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ARYLMETHYLENE DERIVATIVES OF 5-R-3H-FURAN-2-ONES AND N-ARYL-5-R-3H-PYRROL-2-ONES IN REACTION WITH ACETYLACETONE

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Reaction with acetylacetone in the series of 3-arylmethylene-substituted furan-2-ones and pyrrol-2-ones was studied. 8-R-4-Acyl-5-aryl-3-oxo-9-oxabicyclo[4.3.0]nona-1,7-dienes and N-tolyl-8-R-4-acyl-5-aryl-3-oxo-9-azabicyclo[4.3.0]nona-1,7-dienes were synthesized.

Keywords: arylmethylene derivatives, 3H-furan-2-ones, N-aryl-3H-pyrrol-2-ones, acetylacetone, Michael condensation.

The investigated compounds contain a conjugated oxoene fragment involving the exocyclic C=C bond and the double bond of the carbonyl group. Earlier [1] it was shown that the C=C and C=O bonds are fixed in the S-*cis* configuration, making it possible to use 3-arylmethylene-substituted furan-2-ones and pyrrol-2-ones in condensation reactions.

The wide-ranging possibilities of using 3-arylmethylene-3H-furan-2-ones and N-aryl-3-arylmethylene-3H-pyrrol-2-ones in synthesis arise primarily from the presence of the two electrophilic centers. As a result of the delocalization of electron density in the C=C–C=O system these compounds behave as ambident electrophiles, and the addition of nucleophilic particles can take place in two directions, i.e., with attack at the carbon atom of the carbonyl group (1,2-addition) or at the β-carbon atom (1,4-addition).

The relative reactivity of the 3-arylmethylene-3H-furan-2-ones and N-aryl-3-arylmethylene-3H-pyrrol-2-ones in 1,2- and 1,4-addition was examined by means of perturbation molecular orbital theory (PMO). According to this theory, if the electronic structure of the enone fragment is taken into account addition at the C=C group takes place under charge control while 1,4-addition (at the β-carbon atom) takes place under orbital control due to the maximum positive charge at the carbonyl carbon and maximum localization of the LUMO at the β-carbon atom.

Orbital-controlled 1,4-addition is promoted by the increase in the degree of charge delocalization at the electrophilic center of the exocyclic C=C bond in the arylmethylene-substituted furanones, which is accompanied by a decrease in the LUMO energy level. For the initial arylmethylene-substituted 3H-furan-2-ones and N-aryl-3H-pyrrol-2-ones the electron densities of the LUMO at the exocyclic sp^2-hybridized carbon atom were calculated by the LCAO-MO SCF method with PM3 parametrization in the MNDO approximation (Table 1). The results show that the electron density of the LUMO for the carbon atom of the exocyclic C=C bond is higher than that for the carbon atom of the carbonyl group, and on this basis it was concluded that 1,4-addition occurs in the case of the reaction with C-nucleophiles.

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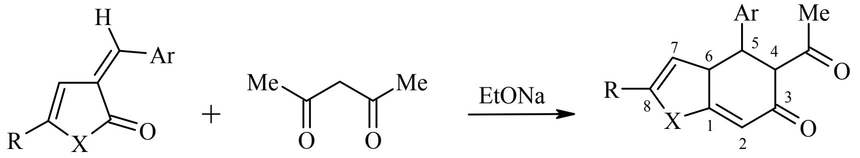
On the basis of the results it can be assumed that the activity is highest in N-aryl-5-R-3-arylidene-3H-pyrrol-2-ones (maximum localization of the LUMO at the exocyclic *sp*^{2}-hybridized carbon atom) compared with other Michael condensation compounds as acceptor.

The use of heterocyclic compounds as acceptors is of particular interest. A similar transformation was examined earlier for the case of the reaction of 3H-furan-2-ones with methyl vinyl ketone and 3-arylmethylene-3H-pyrrol-2-ones with cyclohexanone [2].

Michael condensation of the 5-R-3-arylmethylene-3H-furan-2-ones **1a-c** with the addend that we first used – a diketone (acetylacetone) – by heating (60-65°C) in ethanol under the conditions of base catalysis (sodium ethoxide) leads to the formation of 8-R-4-acyl-5-aryl-3-oxo-9-oxabicyclo[4.3.0]nona-1,7-dienes **3a-c** with yields of 63-71% (Table 2).



1a-c, 2a,b

3a-c, 4a,b

1, **3** **a** X = O, R = *p*-Tol, Ar = Ph; **b** X = O, R = C_5H_{11}, Ar = Ph, **c** X = O, R = Me, Ar = 3,4-$(MeO)_2C_6H_3$; **2**, **4** **a** X = N-*p*-Tol, R = Me, Ar = Ph; **b** X = N-*p*-Tol, R = C_5H_{11}, Ar = Ph

We extended the Michael condensation to the N-heteroanalogs of arylmethylene-substituted furanones, i.e., N-aryl-5-R-3-arylmethylene-3H-pyrrol-2-ones **2a**,**b**. It was established that N-aryl-5-R-3-arylmethylene-3H-pyrrol-2-ones are capable of acting as acceptor in a Michael reaction with acetylacetone with the formation of N-tolyl-8-R-4-acyl-5-aryl-3-oxo-9-azabicyclo[4.3.0]nona-1,7-dienes **4a**,**b** with yields of 76-84% (Table 2). The conditions for the reaction of compounds **2a**,**b** with acetylacetone are similar to the conditions for condensation in the series of oxygen-containing analogs.

The IR spectra of compounds **3a-c** contain the absorption bands of the two carbonyl groups: 1560-1570 ($C=O_{exo}$) and 1665-1685 cm^{-1} (C=O conjugated with the C=C bond) and also the absorption bands of the C–O–C fragment in the region of 1200-1270 cm^{-1}. The vibrations of the lactone carbonyl are absent.

The IR spectra of compounds **4a**,**b** contain the absorption bands of the two carbonyl groups at 1665-1675 cm^{-1} ($C=O_{exo}$) and 1670-1695 cm^{-1} (C=O conjugated with the C=C bond) and also the absorption bands of the C–N–C fragment in the region of 1250-1360 cm^{-1}.

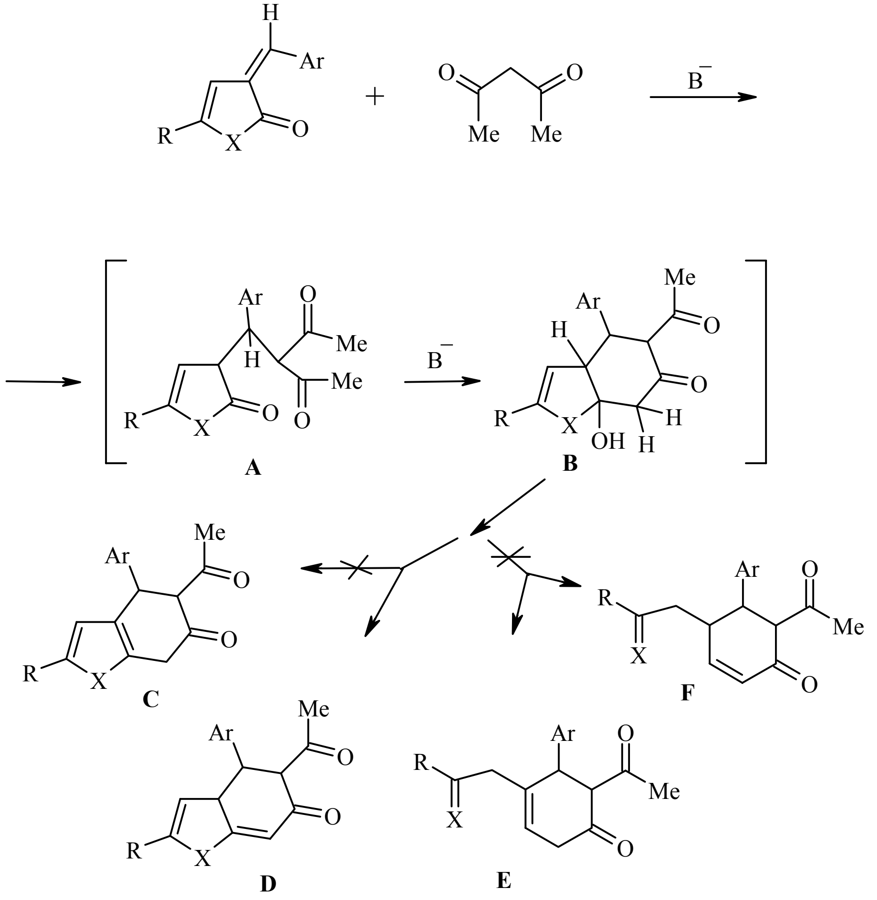
TABLE 1. The Electron Densities at the Carbonyl Carbon Atom (C=O) and the Exocyclic Carbon Atom (C=C) of 5-R-3-Arylmethylene-3H-furan-2-ones and N-Aryl-5-R-3-arylmethylene-3H-pyrrol-2-ones

Compound	LUMO electron densities	
	C=O	C=C
1a	0.051	0.102
1b	0.073	0.296
1c	0.077	0.292
2a	0.072	0.301
2b	0.080	0.310

TABLE 2. The Physicochemical Characteristics of the Products from Michael Condensation **3a-c** and **4a**,**b**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %
		C	H	N		
3a	$C_{23}H_{20}O_3$	80.05 / 80.23	6.03 / 5.81	—	134-135	69
3b	$C_{21}H_{24}O_3$	74.76 / 74.11	7.21 / 6.97	—	145-147	63
3c	$C_{19}H_{20}O_5$	69.12 / 69.51	6.37 / 6.09	—	103-105	71
4a	$C_{28}H_{31}NO_3$	78.54 / 78.32	7.89 / 7.22	3.23 / 3.26	177-179	84
4b	$C_{24}H_{23}NO_3$	77.45 / 77.21	5.87 / 6.16	3.37 / 3.75	164-165	76

The most useful for determination of the structure of compounds **3a-c** and **4a**,**b** are the data from the ^1H and ^{13}C NMR spectra (Tables 3 and 4). Characteristic signals in the ^1H NMR spectra that confirm the formation of the oxabicyclic structures of compounds **3a-c** and **4a**,**b** are the signals of the methine protons H-6 (~3.22) and H-5 (~3.28 ppm) and also the signals of the quaternary atoms C-6 (~44), C-5 (~22), and C-4 (~71 ppm) in the ^{13}C NMR spectra of compounds **3a** and **4b** (Table 4).



X = O, NC_6H_4Me-4

TABLE 3. ^{1}H NMR Spectra of Compounds **3a-c**, **4 a,b**

Compound	H-3, d	H-3a, dd	H-4, dd	H-5, d	H-7, s	CH_3CO, s	Alk	Ar, m
3a	5.07	3.23	3.28	3.59	5.38	2.09	2.35 (3H, s, CH_3)	7.01-7.18 (9H)
	$J_{3,3a}$ = 6.5,	$J_{3a,4}$ = 5.0,	$J_{4,5}$ = 5.4					
3b	4.49	3.23	3.28	3.59	5.38	2.09	0.96-1.96 (11H, m, C_5H_{11})	6.65-6.96 (4H)
	$J_{3,3a}$ = 6.4,	$J_{3a,4}$ = 5.1,	$J_{4,5}$ = 5.5					
3c	4.48	3.24	3.29	3.60	5.37	2.10	2.35 (3H, s, CH_3); 3.73 (6H, s, OCH_3)	6.53-6.58 (3H)
	$J_{3,3a}$ = 6.5,	$J_{3a,4}$ = 5.1,	$J_{4,5}$ = 5.5					
4a	4.08	3.22	3.27	3.58	5.48	2.09	0.96-1.96 (11H, m, C_5H_{11})	6.35-6.96 (8H)
	$J_{3,3a}$ = 6.5,	$J_{3a,4}$ = 5.0,	$J_{4,5}$ = 5.5					
4b	4.50	3.23	3.28	3.59	5.49	2.10	1.71 (3H, s, CH_3); 2.35 (3H, s, CH_3)	6.34-7.10 (8H)
	$J_{3,3a}$ = 6.4,	$J_{3a,4}$ = 5.1,	$J_{4,5}$ = 5.4					

TABLE 4. ^{13}C Spectra of Compounds **3** and **4**

Compound	Chemical shifts, δ, ppm											
	C-8	C-7	C-6	C-5	C-4	C-3	C-2	C-1	C=O	$\underline{C}H_3$-CO	Ar	Alk
3a	149.8	100.5	44.7	22.6	71.5	197.8	98.6	168.3	207.1	22.3	112.8-143.3	24.5
3b	148.6	100.8	44.3	23.1	71.9	198.7	99.5	168.4	206.9	22.5	113.1-144.4	12.3-20.2
3c	148.1	100.1	44.0	23.3	71.4	198.5	99.1	159.5	207.3	22.4	112.3-149.5	15.6
4a	143.2	96.9	43.5	23.5	70.1	197.9	98.7	160.1	207.9	22.3	117.4-143.9	21.9
4b	143.5	97.1	43.3	23.8	70.9	197.5	98.9	159.2	208.1	22.5	116.2-144.1	13.9-20.7

The obtained experimental and spectral data make it possible to put forward a possible reaction scheme. If compounds containing an activated methyl group are used as addend in the Michael condensation it is possible in view of published data [3] to expect an unambiguous reaction path.

The 1,5-dioxo compounds **A** containing the heterocyclic fragment are initially formed under the condition of base catalysis. The process does not stop at the intermediate, and the reaction goes further, leading to the formation of carbocyclization products. This is due to the mobility of the protons in the neighboring methyl group, subsequent dehydration, and the formation of the hypothetical structures **C** and **D**. It was also not possible to rule out possible cleavage of the furan (pyrrolone) ring, leading to compounds **E** and **F**.

However, after analysis of the data from the IR spectra and the ^{1}H and ^{13}C NMR spectra it was possible to rule out the formation of compounds of the **E** and **F** type (Tables 3 and 4) and confirm the formation of structure **D** out of the two most likely forms (**C** and **D**).

This is fully supported by comparison of the chemical behavior of 5-R-3-arylmethylene-3H-furan-2-ones and N-aryl-5-R-3-arylmethylene-3H-pyrrol-2-ones as acceptors in the Michael condensation. It should be noted that the N-heteroanalogs react under milder conditions and the reaction products are formed with higher yields.

Thus, the experimental data fully support the earlier calculations.

EXPERIMENTAL

The IR spectra were recorded on a Specord instrument (Germany) in the region of 400-4000 cm^{-1} with the crystalline compounds as suspensions in vaseline oil. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker MSL-400 spectrometer (400 and 50 MHz respectively) at 25°C in deuterochloroform with TMS as internal standard. Thin-layer chromatography was conducted on Silufol UV-254 plates in the 2:1:1 chloroform–hexane–ether and 2:2:1 ethyl acetate–hexane–chloroform systems with iodine vapor as eluant. Chromatographic separation was realized on a column of silica gel with isopropyl alcohol, ethanol, and hexane as eluants.

The quantum-chemical calculations were performed with MOPAC software by the LCAO-MO SCF method in the MNDO approximation with PM3 parametrization.

The arylmethylene-substituted 3H-furan-2-ones **1a**-**c** were obtained by the procedure in [4], and N-aryl-3H-pyrrolo-2-ones **2a**,**b** by the procedure in [5].

8-R-4-Acyl-5-aryl-3-oxo-9-oxabicyclo[4.3.0]nona-1,7-dienes 3a-c and N-Tolyl-8-R-4-acyl-5-aryl-3-oxo-9-azabicyclo[4.3.0]nona-1,7-dienes 4a,b (General Method). To a mixture of the furanone **1a**-**c** [or pyrrolone **2a**,**b**] (5.4 mmol) and acetylacetone (5.4 mmol) we added dropwise solution of freshly prepared sodium ethoxide in alcohol (5.4 mmol). The reaction mixture was heated for 3-7 h, poured into cold water, neutralized with dilute hydrochloric acid, and extracted with diisopropyl ether. The extract was evaporated, and the crystalline residue was recrystallized from hexane (Table 2).

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