

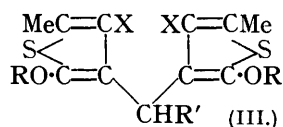
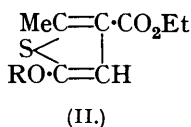
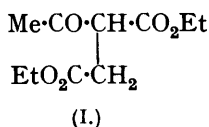
244. Preparation of Thiophen Derivatives from Ethyl β -Carbethoxylævulate.

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5-Alkoxythiophen derivatives are formed by the action of hydrogen sulphide on alcoholic solutions of ethyl β -carbethoxylævulate saturated with hydrogen chloride at 0°. 5-Hydroxy-2-methylthiophen-3-carboxylic acid in its keto-form condenses with carbonyl compounds to give yellow dyes.

In the course of work on the synthesis of complex thiophenoid dyes thiophen derivatives containing groups in convenient positions were required. Their preparation by known methods based on the action of sulphides of phosphorus on γ -diketones, γ -ketonic acids, or anhydrides of dibasic acids was unsatisfactory on account of the low yields of the products and in some cases the failure of the reaction, and Mitra's method (*J. Indian Chem. Soc.*, 1938, 15, 59) was of limited applicability owing to the inaccessibility of the initial unsaturated diketones.

The method adopted utilised a γ -thioketonic ester, prepared by the action of hydrogen sulphide on a solution of the corresponding γ -ketonic ester (Mitra, *ibid.*, 1933, 10, 71; 1938, 15, 31) in an alcohol saturated with hydrogen chloride. The presence of a β -carbethoxy-group (I) so facilitated the ring closure that thiophen formation took place during the process of thionation. The hydroxythiophen thus produced reacted with the solvent alcohol to give a 5-alkoxythiophen derivative (II).



(R = alkyl; R' = alkyl or aryl; X = CO₂H)

The acids corresponding to (II) reacted with aromatic aldehydes, giving *dithienylaryl-methanes* (III), and the acid on dealkylation furnished 5-hydroxy-2-methylthiophen-3-carboxylic acid (IV). This in its keto-form condensed with aldehydes, giving yellow dyes (V).

EXPERIMENTAL.

Preparation of the Ethers (II).—Ethyl β -carbethoxylævulate (I) was dissolved in an alcohol (ROH) (1.2—1.5 g. in 100—200 c.c.), previously saturated with dry hydrogen chloride at 0°, and hydrogen sulphide was passed for 12 hours through the solution, which was then poured

on ice. The oil that separated was extracted in benzene, recovered, and boiled with pyridine. The pyridine solution on acidification gave an oil, which was extracted in benzene and distilled under reduced pressure.

The following ethers of ethyl 5-hydroxy-2-methylthiophen-3-carboxylate were thus prepared : *methyl*, b. p. 125°/5 mm. (Found : C, 53.9; H, 5.9. $C_9H_{12}O_3S$ requires C, 54.0; H, 6.0%); *ethyl*, a greenish-yellow oil, b. p. 150°/5 mm. (Found : C, 55.7; H, 6.6; S, 15.0. $C_{10}H_{14}O_3S$ requires C, 56.1; H, 6.5; S, 14.9%); *n-propyl*, a yellow liquid, b. p. 135°/5 mm. (Found : C, 58.1; H, 7.3. $C_{11}H_{16}O_3S$ requires C, 57.9; H, 7.0%).

The three foregoing ethers (5—10 g.) were refluxed (4—6 hours) with 10% barium hydroxide solution (100—200 c.c.), and the cooled solutions acidified with hydrochloric acid, whereby the corresponding acids were precipitated. *5-Methoxy-2-methylthiophen-3-carboxylic acid*, m. p. 128° (Found : C, 48.9; H, 4.9; OMe, 16.5. $C_7H_8O_3S$ requires C, 48.8; H, 4.6; OMe, 18.0%), and the *5-ethoxy-acid*, m. p. 122° (Found : C, 51.5; H, 5.7; S, 17.2; OEt, 21.4. $C_8H_{10}O_3S$ requires C, 51.6; H, 5.4; S, 17.2; OEt, 24.1%), both formed colourless needles; the *5-n-propoxy-acid* formed colourless plates, m. p. 75° (Found : C, 53.8; H, 6.0. $C_9H_{12}O_3S$ requires C, 54.0; H, 6.0%). The 5-ethoxy-acid formed a *barium* salt crystallising in needles [Found : Ba, 26.6. $(C_8H_9O_3S)_2Ba$ requires Ba, 27.0%].

Preparation of Dithienylarylmethanes (III).—The alkoxy-methylthiophen-carboxylic acid was dissolved in the minimum quantity of alcohol saturated with dry hydrogen chloride at 0°, an alcoholic solution of an aromatic aldehyde added, and the mixture left for 1 hour at 0°. The precipitate was collected and boiled with pyridine (1 minute), the pyridine solution treated with an excess of dilute hydrochloric acid, and the precipitated dithienylarylmethane crystallised from alcohol, forming colourless needles. *Di-(5-ethoxy-3-carboxy-2-methyl-4-thienyl)phenylmethane*, m. p. 233°, was obtained from the 5-ethoxy-acid (3 g.), alcoholic hydrogen chloride (10 c.c.), and benzaldehyde (2 g.) (Found : C, 59.9; H, 5.4; S, 14.2. $C_{23}H_{24}O_6S_2$ requires C, 60.0; H, 5.2; S, 13.9%); *di-(5-ethoxy-3-carboxy-2-methyl-4-thienyl)-4'-hydroxy-3'-methoxyphenylmethane*, m. p. 235°, from the 5-ethoxy-acid (3 g.), alcoholic hydrogen chloride (20 c.c.), and vanillin (4 g.) (Found : C, 56.3; H, 5.2. $C_{24}H_{26}O_8S_2$ requires C, 56.9; H, 5.1%); *di-(5-n-propoxy-3-carboxy-2-methyl-4-thienyl)phenylmethane*, m. p. 232° (decomp.), from the 5-n-propoxy-acid (4 g.), alcoholic hydrogen chloride (20 c.c.), and benzaldehyde (3 g.) (Found : C, 61.3; H, 6.1. $C_{25}H_{28}O_6S_2$ requires C, 61.4; H, 5.75%); and *di-(5-methoxy-3-carboxy-2-methyl-4-thienyl)phenylmethane*, m. p. 250° (decomp.), from the 5-methoxy-acid (1 g.), benzaldehyde (1 g.), and alcoholic hydrogen chloride (Found : S, 14.5. $C_{21}H_{20}O_6S_2$ requires S, 14.8%).

5-Hydroxy-2-methylthiophen-3-carboxylic Acid (IV, X = CO_2H).—5-Methoxy- or 5-ethoxy-2-methylthiophen-3-carboxylic acid (1 g.) was treated with hydrobromic acid (10 c.c., *d* 1.8) at 0°, and the mixture kept at room temperature (22°) for 1 hour; the alkoxy-acid had then almost completely dissolved. On dilution with water (30 c.c.), *5-hydroxy-2-methylthiophen-3-carboxylic acid* separated; it formed colourless needles, m. p. 160°, from water (Found : C, 45.0; H, 3.9; S, 20.4. $C_6H_6O_3S$ requires C, 45.5; H, 3.8; S, 20.2%). It responded to the indophenin test and gave an intense pink coloration with ferric chloride.

Condensation with aldehydes. 5-Hydroxy-2-methylthiophen-3-carboxylic acid (0.5 g.) was dissolved in an alcoholic solution (1—3 c.c.) of the aldehyde, and a few drops of alcoholic hydrogen chloride added. The mixture was left at room temperature (24°) for 1 hour and then made just turbid by addition of water. The precipitated material was crystallised from alcohol. The following compounds were thus prepared; they did not give a coloration with ferric chloride: *5-keto-4-benzylidene-2-methyl-4 : 5-dihydrothiophen-3-carboxylic acid* (V; R' = Ph, X = CO_2H), from benzaldehyde (0.5 g.), bright yellow needles, m. p. 166° (Found : C, 63.0; H, 4.2; S, 12.9. $C_{13}H_{10}O_3S$ requires C, 63.4; H, 4.1; S, 13.0%); the 4-*o*-nitrobenzylidene analogue, from *o*-nitrobenzaldehyde (0.7 g.), bluish-yellow prisms, m. p. 184° (decomp.) (Found : C, 53.1; H, 3.0. $C_{13}H_9O_5NS$ requires C, 53.6; H, 3.0%); the 4-*o*-methoxybenzylidene compound, from anisaldehyde (0.7 g.), brilliant orange-yellow needles, m. p. 152° (Found : C, 61.0; H, 4.8. $C_{14}H_{12}O_4S$ requires C, 60.9; H, 4.4%); the 4-*ethylidene* compound, from saturated aqueous acetaldehyde (1 c.c.), hay-coloured needles, m. p. 124° (Found : C, 51.7; H, 4.7; S, 18.0. $C_8H_8O_3S$ requires C, 52.1; H, 4.4; S, 17.4%); and the 4-*cinnamyldiene* compound, from cinnamaldehyde (1 g.), orange needles, m. p. 204° (Found : S, 11.7. $C_{15}H_{12}O_3S$ requires S, 11.7%).

Our thanks are due to Sir P. C. Rây for his interest in this investigation.