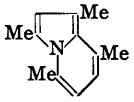
714. *Condensations of 2 : 4-Dimethylpyrrole.*

By J. E. Saxton.

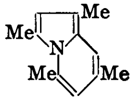
The condensation of 2 : 4-dimethylpyrrole with acetonylacetone and its equivalent self-condensation under the influence of zinc acetate in acetic acid have been re-examined. The products have been shown to be 1 : 3 : 5 : 8- and 1 : 3 : 5 : 7-tetramethylpyrrocoline, respectively.

The condensation of 2 : 4-dimethylpyrrole with acetonylacetone and its self-condensation under the influence of zinc acetate in acetic acid were studied by Plancher (*Ber.*, 1902, **35**, 2606; *Atti R. Accad. Lincei*, 1902, (v), **11**, ii, 210; Plancher and Ciusa, *ibid.*, 1906, (v), **15**, ii, 453), who obtained a base, $C_{12}H_{15}N$, from each reaction. Plancher initially regarded the product from the former condensation as a bridged-ring compound containing a secondary nitrogen atom, but later preferred a tetramethylindolenine structure. This second postulate provided a closer analogy with the self-condensation of 2-methylpyrrole to 2 : 4-dimethylindole, and with the condensation of pyrrole and acetonylacetone with the formation of 4 : 7-dimethylindole.

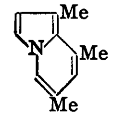
Similarly for the self-condensation of 2 : 4-dimethylpyrrole Plancher assumed partial hydrolysis to α-methyl-lævulic aldehyde, followed by condensation with dimethylpyrrole to give either another bridged-ring compound or a tetramethylindolenine. The condensation of skatole and acetonylacetone to give 1 : 5 : 8-trimethyl-2 : 3-benzopyrrocoline led Sir Robert Robinson and the present author to expect that the above-mentioned compounds would be found to be pyrrocolines (*J.*, 1950, 3136). This expectation has now been verified, and the compounds have been shown to be 1 : 3 : 5 : 8-tetramethylpyrrocoline (I) and 1 : 3 : 5 : 7-tetramethylpyrrocoline (II), respectively.



(I)

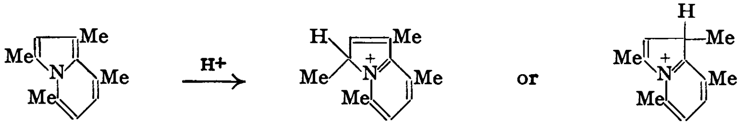


(II)



(III)

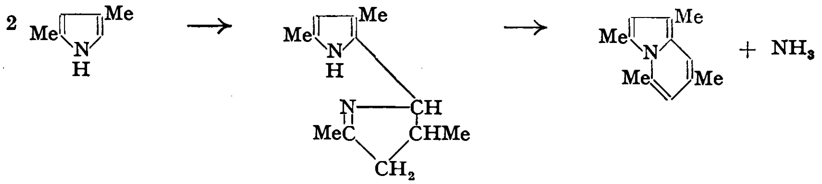
The condensation of 2 : 4-dimethylpyrrole with acetonylacetone was carried out according to the conditions described by Plancher, using zinc acetate in acetic acid for 24 hours at 118°, but a more convenient preparative method was found in the use of ethanolic hydrogen chloride for 15—20 minutes at 0°. The product had the properties of a substituted pyrrocoline : the base did not dissolve in cold dilute acid, but did so when warmed, and neither cooling nor dilution precipitated the base. In light petroleum or ethanol solution the base exhibited a blue fluorescence, and indeed the fluorescent properties of the base were visible in the crystalline solid. Addition of acid to the alcoholic solution destroyed the fluorescence, owing to fixation of the structure in the pyridinoid form :



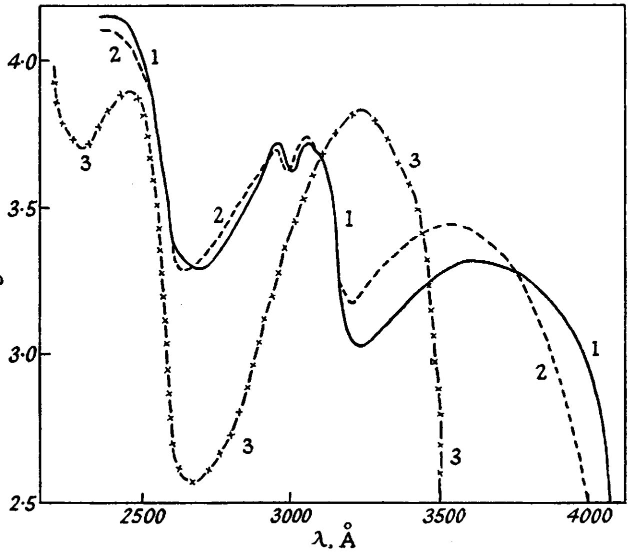
The base gives only a faint pine-shaving reaction, and does not give a coloured melt with anhydrous oxalic acid. It does not give an Ehrlich reaction or the ordinary pyrrole reactions with isatin or phenanthraquinone.

Reduction of the base was easily effected in ethanol, Raney nickel catalyst being used at elevated temperature and pressure, to give a strong tertiary base, $C_{12}H_{23}N$, which gave no reaction with nitrous acid in the cold or with acetic anhydride. Hence Plancher's formulations cannot be entertained, and the product must be 1 : 3 : 5 : 8-tetramethylpyrrocoline.

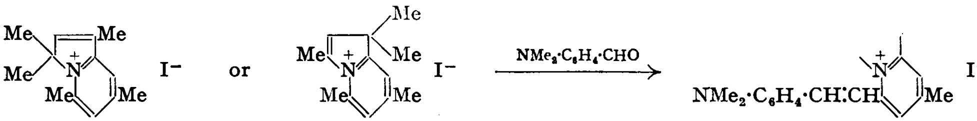
The self-condensation of 2 : 4-dimethylpyrrole gave a base isomeric with (I) and very similar in its chemical behaviour and characteristic ultra-violet absorption. There are two possible formulæ for this product, namely, (II) and (III). Of these, the former is to be preferred, if it may be assumed that the condensation proceeds *via* the initial formation of a dipyrrole, as occurs in the formation of indoles from pyrroles (Allen, Gilbert, and Young, *J. Org. Chem.*, 1937, **2**, 235) :



The methiodide of this base (assumed to be II) has the formula (IV*a* or *b*), the molecule containing a true pyridine ring, bearing methyl groups *ortho* and *para* to the nitrogen atom. These methyl groups should therefore be active, and should condense with aldehydes under the influence of a base. However, there is so far no adequate evidence which can lead to the differentiation of (IV*a*) and (IV*b*) :



1. 1 : 3 : 5 : 7-*Tetramethylpyrrocoline in ethanol solution.*
2. 1 : 3 : 5 : 8-*Tetramethylpyrrocoline in ethanol solution.*
3. 1 : 3 : 5 : 8-*Tetramethylpyrrocoline in* 0·05N-*ethanolic hydrochloric acid.*

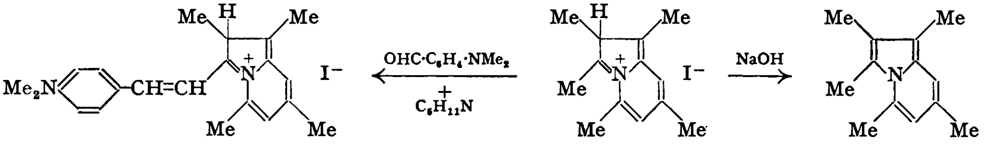


(IV*a*) (IV*b*)

The entering methyl group is assumed to enter either position 1 or 3 (most probably position 3, as in IV*a*), since these are the sites of attack by electrophilic substituents (Borrows, Holland, and Kenyon, *J.*, 1946, 1069 *et seq.*; 1947, 670, 672; Coulson and Longuet-Higgins, *Trans. Faraday Soc.*, 1947, **43**, 87). On the other hand, the methiodide from (III) has two methyl groups *meta* to the nitrogen atom, which are consequently inert.

It should be noted that there is a third formula possible for this methiodide (V), which could also condense with *p*-dimethylaminobenzaldehyde as indicated. However, this formulation is eliminated by the following evidence : if the methiodide has the formula (V), then solution of the substance in water followed by basification should lead to a pyrrocoline base (VI), *i.e.*, the original base with a methyl group in position 2. This type of reaction is not possible with (IV). The base could easily be recognised in solution by the characteristic pyrrocoline fluorescence; this simple experiment showed conclusively that no trace of a pyrrocoline base was obtained on basification, and no ether-soluble material was produced.

Condensation of the methiodide of the pyrrocoline base with *p*-dimethylaminobenzaldehyde in ethanol solution in the presence of piperidine rapidly gave a deep red cyanine dye, thus proving that the product of the self-condensation of 2 : 4-dimethylpyrrole is 1 : 3 : 5 : 7-tetramethylpyrrocoline.



(V) (VI)

The ultra-violet absorption curves of these two pyrrocolines are given in the figure. They show a marked resemblance to the curves for the 2 : 3-benzopyrrocolines (Robinson and Saxton, *loc. cit.*) although absorption does not extend into the visible region. In acid solution, the absorption is entirely different, and the curve is characteristic of a pyridine derivative.

EXPERIMENTAL.

(Analyses are by Drs. G. Weiler and F. B. Strauss, and absorption spectra by Dr. Strauss.)

1 : 3 : 5 : 8-*Tetramethylpyrrocoline* (I) (cf. Plancher, *Atti R. Accad. Lincei*, 1902, (v), **11**, ii, 213).—(*a*) 2 : 4-Dimethylpyrrole (5 g.), acetonylacetone (7·5 g.), and zinc acetate (7·5 g.) were heated under reflux in 90% acetic acid (250 ml.) for 24 hours. The solvent was removed *in vacuo*, the residue made alkaline, and the product distilled in steam. The solid was collected and crystallised from ethanol. 1 : 3 : 5 : 8-Tetramethylpyrrocoline was obtained as long prisms, m. p. 135°.

(*b*) A solution of 2 : 4-dimethylpyrrole (5 g.) and acetonylacetone (7·5 g.) in ethanol (25 ml.) was cooled in ice, and dry hydrogen chloride passed in until a portion of the solution gave no colour with Ehrlich's reagent (approx. 15—20 minutes). The solution was then made alkaline and distilled in steam. The solid was collected and crystallised from ethanol. 1 : 3 : 5 : 8-Tetramethylpyrrocoline (2 g.) was obtained as long prisms, m. p. 135° [Found : C, 83·2; H, 8·5; N, 8·0%; *M* (cryoscopic in camphor), 170. Calc. for $C_{12}H_{15}N$: C, 83·3; H, 8·7; N, 8·1%; *M*, 173].

Solutions of the base in ethanol or light petroleum exhibit a marked blue fluorescence. Addition of acid to the ethanolic solution destroys the fluorescence. As reported by Plancher, the base does not give pyrrole reactions, nor does it combine with methyl iodide in the cold.

Octahydro-1 : 3 : 5 : 8-*tetramethylpyrrocoline*.—1 : 3 : 5 : 8-Tetramethylpyrrocoline (1·5 g.) was reduced in ethanol solution, Raney nickel catalyst being used, with hydrogen at 80 atm. pressure at 100°. The product was isolated by distillation, and *octahydro*-1 : 3 : 5 : 8-*tetramethylpyrrocoline* (1·0 g.) obtained as a colourless oil, b. p. 86—87°/8 mm. (Found : C, 79·5; H, 12·8; N, 7·5. $C_{12}H_{23}N$ requires C, 79·6; H, 12·7; N, 7·7%).

The *picrate* crystallised from ethanol as yellow rhombs, m. p. 172—177° (Found : C, 53·1; H, 6·2; N, 13·5, 13·6. $C_{12}H_{23}N,C_6H_3O_7N_3$ requires C, 52·7; H, 6·3; N, 13·6%).

Octahydro-1 : 3 : 5 : 8-tetramethylpyrrocoline was a strong tertiary base which showed no reaction with nitrous acid in the cold or with acetic anhydride.

1 : 3 : 5 : 7-*Tetramethylpyrrocoline* (II) (cf. Plancher, *Ber.*, 1902, **35**, 2606).—A mixture of 2 : 4-dimethylpyrrole (5 g.), zinc acetate (22·5 g.), and acetic acid (150 ml.) was heated under reflux for 24 hours. The solvent was removed *in vacuo*, and the product, after being made strongly alkaline, was distilled in steam. The solid was collected from the distillate and crystallised from methanol, being obtained as prisms, m. p. 74—75°, which soon develop a delicate green tinge when kept in air. Plancher (*loc. cit.*) reports m. p. 74° and the same property (Found : C, 82·8; H, 8·6. Calc. for $C_{12}H_{15}N$: C, 83·3; H, 8·7%).

The base closely resembled the tetramethylpyrrocoline described above, showing a blue fluorescence in light petroleum solution and a blue-green fluorescence in ethanol. Addition of acid to the alcoholic solution destroyed the fluorescence.

1 : 3 : 5 : 7-*Tetramethylpyrrocoline methiodide* was prepared by heating a solution of the free base in methyl iodide for an hour at 100° in a sealed tube, and was obtained from ethanol or water as rhombs, m. p. 245—248° (Found : C, 49·9; H, 5·7; I, 40·4. $C_{12}H_{15}N,CH_3I$ requires C, 49·5; H, 5·7; I, 40·3%).

This methiodide (0·5 g.) was heated under reflux in ethanol solution for 2 hours with *p*-dimethylaminobenzaldehyde (0·2 g.) and piperidine (2 drops). An intense red colour developed, indicating formation of the dye, which was precipitated in an amorphous state by the addition of ether. Unfortunately it could not be obtained crystalline.

The methiodide (50 mg.) was dissolved in water (2·5 ml.) and excess of sodium hydroxide added. No turbidity was produced, and the solution remained colourless and non-fluorescent. The solution was then warmed for a few minutes, cooled, and extracted with ether. The whole of the material remained in the aqueous layer, which was still colourless and non-fluorescent.

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