RESEARCH ON FURAN ACETAL COMPOUNDS.

VIII.* SYNTHESIS OF (2-FURYL)DIACETAMIDOMETHANES

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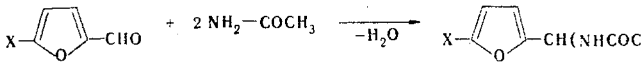
A number of diacetamidomethanes were obtained by condensation of 5-substituted furfurals with acetamides. Previously undescribed 1,3-dioxepanes were synthesized by reaction of the indicated aldehydes with 1,4-butanediol.

It has been shown [1, 2] that five- and six-membered dioxacyclanes formed in the condensation of 5-substituted furfurals with 1,2- and 1,3-diols have physiological activity and that similar cyclic systems with an exocyclic nitrogen atom in the 5 position of the dioxane ring display antimicrobial properties [3].

In order to search for new physiologically active preparations we carried out the condensation of furfural and 5-bromo-, 5-iodo-, 5-methyl-, and 5-nitrofurfurals with 1,4-butanediol and obtained 2-(5-X-fur-2-yl)-1,3-dioxepanes (I-V, Table 1).

The reaction of 5-substituted furfurals with ethylene glycol and acetamide might have led to a seven-membered compound with a nitrogen atom in the ring, inasmuch as it is known [4] that perhydro-1,5-dioxa-5-azepine derivatives are obtained in 9-20% yields as a result of condensation of ethylene glycol with amides (urethanes) and formaldehyde.

However, our attempts to realize the condensation of ethylene glycol, furfural, and acetamide in xylene or benzene, both with sulfuric acid and in the presence of KU-2 ion-exchange resin at various ratios of the starting components, showed that the reaction proceeds without the participation of the diol to give (5-X-fur-2-yl)diacetamidomethanes.



In addition, in benzene the synthesis proceeds without saponification and gives the products in better yields than in xylene. The products (VI-VIII, Table 1) are colorless crystalline substances that are quite soluble in ethanol and boiling benzene but only slightly soluble in water.

The structures of all of the compounds were confirmed by UV and IR spectroscopy.

Acetal lines are observed in the IR spectra of the 1,3-dioxepanes at 1040-1200 cm^{-1} [5, 6]; and the bands at 1150-1180, 1120-1140, and 1063-1100 cm^{-1} are ascribed to ether bonds; whereas those at 1030-1056 and 1105-1116 cm^{-1} are ascribed to acetal bonds [7]. The presence of a furan ring is distinctly apparent [7]: ring ν_{CH} at 3160 and 3130 cm^{-1}, ring stretching vibrations at 1470-1600 cm^{-1} (three or two bands), =C-O-C= band at 1250 cm^{-1}, and pulsation vibrations at 995-1006 cm^{-1}; the bands at 908-934, 735-753, and 704-732 cm^{-1} belong to the deformation vibrations of the furan ring. Deformation vibrations of CH bonds in the 5 position of the furan ring appear at 875-882 cm^{-1}. This band is characteristic only for unsubstituted compounds. A band at 795-810 cm^{-1} appears in its place in the spectra of 2,5-disubstituted furans.

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*See [1] for communication VII.

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TABLE 1. 2-(5-X-Fur-2-yl)-1,3-dioxepanes (I-V) and (5-X-Fur-2-yl)diacetamidomethanes (VI-VIII)

Compound	X	mp, °C	Empirical formula	Found, %				Calc., %				UV spectrum in ethanol		Yield, %
				C	H	X	N	C	H	X	N	λ_{max}, nm	lg ε	
I	H	130 (2)*	$C_9H_{12}O_3$	63,9	7,2	—	—	64,3	7,2	—	—	208	3,95	74
II	CH_3	112 (2)*	$C_{10}H_{14}O_3$	66,0	7,9	—	—	66,0	7,7	—	—	218	3,99	70
III	Br	77	$C_9H_{11}BrO_3$	44,0	4,6	31,9	—	43,7	4,5	32,0	—	217	3,99	76
IV	I	89	$C_9H_{11}IO_3$	37,1	3,9	42,8	—	36,8	3,7	43,2	—	232	3,99	76
V	NO_2	128	$C_9H_{11}NO_5$	51,0	5,4	—	6,8	50,6	5,2	—	6,7	306	3,96	78
VI	H	188	$C_9H_{12}N_2O_3$	54,8	6,3	—	14,5	55,0	6,1	—	14,3	209	4,57	40
VII	CH_3	192	$C_{10}H_{14}N_2O_3$	56,9	7,0	—	12,9	57,1	6,7	—	13,3	217	4,59	38
VIII	Br	202	$C_9H_{11}BrN_2O_3$	39,5	4,2	28,9	10,1	39,2	4,0	29,0	10,1	216	4,60	50

*This is the boiling point (mm).

An amide band at 1655-1659 cm^{-1} and a narrow intense band of the stretching vibrations of an imino group at 3262 cm^{-1} are present in the spectra of VI-VIII.

The UV spectra of I-VIII are similar to the spectra of the corresponding 2-(5-X-fur-2-yl)-1,3-dioxanes [8], and this constitutes evidence that condensation took place at the carbonyl group of the furan aldehydes; the extinction observed for VI-VIII is somewhat higher.

EXPERIMENTAL

The UV spectra of ethanol solutions of the compounds were recorded with an SF-4A spectrophotometer. The IR spectra of thin layers (0.04 mm for I and II) or mineral oil suspensions (III-VIII) were recorded with an IKS-14 spectrometer (with NaCl and LiF prisms).

2-(2'-Furyl)-1,3-dioxepane (I). A 9.6-g (0.1 mole) sample of furfural was added in small portions to a refluxing solution of 9.0 g (0.1 mole) of 1,4-butanediol in 80 ml of dry benzene containing 1.92 g of KU-2 resin. The water formed in the reaction was led off into a trap. The end of the reaction was determined by spectrophotometry. The benzene was removed by distillation, and the product was vacuum distilled.

Compound II was similarly obtained. Dioxepanes III-V were recrystallized from benzene—heptane (1:3).

(2-Furyl)diacetamidomethane (VI). A mixture of 5.9 g (0.1 mole) of acetamide, 4.8 g (0.05 mole) of freshly distilled furfural, 2 g of KU-2 resin, and 100 ml of benzene was refluxed for 30 min on a water bath in a flask equipped with a trap until water liberation ceased. The solution was then separated rapidly from the catalyst, whereupon colorless crystals precipitated immediately. The crystals were removed by filtration and washed thoroughly with water. Compounds VII and VIII were similarly obtained.

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