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SYNTHESIS AND STUDY OF 4-AMINOPYRAZOLONES(5)

II. Acetylation of 1-Phenyl-3-Methyl-4-Aminopyrazolone(5)*

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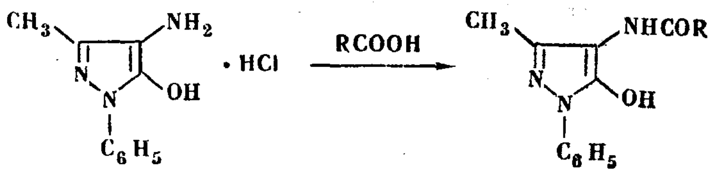
Some 4-N-thioureido- and -ureido derivatives are synthesized by reacting 1-phenyl-3-methyl-4-aminopyrazolone(5) hydrochloride at 40-50°, in alcohol solution, with potassium thiocyanate in the presence of sodium acetate plus carbon disulfide, phenylisothiocyanate, and hexamethylenediisocyanate. Acetylation of 1-phenyl-3-methyl-4-aminopyrazolone(5) with C_1–C_8 aliphatic carboxylic acids takes place under more drastic conditions at 100-150°, to give the corresponding 1-phenyl-3-methyl-4-acylaminopyrazolones(5), isolated in 40-60% yield. The UV spectra of the compounds studied are investigated.

The present authors have previously shown [2], like others [3-6], that 1-phenyl-3-methyl-4-aminopyrazolone(5) hydrochloride (I) reacts with anhydrides and halogenoanhydrides of carboxylic acids to give, depending on the reaction conditions, N-acyl- or O, N-diacylamino derivatives.

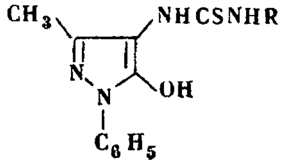
As a development of previous work, a study has been made of the reaction of I with aliphatic carboxylic acids. It was shown that heating I with excess acid gives the 4-acylaminoderivative II in satisfactory yield



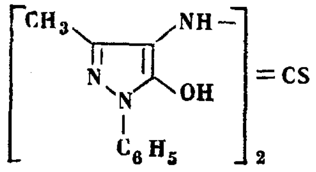
I II

R = H or alkyl(C_1–C_7)

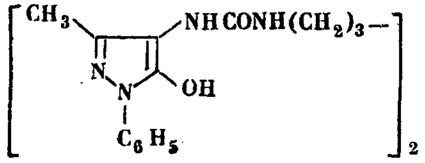
It was also shown that I readily reacts with potassium thiocyanate, though in the presence of sodium acetate, and that it also reacts with phenylisocyanate, carbon disulfide, and hexamethylene diisocyanates, to give the corresponding N-thioureido- and N-ureido derivatives III-VI.



III, IV



V



VI

III, R=H; IV, R=C_6H_5

The products obtained are colorless crystalline compounds, sparingly soluble in water, and compounds IV-VI are sparingly soluble in alcohol. Most of the compounds show an absorption band in alcohol solution, with a maximum at 246-252 mμ.

Experimental

1-Phenyl-3-methyl-4-acylaminopyrazolones(5) (II). A mixture of 1 g 1-phenyl-3-methyl-4-aminopyrazolone(5) hydrochloride (I) and 6–8 g aliphatic carboxylic acid was heated at 100-150° for 4-6 hr. After evaporating off excess acid under reduced pressure, the residue was triturated with dry ether, and recrystallized from a suitable solvent. The

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*For Part I, see [1].

1-Phenyl-3-methyl-4-acylaminopyrazolones(5)

R in formula II	Reaction temperature, °C	M_p, °C	Recrystallization solvent	UV spectrum ($C = 10^{-4}M$)		Formula	Found, %			Calculated, %			% yield
				λ_{max}, mμ	lg ε		C	H	N	C	H	N	
H	100	209—211	xylene, water	250	4.23	$C_{11}H_{11}N_3O_2$	60.95	5.14	19.19	60.83	5.10	19.28	19
CH_3	120	206—208*	water	250	4.23	—	—	—	—	—	—	—	68
C_2H_5	130	201—202	water	246	4.18	$C_{13}H_{15}N_3O_2$	—	—	17.43	—	—	17.12	50
n-C_3H_7	140	198—200	**	246	4.19	$C_{14}H_{17}N_3O_2$	64.85	6.88	15.70	64.85	6.60	16.20	49
n-C_4H_9	140	176—178	**	246	4.17	$C_{15}H_{19}N_3O_2$	65.57	7.30	15.72	65.88	7.00	15.36	45
n-C_5H_{11}	150	173—174	**	250	4.18	$C_{16}H_{21}N_3O_2$	—	—	14.12	—	—	14.62	42
n-C_6H_{13}	150	170—171	**	250	4.18	$C_{17}H_{23}N_3O_2$	68.05	7.63	—	67.76	7.69	—	41
n-C_7H_{15}	150	168—170	**	250	4.18	$C_{18}H_{25}N_3O_2$	68.95	8.20	—	68.56	8.00	—	45

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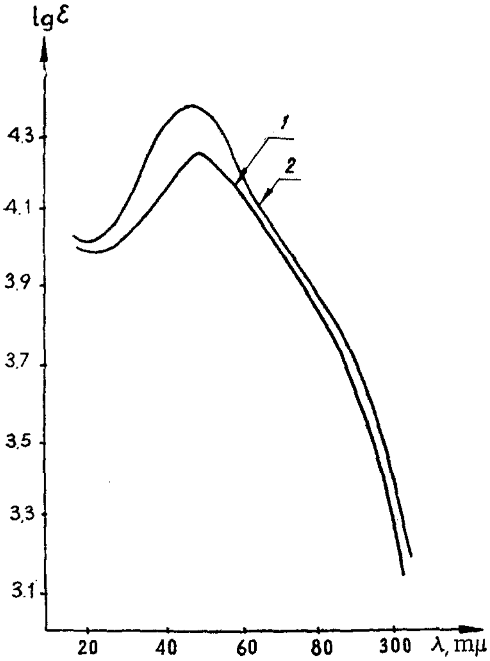
*Literature values: 206-208° [2], 214° [5, 6], approx. 200° [3].

**Purified by dissolving in chloroform and precipitating with petrol ether.

Table below gives reaction temperature, yield, crystallization solvent, mp, absorption maxima positions, and elementary analyses* for the compounds prepared.



UV spectra: 1) II(R = H); 2) III

1-Phenyl-3-methyl-4-N-thioureidopyrazolone(5) (III). 1 g (10 mmole) potassium thiocyanate was added to a suspension of 2.5 g (10 mmole) I in 25 ml absolute alcohol, and the whole stirred for 1 hr at 45-50°. Potassium chloride separated out during the course of the reaction. The solution was filtered, the solvent evaporated off under reduced pressure, and the residue triturated with 100 ml water. The precipitate was filtered off, dried, and washed with 25 ml chloroform. Recrystallization from ethyl acetate gave crystals which decomposed above 80°. Yield 1.62 g (62.7%), λ_{max} 248 mμ, lgε 4.36. Found: S 12.40, 12.80%. Calculated for $C_{11}H_{12}N_4OS$: S 12.51%.

N-phenyl-N'-[1-phenyl-3-methylpyrazolon(5)-yl-4]thiourea (IV). 0.83 g anhydrous sodium acetate was added to a suspension of 2.5 g (10 mmole) I and 1.4 g (10 mmole) phenylisothiocyanate in 25 ml absolute alcohol, and the mixture stirred and held at 45-50° for 30 min. The aminopyrazolone dissolved, and a precipitate was formed; this was filtered off and washed with 100 ml alcohol, 50 ml chloroform, and finally 100 ml water. Yield 2.8 g (85.7%); colorless crystals mp 200-201° (from alcohol), λ_{max} 258 mμ, lgε 4.47. Found: S 10.55, 10.18%. Calculated for $C_{17}H_{16}N_4OS$: S 9.87%.

N, N'-bis[1-phenyl-3-methylpyrazolon(5)-yl-4]thiourea (V). This was prepared in a way similar to that used in preparing the previous compound, using 2.5 g (10 mmole) I, 1.5 g (20 mmole) carbon disulfide. Yield 2 g (94.6%), mp 183-184°. Solution in 36 ml 25% ammonia, followed by filtration and neutralization with acetic acid gave colorless crystals, mp 186-188°. Mass 1.6 g, λ_{max} 252 mμ, lgε 4.63. Found: S 7.75, 7.45%. Calculated for $C_{21}H_{20}N_6O_2S$: S 7.62%.

1, 6-Bis{ N-[1'-phenyl-3'-methylpyrazolon(5)-yl-4']ureido-N'-} hexane (VI). This was prepared in a way similar to that used for the above compounds, starting from 2.5 g (10 mmole) I and 0.9 g (5.3 mmole) hexamethylene diisocyanate. Yield 2.6 g (95.6%); colorless crystals, mp 206-207° (from alcohol), λ_{max} 248 mμ; lgε 4.37. Found: C 61.73, 61.93; H 6.67, 6.77%. Calculated for $C_{28}H_{34}N_8O_4$: C 61.55; H 6.24%.

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