH-CO-CH_2-CN$	$C_{14}H_{10}N_4O_4$	298.3	56.3 56.5	3.38 3.42	18.75 18.61		74	202—203
VIII	3-	$-OH$	$C_{11}H_8N_2O_4$	232.2	56.9 56.86	3.47 3.68	12.05 12.38		85	147—149
IX	3-		$C_{14}H_{11}N_3O_5$	301.2	55.8 55.99	3.68 3.90	13.98 13.95		90	184—186

Table 1 (Continued)

NO.	Position of $-NO_2$	X	Molecular formula	M	Calculated/found % C	% H	% N	% S	Yield [%]	M.p. °C (Boetius)
X	3-		$C_{11}H_{10}N_4O_5$	314.3	53.45 53.67	3.44 3.58	17.82 17.62		77	247 —248
XI	2-	$-NH-CS-NH_2$	$C_{12}H_{10}N_4O_3S$	290.3	49.7 49.95	3.47 3.68	19.3 19.48	11.0 10.78	89	194 —195
XII	2-	$-NH-CO-CH_2-CN$	$C_{14}H_{10}N_4O_4$	298.3	56.3 56.47	3.38 3.46	18.75 19.04		81	159 —160
XIII	2-	$-OH$	$C_{11}H_8N_2O_4$	232.2	56.9 56.86	3.47 3.61	12.05 12.38		90	114 —114.5
XIV	2-		$C_{14}H_{11}N_3O_5$	301.2	55.8 55.77	3.68 3.80	13.98 14,19		89	171.5—172
XV	2-		$C_{14}H_{10}N_4O_5$	314.3	53.45 53.52	3.44 3.56	17.82 18.11		74	224.5—225
XVI	2-	$-NH-CO-NH_2$	$C_{12}H_{10}N_4O_4$	274.2	52.5 52.71	3.65 3.68	20.04 20.25		87	190 —191

M.p. are not corrected; compounds *I* and *VI* were crystallized from ethylene glycol and nitrobenzene; compounds *II* and *VII* from the mixture dimethylformamide and water (1 : 1); others from dioxane or ethanol.

M.p. of compound *III* is reported [9] to be 162—164°C (crystallized from acetic acid).

The reaction mixture was acidified with concentrated hydrochloric acid (1—2 drops) and permitted to stand for several minutes, causing a precipitate of cyanoacetylhydrazone; this was filtered off, washed with ethanol (20 ml), recrystallized and dried at 100°C.

C. Preparation of 5-(nitrophenyl)-2-furfurylidene oximes (III, VIII and XIII)

A mixture of hydroxylamine hydrochloride (0.21 g, 0.003 mole) and natrium acetate (0.41 g) in water (3 ml) was added to an ethanol solution of the appropriate aldehyde prepared according to *A*. The reaction mixture was heated under reflux for 30 minutes; then on concentration of the solution and cooling, the solid was filtered off, and washed with a small amount of water. Evaporation of the solvent gave a further amount of the appropriate oxime. The combined yields of the crude products were recrystallized (Table 1).

D. Preparation of 5-(nitrophenyl)-2-furfurylidene-3-amino-oxazolid-2-ones (IV, IX and XIV)

Benzylidene-3-amino-oxazolid-2-one (commercial product) (0.72 g, 0.0036 mole) was dissolved in water (9 ml) and concentrated sulfuric acid was added (0.3 g, 0.16 ml); then the solution was steam distilled to remove benzaldehyde. The residual solution of 3-amino-oxazolidon-2 was added to ethanolic solution of the appropriate aldehyde prepared according to *A*. The reaction mixture was heated under reflux for 10 minutes and after cooling the solid was filtered off, washed with water (50 ml) and ethanol (10—20 ml) and recrystallized from a suitable solvent (Table 1).

E. Preparation of 5-(nitrophenyl)-2-furfurylidene-1-aminohydantoines (V, X and XV)

Heating of semicarbazide acetic acid (0.46 g, 0.0035 mole) with water (2 ml) and concentrated sulfuric acid (0.6 g, 0.35 ml) for 3 hours yielded 1-aminohydantoine sulfate which was added to ethanol solution of the proper aldehyde prepared according to A. After cooling the solid was filtered off, washed with water (20 ml), recrystallized and dried at 100°C.

F. Preparation of 5-(2-nitrophenyl)-2-furfurylidene semicarbazone (XVI)

A mixture of semicarbazide hydrochloride (0.345 g, 0.003 mole) and crystalline natrium acetate (0.45 g) in water (4 ml) was added to an ethanol solution (140 ml) of 5-(2-nitrophenyl)-2-furaldehyde (0.65 g, 0.003 mole). The reaction mixture was heated under reflux on a steam bath for 10 minutes. After standing for two hours the solid was filtered off, washed with water (100 ml) and ethanol (10 ml); recrystallized and dried at 100°C.

Spectroscopy

Infrared spectra were recorded with a UR-10 Zeiss double beam spectrophotometer in the range of 400—3650 cm^{-1}. With respect to the insolubility of the investigated compounds in CCl_4 and $CHCl_3$, their spectra were measured for Nujol mulls. The calibration was checked against the spectrum of polystyrene (a film of 25 μ thickness was used) after each group of measurements. Frequency measurements for the studied characteristic groups are appear to be accurate to ± 1 cm^{-1}.

Ultraviolet spectra were recorded with a Perkin—Elmer double beam spectrophotometer Model 450 at 20 ± 2°C, using dioxane as solvent (concentration 5×10^{-5} M and cells of 1.0 cm thickness).

Results and Discussion

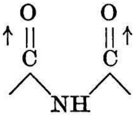
The compounds *V*, *X* and *XV* were also prepared by condensation of 1-aminohydantoine with proper 5-(nitrophenyl)-2-furaldehydes in dimethylformamide with a yield of 16—33% as already reported [7]. *Malinovski* [8] and *Hahn et al.* [9] used in synthetizing the compounds *I* and *III* acetic acid as medium and reported only a yield of compound *III* (above 80%).

In the present work the described condensation of 5-(4-nitrophenyl)-2-furaldehyde, 5-(3-nitrophenyl)-2-furaldehyde and 5-(2-nitrophenyl)-2-furaldehyde with various nitrogen bases in ethanol gives high yields of the condensation products (Table 1). The reaction was found to be completed in 1—2 hours. However, if concentrated hydrochloride acid is added to the reaction mixture, the reaction is completed in a few minutes (compounds *II*, *VII* and *IX*; Table 1).

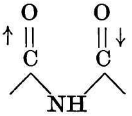
The relatively lower yields of compounds *V*, *X* and *XV* (Table 1) might be explained by the fact that the 1-aminohydantoine sulfate [10] was not isolated from the reaction medium but was directly used in condensation with appropriate aldehydes.

From infrared spectral data of the compounds under investigation (Table 2) may be seen that on passing from *para* derivatives to *ortho* ones (except compounds *V*, *X* and *XV*) the stretching frequencies ν(C=N) are shifted to the lower values. The reverse shift is observed for the compounds *V*, *X* and *XV*. It is known that in many cases the bands of ν(C=N) are not easily to be recognised because they often are overlapped by the bands of ν(C=C). The most intense bands of ν(C=N) are observed for the compounds *I*, *II*, *VI*, *VIII*, *XI* and *XIII*; this might be explained by the fact that the intensity of those bands is mainly dependent on the symmetry of the C=N bond and to a less extent on the nature of the substituents [11].

Compounds *V*, *X* and *XV*, containing the —CO—NH—CO— group in the five-membered ring exhibit two or three absorption bands in the 1700—1800 cm^{-1} region. The relatively high frequencies of the bands can be explained by the fact that the influence of ring strain is superimposed on the other effects. The splitting of the carbonyl frequency in these compounds can be explained in terms of vibrational interactions [12]. Upon analysis one would find that the CO groups vibrate so that either bond stretches and contracts, the other bond remains unchanged in length. Then, they interact with the result that two stretching frequencies are observed, for instance (compound *V*):



ν_s(CO) 1730 cm^{-1}



ν_{as}(CO) 1767 cm^{-1}

Compounds *IV*, *IX* and *XIV*, possessing the $-\overset{|}{\mathrm{N}}-\mathrm{CO}-\mathrm{O}-$ group in the five-membered ring also display two bands in the 1660—1800 cm^{-1} region. The explanation, and perhaps the most likely one, is that the carbonyl frequency and some other fundamental frequency or overtone are coupled together, leading to resonance splitting.

Table 2

Infrared spectral data of 5-(4-nitrophenyl)-, 5-(3-nitrophenyl)- and 5-(2-nitrophenyl)-2-furaldehyde derivatives [cm^{-1}]

No.	$\nu_s(NO_2)$	$\nu_{as}(NO_2)$	$\nu(C{=}N)$	$\nu(C{=}O)$
I	1350(58)	1515(79)	1615(44)	—
II[a]	1336(45)	1515(42)	1630(32)	1656(40) 1692(30)
III	1355(39)	1515(57)	1598(51)[b]	—
IV	1350(57)	1512(55)	1620(18)	1752(58) 1785(49)
V	1352(54)	1519(28)	1600(34)[b]	1730(34) 1767(55))
VI	1350(68)	1525(67)	1608(38)	—
VII[a]	1350(34)	1526(38)	1620(16)	1660(30) 1700(64)
VIII	1350(74)	1525(62)	1635(25)	—
IX	1363(67)	1529(57)	1622(18)	1765(73)
X	1357(49)	1530(30)	1612(19)	1705(31) 1725(37) 1780(30)
XI	1354(47)	1522(52)	1602(43)[b]	—
XII[a]	1368(53)	1534(72)	1608(36)[b]	1695(86)
XIII	1365(61)	1525(80)	1632(41)	—
XIV	1355(52)	1525(40)	1610(22)	1755(54) 1770(44)
XV	1349(65)	1522(65)	1620(24)	1703(65) 1745(72) 1800(56)
XVI	1350(58)	1533(61)	1615(14)	1642(48)

a) $\nu(C{\equiv}N)$ 2265 cm^{-1}.

b) Broad band; $\nu(C{=}N)$ overlapped by $\nu(C{=}C)$.

The values in parenthesis are % of absorption.

The lowest values of the stretching frequencies of the NO_2 groups ν_s and $\nu_{as}(NO_2)$ are observed for *para* derivatives (compounds *I*—*V*) what can be explained by mesomeric effect of the NO_2 group. These results are in accordance with the infrared spectral data of 5-(4-nitrophenyl)-2-furfurylidene benzoylhydrazones reported previously [2, 3]. This assumption is also in good agreement with the ultraviolet spectral data of the compounds under investigation (Table 3); the highest values of λ_{max} having been observed for the *para* derivatives. Infrared and also ultraviolet spectral data of the *ortho* derivatives suggest that the —M effect of the NO_2 group does not play any significant role, which is probably due to some steric hidrance, *e.g.* one requirement for the occurence of mesomeric effects, the coplanarity of the bonds concerned is not fulfilled [2]. Compounds, bearing the NH or NH_2 group

Table 3

Ultraviolet spectral data of 5-(4-nitrophenyl)-, 5-(3-nitrophenyl)- and 5-(2-nitrophenyl)-2-furaldehyde derivatives (in dioxane)

No.	$\lambda_{\max}$	log ε	$\lambda_{\max}$	log ε
I	403	4.41	320	4.18
II	372	4.35	286—290	4.02
III	367	4.37	278	4.00
IV	371	4.35	308	4.02
V	379	4.39	316—320	4.04
VI[a]	363	4.46	260	4.07
VII	335	4.47	242—247	4.10
VIII	314	4.37		
IX	334	4.55	249	4.10
X	337	4.56	255	4.38
XI	346	4.44	246	4.18
XII	320	4.39	245	4.04
XIII	298	4.28	242—247	4.19
XIV	320	4.36	245—247	3.92
XV	323	4.35	248	3.90
XVI[b]	383	4.39	297	3.87

a) Additional band at $\lambda_{\max}$ 248 nm (log ε 4.08).

b) Additional band at $\lambda_{\max}$ 244 nm (log ε 4.04).

$\lambda_{\max}$ and ε are in nm and l mole^{-1} cm^{-1}, respectively.

exhibit several bands in the 3100—3650 cm^{-1} region, assigned to the stretching vibrations of the N—H bonds. However, they were too complex for any precise assignments to be made.

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