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SYNTHESIS AND STEREOCHEMISTRY OF SOME 4-FURYLIDENE-1-PYRIMIDINYL-2-PIRAZOLIN-5-ONES

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ABSTRACT. 1-(4-Hydroxy-6-methyl-2-pyrimidinyl)-3-methyl-pirazolin-5-one has been condensed with heterocyclic aldehydes, derivatives of 5-phenyl-furfural by Knoevenagel reaction, obtaining 4-(5-phenyl-furylidene) -1-(4-hydroxy-6-methyl-2-pyrimidinyl)-3-methyl 2-pyrazolin-5-ones (2a-h). The structures have been confirmed by elemental analysis and spectroscopic data.

INTRODUCTION

It is known that the 4-th position of 1 substituted 3-methyl-pyrazolin-5-ones is very reactive and undergoes a characteristic condensation of the active methylene group with aromatic aldehydes under acidic or basic catalysis, to give 4-arylidene pyrazolones [1,2,3].

The synthesis and chemistry of 4-arylidene pyrazolones have been of great interest because these compounds are very useful intermediates in synthesis of color dyes and substances with biological activity as for instance antibiotics and antipyretics [4,5].

Similary to the condensation reaction with aromatic aldehydes there are possible Knoevenagel condensations with heterocyclic aldehydes [6].

RESULTS AND DISCUSSION

1-(4-Hydroxi-6-methyl-2-pyrimidinyl)-3-methyl-pyrazolin-5-one 1, obtained by using aminoguanidine salts and ethylacetoacetate in basic catalysis with sodium hydroxide (NaOH), undergoes easily a Knoevenagel condensation with aromatic aldehydes to give 1-(4-hydroxy-6-methyl-2-pyrimidinyl)-3-methyl-2-pirazolin-5-ones [7].

We have extended this reaction on heterocyclic aldehydes using instead of aromatic aldehydes some derivatives of 5-phenyl-furfural obtaining 4-(5-phenyl-furylidene)-1-4-hydroxy-6-methyl-2-pyrimidinyl-3-methyl-2-pyrazolin-5-ones (2a-h).

We have studied this reaction using various 5-phenyl-furfurals with different susbtituents attached to the phenyl group.

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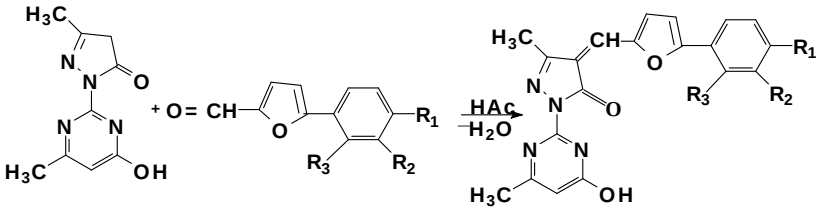

1 1a - h 2 a–h

Table 1

Compound	2a	2b	2c	2d	2e	2f	2g	2h
R_1	NO_2	H	H	COOEt	COOH	Br	Cl	CH_3
R_2	H	NO_2	H	H	H	H	H	H
R_3	H	H	NO_2	H	H	H	H	NO_2

The compounds 2a-h were prepared in various yields by heating under reflux of 1 with (5R-phenyl)-furylaldehydes using EtOH or MeOH as solvent, under acidic catalysis in presence of AcOH.

The reaction was studied also under basic catalysis but the obtained compounds couldn't be separated. The reaction was monitorized by TLC which indicated the presence of only one (stereoisomer) compound [10].

Some physico-chemical data of the obtained compounds are presented in the following table:

Table 2

Compound	Mp(^{0}C)	Yield %	Elementhal analysis Calculated / Found				Colour
			C%		N%		
2a	269	75	59,25	58,60	17,28	16,95	orange
2b	270	80	59,25	60,51	17,28	17,92	orange-red
2c	250	86	59,25	60,35	17,28	17,90	red
2d	218	67	63,88	62,70	12,96	12,36	red
2e	320	53	62,37	61,20	13,86	13,20	red
2f	205	91	54,67	55,70	12,75	12,70	orange-red
2g	190	44	60,83	60,06	14,19	14,23	red
2h	260	84	60,14	60,28	16,70	17,03	orange-red

In acidic catalysis pyrimidyl-pyrazolone (1) reacts in the enol form with heterocyclic aldehydes which are probably orientated with the heterocyclic system in anti to the methyl group, thus affording probably to the Z-isomer. The mechanism of the water elimination is probably E_2 [7].

The obtaining of Z-configuration stereoisomer can be explained by the higher energetic stability of this one, because with the heterocyclic ring in anti position to the methyl group from the third position of pyrazolinone ring the steric hindrance are minimized.

The structure of the synthesized compounds were studied using ^{1}H NMR and IR Spectroscopy. For clarify the stereochemical structure of the exocyclic double bond there were also performed NOE diff measurements and there was observed NOE diff activity for the vinylic proton.

In table 3 are presented the ^1H NMR spectroscopy data of the synthesized compounds.

Table 3

Compound	Pyrazolone-ring $CH_3(C_3)$	Pyrimidine-ring $CH_3(C_6)$	$H(C_3)$	Phenyl-ring H aromatic R	Furyl-ring H_1	H_2
2a	2,56	2,70	6,55	7,9 - 8,5 (m)	7,40(d)	7,62(d)
2b	2,50	2,65	6,55	7,8 - 8,5 (m)	7,45(d)	7,65(d)
2c	2,50	2,70	6,55	7,8 - 8,5 (m)	7,40(d)	7,65(d)
2d	2,55	2,75	6,60	7,9 - 8,4 (m)	7,50(d)	7,70(d)
2e	2,55	2,70	6,55	7,8 - 8,5 (m)	7,40(d)	7,65(d)
2f	2,55	2,65	6,55	7,7 - 8,1 (m)	7,35(d)	7,6)(d)
2g	2,55	2,65	6,50	7,6 - 8,1 (m)	7,35(d)	7,62(d)
2h	2,50	2,65	6,55	7,6 - 7,9 (m)	7,24(d)	7,55(d)

For the obtained compounds were also recorded the UV-VIS spectra in DMF (Table 4):

Table 4

Compound	λ_{max}(nm)	ε
2a	355; 420	7408
2b	310 ; 425	2382
2c	295; 408	11683
2d	325; 438	13926
2e	290; 410	6372
2f	285; 450	24080
2g	305; 435	4552
2h	296; 420	5199

EXPERIMENTAL

Melting points are given uncorrected. The purity of the compounds was checked by thin-layer chromatography on silicagel, using toluene: acetone 8:2 (v:v) as eluent. The elemental analysis for C, H, N, O, S was within $\pm$ 0,4% of the theoretical values for compounds ***2 a-h***.

IR spectra were recorded in KBr pellets on a FT-IR Nicolet 205 spectrophotometer. ^1H-RMN spectra were recorded usind CF_3COOD as solvent with a VARIAN GEMINI 300 MHz Spectrometer.

General procedure for synthesis of compounds 2a-h

1-pyrimidinil-3-methyl-pyrazolin-5-one (1) 0,01 mol and 0,01 mol arylfurfural were dissolved in EtOH and to the reaction mixture was added a small quantity of CH_3COOH. The mixture was refluxed for two hours and then allowed to stand at room temperature and the n cooled with ice. The precipitate was filtered, wash with EtOH (3 times, 3 ml) and dryed at 50^0C. The product was recrystallized from DMF.

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