SYNTHESIS OF α,β-UNSATURATED DIKETONES AND DERIVATIVES OF Δ^2-PYRAZOLINE DERIVED FROM 2, 5-DIACETYLTHIOPHENE

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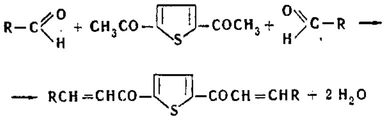
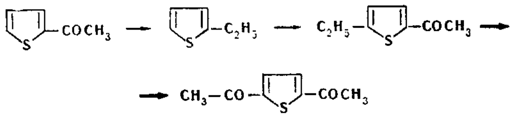
The Claisen reaction of 2, 5-diacetylthiophene with various aromatic and heterocyclic aldehydes was utilized to prepare 15 new unsaturated diketones (diarylidene-2, 5-diacetylthiophenes). Most of them were characterized as their bis-2, 4-dinitrophenylhydrazones, for which λ_{max} values in chloroform solution are given. The reaction of diarylidene-2, 5-diacetylthiophenes with phenylhydrazine hydrochloride has given five 2, 5-bis(1'-phenyl-5'-R-Δ^2-pyrazoline-3"-yl) thiophene showing strong luminescence. A method was developed for the synthesis of 2, 5-diacetylthiophene by the oxidation of 5-ethyl-2-acetothienone.

In continuation of work on the synthesis and examination of the physicochemical properties of unsaturated diketones of the thiophene series [1], we decided to effect the Claisen reaction 2,5-diacetylthiophene with various aromatic and heterocyclic aldehydes according to the scheme:



where R = phenyl (I), 4-tolyl (II), 4-anisyl (III), 2,4-dimethoxyphenyl (IV), 4-hydroxyphenyl (V), 4-dimethylaminophenyl (VI), 4-fluorophenyl (VII), 4-chlorophenyl (VIII), 4-bromophenyl (IX), 4-nitrophenyl (X), 2-furyl (XI), 2-thienyl (XII), 2-selenenyl (XIII), 2-pyrrolyl (XIV), and 2-quinolyl (XV).

The 2,5-diacetylthiophenes required for the condensation may be obtained by the direct acylation of 2-acetothienone [2] or thiophene [3]. The products obtained are, however, impure, and the yields are very low, even according to the literature not exceeding 6% calculated on 2-acetothienone. We have developed a new and much more convenient synthesis of 2,5-diacetylthiophene by the following route:



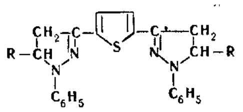
The 2-acetothienone is reduced to ethylthiophene by hydrazine (Wolff-Kizhner) [4]. The ethylthiophene is acetylated by acetic anhydride in presence of anhydrone using a method similar to that in [5]. Finally, the oxidation of 5-ethyl-2-acetothienone with $KMnO_4$ in neutral solution, in a similar way to that described in [6] for 1,4-diacetylbenzene, gives 2,5-diacetylthiophene. By this method, sufficiently pure 2,5-diacetylthiophene is obtained in 15% yield based on 2-acetothienone.

In most cases, the Claisen reaction of the appropriate aromatic or heterocyclic aldehydes with 2,5-diacetylthiophene proceeded readily at room temperature in aqueous-alcoholic solution in presence of a small amount of a 20% solution of NaOH, and were usually complete after a few hours, the only exceptions being the condensation products of 2,5-diacetylthiophene with 4-dimethylaminobenzaldehyde, 4-hydroxybenzaldehyde, and pyrrole-2-aldehyde. Satisfactory yields of diketones VI and XIV were obtained only by the use of 40% NaOH as condensing agent at room temperature for long periods. Compound V was obtained by the use of an acid catalyst (hydrogen chloride) as in [7].

All of the α,β-unsaturated diketones which we have prepared are stable, high-melting, crystalline solids (Table 1), readily soluble in chlorobenzene, less so in benzene, and almost insoluble in alcohol. They show pronounced halochromic behavior, and in solution in conc. H_2SO_4 their color deepens to reddish-violet.

The bis-2,4-dinitrophenylhydrazones were usually formed on boiling the diketones in acetic acid solution with alcoholic 2,4-dinitrophenylhydrazine in the presence of a small quantity of HCl for about 36 hr [8].

On boiling solutions of the diketones I–III, XII and XIII in acetic acid with an alcoholic solution of phenylhydrazine hydrochloride, we obtained the corresponding 2,5-bis(1'-phenyl-5'-R-Δ^2-pyrazolin-3"-yl)thiophenes:



where R = phenyl (XVI), 4-tolyl (XVII), 4-anisyl (XVIII), 2-thienyl (XIX), and 2-selenenyl (XX).

Attempts to react diketones VI, X, XI, and XIV with phenylhydrazine hydrochloride were unsuccessful, resinification being observed.

The dipyrazolinylthiophenes (Table 2) are yellowish, high-melting, crystalline solids, rather sparingly soluble in the usual organic solvents. A positive Knorr [9] reaction (formation of a blue coloration on addition of conc. H_2SO_4 and $FeCl_3$) was obtained for all these dipyrazolinylthiophenes. The structures of these compounds were confirmed by their IR spectra, in which the band at 3200–3500 cm^{-1} characteristic of the N—H stretching frequency was absent. Solutions in benzene and toluene on irradiation with UV show a bright blue (XVI, XVIII–XX) or green (XVII) luminescence.

EXPERIMENTAL

5-Ethyl-2-acetothienone. Into a round-bottomed flask fitted with a reflux condenser were placed 11.2 g (0.10 mole) of 5-ethylthiophene

Table 1

Properties of the α,β-Unsaturated Diketones

Compound	R	Mp, °C	Appearance	Molecular formula	S, %		Yield, %	Bis(2,4-dinitrophenylhydrazones)				
					found	calc.		mp, °C	λmax, nm**	molecular formula	N, %	
											found	calc.
I	Phenyl	243	Greenish-yellow needles	$C_{22}H_{16}O_2S$	9.18; 9.27	9.31	91	311	393	$C_{34}H_{24}N_8O_8S$	15.90	16.07; 16.03
II	4-Tolyl	266	Colorless needles	$C_{24}H_{20}O_2S$	8.53; 8.70	8.61	87	291	394	$C_{36}H_{28}N_8O_8S$	15.29	15.19; 15.22
III	4-Anisyl	212	Yellow cubes	$C_{24}H_{20}O_4S$	8.09; 7.89	7.93	82	301	399	$C_{36}H_{28}N_8O_{10}S$	14.65	14.60; 14.57
IV	2,4-Dimethoxy-phenyl	224	Yellow prisms	$C_{26}H_{24}O_6S$	7.02; 6.82	6.90	78	—	—	—	—	—
V	4-Hydroxy-phenyl	de-comp*	Orange-red needles	$C_{22}H_{16}O_4S$	8.45; 8.61	8.52	59	318	408	$C_{34}H_{24}N_8O_{10}S$	15.21	15.04; 15.14
VI	4-Dimethyl-aminophenyl	216	Deep red prisms	$C_{26}H_{26}N_2O_2S$	7.39; 7.33	7.45	51	—	—	—	—	—
VII	4-Fluorophenyl	271	Greenish-yellow needles	$C_{22}H_{14}F_2O_2S$	8.52; 8.59	8.43	93	322	392	$C_{34}H_{22}F_2N_8O_8S$	15.13	15.06; 15.26
VIII	4-Chlorophenyl	de-comp*	Greenish-yellow plates	$C_{22}H_{14}Cl_2O_2S$	7.66; 7.75	7.75	88	Pde-* comp.	390	$C_{34}H_{22}Cl_2N_8O_8S$	14.48	14.51; 14.54
IX	4-Bromophenyl	de-comp*	Greenish-yellow plates	$C_{22}H_{14}Br_2O_2S$	6.20; 6.39	6.38	90	307	391	$C_{34}H_{22}Br_2N_8O_8S$	12.99	13.02; 13.13
X	4-Nitrophenyl	230	Colorless needles	$C_{22}H_{14}N_2O_6S$	7.47; 7.30	7.38	42	—	—	—	—	—
XI	2-Furyl	227.5	Colorless plates	$C_{18}H_{12}O_4S$	9.90; 9.93	9.88	73	—	—	—	—	—
XII	2-Thienyl	235	Orange plates	$C_{18}H_{12}O_2S_3$	27.08; 26.87	26.98	95	269	405	$C_{30}H_{20}N_8O_8S_3$	15.63	15.55; 15.71
XIII	2-Selenenyl	209	Greenish-yellow prisms	$C_{18}H_{12}O_2SSe_2$	7.02; 7.21	7.12	94	284	408	$C_{30}H_{20}N_8SSe_2$	13.82	13.73; 13.76
XIV	2-Pyrrolyl	221	Yellow needles	$C_{18}H_{14}N_2O_2S$	10.01; 10.07	9.94	38	—	—	—	—	—
XV	2-Quinolinyl	236	Yellowish-green prisms	$C_{28}H_{18}N_2O_2S$	7.24; 7.35	7.18	61	—	—	—	—	—

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*Melts with decomposition at high temperature.

**Measurements were carried out in chloroform solution on an SF-4A spectrophotometer.

Table 2

Properties of 2,5-bis(1'-Phenyl-5'-R-Δ^2-pyrazolin-3"-yl) thiophenes

Compound	R	Mp, °C	Molecular formula	Found, %		Calculated, %		Yield, %
				N	S	N	S	
XVI	Phenyl	194	$C_{34}H_{28}N_4S$	10.44; 10.55	6.22; 6.21	10.67	6.11	67
XVII	4-Tolyl	210	$C_{36}H_{32}N_4S$	9.97; 10.09	5.91; 5.95	10.13	5.80	52
XVIII	4-Methoxyphenyl	174	$C_{36}H_{32}N_4O_2S$	9.40; 9.70	5.40; 5.56	9.58	5.48	48
XIX	2-Thienyl	186	$C_{30}H_{24}N_4S_3$	10.37; 10.54	18.02; 17.85	10.43	17.92	62
XX	2-Selenenyl	192	$C_{30}H_{24}N_4SSe_2$	8.73; 8.91	4.79; 4.92	8.88	5.08	70

[10], 15.3 g (0.15 mole) of acetic anhydride, and 0.45 g (0.002 mole) of anhydrous magnesium perchlorate, and these boiled in the water bath for 30–45 min. The mixture was poured into 100 ml of cold water, the organic layer separated and the aqueous layer was extracted with ether. The combined extracts were washed with water and sodium carbonate solution, and dried over anhydrous sodium sulfate. Fractionation in vacuo gave a fraction bp 120–122° C (12 mm). The yield of 5-ethyl-2-acetothienone was 12.3 g (80%).

2,5-Diacetylthiophene. In a three-necked flask, fitted with a mechanical stirrer, thermometer, and dropping funnel, were placed 8 g of MgO, 240 ml of water, 28 ml of HNO_3 (d 1.40) and 32 g of $KMnO_4$. The mixture was heated at 60° C on the water bath until complete solution was obtained, cooled to 35° C, and 16 g of 5-ethyl-2-acetothienone was added dropwise. Stirring was continued for 2.5 hr at the same temperature. The manganese dioxide which separated was filtered off and the solid washed three times with hot ethyl acetate (30 ml). The aqueous layer was also washed twice with ethyl acetate. The residue, after removal of the solvent, was recrystallized from ethyl acetate to give 2.8 g (15%) of colorless plates, mp 172° C ([2], 172–173° C).

Claisen reaction. Stoichiometric amounts of 2,5-diacetylthiophene (0.01 mole) and the corresponding aromatic or heterocyclic aldehyde (0.02 mole) were dissolved in 20–40 ml of methanol, and 1–3 ml of 20% aqueous sodium hydroxide added dropwise. The solid which separated was filtered off after a few hours, washed, and recrystallized from acetic acid (I–V, XI–XIII), chlorobenzene (VII–X, XIV, XV), or dichloroethane (VI).

Preparation of dipyrazolinylthiophenes. The unsaturated diketone (0.05 mole), dissolved in the minimum amount of acetic acid, and 0.15 mole of an alcoholic solution of phenylhydrazine hydrochloride were boiled under reflux for 10–15 hr. The crystals which separated were filtered off and recrystallized from acetic acid.

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