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SYNTHESIS OF THIOPHENE ANALOGS OF 1, 3, 5-TRIPHENYLPYRAZOLINE DERIVATIVES

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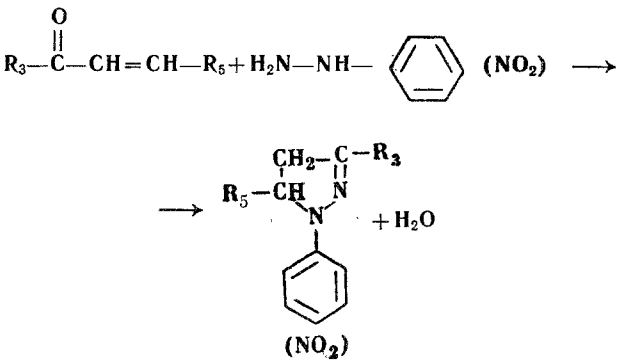
Nineteen Δ^2-pyrazolines hitherto undescribed in the literature are prepared by reacting thiophene and selenophene analogs of chalcones with phenylhydrazine or p-nitrophenylhydrazine. It is shown that thiophene and selenophene chalcones can be more easily cyclized than their furan analogs. The 2, 4, 6-trimethoxy group when present in the 1-(thienyl-2)-3-arylpropenone-1 molecule causes steric hindrance in the corresponding pyrazoline.

Synthesis of furan analogs of 1, 3, 5-triphenylpyrazoline derivatives were described by the present authors in a previous paper [1]. In the present work it was decided to prepare new derivatives of Δ^2-pyrazolines with 2-thienyl, and in some cases, 2-selenienyl at positions 3 and 5. Investigation of the literature relating to the problem showed that there was a small number of papers dealing with the synthesis of a few (thienyl-2)-Δ^2-pyrazolines [2-4], and a paper by Yu. K. Yur'ev and N. K. Sadovaya, [5] which dealt with preparation of 1-phenyl-3-(alkylselenienyl-2)-Δ^2-pyrazolines.

Synthesis of Δ^2-pyrazolines of interest here was effected by reacting isomeric heterocyclic analogs of chalcones with phenylhydrazine or p-nitrophenylhydrazine in acid medium, according to the equation (see Table)

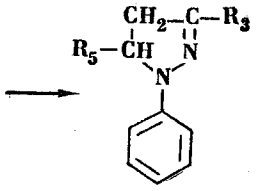


It is important to note that thiophene and selenophene analogs are much less acidophobic than their furan analogs. So where pyrazoline formation was hindered, and prolonged boiling of reactants in acid medium was necessary to bring about reaction, formation of resins was not usually observed. Thus although the nitro group in the aromatic or heterocyclic ring of the furan analog of chalcone hinders cyclization when remote from the carbonyl group, and it was not possible to prepare [1] 1-phenyl-Δ^2-pyrazolines with 4-nitrophenyl or 5-nitrofuryl-2 at position 5, the analogous thiophene derivatives of pyrazolines IV and XII were synthesized. In this connection it may be mentioned that a nitro group in an aromatic ring hinders cyclization more than one in a thiophene ring. This is apparent from the fact that cyclization of 1-(thienyl-2)-3-(4-nitrophenyl) propenone-1 required 25 hr boiling with concentrated hydrochloric acid and acetic acid, whereas only 3 hr were required for 1-phenyl-3-(5-nitrothienyl-2)-propenone-1.

We also prepared the pyrazolines I and VIII, with methoxy groups in the o-positions of the aryl moiety, which methoxy groups hinder cyclization of chalcones, while the corresponding furan analogs could not be prepared. Further, despite a number of experiments under different conditions, it did not prove possible to convert 1-(thienyl-2)-3-(2, 4, 6-trimethoxyphenyl) propenone-1 to a pyrazoline. This was evidently impeded by steric hindrance due to 2, 4, 6-trimethoxyphenyl, and because, as was shown earlier, [6], introduction of three methoxy groups greatly increases the acidophobic nature not only of the furan ring, but also of the thiophene one, so that reaction leads only to formation of resinous products.

The structures of the pyrazolines synthesized were checked by a study of their IR spectra, which were found to lack an absorption band, characteristic of valence vibrations of the N-H group, at 3200-3500 cm^{-1}. Not all of the pyrazolines here described fluoresce, or give the characteristic Knoor reaction. The Table gives some physical and chemical properties of the compounds synthesized.

1-Phenyl-3-R_3-5-R_5-Δ^2-pyrazolines



Serial No.	R_3	R_5	Method of preparation	Refluxing time, hr	Yield, %	Mp, °C	Crystal form	Fluorescence (in n-hexane)	Knorr reaction	Formula	N, %		S, %	
											Found	Calculated	Found	Calculated
I	2-Thienyl	2,4-Dimethoxyphenyl	A	2.5	50	133.5—134	Yellow nodules	Violet	+	$C_{21}H_{20}N_2O_2S$	7.61	7.68	8.73	8.79
II	2-Thienyl	4-Dimethylaminophenyl	A	2	80	149	Yellowish-green flat needles	Violet	+	$C_{21}H_{21}N_3S$	12.22	12.09	9.02	9.22
III	2-Thienyl	4-Chlorophenyl	A	5	85	158.5—159.5	Greenish needles	Dark blue	+	$C_{19}H_{15}ClN_2S$	8.35	8.27	9.64	9.46
IV	2-Thienyl	4-Nitrophenyl	Б	25	87	151.5	Bright orange parallelepipeds	None	+	$C_{19}H_{15}N_3O_2S$	12.22	12.03	9.46	9.18
V	5-Nitro-2-thienyl	Phenyl	A	1.5	36	181.5	Dark red needles	Green	+	$C_{19}H_{15}N_3O_2S$	11.93	12.03	9.24	9.18
VI	Methyl	2-Thienyl	A	5.5	78	96	Slightly yellow minute crystals	None	+	$C_{14}H_{14}N_2S$	11.48	11.56	13.36	13.23
VII	2,4-Dimethoxyphenyl	2-Thienyl	A	3	80	126	Slightly yellow polyhedra	Violet	+	$C_{21}H_{20}N_2O_2S$	7.55	7.68	9.09	8.79
VIII	2,4,6-Trimethoxyphenyl	2-Thienyl	A	5	35	164	Colorless plates	None	+	$C_{22}H_{22}N_2O_3S$	7.13	7.10	8.10	8.13

Table (continued)

Serial no.	R_3	R_5	Method of preparation	Refluxing time, hr	Yield, %	Mp, °C	Crystal form	Fluorescence (in n-hexane)	Knorr reaction	Formula	N, %		S, %	
											Found	Calculated	Found	Calculated
IX	4-Dimethylaminophenyl	2-Thienyl	A	1.5	68	218 —219	Yellowish needles	Violet	+	$C_{21}H_{21}N_3S$	12.12	12.09	9.36	9.22
X	4-Chlorophenyl	2-Thienyl	A	0.6	90	130 —130.5	White needles	Violet	+	$C_{19}H_{15}ClN_2S$	8.39	8.27	9.44	9.46
XI	4-Nitrophenyl	2-Thienyl	A	10	84	169.5	Orange needles	Green	+	$C_{19}H_{15}N_3O_2S$	12.15	12.03	9.20	9.18
XII	Phenyl	5-Nitro-2-thienyl	A	3	80	126 —126.5	Bright yellow needles	None	+	$C_{19}H_{15}N_3O_2S$	11.98	12.03	8.92	9.18
XIII	2-Selenienyl	Phenyl	A	5	89	143.5	Yellow needles	Azure	+	$C_{19}H_{16}N_2Se$	—	—	22.27*	22.48*
XIV	Phenyl	2-Selenienyl	A	5.5	83	124 —124.5	Yellowish green needles	Azure	+	$C_{19}H_{16}N_2Se$	—	—	22.20*	22.48*
XV	2-Selenienyl	2-Selenienyl	A	5.5	68	129.5—130	Yellowish green needles	Azure	+	$C_{17}H_{14}N_2Se_2$		-	39.00*	39.06*
XVI**	2-Thienyl	Phenyl	B	5.5	60	157	Bright yellow needles	None	+	$C_{19}H_{15}N_3O_2S$	11.97	12.03	9.38	9.18
XVII**	2-Thienyl	4-Methoxyphenyl	B	6	35	135	Bright yellow needles	None	+	$C_{20}H_{17}N_3O_3S$	11.34	11.08	8.58	8.40
XVIII**	Phenyl	2-Thienyl	B	5.5	50	169.5—170	Bright yellow minute crystals	None	—	$C_{19}H_{15}N_3O_2S$	11.93	12.03	9.27	9.18
XIX**	4-Methoxyphenyl	2-Thienyl	B	5.5	40	212.5	Bright yellow parellelepipeds	None	—	$C_{20}H_{17}N_3O_3S$	11.28	11.08	8.52	8.40

*% selenium.

**In compounds XVI-XIX, position 1 is occupied by 4-nitrophenyl

Experimental

Previous papers [7-10] have described the synthesis of the starting thiophene and selenophene analogs of chalcones.

Preparation of Δ^2-pyrazolines. a) A mixture of 0.01 mole α,β-unsaturated ketone and 0.015 mole phenylhydrazine hydrochloride was dissolved in a minimum quantity of hot alcohol, and the solution refluxed for the time stated in the table. Next day the crystals which had separated were filtered off, washed with cold alcohol, and recrystallized: I, II, IV, IX-XIX from alcohol-acetone 1 : 1; III from the same, but 1 : 2; VIII from the same but 2 : 1; V, VI, and VII from alcohol.

b) A mixture of 0.01 mole α,β-unsaturated ketone and 0.015 mole phenylhydrazine hydrochloride was dissolved in the minimum quantity of hot alcohol, and heated for 10 hr. 30 ml glacial acetic acid was then added, and the mixture refluxed for 15 hr. Next day the crystals which had separated were filtered off, washed with cold methanol, and recrystallized from alcohol-acetone 1 : 1.

c) A mixture of 0.01 mole α,β-unsaturated ketone and 0.015 mole 4-nitrophenylhydrazine was dissolved in the minimum quantity of hot alcohol, 10 ml concentrated hydrochloric acid added, and the whole refluxed for the time stated in the table. The product was isolated as described in b).

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