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SYNTHESIS OF ARYLIDENE DERIVATIVES OF 1-ARYL-3H-PYRROL-2-ONES

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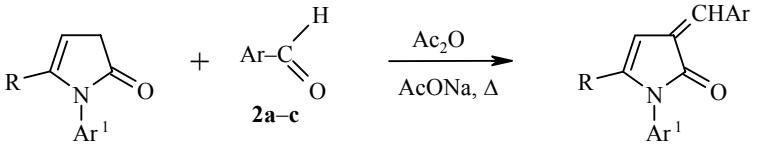
The aminolysis of 5-aryl-3-arylidene-3H-furan-2-ones by the action of aromatic amines leads to the formation of substituted amides of 4-oxo acids, the subsequent azacyclization of which in the presence of acetic anhydride leads to the formation of 1,5-diaryl-substituted 3-arylidene-3H-pyrrol-2-ones. The mechanism of the occurring and alternative transformations is discussed.

Keywords: 4-oxoalkanamides, 5-aryl(alkyl)-3-arylidene-3H-furan-2-ones, 5-aryl(alkyl)-3-arylidene-3H-pyrrol-2-ones, aromatic amines, ammonolysis.

Many examples of the condensation of aromatic aldehydes with 5H- and 3H-furan-2-ones [1-5] are known. At the same time the reaction of aromatic aldehydes with their nitrogen-containing analogs 3H-pyrrol-2-ones has only been described for N-unsubstituted 5-aryl(alkyl)-3H-pyrrol-2-ones [6]; the synthesis of 5-aryl(alkyl)-3-arylidene-3H-pyrrol-2-ones was realized either by ammonolysis of their O-hetero analogs (by the action of ammonia) or by the reaction of N-unsubstituted 5-aryl(alkyl)-3H-pyrrol-2-ones with aromatic aldehydes.

In the present work we studied the condensation of N-aryl-substituted 3H-pyrrol-2-ones **1** with aromatic aldehydes **2a-c**, which requires harsher conditions than in the case of the O,S-hetero analogs. The reaction was conducted in solution in acetic anhydride in the presence of anhydrous sodium acetate with prolonged heating of the reagents.



1 **2a–c** **3a–c**

2 a Ar = 2-HOC_6H_4, **b** Ar = Ph, **c** Ar = 3-$O_2NC_6H_4$

As we established, this reaction takes place slowly, and the yields of the products **3a-c** do not exceed 25-30%, which can be explained by the lower mobility of the protons of the methylene unit compared with the thiophen- and furan-2-ones [7].

In order to increase the yield of the arylidene derivatives **3a-c** we proposed a different method for their production, more convenient in preparative respects than the method described above and based on aminolysis of the respective furan derivatives followed by cyclization of the obtained 4-oxo acids [8].

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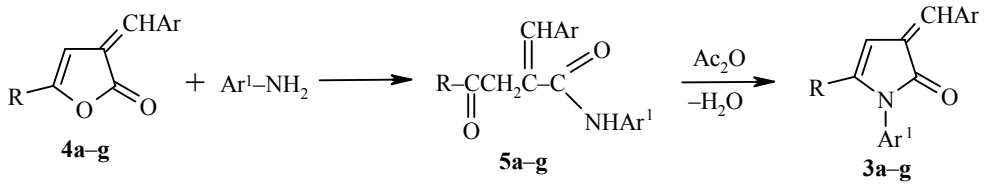
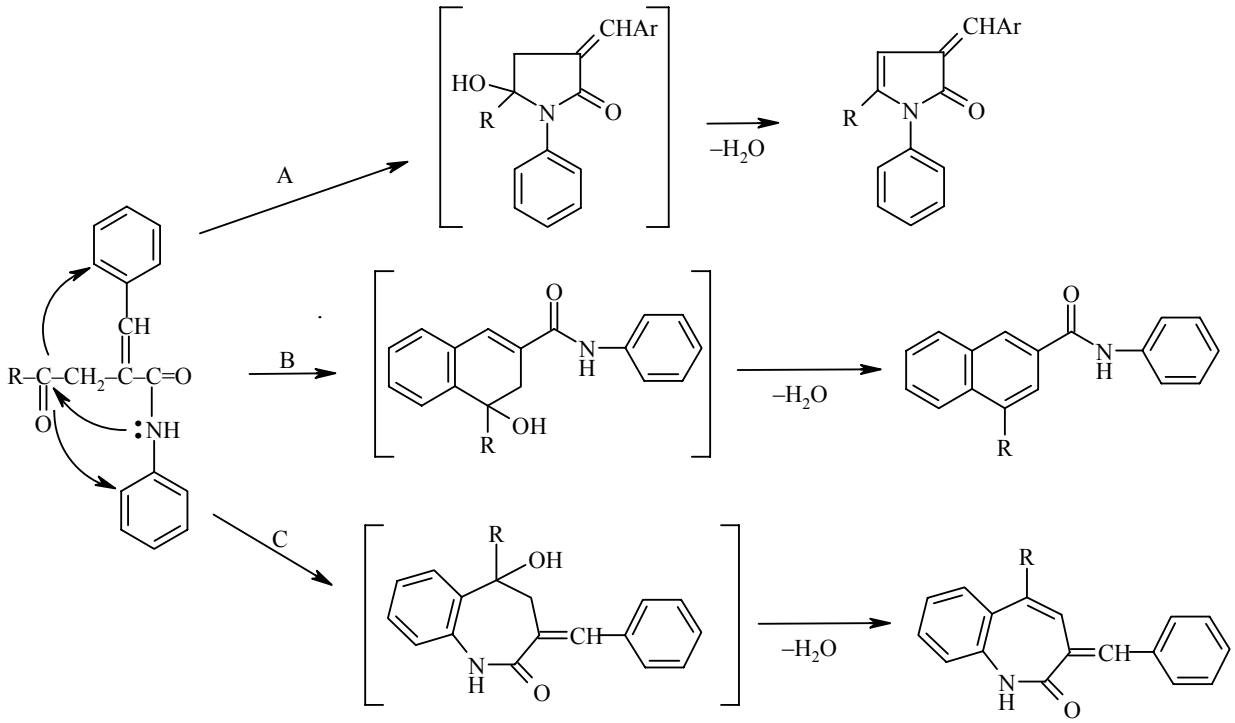


3–**5** **a** R = Ph, Ar = 2-HOC_6H_4; **b** R = Ph, Ar = Ph; **c** R = Ph, Ar = 3-$O_2NC_6H_4$; **d** R = 3-MeC_6H_4, Ar = 4-$MeOC_6H_4$; **e** R = 4-MeC_6H_4, Ar = 3-$O_2NC_6H_4$; **f** R = 4-MeC_6H_4, Ar = Ph; **g** R = C_5H_{11}, Ar = 4-$Me_2NC_6H_4$; **3**, **5** **a**–**c**, **e**, **f** Ar^1 = 3-MeC_6H_4, **d**, **g** Ar^1 = Ph

As starting compounds we used 5-aryl-3-arylidene-3H-furan-2-ones **4a**-**g**, which already contain an arylidene substituent at position 3 of the heterocycle. Compounds **4a**-**g** were obtained by the method in [5], which we developed on the basis of the condensation of aromatic aldehydes with 4-oxoalkanoic acids.

The aminolysis of compounds **4a**-**g** was carried out by refluxing in an excess of the aminating agent in ethanol for 1.5-2 h. We showed that it was possible to isolate the intermediate compounds **5a**-**g**. Such intermediates were not isolated earlier [6] during the reaction of 3-arylidene-substituted 3H-furan-2-ones with ammonia. This is probably due to the fact that the nitrogen atom in the aromatic amines that we used (aniline and *p*-toluidine) has lower nucleophilicity than in ammonia. The formation of the amides **5a**-**g** was proved by the data from elemental analysis and IR spectroscopy.

Further intramolecular cyclization of the amides **5a**-**g** was realized in the presence of dehydrating agents and, in particular, acetic anhydride. The possible formation of a series of products was not excluded; attack by the electron pair of the nitrogen atom may be directed at the electron-deficient carbon atom of the oxo group at position 4 with the formation of 5-hydroxypyrrolidones, from which the elimination of water leads to the targeted 3-arylidene-3H-pyrrol-2-ones (path A); other possible reaction paths are attack on the aromatic fragments of the molecule by the electron-deficient carbon atom of the oxo group with the formation of the amides of naphthenic acids (path B) or benzoazepinones (path C).



Path C is probably not realized on account of the difficulty of closure of the seven-membered ring. Reaction by path B is hindered in connection with the reduced electron density in the aromatic ring on account of the presence of the electron-withdrawing substituent. In actual fact, only path A is realized; the targeted compounds **3a-g** are obtained with quantitative yields when the amides **5a-g** are refluxed in acetic anhydride.

The physicochemical characteristics of the amides **5a-g** and the derivatives of pyrrol-2-ones **3a-g** are given in Table 1.

In the IR spectra of the amides **5a-g** there are absorption bands in the region of 1685-1665 cm^{-1} (the carbonyl group of aromatic ketones), in the region of 1660-1630 cm^{-1} (the amide carbonyl group), and in the region of 3320-3250 cm^{-1} (the absorption band corresponding to the NH group) (Table 2). The IR spectra of

TABLE 1. The Physicochemical Characteristics of 3-Arylidene-3H-pyrrol-2-ones **3a-g** and Amides **5a-g**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, % (method)
		C	H	N		
3a	$C_{24}H_{19}NO_2$	82.12 / 81.59	5.23 / 5.38	4.10 / 3.97	118-120	27 (A), 87 (B)
3b	$C_{24}H_{19}NO$	84.35 / 85.45	5.46 / 5.63	3.64 / 4.15	134-136	30 (A), 53 (B)
3c	$C_{24}H_{20}N_2O_3$	75.35 / 75.00	5.46 / 5.21	7.93 / 7.29	127-130	25 (A), 72 (B)
3d	$C_{25}H_{21}NO_2$	82.07 / 81.74	6.23 / 5.72	3.83 / 3.80	158-160	73 (A)
3e	$C_{25}H_{20}N_2O_3$	76.14 / 75.76	5.00 / 5.06	7.45 / 7.07	145-146	68 A)
3f	$C_{25}H_{21}NO$	85.70 / 85.47	6.15 / 5.98	4.05 / 3.99	139-141	77 (A)
3g	$C_{24}H_{28}N_2O$	80.35 / 80.00	7.86 / 7.78	7.93 / 7.78	147-148	73 (A)
5a	$C_{24}H_{21}NO_3$	77.42 / 77.62	6.00 / 5.66	3.45 / 3.77	162-164	67 (A)
5b	$C_{24}H_{20}NO_2$	88.12 / 88.89	6.34 / 6.94	3.94 / 4.32	160-162	96 (A)
5c	$C_{24}H_{20}N_2O_4$	72.42 / 72.00	5.12 / 5.00	7.10 / 7.00	180-182	87 (A)
5d	$C_{25}H_{23}NO_3$	77.53 / 77.92	5.60 / 5.98	3.82 / 3.64	128-130	56 (A)
5e	$C_{25}H_{22}N_2O_4$	72.75 / 72.46	5.49 / 5.31	6.54 / 6.76	121-123	68 (A)
5f	$C_{25}H_{23}NO_2$	81.03 / 81.30	6.09 / 6.23	3.05 / 3.79	156-158	92 (A)
5g	$C_{24}H_{30}N_2O_3$	76.94 / 76.19	7.78 / 7.94	7.82 / 7.41	128-130	66 (A)

TABLE 2. IR Spectroscopic Data of the Amides **5a-g**

Compound	$\nu_{C=O}$, cm^{-1}	$\nu_{C-N} + \delta_{NH}$, cm^{-1}	ν_{NH}, cm^{-1}
5a	1685	1660	3320-3250
5b	1680	1655	3320-3260
5c	1665	1650	3330-3200
5d	1665	1630	3330-3250
5e	1670	1630	3330-3200
5f	1665	1635	3320-3250
5g	1675	1650	3320-3200

TABLE 3. The Spectral Characteristics of 3-Arylidene-3H-pyrrol-2-ones **3a-g**

Compound	IR spectrum, ν, cm^{-1}	^1H NMR spectrum, δ, ppm		
	C=O, C=C(endocycle), C=C(exocycle), C–H	H-4 (1H, s)	=CHAr (1H, s)	Other signals
3a	1590, 1606, 1550, 3044-3080	6.7	6.9	7.10-7.14 (4H, m, $HOC_6\underline{H}_4$); 7.14-7.30 (5H, m, $C_6\underline{H}_5$); 7.30-7.60 (4H, m, $CH_3C_6\underline{H}_4$); 5.20 (1H, s, $\underline{H}OC_6H_4$); 2.2 (3H, s, $\underline{CH}_3C_6H_4$)
3b	1600, 1606, 1572, 3044-3090	6.3	6.8	7.14-7.30 (10H, m, $2C_6\underline{H}_5$); 7.30-7.50 (4H, m, $CH_3C_6\underline{H}_4$); 2.2 (3H, s, $\underline{CH}_3C_6H_4$)
3c	1580, 1608, 1580, 3050-3080	6.7	6.9	7.14-7.25 (5H, m, $C_6\underline{H}_5$); 7.25-7.50 (4H, m, $CH_3C_6\underline{H}_4$); 7.50-7.70 (4H, m, $O_2NC_6\underline{H}_4$); 2.2 (3H, s, $\underline{CH}_3C_6H_4$)
3d	1580, 1606, 1560, 3050-3030	6.6	6.9	7.00-7.20 (4H, m, $CH_3C_6\underline{H}_4$); 7.20-7.40 (4H, m, $CH_3OC_6\underline{H}_4$); 7.40-7.60 (5H, m, $C_6\underline{H}_5$); 2.2 (3H, s, $\underline{CH}_3C_6H_4$); 2.3 (3H, s, $\underline{CH}_3OC_6H_4$)
3e	1590, 1608, 1580, 3044-3080	6.6	6.9	7.00-7.40 (8H, m, 2 $CH_3C_6\underline{H}_4$); 7.40-7.60 (4H, m, $O_2NC_6\underline{H}_4$); 2.2 (6H, s, 2 $\underline{CH}_3C_6H_4$)
3f	1600, 1606, 1570, 3044-3080	6.6	6.8	7.00-7.30 (8H, m, 2 $CH_3C_6\underline{H}_4$); 7.30-7.60 (5H, m, $C_6\underline{H}_5$); 2.2 (6H, s, 2 $\underline{CH}_3C_6H_4$)
3g	1580, 1608, 1560, 3050-3080	6.6	6.9	7.00-7.20 (5H, m, $C_6\underline{H}_5$); 7.20-7.40 (4H, m, $(CH_3)_2NC_6\underline{H}_4$); 2.3 (6H, s, $(\underline{CH}_3)_2NC_6H_4$); 0.90-2.00 (11H, m, $C_5\underline{H}_{11}$)

compounds **3a-g** contain absorption bands for the amide carbonyl at 1600-1580 cm^{-1}, the stretching vibrations ν_{C-H} of the benzene ring in the region of 3080-3044 cm^{-1}, bands belonging to the absorption of the C=C bond of the heterocycle in the region of 1608-1606 cm^{-1}, and bands corresponding to the exocyclic C=C bond in the region of 1572-1525 cm^{-1}.

In the ^1H NMR spectra of compounds **3a-g** there are singlets for the vinyl protons at position 4 of the heterocycle at 6.30-6.70 ppm, and in the more downfield region (6.80-6.90 ppm) there is a signal for the hydrogen atom of the exocyclic ethylene bond (Table 3). The absence of signals for the protons at the nitrogen atoms and also the absence of additional signals for the vinyl protons make it possible to conclude that the reaction products are 3-arylidene-3H-pyrrol-2-ones **3a-g**.

EXPERIMENTAL

The IR spectra were recorded on an IKS-29 instrument in vaseline oil. The ^1H NMR spectra were recorded on a Varian FT-80A instrument (80 MHz) in deuterochloroform with TMS as internal standard.

The 5-aryl-3-arylidene-3H-furan-2-ones **4a-g** were obtained by the method in [5]. The 1,5-diaryl-3H-pyrrol-2-one **1** was obtained by the method in [8].

N-Aryl-5-aryl-3-arylidene-3H-pyrrol-2-ones (3a-c). A. To a solution of pyrrol-2-one (**1**) (4 mmol) in acetic anhydride we added the respective aromatic aldehyde (4 mmol) and anhydrous sodium acetate (4 mmol). The reaction mixture was heated for 4.5 h. The hot mixture was poured into cold water, and the crystals that separated were filtered off on a Schott filter and recrystallized from hexane.

N-Arylamides of 4-Alkyl- and 4-Aryl-2-arylidene-4-oxobutyric Acid (5a-g). To a solution of 3-arylidene-3H-furan-2-one **4a-g** (3 mmol) in ethanol we added the aromatic amine (9 mmol). The reaction mixture was refluxed for 1.5 h. The crystals that separated were filtered off on a Schott filter and recrystallized from isopropyl alcohol.

N-Aryl-5-alkyl- and N-Aryl-5-aryl-3-arylidene-3H-pyrrol-2-ones (3a-g). B. A 1-mmole sample of the N-arylamide of 2-arylidene-4-aryl(alkyl)-4-oxobutyric acid **5a-g** was refluxed in acetic anhydride (7 ml) for 1 h. The hot mixture was poured into cold water. The crystals that separated were filtered off on a Schott filter and recrystallized from hexane.

REFERENCES

1. Y. S. Rao, *Chem. Rev.*, **64**, 353 (1964).
2. A. A. Avetisyan and G. G. Tokmadzhyan, *Khim. Geterotsikl. Soedin.*, 723 (1987).
3. A. A. Avetisyan and M. T. Dangyan, *Usp. Khim.*, **46**, 1250 (1977).
4. Y. S. Rao, *Chem. Rev.*, **76**, 625 (1976).
5. A. Yu. Egorova, P. V. Reshetov, N. A. Morozova, and V. A. Sedavkina, *Khim. Geterotsikl. Soedin.*, 1043 (1977).
6. A. Yu. Egorova, *Izv. Akad. Nauk. Ser. Khim.*, 172 (2002).
7. V. A. Sedavkina, N. A. Morozova, and A. Yu. Egorova, *Khim. Geterotsikl. Soedin.*, 451 (1987).
8. A. Yu. Egorova, V. A. Sedavkina, and Z. Yu. Timofeeva, *Khim. Geterotsikl. Soedin.*, 755 (2001).