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FUNCTIONAL DERIVATIVES OF THIOPHENE.

17.* SYNTHESIS OF THIENYLHYDRAZINE DERIVATIVES

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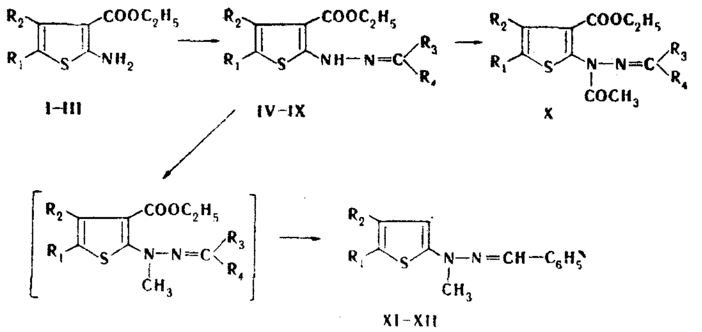
UDC 547.732'733.07

Substituted thienylhydrazones of aromatic aldehydes and cyclohexanone were obtained. It is shown that the sodium salts of the latter are readily acylated and alkylated. The hydrolysis of carbethoxythienylmethylhydrazones of benzaldehyde in alkaline media is accompanied by decarboxylation.

The diazotization of aminothiophene derivatives I-III was carried out by a previously proposed method [2]. The resulting diazonium salts were reduced without isolation with sodium hydrosulfite, after which aqueous suspensions of the products were treated with benzene solutions of aldehydes or ketones. As a result of this reaction, thienylhydrazones (IV-IX) of aldehydes and ketones were obtained. During a study of the properties of benzaldehyde thienylhydrazones it was shown that the latter readily form sodium salts under the influence of sodium methoxide. The sodium salt of benzaldehyde thienylhydrazone V is converted to benzaldehyde N-acetylthienylhydrazone (X) on reaction with acetyl chloride. Hydrolysis of the acetyl group rather than the carbethoxy group, as described in the hydrolysis of ethyl 2-acylaminothiophene-3-carboxylates [3], is observed when X is heated in an alkaline medium, and V is formed. The action of methyl iodide on the sodium salts of IV and V gave N-methyl derivatives, which were subjected to alkaline hydrolysis and decarboxylation without isolation. As a result, benzaldehyde N-methylthienylhydrazones (XI, XII) with a free 4 position were obtained.



I, IV, XI $R_1=R_2=CH_3$; II, V, VI, VII, X, XII $R_1=CH_3$, $R_2=C_6H_5$; III, VIII, IX $R_1+R_2=(CH_2)_4$; IV, V, VIII, X $R_3=H$, $R_4=C_6H_5$; VI, IX $R_3=H$, $R_4=p\text{-}C_6H_4NO_2$; VII $R_3+R_4=(CH_2)_5$

EXPERIMENTAL

Thienylhydrazones of Benzaldehyde (IV, V, and VIII), p-Nitrobenzaldehyde (VI and IX), and Cyclohexanone (VII). A solution of 2.7 g (40.5 mole) of sodium nitrite in 10 ml of water was added dropwise with stirring and cooling to −5°C to a solution of 40 mmole of I-III in a mixture of 90 ml of acetic acid and 30 ml of concentrated HCl, and the mixture was allowed to stand in an ice bath for 30 min. It was then poured into a well-stirred suspension

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*See [1] for Communication 16.

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0009-3122/79/1505-0491$07.50

TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C*	Found, %				Empirical formula	Calc., %				Yield, %
		C	H	N	S		C	H	N	S	
IV	123,5—124,5	63,5	6,0	9,2	10,5	$C_{16}H_{18}N_2O_2S$	63,5	6,0	9,3	10,6	44
V	166—167,5	69,3	5,3	7,6	8,7	$C_{21}H_{20}N_2O_2S$	69,2	5,5	7,7	8,8	71
VI	166—167	61,4	4,7	10,3	7,8	$C_{21}H_{19}N_3O_4S$	61,6	4,7	10,3	7,8	42
VII	94—95	67,2	6,7	7,9	9,0	$C_{20}H_{24}N_2O_2S$	67,4	6,8	7,9	9,0	65
VIII	124—125	65,6	5,9	8,2	9,9	$C_{18}H_{20}N_2O_2S$	65,8	6,1	8,5	9,8	80
IX	193—194	57,8	4,8	11,2	8,6	$C_{18}H_{19}N_3O_4S$	57,9	5,1	11,2	8,6	47
XI	115—116	68,8	6,5	11,2	13,0	$C_{14}H_{16}N_2S$	68,8	6,6	11,4	13,2	45
XII	155—156	74,4	5,8	9,2	10,5	$C_{19}H_{18}N_2S$	74,7	5,6	9,2	10,5	48

*Compounds IV-VIII, XI, and XII were recrystallized from alcohol, and IX was recrystallized from alcohol—dioxane.

of 300 ml of water and 200 ml of benzene containing 27 g (130 mmole) of sodium hydrosulfite and 45 mmole of benzaldehyde, p-nitrobenzaldehyde, or cyclohexanone. The resulting suspension was then stirred for 10 min, the organic layer was separated, and the aqueous layer was extracted with benzene. The benzene extracts were washed with water, and the benzene was removed by distillation to give IV-IX (Table 1).

Benzaldehyde (2-Methyl-3-phenyl-4-ethoxycarbonyl-5-thienyl)acetylhydrazone (X). A solution of 3.64 g (10 mmole) of benzaldehyde (2-methyl-3-phenyl-4-ethoxycarbonyl-5-thienyl)-hydrazone (V) in 15 ml of absolute dioxane was added to a solution of sodium methoxide, obtained from 0.023 g (0.01 g-atom) of sodium and 23 ml of methanol, in 20 ml of absolute dioxane, and the mixture was allowed to stand at room temperature for 15 min. A 3.5-g (45 mmole) sample of acetyl chloride was added, and the mixture was refluxed for 2 h. It was then poured into water, and the resulting precipitate was removed by filtration and recrystallized from alcohol to give 1.6 g (40%) of a product with mp 167-168°C (from alcohol). Found: C 68.2; H 5.5; N 7.1; S 7.9%. $C_{23}H_{22}N_2O_3S$. Calculated: C 67.9; H 5.5; N 6.9; S 7.8%.

Benzaldehyde (2-Methyl-3-phenyl-4-ethoxycarbonyl-5-thienyl)hydrazone (V). A 2.03-g (5 mmole) sample of X and 0.06 g (15 mmole) of sodium hydroxide were dissolved in 30 ml of alcohol, and the solution was refluxed for 2.5 h. It was then cooled, and the precipitate was removed by filtration and recrystallized from alcohol to give 1.45 g (79%) of a product that did not depress the melting point of a previously obtained sample of V. The product had R_f 0.85 (Silufol UV 254, elution with chloroform).

Benzaldehyde (2,3-Dimethyl-5-thienyl)methylhydrazone (XI) and Benzaldehyde (2-Methyl-3-phenyl-5-thienyl)methylhydrazone (XII). A solution of 30 mmole of IV or V in 40 ml of absolute dioxane was added to a solution of sodium methoxide, obtained from 0.069 g (0.03 g-atom) of sodium and 6.9 ml of methanol, in 40 ml of absolute dioxane, and the mixture was allowed to stand at room temperature for 15 min, after which 21.2 g (150 mmole) of methyl iodide was added to it. The mixture was refluxed for 4 h, the precipitate was removed by filtration, and the solvents were removed by distillation. The residue was dissolved in 30 ml of alcohol, a solution of 3 g (75 mmole) of sodium hydroxide in 30 ml of alcohol and 10 ml of water was added, and the mixture was refluxed on a water bath for 1 h. Charcoal was added, the mixture was filtered, and the filtrate was poured into 150 ml of water. The aqueous mixture was acidified with dilute hydrochloric acid, and the resulting precipitate was removed by filtration and recrystallized. Data on XI and XII are presented in Table 1.

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