103. *Methylation of Some Pyrroles and 2-Pyrrolines.*

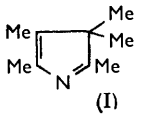
By H. Booth, A. W. Johnson, F. Johnson, and R. A. Langdale-Smith.

The action of methyl iodide on 2,5-dibenzyl-3,4-dimethylpyrrole, like that on 2,3,4,5-tetramethylpyrrole, results in exclusive methylation at the 2-position. Both 1,2- and 1,4-addition of methylmagnesium iodide to the methiodide of 2,2,3,4,5-pentamethyl-2*H*-pyrrole occurs, the latter being the main reaction and thus providing an example of β-methylation in a five-membered nitrogenous ring. A similar reaction with the dipyrromethene (XIII) results in ready 1,6-addition, to give the *meso*-methylated dipyrromethane (XIV). Methylation of 1,2-dialkyl-2-pyrrolines occurs at the exocyclic β-carbon atom even when the double bond is largely endocyclic in the original pyrroline; but allylation of 1,2-dimethyl-2-pyrroline can occur at either the endo- or the exo-cyclic β-carbon atom.

The demonstration that δ-aminolævulic acid and porphobilinogen are intermediates in the biosynthesis of vitamin B_{12}[1] as well as of the natural porphyrins [2] suggests that the methyl groups of the vitamin are introduced after the formation of the macrocycle. Four of these methyl groups are sited on the β-carbons of the five-membered rings and we have endeavoured to ascertain the nature of the intermediate which undergoes β-methylation by examining the methylation of a variety of model pyrroles and pyrrolines, especially as *C*-methylation at the β-position of a five-membered nitrogenous ring has not hitherto been reported. We have already shown [3] that methylation of the Grignard derivatives of *C*-methylpyrroles produces tetra- and penta-methyl-2*H*-pyrroles but we were unable to detect any methylated 3*H*-pyrroles by chemical reactions. A re-examination of the methylation product of 2,3,4,5-tetramethylpyrrole [3] by gas-chromatography has failed to reveal any of the isomeric 2,3,3,4,5-pentamethyl-3*H*-pyrrole (I) as impurity in the main product, 2,2,3,4,5-pentamethyl-2*H*-pyrrole (II). The corresponding "anhydro-base"

[1] Corcoran and Shemin, *Biochim. Biophys. Acta*, 1957, **25**, 661.
[2] For a review, see Gibson, Matthew, Neuberger, and Tait, *Nature*, 1961, **192**, 204.
[3] Booth, Johnson, Markham, and Price, *J.*, 1959, 1587.

from (II), however, has proved to be a mixture of the two isomers A ($\lambda_{max.}$ 212 and 279 mμ) and B($\lambda_{max.}$ 263 mμ), each of which is convertible into the methoperchlorate and methopicrate of (II) when treated with the appropriate acid. Structure (III), possessing the longer chromophore, is suggested for isomer A and (IV) for B.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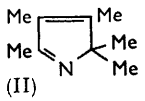
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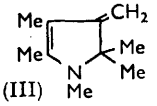
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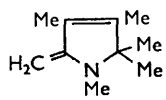
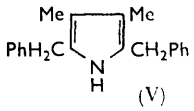

(IV)

Methylation of the Grignard derivative of 2,5-dibenzyl-3,4-dimethylpyrrole (V) has now been studied, as this molecule is more analogous both electronically and sterically to the pyrrole fragment of a porphyrinogen, a possible substrate for biochemical methylation. The main product of the methylation was a weakly basic compound, characterised as a picrate; from its spectral properties, it was either the 2*H*-pyrrole (VI) or the 3*H*-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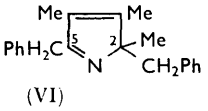
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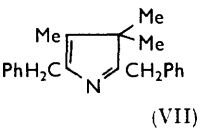
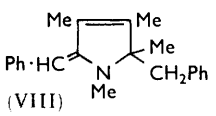

(VII)

pyrrole (VII). The nuclear magnetic resonance spectrum of the base favoured structure (VI). In carbon tetrachloride solution, the methylenic protons appeared as a singlet (area, 2 protons) and a quartet (area, 2 protons) at relatively higher field. The singlet is associated with the methylenic protons of the freely rotating 5-benzyl group of (VI) and the quartet with the methylenic protons of the non-rotating 2-benzyl group. The methylenic protons of isomer (VII) would presumably give rise to two quartets. Further evidence in favour of structure (VI) was provided by the failure to detect acetone in the permanganate-oxidation product and also the position of absorption (335 mμ) in the ultraviolet spectrum of the derived anhydro-base (VIII), whereas the alternative structure (IX) from (VII) would presumably absorb at a lower wavelength.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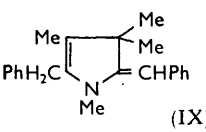
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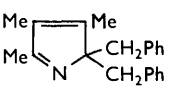
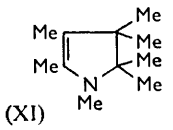

(X)

An attempt to synthesise compound (VI) by benzylation of the Grignard derivative of 2-benzyl-3,4,5-trimethylpyrrole gave a weakly basic product which was not identical with (VI) but from its spectral properties was a 2*H*- or 3*H*-pyrrole. The structure of the benzylation product was shown to be (X) by an examination of the nuclear magnetic resonance spectrum. In carbon tetrachloride solution the methylenic protons appeared as a symmetrical quartet (area, 4 protons), showing that the benzyl groups were in equivalent positions; alternative 3*H*-pyrrolic structures would contain non-equivalent benzyl groups, *e.g.*, (VI).

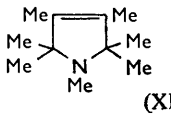
The methiodide of the 2*H*-pyrrole (II) was very susceptible to nucleophilic addition and with methylmagnesium iodide gave a mixture of two bases (XI) and (XII) which were separated by utilisation of their differing basic strengths and by fractional crystallisation of the picrates. The stronger base was the α-enamine (XI) formed by 1,4-addition and identified by its infrared spectrum; the other product (XII) was formed by 1,2-addition. The recognition of the nature of (XI) provides the first example of methylation at a β-carbon in the pyrrole series.

As an extension of this reaction, the addition of methylmagnesium iodide to the salts of dipyrromethenes was investigated. The salts of the dipyrromethenes with the hydrogen halides are merely reconverted into the free base when treated with Grignard reagent, and

the *NN*-dimethyldipyrromethene salts are often difficult to prepare for steric reasons. Corwin and Brunings [4] have, however, described the preparation of salts (XIII) and have shown that addition of hydroxide or methoxide occurs on the *meso*-carbon by 1,6-addition.



(XI)



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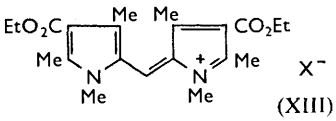
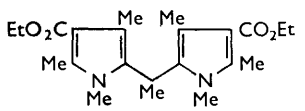
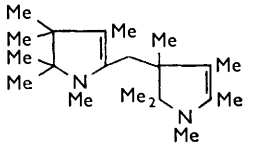


(XIII)

Michael addition of cyanoacetic ester at the *meso*-carbon of dipyrromethenes has also been described,[5] so that it was not surprising to find that the system (XIII) yielded compound (XIV) on reaction with methylmagnesium iodide.



(XIV)



(XV)

An attempt to add the Grignard derivative of 2,3,4-trimethylpyrrole to the methiodide of the 2*H*-pyrrole (II), to produce two directly linked five-membered rings with an angular methyl group as is found in vitamin B_{12}, did not proceed as expected but instead gave a base provisionally formulated as (XV) or an isomer, which accords with the observed ultraviolet absorption, the elementary analysis, and the formation of a dipicrate and diperchlorate. The formation of compound (XV) is visualised as the addition of the anhydro-base (IV) to the methiodide of (II) followed by 1,4-addition of methylmagnesium iodide.

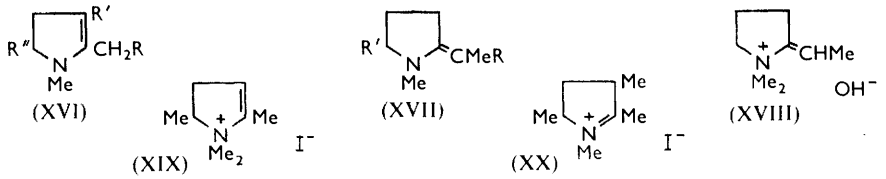
Methylation of the pyrroline ring system has received only scant attention in the past, and, as the pyrrolines are involved in vitamin B_{12} chemistry, some examples of this type of methylation have been investigated. Treatment of 1- and 3-pyrrolines with methyl iodide in neutral solution causes only *N*-methylation.[6-8] 2-Pyrrolines containing unsubstituted nitrogen isomerise spontaneously to the more stable 1-pyrrolines,[9,10] so that the presence of an *N*-alkyl group is necessary to fix the pyrroline double bond in the 2-position. However, if the 1-alkyl-2-pyrroline contains a 2-alkyl substituent possessing a hydrogen atom it may exist as a mixture of tautomers which differ in the position of the double bond. The position of the double bond in such 2-pyrrolines is assigned largely on the basis of infrared spectra.[11] Thus an endocyclic double bond in a 2-pyrroline absorbs at 1632—1643 cm.$^{-1}$, whereas the corresponding exocyclic double bond absorbs at 1663—1685 cm.$^{-1}$, and both types of 2-pyrroline yield the iminium salt which absorbs at 1674—1696 cm.$^{-1}$ ($R{\cdot}C{=}NMe^{+}$). The marked difference between the C=C absorption of 1,2-dimethyl-2-pyrroline (1640 cm.$^{-1}$; endocyclic double bond) (cf. also 1,2,5-trimethyl-2-pyrroline, 1643 cm.$^{-1}$) and 2-ethylidene-1-methylpyrrolidine (1665 cm.$^{-1}$; exocyclic double bond) is not shown by the corresponding hydropyridine derivatives where both alkyl derivatives absorb at 1645 cm.$^{-1}$ (endocyclic double bond).[12]

The 1-alkyl-2-pyrrolines are α-enamines and electrophilic substitution can occur either at nitrogen or at the β-carbon atom which may be endo- or exo-cyclic. Thus protonation

[4] Corwin and Brunings, *J. Amer. Chem. Soc.*, 1942, **64**, 593.
[5] Jain and Kenner, *J.*, 1959, 185.
[6] Evans, *J. Amer. Chem. Soc.*, 1951, **73**, 5230.
[7] Griot and Wagner-Jauregg, *Helv. Chim. Acta*, 1959, **42**, 121, 605.
[8] Sugasawa and Ushioda, *Tetrahedron*, 1959, **5**, 48.
[9] Witkop, *J. Amer. Chem. Soc.*, 1954, **76**, 5597; 1956, **78**, 2873.
[10] Burckhalter and Short, *J. Org. Chem.*, 1958, **23**, 1278.
[11] Lukeš, Dědek, and Novotný, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1117.
[12] Červinka, *Coll. Czech. Chem. Comm.*, 1960, **25**, 1174.

invariably occurs at the β-carbon,[9,13] and *C*-substituted derivatives have been obtained by reaction with ethyl bromoacetate [14] and a variety of αβ-unsaturated carbonyl compounds and esters.[15,16] The 2,3′-dimerisation of the 1-alkyl-2-pyrrolines under acidic conditions [17,18] is a related reaction.

Little work has been carried out on the methylation of 1-alkyl-2-pyrrolines. 2-Ethylidene-1-methylpyrrolidine (XVII; R = R′ = H) which exists largely if not entirely in that form rather than in the tautomeric ethyl form (XVI; R = Me, R′ = R″ = H), was treated with methyl iodide in dry benzene [19] and yielded, after basification, two compounds (XVIII) and (XVII; R = Me, R′ = H), which are the products of *N*- and exocyclic *C*-methylation, respectively.

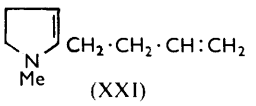


On the other hand, Evans [6] treated 1,2,5-trimethyl-2-pyrroline (XVI; R = R′ = H, R″ = Me) with methyl iodide and obtained a salt for which the *N*- (XIX) and *C*-alkylated structures (XX) were considered. In view of this possible example of β-methylation of the pyrroline ring system, the reaction was re-examined and the product has been shown to have structure (XVII; R = H, R′ = Me) by its infrared spectrum and the identity of derivatives with those of an authentic specimen prepared by the action of ethylmagnesium bromide on 1,5-dimethyl-2-pyrrolidone. At the same time, 1,2,3,5-tetramethyl-2-pyrroline (XVI; R = H, R′ = R″ = Me) and 2-isopropyl-1,5-dimethyl-2-pyrroline were prepared by similar methods for comparison. The infrared spectra of these two pyrrolines each show two maxima in the range 1630—1685 cm.$^{-1}$, suggesting mixtures of tautomers. Thus it appeared that methylation of 1,2-dialkyl-2-pyrrolines occurred on the exocyclic β-carbon atom even when the double bond was largely endocyclic in the original pyrroline.

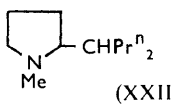
Reaction of allyl, crotyl, and benzyl halides with acyclic enamines is known to cause substitution at the β-carbon atom [20,21] although, in some cases at least, the *C*-alkylated salts are formed by rearrangement of the initially formed *N*-alkylated salts.[22,23] 1,2-Dimethyl-2-pyrroline (XVI; R = R′ = R″ = H) was treated with allyl bromide in benzene solution, and some unchanged starting material could be removed from the product by means of the insoluble styphnate. The unstable basic allylation product was purified further by gas-chromatography and its spectra and molecular weight suggested that it was mainly a diallylated product. When the crude allylation product was hydrogenated over a platinum catalyst and the resulting mixture fractionally distilled, three bases were obtained and isolated as picrates: 1,2-dimethylpyrrolidine, 2-butyl-1-methylpyrrolidine, and an unidentified compound (picrate, m. p. 154—155°). The isolation of 2-butyl-1-methylpyrrolidine proves the presence of 2-but-3′-enyl-1-methyl-2-pyrroline (XXI) in the allylation product, and thus provides another example of alkylation at the exocyclic β-position of a 2-alkyl-2-pyrroline.

[13] Leonard *et al.*, *J. Amer. Chem. Soc.*, 1954, **76**, 2781; 1957, **79**, 5279.
[14] Červinka, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1880.
[15] Ireland, *Chem. and Ind.*, 1958, 979.
[16] Červinka, *Chem. and Ind.*, 1959, 1129; *Coll. Czech. Chem. Comm.*, 1960, **25**, 1183.
[17] Leonard and Cook, *J. Amer. Chem. Soc.*, 1959, **81**, 5627.
[18] Lukeš, Plešek, and Trojánek, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1987.
[19] Lukeš and Dědek, *Coll. Czech. Chem. Comm.*, 1958, **23**, 2046.
[20] Elkik, *Bull. Soc. chim., France*, 1960, 972.
[21] Opitz, Mildenburger, *et al.*, *Annalen*, 1961, **649**, 26, 36; *Angew. Chem.*, 1960, **72**, 169.
[22] Brannock and Burpitt, *J. Org. Chem.*, 1961, **26**, 3576.
[23] Opitz, *Annalen*, 1962, **650**, 122.

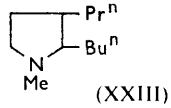
Analysis and molecular-weight determination of the picrate, m. p. 154—155°, suggested that it was a derivative of a base, $C_{12}H_{25}N$, corresponding to a methyldipropylpyrrolidine. The derived base contained an *N*-methyl group (infrared band at 2780 cm.$^{-1}$), and the picrate differed from those of synthetic bases (XXII) and (XXIII). By elimination it



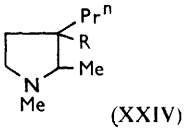
(XXI)



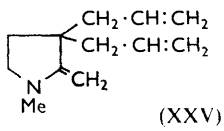
(XXII)



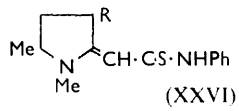
(XXIII)



(XXIV)



(XXV)



(XXVI)

was concluded that the picrate, m. p. 154—155°, was derived from 1,2-dimethyl-3,3-dipropylpyrrolidine (XXIV; R = Pr^n) and this assignment was supported by the presence of a doublet at 8·52 τ (J = 7·3 c./sec.) in the nuclear magnetic resonance spectrum of the picrate, ascribed to the 2-methyl group. A similar doublet at 8·44 τ (J = 6·5 c./sec.) is present in the spectrum of the picrate of 1,2-dimethyl-3-propylpyrrolidine (XXIV; R = H) but is absent from the spectra of the picrates of (XXII) and (XXIII). If structure (XXIV; R = Pr^n) is correct for the hydrogenated base, then the corresponding original diallylation product must have structure (XXV), having been formed by alkylation at the β-carbon of the ring. The nuclear magnetic resonance spectrum of the allylated base showed a singlet (2 protons) at 6·33 τ, ascribed to the olefinic protons on the β-carbon of an enamine (similar signals at about 6 τ, an unusually high value for olefinic protons, were observed in the spectra of other 2-alkyl-2-pyrrolines). The unsplit nature of this signal suggested the unit $>C=CH_2$. These observations are in accord with structure (XXV).

The alkylpyrrolidines (XXII), (XXIII), and (XXIV; R = H) were prepared by standard methods. Reaction of γ-chlorobutyronitrile with 1-propylbutylmagnesium bromide (cf. refs. 23, 25) gave the expected 1-pyrroline, and catalytic hydrogenation of the corresponding methiodide gave the base (XXII) (picrate, m. p. 81—83°). The same Grignard bromide failed to react with 1-methyl-2-pyrrolidone, possibly because of steric factors. For the syntheses of bases (XXIII) and (XXIV; R = H), 1-methyl-2-pyrrolidone was converted into the 3-allyl derivative with allyl bromide in presence of sodamide. Unfortunately attempts to introduce a second allyl group as required for synthesis of compounds (XXIV; R = Pr^n) and (XXV) were unsuccessful. Reaction of 3-allyl-1-methyl-2-pyrrolidone with methylmagnesium iodide and butylmagnesium bromide proceeded normally, and catalytic hydrogenation of the 2-pyrrolines thus obtained gave the bases (XXIV; R = H) and (XXIII), with picrates of m. p. 162—163° and 101—103°, respectively.

Phenyl isothiocyanate reacted with 1,2,5-trimethyl- and 1,2,3,5-tetramethyl-2-pyrroline at the exocyclic β-carbon atoms, to form thiocarbanilides (XXVI; R = H or Me) which were useful solid derivatives. The ultraviolet spectrum of each indicated a conjugated system and the nuclear magnetic resonance spectra showed the presence in each of one olefinic proton.

Experimental

Infrared spectra were determined for liquid films, and ultraviolet spectra for ethanolic solutions, except where otherwise stated. Gas–liquid chromatography was carried out with a Perkin-Elmer vapour fractometer, model 116, with nitrogen as carrier gas. M. p.s were determined on a Kofler hot-stage apparatus.

[24] Maginnity and Cloke, *J. Amer. Chem. Soc.*, 1951, **73**, 49.
[25] Booth, Johnson, and Johnson, *J.*, 1962, 98.

2,2,3,4,5-*Pentamethyl*-2H-*pyrrole*.—The previously reported [3] method was modified by the use of only 1 mol. of methyl iodide. From 2,3,4,5-tetramethylpyrrole (10 g.) was obtained 2,2,3,4,5-pentamethyl-2*H*-pyrrole (7·0 g., 63%), b. p. 84—85°/53 mm., $\nu_{max.}$ 1574, 1588, 1658, and 1663 cm.$^{-1}$. The base showed only one peak when examined by gas–liquid chromatography. The *methoperchlorate*, from the 2*H*-pyrrole methiodide [26] and aqueous silver perchlorate, crystallised from ethanol in rods, m. p. 191—192° (Found: C, 47·4; H, 6·7; N, 5·4. $C_{10}H_{18}ClNO_4$ requires C, 47·7; H, 7·2; N, 5·6%), $\lambda_{max.}$ 205 and 272 mμ (ε 3190 and 5000, respectively), $\nu_{max.}$ (KBr disc) 1600, 1624, 1670, and 1697 cm.$^{-1}$.

1,3,4,5,5-*Pentamethyl*-2-*methylene*-3-*pyrroline and* 1,2,3,5,5-*Pentamethyl*-4-*methylene*-2-*pyrroline*.—Treatment of the foregoing methoperchlorate with aqueous sodium hydroxide, followed by ether-extraction, gave a mixture of anhydro-bases,[3] b. p. 95°/50 mm., n_D^{19} 1·5020, $\lambda_{max.}$ 215, 269, and 287 mμ (ε 9320, 6200, and 5940, respectively, in hexane), $\nu_{max.}$ 1627, 1641, 1670, and 1687 cm.$^{-1}$. Gas–liquid chromatography on a 3 m. silicone–Celite, Perkin-Elmer column at 0·75 atm. at 152° with a flow rate >100 c.c./min., showed the presence of two bases, which were separately collected and examined. 1,2,3,5,5-Pentamethyl-2-methylene-3-pyrroline (retention time 12·4 min.) showed $\lambda_{max.}$ 212 and 279 mμ (ε 8400 and 5500, respectively) and $\lambda_{max.}$ 206 and 272 mμ (ε 3900 and 4900, respectively) in dilute ethanolic hydrochloric acid. The picrate and perchlorate had m. p. 146—148° and 186—189°, respectively, both undepressed when mixed with the methopicrate and methoperchlorate of 2,2,3,4,5-pentamethyl-2*H*-pyrrole. 1,3,4,5,5-Pentamethyl-4-methylene-2-pyrroline (retention time 10·5 min.) showed $\lambda_{max.}$ 263 mμ (ε 9600) and $\lambda_{max.}$ 274 (ε 5000) in ethanolic hydrochloric acid. The picrate and perchlorate had m. p. 146—148° and 189—190°, respectively, both undepressed when mixed with the methopicrate and methoperchlorate of 2,2,3,4,5-pentamethyl-2*H*-pyrrole.

3,4-*Dimethylpyrrole* [with Dr. E. Bullock].—To a suspension of ethyl 3,4,5-trimethylpyrrole-2-carboxylate (36·2 g.) in dry ether (150 c.c.), bromine (11 c.c.) was added with shaking during 10 min. and the mixture was set aside for 1 hr. Sulphuryl chloride (37 c.c.) was then added with shaking in 30 min. and the mixture kept overnight. The ether was removed under reduced pressure at 20° and the sticky residue was hydrolysed with cold water (200 c.c.). The dull purple solid was removed by filtration and hydrolysed with a solution of sodium hydroxide (35 g.) in water (150 c.c.) and ethanol (200 c.c.) under reflux. After 3 hr. the ethanol was removed by distillation, and the residue was neutralised with glacial acetic acid and steam-distilled. 3,4-Dimethylpyrrole was obtained by evaporation of the dried (K_2CO_3) ethereal extract of the distillate, as a pale yellow solid (14 g., 74%), b. p. 65—70°/12 mm. (lit.,[26] 65—66°/14 mm.).

2-*Benzyl*-3,4-*dimethylpyrrole*.—The Grignard derivative of 3,4-dimethylpyrrole (9·5 g.), in dry ether (60 c.c.), was treated during 10 min. with benzyl chloride (12·65 g.) in dry ether (10 c.c.). When the vigorous reaction had subsided, the mixture was heated under reflux for 12 hr. and then cooled to 0°. A saturated solution of ammonium chloride (100 c.c.) was added and the ethereal layer was separated. The aqueous solution was extracted several times with ether, and the ethereal extracts were combined. The dried ($MgSO_4$) extracts were warmed to remove ether and the residual brown oil was then heated at 100°/15 mm. for 5 hr. to remove unchanged benzyl chloride and 3,4-dimethylpyrrole. The residue (15·5 g.) was distilled and two fractions were collected: (i) yellow oil (3·7 g.), b. p. 108—114°/0·3 mm., and (ii) viscous yellow oil (6 g.), b. p. 150—175°/0·3 mm. Redistillation of fraction (i) gave 2-*benzyl*-3,4-*dimethylpyrrole* as a pale yellow oil, b. p. 120°/0·2 mm. (Found: C, 84·5; H, 8·0. $C_{13}H_{15}N$ requires C, 84·3; H, 8·2%), $\nu_{max.}$ (in CCl_4) 1025, 1075, and 3500 cm.$^{-1}$. The 2-*thiocarbanilide*, from the pyrrole and phenyl isothiocyanate, crystallised from light petroleum (b. p. 40—60°) in yellow needles, m. p. 121—122·5° (Found: C, 74·8; H, 6·4; N, 8·6; S, 9·7. $C_{20}H_{20}N_2S$ requires C, 75·0; H, 6·2; N, 8·8; S, 10·0%). Redistillation of fraction (ii) gave 2,5-dibenzyl-3,4-dimethylpyrrole, b. p. 160—170°/0·2 mm. (see below).

2,5-*Dibenzyl*-3,4-*dimethylpyrrole*.—The Grignard derivative of 2-benzyl-3,4-dimethylpyrrole (1 mol.) was treated with benzyl chloride (1 mol.) in ether in the manner described above. The usual method of working up gave 2,5-*dibenzyl*-3,4-*dimethylpyrrole* (59%), b. p. 160—170°/0·2 mm., slowly forming a low-melting solid (Found: N, 5·1. $C_{20}H_{21}N$ requires N, 5·1%). The infrared spectrum (in CCl_4) included max. at 1025s, 1075w, and 3500 cm.$^{-1}$.

2-*Benzyl*-3,4,5-*trimethylpyrrole*.—The Grignard derivative of 2,3,4-trimethylpyrrole (1 mol.)

[26] Fischer and Walach, *Annalen*, 1926, **450**, 109.

was treated in the usual way with benzyl chloride (1 mol.) in ether. 2-*Benzyl*-3,4,5-*trimethylpyrrole* (40%) was obtained as a colourless oil, b. p. 110—120°(bath-temp.)/0·1 mm., m. p. 55—59° (Found: C, 84·4; H, 8·5. $C_{14}H_{17}N$ requires C, 84·4; H, 8·6%). The same compound was prepared from 2-benzyl-3,4-dimethylpyrrylmagnesium iodide and methyl iodide.

2,5-*Dibenzyl*-2,3,4-*trimethyl*-2H-*pyrrole*.—Methyl iodide (2·1 g.) in ether (5 c.c.) was added to the Grignard derivative of 2,5-dibenzyl-3,4-dimethylpyrrole (4 g.) in ether (25 c.c.). The mixture was heated under reflux for 12 hr., cooled, and decomposed by addition of water (50 c.c.). The ethereal layer was separated and the aqueous layer was extracted several times with ether. The combined ethereal extracts were shaken with saturated aqueous potassium dihydrogen phosphate (3 × 100 c.c.), dried ($MgSO_4$), and heated to remove ether. Distillation of the residue gave 2,5-dibenzyl-2,3,4-trimethyl-2*H*-pyrrole (2 g.), b. p. 155°/0·03 mm. The derived *picrate* formed yellow prisms (from acetone), m. p. 166—167° (Found: C, 62·5; H, 4·65. $C_{27}H_{26}N_4O_7$ requires C, 62·5; H, 5·05%). A sample of the base regenerated from the picrate showed $\lambda_{max.}$ 250 mμ (ε 4170) and $\lambda_{max.}$ 265 mμ (ε 5020) in dilute ethanolic hydrochloric acid. The infrared spectrum (in CCl_4) showed bands at 1580, 1600, 1626, and 1653 cm.$^{-1}$. The methiodide had $\lambda_{max.}$ 282 mμ (ε 4370) and $\lambda_{max.}$ 335 mμ (ε 2350) in dilute ethanolic sodium hydroxide.

2,2-*Dibenzyl*-3,4,5-*trimethyl*-2H-*pyrrole*.—The Grignard derivative from 2-benzyl-3,4,5-trimethylpyrrole (10 g.) was treated with benzyl chloride in the usual manner, and the method of working-up followed that used in the previous experiment. The final distillation gave two fractions: (i) (1·5 g.), b. p. 80°/0·05 mm. and (ii) (6·8 g.), b. p. 110—150°/0·05—0·1 mm. Fraction (ii) was converted into the picrate, recrystallisation of which from ethanol gave 2,2-*dibenzyl*-3,4,5-*trimethyl*-2H-*pyrrole picrate*, m. p. 186—188° (decomp.) (Found: C, 62·4; H, 5·25. $C_{27}H_{26}N_4O_7$ requires C, 62·5; H, 5·05%). A sample of the base regenerated from the pure picrate had b. p. 120—130°(bath-temp.)/0·05 mm., $\lambda_{max.}$ 247 mμ (ε 2140) and $\lambda_{max.}$ 265 mμ (ε 4270) in dilute ethanolic hydrochloric acid, $\nu_{max.}$ (in $CHCl_3$) 1570, 1610, and 1669 cm.$^{-1}$. The methiodide showed $\lambda_{max.}$ 271 mμ (ε 3900) and $\lambda_{max.}$ 296 mμ (ε 6770) in dilute ethanolic sodium hydroxide.

Action of Methylmagnesium Iodide on 2,2,3,4,5-*Pentamethyl*-2H-*pyrrole Methiodide*.—The finely powdered methiodide (22·3 g.) was added, with stirring and cooling, to a solution of methylmagnesium iodide, prepared from magnesium (2·88 g.), methyl iodide (16·5 g.), and ether (100 c.c.). The mixture was heated under reflux for 1·5 hr., cooled, and decomposed by addition of a cold saturated solution of ammonium chloride (100 c.c.). The ether layer was separated and the aqueous solution, after being extracted several times with ether, was retained for examination (solution *A*, see below). The combined ethereal extracts were dried (KOH) and distilled, yielding a basic oil (3·35 g.), b. p. 85°/37 mm. Treatment of the oil with aqueous perchloric acid and recrystallisation of the precipitated solid from ethanol gave 1,2,2,3,4,5,5-*heptamethyl*-3-*pyrroline perchlorate* (2·42 g., 11%) as rods, m. p. 252—257° (Found: C, 49·5; H, 7·8. $C_{11}H_{22}ClNO_4$ requires C, 49·4; H, 8·3%), $\nu_{max.}$ (KBr disc) 3100s cm.$^{-1}$ ($^{+}$N–H [27]), no appreciable absorption between 1550 and 1700 cm.$^{-1}$. A sample of the base regenerated from the pure perchlorate had b. p. 155—160°(bath-temp.)/260 mm., n_D^{22} 1·4614, $\lambda_{max.}$ <200 mμ. There was no infrared absorption between 1550 and 1700 cm.$^{-1}$. The *picrate* formed needles, m. p. 226—230°, from ethanol (Found: C, 51·6; H, 6·0; N, 13·8. $C_{17}H_{24}N_4O_7$ requires C, 51·5; H, 6·0; N, 14·1%). Solution *A* was basified with sodium hydroxide, heated under reflux to remove ammonia, and steam-distilled. The distillate was made just acid with 10% hydrochloric acid, evaporated under reduced pressure to a small volume, basified, and extracted several times with ether. Distillation of the dried (KOH) ethereal extracts gave a basic oil (6·35 g.), b. p. 105—110°/55 mm., of which the picrate, after a number of crystallisations from ethanol, gave 1,2,3,4,4,5,5-*heptamethyl*-2-*pyrroline picrate* (4·7 g.), m. p. 210—213° (Found: C, 51·6; H, 5·9. $C_{17}H_{24}N_4O_7$ requires C, 51·5; H, 6·1%). The free base was appreciably volatile in ether, but was satisfactorily isolated from the pure picrate in the following manner. The picrate (0·77 g.) was treated with 4N-hydrochloric acid (4 c.c.), and the mixture was extracted several times with ether saturated with 4N-hydrochloric acid. The aqueous layer remaining was freed from ether at 15°/10 mm. and neutralised to pH 5 with 20% sodium hydroxide solution. The solution was evaporated to 5 c.c. at 40°/10 mm., basified with 40% aqueous sodium hydroxide, and extracted several times with ether. Distillation of the dried (KOH) extracts at 40° removed ether, and the residue, 1,2,3,4,4,5,5-heptamethyl-2-pyrroline

[27] Nuttall, Sharp, and Waddington, *J.*, 1960, 4965.

(0·20 g.), distilled as a pale yellow oil, b. p. 210—220°(bath-temp.)/760 mm., n_D^{23} 1·4746, $\lambda_{max.}$ 241 mμ (ε 6170), $\nu_{max.}$ at 1642s (endocyclic C=C) and 1680w cm.$^{-1}$ (exocyclic C=C). The *perchlorate* had m. p. 285—288° (from ethanol) (Found: N, 5·0. $C_{11}H_{22}ClNO_4$ requires N, 5·2%), $\nu_{max.}$ (KBr disc) 1674 cm.$^{-1}$ (C=N$^+$).

Action of 2,3,4-Trimethylpyrrylmagnesium Iodide on 2,2,3,4,5-Pentamethyl-2H-pyrrole Methiodide.—A solution of 2,3,4-trimethylpyrrole (4·0 g.) in ether (10 c.c.) was added slowly to a solution of methylmagnesium iodide, prepared from magnesium (0·9 g.), methyl iodide (5·0 g.), and ether (20 c.c.). The mixture was kept for 1 hr. at room temperature, then treated with finely powdered 2,2,3,4,5-pentamethyl-2H-pyrrole methiodide (9·3 g.), heated under reflux for 12 hr., cooled, and decomposed by addition of saturated ammonium chloride solution (30 c.c.). The ether layer was separated and the aqueous residue, after being extracted several times with ether, was retained for examination (solution *A*). The combined ethereal extracts were dried (KOH) and distilled. Two fractions were collected: (i) colourless oil (1·8 g.), b. p. 80—82°/12 mm., and (ii) pale yellow oil (1·8 g.), b. p. 150—162°/12 mm. Fraction (i) formed crystals, m. p. 32—38°, on cooling, and redistillation gave 2,3,4-trimethylpyrrole, m. p. and mixed m. p. 36—38°; the picrate, plates (from ethanol), had m. p. 136—137° (decomp.) (lit.,[28] 139—141°). Fraction (ii) on redistillation gave the 2-pyrroline (XV) (0·7 g.), b. p. 160—162°/12 mm. The *dipicrate* had m. p. 185—186° (Found: C, 51·5; H, 5·5. $C_{33}H_{44}N_8O_{14}$ requires C, 51·0; H, 5·7%). A sample of this base, regenerated from the pure dipicrate showed $\lambda_{max.}$ 221 mμ (ε 14,500), $\lambda_{max.}$ <200 mμ in dilute ethanolic hydrochloric acid, and $\nu_{max.}$ 1678 cm.$^{-1}$ (C=C). The *diperchlorate* had m. p. 193—198° (Found: N, 5·4. $C_{21}H_{40}Cl_2N_2O_8$ requires N, 5·4%), $\nu_{max.}$ (KBr disc) 1684 cm.$^{-1}$ (C=N$^+$). Basification and ether-extraction of solution *A* yielded an oil (0·46 g.), b. p. 62—64°/12 mm. (impure picrate, m. p. 172—180°).

Action of Methylmagnesium Iodide on 4,4′-Diethyl-3,3′,5,5′-tetramethyldipyrromethene Hydrobromide.—The reaction, carried out in the usual manner, yielded only the free base, 4,4′-diethyl-3,3′,5,5′-tetramethyldipyrromethene [cobalt complex, m. p. 196—198° (lit.,[29] 198°)]

Ethyl 1,3,4,5-Tetramethylpyrrole-2-carboxylate.—Ethyl 3,4,5-trimethylpyrrole-2-carboxylate (90 g.) was treated with sodium (19 g.) in toluene (600 c.c.), and the sodium salt produced was methylated with dimethyl sulphate (79 g.) by the method of Corwin and Quattlebaum.[30] The crude product was chromatographed in chloroform on alumina (Spence's type H), giving the pyrrole (33 g., 34%), m. p. 35—40°. Sublimation at 70°/0·1 mm. gave colourless plates of pure *ethyl 1,3,4,5-tetramethylpyrrole-2-carboxylate*, m. p. 39—40° (Found: N, 7·1. $C_{11}H_{17}NO_2$ requires N, 7·2%), showing extreme sensitivity to light and air.

Attempts to prepare 1,2,3,4-tetramethylpyrrole by hydrolysis and decarboxylation of this ester failed, the only product being an intractable tar.

Action of Methylmagnesium Iodide on Diethyl 1,1′,3,3′,5,5′-Hexamethyldipyrromethene-4,4′-dicarboxylate Perchlorate.—Ethyl 1,2,4-trimethylpyrrole-3-carboxylate, prepared from the corresponding acid [30] by the method of Chu and Chu,[31] was converted into diethyl 1,1′,3,3′,5,5′-hexamethyldipyrromethene-4,4′-dicarboxylate perchlorate, $\lambda_{max.}$ 500 mμ (in 30% aqueous perchloric acid), by the method of Corwin and Brunings.[4] The finely powdered perchlorate (2·36 g.) was added slowly, with shaking, to methylmagnesium iodide [from magnesium (0·96 g.), methyl iodide (5·7 g.), and ether (40 c.c.)]. Effervescence occurred and a pale yellow viscous oil separated. The mixture was shaken for 3 hr. and then decomposed with saturated aqueous ammonium chloride (25 c.c.). The ethereal layer was dried ($MgSO_4$) and warmed to remove ether; a gum then remained. Crystallisation from ethanol gave *diethyl 1,1′,3,3′,5,5′,α-heptamethyldipyrromethane-4,4′-dicarboxylate* (1·45 g., 63%) as colourless plates, m. p. 136—138° (Found: C, 67·65; H, 8·2; N, 7·2. $C_{22}H_{32}N_2O_4$ requires C, 68·0; H, 8·3; N, 7·2%), $\lambda_{max.}$ 218 and 268 mμ (ε 34,700 and 9500, respectively). A mixed m. p. with 4,4′-diethoxycarbonyl-1,1′,3,3′,5,5′-hexamethyldipyrrylmethanol [4] (m. p. 141—142°) was 116—120°.

The above dipyrromethane (0·39 g.) in dry carbon tetrachloride (20 c.c.) was treated with a 10% w/v solution of bromine in carbon tetrachloride (1·6 c.c.), dropwise during 2—3 min. A deep violet film was deposited during 20 min. on the sides of the vessel. Aqueous perchloric

[28] Piloty and Hirsch, *Annalen*, 1913, **395**, 63.
[29] Fischer, Halbig, and Walach, *Annalen*, 1927, **452**, 268.
[30] Corwin and Quattlebaum, *J. Amer. Chem. Soc.*, 1936, **58**, 1081.
[31] Chu and Chu, *J. Org. Chem.*, 1954, **19**, 266.

acid was added, with shaking, but no crystalline material was obtained. The red solution had $\lambda_{max.}$ 500 mμ, demonstrating oxidation to a dipyrromethene.

Ethyl 5-Acetyl-1,2,4-trimethylpyrrole-3-carboxylate.—Ethyl 1,2,4-trimethylpyrrole-3-carboxylate (0·5 g.) in acetic anhydride (6 c.c.) was treated with 60% aqueous perchloric acid (0·5 c.c.). After 5 min. the mixture was poured into water and the precipitated solid removed. Crystallisation of the solid from ethanol gave the *5-acetyl derivative* (0·45 g.) as needles, m. p. 41—42° (Found: C, 64·2; H, 7·3; N, 6·0. $C_{12}H_{17}NO_3$ requires C, 64·5; H, 7·7; N, 6·3%).

Attempted Preparation of Diethyl 1,1′,3,3′,5,5′,α-Heptamethyldipyrromethene-4,4′-dicarboxylate Salts.—(i) The above acetylpyrrole (0·16 g.) and ethyl 1,2,4-trimethylpyrrole-3-carboxylate (0·12 g.) were dissolved in dry carbon tetrachloride saturated with hydrogen chloride (cf. ref. 4). No dipyrromethene salt was isolated.

(ii) The acetylpyrrole (0·05 g.) and the above ester (0·05 g.) were dissolved in a mixture of methanol (0·5 c.c.) and 40% hydrobromic acid (2·5 c.c.). A bright red colour was produced which slowly became pale orange. No dipyrromethene salt was isolated.

Preparation of Pyrrolines.—*2,5-Dimethyl-1-pyrroline.* This was prepared from 2,5-dimethylpyrrole by catalytic hydrogenation or, better, by reduction with zinc and hydrochloric acid.[6] The mixture of 2,5-dimethyl-3- and 2,5-dimethyl-1-pyrroline was separated through the picrates, the latter having m. p. 134—135° (lit.,[6] 135—137°) (Found: N, 17·5. Calc. for $C_{12}H_{14}N_4O_7$: N, 17·2%), $\nu_{max.}$ (KBr disc) 1678 cm.$^{-1}$ (C=N$^+$). The free base, regenerated from the picrate by lithium hydroxide, had $\nu_{max.}$ 1648 cm.$^{-1}$ (C=N). The methiodide, m. p. 247° (decomp.), formed colourless needles from ethanol.

1,2,5-Trimethyl-2-pyrroline. Prepared by the action of methylmagnesium iodide on 1,5-dimethyl-2-pyrrolidone [32] according to Lukeš and Večerá's directions,[33] the free base had b. p. 141°, n_D^{22} 1·4925, $\lambda_{max.}$ 235 mμ (ε 4450), $\nu_{max.}$ 1643 cm.$^{-1}$ (endocyclic C=C). The perchlorate formed colourless needles, m. p. 225—226° (lit.,[6] 217—218°), from ethanol (Found: C, 39·6; H, 6·5. Calc. for $C_7H_{14}ClNO_4$: C, 39·7; H, 6·8%), the picrate yellow needles, m. p. 174—176° (lit.,[6] 174—178°), from ethanol (Found: C, 46·0; H, 5·05. Calc. for $C_{13}H_{16}N_4O_7$: C, 45·9; H, 4·7%), and the sodium double picrate yellow needles, m. p. 204—205° (lit.,[33] 203—204°), from aqueous ethanol. The *thiocarbanilide* was formed from the free base and phenyl isothiocyanate in heptane; it formed yellow needles, m. p. 153—155°, from cyclohexane (Found: C, 68·0; H, 7·65; S, 11·2. $C_{14}H_{18}N_2S_2$ requires C, 68·3; H, 7·4; N, 11·4%), $\lambda_{max.}$ 222 and 349 mμ (ε 11,330 and 33,100 respectively).

2-Ethyl-1,5-dimethyl-2-pyrroline. Prepared similarly from 1,5-dimethyl-2-pyrrolidone and ethylmagnesium bromide, the free base had b. p. 160—162° and $\nu_{max.}$ 1666 cm.$^{-1}$ (exocyclic C=C). It gave a perchlorate, needles, m. p. 230—232° (lit.,[33] 223—224°), from ethanol (Found: C, 43·2; H, 7·3. Calc. for $C_8H_{16}ClNO_4$: C, 42·9; H, 7·15%), $\nu_{max.}$ (KBr disc) 1682 cm.$^{-1}$ (C=N$^+$), and a sodium double picrate, needles, m. p. 191—193° (lit.,[33] 189—190°), from aqueous ethanol.

2-Isopropyl-1,5-dimethyl-2-pyrroline. Prepared similarly from isopropylmagnesium bromide, the free base had b. p. 162—165°, n_D^{20} 1·4642, $\nu_{max.}$ 1637 (endocyclic C=C) and 1685 (exocyclic C=C) cm.$^{-1}$. The *perchlorate* formed needles, m. p. 228—229°, from ethanol (Found: N, 5·8. $C_9H_{18}ClNO_4$ requires N, 5·8%). The *sodium double picrate*, prepared from the free base and picric acid in the presence of sodium acetate, had m. p. 130·5—132° (Found: C, 40·1; H, 3·8; Na, 3·4. $C_{21}H_{22}N_7NaO_{14}$ requires C, 40·65; H, 3·6; Na, 3·7%). Recrystallisation of the sodium double picrate from aqueous ethanol gave the picrate, m. p. 90—91° (lit.,[34] 86°).

1,3,5-Trimethyl-2-pyrrolidone. 2-Methyl-lævulic acid [35] (80 g.) was hydrogenated in the presence of 40% w/w methylamine (250 c.c.) and Raney nickel (5 g.) at 135°/80 atm. for 20 hr. After cooling, the catalyst was removed and the water evaporated at 30° through a fractionating column. The residue was dried by adding benzene and distilling off the azeotrope. The residue was distilled, to give the *pyrrolidone*, b. p. 85—86°/11 mm., n_D^{21} 1·4619 (Found: N, 10·7. $C_7H_{13}NO$ requires N, 11·0%).

1,2,3,5-Tetramethyl-2-pyrroline. 1,3,5-Trimethyl-2-pyrrolidone was treated with methylmagnesium bromide, and the base was isolated as the *perchlorate* (7 g., 14%), needles, m. p. 203·5° (from ethanol) (Found: N, 6·2. $C_8H_{16}ClNO_4$ requires N, 6·6%), $\nu_{max.}$ 1685 and 1690

[32] *Org. Synth.*, Coll. Vol. III, 1955, p. 328.
[33] Lukeš and Večeřa, *Coll. Czech. Chem. Comm.*, 1954, **19**, 263.
[34] Wallach, *Annalen*, 1901, **319**, 77.
[35] Braude and Timmons, *J.*, 1953, 3313.

cm.$^{-1}$ (C=N$^+$). The regenerated free base had b. p. 146°, $\nu_{max.}$ 1643 (endocyclic C=C) and 1683 cm.$^{-1}$ (exocyclic C=C). The *picrate* formed yellow needles, m. p. 157—158·5°, from ethanol (Found: C, 47·3; H, 4·85. $C_{14}H_{18}N_4O_7$ requires C, 47·45; H, 5·1%), and the *thiocarbanilide* pale yellow granules, m. p. 112·5—114°, from cyclohexane (Found: C, 69·2; H, 7·6; N, 10·5. $C_{15}H_{20}N_2S$ requires C, 69·2; H, 7·7; N, 10·75%), $\lambda_{max.}$ 222 and 354 mμ (ε 10,600 and 29,020, respectively).

Methylation of 1,2,5-*Trimethyl-2-pyrroline*.—The base (7·5 g.) in dry benzene (100 c.c.) was treated with methyl iodide (12 c.c., 2·5 mol.) in benzene (25 c.c.) at 80° with stirring and in an atmosphere of dry nitrogen. Two further portions of methyl iodide (5 c.c.) were added in the next 8 hr. and the stirred mixture was kept at 80° for 20 hr., then cooled. The yellow solid was removed, washed with benzene, and dried *in vacuo* (17 g.); it then had m. p. 160—170°. The methiodide (10 g.) was dissolved in water (25 c.c.), 20% aqueous sodium hydroxide (10 c.c.) was added, and the resulting solution distilled in steam. The basic distillate was neutralised with dilute hydrochloric acid and then the base was converted into the perchlorate which, after several crystallisations from ethanol, had m. p. 225—226°, undepressed on admixture with the authentic perchlorate of 2-ethyl-1,5-dimethyl-2-pyrroline (Found: C, 42·9; H, 6·9. Calc. for $C_8H_{16}ClNO_4$: C, 42·9; H, 7·15%). The sodium double picrate had m. p. and mixed m. p. 191—192·5°.

In another experiment, the crude methylation product was subjected to gas–liquid chromatography on a 2-m. silicone–Celite, Perkin-Elmer column at 167°/1 atm. with a flow rate of 5 c.c./min. The first fraction (retention time 9·8 min.) was unchanged 1,2,5-trimethyl-2-pyrroline (thiocarbanilide, m. p. 152—154°; picrate, m. p. 170—173°; sodium double picrate, m. p. 204—205°), and the second fraction (retention time, 14 min.) was mainly 2-ethyl-1,5-dimethyl-2-pyrroline ($\nu_{max.}$ 1666 cm.$^{-1}$; sodium double picrate, m. p. 189—190°), but the infrared spectrum also indicated the presence of some 2-isopropyl-1,5-dimethyl-2-pyrroline (bands at 1637 and 1685 cm.$^{-1}$).

Reaction of 1,2-*Dimethyl-2-pyrroline with Allyl Bromide*.—Freshly distilled allyl bromide (36 g.) was added dropwise during 1 hr. to a stirred solution of the pyrroline (15 g.) in dry benzene (75 c.c.) in an atmosphere of dry nitrogen, and the mixture was heated under reflux for 2 hr. During the addition of the allyl bromide a red gum was precipitated; after cooling, the gum was dissolved in water (50 c.c.). The layers were separated and the red aqueous layer washed with ether. The ether and the benzene layer were combined and shaken with dilute acid. The aqueous acid layer was then made alkaline with aqueous sodium hydroxide, but no base was liberated. An excess of alkali was then added to the red aqueous layer, and the mixture heated on the steam-bath for 5 min.; a brown oil separated. This oil was removed and extracted five times with ether. After evaporation of the solvent from the dried combined ether extracts, the residue was fractionally distilled to remove unchanged starting material. The product, b. p. 106—120°/15 mm., was a pale yellow oil but all attempts to obtain solid derivatives (perchlorate, picrate) failed. Some further purification was achieved by removal of some starting material as the insoluble styphnate, m. p. 163—168°, or by application of gas–liquid chromatography when again a further small quantity of starting material was removed and the presence of a main component was revealed, but no solid derivatives could be obtained.

The distilled product (fraction b. p. 106—108°/15 mm.; 1·79 g.) in ethanol was acidified to pH 6 with 6N-perchloric acid and hydrogenated for 1½ hr. over Adams platinum catalyst (absorption 610 c.c. at 22°/760 mm.). The catalyst was removed, the resulting salt basified, and the base extracted into ether. After removal of the solvent the residue was distilled and the following fractions were collected: (*a*) b. p. 120—175° (0·223 g.) [picrate, m. p. 235°, identical with 1,2-dimethylpyrrolidine picrate (lit.,[36] m. p. 235°)]; (*b*) b. p. 175—195° (1·015 g.), from which there was isolated a picrate, m. p. 113—114°, not depressed on admixture with the authentic picrate of 2-butyl-1-methylpyrrolidine (lit.,[37] 114—115°) (Found: C, 48·65; H, 6·0; N, 15·1. Calc. for $C_{15}H_{21}N_4O_7$: C, 48·7; H, 6·0; N, 15·4%).

A higher fraction (b. p. 115—120°/15 mm.) was hydrogenated similarly, and distillation of the product gave two fractions, the first of which, b. p. 160—215°, gave a crude picrate, m. p. 220—230°, from which 1,2-dimethylpyrrolidine picrate was isolated as before. The higher-boiling fraction, b. p. 215—220°, gave a crude picrate, m. p. 80—120°, which after repeated crystallisation from ethanol formed yellow rods, m. p. 154—155° [Found: C, 52·8; H, 6·6;

[36] Lukeš, *Coll. Czech. Chem. Comm.*, 1938, **10**, 66.
[37] Craig, *J. Amer. Chem. Soc.*, 1933, **55**, 2543.

N, 13·4%; *M* (from abs. spec.[38]), 408. $C_{18}H_{28}N_4O_7$ requires C, 52·4; H, 6·85; N, 13·6%; *M*, 412].

2-Butyl-1-methylpyrrolidine.—Prepared by hydrogenation, as described above, of 2-butyl-1-methylpyrroline [$\nu_{max.}$ 1668 cm.$^{-1}$ (C=C); picrate, m. p. 64—66° (lit.,[39] 66°)], itself obtained by Craig's method,[39] 2-butyl-1-methylpyrrolidine had b. p. 170—172° (lit.,[40] 40—41°/28 mm.), n_D^{23} 1·4400, and gave a picrate, m. p. 113—114° (lit.,[37] 114—115°).

3-Allyl-1-methyl-2-pyrrolidone.—To a stirred suspension of sodamide (40 g.) in dry benzene (150 c.c.), freshly distilled 1-methyl-2-pyrrolidone (80 g.) in benzene (350 c.c.) was added. The mixture was heated under reflux for 2 hr. on the water-bath and then cooled to 5°; next a solution of freshly distilled allyl bromide (100 g.) in benzene (50 c.c.) was added slowly. The mixture was heated under reflux for 2 hr., cooled, and then treated with 0·1N-nitric acid (100 c.c.). The layers were separated and the aqueous layer further extracted with ether (2 × 50 c.c.). Acidification of the aqueous layer followed by chloroform extraction gave unchanged 1-methyl-2-pyrrolidone (15 g.). The combined organic layers were dried, the solvent was removed and the residue distilled. The main fraction (26 g.), b. p. 103—105°/10 mm., n_D^{25} 1·4790, was redistilled, to give *3-allyl-1-methyl-2-pyrrolidone* (16·6 g.), b. p. 106—108°/11 mm., n_D^{25} 1·4782 (Found: N, 10·4. $C_8H_{13}NO$ requires N, 10·1%), $\nu_{max.}$ 1643 (C=C) and 1699 (amide C=O) cm.$^{-1}$.

1-Methyl-3-propyl-2-pyrrolidone.—This was prepared by hydrogenation of 3-allyl-1-methylpyrrolidone (1·08 g.) over palladium–charcoal at room temperature and pressure. The *product* (0·95 g.) was distilled and had b. p. 103—104°/11 mm., n_D^{25} 1·4614 (Found: C, 68·0; H, 10·7; N, 9·9. $C_8H_{15}NO$ requires C, 67·8; H, 10·7; N, 9·9%).

3-Allyl-1,2-dimethyl-2-pyrroline Perchlorate.—3-Allyl-1-methyl-2-pyrrolidone (13·25 g.) was added to methylmagnesium iodide (from 7·2 g. magnesium) and the mixture kept at 20° for 36 hr. The product was worked up in the usual way and the steam-volatile basic fraction converted into the *perchlorate* (9·0 g.) which formed colourless plates, m. p. 110—111° (Found: C, 45·7; H, 6·5; N, 6·0. $C_9H_{16}ClNO_4$ requires C, 45·5; H, 6·8; N, 5·9%), $\nu_{max.}$ 1645, 1654 cm.$^{-1}$ (C=C) and 1696 cm.$^{-1}$ (C=N$^+$). The free base, b. p. 60—62°/12 mm., showed bands at 1643, 1654, and 1673 cm.$^{-1}$ (C=C).

1,2-Dimethyl-3-propylpyrrolidine Picrate.—The foregoing pyrroline (1 g.) in ethanol was treated with a slight excess of hydrochloric acid (to pH 5) and hydrogenated in the presence of platinum catalyst. The basic product was converted into the *picrate* which formed yellow needles, m. p. 162—163°, from ethyl acetate (Found: C, 49·0; H, 5·7; N, 14·9. $C_{15}H_{22}N_4O_7$ requires C, 48·65; H, 6·0; N, 15·1%).

3-Allyl-2-butyl-1-methyl-2-pyrroline Perchlorate.—3-Allyl-1-methyl-2-pyrrolidone (7·6 g.) was treated with butylmagnesium bromide in the usual manner in benzene. The mixture was heated under reflux for 4 hr. and worked up as before. The basic product was converted into the perchlorate which formed colourless needles (6·7 g., 44%), m. p. 55—57°, from ethanol (Found: N, 5·0. $C_{12}H_{22}ClNO_4$ requires N, 5·0%), $\nu_{max.}$ 1645, 1654 (C=C), and 1685 (C=N$^+$) cm.$^{-1}$, and the corresponding free base, b. p. 190—210°/400 mm. (bulb tube), showed bands at 1640 and 1660 cm.$^{-1}$ (C=C).

2-Butyl-1-methyl-3-propylpyrrolidine Picrate.—The foregoing perchlorate (2 g.) in ethanol was hydrogenated over platinum. The product was converted into the corresponding base and then into the *picrate* which formed yellow rods (2·1 g.), m. p. 101—103°, from ethanol (Found: N, 13·8. $C_{18}H_{28}N_4O_7$ requires N, 13·6%).

2-1′-Propylbutyl-1-pyrroline.—4-Bromoheptane, b. p. 57—60°/18 mm. (lit.,[41] b. p. 60°/18 mm.), was prepared from heptan-4-ol by the method of Coe, Landauer, and Rydon.[42] Magnesium (2·7 g.) was induced to react with 4-bromoheptane by initial treatment with methyl iodide (0·15 c.c.) in ether (10 c.c.). When the reaction had started, ether (65 c.c.) was added and the mixture heated under reflux for 4 hr. γ-Chlorobutyronitrile (8·5 g.) in ether (10 c.c.) was added and the mixture heated under reflux for 1 hr. The ether was replaced by dry xylene (50 c.c.), and the solution then heated at 140°, a vigorous reaction occurring. After 1 hr. at 140° the mixture was cooled and kept overnight. The product was decomposed with saturated aqueous ammonium chloride, and the ether layer separated. The basic products were extracted

[38] Cunningham, Dawson, and Spring, *J.*, 1951, 2305.
[39] Craig, *J. Amer. Chem. Soc.*, 1933, **55**, 295.
[40] Leonard and Locke, *J. Amer. Chem. Soc.*, 1955, **77**, 437.
[41] Shonle, Waldo, Keltch, and Coles, *J. Amer. Chem. Soc.*, 1936, **58**, 585.
[42] Coe, Landauer, and Rydon, *J.*, 1954, 2281; Rydon and Tonge, *J.*, 1956, 3043.

into 6N-hydrochloric acid and then back into ether after the addition of an excess of sodium hydroxide. The solvent was removed from the dried solution and distillation of the residue gave the product as a colourless oil (0·75 g.), b. p. 85—88°/12 mm., n_D^{24} 1·4526, $\nu_{max.}$ 1640 cm.$^{-1}$ (C=N). The *picrate* formed yellow rhombs, m. p. 68—69°, from ethanol (Found: C, 51·3; H, 6·35; N, 13·8. $C_{17}H_{24}N_4O_7$ requires C, 51·5; H, 6·1; N, 14·1%).

1-*Methyl*-2-1′-*propylbutyl*-2-*pyrroline Perchlorate*.—The above 1-pyrroline (1·4 g.) was heated with an excess of methyl iodide in ether under reflux for 2 hr. The pale yellow methiodide (1·9 g.), m. p. 35—40°, was collected and treated with silver perchlorate solution. The *perchlorate* so obtained formed colourless needles, m. p. 127—128°, from ethanol (Found: N, 4·8. $C_{12}H_{24}ClNO_4$ requires N, 5·0%).

1-*Methyl*-2-1′-*propylbutylpyrrolidine Picrate*.—The above methiodide was hydrogenated as before and the product converted into the corresponding *picrate*, which formed yellow plates, m. p. 81—83°, from ethanol (Found: C, 52·5; H, 6·4; N, 13·6. $C_{18}H_{28}N_4O_7$ requires C, 52·4; H, 6·8; N, 13·6%).

1-*Ethyl*-3,4-*dimethylpyrrolidine*.—3,4-Dimethylpyrrole (4·5 g.) in ethanol (30 c.c.) was hydrogenated at 180°/170 atm. in presence of Raney nickel for 12 hr. After cooling, the catalyst was removed and the solution acidified with hydrochloric acid before removal of the ethanol. The aqueous solution of the hydrochloride was basified and extracted with ether. Removal of the solvent from the dried extract gave 1-ethyl-3,4-dimethylpyrrolidine (2·3 g., 40%), b. p. 136—138°. The *picrate* formed yellow needles, m. p. 168—169°, from ethanol (Found: C, 47·1; H, 5·85; N, 15·8. $C_{14}H_{20}N_4O_7$ requires C, 47·2; H, 5·7; N, 15·7%).

1,3,4-*Trimethylpyrrolidine*.—This was prepared as above but with methanol as solvent. From the pyrrole (14 g.), 1,3,4-trimethylpyrrolidine (11 g., 66%), b. p. 116—120°, was obtained; it gave a picrate having m. p. 206—207° (lit.,[17] 203—204°), after crystallisation from ethanol. The *methiodide* formed colourless plates, m. p. 199·5—200·5°, from ethanol (Found: C, 37·7; H, 7·0; N, 5·2. $C_8H_{18}IN$ requires C, 37·7; H, 7·1; N, 5·5%). The *methopicrate* formed yellow needles, m. p. 217—218°, from ethyl acetate (Found: C, 47·2; H, 5·6; N, 15·5. $C_{14}H_{18}N_4O_7$ requires C, 47·5; H, 5·1; N, 15·8%).

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