# SYNTHESIS, KINETICS OF THE FORMATION, AND PHYSICAL PROPERTIES OF 5-ALKOXYFURFURALS

V. N. Novikov and V. E. Polyakov

UDC 547.722.4:541.127.1

The reaction of 5-bromofurfural with potassium alkoxides in an alcohol medium was studied, and 5-alkoxyfurfurals and the products of their condensation with m-nitroacetophenone were obtained. A mechanism for the alkoxylation is proposed on the basis of the kinetic data.

The reaction of aldehydes of the furan series with nucleophilic reagents has been studied quite satisfactorily. The presence of a halogen atom in the 5 position of the ring makes possible its replacement by nucleophilic groupings, owing to which a number of preparative methods for obtaining esters, sulfides, and amines of the furan series have been developed. Thus the reaction of 5-bromofurfural (I) with sodium sulfide or thiosulfate in an aqueous or aqueous alcohol medium leads to bis(5-formyl-2-furyl) sulfide [1, 2]. Sodium thiophenoxide and its derivatives react in alcoholic media with the aldehyde to give the corresponding sulfides in high yields [3], while substituted benzene sulfinates in ethylene glycol monomethyl ether give sulfones [4]. The reaction of sodium phenoxides with the aldehyde in dimethyl sulfoxide (DMSO), which leads to the corresponding ethers, has also been studied [4, 5]. However, the literature does not contain information regarding the synthesis of 5-alkoxyfurfurals by this method. It is known that a halogen atom in furans (Schiff bases [6] and furan-2-carboxylic acid esters [7, 8]) can be replaced by an alkoxy group under conditions that are normal for this reaction, viz. by the action of alkali metal alkoxides in a medium of the corresponding absolute alcohol; however, this reaction has not yet been studied in the case of aldehydes. In one of the earlier studies of aromatic nucleophilic substitution [9] it was pointed out that aromatic aldehydes react with metal alkoxides under the conditions of an S<sub>N</sub>2Ar reaction primarily at the carbonyl group. It will be shown below that this reaction also occurs in the case of aldehydes of the furan series but that it is reversible and does not prevent replacement of a halogen atom in the ring by an alkoxy group.

In the present research we studied the reaction of aldehyde I with potassium alkoxides in the corresponding alcohol (methanol, ethanol, and propyl alcohol). Simultaneously with the development of a method for the preparative isolation of the 5-alkoxyfurfurals we studied the kinetics of this reaction; this made it possible to work out the optimum conditions for carrying out the reaction. With this in mind, we analyzed the reaction mixtures for the percentages of starting and final aldehydes by a spectrophotometric method, as well as for the percentage of ionic halogen by potentiometric titration. The kinetic curves (in "product yield vs time" coordinates) are presented in Fig. 1 in the case of the reaction with potassium methoxide. The yield was calculated in percent of the theoretical value by several methods - from the percentage of alkoxyfurfural in the spectrophotometric solution (curve 3), from the consumption of aldehyde I (curve 1), and from the accumulation of ionic halogen (curve 2). It follows from the data presented above that the reaction is complex in character. It proceeds initially with inductive acceleration, which, as is well known, may constitute evidence for the formation of an intermediate. Its percentage can be determined from the difference between the theoretical yield of the product calculated from the consumption of aldehyde I and the accumulation of ionic halogen. The conjugated "aldehyde-furan ring" system in this product, which contains covalently bonded halogen, is disrupted, since it does not absorb light in the region characteristic for furan aldehydes. We assign to it structure III, which is similar to that of Meisenheimer complexes - intermediates in  $\rm S_N2Ar\ reactions$  . The dynamics of the accumulation of this product (shown by curve 4) are different for the various alkoxides. When  $R = CH_3$ , the yield of intermediate III does not exceed several percent; in the initial period of the reaction its percentage in the mixture passes through a weakly expressed maximum and then remains at an approximately steady-state level. A different pattern is observed for the other alkoxides. For example, when  $R = C_3H_7$ , the overall percentage of reaction product III constantly increases during the reaction and reaches 30%. This apparently constitutes evidence that complex III is a relatively stable compound and that the rate of its conversion to aldehyde IV decreases as R becomes larger.

Rostov State University, Rostov-on-Don 344006. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 747-750, June, 1982. Original article submitted July 28, 1981.



Fig. 1. Kinetics of the reaction of 5-bromofurfural with potassium methoxide in methanol: 1) theoretical yield of the reaction product calculated from the consumption of 5-bromofurfural; 2) yield of the reaction product calculated from the accumulation of ionic bromine; 3) spectrally determined yield of 5-methoxyfurfural; 4) difference in the ordinates of curves 1 and 2 (kinetics of accumulation of complex III); 5) difference in the ordinates of curves 2 and 3 (kinetics of accumulation of complex V).



Another peculiarity of the kinetic curves presented above is the deviation between the spectrally determined yield of alkoxyfurfural IV and the accumulation of ionic halogen. This deviation (shown by curve 5) is minimal only when  $R = CH_3$  and can be virtually disregarded. For the other R the percentage of aldehyde IV in the mixture passes through a maximum and then begins to decrease, although ionic halogen continues to accumulate. We suppose that this is associated with the formation of yet another reaction product, viz. complex V, from the aldehyde by the addition of alkoxide to it. Pathway III  $\rightarrow$  V also is not excluded, since the halogen in intermediate III can be replaced by an alkoxy group via a mechanism involving aliphatic nucleophilic substitution.

It is also important to note that the curves shown in Fig. 1 do not take into account side reaction of the aldehyde with alkoxide ions at the carbonyl group, since the analysis of the mixture was carried out in an aqueous medium, in which a complex of the II type is hydrolyzed. In separate experiments we showed that equilibrium  $I \rightleftharpoons II$  is established instantaneously in an alcohol solution of the alkoxide that contains aldehyde I. The constant of this equilibrium determined at 25°C (for  $R = CH_3$ ) by spectrophotometry (as described for the reaction of aldehyde I with secondary amines [10]) is 2.35 liters-mole<sup>-1</sup>. However, this process is reversible and does not lead to any profound changes in the aldehyde, and it therefore does not prevent irreversible replacement of the halogen atom in the ring by an alkoxy group.

The kinetic data obtained made it possible to more purposefully select the optimum conditions for the preparative isolation of the 5-alkoxyfurfurals. It should only be stipulated that the real yields of the aldehydes (see the experimental section) are depressed as compared with the yields determined from the kinetic data as a consequence of losses during isolation, particularly during vacuum distillation of the preparations because

1	11
x~~_0~	~сно

X	Electronic spectra		IR spectra, $\nu$ , cm <sup>-1</sup>			PMR spectra (δ, ppm; J, Hz)								
	λ <sub>max</sub> , nm	lgε	C=0	C=C	сно	3-H	4-H	1 <sub>34</sub>	Other signals					
H CH <sub>3</sub> Cl Br I CH <sub>3</sub> O C <sub>2</sub> H <sub>5</sub> O C <sub>3</sub> H <sub>7</sub> O (CH <sub>3</sub> ) <sub>2</sub> N Morpholino Piperidino O <sub>2</sub> N	273 284 280 283 294 304 306 307 362 355 364 305	4,19 4,26 4,04 4,28 4,26 4,31 4,33 4,30 4,51 4,52 4,60 4,00	1682 1678 1686 1685 1684 1668 1672 1666 1655 1659 1650 1706	1574 1589 1578 1579 1571 1589 1590 1588 1600 1582 1579 1553	9,65 9,43 9,50 9,50 9,23 9,27 9,20 8,93 9,05 8,99 9,86	7,38 7,23 7,45 7,38 7,28 7,32 7,32 7,31 7,20 7,23 7,27 7,27 7,64	6,68 6,28 6,65 6,75 5,61 5,63 5,63 5,63 5,25 5,41 5,40 7,64	3,8 3,7 4,5 4,2 4,0 3,8 3,8 3,8 3,8 2,7 4,5 3,8	$δ 5.H 7.9; J_{45} = 1.9$ $\delta CH_3 2.33$ 					

TABLE 2. Conditions of Preparation and Properties of Aldehydes

IV	and	Chalcones	$RO \longrightarrow CH = CH - COC_6H_4NO_2 - m$
			VI

	Aldehydes IV									Chalcones VI							
R	n n	bp,°C (4 mm)	mp, C	four %	ound, g		calc	., %	0/0	mp, °C	found, %			empirical	calc., %		
	time			С	н	empi form	с	н	yield		с	Н	N	formula	с	н	N
СН₃	2	112-	22	55,4	4,7	$C_6H_6O_3$	55,4	4,8	35	127	65,4	4,2	5,4	C14H11NO5	65,4	4,3	5,5
C2H5 C3H7	1 0,75	113  109 110	59 17	60,1 61,4	5,6 6,5	$C_7H_8O_3$ $C_8H_{10}O_3$	60,0 62,3	5,7 6,5	25 20	100 79	66,4 67,5	4,7 5,2	5,1 5,0	C <sub>15</sub> H <sub>13</sub> NO <sub>5</sub> C <sub>16</sub> H <sub>15</sub> NO <sub>5</sub>	66,4 67,4	4,8 5,3	5,2 4,9

of their low stabilities. The products of condensation of the aldehydes with m-nitroacetophenone were obtained and characterized.

Data on the spectral properties of the synthesized aldehydes are presented in Table 1. For comparison, the spectral characteristics of a number of 5-N,N-dialkylaminofurfurals obtained by the methods in [11, 12] and of some other widely known and well-studied aldehydes are also presented in Table 1. With respect to all of the parameters 5-alkoxyfurfurals occupy an intermediate position here, as follows from the character of the electronic effect of the alkoxy group on the furan ring.

## EXPERIMENTAL

The electronic spectra of solutions of the compounds in methanol were recorded with an SF-4A spectrophotometer. The IR spectra of solutions in chloroform were obtained with a UR-20 spectrometer. The PMR spectra of solutions in  $d_6$ -acetone were recorded with a Tesla BS-467 spectrometer (60 MHz) with hexamethyldisiloxane as the internal standard.

<u>5-Alkoxyfurfurals (Table 2).</u> A 7-g (0.04 mole) sample of 5-bromofurfural was added to 100 ml of absolute alcohol containing 0.06 mole of potassium alkoxide (prepared by dissolving potassium in the corresponding alcohol), and the mixture was maintained in a thermostat at 50°C (see Table 2 for the reaction times). The precipitated potassium bromide was separated, and the alcohol was then removed at reduced pressure. The residue was treated with hot benzene, and the benzene solution was washed with water and dried with sodium sulfate. The benzene was removed, and the residue was distilled in vacuo (when  $R = CH_3$ ,  $C_3H_7$ ) or recrystallized twice from hexane (when  $R = C_2H_5$ ).

Method of the Kinetic Measurements. A 10-ml solution containing 2.3 mmole of aldehyde I and 4 mmole of the potassium alkoxide in the absolute alcohol was prepared. Immediately after mixing, the reaction mixture was divided into 1-ml portions, which were placed in test tubes with ground glass stoppers. The samples were maintained at 50°C in a thermostat. The reaction was interrupted by adding 9 ml of water to the test tube. A 0.5-ml sample of the resulting solution was diluted further with water up to the spectral concentration (by a factor of 1000), while 9.5 ml, after dilution with water and acidification with nitric acid, was titrated by the method in [13]. The percentages of the starting and final aldehydes in the spectrophotometric solution were determined from Firordt's formulas [14].

#### LITERATURE CITED

- 1. Z. N. Nazarova and Yu. A. Babaeva, Zh. Obshch. Khim., 34, 4010 (1964).
- 2. Z. N. Nazarova and G. F. Potemkin, Zh. Org. Khim., 1, 1709 (1965).
- 3. R. Kada and J. Kovač, Chem. Zvesti, 29, 402 (1975).
- 4. D. R. Shridhar, C. V. R. Sasty, M. Jogbhukta, S. R. Moorty, N. K. Vaidya, and P. G. Reddy, Org. Prep. Proc. Int., <u>8</u>, 302 (1976); Ref. Zh. Khim., 7Zh137 (1978).
- 5. V. Knoppova, A. Beno, R. Kada, and J. Kovač, Collect. Czech. Chem. Commun., 76, 1433 (1980).
- 6. Shin-ichi Shimamura, Yakugaku Zasshi, 80, 429 (1960); Ref. Zh. Khim., 17Zh175 (1961).
- 7. N. K. Kochetkov and É. E. Nifant'ev, Vestn. Mosk. Gos. Univ., Ser. Khim., No. 5, 119 (1958).
- 8. D. Manly and E. D. Amstutz, J. Org. Chem., 21, 516 (1958).
- 9. J. Miller, J. Am. Chem. Soc., 76, 1433 (1954).
- 10. V. N. Novikov, S. V. Borodaev, and L. D. Babeshkina, Khim. Geterotsikl. Soedin., No. 5, 601 (1982).
- 11. Z. N. Nazarova, V. N. Novikov, and V. S. Pustovarov, Zh. Org. Khim., 2, 161 (1966).
- 12. Z. N. Nazarova and V. S. Pustovarov, Khim. Geterotsikl. Soedin., No. 4, 586 (1969).
- 13. V. N. Novikov and Z. N. Nazarova, Khim. Geterotsikl. Soedin., No. 1, 3 (1967).
- 14. I. Ya. Bernshtein and Yu. L. Kaminskii, Spectrophotometric Analysis in Organic Chemistry [in Russian], Khimiya, Leningrad (1975), p. 65.

# SYNTHESIS OF THIIRANE OXIMES FROM 3,4-DIBROMO-

### 3-METHYL-2-BUTANONE OXIME

V. P. Tashchi, T. I. Rukasov, Yu. G. Orlova, Yu. A. Putsykin, and Yu. A. Baskakov UDC 547.712'238: 542.924.5'945. 27'951: 543.422

 $2-(\alpha-\text{Oximinoethyl})-2-\text{methylthiirane}$  was obtained by the reaction of 3,4-dibromo-3-methyl-2butanone oxime with sodium sulfide. At the same time, the O-carbamoyl derivative of the  $\alpha,\beta$ dibromo oxime was converted to the corresponding substituted  $\alpha,\beta$ -unsaturated oxime under the same conditions. Thiirane oxime, like its O-carbamoyl derivative, underwent the desulfuration that is characteristic for thirranes under the influence of tributylphosphine.

It is known [1] that the reaction of vicinal dihaloalkanes with sodium or potassium sulfide does not lead to the expected thiiranes.

By the reaction of 3,4-dibromo-3-methyl-2-butanone oxime (I) with excess sodium sulfide in acetone at 20°C we obtained II, which, according to the results of elementary analysis, corresponds to the product of replacement of the bromine atoms in oxime I by a sulfur atom. The presence in the PMR spectrum of II of singlets at 1.68 and 1.76 ppm (CH<sub>3</sub>C and CH<sub>3</sub>C=N groups, respectively), two doublets with J=1.9 Hz at 2.51 and 2.88 ppm (CH<sub>2</sub> group) [the chemical shifts and the spin-spin coupling constants (SSCC) of the methylene group are characteristic for the thiirane ring [1]], and a broad singlet of an =N-OH group at 9.9 ppm and the IR spectroscopic data made it possible to assign the 2-( $\alpha$ -oximinoethyl)-2-methylthiirane structure to it.

To confirm the structure of thiirane oxime II we carried out the desulfuration of the thiirane under the influence of trialkyl(aryl)phosphines [1]. In fact, treatment of oxime II with tributylphosphine in chloroform led to  $\alpha$ ,  $\beta$ -unsaturated oxime III.

All-Union Scientific-Research Institute of Chemical Agents for the Protection of Plants, Moscow 109088. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 751-753, June, 1982. Original article submitted July 1, 1981.