CONDENSATION OF α-SUBSTITUTED FURFURALS WITH METHYL ETHYL KETONE

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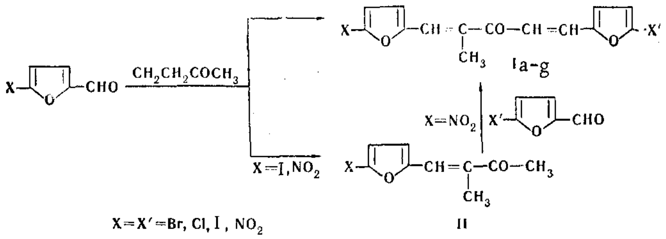
UDC 547.724:542.953

The reaction of 5-halo- and 5-nitrofurfurals with methyl ethyl ketone was investigated. It was established that the 5-halofurfurals form 1,5-bis(5'-halo-2'-furyl)-2-methyl-1,4-pentadien-3-ones in alkaline media. In acid medium, 5-nitrofurfural gives primarily 1-(5'-nitro-2'-furyl)-2-methyl-1-buten-3-one, which readily condenses with halofurfurals in alkaline media. The IR spectra of the pentadienones are presented.

In order to explain the regularities in the synthesis of unsaturated ketones of the furan series and to obtain new biologically active substances, we studied the condensation of 5-halo- and 5-nitrofurfurals with methyl ethyl ketone.

Despite the literature data [1], it turned out that the condensation of 5-halofurfurals with methyl ethyl ketone in alkaline media proceeds just as readily as with acetone [2] to form the previously undescribed stable 1,5-bis(5'-halo-2'-furyl)-2-methyl-1,4-pentadien-3-ones in good yields (up to 80%) (see Table 1). When a large excess of methyl ethyl ketone is used, 1-(5-iodo-2'-furyl)-2-methyl-1-buten-3-one (II, X = I), which is unstable and resinifies on storage, can be isolated.

The condensation of 5-nitrofurfural with methyl ethyl ketone has not yet been described. In view of the fact that 5-nitrofurfural is very sensitive to alkalis, its condensation with methyl ethyl ketone was carried out in acetic acid in the presence of concentrated H_2SO_4. In contrast to the halogen derivatives, 1-(5'-nitro-2'-furyl)-2-methyl-1-buten-3-one (II, X = NO_2) is formed in yields up to 80%. This product is obtained in better yields (90%) directly from 5-nitrofurfural diacetate. It readily undergoes condensation in alkaline media with 5-halofurfurals to form the previously undescribed 1-(5'-nitro-2'-furyl)-2-methyl-5-(5"-halo-2"-furyl)-1,4-pentadien-3-ones (Ie-g).



The compounds obtained, which contain halogen in the furan ring, like bis(halofurfurylidene)acetone [2], evolve halogen quantitatively on heating with concentrated HNO_3 and readily undergo exchange of bromine by iodine with KI and exchange of bromine and iodine by a nitro group with $AgNO_2$.

1,5-Bis(5'-nitro-2'-furyl)-2-methyl-1,4-pentadien-3-one (Id) was obtained in 60% yield by the condensation of II (X = NO_2) with excess 5-nitrofurfural diacetate. It can also be obtained by the condensation of methyl ethyl ketone with a large excess of 5-nitrofurfural diacetate in acidic media.

All of the ketones obtained are yellow, crystalline substances that are slightly soluble in cold ethanol, more soluble in hot ethanol, and quite soluble in benzene, acetone, chloroform, dioxane, dichloro-

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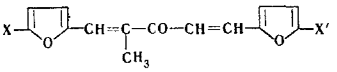
Rostov State University, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 9, pp. 1162-1166, September, 1971. Original article submitted March 3, 1969.

TABLE 1.



Comp.	X	X′	mp, °C	Empirical formula	Element	Found, %	Calc. %	UV spectrum	
								λ_{max}, nm	lg ε
Ia	Cl	Cl	83—84	$C_{14}H_{10}Cl_2O_3$	Cl	24,00	23,87	270 334	4,198 4,313
Ib	Br	Br	95—96	$C_{14}H_{10}Br_2O_3$	Br	41,41	41,45	272 338	4,147 4,223
Ic	I	I	152—153	$C_{14}H_{10}I_2O_3$	I	51,62	52,87	230 395	4,130 4,229
Id	NO_2	NO_2	231,5—232	$C_{14}H_{10}N_2O_7$	N	8,84	8,80	230 348	4,022 4,169
Ie	NO_2	Cl	185,5—186	$C_{14}H_{10}ClNO_5$	Cl N	11,88 4,81	11,62 4,55	228 370	4,004 4,289
If	NO_2	Br	169—169,5	$C_{14}H_{10}BrNO_5$	Br N	22,45 3,50	22,68 3,97	228 370	4,142 4,408
Ig	NO_2	I	140—141	$C_{14}H_{10}INO_5$	I N	31,92 3,49	31,79 3,51	226 355	4,197 4,406

Table 1 (continued)

Comp.	Yield, %	2,4-Dinitrophenylhydrazones			
		mp, °C	empirical formula	N, %	
				found	calculated
I	41	172—172,5	$C_{20}H_{14}Cl_2N_4O_6$	11,22	11,74
Ib	80	163—164	$C_{20}H_{14}Br_2N_4O_6$	10,19	9,88
Ic	82	201,5—202	$C_{20}H_{14}I_2N_4O_6$	8,81	8,50
Id	51	256—257	$C_{20}H_{14}N_6O_{10}$	16,91	17,06
Ie	58	220—221	$C_{20}H_{14}ClN_5O_8$	14,78	14,35
If	62,7	193,5—194	$C_{20}H_{14}BrN_5O_8$	13,00	13,16
Ig	71	188,5—189	$C_{20}H_{14}IN_5O_8$	12,13	12,09

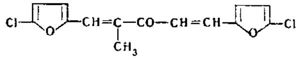
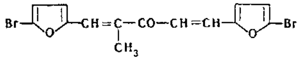
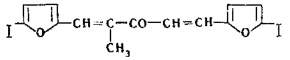
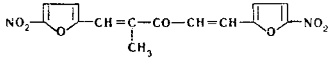
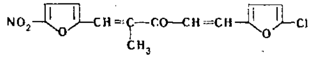
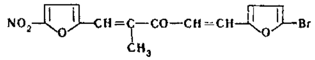
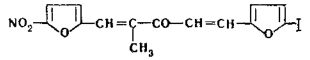
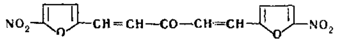
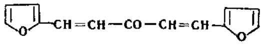
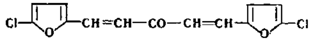
ethane, and glacial acetic acid, and insoluble in water. Brightly colored solutions form when they are dissolved in concentrated H_2SO_4. The solutions are decomposed by a solution of bromine in carbon tetrachloride.

The physical constants, analytical results, and UV spectra for all of the newly obtained compounds are presented in Table 1.

Compound II ($X = NO_2$) has clearly expressed bacteriostatic activity [3].

For a more detailed study of the structures of the compounds obtained, we recorded their IR spectra (Table 2) from 600 to 1800 cm^{-1}, which encompasses the characteristic vibrations of the carbonyl group, the furan ring, the double bonds, the nitro group, the methyl group, etc. The IR spectra of mineral oil suspensions were measured with an IKS-14 spectrophotometer. For comparison, we recorded the spectra of 1,5-bis(5'-nitro-2'-furyl)- [4] and 1,5-bis(5'-chloro-2-furyl)-substituted [2] 1,4-pentadien-3-ones (Ih and Ij). The unsaturated ketones that we investigated have absorption maxima at 1625-1646 cm^{-1}, which are characteristic for the valence vibrations of the carbonyl group. The introduction of electron-donor or electron-acceptor groups into the 5- and 5'-positions of the furan ring results in a reduction of the $\nu_{C=O}$ band. (For example, $\nu_{C=O}$ is 1670 cm^{-1} for Ii, but 1625 and 1639 cm^{-1} for Ih and Ij, respectively.) The presence of a methyl group attached to the secondary carbon atom in 1,4-pentadien-3-ones (Ia-c) is not appreciably reflected in $\nu_{C=O}$ (for example, 1639 cm^{-1} for Ij, and 1635-1638 cm^{-1} for Ia-c), while the presence of a nitro group in the 5-position of the furan ring has an appreciable effect on $\nu_{C=O}$ (compare 1625 cm^{-1} for Ih and 1631-1646 cm^{-1} for Id-g). The frequency of the symmetric stretching vibrations of the nitro group in Id-h is somewhat lower as compared with the known value (1347-1365 cm^{-1} [5]). The asymmetric stretching vibrations of the nitro group in the same compounds are manifested as intense bands at 1528-1547 cm^{-1} (as compared with 1518-1594 cm^{-1} [5]). The furan ring can be detected in Ia-h and Ij from its in-plane deformation vibrations at 1235-1264 cm^{-1} (1215-1252 cm^{-1} [6]), the pulsation vibrations of the ring at 1006-1025 cm^{-1} (1013-1022 cm^{-1} [7]), the out-of-plane CH deformation vibrations at 962-976 cm^{-1}(1945-970 cm^{-1} [6]),

TABLE 2. Characteristic Vibrational Frequencies in the IR Spectra of 1,5-Difuryl-1,4-pentadien-3-ones

Comp.	Structural formula	$\nu_{C=O}$, cm^{-1}	$\nu_{C=C}$, cm^{-1}	ν_{CH_3}, cm^{-1}	NO_2 group, cm^{-1}		2,5-Disubstituted furan ring, cm^{-1}			
					symmetric stretching vibrations	asymmetric stretching vibrations	β_{CH}	pulsation vibrations	γ_{CH}	out-of-plane deformation vibrations
I a		1635	1586	1375	—	—	1264	1016	972	782
Ib		1638	1579	1372	—	—	1259	1008	967	785
Ic		1636	1574	1384	—	—	1253	1006	970	787
Id		1646	1598	1382	1345	1547	1235	1009	976	733
Ie		1643	1586	1381	1344	1537	1251	1018	969	732
If		1631	1576	1382	1340	1528	1258	1008	970	734
I g		1638	1589	1384	1339	1532	1259	1015	971	730
Ih		1625	1595	—	1354	1567	1239	1020	970	736
I i*		1670	1589	—	—	—	—	—	—	—
Ij		1639	1589	—	—	—	1254	1015	963	730

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*See [5].

and the out-of-plane deformation vibrations of the furan ring at 730-790 cm^{-1} (740-800 cm^{-1} [8]); replacement of the halogen by a nitro group in the 5 position of the furan ring lowers the frequency of the out-of-plane deformation vibrations by 52-53 cm^{-1}.

EXPERIMENTAL

1,5-Bis(5'-halo-2'-furyl)-2-methyl-1,4-pentadien-3-ones (Ia-c). Methyl ethyl ketone (0.02 mole) and 3 ml of a 4% aqueous sodium hydroxide solution were added with stirring at room temperature to a solution of 0.02 mole of the appropriate halofurfural in the minimum amount of ethanol. After 20-25 min, the mixture gradually darkened, and fine yellowish crystals began to precipitate. The reaction mixture was stirred for another 30 min. The precipitate was removed by filtration, washed with water, hydrochloric acid, and again with water until it gave a neutral reaction to Congo, and recrystallized from alcohol.

1-(5'-Iodo-2'-furyl)-2-methyl-1-buten-3-one (II, X = I). Methyl ethyl ketone [2.16 g (0.03 mole)] and 3 ml of 4% aqueous sodium hydroxide were added dropwise with stirring to a solution of 2.21 g (0.01 mole) of 5-iodofurfural in the minimum amount of ethanol, and the mixture was stirred for 2 h. The dark-yellow crystals were removed by filtration and washed with water, dilute hydrochloric acid, and again with water until they were neutral to Congo to give 1.38 g (50%) of a product with mp 130-131° (from benzene). Found %: I 46.25. $C_9H_9IO_2$. Calculated %: I 45.96. UV spectrum: λ_{max} 222, 278, 350 nm, log ε 3.98, 3.93, 4.05. IR spectrum: $\nu_{C=O}$ 1621 cm^{-1}, $\nu_{C=C}$ 1576 cm^{-1}, ν_{CH_3} 1365 cm^{-1}, and, for the furan ring, 1247, 1006, 973, and 790 cm^{-1}.

The 2,4-dinitrophenylhydrazone was obtained as dark bordeaux-red crystals with mp 186° (from acetic acid). Found %: N 12.08. $C_{15}H_{15}IN_4O_5$. Calculated %: N 12.28.

1-(5'-Nitro-2'-furyl)-2-methyl-1-buten-3-one (II, X = NO_2). A. Methyl ethyl ketone [36 g (0.5 mole)] and 5.8 ml of concentrated H_2SO_4 were added dropwise with stirring to a solution of 70.5 g (0.5 mole) of 5-nitrofurfural in 125 ml of glacial acetic acid. The reaction mixture was allowed to stand in sunlight for 5 h and was then diluted with cold water. The precipitated dark-brown crystals were removed by filtration and washed with water to give 117.1 g (60%) of a product with mp 124.5-125° (from benzene). Found %: C 55.85; H 4.90; N 7.23. $C_9H_9NO_4$. Calculated %: C 55.38; H 4.64; N 7.17. UV spectrum: λ_{max} 240, 355 nm, log ε 4.65, 4.87. IR spectrum: $\nu_{C=O}$ 1649 cm^{-1}, $\nu_{C=C}$ 1615 cm^{-1}, ν_{CH_3} 1371 cm^{-1}, and, for the furan ring, 1236, 1025, 962, and 809 cm^{-1}.

B. Concentrated H_2SO_4 (2.7 ml) was added to a solution of 33 g of 5-nitrofurfural diacetate in 75 ml of glacial acetic acid, and the mixture was heated on a water bath with stirring. The mixture was cooled, and 12.5 ml of methyl ethyl ketone and 3.3 ml of concentrated H_2SO_4 were added. The mixture was worked up as in method A to give 78% of a product with mp 124.5-125° (from benzene). This product did not depress the melting point of the product obtained by method A. The semicarbazone was obtained as yellow crystals with mp 245-246° (from alcohol). Found %: N 22.00. $C_{10}H_{12}N_4O_4$. Calculated %: N 22.21. The thiosemicarbazone was obtained as orange crystals with mp 237-238.5° (from acetic acid). Found %: N 21.02. $C_{10}H_{12}N_4O_3S$. Calculated %: N 20.80. The 2,4-dinitrophenylhydrazone was obtained as dark-red crystals with mp 265-266° (from acetic acid). Found %: N 18.92. $C_{15}H_{13}N_5O_7$. Calculated %: N 18.66.

Oxidation of II (X = NO_2) with concentrated HNO_3 by the method in [9] (a) gave 5-nitrofurancarboxylic acid with mp 181-183° (from alcohol) (mp 183-184° [10]), while oxidation of II with sodium hypochlorite by the method in [11] (b) results in hydrolytic cleavage to form 5-nitrofurfural (proved by chromatography).

1,5-Bis(5'-nitro-2'-furyl)-2-methyl-1,4-pentadien-3-one (Id). A. This compound was obtained in 12% yield as a side product during the chromatographic purification of II (X = NO_2).

B. 5-Nitrofurfural [1.41 g (0.01 mole)] and 2.5 ml of concentrated H_2SO_4 were added to a solution of 1.95 g (0.01 mole) of II (X = NO_2) in 6 ml of glacial acetic acid. The mixture was allowed to stand in sunlight for 5 h and was then poured into cold water. The resulting dark-brown crystals were removed by filtration and washed with water to give 1.63 g (51%) of a product with mp 231-232.5° (from benzene). This product did not depress the melting point of the product obtained by method A.

C. Silver nitrite [0.040 g (0.002 mole)] was added to a solution of 0.049 g (0.001 mole) of Ic (X = X' = I) in 3 ml of glacial acetic acid. The mixture was allowed to stand for 24 h and was then heated on a boiling-water bath. The resulting precipitate was removed by filtration, and the filtrate was diluted with cold water to precipitate yellow crystals. A chromatographic comparison of this product with the products obtained by methods A and B demonstrated their identical character. This product did not depress the melting point of the products obtained by methods A and B.

1-(5'-Nitro-2'-furyl)-5-(5"-halo-2"-furyl)-2-methyl-1,4-pentadien-3-ones (Ie-g, $X = NO_2$, $X' = Cl$, Br, I). A solution of 0.05 mole of 5-halofurfural in ethanol and 1 ml of 10% aqueous sodium hydroxide were added with stirring at room temperature to a solution of 0.05 mole of II ($X = NO_2$) in the minimum amount of ethanol. The reaction mixture was stirred for 5-6 h and allowed to stand for 24 h. The resulting precipitate was removed by filtration.

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