

# Furan Derivatives. XXX.

## Preparation of Substituted 5-Phenyl-2-furfuryl Alcohols

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The preparation of 5-(X-phenyl)-2-furfuryl alcohols from the corresponding aldehydes is described by a) reduction with  $\text{NaBH}_4$ , when  $\text{X} = 2\text{-NO}_2$ ,  $3\text{-NO}_2$ , and  $4\text{-NO}_2$ ; b) reduction with  $\text{LiAlH}_4$ , when  $\text{X} = 2\text{-Cl}$ ,  $3\text{-Cl}$ ,  $4\text{-Cl}$ ,  $4\text{-Br}$ ,  $4\text{-CH}_3$ ,  $4\text{-OCH}_3$ , H; c) modified Cannizzaro reaction, when  $\text{X} = 2\text{-NO}_2$ ,  $3\text{-NO}_2$ ,  $4\text{-NO}_2$ ,  $4\text{-CH}_3$ ,  $4\text{-OCH}_3$ , H. Infrared and ultraviolet spectra of the final products are interpreted.

Formation of some substituted 5-phenyl-2-furfuryl alcohols by reduction of the corresponding 5-phenyl-2-furaldehydes with  $\text{LiAlH}_4$  has been described by *Kaltenbronn* and *Rhee* [1] and others [2, 3]. Instead of isolating the alcohols previous workers used these substances as intermediates for the synthesis of substituted 5-phenyl-2-furylacetic acids which show pronounced antiinflammation effects.

The above-mentioned method is not suitable when the substrate is a nitro derivative of 5-phenyl-2-furaldehyde since, simultaneously with the carbonyl group, the nitro group also undergoes reduction [4]. *Malinowski* [5] has attempted the reduction of 5-(4-nitrophenyl)-2-furaldehyde by modified Cannizzaro reaction but the only product isolated was 5-(4-nitrophenyl)-2-furancarboxylic acid. We showed previously [6] that direct arylation of 2-furfuryl alcohol, using Meerwein's method, did not produce the wanted product, though the reaction was carried out at various pH. Neither 5-(nitrophenyl)-2-furfuryl alcohol nor any other arylated product could be isolated from the resinous reaction mixture.

The desired 5-(2-, 3-, 4-nitrophenyl)-2-furfuryl alcohols were then prepared by reduction of the corresponding aldehydes with  $\text{NaBH}_4$  which, under mild conditions, selectively reduces the carbonyl group [7–13]. Good results have also been obtained using modified Cannizzaro reaction.

### Experimental

Melting points were determined on a Koffler hot stage.

Infrared spectra ( $700\text{--}3650\text{ cm}^{-1}$ ) were measured in chloroform with a double-beam UR-10 Zeiss spectrometer at a concentration of 0.01 M. The spectra of compound VIII were, in addition, measured at various concentrations in carbon tetrachloride. Ultraviolet absorption spectra were measured in 1,4-dioxan ( $2 \times 10^{-5}\text{--}4 \times 10^{-5}\text{ mol l}^{-1}$ ) with a JASCO ORD spectrometer.

The starting phenylsubstituted 2-furaldehydes were prepared as described in [14–19].

## Substituted 5-phenyl-2-furfuryl alcohols

A. Reduction of aldehydes with  $\text{LiAlH}_4$ 

To a suspension of  $\text{LiAlH}_4$  (1.4 g; 0.04 mole) in dry ether (40 ml) 5-(X-phenyl)-2-furaldehyde (0.02 mole) dissolved in dry ether or tetrahydrofuran was added dropwise. The reaction mixture was heated under reflux for 90 minutes, cooled, and the excess of the reducing agent was decomposed by slow addition of ethyl acetate and water. The organic phase was separated and the inorganic residue was extracted with several portions of ether. The combined extracts were washed with a saturated solution of sodium chloride, dried with anhydrous sodium sulfate, and concentrated under reduced pressure. Compounds *IV*–*X* were prepared using this procedure.

B. Reduction of aldehydes with  $\text{NaBH}_4$ 

Nitrosubstituted 5-phenyl-2-furaldehyde (21.7 g; 0.1 mole) dissolved in 96% ethanol or tetrahydrofuran was slowly added to a suspension of  $\text{NaBH}_4$  (5.6 g; 0.15 mole) in ethanol or tetrahydrofuran (100 ml). When tetrahydrofuran was used the pH of the reaction mixture was kept at 5–6 [10] by intermittent addition of 0.1 N- $\text{H}_2\text{SO}_4$ . The reaction mixture was refluxed for 5 hours during which time 2-propanol (100 ml) was added, cooled, and when ethanol was used as solvent the mixture was neutralized with 0.1 N- $\text{H}_2\text{SO}_4$ , filtered, and concentrated. The residue was extracted with ether, filtered, and the filtrate

Table 1

Synthesized 5-(X-phenyl)-2-furfuryl alcohols

No.	X	Formula	M	Calculated/found				Yield [%]	M.p. [°C]
				% C	% H	% N	% Hal.		
<i>I</i>	4-NO <sub>2</sub>	C <sub>11</sub> H <sub>9</sub> NO <sub>4</sub>	219.19	60.27	4.14	6.39		85.3 (40)	139–141
				60.38	4.28	6.58			
<i>II</i>	3-NO <sub>2</sub>	C <sub>11</sub> H <sub>9</sub> NO <sub>4</sub>	219.19	60.27	4.14	6.39		83 (45)	90–92
				60.50	4.24	6.30			
<i>III</i>	2-NO <sub>2</sub>	C <sub>11</sub> H <sub>9</sub> NO <sub>4</sub>	219.19	60.27	4.14	6.39		81 (54)	40–41
				60.32	4.20	6.42			
<i>IV</i>	4-Cl	C <sub>11</sub> H <sub>9</sub> ClO <sub>2</sub>	208.639	6.32	4.35	—	16.99	88.3 (59)	91.5–92.5
				63.41	4.48	—	16.89		
<i>V</i>	3-Cl	C <sub>11</sub> H <sub>9</sub> ClO <sub>2</sub>	208.639	6.32	4.35	—	16.99	90.0	71–72
				63.50	4.46	—	17.20		
<i>VI</i>	2-Cl	C <sub>11</sub> H <sub>9</sub> ClO <sub>2</sub>	208.639	63.32	4.35	—	16.99	92.3	48–49
				63.38	4.50	—	17.19		
<i>VII</i>	4-Br	C <sub>11</sub> H <sub>9</sub> BrO <sub>2</sub>	253.098	52.20	3.58	—	31.57	91.6	105–106
				52.46	3.76	—	31.39		
<i>VIII</i>	H	C <sub>11</sub> H <sub>10</sub> O <sub>2</sub>	174.19	75.84	5.78	—	—	96 (78)	63–64
				75.62	5.66	—	—		
<i>IX</i>	4-CH <sub>3</sub>	C <sub>12</sub> H <sub>12</sub> O <sub>2</sub>	188.226	76.57	6.42	—	—	96 (70)	59–61
				76.30	6.43	—	—		
<i>X</i>	4-OCH <sub>3</sub>	C <sub>12</sub> H <sub>12</sub> O <sub>3</sub>	204.226	70.57	5.92	—	—	90	99–100
				70.31	6.06	—	—		

Compounds *I* and *II* were crystallized from benzene, *III* from ether–petroleum ether (1 : 1), *IV*–*X* from heptane or hexane.

Table 2  
Ultraviolet and infrared data of the synthesized compounds

No.	$\lambda_{\max}$ [nm]	$\log \epsilon$	$\lambda_{\max}$ [nm]	$\log \epsilon$	$\lambda_{\max}$ [nm]	$\log \epsilon$	$\lambda_{\max}$ [nm]	$\log \epsilon$	$\lambda_{\max}$ [nm]	$\log \epsilon$	$\bar{\nu}_{\text{as}}(\text{C}-\text{O}-\text{C})$ [cm <sup>-1</sup> ]	$\bar{\nu}(\text{C}=\text{C})_{\text{arom}}$ [cm <sup>-1</sup> ]	$\bar{\nu}(\text{OH})$		
													assoc. [cm <sup>-1</sup> ]	free	
I	354	4.28	243	4.0											
II	330 i	3.34	298 sh	4.30	288	4.38	276 sh	4.37			1270 (37)	1618 (91)	3432 (34)	3617 (50)	
III	330 i	3.46	280 sh	4.16	268	4.18					1280 (48)	1611 (35)	3426 (37)	3616 (52)	
IV	303 sh	4.43	291	4.57	285 i	4.54	229 sh	4.02	224	4.07	1290 (45)	1620 (45)	3420 (34)	3615 (48)	
V	300 sh	4.24	288	4.38	282 sh	4.36	236 sh	3.94	231	4.03	1290 (32)	1610 (30)	3422 (36)	3617 (52)	
VI	297 sh	4.24	286	4.35	280 sh	4.31	229	4.05	228	4.09	1267 (35)	1600 (59)	3428 (32)	3617 (50)	
VII	305 sh	4.31	293	4.44	287 sh	4.41	230 sh	3.86	225	3.92	1288 (25)	1609 (24)	3427 (31)	3619 (41)	
VIII	298 sh	4.19	286	4.36	281 sh	4.35	228 sh	3.89	222	3.97	1290 (23)	1616 (26)	3430 (32)	3618 (50)	
IX	300 sh	4.20	287	4.41	283 sh	4.39	228 sh	3.88	222	3.94	1289 (32)		3428 (30)	3620 (54)	
X	303 sh	4.20	290	4.41	285 sh						1260 (76)	1608 (80)	3450 (32)	3620 (54)	

The values in parentheses refer to the absorption in %.  
sh — shoulder, i — point of inflexion.

was washed with water. The ethereal solution was dried with anhydrous sodium sulfate and concentrated. This procedure was used to prepare compounds *I–III*.

### C. Modified Cannizzaro reaction

To a suspension of 5-(*X*-nitrophenyl)-2-furaldehyde (10.85 g; 0.05 mole) in 100 ml of an alcohol (2-nitro derivative in methanol, 3-nitro derivative in ethanol, 4-nitro derivative in ethanol or *n*-propanol) formaldehyde (30% solution; 8.6 g) was added and the reaction mixture was warmed to the boiling point of the mixture. A solution of potassium hydroxide (12 g in 8 ml of water) was added dropwise with stirring while the solution was kept under reflux for 2 1/2 hours. The reaction mixture was cooled, diluted with water and extracted with ether. The ethereal solution was dried with anhydrous sodium sulfate and concentrated under reduced pressure. According to this procedure compounds *I–IV*, *VIII*, and *IX* were prepared. The yields, physical constants, and analytical figures are given in Table 1.

## Results and Discussion

Reduction of 5-(*X*-phenyl)-2-furaldehydes with  $\text{LiAlH}_4$  gave high yields of 5-(*X*-phenyl)-2-furfuryl alcohols (compounds *IV–X*; Table 1). Although no marked effect of the solvent upon the yield of the products was observed tetrahydrofuran was found to be more suitable in these reactions than ether as the latter is not such a good solvent for the components of these reaction mixtures.

To avoid unwanted modifications of the nitro derivatives [4] by the reduction with  $\text{LiAlH}_4$ , these starting materials were successfully reduced (preparation of *I–III*; Table 1) with half molar excess of  $\text{NaBH}_4$  which is known to attack a nitro group only in exceptional cases [20–22]. The temperature of the reaction mixtures was kept at appropriate level according to the solubility of the respective starting material in the used solvent. Of these most suitable was found to be tetrahydrofuran containing 2-propanol [23].

As an alternative for making the alcohols, 5-(nitrophenyl)-2-furaldehydes were reduced

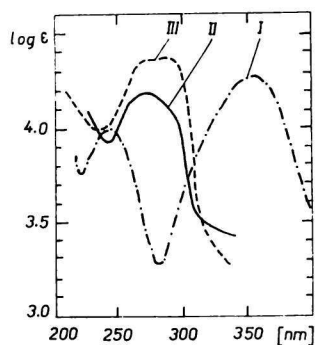


Fig. 1. Ultraviolet spectra of compounds *I–III*.

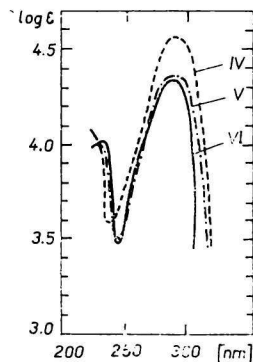


Fig. 2. Ultraviolet spectra of compounds *IV–VI*.

by modified Cannizzaro reaction. The yields were, however, by 30–40% lower than those obtained by the reduction with  $\text{NaBH}_4$ . The conditions of the modified Cannizzaro reaction were used also for the preparation of *IV*, *VIII*, and *IX*, though the yields were again markedly lower (Table 1, the figures in parentheses). The prepared 5-phenyl-2-furfuryl alcohols are crystalline, stable substances. Compounds *I–III* are yellow, the others are colourless.

The infrared spectral data of the synthesized 5-phenyl-2-furfuryl alcohols are given in Table 2. Bands corresponding to the free hydroxyl groups ( $3615\text{--}3620\text{ cm}^{-1}$ ) as well to those involved in hydrogen bonds ( $3450\text{--}3420\text{ cm}^{-1}$ ) can be independently seen in the spectra. The bands of the free OH groups of *VIII*, measured in carbon tetrachloride at the concentration of  $0.1\text{--}0.0025\text{ M}$ , are, as expected, shifted to  $3643\text{ cm}^{-1}$ . In the range of the associated hydroxyl groups there are two absorption bands present: the one at  $3390\text{ cm}^{-1}$ , being greatly dependent upon the concentration of the compound, indicates the presence of intermolecular hydrogen bonding, the other one (at  $3510\text{ cm}^{-1}$ ) is probably that of the hydroxyl groups involved in intramolecular hydrogen bonds, which is in agreement with data given by *Nazarova* [25, 26].

The ultraviolet spectra of the compounds under investigation show two main absorption bands (Figs. 1 and 2). One is in the range of  $280\text{--}350\text{ nm}$  and it obviously belongs to the whole conjugated system of the molecule. The effect of the substituents showed itself in the same manner as reported in our previous works [24, 27, 28].

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