438. *Thiophen Derivatives of Potential Biological Interest. Part I. Thiophen Analogues of Stilbene and of Related Compounds.*

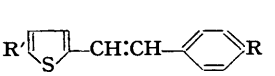
By Ng. Ph. Buu-Hoï, Ng. Hoán, and Denise Lavit.

Several new derivatives of thiophen akin to stilbene and to αβ-diphenylacrylonitrile have been prepared by known methods for biological investigation. The properties of some aldehydes of the thiophen series have been examined, particularly the reaction with ethyl acetoacetate and the Ullmann acridine synthesis.

Numerous investigations have concerned the influence, on biological activity, of the replacement of phenyl nuclei by thiophen groups in the molecules of various pharmacologically active substances (see Steinkopf, "Die Chemie des Thiophens," Dresden, 1941, p. 29; Buu-Hoï and Hoán, *Rec. Trav. chim.*, 1948, **67**, 309). The chief result has been to show that generally the thiophen nucleus is a less potent toxophore than the benzene nucleus. Some results of practical significance have been gathered in that respect, such as the recent discovery of Chlorothene and Bromothene, two substances of the pyribenzamine series which have greater antihistamine activity and lower toxicity than their benzene analogues (Lichtfield, Adams, Goddard, Jaeger, and Alonso, *Bull. Johns Hopkins Hosp.*, 1947, **81**, 55). Such facts are bringing renewed incentive to a broader investigation of series of thiophen compounds with potential biological interest. The present paper deals mainly with the preparation of substances akin to stilbene.

The aldehydes used as intermediates in this work were 2-formyl-, 2-formyl-5-methyl-, 5-chloro-2-formyl-, and 3-formyl-2 : 5-dimethyl-thiophen. These were readily prepared by a modification of King and Nord's method (*J. Org. Chem.*, 1948, **13**, 635) involving the use of phosphorus oxychloride and *N*-methylformanilide, which was much superior to the reaction of ethyl orthoformate with the appropriate thiophen Grignard reagents (Grischkewitsch-Trochimowski, *J. Russ. Phys. Chem. Ges.*, 1911, **43**, 204; 1912, **44**, 570) and to the more recent method of Emerson and Patrick (*J. Org. Chem.*, 1949, **14**, 790) based on the oxidation of primary thiophen alcohols.

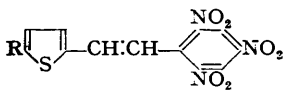
Reaction of 2-formylthiophen with benzylmagnesium chloride, followed by dehydration of the secondary alcohol thus formed, gave as the main product a solid 2-styrylthiophen (I; R = R′ = H) assumed to be the *trans*-form by reason of its high melting point (111°; *trans*-stilbene

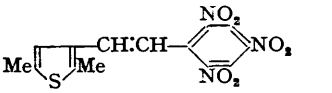
(I).   (II.)

has m. p. 124°); in the same way, 2-styryl-5-methyl (I; R = H; R′ = Me), 2-4′-methylstyryl-5-methyl- (I; R = R′ = Me), 2-4′-ethylstyryl- (I; R = Et; R′ = H), 3-styryl-2 : 5-dimethyl- (II; R = H) and 3-4′-methylstyryl-2 : 5-dimethyl-thiophen (II; R = Me) were obtained. In some cases, there were signs of the simultaneous formation of a second isomer (probably the *cis*-).

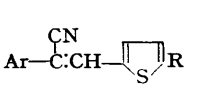
Another route to analogues of stilbene was the condensation of thiophen aldehydes with 2 : 4 : 6-trinitrotoluene in the presence of piperidine, according to a procedure used in the aro-

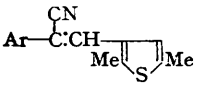
matic series by Pfeiffer and Monath (*Ber.*, 1906, **39**, 1306). The compounds (III; R = H, Me, and Cl) and (IV) were thus readily obtained. A third route was the condensation of thiophen

(III.) 

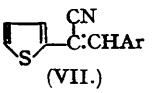
 (IV.)

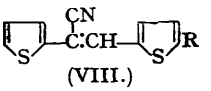
aldehydes in the presence of mineral or organic bases with arylacetonitriles. A series of α-aryl-β-2-thienylacrylonitriles (as V) and α-aryl-β-3-thienylacrylonitriles (as VI) was thus easily

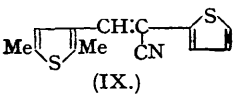
(V.) 

 (VI.)

prepared and is listed in Table I. The analogous condensation of various aromatic aldehydes with 2-thienylacetonitrile yielded a series of β-aryl-α-2-thienylacrylonitriles of type (VII),

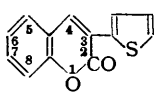

(VII.)

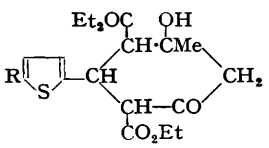

(VIII.)


(IX.)

listed in Table II. When thiophen aldehydes were used in the latter process, αβ-dithienylacrylonitriles of types (VIII) and (IX) were obtained (see Table II).

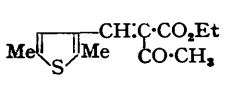
It is worth mention that although β-*p*-methoxyphenyl-α-2-thienylacrylonitrile (VII; Ar = (*p*-MeO·C_6H_4) was readily demethylated by pyridine hydrochloride, the isomeric nitrile (VII; Ar = *o*-MeO·C_6H_4) was completely converted into 3-2′-thienylcoumarin (X). This abnormal behaviour was also found in the aromatic series, 1-phenyl-2-*o*-methoxyphenylacrylonitrile being similarly transformed into 3-phenylcoumarin by heating it for a short time with pyridine hydrochloride.

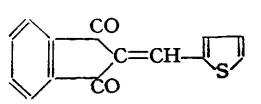
(X.) 

 (XI.)

The ready accessibility of thiophen aldehydes by the *N*-formanilide method led us to investigate their properties further. When 2-formylthiophen and ethyl acetoacetate in equimolecular amounts were treated with a few drops of piperidine, the expected ethyl 2-thienylideneacetoacetate was not formed, but instead ethyl 4-hydroxy-6-keto-2-2′-thienyl-4-methyl*cyclo*hexan-1 : 3-dicarboxylate (XI; R = H) was obtained; similarly, the 5-chloro-2-thienyl compound (XI; R = Cl) was formed from an equimolecular mixture of 5-chloro-2-formylthiophen, ethyl acetoacetate, and piperidine. Both compounds (XI) were of course obtained when one molecule of aldehyde was allowed to react with two molecules of ethyl acetoacetate.

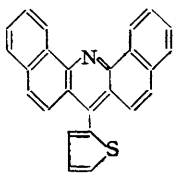
It may be recalled that, in the benzene series, ethyl benzylideneacetoacetate was readily obtained when equimolecular amounts of benzaldehyde and ethyl acetoacetate were treated with piperidine (Knoevenagel, *Ber.*, 1896, **29**, 172), and we found that *p*-chlorobenzaldehyde behaved similarly. An unexpected result was therefore recorded with 3-formyl-2 : 5-dimethylthiophen, which behaved like an aromatic aldehyde, and yielded ethyl (2 : 5-dimethyl-3-thienylidene)acetoacetate (XII).

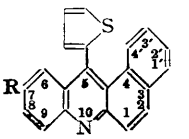
(XII.) 

 (XIII.)

In some other reactions, 2-formylthiophen behaved like benzaldehyde, yielding, for instance, the 2-thienylidene derivative (XIII) with indane-1 : 3-dione, and with an equimolecular mixture of α-naphthol and α-naphthylamine 5-2′-thienyl-1 : 2 : 8 : 9-dibenzacridine (XIV) (cf. the synthesis of 5-phenyl-1 : 2 : 8 : 9-dibenzacridine by Senier and Austin, *J.*, 1906, **89**, 1395).

Extensions of this acridine synthesis were the ready preparation of 5-2′-thienyl- (XV; R = H) and 5-2′-thienyl-7-methyl-3 : 4-benzacridine (XV; R = Me).

(XIV.) 

 (XV.)

Many of our new compounds are under biological investigation in this Institute by Professor A. Lacassagne, in particular 2-(*p*-dimethylaminophenyl)-1-2′-thienylacrylonitrile, which is isosteric with the carcinogenic 1-phenyl-2-(*p*-dimethylaminophenyl)acrylonitrile.

Experimental.

Preparation of 2-Formylthiophen and its Homologues.—The following modification of the King–Nord procedure (*loc. cit.*) was used throughout. To a mixture of thiophen (84 g.) and *N*-methylformanilide (180 g.), in a flask fitted with a reflux condenser and a mechanical stirrer, phosphorus oxychloride (192 g.) was added; reaction set in immediately and the liquid boiled. The reaction subsided after about 30 minutes, and the mixture was then refluxed for 1 hour on a water-bath. After cooling, it was treated with sodium acetate (300 g.) in water (500 c.c.) and steam-distilled. 2-Formylthiophen was extracted from the distillate with ether, with dilute hydrochloric acid, then with dilute aqueous sodium carbonate, dried (Na_2SO_4), and freed from solvent, and the residue was distilled *in vacuo*. The yields were generally superior by 10—15 g. to those recorded by King and Nord. The aldehyde had b. p. 93—94°/20 mm.

5-Chloro-2-formyl-, b. p. 103—105°/13 mm., and 2-formyl-5-methyl-thiophen, b. p. 107°/13 mm., were prepared similarly, with the same yields. The condensation of 2 : 5-dimethylthiophen to give 3-formyl-2 : 5-dimethylthiophen, b. p. 115°/13 mm., was less easy and required 2 hours' refluxing to afford good yields, probably because of the lower reactivity at the 3-position.

2-Styrylthiophen and its Analogues.—A solution of 2-formylthiophen (5 g.) in anhydrous ether (10 c.c.) was added in small portions to a cooled Grignard solution [from magnesium (1·3 g.) and benzyl chloride (6·8 g.) in ether (50 c.c.)]. After 15 minutes' refluxing, the reaction product was poured into 10% aqueous sulphuric acid, and the crude carbinol from the ethereal layer was refluxed for 5 minutes with 98% formic acid (20 c.c.). The mixture was poured into water, and the *styryl* compound taken up in benzene and purified by vacuum-fractionation (b. p. 170—180°/13 mm.). It formed, from ethanol, light colourless leaflets (5 g.), m. p. 111°, giving an orange-red colour with sulphuric acid (Found: C, 77·2; H, 5·4. $C_{12}H_{10}S$ requires C, 77·4; H, 5·4%).

2-Styryl-5-methylthiophen, prepared in the same way, had b. p. 185—190°/13 mm. and crystallised from ethanol in colourless leaflets m. p. 85°, giving a bright red colour with sulphuric acid (Found: C, 78·0; H, 6·2. $C_{13}H_{12}S$ requires C, 78·0; H, 6·0%). *2-4′-Methylstyryl-5-methylthiophen* had b. p. 185—195°/13 mm. and formed from ethanol glistening colourless leaflets, m. p. 94° (Found: C, 78·3; H, 6·6. $C_{14}H_{14}S$ requires C, 78·5; H, 6·5%). The isosteric 4 : 4′-dimethylstilbene (Anschütz and Wirtz, *Ber.*, 1885, **18**, 1948) has m. p. 179° and b. p. 304—305°. *2-4′-Ethylstyrylthiophen* was a pale yellow oil, b. p. 190—195°/13 mm., giving an orange-red colour with sulphuric acid (Found: C, 78·3; H, 6·6. $C_{14}H_{14}S$ requires C, 78·5; H, 6·5%). *3-Styryl-2 : 5-dimethylthiophen* had b. p. 195—205°/13 mm. and formed from ethanol colourless needles, m. p. 55°, giving with sulphuric acid a deep orange-red colour (Found: C, 78·5; H, 6·9. $C_{14}H_{14}S$ requires C, 78·5; H, 6·5%). *3-4′-Methylstyryl-2 : 5-dimethylthiophen* formed from ethanol colourless leaflets, m. p. 101°, b. p. 200—210°/13 mm., giving a crimson-red colour with sulphuric acid (Found: C, 78·6; H, 7·0. $C_{15}H_{16}S$ requires C, 78·9; H, 7·0%). Crystallisation of the mother-liquors of all the foregoing solid compounds yielded small amounts of oily, sulphur-containing substances which have approximately the same b. p. as the crystals and which are stereoisomers thereof.

2-2′-Thienylideneindane-1 : 3-dione (XIII).—One drop of piperidine was added to a stirred mixture of indane-1 : 3-dione (1 g.) and 2-formylthiophen (0·9 g.) in ethanol (10 c.c.). An exothermic reaction at once set in. The *thienylidene* derivative formed was collected, washed with methanol, and recrystallised from ethanol in long golden-yellow needles, m. p. 177°, giving an orange-red colour with sulphuric acid (Found: C, 69·8; H, 3·5. $C_{14}H_8O_2S$ requires C, 70·0; H, 3·3%).

5-2′-Thienyl-1 : 2 : 8 : 9-dibenzacridine (XIV).—To a boiling mixture of α-naphthylamine (7 g.) and α-naphthol (7 g.), 2-formylthiophen (5·5 g.) was added drop-wise with stirring. Boiling was then continued for 5 minutes, and the reaction product distilled in a high vacuum; crystallisation from benzene of the resin, b. p. >280°/2 mm., gave yellow prisms, m. p. 224° (yield, 40%), producing an orange-yellow colour with sulphuric acid (Found: N, 3·6. $C_{25}H_{15}NS$ requires N, 3·9%). The picrate formed yellow prisms, m. p. 236—237° (decomp.), from xylene.

5-2′-Thienyl-3 : 4-benzacridine.—Similarly prepared by addition of 2-formylthiophen (5·5 g.) to a boiling mixture of β-naphthol (7 g.) and aniline (4·8 g.), this *base* crystallised from ethanol in fine pale yellow prisms, m. p. 191° (Found: N, 4·2. $C_{21}H_{13}NS$ requires N, 4·5%), giving a picrate, fine yellow needles, m. p. 235—236° (decomp.) (Buu-Hoï and Hoán, *Rec. Trav. chim.*, 1949, **68**, 5, gave m. p. 237°). *5-2′-Thienyl-7-methyl-3 : 4-benzacridine* (from the same aldehyde, β-naphthol, and *p*-toluidine) formed

from ethanol pale yellow needles, m. p. 237° (sublimation above 210°) (Found: N, 4·2. $C_{22}H_{15}NS$ requires N, 4·3%), giving a picrate, m. p. *ca.* 245° (decomp.).

2-(2 : 4 : 6-*Trinitrostyryl*)*thiophen and its Analogues.*—A solution of 2 : 4 : 6-trinitrotoluene (1 g.) and 2-formylthiophen (0·5 g.) in dry benzene (10 c.c.) was gently refluxed for 3 hours with 2 drops of piperidine; the solvent was distilled off, and the residue recrystallised twice from ethanol, giving glistening dark yellow elongated prisms, m. p. 140° (1·2 g.); sulphuric acid produced an orange colour. This compound has recently been described by Emerson and Patrick (*loc. cit.*).

2-(2 : 4 : 6-*Trinitrostyryl*)-5-*methylthiophen*, similarly prepared from 2-formyl-5-methylthiophen, formed from ethanol reddish-yellow needles, m. p. 164—165° (Found: N, 12·2. $C_{13}H_9O_6N_3S$ requires N, 12·5%). 5-*Chloro*-1-(2 : 4 : 6-*trinitrostyryl*)*thiophen* formed from ethanol brownish-yellow needles, m. p. 150°, giving a brown colour with sulphuric acid (Found: N, 11·6. $C_{12}H_6O_6N_3ClS$ requires N, 11·8%). 3-(2 : 4 : 6-*Trinitrostyryl*)-2 : 5-*dimethylthiophen* (24 hours' heating) formed from ethanol long red needles, m. p. 175°, giving a brownish-yellow colour with sulphuric acid (Found: N, 11·9. $C_{14}H_{11}O_6N_3S$ requires N, 12·0%).

Ethyl 4-*Hydroxy*-6-*keto*-2-2′-*thienyl*-4-*methyl*cyclo*hexane*-1 : 3-*dicarboxylate.*—An equimolecular mixture of 2-formylthiophen (8 g.) and ethyl acetoacetate (10 g.) was cooled in ice, and 5 drops of piperidine were stirred in. After 12 hours at room temperature, the cyclic *ester*, which had solidified, was filtered off and recrystallised twice from ether; fine colourless needles, m. p. 106°, were obtained, giving an orange-yellow colour with sulphuric acid (Found: C, 57·6; H, 6·3. $C_{17}H_{22}O_6S$ requires C, 57·6; H, 6·2%). The same compound was obtained in almost quantitative yield when the proportion of ethyl acetoacetate was doubled, and the mixture kept for 48 hours.

The 5-*chloro*-2-*thienyl* analogue crystallised from ether in glistening colourless needles, m. p. 150°, giving with sulphuric acid a yellow colour (Found: C, 52·4; H, 5·5. $C_{17}H_{21}O_6ClS$ requires C, 52·4; H, 5·4%).

Ethyl p-*Chlorobenzylideneacetoacetate.*—A mixture of *p*-chlorobenzaldehyde (5 g.), ethyl acetoacetate (4·6 g.), and piperidine (4 drops) was kept at room temperature for 24 hours; the *ester* obtained crystallised from ether in long colourless needles (8 g.), m. p. 87°, giving with sulphuric acid a yellow colour (Found: C, 61·5; H, 5·2. $C_{13}H_{13}O_3Cl$ requires C, 61·7; H, 5·1%).

Ethyl (2 : 5-*Dimethyl*-3-*thienylidene*)*acetoacetate.*—Obtained from 3-formyl-2 : 5-dimethylthiophen (2·6 g.), ethyl acetoacetate (2·3 g.), and piperidine (2 drops) (24 hours at room temperature), this *compound* formed from ether colourless prisms (4 g.), m. p. 72°, giving with sulphuric acid an orange-red colour (Found: C, 61·6; H, 6·5. $C_{13}H_{16}O_3S$ requires C, 61·9; H, 6·3%).

TABLE I.

Acrylonitriles of types (V) *and* (VI).

Acrylonitrile.[a]	M. p. (b. p.).	Formula.	Found, %. C.	Found, %. H.	Reqd., %. C.	Reqd., %. H.
α-*Phenyl*-β-2-*thienyl*-	90° (200—210°/13 mm.)	$C_{13}H_9NS$	73·6	4·6	73·9	4·3
α-*Phenyl*-β-(5-*methyl*-2-*thienyl*)-	83 (210—220°/13 mm.)	$C_{14}H_{11}NS$	74·5	5·0	74·7	4·9
α-*Phenyl*-β-(5-*chloro*-2-*thienyl*)-[b]	149	$C_{13}H_8NClS$	63·1	3·5	63·4	3·3
α-*Phenyl*-β-(2 : 5-*dimethyl*-3-*thienyl*)-	85	$C_{15}H_{13}NS$	75·2	5·6	75·3	5·4
α-p-*Tolyl*-β-2-*thienyl*-	118	$C_{14}H_{11}NS$	74·4	5·1	74·7	4·9
α-p-*Tolyl*-β-(5-*methyl*-2-*thienyl*)-	110	$C_{15}H_{13}NS$	75·1	5·4	75·3	5·4
α-p-*Tolyl*-β-(2 : 5-*dimethyl*-3-*thienyl*)-	91	$C_{16}H_{15}NS$	75·6	5·9	75·9	5·9
α-p-*Tolyl*-β-(5-*chloro*-2-*thienyl*)-[b]	154	$C_{14}H_{10}NClS$	64·4	3·9	64·6	3·8
α-1-*Naphthyl*-β-2-*thienyl*-[c]	97 (270—275°/13 mm.)	$C_{17}H_{11}NS$	78·1	4·4	78·2	4·2
α-1-*Naphthyl*-β-(5-*methyl*-2-*thienyl*)-[d]	145	$C_{18}H_{13}NS$	78·5	4·8	78·5	4·7
α-1-*Naphthyl*-β-(2 : 5-*dimethyl*-3-*thienyl*)-	76	$C_{19}H_{15}NS$	75·2	5·3	75·4	5·2
α-1-*Naphthyl*-β-(5-*chloro*-2-*thienyl*)-	152	$C_{17}H_{10}NClS$	68·8	3·6	68·9	3·4
α-p-*Nitrophenyl*-β-2-*thienyl*-	204	$C_{13}H_8O_2N_2S$	60·0	3·2	60·1	3·1
α-p-*Nitrophenyl*-β-(5-*methyl*-2-*thienyl*)-[c]	227 (subl. >200°)	$C_{14}H_{10}O_2N_2S$	62·1	3·9	62·2	3·7
α-p-*Nitrophenyl*-β-(2 : 5-*dimethyl*-3-*thienyl*)-	188	$C_{15}H_{12}O_2N_2S$	63·1	4·2	63·4	4·2
α-p-*Nitrophenyl*-β-(5-*chloro*-2-*thienyl*)-[b]	234 (subl.)	$C_{13}H_7O_2N_2SCl$	53·5	2·6	53·6	2·4
α-p-*Methoxyphenyl*-β-2-*thienyl*-	77	$C_{14}H_{11}ONS$	69·8	4·4	69·7	4·4
α-p-*Methoxyphenyl*-β-(5-*methyl*-2-*thienyl*)-	88	$C_{15}H_{13}ONS$	70·4	5·3	70·6	5·1
α-p-*Methoxyphenyl*-β-(5-*chloro*-2-*thienyl*)-	134	$C_{14}H_{10}ONSCl$	50·8	3·6	50·9	3·6
α-p-*Methoxyphenyl*-β-(2 : 5-*dimethyl*-3-*thienyl*)-	96	$C_{16}H_{15}ONS$	71·2	5·6	71·4	5·6
α-p-*Hydroxyphenyl*-β-2-*thienyl*-[c]	166	$C_{13}H_9ONS$	68·6	4·0	68·7	3·9
α-p-*Hydroxyphenyl*-β-(5-*methyl*-2-*thienyl*)-	208	$C_{14}H_{11}ONS$	69·8	4·8	69·7	4·6
α-p-*Hydroxyphenyl*-β-(5-*chloro*-2-*thienyl*)-	206	$C_{13}H_8ONSCl$	59·3	3·2	59·5	3·1
α-p-*Hydroxyphenyl*-β-(2 : 5-*dimethyl*-3-*thienyl*)-	187	$C_{15}H_{13}ONS$	70·3	5·1	70·6	5·0

[a] All yellow needles, unless otherwise stated. [b] Leaflets. [c] Prisms. [d] Orange.

TABLE II.

Acrylonitriles [a] *of types* (VII), (VIII), *and* (IX).

α-(2-Thienyl)acrylonitriles.[b]	M. p.	Formula.	Found, %. C.	Found, %. H.	Reqd., %. C.	Reqd., %. H.
β-2-*Furyl*- [c]	80°	$C_{11}H_7ONS$	65·6	3·8	65·7	3·5
β-(p-*Dimethylaminophenyl*)- [d]	160	$C_{15}H_{14}N_2S$	70·1	5·7	70·1	5·6
β-p-*Chlorophenyl*-	90	$C_{13}H_8NSCl$	63·2	3·5	63·4	3·3
β-p-*Methoxyphenyl*-	74	$C_{14}H_{11}ONS$	69·6	4·8	69·7	4·6
β-(3 : 4-*Dimethoxyphenyl*)- [c]	86	$C_{15}H_{13}O_2NS$	66·3	4·9	66·4	4·8
β-(3 : 4-*Methylenedioxyphenyl*)- [c]	106	$C_{14}H_9O_2NS$	65·6	3·7	65·9	3·5
β-o-*Methoxyphenyl*-	81	$C_{14}H_{11}ONS$	59·4	4·8	49·7	4·6
β-(5-*Methyl*-2-*thienyl*)- [c]	87	$C_{12}H_9NS_2$	62·2	3·8	62·3	3·9
β-(2 : 5-*Dimethyl*-3-*thienyl*)- [c]	105	$C_{13}H_{11}NS_2$	63·7	4·8	63·7	4·5
β-(5-*Chloro*-2-*thienyl*)-	115	$C_{11}H_6NS_2Cl$	52·3	2·6	52·4	2·4
β-p-*Hydroxyphenyl*-	176	$C_{13}H_9ONS$	68·5	4·1	68·7	4·0
β-(3 : 4-*Dihydroxyphenyl*)-	179—181	$C_{13}H_9O_2NS$	64·0	3·8	64·2	3·7

[a] Acrylonitriles of type (VIII) are functional derivatives of 1 : 2-di-2′-thienylethylene (Nahke, *Ber.*, 1897, **30**, 2041). [b] Yellow needles unless otherwise stated. [c] Prisms. [d] Leaflets. [e] B. p. 230—240°/13 mm.

Preparation of Acrylonitriles of Types (V), (VI), (VIII), and (IX).—These were prepared in the usual way by shaking the aldehyde and arylacetonitrile in warm ethanol, with a few drops of 30% aqueous potassium hydroxide. In most instances, there was an almost immediate separation of an oil which solidified when kept. The substance was collected, washed with water, and recrystallised from ethanol. In the case of *p*-nitrophenylacetonitrile, piperidine was used instead of potassium hydroxide, and the reaction was effected by 3 hours' boiling. 2-Thienylacetonitrile was condensed with aldehydes in the same way; it was prepared from 2-chloromethylthiophen (Blicke and Burchkalter, *J. Amer. Chem. Soc.*, 1942, **64**, 477) by Blicke and Zienty's method (*J. Amer. Chem. Soc.*, 1941, **63**, 2945). The products are recorded in Tables I and II. All these compounds give brown, red, or violet colours in sulphuric acid.

Demethylation of Acrylonitriles bearing Methoxy-groups.—This was effected by refluxing for 15 minutes a mixture of the required methoxy-compound (1 part) with redistilled pyridine hydrochloride. After dilution of the mixture with water, the precipitate formed was collected, washed thoroughly with water, dried, and crystallised from benzene; the yields were almost quantitative.

3-2′-*Thienylcoumarin* (X).—Demethylation of β-*o*-methoxyphenyl-α-2-thienylacrylonitrile (1·5 g.) with pyridine hydrochloride in the foregoing way, and crystallization of the reaction product from ethanol, yielded 3-2′-*thienylcoumarin* as pale yellow, fluffy needles (1·3 g.), m. p. 167°, giving a red colour with sulphuric acid (Found: C, 68·4; H, 2·8; N, 0. $C_{13}H_8O_2S$ requires C, 68·4; H, 3·5%). This compound was insoluble in dilute aqueous sodium hydroxide solutions in the cold.

1-*Phenyl*-2-o-*methoxyphenylacrylonitrile*, prepared from *o*-methoxybenzaldehyde and phenylacetonitrile, formed, from ethanol, silky, pale yellow needles, m. p. 46°, b. p. 222°/13 mm. (Found: N, 6·0. $C_{15}H_{13}ON$ requires N, 6·2%). On treatment with pyridine hydrochloride as above, it gave a quantitative yield of 3-phenylcoumarin, m. p. 140° (Oglialoro, *Ber.*, 1879, **12**, 2367).

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[*Received, April 5th*, 1950.]