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3-ARYLIDENE DERIVATIVES OF 3H-FURAN-2-ONES. SYNTHESIS AND REACTION WITH MALEIC ANHYDRIDE

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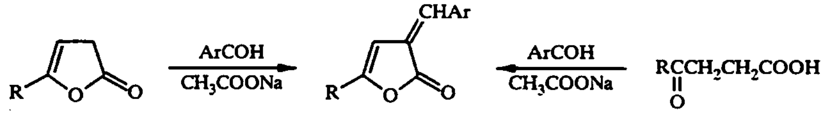
The synthesis of 5-alkyl(aryl)-3-arylidene-3H-furan-2-ones was accomplished, and their reaction with maleic anhydride was studied. The configuration of the initial arylidene derivatives was established on the basis of the PMR spectra of the adducts obtained.

The literature has considered in detail the condensation reactions of aromatic aldehydes with 5H-furanones [1, 2]. Condensations of 5-substituted 3H-furanones have insufficient description in the literature, and only relate to 5-aryl- and 5-methyl-3H-furan-2-ones [2, 3]; this is explained by the low availability of 5-alkyl-3H-furan-2-ones.

On the basis of 4-oxoalkanoic acids, we obtained a series of 5-alkyl-3H-furan-2-ones, with the alkyl substituent from C_3H_7 to C_6H_{13}, in yields up to 75% [4]. That allowed the study of their reaction with aldehydes of the benzene and furan series. All the indicated furanones (Ia-e) react by the crotonic type of condensation at the position 3 of the heterocycle.

The isolation of the 5-alkyl(aryl)-3-arylidene-3H-furan-2-ones (IIa-*l*) was accomplished in acetic anhydride in the presence of anhydrous sodium acetate. The synthesis of the compounds (II) is also possible by the treatment of 4-oxoalkanoic acids with the equimolecular amount of aldehydes in the presence of sodium acetate under conditions analogous to those described for the condensation of furanones.



Ia-e IIa-*l* IIIa-e

I, III a R = C_6H_5, b R = CH_3, c R = C_3H_7, d R = C_4H_9, e R = C_5H_{11}-*i*; II a R = C_6H_5, Ar = C_6H_5;
b R = CH_3, Ar = C_6H_5; c R = C_3H_7, Ar = C_6H_5; d R = C_4H_9, Ar = C_6H_5; e R = C_3H_7, Ar = C_6H_4-Cl-*o*;
f R = C_3H_7, Ar = C_6H_4-NO_2-*o*; g R = C_4H_9, Ar = $C_6H_4N(CH_3)_2$; h R = C_3H_7, Ar = 2-furyl
i R = C_4H_9, Ar = 2-furyl ; j R = C_5H_{11}-*i*, Ar = 2-furyl ; k R = C_4H_9, Ar = α-NO_2- 2-furyl
l R = C_4H_9, Ar = 5-iodo-2-furyl

The scheme for the formation of compounds (IIa-e) based on the 4-oxoalkanoic acids (IIIa-e) assumes the initial lactonization of the acids to the 3H-furan-2-ones (Ia-e), undergoing the subsequent condensation reaction with aldehydes, without the isolation of the intermediate products.

It should be noted that an ambiguous path can occur for the process in the case of 4-oxoalkanoic acids. However, the alternative reaction direction, the first stage of which is the condensation of the aldehydes at the methylene group of the β-position of the acid, characterized by higher C−H acidity than the α-methylene group, and the subsequent lactonization of the product leading to the 5-alkenyl-4-arylidenetetrahydrofuran-2-one (IV), is not realized.

All the synthesized compounds (IIa-*l*) have very specific spectral characteristics.

The IR spectra of the compounds (IIa-*l*) contain absorption bands in the region of 1805-1800 cm^{-1}, corresponding to vibrations of the C=O group of β,γ-unsaturated lactones. They also contain the ν_{CH} stretching vibrations of the benzene ring

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TABLE 1. ^1H NMR Spectra of the 5-R-3-Arylidene-3H-furan-2-ones (II)

Compound	Chemical shifts, δ, ppm			
	4-H	=CH—Ar	Ar	R
IIc	6,20	6,90	7,25...7,65	0,92...2,10
IId	6,40	6,95	7,25...7,70	0,92...2,20
IIe	6,40	7,23	7,28...7,80	0,87...2,40
IIg	6,35	7,21	7,22...7,76	0,87...2,20
IIh	6,00	7,20	7,25...7,30	0,97...2,00
IIi	6,10	7,22	7,25...7,35	0,92...2,10
IIj	6,10	7,20	7,25...7,35	0,87...2,20

TABLE 2. ^1H NMR Spectra of the 4-Phenyl(furyl)-6-R-3,4-dihydro-2H-furo[2,3-b]pyran-2,3-dicarboxylic Anhydrides (Va-d)

Compound	Chemical shifts, δ, ppm					
	5-H	4-H	3-H	2-H	6-R	4-Ar
Va	6,51	2,89	2,60	2,70	7,12...7,35	7,12...7,35
Vb	6,32	2,91	2,61	2,72	2,52	7,22...7,30
Vc	6,30	2,90	2,62	2,75	0,89...2,20	7,20...7,33
Vd	6,33	2,90	2,61	2,70	0,87...2,10	7,25...7,27

TABLE 3. Characteristics of the Compounds (IIe-g,k,*l*)* and the Compounds (Va-d)

Compound	Empirical formula	Found, % Calculated, %				mp, °C	Yield, %
		C	H	N	Cl		
IIe	$C_{14}H_{13}ClO_2$	67,89 67,61	5,89 5,23	—	14,67 14,28	104...105	62
IIf	$C_{14}H_{13}NO_4$	65,02 64,92	5,36 5,06	5,58 5,41	—	127...129	55
IIg	$C_{17}H_{21}NO_2$	78,33 78,23	7,94 8,11	5,42 5,97	—	109...110	68
IIk	$C_{13}H_{13}NO_5$	59,72 59,31	5,10 4,94	5,68 5,32	—	114...115	45
IIl	$C_{13}H_{13}IO_3$	45,71 45,35	3,92 3,78	5,68 5,32	—	120...121	51
Va	$C_{16}H_{12}O_5$	68,02 67,66	4,53 4,26	—	—	85...86	82
Vb	$C_{21}H_{14}O_5$	72,95 72,80	4,12 4,05	—	—	102...103	87
Vc	$C_{18}H_{16}O_5$	69,50 69,23	5,24 5,12	—	—	107...109	80
Vd	$C_{16}H_{14}O_6$	63,68 63,57	4,78 4,63	—	—	91...93	70

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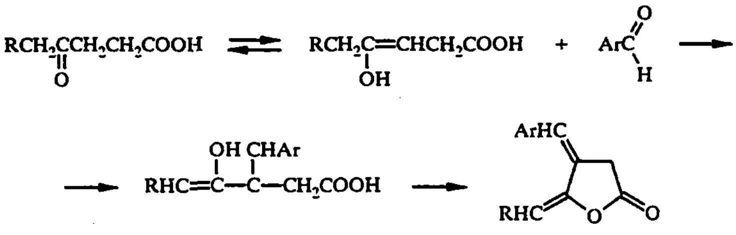
*The characteristics of the compounds (IIa-d,h-j) correspond with those obtained previously [3, 4].

in the region of 3080-3060 cm^{-1} for the compounds (IIa-g), and those of the furan ring in the region of 3130-3110 cm^{-1} for the compounds (IIh-*l*).

In the ^1H NMR spectra of 3-arylidene-substituted 3H-furan-2-ones, the signals of the alkyl groups at the position 5 of the ring occur in the region of 0.92-2.39 ppm. The vinyl proton at C-4 forms a singlet in the region of 6.00-6.40 ppm. The position of the proton signal at the exocyclic sp^2-carbon atom (7.00-7.21 ppm) is determined by the influence of the aryl substituent; the presence of an electron-accepting substituent in the benzene ring shifts the signal to lower field (Table 1).

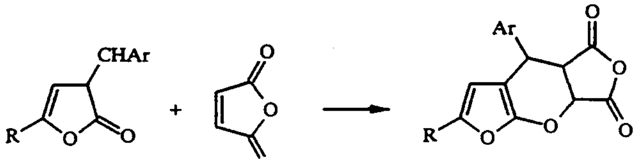


IV

The assignment of signals in the ^{13}C NMR spectrum of the compounds (IIc) was made by comparison with known data as well as the utilization of the method of off-resonance. The number, position, and multiplicity of the signals correspond with the proposed structure. The signal of the carbonyl group is observed at low field at 162.61 ppm. The signals of the $C_{(3)}$, $C_{(4)}$, and $C_{(5)}$ atoms appear at 121.88, 100.85, and 133.39 ppm correspondingly, whereby the signal of the $C_{(4)}$ atom in the off-resonance spectrum is split into a doublet, and the signals of the quaternary $C_{(3)}$ and $C_{(5)}$ atoms remain as singlets. The exocyclic sp^2-hybridized C atom is characterized by resonance at 133.70 ppm (a doublet in the off-resonance spectrum). The carbon atoms of the benzene ring absorb at 134.61, 128.59, 128.8, and 128.02 ppm, and the atoms of the alkyl substituent absorb in the region of 30.37-12.31 ppm.

However, these data are insufficient to determine the configuration of the compounds (IIa-*l*), which can exist either in the Z- or E-configuration.

Considering that the 1,3-oxadiene portion, formed from the exocyclic C═O bond and the carbonyl group of the lactone ring in the molecule of the 3-arylidene-3H-furan-2-ones, rigidly fixed in the S-cis-position, guarantees the possible [4+2]-cycloaddition reaction with different dienophiles, we investigated the reaction of compounds (IIa-c,h) with maleic anhydride under conditions of the Diels–Alder reaction. The study of the given reaction allows not only the development of the chemistry of arylidene derivatives of furanones, but also the response to the question of the configuration of the last.



IIa-c,h

Va-d

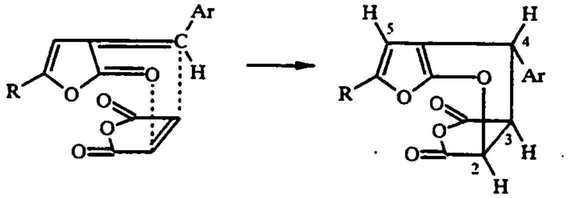
V a R = C_6H_5, Ar = C_6H_5; b R = CH_3, Ar = C_6H_5; в R = C_3H_7, Ar = C_6H_5; d R = C_3H_7, Ar = 2-furyl

Of the 3-arylidene-3H-furan-2-ones, special interest in the Diels–Alder reaction is presented by the 3-furfurylidene-substituted furanone (IIh). When the indicated compound is utilized as a diene, the [4+2]-cycloaddition reaction at the endo C═C double bonds of the furyl substituent can be expected. However, the Diels–Alder heteroreaction at the 1,3-oxodiene portion also takes place in that case.

Products of the reaction performed by heating equimolecular amounts of the diene and the dienophile in benzene solution were found to be 4-phenyl-6-R-3,4-dihydro-2H-furo[2,3-b]pyran-2,3-dicarboxylic anhydrides (Va-d), the structure of which was shown on the basis of the data of ^{1}H NMR spectroscopy (Table 2).

The ^{1}H NMR spectrum of compound (Vb) showed signals of the protons of the phenyl ring as a multiplet in the region of 7.22-7.27 ppm. The singlet at 6.32 ppm is attributed to the 5-H vinyl proton, and the protons of the methyl substituent at the ring position 5 give a singlet at 2.52 ppm. The signal at 2.61 ppm appears as a multiplet and can, on this basis, be assigned to the 3-H proton; two other protons are characterized by signals in the form of a doublet at 2.91 and 2.72 ppm. The assignment of the last two signals was made from the study of spin–spin interaction and stereochemical features of the diene synthesis.

It is known [5] that the Diels–Alder reaction proceeds stereospecifically as the cisoid addition of the diene to the dienophile, and the C═C bond in the adduct tends to be disposed closer to the activating group of the substituent. Taking into account that the five-membered heterocycle containing the anhydride group is planar, it can be concluded that the 2H-pyran ring of the adduct is stabilized in the "bath" conformation. In that case, the hydrogen atoms $H_{(3)}$ and $H_{(2)}$ occur in the shielded conformation. On the basis of the spin–spin coupling constants, the signal at 2.72 ppm can be assigned to the $H_{(2)}$ atom (J_{23} = 13 Hz), and the signal at 2.91 ppm can be assigned to the $H_{(4)}$ atom (J_{34} = 5 Hz). The SSCC of the $H_{(4)}$ and $H_{(3)}$ protons (5 Hz) shows that the $H_{(4)}$ atom in the compounds (V) has the pseudoaxial orientation.



The structure of the adduct and the stereospecificity of the given reaction allow the structure of the initial 3-arylidene-substituted 3H-furan-2-ones (IIa-*l*) to be inferred.

Therefore, taking into account the axial disposition of the phenyl substituent in the compounds (Va-c,h), as well as the principles indicated above, it can be concluded unambiguously that the 5-alkyl(aryl)-3-arylidene-3H-furan-2-ones utilized in the Diels–Alder reaction have the E-configuration.

EXPERIMENTAL

The IR spectra were taken on the IKS-29 instrument. The NMR spectra were recorded on the Varian FT-80A instrument at the working frequency of 80 MHz, and using the solvent $CDCl_3$; chemical shifts are presented using the δ scale, and the internal standard was TMS. The yields and characteristics of the compounds obtained are presented in Table 3.

The 5-alkyl(aryl)-3-arylidene-3H-furan-2-ones (IIe,f,g,k,*l*) were obtained by the method of [4].

4-Phenyl(furyl)-6-R-3,4-dihydro-2H-furo[2,3-b]pyran-2,3-dicarboxylic Anhydrides (Va-d). To 0.005 mole of the 5-alkyl(aryl)-3-arylidene-3H-furan-2-one (IIa-c,h) in benzene is added 0.005 mole of maleic anhydride. The reaction mixture is heated on a water bath for 1 h. The solvent is removed, and the crystals are recrystallized from hexane.

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