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SYNTHESIS AND CONFIGURATION OF 6-ARYLIDENE-2-FURFURYLIDENE-CYCLOHEXANONES

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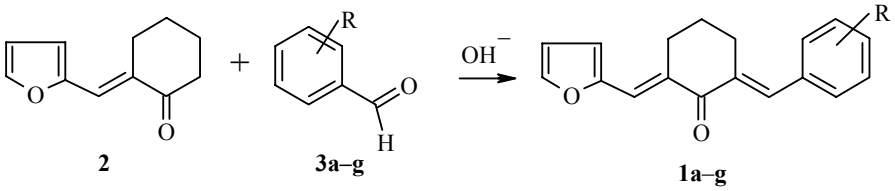
6-Arylidene-2-furfurylidenecyclohexanones were obtained by the condensation of cyclohexanone with aldehydes of the aromatic and furan series under conditions of base or acid catalysis. The effect of substituents in the aromatic ring on the activity of the initial aldehyde was studied. According to data from the IR spectra, the obtained ketones exist in the form of trans,trans isomers.

Keywords: 6-arylidene-2-furfurylidenecyclohexanones, aromatic aldehydes, α,β-unsaturated ketones, 5-nitrofurfural, furfural, crotonic condensation.

Diarylidene(dihetarylidene)cyclanones have various types of biological activity [1], are pesticides [2], and are used in organic synthesis for the construction of practically important heterocyclic compounds [3]. The possibility of using compounds of this type as antioxidant additives [2] and as components of rocket fuel [4] has been reported. New polymers based on furfurylidenecyclohexanones are stable and resistant to the action of laser radiation [5].

The literature contains fairly comprehensive data on the synthesis and properties of symmetrical diarylidene- and difurfurylidenecyclohexanones (see, for example, [6]). The amount of information on unsymmetrical arylidenecyclohexanones is significantly smaller [7]. Furfurylidenearylidenecyclohexanones have hardly been studied at all.

In the present work we describe the synthesis of previously unknown 6-arylidene-2-furfurylidenecyclohexanones **1a-h** and discuss their stereochemistry. The ketones **1a-g** were obtained by crotonic condensation of 2-furfurylidenecyclohexanone (**2**) with aromatic aldehydes **3a-g** in solution in isopropyl alcohol under conditions of base catalysis (an aqueous solution of sodium hydroxide) at room temperature.



2 **3a–g** **1a–g**

1, **3 a** R = H; **b** R = 4-OMe; **c** R = 4-NMe_2; **d** R = 4-Br; **e** R = 3-NO_2; **f** R = 2-Cl; **g** R = 2-F

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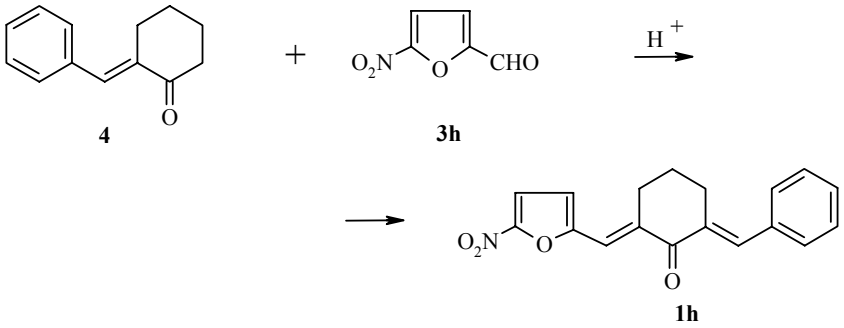
Here, it was found that the nature of the substituent R has a substantial effect on the reactivity of the aldehyde and, consequently, on the yields of the products **1**, which vary between 60 and 92%. The ketones **1a**,**d-g** (R = H or R = electron-withdrawing groups 4-Br, 3-NO_2, 2-Cl, and 2-F respectively) were obtained with the highest yields (79-92%).

The yields of the ketones **1b**,**c** (R is an electron-donating group, OMe and NMe_2 respectively) were considerably lower (60-68%), while a more concentrated catalyst (a 40% solution of sodium hydroxide) was used for the production of **1c**.

In the case of the aldehyde **3h** under the conditions of base catalysis strong resinification of the reaction mass was observed. The synthesis of compound **1h** from 2-benzylidenecyclohexanone (**4**) and 5-nitrofurfural (**3h**) was therefore realized in acetic acid in the presence of sulfuric acid.



The yield of the product **1h** amounted to 32%. The characteristics of the synthesized compounds **1a-h** are given in Table 1.

The composition and structure of the ketones **1a-h** were confirmed by the results of elemental analysis and also by data from the IR and ^{1}H NMR spectra.

TABLE 1. The Characteristics of 6-Arylidene-2-furfurylidenecyclohexanones **1a-h**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
1a	$C_{18}H_{16}O_2$	82.05 / 81.82	6.01 / 6.06	—	109-110	88
1b	$C_{19}H_{18}O_3$	77.55 / 77.55	6.50 / 6.12	—	99-100	68
1c	$C_{20}H_{21}NO_2$	78.01 / 78.18	7.09 / 6.84	4.93 / 4.56	153-168 (dec.)	60
1d*	$C_{18}H_{15}BrO_2$	63.11 / 62.97	4.67 / 4.37	—	134-136	87
1e	$C_{18}H_{15}NO_4$	70.26 / 69.90	4.94 / 4.85	4.48 / 4.53	129-130	92
1f*[2]	$C_{18}H_{15}ClO_2$	72.54 / 72.36	5.35 / 5.03	—	85-86	86
1g	$C_{18}H_{15}FO_2$	76.50 / 76.60	5.54 / 5.32	—	86-87	79
1h	$C_{18}H_{15}NO_4$	70.17 / 69.90	5.57 / 4.85	4.32 / 4.53	175-176	32

* Found, %: Br 23.08. Calculated, %: Br 23.32.

*[2] Found, %: Cl 11.76. Calculated, %: Cl 11.89.

In the IR spectra (Table 2) there is a band for the stretching vibrations of the carbonyl group, which undergoes a bathochromic shift as a result of conjugation and appears in the region of 1652-1664 cm^{-1}. The bands of the stretching vibrations of the olefinic C=C bonds are observed in the region of 1526-1610 cm^{-1}.

Their high intensity compared with the intensity of the bands for the vibrations of the carbonyl C=O bond, which in compounds **1** is determined by the cyclohexanone fragment, provides an analytical indication for the *s-cis* arrangement of the carbonyl and vinylene groups [8]. The presence of bands for the out-of-plane deformation vibrations of the C=C bond at 972-984 cm^{-1} of the ketones **1a-h** indicates the *trans*,*trans* configuration for the latter (see [9, 10]), in which both the furyl and the aryl substituents are located with the carbonyl group on different sides of the C=C bond.

Strong conjugation in a system of π-bonds can be traced in the ^{1}H NMR spectra of the ketones (Table 3), and this shows up in the almost identical screening of the protons of the CH groups of the arylidene and furfurylidene fragments. The chemical shifts of these protons have close values (7.48-7.70 ppm), and their signals frequently overlap with the signals of the aromatic protons, which are in the region of 6.50-8.30 ppm.

The proximity of the chemical shifts of the signals of =C<u>H</u>Ar and =C<u>H</u>Het indicates that of various types of substituents in Ar have a weak effect on the conjugated system. It is only possible to note a small upfield shift of these signals in the presence of electron-donating groups OMe and NMe_2 in Ar (see compounds **1b**,**c**).

Thus, we have synthesized previously unknown 6-arylidene-2-furfurylidenecyclohexanones and investigated their stereochemistry. It should be noted that the alternative transformations that arise during investigation of the reactions of the obtained compounds with the conjugated C=C–C=O system will form the subject of future investigations.

EXPERIMENTAL

The IR spectra were recorded on a Specord M-80 instrument. The ^{1}H NMR spectra were obtained on Bruker AC-300 (300 MHz) and Varian FT-80A (80 MHz) spectrometers. The reactions and the purity of the products were monitored by TLC on Silufol UV-254 plates with a 3:1:1 mixture of hexane, diisopropyl ether, and chloroform as eluent, iodine as developer, and UV irradiation.

TABLE 2. The IR Spectra of the Ketones **1a-h***

Compound	ν, cm^{-1}				
	C=O	C=C–Het, C=C–Ar	C=CH (nonplanar)	C–O–C (furan)	Other vibrations
1a	1660	1580, 1568	984	1036	—
1b	1656	1596, 1526	982	1030	1258 (=C–O–C), 1460, 1388 (Me)
1c	1652	1570, 1552	980	1028	1460, 1364 (Me)
1d	1664	1610, 1574	980	1028	628 (C–Br)
1e	1656	1584, 1562	974	1020	1524, 1346 (NO_2)
1f	1656	1580, 1556	982	1036	762 (C–Cl)
1g	1662	1582, 1570	972	1026	1105 (C–F)
1h	1662	1575, 1554	974	1020	1508, 1348 (NO_2)

* Recorded in a thin layer of vaseline oil and hexachlorobutadiene.

TABLE 3. The ^{1}H NMR Spectra of the Ketones **1a-h**

Compound	Chemical shifts, δ, ppm *					
	$C_{(4)}$–H_2 (2H, m)	$C_{(3)}$–H_2, $C_{(5)}$–H_2 (4H, m)	=CH–Ar (1H, s)	=CH–Het (1H, s)	H_{Ar}	H_{Het}*[2]
1a	1.85	2.50-3.00	7.62	7.68	7.40 (5H, m)	6.55; 6.75; 7.40*[3]
1b	1.85	2.50-3.00	7.58	7.68	6.90 (2H, d, *J* = 10); 7.42 (2H, d, *J* = 10)	6.55; 6.70; 7.40 *[3]
1c	1.85	2.50-2.95	7.48	7.70	6.75 (2H, d, *J* = 10); 7.50 (2H, d, *J* = 10)	6.55; 6.70; 7.40
1d	1.85	2.50-3.00	7.58	7.68	7.38 (2H, d, *J* = 10); 7.55 (2H, d, *J* = 10)	6.55; 6.70; 7.40
1e	1.85	2.50-3.10	7.70		7.85 (1H, d, *J* = 10); 7.70 (1H, s); 8.20 (1H, d, *J* = 10); 8.30 (1H, s)	6.60; 6.80; 7.45
1f	1.85	2.50-3.10	7.70		7.30 (4H, m)	6.60; 6.80; 7.45
1g	1.75	2.30-3.05	7.70		7.35 (4H, m)	6.60; 6.80; 7.40*[3]
1h	1.81	2.79-3.16	7.68		7.42 (5H, m)	6.80; 7.42*[3]

* The ^{1}H NMR spectra were recorded in DMSO-d_6 (compounds **1a**,**b**,**d-f**) and deuterochloroform (compounds **1c**,**g**,**h**).
*[2] The chemical shifts of the one-proton broad signals are given.
*[3] The H_{Het} signals overlap with the H_{Ar} signals.

6-Benzylidene-2-furfurylidenecyclohexanone (1a). To a solution of 2-furfurylidenecyclohexanone (**2**) (40 g, 0.23 mol) and benzaldehyde (35 g, 0.33 mol) in isopropyl alcohol (40 ml) at room temperature and with stirring we added a 20% aqueous solution of sodium hydroxide (45 ml). The mixture was kept at the same temperature for 2 h and neutralized with a 3% aqueous solution of hydrochloric acid. The crystals of the product **1a** that separated were washed with water and isopropyl alcohol and recrystallized from isopropyl alcohol.

The ketones **1b-g** were obtained similarly. During the synthesis of the ketone **1c** a 40% aqueous solution of sodium hydroxide was used.

6-Benzylidene-2-(5-nitrofurfurylidene)cyclohexanone (1h). To a solution of 2-benzylidenecyclohexanone (**4**) (6.33 g, 0.03 mol) and 5-nitrofurfural (4.25 g, 0.03 mol) in glacial acetic acid (25 ml) we added one drop of concentrated sulfuric acid. The mixture was stirred at room temperature for 2 h and was then kept at the same temperature for 22 h. The crystals of the product **1h** that separated were filtered off, washed with acetic acid, and recrystallized from acetic acid and then from isopropyl alcohol.

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