427. *Heterocyclic Derivatives of Guanidine. Part I.* 2H-*Pyrroles and* 1H-*Isoindoles.*

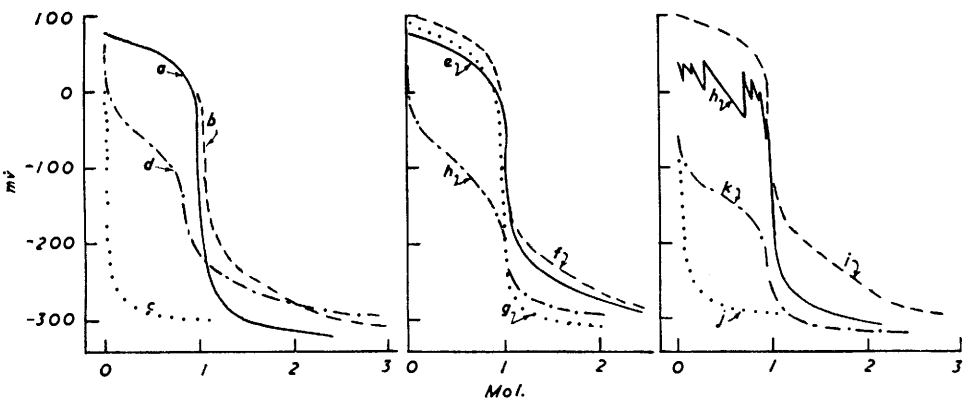
By J. E. Banfield.

Guanidine and its mono- and di-alkyl derivatives with *trans*-αβ-dicyanostilbene give 5-guanidino-2-imino-3,4-diphenyl-2*H*-pyrroles (IV), which with ethyl cyanoacetate gave 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-Δ³-pyrroline (XVII; R = Et). 5-Guanidino- and 5-*N*-methylguanidino-2-imino-3,4-diphenyl-2*H*-pyrroles with nitrous acid gave the imino-oxopyrroline (V; X = NH), whereas the *NN'*-dimethyl and the piperidino-analogue gave the guanidino-oxo-2*H*-pyrroles (IX). All three keto-compounds reacted with ethyl cyanoacetate, to give 5-(α-cyano-α-ethoxycarbonylmethylene)-2-oxo-3,4-diphenyl-Δ³-pyrroline (VI).

Guanidine and phthalonitrile afforded 3-guanidino-1-imino-1*H*-isoindole (III) which with ethyl cyanoacetate gave the known [1] 1,3-di-(α-cyano-α-ethoxycarbonylmethylene)isoindoline (XV).

A substance previously obtained by the author from guanidine and α-cyanobenzyl bromide was shown to give diphenylmaleinimide on hydrolysis,[2] leading to the suggestion that *trans*-αβ-dicyanostilbene was an intermediate in its formation. Guanidine has now been shown to yield with *trans*-αβ-dicyanostilbene a yellow crystalline 1 : 1 adduct which gives diphenylmaleinimide on hydrolysis. This adduct was very sparingly soluble in non-acidic solvents and could not be purified by recrystallisation; the molecular weight in phenol (in which it is undoubtedly ionised but would be expected to dissociate only slightly) corresponded to the monomer. In phenol liquefied by 10% of water it titrated as a strong monoacid base with a second much weaker basic function (Fig. 1, cf. curve *b*).

Fig. 1. Fig. 2. Fig 3.



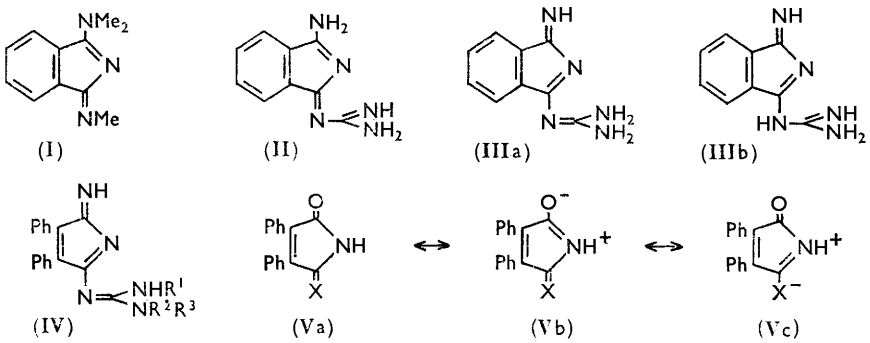
Figs. 1—3. *Potentiometric titrations in phenol–water with* 0·04M-*perchloric acid.* (*a*) *Compound* (IX; R^1 = H, R^2R^3 = <[CH_2]$_5$), (*b*) *compound* (IV; R^1 = R^2 = Me, R^3 = H), (*c*) trans-αβ-*dicyanostilbene*, (*d*) p-*phenylenediamine*, (*e*) *compound* (XIII; R^1 = H, R^2R^3 = <[CH_2]$_5$), (*f*) *compound* (IV; R^1 = H, R^2R^3 = <[CH_2]$_5$), (*g*) 1,3-*di-iminoisoindoline*, 2(*h*) *the triacetyl derivative* (XIII; R^1 = R^2 = Ac, R^3 = H), 3(*h*) *compound* (XIV), (*i*) *compound* (III), (*j*) *guanidine nitrate, and* (*k*) *compound* (V; X = NH).

The acetate of this base had a molecular weight in water corresponding to the monomer (*i* being assumed to be 2), and basification of its aqueous solution regenerated the base as the monohydrate. The anhydrous or hydrated base yielded a triacetyl derivative,

[1] Elvidge, Fitt, and Linstead, *J.*, 1956, 235.
[2] Banfield, *J.*, 1960, 456.

which like the parent base had no C≡N absorption at *ca.* 2200 cm.$^{-1}$ whilst both absorbed strongly at *ca.* 3160 cm.$^{-1}$ (NH). A similar base was obtained from *trans*-αβ-dicyanostilbene and *N*-methylguanidine; this base was reprecipitated in anhydrous form from aqueous solution and yielded a diacetyl derivative. 1-Amidinopiperidine gave a similar basic adduct which yielded a strongly basic monoacetyl derivative.

Although *NN*-dimethylguanidine yielded an adduct with properties similar to the above-mentioned bases, *NN'*-dimethylguanidine gave an isomeric yellow base which was very soluble in ethanol, acetone, dioxan, etc., and was monomeric in chloroform. However,



the similarity of its ultraviolet absorption to those of the above compounds indicated that the structures were analogous and that the lower solubility was due to restriction of hydrogen bonding in the solid state.

Ultraviolet absorption maxima (mμ) ($\log_{10}$ ε *in parentheses*).

Phthalonitrile–guanidine adduct	229 (4·66), 279 (4·30), 332 (4·05)
3-Dimethylamino-1-methylimino-1*H*-isoindole [3] (I)	279 (4·09), 348 (3·59)
Phthalonitrile–guanidine adduct in AcOH	227 (4·23), 318 (3·98), 345 * (3·84)
Hydrochloride of (I) [3]	227 (4·50), 280 (4·11), 318 * (3·70), 354 (3·58)
1,3-Di-iminoisoindoline (in MeOH) †	251 (4·10), 265 (4·10), 303 (3·66)

* Inflexion. † Elvidge and Golden, *J.*, 1957, 700.

Phthalonitrile reacted, albeit slowly, with an excess of guanidine in ethanol to give a similar, insoluble, basic 1 : 1 adduct which gave phthalimide on hydrolysis. This was a monohydrate, but the acetate, benzoate, and triacetyl derivative were anhydrous. This adduct has absorption in ethanol similar to that [3] of 3-dimethylamino-1-methylimino- 1*H*-isoindole (I) in both neutral and acid solution (cf. the Table), and thus must be formulated as (II) or (III). Accordingly the αβ-dicyanostilbene adducts can be formulated as derivatives (IV) of 5-guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (IV; $R^1 = R^2 = R^3 = H$); use of such names in this paper is not intended to prejudice questions of tautomerism.

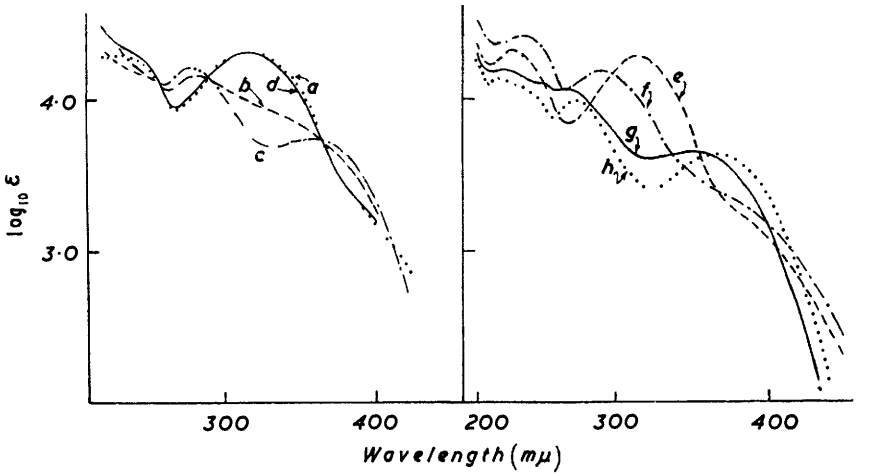
Each of the dicyanostilbene adducts yielded diphenylmaleinimide on hydrolysis. With nitrous acid the parent compound (IV; $R^1 = R^2 = R^3 = H$) gave 2-imino-5-oxo-3,4-diphenyl-Δ^3-pyrroline (V; X = NH), also obtained in lower yield from the *N*-methyl compound (IV; R^1 = Me, $R^2 = R^3 = H$) with nitrous acid, The structure of the product (V; X = NH) follows from its hydrolysis to diphenylmaleinimide and its reaction with ethyl cyanoacetate to give the α-cyano-α-ethoxycarbonylmethylene analogue (VI). The imino-compound (V; X = NH) is a weak base (Figs. 3*k*, 8*b*), the protonated form (V; X = NH_2^+) being little stabilised by resonance. The spectrum of the mesomeric anion (VII) (Fig. 8*c*) is very similar to that of the structurally related guanidinoimino-2*H*-pyrrole (IV) (Fig. 5*e*) (designated below as type E) and easily distinguishable from the spectra

[3] Clarke, Elvidge, and Golden, *J.*, 1956, 4135.

of the pyrrolines (type I), *e.g.* (V; X = NH) (Fig. 8*a*) and *N*-methyl-αα′-diphenylmaleinimide (Fig. 5*h*).

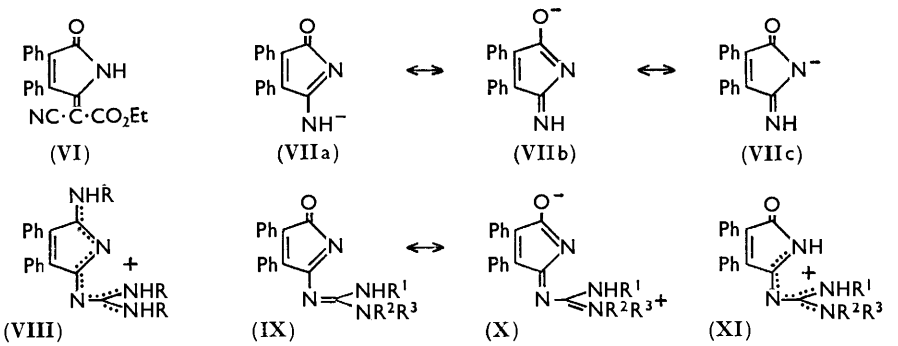
The strongly basic guanidinoimino-2*H*-pyrrole (IV; $R^1 = R^2 = R^3 = H$) must exist in ethanol substantially as the cation which is presumably (VIII; R = H) formed by

FIG. 4. FIG. 5.



FIGS. 4 *and* 5. *Ultraviolet absorption spectra.* (*a*) *Compound* (IX; $R^1 = H$, $R^2R^3 = <[CH_2]_5$), (*b*) *its nitrite,* (*c*) *its nitrite in acid,* (*d*) *its nitrite in alkali,* (*e*) *compound* (IV; $R^1 = R^2 = R^3 = H$), (*f*) *compound* (XIII; $R^1 = R^2 = Ac$, $R^3 = H$), (*g*) *5-guanidino-2-imino-3,4-diphenyl-2H-pyrrole in perchloric acid extrapolated to zero time, and* (*h*) *N-methyl-αα′-diphenylmaleinimide.*

terminal protonation. However, the type E spectrum of the monocation gives way to a type I spectrum in perchloric acid (Fig. 5*g*, which is the spectrum extrapolated to the time of addition of the acid, the product presumably hydrolysing at an appreciable rate) and thus formation of a dication (XII; $R^1 = R^2 = R^3 = R^4 = H$) is implied; protonation at a terminal nitrogen is in any case considered unlikely as, change from sp^2- to sp^3-hybridis-



ation being then required, overlap with the shorter π-system would be restricted to NH_3 hyperconjugation (guanidinium ion is not further protonated in less than 99% sulphuric acid [4]). As the second basic function of these compounds is rather weaker than the second of *p*-phenylenediamine (Fig. 1*d*) (cf. p-$Me_3N^+{\cdot}C_6H_4{\cdot}NH_3^+$,[5] pK_a 2·51), diprotonation in ethanolic acetic acid (~1000 mol. in excess) would be substantial but incomplete (Fig. 7*f*).

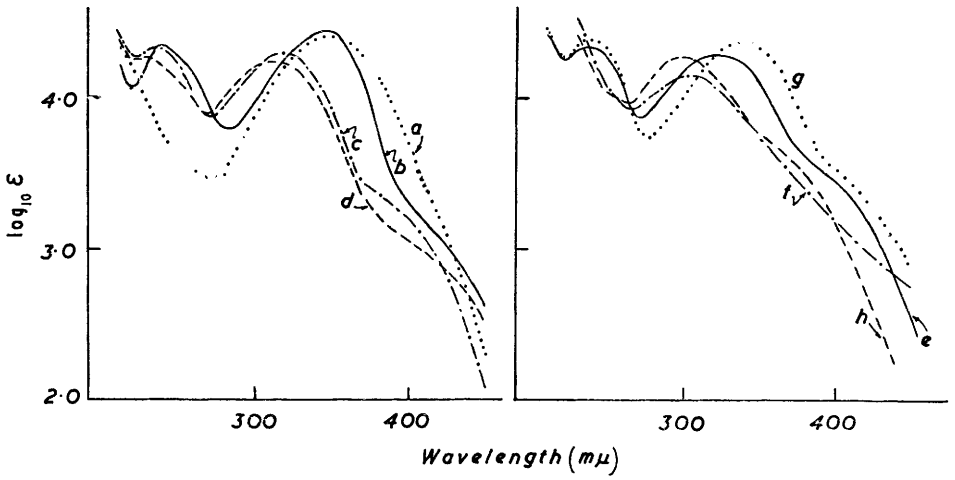
Reaction of the *NN′*-dimethyl compound (IV; $R^1 = R^2 = Me$, $R^3 = H$) with nitrous

[4] Williams and Hardy, *J.*, 1953, 2560.
[5] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 746.

acid gave the nitrite of 5-*NN'*-dimethylguanidino-2-oxo-3,4-diphenyl-2*H*-pyrrole (stable to hot ethanol), and basification of the reaction mixture gave the free base (IX; $R^1 = R^2 = Me$, $R^3 = H$) as the monohydrate. Carbonyl absorption of the salt at 1749 cm.$^{-1}$ and of the base at 1691 cm.$^{-1}$, and the reaction of the salt with ethyl cyanoacetate to give the ester (VI), confirm the structure of this compound.

Reaction of the piperidino-compound (IV; $R^1 = H$, $R^2R^3 = <[CH_2]_5$) with nitrous acid gave a nitrite which was readily hydrolysed to a base by hot ethanol or by addition of ether to the chloroform solution. The salt as first prepared was contaminated by starting material, as shown by reaction with ethyl cyanoacetate; it was best purified by a second treatment with nitrous acid and then reacted with ethyl cyanoacetate to give the ester (VI) uncontaminated by the bis-compound (XVII; R = Et). Formulation of

FIG. 6. FIG. 7.



FIGS. 6—7. *Ultraviolet absorption spectra.* (*a*) *Compound* (VI), (*b*) *compound* (XIV), (*c*) *compound* (IV; $R^1 = Me$, $R^2 = R^3 = H$), (*d*) *its acetate*, (*e*) *compound* (IV; $R^1 = H$, $R^2R^3 = <[CH_2]_5$), (*f*) *the same in acid*, (*g*) *compound* (XIII; $R^1 = H$, $R^2R^3 = <[CH_2]_5$), *and* (*h*) *the same in acid.*

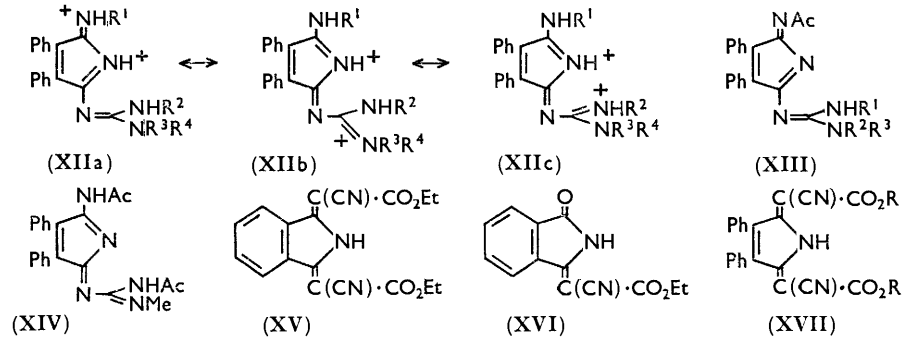
the base as (IX; $R^1 = H$, $R^2R^3 = <[CH_2]_5$) was confirmed by hydrolysis of its nitrite to diphenylmaleinimide (98%) and 1-amidinopiperidine (65%) under conditions shown to hydrolyse the related imine (IV) to the same products. Both compounds of type (IX) titrated in phenol–water as strong monoacid bases (Fig. 1*a*); differences in the ease of hydrolysis of their salts are now ascribed to the very low solubility of compound (IX; $R^1 = H$, $R^2R^3 = <[CH_2]_5$). The bases (IX) have spectra of type E (Figs. 4*a*, 9*f*), little different from those of the parent guanidinoimino-2*H*-pyrroles, suggesting that polar forms of type (X) make substantial contributions; these forms can be considered as the guanidinium enolate derived from the enolic tautomer of bases (IX), the negligible change in spectra of the bases (IX) on basification (Fig. 4*a*, *d*) being explicable in terms of the negligible acidity of the guanidinium enolate. However, the spectra of the monoacid salts are complicated by hydrolysis (Figs. 4*b*, 9*g*): the spectra (Fig. 4*c*, 9*h*) of the monocations in an excess of acetic acid (cf. Fig. 1*a*) are of type I, indicating structures of type (XI).

In the formation of 5-guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole from guanidine and the dinitrile, the five hydrogen atoms from guanidine-nitrogen atoms must be redistributed between the five nitrogen atoms of the product. If the formation of the triacetyl derivative is evidence that these five hydrogen atoms are located on only three of the nitrogen atoms, then its functional groups must be NHAc, NHAc, and C:NAc. Sharp absorption of the acetyl derivative at 3172 cm.$^{-1}$ as the only peak in the NH stretching region confirms that

an alternative distribution C:NAc, C:NAc, NHAc, and NH is not involved; the distribution NH, NH, etc., is considered not to be in accord with the ultraviolet absorption (type E) (Fig. 5*f*). Thus two C=O stretching frequencies are to be expected for this compound and, by analogy with the relative frequencies of C=O stretching modes in secondary and tertiary amides (1688—1711 cm.$^{-1}$ for Ar·NHAc, 1653—1682 cm.$^{-1}$ for Ar·NMeAc),[6] the band at 1706 cm.$^{-1}$ is assigned to the NHAc group, that at 1661 cm.$^{-1}$ to C:NAc, and the structure (XIII; $R^1 = R^2 = Ac$, $R^3 = H$) is proposed. Protonation of this acetyl compound to give the symmetrical cation (VIII; R = Ac) is hindered by the electronic withdrawal of the acetyl substituents (Fig. 2*h*).

The monoacetyl derivative of the piperidino-compound (IV; $R^1 = H$, $R^2R^3 = <[CH_2]_5$) lacks absorption in the 1700 cm.$^{-1}$ region and thus a strong shoulder at 1668 cm.$^{-1}$ must be due to a C:NAc function, and strong peaks at 1655 and 1648 cm.$^{-1}$ to $\delta(NH_2)$ modes. Structure (XIII; $R^1 = H$, $R^2R^3 = <[CH_2]_5$) is supported for this compound as with nitrous acid it yielded the oxo-compound (IX; $R^1 = H$, $R^2R^3 = <[CH_2]_5$), also formed as a by-product in its synthesis. In view of the strong basic function of this monoacetyl derivative (Fig. 2*e*) the type E spectrum (Fig. 7*g*) of the ethanolic solution must be due to the monocation of type (VIII), the displacement by acid (Fig. 7*h*) being due to partial formation of the dication (XII; $R^1 = Ac$, $R^2 = H$, $R^3R^4 = <[CH_2]_5$), a slightly stronger acid than (XII; $R^1 = R^2 = H$, $R^3R^4 = <[CH_2]_5$) (Figs. 2*c*, *f*).

The diacetyl derivative of compound (IV; $R^1 = Me$, $R^2 = R^3 = H$) has a single



very sharp peak in the NH stretching region, and thus similar location of the hetero-hydrogen atoms is suggested. In view of the strong band at 1706 cm.$^{-1}$, two NHAc groups are implied for this compound and structure (XIV) is supported for the solid state. Potentiometric titration of this compound (XIV) gave readings which changed with time; Fig. 3*h* gives both instantaneous and equilibrium readings obtained after each addition of acid, the latter corresponding to a moderately strong monoacid base, the former to (possibly) a weaker pseudo-base. The weakly basic acylguanidino-residue of (XIV) is apparently less able than the amide function to compete for the proton in the solid state than is the corresponding guanidino-residue of (XIII; $R^1 = H$, $R^2R^3 = <[CH_2]_5$).

Reaction of the guanidinoimino-2*H*-isoindole (III) with ethyl cyanoacetate gave a high yield of 1,3-di-(-α-cyano-α-ethoxycarbonylmethylene)isoindoline (XV), the structure of which follows * from its oxidation under controlled conditions to 1-α-cyano-α-ethoxycarbonylmethylene-3-oxoisoindoline [7] (XVI), synthesis from the condensation of ethyl cyanoacetate with phthalonitrile in the presence of sodium ethoxide, and identity with the product obtained by Elvidge, Fitt, and Linstead [1] by condensation of di-iminoisoindoline with ethyl cyanoacetate. The dimethyl ester analogous to (XV) was obtained from (III) and from phthalonitrile and methoxide.

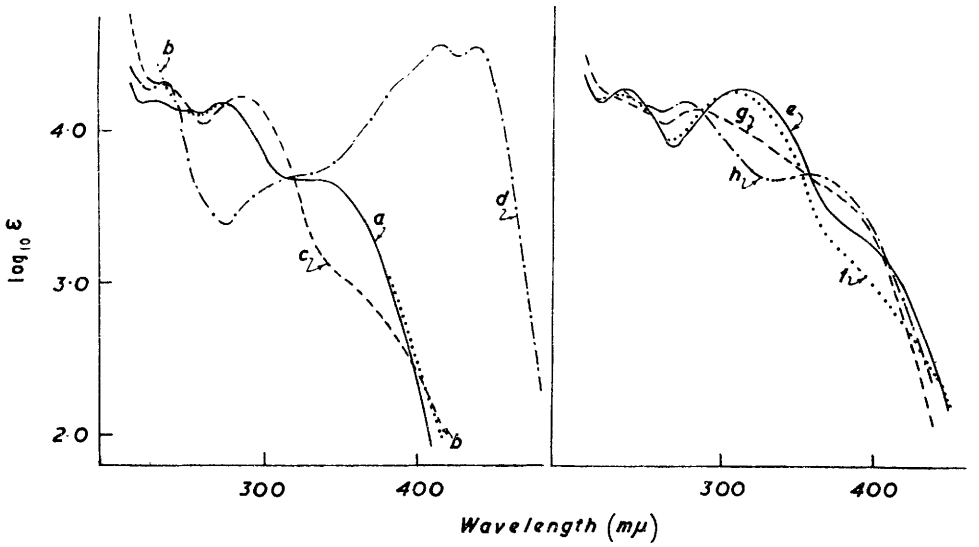
* This argument is given in greater detail elsewhere (Banfield, Thesis, Melbourne, 1951).

[6] Katritzky and Jones, *J.*, 1959, 2067.

[7] Barrett, Linstead, Leavitt, and Rowe, *J.*, 1940, 1079.

Each of the guanidinoimino-2*H*-pyrroles (IV; $R^1 = R^2 = R^3 = H$, and its hydrate; $R^1 = Me$, $R^2 = R^3 = H$; $R^1 = H$, $R^2 = R^3 = Me$; $R^1 = R^2 = Me$, $R^3 = H$; and $R^1 = H$, $R^2R^3 = <[CH_2]_5$) gave with ethyl cyanoacetate 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-Δ^3-pyrroline (XVII; R = Et) with loss of its imino- and guanidino-residues. The compound (IV; $R^1 = R^2 = R^3 = H$) with ethyl cyanoacetate in acetic acid gave the same pyrroline (XVII). This pyrroline diester was recovered after being refluxed in acetic anhydride, and was hydrolysed by aqueous-ethanolic alkali to the dicarboxylic acid (XVII; R = H), which was oxidised to benzoic acid by alkaline permanganate. The methyl ester was obtained similarly.

FIG. 8. FIG. 9.



FIGS. 8—9. *Ultraviolet absorption spectra.* (*a*) *Compound* (V; X = NH), (*b*) *the same in acid,* (*c*) *the same in alkali,* (*d*) *compound* (XVII; R = Et), (*e*) *compound* (IV; $R^1 = R^2 = Me$, $R^3 = H$), (*f*) *compound* (IX; $R^1 = R^2 = Me$, $R^3 = H$), (*g*) *its nitrite, and* (*h*) *its nitrite in acid.*

Although Thorpe-type condensations of nitriles with compounds containing active methylene groups are well known [1,8,9] no such reactions are recorded for *trans*-αβ-dicyanostilbene. The outcome of the reaction of *trans*-αβ-dicyanostilbene with ethyl cyanoacetate in the presence of ethoxide proved critically dependent on both the conditions of the reaction and the method of working up, either the bis-cyanoacetate derivative (XVII; R = Et) or the mono-derivative (VI) being obtained. The final step in this synthesis of the ester (XVII· R = Et) is presumably the condensation of 2-α-cyano-α-ethoxycarbonylmethylene-5-imino-3,4-diphenyl-Δ^3-pyrroline with ethyl cyanoacetate, a reaction of a type which in the isoindoline and 3,4-diphenylpyrroline series frequently occurs at positions occupied by N but apparently not at positions occupied by O; the greater reactivity of C:NH than of C:O in such reactions has been noted,[10] a further example being the ready reaction of diphenylketimine with malononitrile and with ethyl cyanoacetate under conditions where benzophenone is inert.[11] However, care must be exercised in the use of this generalisation in view of the condensation of isatin with cyanoacetic acid to give 2,3-di(carboxycyanomethylene)indoline.[12]

[8] Elvidge and Golden, *J.*, 1956, 4135.
[9] Atkinson, Ingram, and Thorpe, *J.*, 1907, **91**, 578.
[10] Elvidge and Linstead, *J.*, 1952, 5000.
[11] Ramsay, M.Sc. Thesis, Melbourne, 1949.
[12] Yokayama, *J. Chem. Soc. Japan*, 1936, **57**, 251.

Experimental

Infrared spectra were kindly determined by Dr. D. L. Ford, Timbrol Company, Sydney, whom we thank, for Nujol mulls; a Perkin–Elmer Model 21 double-beam spectrophotometer fitted with a rock-salt prism was used. Ultraviolet absorption spectra were determined for 95% EtOH solutions on an Unicam S.P. 500 spectrophotometer by Mrs. J. E. Banfield, B.Sc.

*5-Guanidino-2-imino-3,4-diphenyl-*2H*-pyrrole* (IV; $R^1 = R^2 = R^3 = H$).—*trans*-αβ-Dicyanostilbene (0·5 g.) in dry ethanol was treated with ethanolic guanidine (from the nitrate; 0·3 g.) at 37° for 6 days to yield the 2H-*pyrrole* in yellow needles, m. p. 210° (decomp.) [Found: C, 70·6; H, 5·4; N, 23·6%; *M* (cryoscopic, in phenol), 256 (0·36% solution), 239 (0·67% solution). $C_{17}H_{15}N_5$ requires C, 70·6; H, 5·2; N, 24·2%; *M*, 289]. Sodium hydroxide precipitated the *monohydrate* of the pyrrole from the acetic acid solution as a pale yellow microcrystalline powder, m. p. 210° (decomp.) [Found: C, 65·4; H, 5·6; N, 21·9%; *M* (cryoscopic, in phenol), 168 (0·32% solution), 170 (0·76% solution), 165 (1·25% solution), 165 (2·3% solution). $C_{17}H_{15}N_5,H_2O$ requires C, 66·4; H, 5·58; N, 22·8%; *M*, 308]. The *acetate* (from ethanol–light petroleum) had m. p. 170° (decomp.) [Found: C, 65·4; H, 5·8; N, 19·2%; *M* (cryscopic, in phenol), 194 (0·27%), 177, 216 (0·28%), 207 (0·78%), 194, 198 (1·24%); *M* (cryoscopic, in water), 136 (0·36%), 124 (0·44%). $C_{17}H_{15}N_5,C_2H_4O_2$ requires C, 65·3; H, 5·5; N, 20·0%; *M* (van't Hoff *i* factor = 2), 175], $\lambda_{max.}$ 230, 313, $\lambda_{infl.}$ 374 mμ (log ε 4·28, 4·26, 3·27). A solution of the acetate, when basified, gave the 2*H*-pyrrole monohydrate (Found: C, 67·2; H, 5·9; N, 22·2; ash, 0·3%). The *oxalate* was obtained in yellow needles, m. p. >260° (darkens at *ca.* 185°) (Found: C, 64·0; H, 5·0; N, 20·2. $C_{17}H_{15}N_5,\frac{1}{2}C_2H_2O_4$ requires C, 64·6; H, 4·8; N, 20·9%).

The 2*H*-pyrrole (0·5 g.) in acetic anhydride (4 ml.) was heated to the b. p. and then cooled rapidly, giving the *triacetyl derivative* (0·3 g.), which separated from benzene–light petroleum in yellow needles, m. p. 185—186° (decomp.) [Found: C, 67·1; H, 5·2; N, 16·3%; *M* (isothermal distillation in chloroform), 318. $C_{23}H_{21}O_3N_5$ requires C, 66·5; H, 5·1; N, 16·8%; *M*, 415]. This derivative, m. p. 185° (decomp.), was also obtained from the precipitated 2*H*-pyrrole hydrate (Found: C, 66·9; H, 5·2; O, 12·3; N, 16·5. $C_{23}H_{21}O_3N_5$ requires O, 11·6%; cf. above). The 2*H*-pyrrole, refluxed for 1 min. in 75% sulphuric acid, gave diphenylmaleinimide, m. p. 218—218·5° (from aqueous ethanol), $\lambda_{max.}$ 224, 305, 355, $\lambda_{infl.}$ 247, 263, 320 mμ (log ε 4·236, 3·544, 3·737, 4·12, 3·98, 3·57), hydrolysed by aqueous sodium hydroxide to diphenylmaleic anhydride, m. p. 147·5—148°, $\lambda_{max.}$ 256, 275, 349, $\lambda_{infl.}$ 214 mμ (log ε 3·923, 3·888, 3·519, 4·26).

*2-Imino-5-N-methylguanidino-3,4-diphenyl-*2H*-pyrrole* (IV; $R^1 = Me$, $R^2 = R^3 = H$).—Methylguanidinium sulphate (4 g.) was shaken with sodium ethoxide (from sodium, 0·9 g.) and a " Teflon " ball, and the solution was filtered and then shaken with *trans*-αβ-dicyanostilbene (5 g.), to yield the *pyrrole* in yellow needles (5·2 g.), m. p. 210° (decomp.). A sample prepared in dilute solution had m. p. 213° (decomp.) [Found: C, 71·3; H, 5·8; N, 23·0%; *M* (cryoscopic, in phenol), 261 (0·5%), 256 (0·98%); 253 (1·46%). $C_{18}H_{17}N_5$ requires C, 71·3; H, 5·7; N, 23·1%; *M*, 303]. Hydrolysis as above gave diphenylmaleinimide, m. p. and mixed m. p. 215—216·5°, and methylamine (identified as *N*-methyl-2,4-dinitroaniline).

The 2*H*-pyrrole was reprecipitated from its ethanolic acetic acid solution as a pale yellow powder, m. p. 195° (decomp.) (Found: C, 71·0; H, 5·9; N, 22·4%). The yellow *acetate*, m. p. 180° (decomp.), was prepared in ethanol–light petroleum [Found: C, 65·7; H, 5·9; N, 19·0; *M* (cryoscopic, in water), 200, 158, 170 (0·85%), 167, 152 (0·44%). $C_{20}H_{21}O_2N_5$ requires C, 66·1; H, 5·8; N, 19·3%; *M* (van't Hoff factor *i* = 2), 182]. The *benzoate* crystallised from ethanol–light petroleum in yellow rhombs, m. p. *ca.* 160° (decomp.) (Found: C, 70·0; H, 5·7; N, 16·5. $C_{25}H_{23}O_2N_5$ requires C, 70·6; H, 5·4; N, 16·5%).

The 2*H*-pyrrole (1 g.) was heated in acetic anhydride (8 ml.) at the b. p. for 25 sec., then cooled immediately in ice to give *5-acetamido-2-(N-acetyl-N′-methylamidinoimino)-3,4-diphenyl-*2H*-pyrrole* (XIV) in yellow needles (from benzene–light petroleum), m. p. 211° (decomp.) [Found: C, 68·5; H, 5·14; N, 17·8%; *M* (isothermal distillation in chloroform), 340, 359, 351. $C_{22}H_{21}O_2N_5$ requires C, 68·2; H, 5·5; N, 18·1%; *M*, 387]; the reaction conditions were critical.

2-Imino-3,4-diphenyl-5-oxo-Δ^3*-pyrroline* (V; X = NH).—(*a*) 5-Guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (10 g.) in ethanolic acetic acid was treated with sodium nitrite (20 g.) in water at 5°, giving the *pyrroline* (5·7 g.) in pale yellow spears (from ethanol), m. p. 244—249° (decomp.) [Found: C, 77·6; H, 4·9; O, 7·2; N, 11·0%; *M* (Rast), 255 (2·5%), 288 (5·9%). $C_{16}H_{12}ON_2$ requires C, 77·4; H, 4·9; O, 6·4; N, 11·3%; *M*, 248].

(*b*) 2-Imino-5-*N*-methylguanidino-3,4-diphenyl-2*H*-pyrrole (0·5 g.) gave, by the above method, a low yield (0·05 g.) of the pyrroline, m. p. 241—249·5° (decomp.) (Found: C, 77·8; H, 5·0%).

The pyrroline in refluxing acetic anhydride rapidly yielded diphenylmaleinimide, yellow rods, m. p. 222—223° (from benzene) undepressed on admixture with an authentic sample of m. p. 217—217·5° (pale yellow needles) (Found: C, 77·4; H, 4·5; N, 5·8. Calc. for $C_{16}H_{11}O_2N$: C, 77·1; H, 4·45; N, 5·6%); this reaction was analogous to the acetylation of 1-imino-3-oxoisoindoline which gave a small yield of the acetyl derivative accompanied by much phthalimide.[13]

5-NN′-*Dimethylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole* (IV; $R^1 = R^2 = Me$, $R^3 = H$).—*NN*′-Dimethylguanidinium sulphate (4 g.) was treated with *trans*-αβ-dicyanostilbene (5 g.) as above. The dicyanostilbene dissolved slowly to give (after 10 days) a small quantity of the *pyrrole* in yellow rhombs, m. p. 220° (decomp.) (Found: C, 71·9; H, 6·0; N, 21·8. $C_{19}H_{19}N_5$ requires C, 71·9; H, 6·0; N, 22·1%). Evaporation of the filtrate yielded more pyrrole (total 4·0 g.), m. p. 220° (decomp.) (from ethanol) [Found: *M* (isothermal distillation in chloroform at 37°), 321, 359. $C_{19}H_{19}N_5$ requires *M*, 317].

5-NN′-*Dimethylguanidino*-2-*oxo*-3,4-*diphenyl*-2H-*pyrrole* (IX; $R^1 = R^2 = Me$, $R^3 = H$).—5-*NN*′-Dimethylguanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (0·5 g.) in ethanol–acetic acid was diluted with water and treated with sodium nitrite (1 g.) at 0—5° for 5 days: it gave the *nitrite*, m. p. 204—209° (decomp.) (0·45 g.), of the oxo-2*H*-pyrrole in golden-yellow needles (from ethanol–light petroleum) (Found: C, 61·7; H, 5·2; N, 18·9. $C_{19}H_{19}O_3N_5$ requires C, 62·4; H, 5·2; N, 19·2%).

In a longer experiment a reduced yield of the nitrite was obtained (0·25 g. from 0·6 g.); basification of the supernatant layer gave the *base monohydrate* (0·45 g.) in yellow needles (from methanol), m. p. 249—250° (decomp.) (Found: C, 67·9; H, 5·8; O, 9·8; N, 16·9. $C_{19}H_{20}O_2N_4$ requires C, 67·8; H, 6·0; O, 9·5; N, 16·7%).

The nitrite (0·15 g.) was refluxed in ethyl cyanoacetate (0·5 ml.) for 3 min., cooled, and diluted with ethanol, to yield 2-α-cyano-α-ethoxycarbonylmethylene-5-oxo-3,4-diphenyl-Δ^3-pyrroline (VI) (0·07 g.) m. p. and mixed m. p. 169·5—170°.

5-NN-*Dimethylguanidino*-2-*imino*-3,4-*diphenyl*-2H-*pyrrole* (IV; $R^2 = R^3 = Me$, $R^1 = H$).—*NN*-Dimethylguanidinium sulphate (4·5 g.) and *trans*-αβ-dicyanostilbene (6 g.) gave by the above method the pyrrole, m. p. 244° (decomp.) (Found: C, 72·08; H, 6·12; N, 21·94%) (7·6 g.), $\lambda_{max.}$ 228 311, $\lambda_{infl.}$ 373 mμ (log ε 4·21, 4·18, 3·42) displaced by acetic acid to $\lambda_{max.}$ 307, $\lambda_{infl.}$ 391 mμ (log ε 4·17, 3·11). Basification of the acetic acid solution regenerated the pyrrole, m. p. 235° (decomp.) (from 2-methoxyethanol) (Found: C, 71·0; H, 6·0%). Hydrolysis gave diphenylmaleinimide, m. p. and mixed m. p. 213—215°.

The Piperidine Analogue (IV; $R^1 = H$, $R^2R^3 = <[CH_2]_5$).—1-Amidinopiperidine sulphate had m. p. 302—303° (Found: N, 24·1. Calc. for $C_6H_{13}N_3,\frac{1}{2}H_2SO_4$: N, 23·9%). This (9 g.) and *trans*-αβ-dicyanostilbene gave as above the *pyrrole* (12·1 g.) in yellow needles, m. p. 226° (decomp.) [Found: C, 73·7; H, 6·5; N, 19·3%; *M* (cryoscopic, in phenol), 274 (0·36%), 267 (0·31%), 297 (0·66%), 327 (1·24%), 317, 313 (2·06%). $C_{22}H_{23}N_5$ requires C, 73·9; H, 6·5; N, 19·6%; *M*, 357].

trans-αβ-Dicyanostilbene (1 g.) and ethanolic 1-amidinopiperidine [from the sulphate (1 g.)] were refluxed for a short time, to yield the pyrrole (1·15 g.), m. p. 228° (decomp.), in brownish-yellow needles.

The pyrrole, recovered from its ethanolic acetic acid solution on basification, had m. p. 214° (decomp.) (Found: C, 73·1; H, 6·6; N, 19·1; ash, 0·2%).

A solution of the pyrrole (0·5 g.) in 70% sulphuric acid (10 ml.) was refluxed for 5 min. and when cold diluted with water, to yield a solid (0·35 g.), m. p. 217—217·5°, which afforded (from aqueous ethanol) diphenylmaleinimide (0·3 g.). The filtrate was basified with sodium carbonate and treated with sodium picrate solution, to give 1-amidinopiperidine picrate (0·53 g.), m. p. and mixed m. p. 250—252° (from ethanol) (Found: C, 40·9; H, 4·7. Calc. for $C_{12}H_{16}O_7N_6$: C, 40·5; H, 4·5%).

1-[*N*′-(2-*Acetimido*-3,4-*diphenyl*-2H-5-*pyrrolyl*)*amidino*]*piperidine* (XIII, $R^1 = H$, $R^2R^3 = <[CH_2]_5$).—The preceding base (IV) (2 g.) was refluxed in acetic acid–acetic anhydride for 30 sec., the mixture was immediately cooled in ice and added to ice-water without delay, and the yellow solution was basified by rapid addition of sodium carbonate solution. The precipitate

[13] Possner, *Ber.*, 1897, **30**, 1699.

was collected and dried (2·3 g.) and then extracted with cold chloroform. The solution was filtered from a very small residue of the oxo-compound (IX), and diluted with light petroleum, to yield the *monoacetyl compound*, m. p. 227° (from benzene) [Found: C, 72·2; H, 6·2; O, 4·5; N, 17·3; Ac, 10·7%; *M* (isothermal distillation, in chloroform), 479. $C_{24}H_{25}ON_5$ requires C, 72·2; H, 6·3; O, 4·0; N, 17·5; Ac, 10·8%; *M*, 399].

Compound (IX; $R^1 = H$, $R^2R^3 = <[CH_2]_5$).—(*a*) The compound (IV; $R^1 = H$, $R^2R^3 = <[CH_2]_5$) (4 g.) in ethanolic acetic acid was treated with aqueous sodium nitrite (4 g.) at 0—5° for 10 days and then at room temperature for one week, to give the *nitrite* (4 g.), m. p. 200° (decomp.), of the oxo-2*H*-pyrrole (Found: C, 65·4; H, 5·6; N, 17·5. $C_{22}H_{23}O_3N_5$ requires C, 65·2; H, 5·7; N, 17·3%). The nitrite extracted with hot ethanol afforded a small amount of the *compound* (IX) in yellow needles, m. p. 252·5—253° (slight decomp.) (Found: C, 74·0; H, 6·4; N, 15·7. $C_{22}H_{22}ON_4$ requires C, 73·7; H, 6·2; N, 15·6%). The nitrite in chloroform was diluted with ether, giving the same base, which recrystallised from ethanol had m. p. 253—255° (decomp.). This base (unrecrystallised), heated with ethyl cyanoacetate, gave a minute quantity of the pyrroline (XVII; R = Et), m. p. 253—254° (decomp.), and an impure sample, m. p. and mixed m. p. 164—167°, of compound (VI) contaminated with the former pyrroline (spectroscopic).

Attempted purification of the nitrite by recrystallisation from organic solvents caused hydrolysis; the salt was sparingly soluble in water, more readily in hot water although the hot solution rapidly deposited the base. A sample of the nitrite (2 g.; containing at least 5% of the iminopyrrole, estimated by reaction with ethyl cyanoacetate and spectroscopic analysis of the resulting crude product) in ethanolic acetic acid was diluted with water and treated with sodium nitrite (3 g.) at 5°. An oil separated which solidified at 0—5°, to give (probably) the monohydrate, m. p. 193—207° (decomp.), of the nitrite of the oxo-2*H*-pyrrole. This, when dried over P_2O_5, afforded the *hemihydrate* (Found: C, 64·0; H, 5·6; O, 13·8; N, 17·0. $C_{22}H_{23}O_3N_5,\frac{1}{2}H_2O$ requires C, 63·8; H, 5·8; O, 13·5; N, 16·9%). The *monohydrate* lost 4·3% when dried to constant weight at 80—90°/0·5 mm. ($C_{23}H_{23}O_3N_5,H_2O$ requires H_2O, 4·3%), leaving the *anhydrous salt*, m. p. 194—205° (decomp.) (Found: C, 65·3; H, 5·9; N, 16·6%), the slightly low nitrogen content indicating some loss of nitrous acid. At 120—130°/0·5 mm. the monohydrate lost 14·8% (constant weight) ($C_{23}H_{22}ON_4,HNO_2,H_2O$ requires: loss of H_2O + HNO_2, 15·3%); the residue, presumably impure oxopyrrole base, had m. p. *ca.* 228° (decomp.).

The nitrite monohydrate, taken up in chloroform and diluted with ether, gave the oxo-2*H*-pyrrole (from ethanol), m. p. 253—255° (decomp.).

The monohydrate (0·3 g.) of the nitrite, refluxed with ethyl cyanoacetate, gave yellow needles, m. p. 160—166° (0·12 g.), whose spectrum was identical with that of compound (VI) in the region 320—450 mμ, indicating the absence of compound (XVII; R = Et). Recrystallisation from ethanol afforded the last pyrroline pure with m. p. and mixed m. p. 169—169·5°.

The nitrite monohydrate (0·33 g.), heated in boiling 75% sulphuric acid for 5 min., gave diphenylmaleinimide (0·19 g., 98%), m. p. 212—215°, and 1-amidinopiperidine as the picrate (0·18 g., 65%) which (from ethanol) had m. p. and mixed m. p. 249—249·5° (Found: C, 40·7; H, 4·6%).

(*b*) The compound (IV; $R^1 = H$, $R^2R^3 = <[CH_2]_5$) (2 g.) was heated with acetic anhydride–acetic acid and then added to water and set aside for some time. The solution was basified with sodium hydroxide, to yield a solid (1·6 g.), part of which afforded (from benzene) the oxo-2*H*-pyrrole, m. p. 252—253° (decomp.). The solid gave with acetic acid in benzene–light petroleum the *acetate monohydrate* in yellow needles, m. p. 252—253° (decomp.) (Found: O, 14·5; N, 12·7. $C_{24}H_{28}O_4N_4$ requires C, 14·7; N, 12·8%), $\lambda_{max.}$ 284, $\lambda_{infl.}$ 222, 310 mμ, displaced by acetic acid to 278, 355, and by alkali to 302 mμ ($\lambda_{infl.}$ 229, 372 mμ); this (0·33 g.) with ethyl cyanoacetate gave compound (VI) (0·20 g.), m. p. 168·5—169·5°.

(*c*) The acetyl derivative (0·3 g.; Ac, 10·7%) of the preceding compound (IV) in ethanolic acetic acid was treated with sodium nitrite (0·6 g.) in water at 0—5° for one week; it gave the nitrite (0·15 g.), m. p. 197° (decomp.) (Found: C, 64·2; H, 5·5; N, 16·95%), which in chloroform with ether afforded the base, m. p. 255° (decomp.) (from ethanol) (Found: C, 73·8; H, 6·1; N, 15·55%). The filtrate from the nitrite was basified to give a further amount of base (0·18 g.), m. p. 248° (decomp.).

3-*Guanidino*-1-*imino*-1H-*isoindole*.—A mixture of guanidine (8 g.), phthalonitrile (9 g.), and methanol (100 ml.) was kept at 37° during 1 week; it yielded the crude isoindole (8·9 g.), m. p. 183° (decomp.). A *monohydrate* was obtained in yellow prisms, m. p. 192° (decomp.)

[Found: C, 52·5; H, 5·8; N, 34·1%; *M* (cryoscopic, in phenol), 106, 109 (0·25%), 108, 110 (0·7%), 111 (1·02%). $C_9H_9N_5,H_2O$ requires C, 52·7; H, 5·4; N, 34·1%; *M*, 206]. The *benzoate*, needles from ethanol, had m. p. 194—194·5° (Found: C, 62·5; H, 4·9; N, 22·4. $C_{16}H_{15}O_2N_5$ requires C, 62·1; H, 4·9; N, 22·6%). The *acetate* had m. p. 190·5—192° [Found: C, 54·0; H, 5·5; N, 28·4%; *M* (cryoscopic, in water), 130 (0·38%). $C_{11}H_{13}O_2N_5$ requires C, 53·4; H, 5·3; N, 28·3%; *M* (van't Hoff *i* factor = 2), 124], $\lambda_{max.}$ 230, 280, 314, 327, $\lambda_{infl.}$ 344 mμ (log ε 4·50, 4·16, 3·96, 3·94, 3·81). The *triacetyl derivative* (from benzene–light petroleum) was obtained in pale yellow needles, m. p. 164° (decomp.) (Found: C, 57·8; H, 4·8; N, 22·0. $C_{15}H_{15}O_3N_5$ requires C, 57·5; H, 4·8; N, 22·3%), $\lambda_{max.}$ 222, 247, 298, $\lambda_{infl.}$ 332 mμ (log ε 4·51, 4·36, 3·74, 3·34), changed to $\lambda_{max.}$ 293, $\lambda_{infl.}$ 248, 330 mμ (log ε 3·42, 4·10, 3·03), by acetic acid.

The isoindole, refluxed in 30% sulphuric acid for 1 min., gave phthalimide, m. p. and mixed m. p. 232·5—234·5°.

Potentiometric Titrations in Phenol–Water.—Phenol was freshly redistilled. 0·04M-Perchloric acid was prepared from a 90% phenol solution. The base (*ca.* 30 mg.) was dissolved in 90% phenol solution in a cell compartment containing a glass electrode (Cambridge Instrument Co. Yellow Cap, wide range) and a mechanical stirrer. Connection with the reference calomel electrode was made by a strip of filter paper arranged so that the liquid junction was *ca.* 1 cm. above the level of the phenol–water in the cell; a Weston standard cell was used for bias as required. No attempt was made to set up a pH type scale in view of the large liquid-junction potential expected for this system.

2,5-*Di*-α-(*cyano*-α-*ethoxycarbonylmethylene*)-3,4-*diphenyl*-Δ^3-*pyrroline* (XVII; R = Et).—(*a*) 5-Guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (10 g.) was stirred with ethyl cyanoacetate (30 ml.), and the mixture was warmed to initiate the reaction; when cold, the mixture was treated with ethanol, to give the *pyrroline* (9·8 g.) which, purified from ethanol (orange needles), had m. p. 253·5—255° [Found: C, 70·9, 71·0; H, 5·0, 4·3; N, 9·6, 9·9; O, 14·9; OEt, 21·9%; *M* (isothermal distillation in chloroform), 417, 400. $C_{26}H_{21}O_4N_3$ requires C, 71·1; H, 4·8; N, 9·6; O, 14·6; 2EtO, 20·5; *M*, 439].

(*b*) A mixture of 5-guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (0·5 g.), acetic acid (6 ml.), and ethyl cyanoacetate (3 ml.) was refluxed for ¾ hr., giving the pyrroline (0·4 g.), m. p. and mixed m. p. 254—255°.

(*c*) To a solution of sodium (0·5 g.) and ethyl cyanoacetate (2·5 ml.) in dry ethanol was added *trans*-αβ-dicyanostilbene (5·5 g.), and the mixture was distilled at the steam-bath during 30 min. Acetic acid (6 ml.) was added to the warm mixture which deposited the crude pyrroline (1·6 g.), m. p. 156—160°; recrystallised from ethyl acetate and then from ethanol, this had m. p. 252—255° (Found: C, 70·2; H, 4·85; N, 9·8%).

An attempt to prepare the pyrroline (VI) by reducing the time of distillation in the above preparation to 5 min. was not successful, the pyrroline (XVII; R = Et) (0·07 g.), m. p. and mixed m. p. 253—255°, being obtained.

Reaction as in (*a*) of ethyl cyanoacetate with all our derivatives (IV) yielded the above pyrroline, m. p. and mixed m. p. 254—255°.

The pyrroline was recovered after being heated in acetic anhydride on the steam-bath for 3 hr., and after being refluxed with chromic acid in acetic acid or in concentrated hydrochloric acid for 15 min.

2,5-*Di*-(α-*cyano*-α-*methoxycarbonylmethylene*)-3,4-*diphenyl*-Δ^3-*pyrroline* (XVII; R = Me).—5-Guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole (4 g.) and methyl cyanoacetate afforded the *pyrroline* (XVII; R = Me) (4·2 g.) in yellow needles (from 2-methoxyethanol), m. p. 284° (decomp.) (Found: C, 70·2; H, 4·1; N, 9·6. $C_{24}H_{17}O_4N_3$ requires C, 70·1; H, 4·2; N, 10·2%).

Refluxing a mixture of the pyrrole (10 g.), methyl cyanoacetate (15 ml.), and di-n-butyl phthalate (30 ml.) for 0·5 hr. gave the same pyrroline (8·4 g.), m. p. 280° (decomp.).

Hydrolysis of the pyrroline gave the acid, m. p. 242°, described below.

2,5-*Di*-(α-*carboxy*-α-*cyanomethylene*)-3,4-*diphenyl*-Δ^3-*pyrroline* (XVII; R = H).—2,5-Di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-Δ^3-pyrroline (6 g.) in 2N-sodium hydroxide solution (30 ml.) and ethanol (30 ml.) at 30° afforded the acid (5·1 g.), m. p. 245° (decomp.), which recrystallised from ethanol in yellow needles of the *hemihydrate*, m. p. 240° (decomp.) (Found: C, 67·5; H, 3·9; N, 10·2%; equiv., 204. $C_{22}H_{13}O_4N_3,\frac{1}{2}H_2O$ requires C, 67·3; H, 3·6; N, 10·7%; equiv., 196), or from aqueous ethanol in orange prisms, m. p. 242° (decomp.) (Found: C, 64·0; H, 4·2; N, 9·8; loss in wt. at 160—175° in a high vacuum, 9·0%. $C_{22}H_{13}O_4N_3,2H_2O$ requires C, 63·0; H, 4·1; N, 10·0; $2H_2O$, 8·6%), $\lambda_{max.}$ 232, 413, 436, $\lambda_{infl.}$ 337, 397 in ethanol containing

0·1M-hydrochloric acid, changed to $\lambda_{max.}$ 411, 434 mμ in aqueous sodium metaborate buffer. The anhydrous *acid* had m. p. 249° (decomp.) (Found: C, 68·4; H, 3·4; N, 10·6. $C_{22}H_{13}O_4N_3$ requires C, 68·9; H, 3·4; N, 11·0%). The acid was refluxed with copper chromite in quinoline, giving a black solid soluble in sulphuric acid to an intensely blue solution. The acid was recovered from boiling ethanolic sulphuric acid; gas was not evolved when the acid was suspended in ethereal diazomethane.

The diethyl ester (0·3 g.) in ethanolic potassium hydroxide, refluxed with 1-chloro-2,4-dinitrobenzene (0·2 g.), yielded an acid, presumably the *N*-2,4-dinitrophenyl derivative, in yellow needles (from ethanol) which exploded at >300° (Found: N, 11·9. Calc. for $C_{28}H_{15}O_8N_5,2H_2O$: N, 11·9%).

A solution of the acid (from 1 g. of the diethyl ester) in 10% sodium hydroxide solution (80 ml.) was oxidised with potassium permanganate (3 g.); it yielded benzoic acid (0·2 g.), m. p. and mixed m. p. 120·5—121·5°.

2-α-*Cyano*-α-*ethoxycarbonylmethylene*-5-*oxo*-3,4-*diphenyl*-Δ^3-*pyrroline* (VI).—(*a*) *trans*-αβ-Dicyanostilbene (5·8 g.) was added to a solution from sodium (0·6 g.) in ethanol (20 ml.) containing ethyl cyanoacetate (2·5 ml.), and the mixture was distilled during 5 min., cooled, and stirred into dilute acid, giving a solid and an oil; the former afforded the *pyrroline* (from ethyl acetate–light petroleum) in yellow needles, m. p. 168·5—169·5° (Found: C, 72·7; H, 4·9; N, 8·1; OEt, 13·55. $C_{21}H_{16}O_3N_2$ requires C, 73·2; H, 4·7; N, 8·1; OEt, 13·1%). *trans*-αβ-Dicyanostilbene was also isolated but not the bis-derivative (XVII). Attempted repetition of this experiment was not successful, the last-named compound being isolated as described above.

(*b*) *trans*-αβ-Dicyanostilbene (3 g.) was dissolved in a hot solution from sodium (0·3 g.) in ethanol (200 ml.), and a solution of ethyl cyanoacetate (1·5 ml.) in ethanol was added; the mixture was distilled on the steam-bath during 45 min. and then added to aqueous acetic acid, giving a black tar which afforded the above pyrroline (0·15 g.), m. p. 168—169° (from ethanol) (Found: C, 73·3; H, 4·73; O, 14·0; N, 8·4. $C_{21}H_{16}O_3N_2$ requires O, 13·9%; cf. above), which from the absorption spectrum was probably contaminated by *ca.* 7% of bis-ester (XVII; R = Et).

(*c*) 2-Imino-5-oxo-3,4-diphenyl-Δ^3-pyrroline (1 g.) was refluxed with ethyl cyanoacetate (1 ml.) for 1 min., an ammoniacal gas being evolved; the mixture was cooled and diluted with ethanol, to yield the pyrroline (0·7 g.), m. p. 169·0—170·5° (Found: N, 8·1; OEt, 12·9%).

1,3-*Di*-(α-*cyano*-α-*ethoxycarbonylmethylene*)*isoindoline* (XV).—(*a*) 3-Guanidino-1-imino-1*H*-isoindole (2 g.) reacted with ethyl cyanoacetate (5 ml.), to give the ester (XV) (2·9 g.) in yellow needles (from ethyl methyl ketone), m. p. 233·5—234° (lit.,[1] 231°) [Found: C, 64·1; H, 4·5; O, 19·1; N, 12·7; OEt, 26·9%; *M* (Rast), 344. Calc. for $C_{18}H_{15}O_4N_3$: C, 64·1; H, 4·5; O, 19·0; N, 12·5; 2EtO, 26·7%; *M*, 337]. When refluxed in aqueous-ethanolic sodium hydroxide it (1 g.) yielded 1,3-di-(α-carboxy-α-cyanomethylene)isoindoline (0·3 g.), m. p. 260° (decomp.) (crude or purified *via* the sparingly soluble sodium salt) (Found: C, 58·5; H, 2·6; N, 14·7. Calc. for $C_{14}H_7O_4N_3$: C, 59·8; H, 2·5; N, 14·9%) (Elvidge, Fitt, and Linstead [1] state that the m. p. of this acid is not characteristic).

(*b*) To a solution from sodium (0·67 g.) in ethanol (13 ml.) were added phthalonitrile (3·2 g.) and ethyl cyanoacetate (5 ml.), and the mixture was refluxed for 15 min., treated with ammonium chloride (5 g.) and ethanol (25 ml.), and refluxed for a further hr.; this gave the ester, m. p. and mixed m. p. 233° (3·3 g.), which was hydrolysed to the acid, m. p. 260° (decomp.).

(*c*) Use of methyl cyanoacetate in method (*b*) gave, by transesterification, the diethyl ester, m. p. and mixed m. p. 231—232·5°.

1,3-*Di*-(α-*cyano*-α-*methoxycarbonylmethylene*)*isoindoline*.—(*a*) 3-Guanidino-1-imino-1*H*-isoindole (2 g.) and methyl cyanoacetate afforded the *dimethyl ester* (2 g.), m. p. 276—279° (decomp.) (from acetic acid) (Found: C, 62·0, 61·9; H, 4·2, 3·9; N, 13·5; OMe, 20·2. $C_{16}H_{11}O_4N_3$ requires C, 62·1; H, 3·6; N, 13·6; 2MeO, 20·1%), which was hydrolysed to the acid, m. p. 261° (decomp.).

(*b*) Phthalonitrile (3·2 g.) afforded with ethyl or methyl cyanoacetate and sodium methoxide the dimethyl ester (2·35 g.) in yellow plates, m. p. 279—280° (decomp.) (Found: N, 13·6; OMe, 20·1%).

Oxidation of 1,3-*Di*-(α-*cyano*-α-*ethoxycarbonylmethylene*)*isoindoline* (XV).—A solution of the ester (1 g.) in acetone (500 ml.) was stirred whilst a solution of potassium permanganate (0·55 g.) was dropped in during 15 min.; the mixture was decolorised with sodium hydrogen sulphite, then neutralised with acetic acid, and the acetone was removed by slow evaporation to give

four fractions: (i) m. p. 230·5—233° (0·4 g.); (ii) m. p. 169—170° (0·3 g.); (iii) m. p. 167·5—169° (0·03 g.), and (iv) m. p. 167·5—169° (0·07 g.). Fractions (iii) and (iv) were combined to give the isoindoline (XVI) (from benzene), m. p. and mixed m. p. 169—170·5° with a specimen prepared as described by Barrett, Leavitt, Linstead, and Rowe.[7] Use of an excess of permanganate afforded phthalimide, m. p. and mixed m. p. 233—234°.

Identity of the Substance from Guanidine and α-Cyanobenzyl Bromide.[2]—The following evidence indicated that this substance was impure 5-guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole.

Recrystallised with great difficulty from ethyl methyl ketone it had m. p. 162° (Found: C, 63·1; H, 5·7; N, 18·8%). It dissolved in warm acetic anhydride, to yield (probably) the triacetyl derivative of 5-guanidino-2-imino-3,4-diphenyl-2*H*-pyrrole in orange needles, m. p. 192·5° (decomp.) (Found: C, 65·9; H, 5·3; N, 16·2%). When the substance (0·2 g.) was refluxed for 2 min. in benzene (2 ml.) containing acetic anhydride (1 ml.) it yielded the triacetyl derivative, m. p. 182·5° (decomp.) (Found: C, 66·0; H, 4·8; N, 16·3%), which was hydrolysed to diphenylmaleinimide, m. p. and mixed m. p. 215·5—216·5°.

The substance with warm ethyl cyanoacetate gave 2,5-di-(α-cyano-α-ethoxycarbonylmethylene)-3,4-diphenyl-Δ^3-pyrroline (XVII; R = Et), m. p. and mixed m. p. 254—255°.

The substance (0·1 g.) was suspended in ethanol (2 ml.) and treated with dry hydrogen chloride until most of the solid had dissolved. The solution was clarified at the centrifuge and ether was added, giving the hydrochloride (from benzene–ether), m. p. 129° (decomp.) (Found: C, 50·5; H, 5·3; N, 17·2. Calc. for $C_{17}H_{18}N_5Cl_3$: C, 51·2; H, 4·6; N, 17·5%).

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