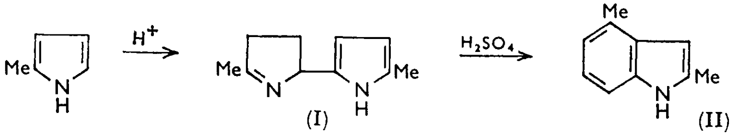
308. *The Reductive Condensation of 2,5-Dimethylpyrrole. A Novel Isoindoline Synthesis.*

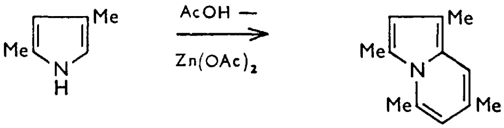
By R. Bonnett and J. D. White.

Two bases, $C_{12}H_{17}N$, formed by the reductive self-condensation of 2,5-dimethylpyrrole in metal–acid systems, are identified as the geometrical isomers of 1,3,4,7-tetramethylisoindoline. Observations which give some indication of the path of the reaction are discussed.

The acid-catalysed condensation of alkylpyrroles leads to a remarkable variety of heterocyclic compounds. Thus, 2-alkyl- and 2,3-dialkyl-pyrroles are reported[1,2] to give initially the corresponding dimers (*e.g.*, I) which under more vigorous conditions are converted[3] into indoles (*e.g.*, II). 2,4-Dimethylpyrrole, on the other hand, undergoes self-condensation[4]



to give the indolizine (III), while tri- and tetra-substituted pyrroles are reported to give dimeric products,[5] the structures (and, indeed, existence[2]) of which remain to be convincingly demonstrated. It is evident that in each of the formulated series, and also in the trimerisation of pyrrole itself,[6] the product may be derived from a pyrrole dimer,



(III)

which in turn can arise by the nucleophilic attack of one pyrrole ring, through an unsubstituted α-position, upon an unsubstituted α-position of a β-protonated pyrrole molecule. It was of interest to determine the course of the reaction, if any, when both of the α-positions were substituted, and for this purpose the condensation of 2,5-dimethylpyrrole was investigated.

It had already been shown[7] that 2,5-dimethylpyrrole, when treated with anhydrous hydrogen chloride in ether, gives an unstable salt from which the pyrrole may be regenerated in moderate yield. It is to be noted, however, that the proton magnetic resonance spectrum of this pyrrole in an aqueous acidic medium cannot readily be interpreted in terms of a simple protonation[8] and, indeed, evidence for the formation of an unstable condensation product under forcing conditions has been given.[9] A reasonably stable product may be obtained if reduction is carried out concomitantly. Earlier work, with zinc and acetic acid for this purpose, resulted[10] in the formation of a base $C_{12}H_{17}N$ obtained as colourless needles, m. p. 74—75°. Plancher and Tornani originally[9] formulated

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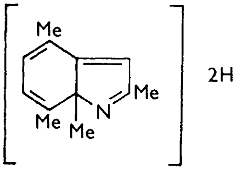
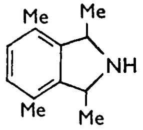
[1] Allen, Gilbert, and Young, *J. Org. Chem.*, 1938, **2**, 227.
[2] Booth, Johnson, and Johnson, *J.*, 1962, 98.
[3] Dennstedt, *Ber.*, 1888, **21**, 3429; 1889, **22**, 1920.
[4] Saxton, *J.*, 1951, 3239.
[5] Fischer and Orth, " Die Chemie des Pyrrols," Akademische Verlagsgesellschaft, Leipzig, 1934, Vol. I, p. 38.
[6] Potts and Smith, *J.*, 1957, 4018.
[7] Bullock, *Canad. J. Chem.*, 1958, **36**, 1686.
[8] Abraham, Bullock, and Mitra, *Canad. J. Chem.*, 1959, **37**, 1859.
[9] Plancher and Tornani, *Gazzetta*, 1905, **35**, 461.
[10] Zanetti and Cimatti, *Ber.*, 1897, **30**, 1588.

this with an isoindole skeleton, but later[11] expressed a preference for structure (IV) largely on the basis of the analogy to the known examples of indole formation from certain other pyrroles.[3,12] The present work indicates that an isoindoline is in fact formed. Two products, which are formulated as the geometrical isomers of 1,3,4,7-tetramethylisoindoline (V), have been obtained.

It was found convenient to replace the metal–acid system of earlier workers by tin in refluxing aqueous hydrochloric acid. The product, isolated after basification and steam-distillation, was a viscous oil possessing an unpleasant mouse-like odour. Vapour-phase chromatography separated two major components: a solid, m. p. 72—73°, in small amount (15%), which was presumed to be the material of m. p. 74—75° reported by previous workers; and a viscous oil (85%) which solidified on cooling but remelted at the ambient temperature or just above (~35°) and then readily became supercooled. Both substances were basic and gave positive nitroprusside tests for the secondary amino-function.[13] They had practically identical ultraviolet spectra, and had similar but not identical infrared spectra. Both reddened on storage at room temperature.



(IV)



(V)

The major part of the investigation was carried out with the lower-melting product which could be readily obtained pure from the mixture through the hydrochloride, and to which, it became clear, the higher-melting base was closely related. The lower-melting base readily absorbed carbon dioxide from the atmosphere forming a solid adduct, a phenomenon which had previously been noticed with liquid bases of the isoindoline type,[14] as, incidentally, had the development of a red colour on storage.[15] The base had pK_a ~9 in aqueous ethanol: it formed a benzenesulphonamide which was insoluble in alkali, and an *N*-nitroso-derivative, observations which suggested the presence of an aliphatic secondary amino-function. Analyses of the base itself, the benzenesulphonamide, the nitrate, and the hydrochloride indicated the formula $C_{12}H_{17}N$, while titration gave an equivalent of 178 (calc., 175). The benzenesulphonamide had a molecular weight of 305 (Rast), confirming the monomeric nature of the compound. The ultraviolet spectra of the base and its salts were similar, although the protonated species showed rather more fine structure. In form, position, and intensity the absorption suggested the presence of a benzenoid unit (base in ethanol: $\lambda_{\max.}$ 263·5, 271 mμ; log ε 2·39, 2·25, respectively. On acidification: $\lambda_{\max.}$ 265·5, 271, 274·5 mμ; log ε 2·46, 2·39, 2·36, respectively. Cf. 4,7-dimethylindane in " iso-octane "[16]). Moreover, the ultraviolet spectrum of the *N*-methyl methiodide of the base closely resembled that of 2,4,7-trimethylisoindolinium methiodide. The infrared spectrum of the base provided further evidence for a benzenoid chromophore: peaks occurred at 3322 (NH), 1866, 1605, 1493, and 807 cm.$^{-1}$, the last, strong absorption (in the absence of strong absorption in the 700—750 cm.$^{-1}$ region) together with a weak band at 1866 cm.$^{-1}$, being taken to indicate a benzene ring with two, but not more, adjacent hydrogen atoms.[17]

The nature of the benzenoid unit was determined by permanganate oxidation. Under

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[11] Plancher and Cuisa, *Atti R. Accad. Lincei, Rend. Classe Sci. fis. mat. nat.*, 1906, **15**, 447; cf. Beilstein's " Handbuch der Organischen Chemie," Julius Springer, Berlin, Vol. XX, p. 299.

[12] Plancher, *Ber.*, 1902, **35**, 2606.

[13] Feigl, " Spot Tests," Elsevier, London, 1954, Vol. II, p. 189.

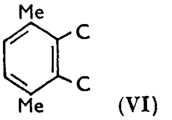
[14] Gabriel and Neumann, *Ber.*, 1893, **26**, 705.

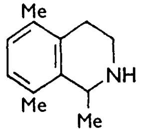
[15] Linstead and Noble, *J.*, 1937, 933.

[16] Entel, *Analyt. Chem.*, 1954, **26**, 612.

[17] Bellamy, " The Infra-red Spectra of Complex Molecules," Methuen, London, 1958, chap. 5.

different conditions of oxidation and extraction, the reaction with alkaline permanganate furnished 3,6-dimethylphthalic anhydride (7% yield) and benzene-1,2,3,4-tetracarboxylic acid (16% as the tetramethyl ester), which strongly supported the partial structure (VI) for the original base. That the structure corresponded to expression (V) rather than less reasonable structures such as (VII), which accorded with observations up to this point,

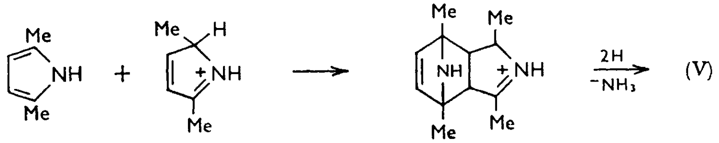

(VI)


(VII)

was indicated by the proton magnetic resonance spectrum (recorded at 60 Mc. sec.$^{-1}$ in carbon tetrachloride solution) which showed peaks with τ values of 3·21 (singlet; aromatic H), 5·65 (quadruplet; $J = 6{\cdot}5$ c./sec.: H at positions 1 and 3 split by CH_3 at those positions), 7·80 (singlet; aromatic methyl groups), 7·95 (singlet; NH), and 8·62 (doublet; $J = 6{\cdot}5$ c./sec.; CH_3 at positions 1 and 3 split by H at those positions). The area ratio of the five groups of signals approximated to 1 : 1 : 3 : 0·5 : 3, again in agreement with structure (V). The neat molten base showed (at 40 Mc. sec.$^{-1}$) signals similarly distributed but shifted upfield by about 0·3 τ unit.[18] The spectrum of 1-phenylethylamine was measured for comparison (60 Mc. sec.$^{-1}$; 30% solution in carbon tetrachloride): it also showed a quadruplet at 6·06 τ and a doublet at 8·76 τ, both with a splitting constant of 6·5 c./sec., while the NH_2 signal appeared as a singlet at 8·78 τ.

The higher-melting base gave analyses for $C_{12}H_{17}N$ and it was also characterised as the nitrate and the benzenesulphonamide, the molecular weight (Rast) of the latter indicating the monomeric formulation. The basicity and ultraviolet spectrum were very similar to those of the lower-melting isomer, and the main features of the infrared spectrum already detailed were also present, although the finger-print regions of the two spectra were not identical. The two bases were formulated as the geometrical isomers of 1,3,4,7-tetramethylisoindoline. This assignment was confirmed by the proton magnetic resonance spectrum of the higher-melting base which had the same general appearance as that of the lower-melting isomer: the position of the signals associated with the aromatic protons and the aromatic methyl groups had not been significantly altered, but the signals associated with groups at the seat of the configurational differences had shifted. Thus, slight shifts in the positions of the quadruplet (to 5·53 τ) and the doublet (to 8·75 τ) had occurred, while the NH absorption had been displaced upfield to 8·44 τ. It has not been possible as yet to assign the individual configurations with certainty: attempted resolution under the conditions used for 1-phenylethylamine[19] have failed in each case, but the problem is being examined further.

Although the details of the reaction pathway of this remarkable condensation are not clear at present, certain observations may be made. The structure of the product suggests that a reaction of the Diels–Alder type has occurred, perhaps according to the scheme I.[18]



Scheme I

Elimination of the ammonium ion in this way is well known,[20] and overall the reaction has considerable analogy to the Diels–Alder reaction of 2,5-dimethylfuran with maleic

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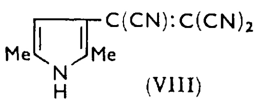
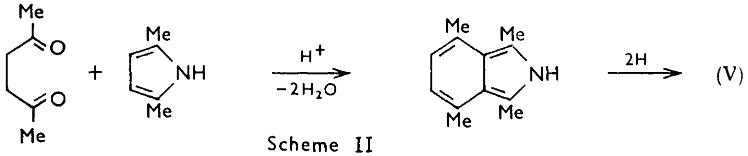
[18] Bonnett and White, *Proc. Chem. Soc.*, 1961, 119.
[19] Cf. Theilacker and Winkler, *Chem. Ber.*, 1954, **87**, 690.
[20] *E.g.*, Harries and Antoni, *Annalen*, 1903, **328**, 88.

anhydride, followed by the acid-catalysed elimination of water to yield 3,6-dimethylphthalic anhydride.[21] However, an aqueous medium, though not unknown, is atypical. Moreover, pyrroles have little dienic character, and the few recent examples [22] in which they are reported to partake in this reaction may be attributed to steric and electronic factors which do not operate here. The reaction of 2,5-dimethylpyrrole with maleic anhydride has been reported [23] to give no isolable adduct: this is not definitive however, since, if formed, such an adduct might well give a polymeric amide. As a more useful demonstration of the absence of the dienic character of the pyrrole, the reaction with tetracyanoethylene, which is both a very highly reactive dienophile and one less likely to produce polymers in this instance, has been employed. Tetracyanoethylene reacted with 2,5-dimethylpyrrole in tetrahydrofuran at room temperature to give in good yield a coloured compound which was not an adduct. This is formulated as the tricyanovinyl compound (VIII) since the infrared spectrum indicated the presence of NH (3236 cm.$^{-1}$). An analogous reaction, with substitution at the 2-position, occurs with pyrrole itself.[24] Since tetracyanoethylene, which would be expected to be a much stronger dienophile than the protonated pyrrolenine in Scheme I, failed to elicit any dienic character from 2,5-dimethylpyrrole, this scheme must be considered unlikely.



(VIII)

One of the most plausible alternatives involves acetonylacetone or its equivalent (*e.g.*, β-protonated 2,5-dimethylpyrrole). It has been shown [1] that 2,5-dimethylpyrrole readily gives the bis-2,4-dinitrophenylhydrazone of acetonylacetone when treated with acidic alcoholic 2,4-dinitrophenylhydrazine. Since, as a recently published [25] spectrum suggests, 2,5-dimethylpyrrole is frequently contaminated with the dione from which it is prepared, it was considered desirable to repeat the observation with the carefully purified pyrrole. This showed no carbonyl absorption in the infrared region, but nevertheless gave the bishydrazone readily. Hence in an acid solution of the pyrrole, acetonylacetone or its equivalent is available for reaction, and it may, indeed, be regarded as being subject to the nucleophilic attack of another pyrrole molecule to give an isoindole (or 1*H*-isoindole) which is then reduced to the benzenoid system (Scheme II).



Scheme II

This bidentate condensation has a direct analogy in the thiophen series, where the acid-catalysed condensation of acetonylacetone and 2,5-dimethylthiophen has been shown [26] to give 1,3,4,7-tetramethylbenzo[*c*]thiophen. Further support for the scheme comes from observations with a less reactive pyrrole. It has been shown that 2,5-diphenylpyrrole does not give a diketone derivative with Brady's reagent, and, consistently with this, it does not give a self-condensation product with tin and hydrochloric acid, but is largely recovered. However, when acetonylacetone and 2,5-diphenylpyrrole are heated together under acidic reducing conditions, a compound $C_{22}H_{21}N$ may be isolated, and the formulation of this as 4,7-dimethyl-1,3-diphenylisoindoline is in accord with its spectral characteristics and with the observation that it gives a *N*-nitroso-derivative. The proton magnetic resonance spectrum of the base (60 Mc. sec.$^{-1}$; in deuterochloroform) is of interest since it

[21] Newman and Lord, *J. Amer. Chem. Soc.*, 1944, **66**, 733.

[22] Mandell and Blanchard, *J. Amer. Chem. Soc.*, 1957, **79**, 6198; Wittig and Behnisch, *Chem. Ber.*, 1958, **91**, 2358; Acheson and Vernon, *J.*, 1961, 457.

[23] Allen and Young, *Canad. J. Res.*, 1934, **10**, 771.

[24] Sausan, Engelhart, and Middleton, *J. Amer. Chem. Soc.*, 1958, **80**, 2815.

[25] Kreutzberger and Kalter, *J. Phys. Chem.*, 1961, **65**, 624.

[26] Dann, Kokorudz, and Gropper, *Chem. Ber.*, 1954, **87**, 140.

manifests both the deshielding and the shielding effect of the phenyl groups. Thus the C-1 and C-3 protons now appear at 4·61 τ (singlet: cf. 4·46 τ of *trans*-1,3-diphenylisoindoline[27]), while the aromatic methyl groups, which for steric reasons are exposed predominantly to the faces, rather than the edges, of the phenyl rings, come within the region of shielding influence and appear at 8·19 τ.

EXPERIMENTAL

Unless otherwise stated, infrared spectra were determined (as liquid films or liquid paraffin mulls) with a Perkin-Elmer Infracord instrument, and ultraviolet spectra were measured for 95% ethanol solutions with a Cary 11 recording spectrophotometer. Proton magnetic resonance spectra were measured on an A60 Varian spectrophotometer, and were calibrated with an internal standard of tetramethylsilane (10 τ).

Preparation of the 1,3,4,7-*Tetramethylisoindolines* (V).—2,5-Dimethylpyrrole (25 g.) was added in small portions to a refluxing mixture of granulated tin (125 g.) and 6N-hydrochloric acid (500 ml.), and the mixture was refluxed for 22 hr. An excess of 30% aqueous sodium hydroxide was carefully added to the cooled mixture, which was then steam-distilled until 1·5—2 l. of distillate had collected. Addition of sodium hydroxide (20 g.) to the distillate was followed by continuous ether-extraction (10 hr.). Fractional distillation of the dried ether extract under nitrogen gave a colourless basic oil (11·4 g., 50%), b. p. 85—90°/0·6 mm., which reddened on storage at room temperature.

Separation of the Components.—(*a*) *By vapour-phase chromatography.* Vapour-phase chromatography (Aerograph A-100-C instrument, 5′ Ucon Polar column, 180°, helium carrier gas) of the oil gave two main fractions present in the ratio of 15 : 85 as determined by measurement of peak areas. The smaller fraction had a retention volume of 1050 ml. and was collected as colourless needles, m. p. 72—73°, which became pink on storage (Found: C, 82·3; H, 9·7; N, 7·9. $C_{12}H_{17}N$ requires C, 82·2; H, 9·8; N, 8·0%), $\nu_{max.}$ 3247, 1855w, 1595w, 1484, 802s cm.$^{-1}$, $\lambda_{max.}$ 263 and 271 mμ (log ε 2·45 and 2·33, respectively). Titration in 20% aqueous ethanol gave an equivalent of 187 (calc., 176) and an apparent pK_a of 8·85. The *base* gave a positive nitroprusside test for secondary amines.[13] The *nitrate*, m. p. 250—251° (decomp.), was prepared in aqueous medium and recrystallised from ethanol–benzene (Found: C, 60·2; H, 7·6; N, 11·6. $C_{12}H_{18}N_2O_3$ requires C, 60·5; H, 7·6; N, 11·8%) and had $\lambda_{max.}$ 265·5, 271, and 275 mμ (log ε 2·54, 2·46, and 2·45, respectively). The *benzenesulphonyl derivative*, m. p. 139° (from ethanol), was insoluble in alkali [Found: C, 68·6; H, 6·9; N, 4·5%; *M* (Rast), 303. $C_{18}H_{21}NO_2S$ requires C, 68·5; H, 6·7; N, 4·4%; *M*, 315].

The second fraction had a retention volume of 1320 ml. and was identified with the base prepared from the hydrochloride (below).

(*b*) *By salt formation.* Treatment of the mixed bases with hydrochloric acid in anhydrous ether, or in concentrated aqueous solution, gave the *hydrochloride*, white plates, m. p. 267—268° (decomp.) (Found: C, 68·3; H, 8·75; Cl, 16·4; N, 6·8. $C_{12}H_{18}ClN$ requires C, 68·1; H, 8·6; Cl, 16·8; N, 6·6%). Regeneration of the base gave 1,3,4,7-*tetramethylisoindoline* as a colourless liquid, b. p. 90—91°/0·35 mm., which solidified when kept at 0° to a crystalline mass (m. p. ~35°). At room temperature the liquid or semisolid base slowly became red. It was best kept at 0° or below under nitrogen (Found: C, 82·6; H, 10·0; N, 8·1%). It had retention volume (conditions above) 1316 ml., $\nu_{max.}$ [identical with second fraction under (*a*) above] 3322, 1866w, 1605w, 1493, and 807s cm.$^{-1}$, and $\lambda_{max.}$ 263·5 and 271 mμ (log ε 2·39 and 2·25, respectively). Electrometric titration in 20% aqueous ethanol gave an equivalent of 178 and an apparent pK_a of 9·1. The base gave a positive nitroprusside test.

Further Reactions of the Major Product (*Lower-melting Isomer*).—(*a*) *Derivatives.* The *nitrate*, prepared in water, formed colourless blades, m. p. 176—178° (from ethanol) (Found: C, 60·8; H, 7·4; N, 11·9. $C_{12}H_{18}N_2O_3$ requires C, 60·5; H, 7·6; N, 11·8%), $\lambda_{max.}$ 265·5, 270·5, 274·5 mμ (log ε 2·52, 2·46, and 2·45, respectively).

The *nitrosamine* recrystallised from ethanol as prisms, m. p. 94°, and gave a positive Liebermann test (Found: N, 13·5. $C_{12}H_{16}N_2O$ requires N, 13·7%).

The *benzenesulphonyl derivative*, colourless blades, m. p. 127—128°, from ethanol, was insoluble in alkali [Found: C, 68·5; H, 6·5; N, 4·35%; *M* (Rast) 305]. The mixed m. p. with the isomeric benzenesulphonyl derivative (above) was 100—105°.

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[27] Carpino, *J. Amer. Chem. Soc.*, 1962, **84**, 2196.

Eschweiler–Clarke methylation of the base was carried out according to Icke, Wisegarver, and Alles [28] and gave a 22% yield of 1,2,3,4,7-pentamethylisoindoline, b. p. 56°/0·2 mm., $\nu_{max.}$ 2760 cm.$^{-1}$. The *methiodide* formed colourless needles, m. p. 264—266° (from ethanol) (Found: C, 51·0; H, 6·5. $C_{14}H_{22}IN$ requires C, 50·8; H, 6·65%), $\lambda_{max.}$ 266·5, 271, and 275·5 mμ (log ε 2·53, 2·45, and 2·50, respectively).

A white solid *substance* separated when carbon dioxide was passed into an ethereal solution of the base. It could not be recrystallised without decomposition, but was washed with ether and dried at room temperature. It decomposed at 85—90° (Found: C, 71·0; H, 7·8; N, 6·2. $C_{13}H_{17}NO_2$ requires C, 71·2; H, 7·8; N, 6·4%).

(*b*) *Oxidation.* (i) The tetramethylisoindoline (0·45 g.) was set aside with potassium permanganate (10 g.) and potassium carbonate (2·8 g.) in water (150 ml.) for 3 days. The mixture was then refluxed for 6 hr., cooled, acidified to pH 4, and extracted continuously with ether. Removal of the ether and sublimation of the gummy residue gave 0·03 g. (7%) of 3,6-dimethylphthalic anhydride, m. p. 142—144°, mixed m. p. 143—144° (lit.,[21] 142—143°).

(ii) The tetramethylisoindoline (0·72 g.) was added to a mixture of potassium permanganate (20 g.) and potassium carbonate (2·6 g.) in water (100 ml.) at 60°. The mixture was maintained at this temperature for 4 hr. and then refluxed for 16 hr. After decomposition of the excess of permanganate with sulphur dioxide the solution was extracted continuously with ether at pH 4. The solution was then extracted at pH 1 with ether for 44 hr. The dried ethereal solution from the second extraction was evaporated to give 0·34 g. of crude crystalline benzene-1,2,3,4-tetracarboxylic acid, which was esterified (diazomethane) to give 0·19 g. (16%) of tetramethyl benzene-1,2,3,4-tetracarboxylate, m. p. 129—131°, mixed m. p. 129—132° (lit.,[29] 129—130°, 131—133°, 128—129°). The infrared spectrum (Perkin-Elmer 21) was identical with that of an authentic sample prepared by similar treatment of 1,2,3,4-tetramethylbenzene.

Preparation of 2,4,7-*Trimethylisoindolinium Methiodide.*—3,6-Dimethylphthalic anhydride [21] (4·6 g.) was dissolved in 20% aqueous methylamine (40 ml.), and the solution was warmed to 50°. The precipitate was collected. The filtrate was refluxed with intermittent filtration (to prevent excessive bumping) until no more solid was formed. The combined solid materials were dried and then heated at 130° for 2 hr., to give a quantitative yield of 3,6,N-*trimethylphthalimide*, m. p. 176—177° after vacuum-sublimation (Found: C, 70·1; H, 5·6; N, 7·5. $C_{11}H_{11}NO_2$ requires C, 69·8; H, 5·9; N, 7·4%).

Reduction of the phthalimide with lithium aluminium hydride in ether gave a 48% yield of 2,4,7-trimethylisoindoline, which was converted into the *methiodide*, colourless plates, m. p. 231—232° (from ethanol) (Found: C, 47·3; H, 6·0; I, 41·5; N, 4·4. $C_{12}H_{18}IN$ requires C, 47·5; H, 6·0; I, 41·9; N, 4·6%), $\lambda_{max.}$ 265·5, 270·5, and 274·5 mμ (log ε 2·47, 2·40, and 2·43, respectively).

Reactions of 2,5-*Disubstituted Pyrroles.*—(i) Freshly distilled 2,5-dimethylpyrrole, which had no peak at 1730 cm.$^{-1}$ in the infrared region, on treatment with a solution of 2,4-dinitrophenylhydrazine in acidic ethanol gave the bis-2,4-dinitrophenylhydrazone of acetonylacetone, identical with that prepared from acetonylacetone itself.[23] In similar conditions 2,5-diphenylpyrrole did not give a carbonyl derivative.

(ii) Freshly distilled 2,5-dimethylpyrrole (0·75 g.) in dry tetrahydrofuran (5 ml.) was added to tetracyanoethylene (1 g.) in tetrahydrofuran (10 ml.). The solution became blue initially, but finally orange. The solvent was removed, leaving an orange product which crystallised from 1% ethanol in benzene to give 1·2 g. (77%) of 2,5-*dimethyl*-3-*tricyanovinylpyrrole* (VIII) as brick-red needles, m. p. 192—194° (Found: C, 67·1; H, 4·1; N, 28·6. $C_{11}H_8N_4$ requires C, 67·3; H, 4·1; N, 28·55%), $\nu_{max.}$ 3236, 2217 cm.$^{-1}$, $\lambda_{max.}$ 251·5, 362, and 433 mμ (log ε 3·66, 4·13, and 4·21, respectively).

4,7-*Dimethyl*-1,3-*diphenylisoindoline.*—A solution of 2,5-diphenylpyrrole [30] (10 g.) and acetonylacetone (6 g.) in ethanol (150 ml.) was added in small portions to tin (65 g.), 6N-hydrochloric acid (250 ml.), and ethanol (250 ml.) under reflux. A deep red colour formed initially but was discharged as reduction took place. Refluxing was continued for 40 hr., then the ethanol was distilled off, yielding a thick slurry. This was made strongly basic with 30% aqueous sodium hydroxide, and the aqueous layer and solid material were separated and

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[28] Icke, Wisegarver, and Alles, *Org. Syn.*, Coll. Vol. III, 723.

[29] Fieser and Peters, *J. Amer. Chem. Soc.*, 1932, **54**, 4347; Smith and Carlson, *ibid.*, 1939, **61**, 288; Elsner and Parker, *J.*, 1957, 592.

[30] Kreutzberger and Kalter, *J. Org. Chem.*, 1960, **25**, 554.

extracted vigorously with benzene. Removal of the benzene, and recrystallisation of the solid product from ethanol, gave off-white needles of 4,7-*dimethyl*-1,3-*diphenylisoindoline*, m. p. 172—174° (8·8 g., 64%) [Found: C, 88·0; H, 6·9; N, 4·85%; *M* (Rast), 295. $C_{22}H_{21}N$ requires C, 88·2; H, 7·1; N, 4·7%; *M*, 299], $\lambda_{max.}$ 253, 258, and 265 mμ (log ε 2·87, 2·91, and 2·87, respectively), $\nu_{max.}$ 3344, 1595, 1493, 817, and 698 cm.$^{-1}$.

The *nitrosamine* was prepared by adding concentrated hydrochloric acid (1·5 ml.) to an ice-cold solution of the isoindoline (2·1 g.) in ethanol (120 ml.), followed immediately by a cold solution of sodium nitrite (1·5 g.) in water (3 ml.). The mixture was set aside for 15 min., the precipitated inorganic salt was filtered off, and the nitrosamine was precipitated from the filtrate by addition of water. Recrystallisation of the solid from ethanol–benzene (3 : 1) gave 2·05 g. (89%) of the nitrosamine, pale yellow blades, m. p. 183—185° (Found: C, 80·7; H, 6·0; N, 8·5. $C_{22}H_{20}N_2O$ requires C, 80·5; H, 6·1; N, 8·5%).

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