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FURFURYLIDENECYCLANONES IN REACTIONS WITH HYDRAZINES

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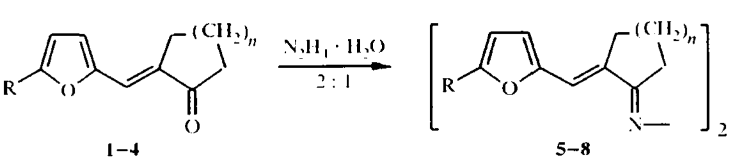
The reaction of cyclopenta(hexa)nones with hydrazine and aryl hydrazines has been studied. Depending on the structure and the conditions, reaction occurs with the formation of the corresponding azines, hydrazones, and pyrazolines.

Keywords: azines, hydrazones, pyrazolines, furfurylidenecyclopenta(hexa)nones, amination.

The reactions of α,β-unsaturated ketones of the furan series with hydrazines have been well studied on examples of substrates with open side chains (furfurylideneacetone, -pinacoline, -acetophenone) [1]. There are individual publications regarding participation of furfurylidenecyclanones in this reaction [2,3].

The aim of the present work was to study the reaction of monofurfurylidenecyclopenta(hexa)nones with hydrazines, to clarify the direction of the reaction in relation to the nature of the nucleophilic reagent (hydrazine, phenylhydrazine), the ratio of the substances reacting, and other conditions.

We have established that on reacting furfurylidenecyclopentanone (**1**), furfurylidenecyclohexanone (**2**), and their homologs **3** and **4** containing methyl group in the α-position of the furan ring, with hydrazine hydrate in ratio of 2 : 1, azines **5-8** are formed readily and in high yield.



1, **5** R = H, *n* = 1; **2**, **6** R = H, *n* = 2; **3**, **7** R = Me, *n* = 1; **4**, **8** R = Me, *n* = 2

The reaction was effected by heating alcohol solutions of the reactants for 1 h. On using an excess of hydrazine the reaction takes place with the participation of the conjugated C=C–C=O bond system of the substrate. The reaction products are the condensed pyrazolines **9** and **10**.

NH-Pyrazolines **9** and **10** are unstable compounds, readily resinifying in air, and decomposing partially on distillation in vacuum with the evolution of nitrogen. The yields of pyrazolines **9**, **10** amount to 10-40%. The compounds of this type are expediently isolated as their N-acyl derivatives. We obtained N-maleyl-3-(2-furyl)-3,4-trimethylene-2-pyrazoline (**11**) by adding maleic anhydride at the end of the reaction (TLC control). Compound **11** was isolated as well-separated and purified crystals in 65% yield. The reverse synthesis of the latter was effected from azine **5** under transhydrazination conditions. The probable scheme of obtaining pyrazolines may be through the formation of hydrazone and its subsequent cyclization. Confirmation of this scheme was the isolation of

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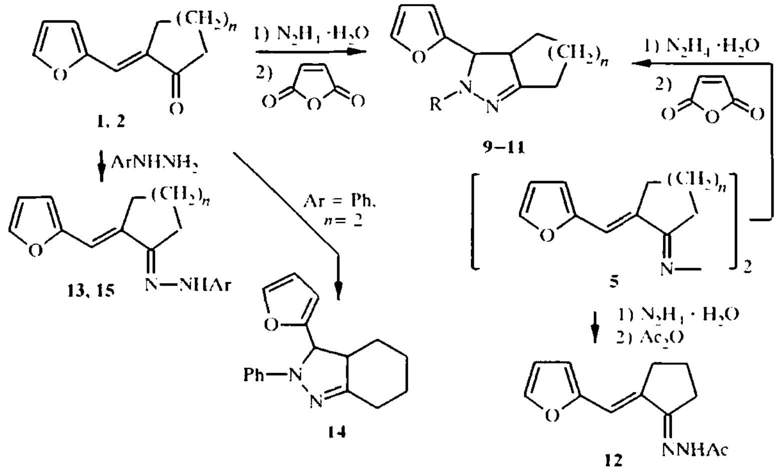

9 R = H, n = 1; **10** R = H, n = 2; **11** R = COCH=CHCOOH, n = 1;
13 Ar = Ph, n = 1; **15** Ar = p-$O_2NC_6H_4$, n = 2

N-acetyl-substituted hydrazone of furfurylidenecyclopentanone (**12**) on reducing the reaction time and treating the mixture with acetic anhydride.

On reacting ketones **1** and **2** with phenylhydrazine, which is less reactive than hydrazine, formation of phenylhydrazones, or the products of their cyclization, *viz.* the corresponding pyrazolines might be expected.

On boiling alcohol solution of ketone **1** and phenylhydrazine furfurylidenecyclopentanone phenylhydrazone (**13**) was obtained in 75% yield. Aza cyclization of the latter probably does not occur due to the planar structure of the molecule analogous to the initial ketone [4] and the *E*-configuration of the hydrazone fragment in connection with the low nucleophilicity of the nitrogen atom of the aminophenyl fragment. It was not possible to isolate any products from the reaction of furfurylidenecyclohexanone with phenylhydrazine under the same conditions due to strong resinification. On carrying out the reaction under mild conditions in an aprotic solvent (ether–hexane, 1 : 1) and maintaining the reaction mixture at 10-15°C N-phenyl-5-(2-furyl)-3,4-tetramethylene-2-pyrazoline (**14**) was obtained.

Further decrease in the reactivity of phenylhydrazine by introducing an electron-withdrawing nitro group into the *p*-position of the aromatic ring reduces the possibility of forming cyclic compounds. On using furfurylidenecyclohexanone **2** under fairly drastic conditions (boiling in alcohol) the corresponding hydrazone **15** is formed on reaction with *p*-nitrophenylhydrazine. The characteristics of the compounds obtained are given in Table 1.

The structures of the compounds synthesized were confirmed by data of IR and ^{1}H NMR spectroscopy. The IR spectra of azines **5-8** contain absorption bands at 1635-1640 cm^{-1} corresponding to the stretching vibrations of the C=N bond, and those of the furan ring at 1120-1160 and 1030 cm^{-1}. The signal of the vinylic H_β hydrogen atom in the ^{1}H NMR spectrum of these compounds is found at 6.35-6.45 ppm as a doublet of singlets corresponding in area to two protons. The signals from the furan ring protons are displayed at 7.25-7.45 ppm, and those of the methylene units as three multiplets at 2.85, 2.68, and 1.8 ppm.

Furylpyrazolines **9** and **10** have absorption bands of secondary amino group at 3200-3400 cm^{-1} in the IR spectra and in the ^{1}H NMR spectrum hydrogen atoms attached to nitrogen atoms resonate at 3.18-3.54 ppm. Stretching vibrations of NH groups are present in the IR spectra of hydrazones **13** and **15** at 3308-3348 cm^{-1}.

Therefore the hydrazination of furfurylidenecyclanones leads to the formation of azines, pyrazolines, or hydrazones depending on the structure of the substrate, the nucleophilicity of the aminating reactant, and the reaction conditions.

TABLE 1. Characteristics of the Obtained Compounds **5-15**

Compound	Empirical formula	Found, % / Calculated, %			mp, °C or bp, °C/mm	Yield, %
		C	H	N		
5	$C_{20}H_{20}N_2O_2$	75.0 / 74.2	6.83 / 6.3	9.18 / 8.75	195-197	98
6	$C_{22}H_{24}N_2O_2$	73.54 / 73.06	7.43 / 6.89	8.36 / 8.04	123-125	96
7	$C_{22}H_{24}N_2O_2$	76.65 / 75.84	6.94 / 6.94	8.02 / 8.04	156-158	80
8	$C_{24}H_{28}N_2O_2$	76.22 / 76.61	7.12 / 7.5	8.01 / 7.44	130-132	96
9	$C_{10}H_{12}N_2O$	67.72 / 68.18	6.72 / 6.81	16.2 / 15.9	112-115/5	10
10	$C_{11}H_{14}N_2O$	69.05 / 69.47	6.92 / 7.36	14.92 / 14.73	175-177/3	40
11	$C_{14}H_{14}N_2O_4$	60.97 / 61.31	5.53 / 5.1	10.05 / 10.22	148-150	65
12	$C_{12}H_{14}N_2O_2$	65.50 / 66.05	6.89 / 6.42	13.35 / 12.85	161-164	25
13	$C_{16}H_{16}N_2O$	74.97 / 76.0	6.93 / 6.4	11.78 / 11.12	101-104	75
14	$C_{17}H_{18}N_2O$	77.02 / 76.69	6.92 / 6.76	10.37 / 10.52	80-82	26
15	$C_{17}H_{18}N_3O_3$	64.98 / 65.5	6.02 / 5.46	13.8 / 13.5	129-132	40

EXPERIMENTAL

The IR spectra were recorded on a Specord M 80 spectrometer in thin films (nujol, hexachlorobutadiene). The ^{1}H NMR spectra were recorded on a Varian FT 80A spectrometer in $CDCl_3$ solution, internal standard was TMS. A check on the progress of reactions and on the purity of products was effected by TLC on Silufol UV 254 plates in the hexane–ether–chloroform, 2 : 2 : 1 system. Furfurylidenecyclanones **1** and **2** were obtained by the procedure [5,6].

2-Furfurylidenecyclopentanone Azine (5). Solution of hydrazine hydrate (1.3 g, 0.05 mol) in alcohol (5 ml) was added with stirring to boiling solution of ketone **1** (16.2 g, 0.1 mol) in ethanol (25 ml). The mixture was heated for 1 h. Crystals of compound **5** separated after removing part of the solvent under reduced pressure. Azines **6-8** were obtained analogously.

1-Phenyl-3,4-tetramethylene-5-(2-furyl)-2-pyrazoline (14). Solution of phenylhydrazine (1 g, 0.0092 mol) in ether (5 ml) and *n*-hexane (20 ml) was added to solution of ketone **2** (1.6 g, 0.0092 mol) in ether (15 ml). The solvent was removed under reduced pressure and crystals of pyrazoline **14** were isolated.

1-Maleyl-3,4-trimethylene-5-(2-furyl)-2-pyrazoline (11). Solution of ketone **1** (5 g, 0.03 mol) in alcohol (5 ml) was added with stirring to solution of hydrazine hydrate (3 g, 0.06 mol) in alcohol (5 ml). The mixture was boiled for 24 h, the solvent was removed under reduced pressure. The residue was dissolved in benzene and acylated with solution of maleic anhydride (5.53 g, 0.06 mol) in benzene (20 ml). The precipitated crystals of compound **11** were filtered off (compound **11** was also obtained by an analogous procedure starting from the azine **5**).

3,4-Tetramethylene-5-(2-furyl)-2-pyrazoline (10). Solution of ketone **2** (8.3 g, 0.047 mol) was added with stirring to boiling solution of hydrazine hydrate (5.93 g, 0.47 mol) in alcohol (25 ml) and the solution boiled for 1 h. The solvent was distilled off, and the residue redistilled in vacuum to give pyrazoline **10**. Pyrazoline **9** was obtained analogously.

2-Furfurylidenecyclopentanone Phenylhydrazone (13). Solution of phenylhydrazine (2.2 g, 0.02 mol) in alcohol (5 ml) was added to boiling solution of ketone **1** (3.2 g, 0.02 mol) in alcohol (5 ml) and the solution boiled for 1 h. Crystals of compound **13** precipitated on cooling. Nitrophenylhydrazone **15** was obtained analogously.

2-Furfurylidenecyclopentanone N-Acetylhydrazone (12). Solution of ketone **1** (9.6 g, 0.06 mol) in alcohol (20 ml) was added to solution of hydrazine hydrate (3 g, 0.06 mol) in alcohol (15 ml), and the solution boiled for 18 h. The solvent was distilled off under reduced pressure, the residue was treated with acetic anhydride (4 g, 0.04 mol), and crystals of compound **12** were isolated.

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