SYNTHESIS OF α,β-UNSATURATED DIKETONES AND DERIVATIVES OF 2-PYRAZOLINE FROM 2,5-DIFORMYLTHIOPHENE

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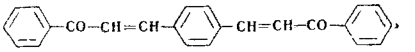
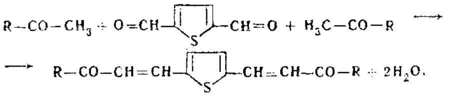
The crotonic condensation of 2,5-diformylthiophene with various aromatic and heterocyclic methyl ketones has given 15 α,β-unsaturated diketones. By the reaction of the latter with phenylhydrazine, ten 2,5-di(1'-phenyl-3'-R-Δ^2-pyrazolin-5'-yl)thiophenes possessing a bright blue-violet or green luminescence have been synthesized.

Continuing our work on the synthesis and study of various properties of α,β-unsaturated ketones and their derivatives, we decided to obtain a number of heterocyclic analogs of the so-called p-dichalcone [1]



in which the central aromatic nucleus was to be replaced by thiophene and the terminal nuclei were to be various substituted aromatic or heterocyclic radicals. For this purpose we have carried out the crotonic condensation of 2,5-diformylthiophene with the appropriate aromatic and heterocyclic methyl ketones.



R = phenyl (I), 4-tolyl (II), 4-methoxyphenyl (III), 2,4-dimethoxyphenyl (IV), 4-hydroxyphenyl (V), 4-dimethylaminophenyl (VI), 4-chlorophenyl (VII), 4-bromophenyl (VIII), 4-nitrophenyl (IX), 2-furyl (X), 2-thienyl (XI), 2-selenienyl (XII), 2-pyrryl (XIII), 2-pyridyl (XIV), or 3-pyridyl (XV).

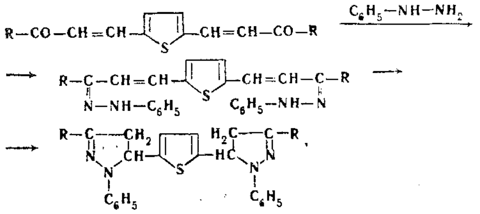
When we had already begun this work, we became aware that Vaysse and Pastour [2] had performed the condensation of 2,5-diformylthiophene with acetophenone and 2-acetothienone and had isolated the corresponding analogs of the p-dichalcones I and XI.

In almost all cases, the crotonic condensation took place fairly smoothly with satisfactory yields under the influence of small amounts of a 20–40% solution of caustic soda with brief boiling in methanol. It is interesting that analogous condensations with the participation of 2-thiophenealdehyde take place under milder conditions, at room temperature using a 5–10% solution of caustic potash as catalyst [3]. It is known that strong electron-donating substituents in the ketone reactant interfere with the crotonization reaction [4]. In actual fact, in the reaction of 4-dimethylamino- and 4-hydroxyacetophenone and also of 2-acetylpyrrole (it has recently been shown that 2-pyrryl possesses strong electron-donating properties [5, 6]) with 2,5-diformylthiophene, satisfactory yields of the corresponding diketones V, VI, and XIII could be obtained only after the reaction mixture had been allowed to stand at room temperature for a long time (up to 36 hr) with the use of a 40–60% solution of caustic soda as condensing agent. The diketone V can, however, also be obtained in 60% yield in an acid medium, as has been shown previously [7]. The condensation of 3-acetylpyridine with 2,5-diformylthiophene takes place most readily in an aqueous pyridine medium in the presence of diethylamine [8].

All the α,β-unsaturated diketone derivatives of thiophene that we synthesized consisted of fairly high-melting colored crystalline substances (see Table 1) readily soluble in benzene, less readily in ethanol, and insoluble in water. The majority of them possessed well-defined halochromic properties and in concentrated sulfuric acid solutions their color deepened to red or red-violet.

We attempted to characterize the unsaturated diketones that we had produced by means of the corresponding 2,4-dinitrophenylhydrazones. However, in spite of all our attempts to obtain the dinitrophenylhydrazones by using various severe conditions [9], in each case we were able to isolate only sparingly soluble and high-melting products with nitrogen contents somewhat (1–2%) lower than those calculated for the dihydrazones, and we were unable to purify these.

The α,β-unsaturated diketones of the thiophene series reacted considerably more readily with phenylhydrazine. The reaction did not stop at the stage of the formation of the phenylhydrazones but cyclization took place and 2,5-di(1'-phenyl-3'-R-Δ^2-pyrazolin-5'-yl)thiophenes were isolated.



R = phenyl (XVI), 4-tolyl (XVII), 4-methoxyphenyl (**XVIII**), 4-hydroxyphenyl (XIX), 4-dimethylaminophenyl (XX), 4-chlorophenyl (XXI), 4-bromophenyl (XXII), 2-furyl (XXIII), 2-thienyl (XXIV), and 2-selenienyl (XXV).

Table 1

Characteristics of the α,β-unsaturated Diketones 2,5-Di(2'-acylvinyl)thiophenes

Compound	Acyl	Mp, °C	Method of synthesis	Form of the crystals	Empirical formula	S, %		Yield, %
						found	calculated	
I	Benzoyl	185*	A	Light green plates	$C_{22}H_{16}O_2S$	—	—	80
II	4-Tolyl	201	A	Yellow-green plates	$C_{24}H_{20}O_2S$	8.51; 8.56	8.60	85
III	4-Methoxybenzoyl	204	A	Pale green plates	$C_{24}H_{20}O_4S$	8.04; 8.01	7.93	69
IV	2,4-Dimethoxybenzoyl	172	A	Yellow-orange plates	$C_{26}H_{24}O_6S$	6.95; 6.85	6.90	39
V	4-Hydroxybenzoyl	232.5	B, C	Pale yellow prisms	$C_{22}H_{16}O_4S$	8.44; 8.61	8.51	20/60
VI	4-Dimethylaminobenzoyl	191	B	Red needles	$C_{26}H_{26}N_2O_2S$	7.56; 7.47	7.48	51
VII	4-Chlorobenzoyl	202	A	Green needles	$C_{22}H_{14}Cl_2O_2S$	7.61; 7.78	7.75	59
VIII	4-Bromobenzoyl	198	A	Green plates	$C_{22}H_{14}Br_2O_2S$	6.38; 6.36	6.38	65
IX	4-Nitrobenzoyl	187.5	A	Dark red cubes	$C_{22}H_{14}N_2O_6S$	7.17; 7.37	7.38	49
X	2-Furoyl	195.5	A	Yellow prisms	$C_{18}H_{12}O_4S$	9.66; 9.96	9.88	80
XI	2-Thenoyl	209.5*	A	Yellow plates	$C_{18}H_{12}O_2S_3$	—	—	85
XII	2-Selenoyl	200	A	Yellow-green plates	$C_{18}H_{12}O_2SSe_2$	7.11; 7.17	7.12	50
XIII	2-Pyrroyl	261	B	Bright yellow needles	$C_{18}H_{14}N_2O_2S$	9.94; 10.10	9.94	53
XIV	Picolinoyl	192	A	Green needles	$C_{20}H_{14}N_2O_2S$	9.42; 9.25	9.25	78
XV	Nicotinoyl	186	D	Yellow needles	$C_{20}H_{14}N_2O_2S$	9.36; 9.18	9.25	24

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*According to the literature [2], mp for I 184° C, for XI 211° C.

Table 2

Characteristics of the 2, 5-Di(1'-phenyl-3'-R-Δ^2-pyrazolin-5'-yl)thiophenes

Compound	R	Mp, °C	Time of boiling, hr	Knorre reaction	Form of the crystals	Fluorescence in benzene	Empirical formula	N, %		S, %		Yield, %
								calculated	found	calculated	found	
XVI	Phenyl	225.5	0.5	+	Colorless needles	Violet	$C_{34}H_{28}N_4S$	10.71; 10.94	10.67	5.95; 5.97	6.11	82
XVII	4-Tolyl	176	0.6	+	Yellowish needles	Violet	$C_{36}H_{32}N_4S$	10.10; 10.07	10.13	5.87; 5.74	5.80	79
XVIII	4-Methoxy-phenyl	169	1	–	Yellow plates	Blue-violet	$C_{36}H_{32}N_4O_2S$	9.57; 9.69	9.58	5.54; 5.65	5.48	71
XIX	4-Hydroxy-phenyl	216	4	+	Pale yellow needles	Violet	$C_{34}H_{28}N_4O_2S$	10.03; 9.87	10.06	5.89; 5.81	5.76	25
XX	4-Dimethyl-aminophenyl	223	2	+	Yellowish needles	Blue-green	$C_{38}H_{38}N_6S$	13.79; 13.77	13.75	5.31; 5.15	5.24	40
XXI	4-Chlorophenyl	166	0.75	–	Yellow-green plates	Green	$C_{34}H_{26}Cl_2N_4S$	9.55; 9.52	9.43	5.47; 5.42	5.40	76
XXII	4-Bromophenyl	172.5	0.75	–	Yellow needles	Bright green	$C_{34}H_{26}Br_2N_4S$	7.94; 8.10	8.20	4.73; 4.77	4.69	74
XXIII	2-Furyl	221	3	–	Pale yellow plates	Violet	$C_{30}H_{24}N_4O_2S$	11.06; 11.08	11.10	6.20; 6.22	6.35	38
XXIV	2-Thienyl	197.5	3.5	–	Yellow plates	Green	$C_{30}H_{24}N_4S_3$	10.55; 10.22	10.43	17.72; 17.73	17.92	36
XXV	2-Selenienyl	186	3	–	Yellow plates	Green	$C_{30}H_{24}N_4SSe_2$	9.01; 8.96	8.88	4.91; 4.89	5.08	31

The formation of derivatives of 2-pyrazoline took place when the initial unsaturated diketones were boiled with phenylhydrazine hydrochloride in a mixture of ethanol and acetic acid. The reaction apparently takes place more readily than was found by two of us in the synthesis of the analogous furan [10] and thiophene [11] derivatives of 1, 3, 5-triphenylpyrazoline.

The structure of the pyrazolines that we obtained was confirmed by a study of their IR spectra, which lacked the absorption band characteristic for N—H stretching vibrations in the 3200–3500 cm^{-1} region.

All the dipyrazolinylthiophenes that we synthesized (Table 2) consisted of colorless or slightly yellowish crystalline substances luminescing brightly in solution in benzene or toluene. The Knorr reaction is not characteristic for the majority of them (see Table 2). The optical properties of the pyrazoline derivatives will be studied in detail subsequently.

EXPERIMENTAL

2, 5-Diformylthiophene was obtained by Tuo Sone's method [12].

Crotonic condensation. a) Stoichometric amounts of 2, 5-diformylthiophene (0.01 mole) and a methyl ketone (0.02 mole) were dissolved in a small amount of methanol (20–40 ml), 20% caustic soda solution (1–3.5 ml) was added in drops, and the mixture was heated under reflux for 10–15 min. After 10–15 hr, the precipitate that had deposited was filtered off, washed with aqueous ethanol, and recrystallized from a suitable solvent (acetic acid for I–IV, VI, VIII, X, XIII, aqueous methanol for V, XV, and chlorobenzene for XIV) to constant melting point.

b) This was analogous to method (a) except that the 20% caustic soda solution was replaced by a 40–60% solution, and the reaction product was filtered off after 30–36 hr.

c) Equimolar amounts of 2, 5-diformylthiophene and 4-hydroxyacetophenone were dissolved in the minimum amount of methanol, and the solution was saturated with gaseous hydrogen chloride at 0° C.

On the following day the crystalline precipitate that had deposited was filtered off, washed with aqueous ethanol, and recrystallized from methanol with the addition of activated carbon.

d) With stirring, 1 ml of diethylamine was added to a solution of 0.01 mole of 2, 5-diformylthiophene and 0.02 mole of 3-acetylpyridine in 3 ml of pyridine and 200 ml of water, and the mixture was left overnight. The precipitate that had deposited was filtered off and recrystallized.

Preparation of the pyrazoline derivatives. A mixture of 0.01 mole of one of the ketones and 0.03 mole of phenylhydrazine hydrochloride was dissolved in the minimum amount of ethanol and acetic acid (1:1). The solution was heated under reflux for 1/2–3 hr. On the following day the crystals that had deposited were filtered off, washed with ethanol, and recrystallized from acetic acid.

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