224. *β-Cycloylpropionitriles. Part I. A General Synthesis and Conversion into Pyrrole Dyes.*

By Edward B. Knott.

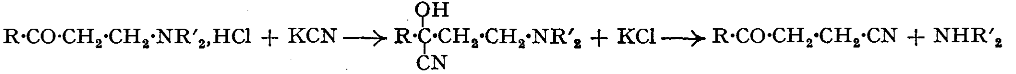
Cyclyl β-dialkylaminoethyl ketone hydrochlorides, readily obtained by the Mannich reaction, are converted to *β-cycloylpropionitriles* by refluxing with aqueous potassium cyanide. The nitriles on hydrolysis yield *β-cycloylpropionic acids* some of which are not otherwise readily available. β-Benzoylpropionitrile readily absorbs hydrogen chloride to give a crystalline *chloroimide* salt which on treatment with alcohol gives an *alkyl β-benzoylpropimino-ether hydrochloride.* The latter, also formed by the conventional method, gives with hot alcoholic ethyl orthoformate, red 3 : *3′-pyrromethin* and with β-ethoxyacraldehyde acetal, a blue 3 : *3′-pyrrotrimethin* dye.

The preparation of β-cycloylpropionic acids is normally achieved by a Friedel–Crafts condensation of an unsaturated carbocycle or heterocycle with succinic anhydride. This method gives positive results with most suitable carbocyclic and stable heterocyclic compounds. The same acids can also be prepared from the cyclyl bromomethyl ketone by condensation with ethyl sodiomalonate followed by hydrolysis and decarboxylation. Both of these methods fail, however, when the cyclic component is relatively unstable. Thus furan or 2-bromoacetylfuran gave only tars when submitted to either of the above processes. Since β-2-*furoylpropionic acid* was required, an alternative method of preparation was sought.

One method would be by the hydrolysis of β-2-furoylpropionitrile if such a compound were readily available. No general method for the preparation of β-cycloylpropionitriles has been developed, although one such nitrile, β-benzoylpropionitrile (β-cyanopropiophenone) was prepared by Allen, Gilbert, and Young (*J. Org. Chem.*, 1937, **2**, 227) by the addition of hydrogen cyanide to phenyl vinyl ketone.

It is well known (Mannich and Hönig, *Arch. Pharm.*, 1927, **265**, 598) that cyclyl β-dialkylaminoethyl ketones vary in their stability and that many of them, on steam distillation, lose dialkylamine to give cyclyl vinyl ketones. It is also known (Reichert and Posemann, *ibid.*, 1937, **275**, 67) that Mannich salts react with sodionitromethane to give γ-nitrobutyrophenones. It appeared fruitful, therefore, to investigate the action of alkali cyanides on Mannich salts, since such alkalis should release the Mannich bases, and under certain conditions the latter, by loss of dialkylamine followed by hydrogen cyanide addition, might be converted into the desired nitriles.

It has been reported (Mannich and Braun, *Ber.*, 1920, **53**, 1874) that the Mannich salt obtained from *cyclo*hexanone on treatment with aqueous potassium cyanide yields a cyanohydrin of the Mannich base. The β-dialkylaminopropiophenone hydrochlorides (I; R = Ph) which were chosen for model experiments also gave oils on the addition of aqueous potassium cyanide. These are believed to be the cyanohydrins (II; R = Ph) but they readily decomposed on attempted distillation and were not analysed. The product from 2-furyl β-dimethylamino ethyl ketone hydrochloride (I; R = 2-C_4H_3O) and cold aqueous potassium cyanide, however, was obtained crystalline and found to be 2-*furyl* β-*dimethylaminoethyl ketone cyanohydrin* (II; R = 2-C_4H_3O, R′ = Me).



$$R{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}NR'_2{,}HCl + KCN \longrightarrow R{\cdot}\overset{OH}{\underset{CN}{C}}{\cdot}CH_2{\cdot}CH_2{\cdot}NR'_2 + KCl \longrightarrow R{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CN + NHR'_2$$

(I.) (II.) (III.)

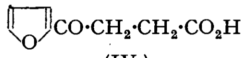
The decomposition of (II; R = Ph), with or without its isolation, was readily brought about by short heating under reflux in water, preferably in the presence of excess alkali cyanide. Dialkylamine was evolved, and β-benzoylpropionitrile formed in reasonably good yield. The yield and the state of purity of the crude product, as well as the optimal reaction time, depended primarily on the concentration of the aqueous cyanide. The greater the dilution the purer was the product, and up to a point the higher the yield. Too great a dilution lowered the yield, owing to the solubility of the nitrile in water. Replacement of water as solvent by aqueous alcohol, and other combinations, always gave lower yields.

The application of this method to other salts (I; R = aryl, or 2-thienyl) gave similar yields of nitrile. β-2-*Furoylpropionitrile* is much more soluble than the other nitriles and must be extracted from the reaction mixture. 2-*Benzfuryl* β-*cyanoethyl ketone* (VI) was also obtained by this method. The reaction appears to be fairly general and the only exception amongst the salts used involved 3-nitro-β-dimethylaminopropiophenone hydrochloride. This salt, the base of which is known to be very unstable, readily releasing amine and formaldehyde (Mannich and Dannehl, *Arch. Pharm.*, 1938, **276**, 206), gave only resins with potassium cyanide. 1-*Naphthyl* β-*dimethylaminoethyl ketone hydrochloride*, which decomposed rapidly on heating in aqueous solution, gave the expected nitrile only when a large excess of cyanide was present.

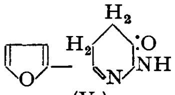
The reaction applied to *p*-chloro-β-dimethylaminopropiophenone hydrochloride gave only a 16·5% yield of the required nitrile and a second solid, analysis of which indicated the empirical formula $C_{19}H_{15}O_2NCl_2$. It formed a monophenylhydrazone and was decomposed to an oil by boiling 18% hydrochloric acid. The simplest substance of this composition, *viz.*, $Cl{\cdot}C_6H_4{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}C(\colon NH){\cdot}CH\colon CH{\cdot}CO{\cdot}C_6H_4Cl$, would be formed by addition of the intermediate *p*-chlorophenyl vinyl ketone to the *p*-chlorobenzoylpropionitrile, giving 4-imino-1 : 7-diketo-1 : 7-di-*p*-chlorophenylhept-2-ene.

This method of preparation of the nitriles appears to apply only where R′ is alkyl. Such Mannich salts obtained by the substitution of dialkylamines by piperidine or morpholine do not decompose under the conditions employed here. Similarly, Mannich salts from cyclic ketones or propiophenone gave only oils or resins on similar treatment.

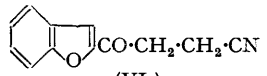
In all cases the nitrile was readily hydrolysed to the β-cycloylpropionic acid (cf. Allen *et al.*, *loc. cit.*). β-2-*Furoylpropionic acid* (IV) resembles β-benzoylpropionic acid in its melting point and physical appearance. It was characterised by its *ethyl* ester and its conversion into 3-*keto*-6-(2′-*furyl*)-2 : 3 : 4 : 5-*tetrahydropyridazine* (V) by hydrazine hydrate.



(IV.)



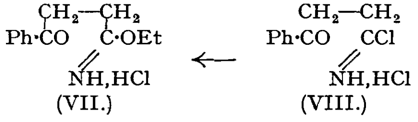
(V.)



(VI.)

On treating an alcoholic solution of β-benzoylpropionitrile with hydrogen chloride, *ethyl* β-*benzoylpropimino-ether hydrochloride* (VII) was obtained, the *base* of which is crystalline but not very stable; (VII) was also obtained by treating the nitrile with hydrogen chloride in dry benzene and dissolving the resulting, crystalline *chloroimide* salt (VIII) in ethyl alcohol. The chloroimide fumed strongly in air, slowly releasing hydrogen chloride to give the original nitrile. It was decomposed by water to give chiefly the original nitrile together with some β-benzoylpropionamide.

On warming (VII) with 18% hydrochloric acid, ethyl β-benzoylpropionate was formed in quantitative yield, whilst its base, on heating with acetic anhydride, gave the expected N-β-*benzoylpropionylacetamide* (IX). The corresponding *imino-ether* salts from β-4-*methoxy-benzoylpropionitrile* and β-4-*hydroxybenzoylpropionitrile* are very sensitive to moisture, and on dissolving in 99% alcohol were converted into β-4-*methoxy*- and β-4-*hydroxy-benzoylpropionamides*.



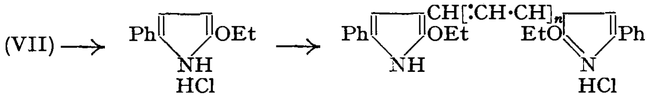
(VII.) (VIII.)

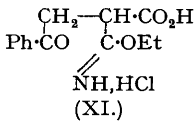
$Ph{\cdot}CO{\cdot}CH_2{\cdot}CH_2{\cdot}CO{\cdot}NH{\cdot}CO{\cdot}CH_3$

(IX.)

All the imino-ether hydrochlorides showed a strong Ehrlich reaction in warm alcohol, indicating ring closure to pyrrole derivatives. The latter could not be isolated, although a yellow crystalline substance together with ammonium chloride was formed on refluxing (VI) in absolute alcohol. Its constitution was not determined.

On refluxing (VII) with alcoholic ethyl orthoformate a brilliant red dye was formed. Analysis suggested the empirical formula $C_{25}H_{25}O_2N_2Cl$ which is the *hydrochloride* of a *base* $C_{25}H_{24}O_2N_2$. Since it is apparent that pyrrole ring formation occurs on heating (VII) in alcohol, the dye is therefore *bis*-3-(2-*ethoxy*-5-*phenylpyrrole*)*methin hydrochloride* (X; $n = 0$) or the *bis*-4-*isomer*. The 3-position of the methin bridge was established with a fair amount of certainty by preparing the imino-ether of α-cyano-β-benzoylpropionic acid (XI) and treating it with *p*-dimethylaminobenzaldehyde and also with ethyl orthoformate. Although (XI), obtained as an oil, was not purified, it gave a strong Ehrlich reaction but no dye with ethyl orthoformate. Since the 3-position in the potential pyrrole ring is blocked by the carboxyl group it follows that the reaction with *p*-dimethylaminobenzaldehyde must take place in the 4-position, and that either steric hindrance or lower activity of the 4-position precludes dye formation with ethyl orthoformate.


(VII) (XII.) (X.)


(XI.)

Analogues of (X) were prepared from *methyl* β-*benzoylpropimino-ether hydrochloride* and *ethyl* β-4-*methoxybenzoylpropimino-ether hydrochloride*. The salt (VII) and β-ethoxyacraldehyde acetal gave a blue dye which by analogy is *bis*-3-(2-*ethoxy*-5-*phenylpyrrole*)*trimethin hydrochloride* (X; $n = 1$). The formation of these dyes is interesting. It appears that the initial step of pyrrole ring formation occurs on warming in alcohol; the 2-ethoxy-5-phenylpyrrole hydrochloride (XII) thus formed probably decomposes rapidly to ammonium chloride and the above-mentioned yellow crystalline substance; in the presence of *p*-dimethylaminobenzaldehyde, ethyl orthoformate or β-ethoxyacraldehyde acetal, however, dye formation, occurring immediately the pyrrole ring has formed, stabilises the rings. This stability may be connected with the resonance of the new systems.

Degradation experiments failed to give any simpler pyrrole derivatives. The dye salts are stable in aqueous alcoholic solution at pH 3 but are readily hydrolysed by water at higher pH values. On the addition of alkali to the aqueous-alcoholic solution of the dye, the intense red colour, lost on initial hydrolysis of the salt, is restored; this must be due to salt formation although the identity of the absorption curves indicates no great structural change.

The blue dye (X; $n = 1$) weakly sensitised a photographic silver chloride emulsion at low pH values with a broad maximum sensitivity at 5000—6000 A. extending to 7000 A.

EXPERIMENTAL.

(Microanalyses are by Drs. Weiler and Strauss, Oxford; m. p.s are uncorrected.)

1-*Naphthyl β-Dimethylaminoethyl Ketone Hydrochloride* (I; $R = 1\text{-}C_{10}H_7$).—1-Naphthyl methyl ketone (85 g.), dimethylamine hydrochloride (42 g.), paraformaldehyde (22·5 g.), concentrated hydrochloric acid (1 c.c.), and ethyl alcohol (150 c.c.) were heated under reflux for 4 hours, poured into acetone (800 c.c.), and chilled. Colourless crystals (45 g.; 34%) were obtained which formed colourless prisms, m. p. 165°, from ethyl alcohol (Found: N, 4·9. $C_{15}H_{18}ONCl$ requires N, 5·3%).

β-Dimethylamino-3-hydroxypropiophenone Hydrochloride (I; $R = 3\text{-}OH{\cdot}C_6H_4$).—*m*-Hydroxyacetophenone (50 g.), dimethylamine hydrochloride (40 g.), paraformaldehyde (14·4 g.), concentrated hydrochloric acid (1·5 c.c.), and ethyl alcohol (100 c.c.) were heated under reflux for 1 hour. The *salt* had then partly crystallised. It (44·2 g.; 52·5%) was collected when cold and formed long, fine needles, m. p. 176°, after two recrystallisations from ethyl alcohol (Found: N, 6·1. $C_{11}H_{16}O_2NCl$ requires N, 6·1%).

β-Dimethylamino-3-methoxypropiophenone Hydrochloride (I; $R = 3\text{-}MeO{\cdot}C_6H_4$).—*m*-Methoxyacetophenone (23·5 g.), dimethylamine hydrochloride (16·6 g.), paraformaldehyde (6·3 g.), concentrated hydrochloric acid (0·3 c.c.), and ethyl alcohol (50 c.c.) were heated under reflux for 2 hours. The clear liquor was poured into acetone (400 c.c.), and the required *salt* (23 g.; 60·5%) obtained on scratching. It formed cream needles, m. p. 160°, from ethyl alcohol (Found: N, 5·55. $C_{12}H_{18}O_2NCl$ requires N, 5·75%).

β-Dimethylamino-4-hydroxypropiophenone Hydrochloride (I; $R = 4\text{-}OH{\cdot}C_6H_4$).—*p*-Hydroxyaceto phenone (25 g.), dimethylamine hydrochloride (20 g.), paraformaldehyde (7·2 g.), concentrated hydrochloric acid (0·75 c.c.), and ethyl alcohol (30 c.c.) were heated under reflux for 1 hour. After 10 minutes a mass of crystals had separated. They (32 g.; 76%) were collected when cold and washed with cold ethyl alcohol. A sample was obtained as glistening plates, m. p. 192°, from ethyl alcohol, in which it is sparingly soluble (Found : N, 6·2; Cl, 15·2. $C_{11}H_{16}O_2NCl$ requires N, 6·1; Cl, 15·45%).

4-*Bromo-β-dimethylaminopropiophenone Hydrochloride* (I; R = 4-BrC_6H_4).—*p*-Bromoacetophenone (25 g.), dimethylamine hydrochloride (12 g.), paraformaldehyde (4·5 g.), concentrated hydrochloric acid (0·5 c.c.), and ethyl alcohol (30 c.c.) were refluxed together for 2 hours, then chilled, and acetone (50 c.c.) added; the *salt* (17·9 g.; 49%) crystallised, and formed jagged needles, m. p. 196°, from ethyl alcohol (Found : N, 4·7. $C_{11}H_{15}ONClBr$ requires N, 4·8%).

2-*Benzfuryl β-Dimethylaminoethyl Ketone Hydrochloride* (I; R = 2-*benzfuryl*).—2-Acetylbenzfuran (34 g.) (Stoermer and Schäffer, *Ber.*, 1903, **36**, 2863), dimethylamine hydrochloride (17·3 g.), paraformaldehyde (7·2 g.), and ethyl alcohol (100 c.c.) were refluxed together for 2 hours. The clear solution was concentrated to half its volume, acetone (200 c.c.) added, and the mixture chilled. The crystals (21 g.; 39%) were washed with acetone and obtained as tiny needle rosettes (Found : N, 5·15; Cl, 13·5. $C_{13}H_{16}O_2NCl$ requires N, 5·5; Cl, 14·0%), m. p. 188°, from ethyl alcohol. The filtrates gave unchanged acetylbenzfuran (16·5 g.) on dilution with water.

a-Dimethylaminomethylpropiophenone Hydrochloride.—Propiophenone (134 g.), dimethylamine hydrochloride (106 g.), paraformaldehyde (40 g.), concentrated hydrochloric acid (2 c.c.) and ethyl alcohol (160 c.c.) were heated under reflux for 2 hours. After cooling, ether was added to precipitate an oil, which solidified on shaking (184 g.; 81%). It formed tiny needles, m. p. 142·5°, from ethyl alcohol–ether (Found : N, 6·35. $C_{12}H_{18}ONCl$ requires N, 6·15%).

β-Benzoylpropionitrile (III; R = Ph).—(*a*) β-Dimethylaminopropiophenone hydrochloride (213·5 g.; 1 mol.) (*Org. Synth.*, **23**, 30) and potassium cyanide (130 g.; 2 mols.) were placed in a flask and boiling water (2600 c.c.) added rapidly. The whole, consisting of an aqueous and an oily layer, was refluxed for 30 minutes. Part of the dimethylamine distilled and was collected in dilute hydrochloric acid. On chilling, the oil crystallised, and crystals formed from the aqueous layer. The nitrile (67% yield) formed almost colourless blades, m. p. 76°, from benzene–light petroleum (Found : C, 75·2; H, 5·85; N, 8·6. Calc. for $C_{10}H_9ON$: C, 75·5; H, 5·65; N, 8·8%). Allen *et al.* (*loc. cit.*) give m. p. 76° from ethyl alcohol.

(*b*) Crude β-diethylaminopropiophenone hydrochloride contaminated with diethylamine hydrochloride (900 g.) was obtained by refluxing for 2 hours a mixture of acetophenone (422 g.), diethylamine hydrochloride (500 g.), paraformaldehyde (138 g.), concentrated hydrochloric acid (7 c.c.), and ethyl alcohol (280 c.c.) and adding dry ether to the cooled reaction mixture until no more solid precipitated. The crude salt (24·1 g.), potassium cyanide (13 g.), and boiling water (520 c.c.) were refluxed for 20 minutes, and the nitrile, m. p. 76°, isolated and purified as under (*a*). The yield of nitrile was 48% based on the diethylamine hydrochloride.

*β-*p*-Toluoylpropionitrile* (II; R = *p*-MeC_6H_4).—β-Dimethylamino-4-methylpropiophenone hydrochloride (22·7 g.; 0·1 mol.), potassium cyanide (13·0 g.; 0·2 mol.), and boiling water (520 c.c.) were refluxed for 20 minutes. The crystalline *nitrile* (9·0 g.; 52%) obtained on chilling formed glossy needles, m. p. 76°, from ethyl alcohol (Found : N, 8·15. $C_{11}H_{11}ON$ requires N, 8·2%).

*β-*p*-Chlorobenzoylpropionitrile* (II, R = *p*-ClC_6H_4).—*p*-Chloro-β-dimethylaminopropiophenone hydrochloride (124 g.) (Dhont and Wibaut, *Rec. Trav. chim.*, 1944, **63**, 81), potassium cyanide (65 g.), and boiling water (2600 c.c.) were refluxed together for 30 minutes. On chilling, the oil solidified. It was washed, and dissolved in ethyl alcohol. On cooling, the *nitrile* (16 g., 16·5%) crystallised. It formed flat, colourless needles, m. p. 72·5°, from ethyl alcohol (Found : N, 7·35. $C_{10}H_8ONCl$ requires N, 7·25%). The primary filtrate on prolonged standing gave a second solid (18·0 g.) which was obtained as fine white needles, m. p. 115°, from ethyl alcohol (Found : C, 63·35; H, 4·3; N, 3·95; Cl, 19·45. $C_{19}H_{15}O_2NCl_2$ requires C, 63·35; H, 4·15; N, 3·9; Cl, 19·7%). Its *monophenylhydrazone* formed pale yellow, feathery needles, m. p. 146—148°, from alcohol (Found : N, 8·95. $C_{25}H_{21}ON_3Cl_2$ requires N, 9·35%). The filtrates from the second crystallisation, on concentration, gave a further crop of nitrile (14·4 g.), m. p. 72·5°, so the total yield of the required nitrile was 31·5%. It was readily hydrolysed to β-*p*-chlorobenzoylpropionic acid, m. p. 134° (Skraup and Schwamberger, *Annalen*, 1928, **462**, 135, give m. p. 134°).

*β-*p*-Bromobenzoylpropionitrile* (II; R = *p*-BrC_6H_4).—*p*-Bromo-β-dimethylaminopropiophenone hydrochloride (14·6 g.), potassium cyanide (6·5 g.), and boiling water (130 c.c.) were refluxed for 20 minutes. On chilling, the oil crystallised. The *nitrile* (7·2 g.; 62·5%) formed tiny needles, m. p. 81°, from ethyl alcohol (Found : N, 5·65. $C_{10}H_8ONBr$ requires N, 5·9%).

*β-*p*-Bromobenzoylpropionic Acid*.—The nitrile (1 g.) was refluxed for 1 hour with concentrated hydrochloric acid (10 c.c.), and the *acid* which crystallised on cooling was dissolved in aqueous sodium carbonate, and the solution filtered and acidified. The acid formed colourless needles, m. p. 148° from water (Found : Br, 31·2. $C_{10}H_9O_3Br$ requires Br, 31·1%).

β-3-Hydroxybenzoylpropionitrile; (III; R = 3-$OH{\cdot}C_6H_4$).—β-Dimethylamino-3-hydroxypropiophenone hydrochloride (41 g.), potassium cyanide (23·2 g.), and boiling water (900 c.c.) were refluxed for 30 minutes. The chilled liquor gave on acidification with acetic acid an oil which slowly solidified. It crystallised as needles, m. p. 98°, from aqueous alcohol (Found : N, 8·2. $C_{10}H_9O_2N$ requires N, 8·0%). The *acid*, obtained by refluxing the *nitrile* (2 g.) with 18% hydrochloric acid (20 c.c.), for 1 hour, formed irregular plates, m. p. 146·5°, from water (Found : C, 61·75; H, 5·0. $C_{10}H_{10}O_4$ requires C, 61·85; H, 5·15%).

β-4-Hydroxybenzoylpropionitrile (III; R = 4-$OH{\cdot}C_6H_4$).—Prepared as for the 3-isomer, this *nitrile* was precipitated as a crystalline solid on the addition of acetic acid to the reaction mixture. It was obtained as colourless, flat needles, m. p. 162°, from a little ethyl alcohol in 59% yield (Found : C, 68·35; H, 5·35; N, 7·95. $C_{10}H_9O_2N$ requires C, 68·55; H, 5·15; N, 8·0%). The acid formed colourless needles, m. p. 157°, from hot water. Fieser *et al.* (*J. Amer. Chem. Soc.*, 1940, **62**, 2966) give m. p. 154—156° (Found : C, 61·55; H, 5·05. Calc. for $C_{10}H_{10}O_4$: C, 61·85; H, 5·15%).

β-3-Methoxybenzoylpropionitrile (III; R = 3-$MeO{\cdot}C_6H_4$).—β-Dimethylamino-3-methoxypropiophenone hydrochloride (12·2 g.; 0·05 mol.), potassium cyanide (13 g.; 0·2 mol.), and boiling water (520 c.c.) were refluxed for 10 minutes. On chilling, the oil crystallised. It formed colourless needles, m. p. 54°, in 73% yield from methyl alcohol by repeated concentration of the filtrates (Found : N, 7·2. $C_{11}H_{11}O_2N$ requires N, 7·4%). The *acid* was obtained on hydrolysis of the *nitrile* with 18% hydrochloric acid as colourless needles, m. p. 108°, from water (Found : C, 63·2; H, 5·95. $C_{11}H_{12}O_4$ requires C, 63·45; H, 5·75%).

β-4-*Methoxybenzoylpropionitrile* (III; R = 4-MeO·C_6H_4).—β-Dimethylamino-4-methoxypropiophenone hydrochloride (24·35 g.; 0·1 mol.), obtained in 86% yield by the method given for the unsubstituted product (*Org. Synth.*, **23**, 31) (cf. Mannich and Lammering, *Ber.*, 1922, **55**, 3510), potassium cyanide (13·0 g.; 0·2 mol.), and boiling water (520 c.c.) were refluxed for 20 minutes and chilled. The *nitrile* was obtained as glassy needles, m. p. 95°, from ethyl alcohol in 71% yield (Found : C, 69·6; H, 5·7; N, 7·65. $C_{11}H_{11}O_2N$ requires C, 69·85; H, 5·8; N, 7·4%). The acid had m. p. 144°, alone, and mixed with a specimen prepared from anisole and succinic anhydride (Poppenberg, *Ber.*, 1901, **34**, 5257).

β-3 : 4-*Dimethoxybenzoylpropionitrile* [II, R = $(MeO)_2C_6H_3$].—β-Dimethylamino-3 : 4-dimethoxypropiophenone hydrochloride (21 g.) (Mannich and Lammering, *loc. cit.*), potassium cyanide (10 g.), and boiling water (400 c.c.) were refluxed for 20 minutes. The *nitrile* (13·3 g., 85%) was obtained as glassy needles, m. p. 118°, from ethyl alcohol (Found : N, 6·5. $C_{12}H_{13}O_3N$ requires N, 6·4%).

β-1-*Naphthoylpropionitrile* (III; R = 1-$C_{10}H_7$).—1-Naphthyl β-dimethylaminoethyl ketone hydrochloride (5 g.; 1 mol.), potassium cyanide (5·0 g.; 4 mols.), and boiling water (200 c.c.) were refluxed for 30 minutes. The solid obtained on chilling (1·7 g.; 42·5%) formed tiny needle rosettes, m.p. 113 114°, from methyl alcohol (Found : C, 79·8; H, 5·3; N, 6·9. $C_{14}H_{11}ON$ requires C, 80·4; H, 5·25; N, 6·7%).

β-2-*Naphthoylpropionitrile* (III; R = 2-$C_{10}H_7$).—2-Naphthyl β-dimethylaminoethyl ketone hydrochloride (50 g.) (Blicke and Maxwell, *J. Amer. Chem. Soc.*, 1942, **64**, 431), potassium cyanide (50 g.), and boiling water (1 l.) were refluxed for 30 minutes. The *nitrile* (15·1 g., 38%), obtained on chilling, formed clusters of yellow needles, m. p. 114°, from ethyl alcohol (Found: N, 6·65%).

2-*Furyl β-Dimethylaminoethyl Ketone Cyanohydrin* (II; R = 2-C_4H_3O, R′ = Me).—2-Furyl β-dimethylaminoethyl ketone hydrochloride (8·15 g.; 0·04 mol.) (Levvy and Nisbet, *J.*, 1938, 1055) was dissolved in cold water (5 c.c.), and a solution of potassium cyanide (5·2 g.; 0·08 mol.) in water (10 c.c.) added. Colourless crystals of the *cyanohydrin* separated. It formed colourless needles, m. p. 45°, from ligroin (Found : C, 62·2; H, 7·2; N, 14·3. $C_{10}H_{14}O_2N_2$ requires C, 62·0; H, 7·2; N, 14·45%).

β-2-*Furoylpropionitrile* (III; R = 2-C_4H_3O).—2-Furyl β-dimethylaminoethyl ketone hydrochloride (81·5 g.; 0·4 mol.), potassium cyanide (52 g.; 0·8 mol.), and boiling water (2850 c.c.) were refluxed for 30 minutes, and the clear orange liquor was cooled and extracted 4 times with chloroform (100 c.c.). The dried (Na_2SO_4) extract was freed from chloroform to give a brown oil (32 g.; 57%) which crystallised completely. It formed colourless needles, m. p. 74—76°, from ethyl alcohol after treatment with charcoal (Found : C, 64·65; H, 4·65; N, 9·45. $C_8H_7O_2N$ requires C, 64·5; H, 4·7; N, 9·4%).

β-2-*Furoylpropionic Acid* (IV).—The nitrile (2 g.) was refluxed for 1 hour with 18% hydrochloric acid (20 c.c.), charcoal was added, and after a further 10 mins.' refluxing the liquor was diluted with water (50 c.c.), filtered, and the light yellow solution concentrated. The *acid* (2·1 g., 93%) separated as yellow grains. It had m. p. 115° and was pure. On recrystallising from hot water it was obtained as almost colourless, glistening flakes, m. p. 115°, lowered to 106° with previous softening on repeated crystallisation (Found: C, 57·25; H, 4·75. $C_8H_8O_4$ requires C, 57·15; H, 4·75%).

The acid (2 g.) was boiled for 15 minutes with 10% ethyl-alcoholic sulphuric acid (10 c.c.), cooled, and poured into water. The precipitated oil crystallised rapidly. The *ethyl* ester formed glistening, colourless plates, m. p. 52—53°, from aqueous alcohol (Found : C, 61·05; H, 5·95. $C_{10}H_{12}O_4$ requires C, 61·2; H, 6·1%).

3-*Keto*-6-(2′-*furyl*)-2 : 3 : 4 : 5-*tetrahydropyridazine* (V).—β-2-Furoylpropionic acid (1·68 g.; 0·01 mol.), aqueous hydrazine hydrate (1 c.c. of 85%), and ethyl alcohol (5 c.c.) were refluxed for 1 hour, then diluted with water (100 c.c.). The *pyridazone* which separated formed yellow, glassy needles, m. p. 145°, from ethyl alcohol (Found : C, 58·8; H, 4·7; N, 17·0. $C_8H_8O_2N_2$ requires C, 58·55; H, 4·9; N, 17·1%).

β-2-*Thienoylpropionitrile* (III; R = 2-C_4H_3S).—2-Thienyl β-dimethylaminoethyl ketone hydrochloride (2·2 g.; 0·01 mol.) (Blicke and Burckhalter, *J. Amer. Chem. Soc.*, 1942, **64**, 453), potassium cyanide (1·3 g.; 0·02 mol.), and boiling water (52 c.c.) were heated under reflux for 20 minutes. On cooling, the *nitrile* (67% yield) crystallised. It formed colourless needles, m. p. 66°, from benzene–light petroleum (Found : N, 8·4; S, 19·2. C_8H_7ONS requires N, 8·5; S, 19·45%). The acid, obtained on hydrolysis of the nitrile, formed flat needles, m. p. 120°, alone, and mixed with a specimen prepared from thiophen and succinic anhydride (Fieser and Kenelly, *J. Amer. Chem. Soc.*, 1935, **57**, 1615) (Found : S, 17·3. Calc. for $C_8H_8O_3S$: S, 17·4%).

2-*Benzfuryl β-Cyanoethyl Ketone* (VI).—2-Benzfuryl β-dimethylaminoethyl ketone hydrochloride (5·07 g.), potassium cyanide (5·2 g.), and boiling water (130 c.c.) were refluxed for 10 minutes. The hot aqueous layer was decanted from an oil which thickened on chilling. The chilled aqueous layer deposited a mass of crystals which formed colourless needles, m. p. 110—111°, after repeated recrystallisation from methyl alcohol, in 21% yield. The oil was not investigated further (Found : N, 6·9. $C_{12}H_9O_2N$ requires N, 7·05%). The *acid* formed faintly yellow needles, m. p. 148°, from hot water (Found : C, 65·75; H, 4·55. $C_{12}H_{10}O_4$ requires C, 66·05; H, 4·6%).

Chloroimide from β-Benzoylpropionitrile (VIII).—The nitrile (10 g.) and dry benzene (50 c.c.) were cooled in ice, and a rapid stream of dry hydrogen chloride passed into the suspension. The solid dissolved, and crystals soon commenced to separate. After 30 minutes the solid was collected, washed with dry ether, and dried rapidly in a vacuum. The *chloroimide* salt (7·2 g.) formed pale yellow leaflets, m. p. 99° (efferv.) (Found, for the freshly prepared substance : C, 52·0; H, 4·95; N, 6·35; Cl, 29·6. $C_{10}H_{11}ONCl_2$ requires C, 51·75; H, 4·75; N, 6·05; Cl, 30·55%). On standing over aqueous potassium hydroxide for 14 days the original nitrile, m. p. 76°, was recovered.

Ethyl β-Benzoylpropimino-ether Hydrochloride (VII).—(*a*) The nitrile (25 g.) was suspended in ethyl alcohol (50 c.c.), and a rapid stream of dry hydrogen chloride was passed into the suspension cooled in ice. The temperature rose to 40°, the solid dissolved, and a deep yellow colour developed. When saturated, the solution was left to stand for 1 hour, and the *salt* was precipitated by addition of dry ether. It formed colourless needles, m. p. 130°, in 60% yield after recrystallisation from cold ethyl alcohol–ether. The yield was not improved by keeping the reaction temperature below 10° (Found: C; 58·95; H, 6·7; N, 5·95; Cl, 14·55. $C_{12}H_{16}O_2NCl$ requires C, 59·5; H, 6·65; N, 5·8; Cl, 14·7%).

(*b*) The chloroimide hydrochloride (VIII) was dissolved in a minimum of hot ethyl alcohol, chilled immediately, and (VII) precipitated as colourless needles, m. p. 130°, by the addition of ether.

The *base* was obtained as an oil on adding aqueous sodium carbonate to an aqueous solution of the salt. It solidified rapidly and was obtained as colourless, glassy crystals, m. p. 60°, from light petroleum. The crystals turned magenta on keeping (Found: C, 70·4; H, 7·2; N, 7·05. $C_{12}H_{15}O_2N$ requires C, 70·5; H, 7·2; N, 6·85%).

Methyl β-Benzoylpropimino-ether Hydrochloride.—This *salt* was obtained from (VIII), in the same way as the ethyl homologue, by using methyl alcohol as solvent. It formed colourless needles, m. p. 127°, from methyl alcohol–ether (Found: Cl, 15·55. $C_{11}H_{14}O_2NCl$ requires Cl, 15·6%).

Ethyl β-4-Methoxybenzoylpropimino-ether Hydrochloride.—β-4-Methoxybenzoylpropionitrile (5 g.) and ethyl alcohol (10 c.c.) were treated with dry hydrogen chloride whilst cooling in ice. Precipitation of the salt commenced after a short time and was completed by addition of dry ether. It (5·5 g., 77%) was dissolved in absolute alcohol, the solution saturated with hydrogen chloride, and the *salt* reprecipitated by ether. It formed colourless needles, m. p. 133° (effervescence) (Found: Cl, 12·1. $C_{13}H_{18}O_3NCl$ requires Cl, 13·1%). On dissolving the salt in alcohol containing 1% water, *β-4-methoxybenzoylpropionamide* separated. It formed glistening plates or flat needles, m. p. 136°, from ethyl alcohol (Found: C, 63·95; H, 6·2; N, 6·55. $C_{11}H_{13}O_3N$ requires C, 63·75; H, 6·35; N, 6·75%).

β-4-Hydroxybenzoylpropionamide.—The imino-ether hydrochloride prepared analogously from β-4-hydroxybenzoylpropionitrile was dissolved in ethyl alcohol containing 1% of water, and on cooling the *amide* separated. It formed colourless irregular crystals, m. p. 218° (blue at 210°), from ethyl alcohol (bluish solution) (Found: N, 7·8. $C_{10}H_{11}O_3N$ requires N, 7·5%).

Decomposition of (VII).—(*a*) The hydrochloride (VII) (3·9 g.) was refluxed in absolute alcohol (20 c.c.) for 30 minutes. The solution turned orange, and ammonium chloride (0·4 g.) separated. On concentration a further crop (0·2 g.) separated. This represented 70% of the total nitrogen. The residue gave an oil on dilution with water, which solidified almost completely. It formed long, orange needles, m. p. 150° (0·6 g.), from ethyl alcohol (Found: C, 76·0; H, 6·1; N, 4·9%).

(*b*) The same hydrochloride (10 g.) was dissolved in concentrated hydrochloric acid (10 c.c.) and water (20 c.c.), and warmed on the steam-bath. The oil which slowly separated was taken up in ether, dried, and distilled. It (7·5 g.) had b. p. 165°, and was ethyl β-benzoylpropionate (Found: C, 69·6; H, 7·0. Calc. for $C_{12}H_{14}O_3$: C, 70·0; H, 6·8%).

N-*β-Benzoylpropionylacetamide* (IX).—Ethyl β-benzoylpropimino-ether (1 g.) and acetic anhydride (10 c.c.) were heated for 2 hours on the steam-bath. On decomposition with water, an oil was obtained which partly crystallised. It formed colourless, silky needles, m. p. 139—140°, from ethyl alcohol (Found: C, 65·9; H, 6·0; N, 6·3. $C_{12}H_{13}O_3N$ requires C, 65·75; H, 5·95; N, 6·4%).

Bis-3-(2-ethoxy-5-phenylpyrrole)methin Hydrochloride (X; $n = 0$).—Ethyl β-benzoylpropimino-ether hydrochloride (4·83 g.; 0·02 mol.), ethyl orthoformate (5·92 g.; 0·04 mol.), and 99% ethyl alcohol (10 c.c.) were refluxed for 15 minutes, by which time the whole had solidified to a mass of red needles. From ethyl alcohol this formed bright red needles, m. p. 175—176°, turning bronze on contact with air (Found: C, 71·2; H, 5·9; N, 6·95; Cl, 8·65. $C_{25}H_{25}O_2N_2Cl$ requires C, 71·5; H, 5·95; N, 6·65; Cl, 8·45%). Its absorption maximum in methyl alcohol lies at 4700 A. After standing in contact with moist air for 48 hours it shows no absorption peak. Its sodium hydroxide–methyl alcohol solution also give a maximum absorption at 4700 A. and an absorption curve almost identical with that of the freshly prepared dye in neutral or acid solution. The mother-liquor, freed from *dye*, deposited yellow needles, m. p. 150°, identical with the product obtained by heating the starting material in ethyl alcohol.

Bis-3-(2-methoxy-5-phenylpyrrole)methin Hydrochloride.—Prepared in the same way as the ethoxy-analogue, but with methyl alcohol as solvent, the *dye* formed red needles, m. p. 176° (for the freshly prepared substance; 163—164°, after standing in air for 1 hour), on recrystallisation from methyl alcohol (Found: Cl, 9·0. $C_{23}H_{21}O_2N_2Cl$ requires Cl, 9·05%).

Bis-3-(2-ethoxy-5-4′-methoxyphenylpyrrole)methin Hydrochloride.—Ethyl β-4-methoxybenzoylpropimino-ether hydrochloride (2·7 g.), ethyl orthoformate (3·0 g.), and ethyl alcohol (25 c.c.) were refluxed for 30 minutes. The red solution had, by this time, become brown, owing to complete crystallisation of the *dye*. It is very insoluble and was purified by boiling with *n*-butyl alcohol for 15 minutes and collecting whilst hot. It formed green crystals, m. p. 266° (Found: N, 6·05; Cl, 7·65. $C_{27}H_{29}O_4N_2Cl$ requires N, 5·8; Cl, 7·35%).

Bis-3-(2-ethoxy-5-phenylpyrrole)trimethin Hydrochloride (X; $n = 1$).—Ethyl β-benzoylpropimino-ether hydrochloride (2·4 g.; 2 mols.), β-ethoxyacraldehyde acetal (0·8 g.; 1 mol.), and ethyl alcohol (10 c.c.) were refluxed for 10 minutes. The blue solution had then deposited crystals of the *dye*. They (0·4 g.) were collected after cooling and obtained as green crystals, m. p. 162°, from ethyl alcohol (Found: C, 72·65; H, 6·05; N, 6·0; Cl, 7·55. $C_{27}H_{27}O_2N_2Cl$ requires C, 72·55; H, 6·05; N, 6·25; Cl, 7·95%). In moist methyl alcohol the dye shows a maximum absorption at 4750—4800 A.; in methyl alcohol containing a little concentrated hydrochloric acid the maximum lies at 6050 A.; in methyl alcohol containing a little aqueous sodium hydroxide the maximum is also at 6050 A. but fades rapidly.

RESEARCH LABORATORY, KODAK LIMITED,
WEALDSTONE, MIDDLESEX.

[*Received, November* 28*th*, 1946.]