736. *Studies in the Pyrrocoline Series.*

By E. D. Rossiter and J. E. Saxton.

2-Methylpyrrocoline has been formylated to give 3-formyl- or 1 : 3-diformyl-2-methylpyrrocoline. The former was identified by reduction to 2 : 3-dimethylpyrrocoline.

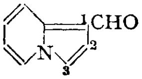
2 : 3-Dimethylpyrrocoline has been formylated to 1-formyl-2 : 3-dimethylpyrrocoline, Wolff–Kishner or lithium aluminium hydride reduction of which gives 1 : 2 : 3-trimethylpyrrocoline. This behaviour is analogous to that of 3-formylindole and 3-acetylindole.

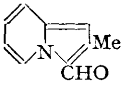
When 2-methylpyrrocoline reacts with methyl iodide the first methyl group enters the 3-, and the second the 1-position.

2 : 3-Dimethylpyrrocoline gives a Mannich base with formaldehyde and dimethylamine, the methiodide of which behaves as an alkylating agent in a manner analogous to that of gramine methiodide in the indole series.

There have hitherto been no reports of the preparation and properties of aldehydes in the pyrrocoline series. While they may be regarded simply as aromatic aldehydes, it is conceivable that their properties may be influenced by the presence of nitrogen in the molecule. For example, 1-formylpyrrocoline (I) may be regarded as the vinylogue of an amide. For the first experiments, the readily available 2-methylpyrrocoline was chosen.

(I)

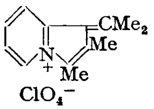




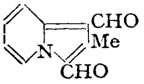
(II)

Since the pyrrocoline and the indole ring system frequently show similar reactivity, the 1- and the 3-position of pyrrocoline being analogous to the 2- and the 3-position of indole, it should be possible to formylate 2-methylpyrrocoline with the reagents successful in the indole series. In general, electrophilic reagents attack pyrrocolines in the 3-position, and, if this is substituted, the 1-position. There is one known exception, namely, the nitration of 2-methylpyrrocoline, which gives 2-methyl-1-nitropyrrocoline in addition to the 3-nitro-isomer (Borrows, Holland, and Kenyon, *J.*, 1946, 1077). Hence the structure of any formylation product requires proof. 2-Methylpyrrocoline with *N*-methylformanilide and phosphorus oxychloride gave 3-formyl-2-methylpyrrocoline (II), though the yield was small owing, probably, to the acid medium used in the reaction: the formyl group was quantitatively removed by hot dilute mineral acid in 2 min.

The structure of (II) was proved by Wolff–Kishner reduction to 2 : 3-dimethylpyrrocoline, and preparation of the latter according to Ochiai and Tsuda's method (*Ber.*, 1934, **67**, 1011). The melting point (39·5—40·5°) of our samples of 2 : 3-dimethylpyrrocoline was somewhat higher than that recorded by Ochiai and Tsuda (35—36°). This may be due partially to the use of purer starting material, but is probably mainly due to purification of the product by sublimation, by far the most satisfactory technique for low-melting pyrrocolines.



(III)



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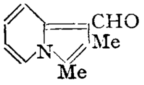
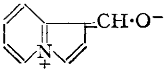


(V)



(V*a*)

2 : 3-Dimethylpyrrocoline is a weaker base than 2-methylpyrrocoline, and under ordinary conditions does not form a picrate; it was therefore characterised as the perchlorate. Crystallisation of the latter from acetone containing perchloric acid gave a derivative, $C_{13}H_{16}O_4NCl$, which is presumably 2 : 3-dimethyl-1-*iso*propylidene-pyrrocolinium perchlorate (III).

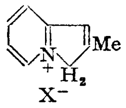
Under Reimer–Tiemann conditions 2-methylpyrrocoline gave 1 : 3-diformyl-2-methylpyrrocoline (IV). It was hoped that the formyl group in the more reactive 3-position might be removed preferentially by acid hydrolysis, but this proved to be impracticable.

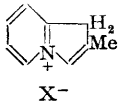
2 : 3-Dimethylpyrrocoline was formylated to 1-formyl-2 : 3-dimethylpyrrocoline (V), the structure of which was proved by Wolff–Kishner reduction to 1 : 2 : 3-trimethylpyrrocoline and unambiguous synthesis of the latter. Reduction of (V) with lithium aluminium hydride gave mainly 1 : 2 : 3-trimethylpyrrocoline. In this respect it behaves more like an amide than an aldehyde, possibly owing to participation in the structure of canonical forms such as (V*a*). This is reflected in the decreased tendency of both (II) and (V) to yield derivatives of the carbonyl group. Thus 1-formyl-2 : 3-dimethylpyrrocoline reacts only sluggishly with semicarbazide in ethanol, fails to undergo the Cannizzaro reaction (this may, however, be partly due to steric hindrance), and cannot be oxidised by silver oxide. 3-Formyl-2-methylpyrrocoline is even less reactive, and could not even be induced to form a semicarbazone.

The complete elimination of oxygen on reduction of the carbonyl group with lithium aluminium hydride is found also in the indole series. 3-Formylindole and 3-acetylindole are reduced by an excess of reducing agent to skatole and 3-ethylindole. These carbonyl compounds can again be regarded as vinylogues of amides.

It was pointed out by one of the present authors (*J.*, 1951, 3240) that the pyrrocolinium ion contains a true pyridine ring. Thus 2-methylpyrrocolinium salts can be represented by VI(*a* or *b*), the former being the more probable. Reaction of 2-methylpyrrocoline with

(VI*a*)

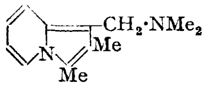




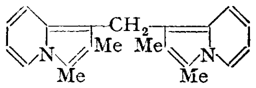
(VI*b*)

methyl iodide at room temperature gave a crystalline product, identified as the hydriodide of 2-methylpyrrocoline. The much weaker basic product of methylation remained in the mother-liquors, and could not be separated from unchanged 2-methylpyrrocoline by fractional crystallisation of base or picrate, by fractional sublimation, or by chromatography. The methylation product was finally identified as 2 : 3-dimethylpyrrocoline by formylation of the mixture of bases obtained from the mother-liquors. 1-Formyl-2 : 3-dimethylpyrrocoline was isolated and identified, thus showing that attack by methyl iodide was first at the 3-position. This favours (VI*a*) as the formula of the ion from 2-methylpyrrocoline. Further methylation with methyl iodide at elevated temperatures gave 1 : 2 : 3-trimethylpyrrocoline and its methiodide.

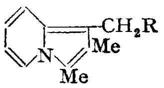
The analogy between pyrrocolines and indoles has been further demonstrated by preparation of the Mannich base (VII) from 2 : 3-dimethylpyrrocoline. A by-product $C_{21}H_{22}N_2$ is considered to be di-(2 : 3-dimethyl-1-pyrrocolinyl)methane (VIII) and was readily obtainable by the direct condensation of 2 : 3-dimethylpyrrocoline and formaldehyde. The salts of the Mannich base are very unstable, and decompose more readily than the corresponding salts of gramine. In consequence the methiodide of (VII) behaves as an alkylating agent : with sodium methoxide it gives 1-methoxymethyl-2 : 3-dimethylpyrrocoline (IX; R = OMe), and with potassium cyanide it readily gives 1-cyanomethyl-2 : 3-dimethylpyrrocoline (IX; R = CN).



(VII)



(VIII)



(IX)

1 : 2-Dimethyl- and 2-ethyl-pyrrocoline and their derivatives are also described below.

EXPERIMENTAL

3-*Formyl*-2-*methylpyrrocoline*.—*N*-Methylformanilide (15·6 g.) and phosphorus oxychloride (17·8 g.) were mixed, with mechanical stirring and exclusion of atmospheric moisture. After 15 min. at room temperature, ethylene dichloride (75 g.) was added and the solution cooled in an ice-bath. When the internal temperature had reached 0°, 2-methylpyrrocoline (6 g.), dissolved in a small amount of ethylene dichloride, was added dropwise at such a rate that the temperature did not rise above 10°. The mixture was kept at 0° for a further hour with stirring, finely divided calcium carbonate (20 g.) was added, and the ice-bath removed. The mixture was gently heated, with stirring; a violent reaction occurred, external cooling sometimes being necessary. When the reaction had subsided the mixture was heated under reflux for 2 hr., then cooled and poured into a mixture of sodium acetate (75 g.), water (75 c.c.), and ice (15 g.). The ethylene dichloride and unchanged 2-methylpyrrocoline were removed in steam (500 c.c. of distillate): continuation of the distillation gave a pale green distillate, from which needles gradually separated. The solid was collected and crystallised from light petroleum (b. p. 40—60°). 3-*Formyl*-2-*methylpyrrocoline* (0·6 g., 8·2%) was obtained as pale green rhombs, m. p. 56·5—57·5° (Found: C, 75·6; H, 5·5; N, 8·6. $C_{10}H_9ON$ requires C, 75·4; H, 5·7; N, 8·8%).

The aldehyde (0·05 g.) was triturated with a few drops of 60% aqueous perchloric acid. Addition of ether gave a yellow precipitate of the *hemi-perchlorate*, m. p. 173—175° (decomp.) after darkening at 140° and sintering at 160° (Found: C, 57·2, 57·7; H, 4·7, 4·5; N, 7·2; Cl, 9·0. $C_{20}H_{19}O_6N_2Cl$ requires C, 57·3; H, 4·5; N, 6·7; Cl, 8·5%). 3-Formyl-2-methylpyrrocoline failed to give a silver mirror or a semicarbazone, but gave a dark red precipitate, decomp. 200°, with 2 : 4-dinitrophenylhydrazine in concentrated sulphuric acid and ethanol. Attempts to purify this derivative by recrystallisation from ethyl acetate were unsuccessful.

The formyl group was quantitatively removed in 2 min. by an excess of boiling 2N-hydrochloric acid.

In the infra-red region the carbonyl band is at 6·10 μ.

Reduction of 3-*Formyl*-2-*methylpyrrocoline*.—3-Formyl-2-methylpyrrocoline (1 g.), 100% hydrazine hydrate (4·3 c.c.), ethanol (40 c.c.), and sodium ethoxide (from 2 g. of sodium) were heated together at 180° for 22 hr. The *azine* which separated was collected at the pump, recrystallised from tetrahydrofuran, and obtained as orange needles, m. p. 254° (decomp.) (1 g., 51%) (Found: C, 76·8, 76·2; H, 6·0, 5·8; N, 17·8. $C_{20}H_{18}N_4$ requires C, 76·4; H, 5·7; N, 17·8%).

The filtrate from the reaction mixture was diluted with water, and the base isolated by means of ether and purified by sublimation at 100°/20 mm. 2 : 3-Dimethylpyrrocoline (0·1 g.) was obtained as colourless plates with a blue fluorescence, m. p. 39·5—40·5°, alone or mixed with authentic 2 : 3-dimethylpyrrocoline (Found: C, 82·9; H, 7·8; *C*-Me, 20·4. Calc. for $C_{10}H_{11}N$: C, 82·8; H, 7·6; 2*C*-Me, 20·8%).

2 : 3-*Dimethylpyrrocoline*.—This was prepared according to Ochiai and Tsuda's method (*Ber.*, 1934, **67**, 1011) from pure 1-bromoethyl methyl ketone and α-picoline, and purified by sublimation at 100°/20 mm. 2 : 3-Dimethylpyrrocoline was obtained as colourless plates with a blue fluorescence, m. p. 39·5—40·5°.

Freshly sublimed 2 : 3-dimethylpyrrocoline (0·05 g.) was triturated with aqueous perchloric acid (0·2 c.c. of 60%), then ether was added to complete the precipitation. The *perchlorate* of 2 : 3-dimethylpyrrocoline was obtained from methanol as colourless rhombs with a slight blue tinge, m. p. 74—75·5° (Found: C, 49·1; H, 5·1. $C_{10}H_{12}O_4NCl$ requires C, 48·9; H, 4·9%). Recrystallisation of this from acetone containing an excess of perchloric acid yielded 2 : 3-*dimethyl*-1-iso*propylidenepyrrocolinium perchlorate*, yellow needles, which darkened above 225°, decomp. 230—233° (Found: C, 54·7; H, 5·5. $C_{13}H_{16}O_4NCl$ requires C, 54·6; H, 5·6%).

1 : 3-*Diformyl*-2-*methylpyrrocoline*.—A boiling solution of 2-methylpyrrocoline (10 g.) in chloroform (85 c.c.) and ethanol (200 c.c.) was stirred, and a solution of potassium hydroxide (125 g.) in water (150 c.c.) added during 2½ hr.; boiling was continued for a further 30 min. and the mixture then cooled. The potassium chloride which separated was removed by filtration, the solid was washed with chloroform, and the washings were added to the filtrate, which was then distilled in steam. When all the chloroform had been removed the steam-distillation was continued until approx. 500 c.c. of pale green distillate had been collected. This was extracted with ether, the ethereal layer was dried (Na_2SO_4), the ether removed, and the residue recrystallised from light petroleum (b. p. 40—60°). A small amount of 3-formyl-2-methylpyrrocoline was obtained as pale green needles, m. p. and mixed m. p. 56·5—57·5°. The mother-liquors from the steam-distillation were filtered whilst hot, and the residue extracted with boiling water (6 × 500 c.c.) (charcoal). The solid which separated from the combined filtrates was recrystallised from tetrahydrofuran, giving 1 : 3-*diformyl*-2-*methylpyrrocoline* (7 g., 49%) as pale yellow needles, m. p. 210° (Found: C, 70·8; H, 4·8; N, 7·3. $C_{11}H_9O_2N$ requires C, 70·6; H, 4·8; N, 7·5%).

1 : 3-Diformyl-2-methylpyrrocoline failed to give a silver mirror but gave a dark-red precipitate with 2 : 4-dinitrophenylhydrazine in concentrated sulphuric acid and ethanol. The *phenylhydrazone*, prepared in 30% acetic acid, formed golden-yellow plates (from methanol),

m. p. 177—179° (decomp.) (sintering above 170°) (Found: C, 74·0; H, 5·5; N, 14·8. $C_{17}H_{15}ON_3$ requires C, 73·6; H, 5·4; N, 15·2%). Attempts to remove the 3-formyl group selectively by various mixtures of hydrochloric and acetic acids failed.

1-*Formyl*-2 : 3-*dimethylpyrrocoline*.—2 : 3-Dimethylpyrrocoline (6 g.) was formylated with *N*-methylformanilide (15·6 g.) and phosphorus oxychloride (17·8 g.) as described for 2-methylpyrrocoline. After removal of the ethylene dichloride in steam, the mother-liquors were diluted with water (750 c.c.), boiled (charcoal), and filtered. The residue was extracted with boiling water (2 × 500 c.c.). The solid which separated from the cooled filtrates was dried and recrystallised from light petroleum (b. p. 60—80°) (charcoal). 1-*Formyl*-2 : 3-*dimethylpyrrocoline* (2·6 g., 36%) was obtained as colourless needles, m. p. 94—95° (Found: C, 76·3; H, 6·4; N, 7·9. $C_{11}H_{11}ON$ requires C, 76·5; H, 6·3; N, 8·0%). 1-Formyl-2 : 3-dimethylpyrrocoline failed to give a silver mirror, but gave a dark red precipitate with 2 : 4-dinitrophenylhydrazine in concentrated sulphuric acid and ethanol. In the infra-red region the carbonyl bands are at 6·08 and 6·17 μ.

The *semicarbazone*, prepared in anhydrous ethanol, was obtained from tetrahydrofuran as yellow-green prisms, m. p. 209° (Found: C, 63·2, 63·5; H, 6·8, 6·7; N, 21·4, 21·4. $C_{12}H_{14}ON_4,\frac{1}{2}C_4H_8O$ requires C, 63·2; H, 6·8; N, 21·1%) (Found, on sample dried at 100° for 4 hr.: C, 61·9; H, 6·0; N, 25·3. $C_{12}H_{14}ON_4$ requires C, 62·6; H, 6·1; N, 24·4%). The *perchlorate* crystallised from water as pale yellow needles, decomp. 194—196° (sinters at 155°, becomes green at 185°) (Found: C, 45·1; H, 4·7. $C_{11}H_{14}O_6NCl$ requires C, 45·6; H, 4·8%).

Reduction of 1-*Formyl*-2 : 3-*dimethylpyrrocoline*.—1-Formyl-2 : 3-dimethylpyrrocoline (1 g.), 100% hydrazine hydrate (4·3 c.c.), and metallic sodium (2 g.), dissolved in ethanol (40 c.c.), were heated together at 200° for 24 hr. The resulting solution was filtered, diluted with water, and extracted with ether. The semi-solid amber product obtained on removal of the ether was sublimed at 100°/20 mm. on to a cold finger cooled with solid carbon dioxide and ethanol. 1 : 2 : 3-*Trimethylpyrrocoline* was obtained as colourless plates, m. p. 12—13° (Found: N, 8·8. $C_{11}H_{13}N$ requires N, 8·8%). The *perchlorate* formed colourless prisms, m. p. 126—128°, from methanol (Found: C, 50·8; H, 5·6; N, 5·4; Cl, 13·8. $C_{11}H_{14}O_4NCl$ requires C, 50·9; H, 5·4; N, 5·4; Cl, 13·7%).

Reduction of 1-*Formyl*-2 : 3-*dimethylpyrrocoline with Lithium Aluminium Hydride*.—1-Formyl-2 : 3-dimethylpyrrocoline (1 g.) in dry ether (100 c.c.) was added dropwise to a stirred solution of lithium aluminium hydride (1 g.) in dry ether (100 c.c.). The mixture was then heated under reflux for 2 hr. and set aside for a further 36 hr. Dilute sulphuric acid (100 c.c.) was added, the ethereal layer was dried, and the solvent removed. The residual oil (0·5 g.) was distilled, and collected at 55°/0·07 mm. (bath-temp.). The crude 1 : 2 : 3-trimethylpyrrocoline so obtained was purified by sublimation at 100°/20 mm. on to a cold finger, and obtained as colourless plates with a blue fluorescence, m. p. 12—13°. The perchlorate formed colourless prisms, m. p. and mixed m. p. 126—128°, from methanol (Found: C, 50·9; H, 5·7; N, 5·3; Cl, 13·8%).

1 : 2 : 3-*Trimethylpyrrocoline*.—A mixture of 2-ethylpyridine (10 g.) and 1-bromoethyl methyl ketone (15·5 g.) was heated on a steam-bath for 3 hr. and allowed to cool. The resulting brown solid was washed with ethanol–ether (1 : 1; 20 c.c.) and dissolved in distilled water (400 c.c.). Sodium hydrogen carbonate (25 g.) was added to the solution, which was heated on a steam-bath for 1 hr. and then distilled in steam. The pale yellow oil which separated from the aqueous distillate was extracted with ether, and the ethereal layer was dried and distilled. 1 : 2 : 3-Trimethylpyrrocoline (10 g., 67%), b. p. 85—87°/0·095 mm., was obtained as a pale yellow oil, rapidly darkening in air and light (Found: C, 82·9; H, 8·0; N, 9·2. Calc. for $C_{11}H_{13}N$: C, 83·0; H, 8·2; N, 8·8%). The perchlorate formed prisms, m. p. and mixed m. p. 126—128°. The *picrate* was obtained from ethanol as a yellow microcrystalline solid, m. p. 94—95° (decomp.) (Found: C, 52·8; H, 4·2. $C_{17}H_{16}O_7N_4$ requires C, 53·1; H, 4·1%).

Reduction of 3-*Formylindole*.—3-Formylindole (0·19 g.) in pure tetrahydrofuran (25 c.c.) was added dropwise during 90 min. to lithium aluminium hydride (0·2 g.) in ether (80 c.c.). The solution was heated under reflux for 2 hr., then cooled, and the excess of reagent destroyed by addition of ethanol and dilute hydrochloric acid. The organic layer was dried and evaporated. The residue crystallised from light petroleum (b. p. 40—60°) as colourless plates, m. p. 92—94°, having a pronounced skatole odour. The picrate was prepared in benzene, and obtained as red needles, m. p. and mixed m. p. with skatole picrate, 171—172°.

Reduction of 3-*Acetylindole*.—This was reduced with excess of lithium aluminium hydride as described above for 3-formylindole. The product was converted into its picrate, which was obtained from benzene as red needles, m. p. and mixed m. p. with authentic 3-ethylindole picrate, 120—121° (Found : C, 51·7; H, 3·9; N, 14·7. Calc. for $C_{10}H_{11}N,C_6H_3O_7N_3$: C, 51·35; H, 3·75; N, 15·0%).

Reaction of 2-*Methylpyrrocoline with Methyl Iodide*.—(a) 2-*Methylpyrrocoline hydriodide*. A solution of freshly sublimed 2-methylpyrrocoline (6 g.) in methyl iodide (20 c.c.) was set aside overnight. Ether was then added to complete the precipitation of the salt, which was collected, washed with ether, and recrystallised from ethanol. 2-*Methylpyrrocoline hydriodide* (5·5 g., 42%) was obtained as colourless rhombs, m. p. 165—170° (decomp.), which in air and light became dark green (Found : C, 41·9; H, 4·1; I, 48·9. $C_9H_{10}NI$ requires C, 41·7; H, 3·9; I, 49·0%).

(b) *Identification of* 2 : 3-*dimethylpyrrocoline*. A solution of freshly sublimed 2-methylpyrrocoline (4·3 g., 2 mols.) and methyl iodide (2·85 g., 1 mol.) in methanol (30 c.c.) was heated at 100° for 3 hr. The solvent was then removed, the crude 2-methylpyrrocoline hydriodide was washed well with dry ether, and the combined ethereal washings were dried and evaporated. The mixture of 2-methylpyrrocoline and 2 : 3-dimethylpyrrocoline was sublimed at 100°/20 mm. This mixture (1·5 g.) was then formylated as described above for pure 2 : 3-dimethylpyrrocoline, the 3-formyl-2-methylpyrrocoline being removed in the steam-distillation. 1-Formyl-2 : 3-dimethylpyrrocoline (0·1 g.) was obtained from light petroleum (b. p. 60—80°) as colourless needles, m. p. and mixed m. p. 93—94°, identity being confirmed by comparison of infra-red spectra.

(c) 1 : 2 : 3-*Trimethylpyrrocoline methiodide*. 2-Methylpyrrocoline (7 g.), methyl iodide (25 c.c.), and methanol (30 c.c.) were heated together at 100° for 24 hr. The solvent was removed and the residue triturated with acetone until crystallisation was complete. The solid was collected, washed with acetone, and recrystallised from the same solvent. 1 : 2 : 3-*Trimethylpyrrocoline methiodide* (4 g.) was obtained as pale brown rhombs, m. p. 197·5° (sinters above 180°) (Found : C, 47·9; H, 5·6; I, 42·3. $C_{12}H_{16}NI$ requires C, 47·8; H, 5·3; I, 42·2%). A solution of the pure methiodide in water gave no precipitate on basification with sodium hydroxide solution.

(d) 1 : 2 : 3-*Trimethylpyrrocoline*. 2-Methylpyrrocoline (2·1 g.), methyl iodide (10 c.c.), and methanol (10 c.c.) were heated together at 100° for 24 hr. The solvent was then removed, the crude methiodide (2 g.) dissolved in water, and excess of dilute sodium hydroxide solution added. The liberated base was extracted with ether, the ethereal layer dried, and the solvent removed. Distillation of the residue gave 1 : 2 : 3-trimethylpyrrocoline (0·1 g.) as a viscous yellow oil, b. p. 150°/15 mm. (bath-temp.), m. p. 12—13° (Found : C, 83·1; H, 8·4; N, 8·3. Calc. for $C_{11}H_{13}N$: C, 83·0; H, 8·2; N, 8·8%). The perchlorate formed prisms, m. p. and mixed m. p. 126—128°.

1-*Dimethylaminomethyl*-2 : 3-*dimethylpyrrocoline*.—A mixture of 30% aqueous dimethylamine (16·3 g., 1·05 mols.) and glacial acetic acid (14·5 g., 2·33 mols.) was cooled in an ice-bath. When the temperature had fallen to 5°, 40% aqueous formaldehyde (7·9 g., 1·0 mol.) was added. The resulting mixture was cooled to 5° and added to 2 : 3-dimethylpyrrocoline (15 g.). The mixture was shaken gently until it became homogeneous, set aside at room temperature for 45 hr., and then poured into a solution of sodium hydroxide (14·5 g.) in water (100 c.c.). The oil which separated was extracted with ether, the ethereal extracts were washed exhaustively with 2N-hydrochloric acid, and the combined acid extracts made alkaline by the addition of an excess of 2N-sodium hydroxide. The liberated base was extracted with ether, and the ethereal layer dried and concentrated. The yellow prisms which separated were collected, washed with ether, and crystallised from light petroleum (b. p. 60—80°), giving *di*-(2 : 3-*dimethyl*-1-*pyrrocolinyl*)*methane* (0·35 g.) as yellow needles, m. p. 109—110° (Found : C, 83·2; H, 7·4; N, 9·4. $C_{21}H_{22}N_2$ requires C, 83·5; H, 7·3; N, 9·3%).

A further amount (2·5 g.) of less pure di-(2 : 3-dimethyl-1-pyrrocolinyl)methane was obtained on removal of the solvent from the ethereal extracts which had been washed with hydrochloric acid. A small amount of the pure base was triturated with a few drops of 60% aqueous perchloric acid, and ether was added to complete the precipitation. The colourless *diperchlorate* which separated was washed thoroughly with ether and dried in a vacuum-desiccator; it had m. p. 179—181° (decomp.) (Found : C, 50·3; H, 5·0. $C_{21}H_{24}O_8N_2Cl_2$ requires C, 50·1; H, 4·8%). This compound decomposed on crystallisation from water or methanol.

The ethereal filtrate after removal of di-(2 : 3-dimethyl-1-pyrrocolinyl)methane was concentrated and the residue (11 g.) distilled; 1-*dimethylaminomethyl*-2 : 3-*dimethylpyrrocoline* (5·3 g.) was obtained as pale yellow oil, b. p. 85—92°/0·05 mm., which on exposure to air and light became dark brown (Found : C, 77·1; H, 9·1; N, 13·9. $C_{13}H_{18}N_2$ requires C, 77·2; H, 8·9; N, 13·9%). In concentrated ethanolic solution it gave a *picrate* as a red microcrystalline solid, sintering at 133°, m. p. 137—139° (decomp.) (Found : C, 53·4; H, 4·9; N, 16·3. $C_{19}H_{21}O_7N_5$

requires C, 52·9; H, 4·9; N, 16·2%). An attempt was made to crystallise the picrate from benzene, but decomposition occurred and the picrate of dimethylamine was isolated as golden-yellow rhombs, m. p. 155·5—156·5° (reported m. p. 156°) (Found: C, 35·2; H, 3·7; N, 20·4. Calc. for $C_8H_{10}O_7N_4$: C, 35·0; H, 3·7; N, 20·4%).

Di-(2 : 3-*dimethyl*-1-*pyrrocolinyl*)*methane*.—Formaldehyde (40% aqueous; 2 g.) was added to a solution of 2 : 3-dimethylpyrrocoline (2·5 g.) in ethanol (20 c.c.) and concentrated hydrochloric acid (1 c.c.), kept for 4 hr., and then basified with dilute sodium hydroxide solution. The yellow needles which separated were collected, washed with ether, and recrystallised from light petroleum (b. p. 60—80°); di-(2 : 3-dimethyl-1-pyrrocolinyl)methane (2·0 g., 76·8%) was obtained as yellow needles, m. p. 109—110°, undepressed on admixture with a sample obtained as above. The identity of the product was confirmed by the m. p. of the perchlorate.

1-*Methoxymethyl*-2 : 3-*dimethylpyrrocoline*.—Freshly distilled 1-dimethylaminomethyl-2 : 3-dimethylpyrrocoline (0·5 g.) was added to a cooled solution of sodium (0·18 g.) in methanol (10 c.c.). After the addition of methyl iodide (1·05 g.), a stream of dry nitrogen was passed for 24 hr. through the solution. The tetramethylammonium iodide which separated from the reaction mixture was removed by filtration, the alcoholic filtrate poured into water and extracted with ether, and the ethereal layer separated and dried. The solvent was removed and the brown oil which remained was distilled. 1-*Methoxymethyl*-2 : 3-*dimethylpyrrocoline* (0·15 g.) was obtained as a pale yellow oil (which became dark brown in air and light), b. p. 110°/0·05 mm. (bath-temp.) (Found: C, 76·1; H, 7·8. $C_{12}H_{15}ON$ requires C, 76·2; H, 7·9%)

1-*Cyanomethyl*-2 : 3-*dimethylpyrrocoline*.—Potassium cyanide (5·5 g.) in water (60 c.c.) was added to a mixture of freshly distilled 1-dimethylaminomethyl-2 : 3-dimethylpyrrocoline (6·5 g.), methyl iodide (13·65 g.), and ethanol (100 c.c.). A stream of dry nitrogen was passed through the reaction mixture for 24 hr. The pale yellow needles which separated were collected, and washed once with ethanol, and then thoroughly with water. Recrystallisation from light petroleum (b. p. 40—60°) gave 1-*cyanomethyl*-2 : 3-*dimethylpyrrocoline* (2 g.) as pale yellow needles m. p. 78—79° (Found: C, 78·4; H, 6·6. $C_{12}H_{12}N_2$ requires C, 78·3; H, 6·5%). A further amount (0·5 g.) of the nitrile was obtained on removal of the ethanol from the mother-liquors. In the infra-red region the nitrile band is at 4·48 μ.

1 : 2-*Dimethylpyrrocoline*.—A mixture of 2-ethylpyridine (10·7 g.) and chloroacetone (9·3 g.) was heated on a steam-bath for 3 hr. and allowed to cool. The resulting brown solid was washed with ethanol–ether (1 : 1; 20 c.c.) and dissolved in distilled water (400 c.c.). Sodium hydrogen carbonate (25 g.) was added to the solution, which was heated on a steam-bath for 1 hr., and then distilled in steam. The cream-coloured solid which separated from the aqueous distillate was extracted with ether, the ethereal layer was dried, and the solvent removed. 1 : 2-*Dimethylpyrrocoline* (8 g., 55%) was purified by sublimation at 100°/20 mm., and obtained as colourless plates with a blue fluorescence, m. p. 57—58° (Found: C, 82·6; H, 7·6; N, 9·6. $C_{10}H_{11}N$ requires C, 82·8; H, 7·6; N, 9·6%). The *perchlorate* was obtained from methanol as colourless rhombs with a slight pink tinge, m. p. 128—129° (sintering at 125°) (Found: C, 48·8; H, 5·0. $C_{10}H_{12}O_4NCl$ requires C, 48·9; H, 4·9%). The *picrate* was obtained from ethanol as yellow rhombs, m. p. 130—132° (decomp.) (Found: C, 51·4; H, 3·9. $C_{16}H_{14}O_7N_4$ requires C, 51·3; H, 3·7%).

2-*Ethylpyrrocoline*.—A mixture of α-picoline (10 g.) and bromomethyl ethyl ketone (16·4 g.) was heated on the water-bath for 2 hr. and then cooled. The solid quaternary salt which separated was washed once with ethanol–ether (1 : 1; 50 c.c.). The crude product was dissolved in water (200 c.c.), sodium hydrogen carbonate (20 g.) was added, and the mixture was heated on the steam-bath for 1 hr. and then distilled in steam. The cream-coloured solid which separated from the distillate was collected and dissolved in ether, the solution dried, and the ether removed. The crude product (14·5 g., 93%) was purified by sublimation at 100°/20 mm., 2-*ethylpyrrocoline* being obtained as colourless plates becoming dark brown in air and light, m. p. 41° (Found: C, 82·9; H, 7·6. $C_{10}H_{11}N$ requires C, 82·8; H, 7·6%). The *perchlorate* was obtained from methanol as pale blue needles, m. p. 121—123° to a blue liquid (Found: C, 48·5; H, 4·9; N, 5·8; Cl, 14·6. $C_{10}H_{12}O_4NCl$ requires C, 48·9; H, 4·9; N, 5·7; Cl, 14·5%). The *picrate*, prepared in ethanol, was obtained from ethanol as yellow plates, m. p. 104—105·5° (Found: C, 51·2; H, 4·0. $C_{16}H_{14}O_7N_4$ requires C, 51·3; H, 3·7%).

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