FORMYLATION OF 5-ALKYL-3H-FURAN-2-ONES

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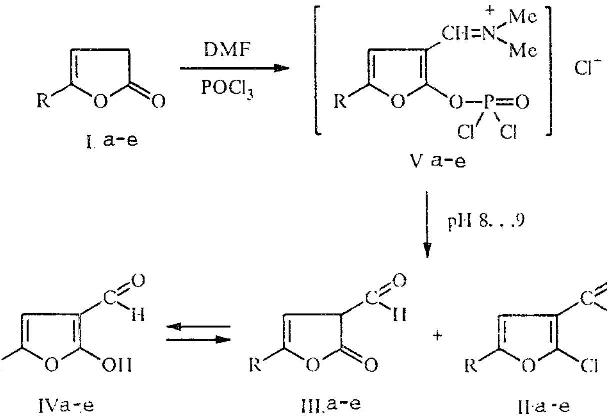
3-Formyl derivatives of 3H-furanones and 2-chlorofurans are formed in the reaction of 5-alkyl-3H-furan-2-ones with $POCl_3$ and DMF. The conditions for the purposeful synthesis of these compounds were found. The transformations of the formyl group in reactions with dinitrophenylhydrazine and aniline were studied.

We have previously demonstrated the ability of 5-R-3H-furan-2-ones to undergo condensation with aromatic aldehydes, aminomethylation, and alkylthiomethylation, which are realized due to the C—H acidity of the methylene group of the lactone ring [1].

In continuing our research on the reactivities of the indicated heterocycles we examined the possibilities of introduction of a formyl group into the 3 position of the ring. One of the pathways that we selected is the Vilsmeier—Haack formylation of 5-alkyl-3H-furan-2-ones Ia-e (see Scheme 1).

Scheme 1



I—V a R = C_4H_9, b R = C_4H_9-*i*, c R = C_5H_{11}, d R = C_6H_{13}, e R = $(CH_2)_3CH(CH_3)_2$

The reaction was accomplished in dry benzene at 70-80°C with a I:dimethylformamide:phosphorus oxychloride ratio of 1:1:2. The results of a study of the structures of the products obtained by means of physicochemical methods showed that under the formylation conditions the transformations take place simultaneously at two reaction centers of I — the methylene group and the lactone carbonyl group — to give 5-alkyl-3-formyl-2-chlorofurans II, as well as 5-alkyl-3-formyl-3H-furan-2-ones III, which exist in equilibrium with their tautomers — 5-alkyl-2-hydroxy-3-formylfurans IV. The relative amounts of products II and III/IV are determined by the conditions under which the reaction products are worked up. Thus at pH 7 only II are obtained in all variations (a-e), while at pH 8-9 mixtures of II and III/IV are obtained. Intermediate salts V are probably initially formed during the reaction, whereas hydrolysis of them (pH 7) gives 2,3,5-substituted furans II, which at higher pH values are converted to mixtures of tautomers III and IV.

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0009-3122/93/2904-0383$12.50

TABLE 1. Characteristics of IIa-e and IIIa-e

Compound	Empirical formula	bp (°C)/mm	^{13}C NMR spectrum, ppm					Yield, %
			$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$	CHO	
IIa	$C_9H_{11}O_2Cl$	92...93/4	143,38	121,28	104,62	156,73	182,91	47
IIб	$C_9H_{11}O_2Cl$	120...122/5	143,35	121,28	104,62	156,72	182,90	30
IIв	$C_{10}H_{13}O_2Cl$	126...128/5	143,25	120,14	102,16	157,29	183,23	40
IIг	$C_{11}H_{15}O_2Cl$	125...127/5	143,20	120,14	105,42	156,24	183,10	39
IIд	$C_{11}H_{15}O_2Cl$	122...124/5	143,40	120,26	105,50	156,27	183,20	40
IIIa	$C_9H_{12}O_3$	77...78/4	174,94	83,15	120,07	156,53	180,05	50
IIIб	$C_9H_{12}O_3$	113...114/5	174,93	83,15	120,67	156,53	180,91	40
IIIв	$C_{10}H_{14}O_3$	115...117/5	175,20	83,65	121,67	156,50	180,75	40
IIIг	$C_{11}H_{16}O_3$	115...117/5	176,17	84,20	122,15	156,80	180,80	36
IIIд	$C_{14}H_{16}O_3$	114...115/5	175,20	84,10	122,65	156,85	181,10	35

TABLE 2. Characteristics of VIc, e, VIIc, e, and VIIIc, d

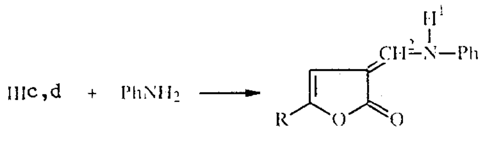
Compound	Empirical formula	mp, °C	Yield %	Compound	Empirical formula	mp, °C	Yield, %
VIc	$C_{16}H_{20}N_4O_6$	175...176	65	VIIe	$C_{17}H_{19}ClN_4O_5$	172...173	85
VIe	$C_{17}H_{20}N_4O_6$	176...177	85	VIIIc	$C_{16}H_{19}NO_2$	91...93	57
VIIc	$C_{16}H_{17}ClN_4O_5$	170...171	80	VIIId	$C_{17}H_{21}NO_2$	93...95	55

The reasoning presented above is based on an analysis of the IR and ^1H and ^{13}C NMR spectra of the synthesized products. Thus the IR spectra of IIIa-e contain absorption bands that are characteristic for 3H-furan-2-ones at 1805 cm^{-1} (C=O group of a β,γ-unsaturated lactone), 1695 cm^{-1} (unconjugated C=C bond of a lactone), and 1070 and 1125 cm^{-1} (ring C—O), as well as absorption bands at 1700 and 2700 cm^{-1} (CHO) and 3400 cm^{-1} (OH). The presence of absorption at 3400 cm^{-1} makes it possible to conclude that its tautomeric enol form IV is present in 3-formyl-substituted furanone III. This conclusion is also confirmed by data from the PMR spectra of III/IVa-e: the presence of two signals of protons of formyl groups constitutes evidence in favor of the existence of carbonyl and enol forms. The following signals (δ, ppm) are observed for carbonyl forms IIIa-e: 7.18-7.26 (1H, d, 1-H), 3.61 (1H, t, 2-H), and 10.36 (1H, d, CHO). The following signals (δ, ppm) are observed for enol forms IVa-e: 6.11 (1H, s, 1-H), 10.76 (1H, s, CHO), and 8.17 (1H, s, 2-H). The percentages of tautomers IV in the mixtures are very small. These mixtures will therefore subsequently be designated as III. The characteristics of II and III are presented in Table 1.

Formylfuranones IIIc, e and chlorofurans IIc, e readily react at the formyl group to give the corresponding 2,4-dinitrophenylhydrazones VIc, e and VIIc, e, the characteristics of which are presented in Table 2.

Aniline was also used as a nitrogen-containing nucleophile in the reaction with 3-formyl-substituted 3H-furan-2-ones IIIc, d; enamines VIIIc, d, which correspond to the expected Schiff bases, were isolated (see Scheme 2).

Scheme 2



VIIIc,d

The IR spectra of VIIIc, d contain a broad band at 3220-3350 cm^{-1}, which should be ascribed to vibrations of an NH group involved in an intramolecular hydrogen bond. The PMR spectra of these compounds contain 4-H signals at 6.26 ppm, as well as protons of =CH—N— and NH groups at 7.20 and 10.84 ppm, respectively, with J_{H1H2} = 12.5 Hz. The existence of H^1 and H^2 coupling constitutes evidence for localization of the H^1 proton attached to the nitrogen atom, and, consequently, VIII exist primarily in the enamine form in solution in $CDCl_3$.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with an IR-20 spectrometer. The PMR and ^{13}C NMR spectra of solutions in $CDCl_3$ were recorded with a Varian FT-80A spectrometer with tetramethylsilane (TMS) as the internal standard.

The results of elementary analysis of II, IIIa-e, VI, VIIc, e, and VIIIc, d were in agreement with the calculated values. Starting furanones Ia-e were obtained by the method described in [1].

5-Butyl-3-formylfuran-2-one (IIIa) and 5-Butyl-3-formyl-2-chlorofuran (IIa). A 7-g (0.05 mmole) sample of 5-butyl-3H-furan-2-one and 3.6 ml (0.05 mmole) of DMF in 10 ml of absolute benzene were added with stirring and cooling (−5°C to 0°C) to a solution of 17 g (0.11 mmole) of $POCl_3$ in 10 ml of absolute benzene, and the reaction mixture was maintained at 75-80°C for 6 h. It was then cooled and treated with 50 ml of saturated aqueous K_2CO_3 solution (pH 8), and the resulting aqueous and organic layers were separated. The aqueous layer was extracted with benzene, and the extract was combined with the organic layer and dried over $MgSO_4$. The solvent was removed, and the residue was fractionated in vacuo to give 4.7 g of IIIa and 4 g of IIa.

5-Butyl-3-formyl-2-chlorofuran (IIa) was similarly obtained, but the reaction mixture was worked up at pH 7.

5-Butyl-3-formyl-3H-furan-2-one (IIIa). A saturated aqueous solution of K_2CO_3 was added with stirring to 5 g (0.027 mole) of IIa up to pH 9, after which the organic layer was separated, dried over $MgSO_4$, and fractionated in vacuo to give 3.3 g of IIIa.

5-Alkyl-3-formyl-3H-furan-2-one Hydrazones VIc, e. A 0.003-mole sample of 2,4-dinitrophenylhydrazine was dissolved in 8 ml of ethanol acidified with a few drops of H_2SO_4, after which 0.003 mole of IIIc, e in 4 ml of ethanol was added dropwise with stirring. The product was crystallized from ether—ethanol (3:2).

5-Alkyl-3-formyl-2-chlorofuran Hydrazones VIIc, e. Compounds VIIc, e were obtained in the same way as hydrazones VIc, e.

Enamines VIIIc, d. A 0.026-mole sample of the 5-alkyl-3-formyl-3H-furan-2-one and 0.035 mole of freshly distilled aniline in 20 ml of absolute benzene were placed in a round-bottomed flask equipped with a Dean—Stark adapter, and the reaction mixture was refluxed for 2 h. The crystalline product was then separated and washed with ether.

REFERENCES

1. V. A. Sedavkina, N. A. Morozova, A. Yu. Egorova, and I. G. Ostroumov, Khim. Geterotsikl. Soedin., No. 4, 451 (1987).