# CCLIII.—*The Lupin Alkaloids. Part II.*

By GEORGE ROGER CLEMO and RICHARD RAPER.

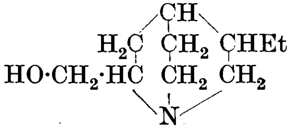
SINCE the publication of Part I of this investigation (Clemo and Leitch, J., 1928, 1811), dealing mainly with lupanine, papers by Schöpf (*Annalen*, 1928, **465**, 97) and Karrer (*Helv. Chim. Acta*, 1928, **11**, 1061) and collaborators have appeared in this field. It is deemed advisable, therefore, to record some of the results we have obtained on the degradation of lupinine and sparteine, and in particular those bearing on the formula advanced by Karrer for lupinine.

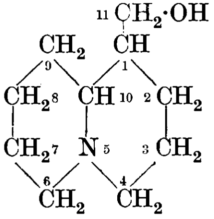
Schöpf and his collaborators (*loc. cit.*) show that lupinine has no primary alcoholic group attached to the quinuclidine ring system as in (I), and they have prepared a third methylsparteine, which is different from the isomeric α- and β-bases described by Moureu and Valeur (*Compt. rend.*, 1907, **145**, 929), and a fourth base which gives the analytical results required for a methylsparteine combined with a molecule of water. Karrer and his co-workers subjected lupinine methiodide to the Hofmann degradation reaction, reduced the resulting mixture of methyl-lupinines (compare Willstätter and Fourneau, *Ber.*, 1902, **35**, 1922) to the dihydro-derivatives, repeated the operations three times to remove the nitrogen, and obtained a 46%

yield of a mixture of two optically active, unsaturated $C_{10}H_{20}O$ alcohols. The range in boiling point of this mixture, 20°/11 mm., seems a wide one. No attempt was made to separate any of the mixtures of bases or their methiodides.

Reduction of the alcohols gave the decanol, and from this, by successive treatment with phosphorus pentabromide and trimethylamine, a quaternary salt was obtained which, when submitted to the Hofmann degradation process, yielded the optically active decene $C_8H_{18}{>}C{:}CH_2$. This on ozonolysis and hydrolysis gave a liquid nonanone $C_8H_{18}{>}CO$, which always gave analytical results 2% low in carbon. The liquid nonanoneoxime was subjected to the Beckmann transformation, the resulting non-crystalline amide hydrolysed, and the calcium salt of a fatty acid prepared which is stated to be doubtless calcium butyrate, although no analytical data are given to support the statement. The base formed at the same time was analysed as the hydrochloride and as the picrate and shown to be *n*-amylamine. The inference is that the nonanone is *n*-propyl *n*-amyl ketone, and this was confirmed by synthesis. This result is interpreted to mean that lupinine has probably the structure (II), although (III) and (IV) are given as unlikely alternatives.

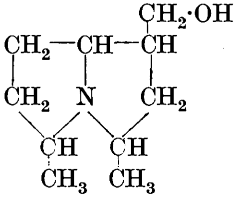
(I.)

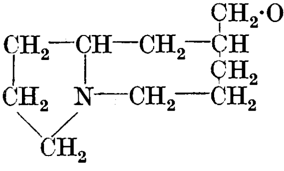




(II.)

(III.)

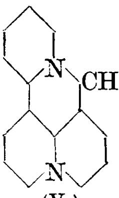


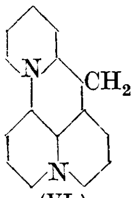


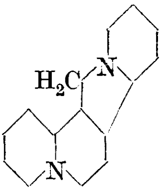
(IV.)

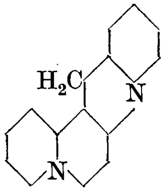
The constitution (II), containing as it does a ring system present in the berberine alkaloids with the $CH_2{\cdot}OH$ group in the same position as the methyl group in corydaline, is an attractive one.

It will be shown subsequently, however, that under certain conditions the lupinine molecule can undergo a structural change in the Hofmann degradation, and hence the promised synthesis of the structure (II) is awaited with interest. A natural extension of the above is the condensation of (II) with the piperidine ring, and Karrer advances the following four possible formulæ for sparteine:

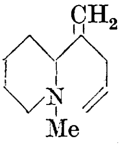

(V.)

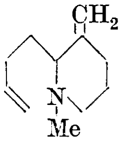

(VI.)

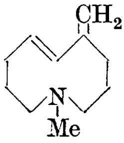

(VII.)


(VIII.)

Prior to the publication of Karrer's results, an extensive study of the Hofmann degradation of *chlorolupinine methiodide* had been in progress in this laboratory. If the treatment with silver oxide be carried out at the ordinary temperature, subsequent vacuum distillation of the methohydroxide gives a good yield of an optically active base $C_{10}H_{17}N$, isomeric with, but more stable than anhydrolupinine (Willstätter and Fourneau, *loc. cit.*), and subsequently called *ψ-anhydrolupinine*. This base gives two stereoisomeric *methiodides*, and is reduced by hydrogen and palladium to the saturated compound $C_{10}H_{19}N$. If, however, the treatment with silver oxide is carried out at 100°, or first as above and then at 100°, subsequent degradation, a much more facile operation than for lupininemethylammonium hydroxide, gives an optically active basic mixture $C_{11}H_{19}N$, identical with that obtained in the Hofmann degradation of anhydrolupinine methiodide. Assuming, as will be done throughout for the purpose of discussion, the correctness of formula (II) for lupinine, the three structures (IX), (X), and (XI) are


(IX.)

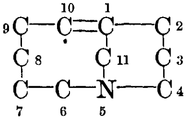

(X.)

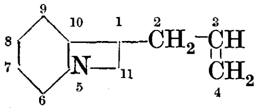

(XI.)

possible for *anhydromethyl-lupinine*. That the basic mixture obtained contains a preponderating amount of one anhydromethyl-lupinine (α) is indicated by the fact that it gives a good yield of an almost pure *methiodide*, but absence of complete homogeneity is evidenced by the necessity of a few recrystallisations before a pure picrate can be obtained. The anhydromethyl-lupinine mixture is not reduced by sodium amalgam, undergoes a complex change, including the formation of an isomeric base, on treatment with hydrochloric acid, and in presence of palladium and hydrogen absorbs two atoms of hydrogen. Under similar conditions anhydrolupinine is reduced to two isomeric lupinanes (compare D.R.-P. 396508; Schöpf, *loc. cit.*), and it is difficult to understand from structures (IX), (X), and (XI) why both double bonds are not reduced in the anhydromethyl-lupinines to give a mixture of methyl-lupinanes. The actual $C_{11}H_{21}N$ mixture, as might be expected from its derivation largely from α-anhydromethyl-lupinine, gives mainly two isomeric *methiodides*, although a small amount of a third form, doubtless derived from the reduction of β-anhydromethyl-lupinine, has been isolated.

The formation of ψ-anhydrolupinine, $C_{10}H_{17}N$, from chlorolupininemethylammonium hydroxide apparently occurs in two stages, water being first lost, and a methochloride formed which then decomposes in the normal manner with loss of methyl chloride. The loss of water can occur in four different ways dependent on whether the β-hydrogen atom involved in the change occupies the 1, 3, 7, or 9 position, but in any case the subsequent formation and decomposition of a methochloride to give (XII), (XIII), (XIV), or (XV) seems at first sight improbable.

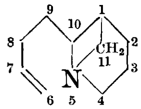
(XII.)

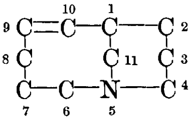




(XIII.)

(XIV.)



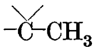


(XV.)

The literature contains little or no guidance as to how a ring structure such as (II) might be expected to rupture in the Hofmann degradation. On general electronic grounds the oxygen electron source might be expected to decrease the activity of the hydrogen atom attached to carbon atom 1 more than that of those attached to 3 and 9, and the effect on the hydrogen atoms attached to 7 would be still less. The fact that tetrahydroberberine methohydroxide with its additional fused ring systems and minus the oxygen atom in (II) gives the ten-membered ring compound anhydrotetrahydromethylberberine (Perkin, J., 1916, **109**, 952) is no guide in the present case. Hanhart and Ingold (J., 1927, 977) and Ingold and Vass (J., 1928, 3125) deal with the mechanism of the Hofmann degradation reaction, and state that in the general case the normal (A) reaction involves a

$$[R_1R_2CH\cdot CR_3R_4\cdot\overset{+}{N}Me_3]\overset{-}{O}H - \left| \begin{array}{ll} \rightarrow R_1R_2C{:}CR_3R_4 + NMe_3 + H_2O & (A) \\ \rightarrow R_1R_2CH\cdot CR_3R_4\cdot NMe_2 + MeOH & (B) \end{array} \right.$$

β-hydrogen atom, whereas reaction (B) is mainly dependent on the influence of $R_1$ and $R_2$, being favoured by their increasing molecular weight, and also if $R_1$ or $R_2$ contains a branched chain. If lupanine contains one of the structures (V), (VI), (VII), and (VIII), this might explain why lupaninemethylammonium hydroxide undergoes only the (B) reaction, but against this must be placed the fact that sparteine and oxysparteine undergo the normal (A) reaction only.

Although Willstätter (*loc. cit.*) prepared only one pure methyl-lupinine methiodide—now found to be much more conveniently prepared from the base obtained by distilling lupinine methiodide with potash in a vacuum—from his mixture of methyl-lupinines, it has been found possible to prepare two crystalline *chloromethyl-lupinine methiodides*, both of which on subjection to the Hofmann degradation give a *chlorodimethyl-lupinine*. Under these conditions, therefore, the chlorine atom does not react with the nitrogen atom as in the formation of ψ-anhydrolupinine. On studying the formation of the latter with the aid of models, it is evident that systems (XIII) and (XIV) would be very strained and hence unlikely to be formed. If, however, the configurations are considered into which the chloro-methyl-lupinine can pass by strain-free rotations, it is found that carbon atom 11 comes into such a position that quaternary ion formation is possible between it and the nitrogen atom, and the resulting methochloride gives, with loss of methyl chloride, one or other of the strain-free structures (XII) and (XV) according as the double bond in the chloromethyl-lupinine occupies positions 1—10 or 9—10. The strain-free character of these systems would seem to lessen the necessity for extrusion of carbon atoms from the ring in the form of  $-\overset{\diagdown\,\diagup}{C}-CH_3$. In addition, as the base gives two stereoisomeric methiodides and is optically active, and as so far it has not been possible to prepare a carbonyl derivative from it through its amine oxide (compare the conversion of anhydrotetrahydroberberine into β-homochelidonine; Haworth and Perkin, J., 1926, 466), structure (XV) and not (XII) is indicated for ψ-anhydrolupinine.

N-*Piperidyl-lupinine* has been prepared for comparison with sparteine. It readily yields a *dimethiodide*, whereas sparteine only gives monomethiodides, and also differs from sparteine in not containing a $>CH_2$ group easily oxidisable by potassium ferricyanide. An ethereal solution of *N*-piperidyl-lupinine containing a trace of sulphur in suspension, however, gives with hydrogen sulphide a light orange precipitate similar to that from lupinine, in contrast to the deep orange one given by sparteine. A comparison of the degradation products of *N*-piperidyl-lupinine with those of sparteine and lupanine is being carried out.

Although Moureu and Valeur describe α- and β-methylsparteines, and Schöpf a third form, it has now been found that, on distilling either sparteine α- or α′-methiodide with potassium hydroxide in a vacuum, a base passes over in good yield which redistils within 1°/1 or 26 mm., gives the analytical results of a methylsparteine, and appears to be different from its known isomerides. For instance, the new *base* is easily soluble in methyl alcohol, cannot be induced to crystallise, and gives a mercurichloride decomposing at 179—182°, whereas Moureu's α-base is not very soluble in this solvent, can easily be obtained crystalline, and gives a mercurichloride, m. p. 270°. Moureu's β-base is dextrorotatory, whereas the new base is lævorotatory. Schöpf's third methylsparteine is lævorotatory and gives a mercurichloride melting at 182—185°, but it gives a dihydriodide (yield not stated) of m. p. 223—225°, whereas the new base under the same conditions gave only a trace of solid after several days. Moureu's α-methylsparteine methiodide has m. p. 242° (Schöpf gives 239°), whereas the methiodide of the new base decomposes at 247° and a mixture of the two at 232°.

When sparteine is oxidised with chromic acid (Willstätter and Marx, *Ber.*, 1905, **38**, 1772) or alkaline ferricyanide (Ahrens, *Ber.*, 1905, **38**, 3268; Schöpf, *Annalen*, 1928, **465**, 132), oxysparteine is produced. Oxysparteine is destroyed completely by potassium permanganate, but resembles *iso*lupanine (Clemo and Leitch, *loc. cit.*) in resisting all attempts at reduction, including sodium amalgam, treatment in the electrolytic cell, and heating with fuming hydriodic acid and red phosphorus at 240° for 28 hours in sealed tubes. It is also stable to potash fusion and to hydrochloric acid at 140°. Oxysparteine gives a monomethiodide and a *methosulphate*, and by means of the Hofmann degradation of the former, or treatment of the latter with sodium amalgam, *α-methyloxysparteine* is obtained, which, like oxysparteine, is monobasic and forms a *methosulphate*, although it has not been possible to obtain from it a crystalline methiodide. If, however, oxysparteine methiodide or α-methyloxysparteine is distilled slowly with potassium hydroxide in a vacuum, an isomeric base, *β-methyloxysparteine*, is formed. This substance gives a *monopicrate* and a crystalline *methiodide*. The latter, when submitted to the Hofmann degradation, undergoes both reactions (A) and (B) (p. 1930), but from the resulting mixture of bases a crystalline *methiodide* has been obtained which gives the analytical figures required for dimethyloxysparteine methiodide. This, unfortunately, undergoes reaction (B) almost entirely in the Hofmann degradation, and hence it has not yet been possible to eliminate one of the nitrogen atoms of oxysparteine.

In an attempt to demethylate α-methyloxysparteine with cyanogen bromide a surprising result has been obtained. When an acetone solution of the base and cyanogen bromide is kept over-night, a crystalline mass is formed, which, on fractional crystallisation from methyl alcohol, can be separated into an addition product of two molecules of cyanogen bromide with one of base, and a second substance which has the composition of methyloxysparteine in which the methyl group has been replaced by cyanogen.

It seems probable that sparteine and lupanine are in the main structurally similar, and it is of interest to consider briefly how their chemistry, and particularly that of their oxy-compounds, fits in with the proposed formulæ (V), (VI), (VII), and (VIII) for sparteine. Evidence, as yet incomplete, points to the fact that lupanine probably contains the lactam group $>N\cdot CO^-$, and the existence of oxylupanine (Clemo and Leitch, *loc. cit.*, p. 1815), and also of *iso*lupanine and oxysparteine, indicates the possibility of a second non-reactive carbonyl group in the latter compounds. The fact that these oxy-derivatives do not give the hydrogen sulphide reaction of lupinine, *N*-piperidyl-lupinine, and sparteine points to the oxygen atom, and therefore the easily oxidisable $>CH_2$, being in the lupinine part of the molecule, and yet neither chlorolupinine nor *N*-piperidyl-lupinine gives an oxy-derivative when treated with alkaline ferricyanide. None of the suggested formulæ for sparteine appears to explain the facts, and, further, sparteine and lupanine form only monomethiodides, whereas (V) and (VII), by analogy with *N*-piperidyl-lupinine, and (VI), by analogy with lupinine itself, would be expected to form dimethiodides.

The degradation of sparteine and lupanine is being continued along the lines indicated.

## EXPERIMENTAL.

The seed of *Lupinus luteus* has been found to be a better source of *l*-lupinine than *L. pilosus*, and 1 cwt. of the former (kindly extracted by Messrs. T. and H. Smith, Ltd., of Edinburgh) gave 2 l. of extract as sulphate, 100 c.c. of which, made alkaline with potassium hydroxide, on extraction with chloroform and fractionation, gave 23—24 g. of crystalline lupinine and 5—6 g. of sparteine. The lupinine (24 g.) was recrystallised from ligroin (15 c.c., b.p. 40—60°) and gave colourless prisms (17 g.), m. p. 70—71° (Found: C, 71·1; H, 10·95. Calc. for $C_{10}H_{19}ON$: C, 71·0; H, 11·2%). Lupinine is readily soluble in cold water, less soluble in hot, and gives a solution strongly alkaline to litmus. An ethereal solution containing sulphur gives a light orange precipitate when hydrogen sulphide is passed in.

Lupinine methiodide was obtained when lupinine (5 g.) was dissolved in acetone (15 c.c.), methyl iodide (2 c.c.) in acetone (2 c.c.) added, and the mixture cooled. The crystalline mass produced was warmed for 30 minutes on the water-bath, collected, washed with a little ethyl alcohol, and dried on the steam-bath; wt., 8·9 g., m. p.

305—306° (with decomp.). The compound can be recrystallised from ethyl alcohol–water, but is practically pure as obtained.

Powdered lupinine methiodide (2 g.) and potassium hydroxide (3 g.) were mixed and carefully heated with a free flame for 15 minutes under 1 mm. pressure *; a colourless oil with a terpene-like odour, due to a trace of decomposition product, then passed over. This redistilled at 108—110°/1 mm. (1·1 g.), and with methyl iodide in acetone gave 1·7 g. of α-methyl-lupinine methiodide, m. p. 216° after softening at 200°. One recrystallisation from ethyl alcohol (30 c.c.) gave 1·2 g. of colourless prisms, m. p. 224—225°. By the Hofmann method with silver oxide (1 g.) the corresponding amounts were 1·1 g. of base, b. p. 105—110°/1 mm., 1·25 g. of methiodide, m. p. 190—205°, 0·75 g. of m. p. 218—223° after recrystallisation, and a further recrystallisation was necessary to obtain the pure α-methiodide.

*α- and β-Chloromethyl-lupinine Methiodides.*—The mixture of methyl-lupinines from the silver oxide method (3 g.), when dissolved in benzene (15 c.c.) and treated with phosphorus pentachloride (2 g.) as described below for chlorolupinine, gave 2·3 g. of chloromethyl-lupinines, b. p. 90—92°/1 mm. (Found: C, 65·4; H, 10·2. $C_{11}H_{20}NCl$ requires C, 65·5; H, 9·9%). This mixture (2 g.) was dissolved in acetone (4 c.c.), methyl iodide (1 c.c.) added, and the crystalline precipitate (1·7 g.), m. p. 195—200° (decomp.) after softening at 180°, collected after 3 hours. Pure *α-chloromethyl-lupinine methiodide* was obtained from this by recrystallisation from ethyl alcohol as colourless prisms, m. p. 215—216° (Found: C, 42·2; H, 7·1. $C_{12}H_{23}NClI$ requires C, 42·0; H, 6·7%). The acetone filtrate from the above at once deposited 0·7 g. of the *β-methiodide* as prisms, m. p. 180—182°; a further 0·1 g. separated over-night. Recrystallised from acetone, it formed prisms, m. p. 182° (Found: C, 42·1; H, 6·5%). Both the α- and the β-methiodide when subjected to the Hofmann degradation gave bases, b. p. 100°/1 mm., approx., and as a crystalline picrate or methiodide could not be prepared from them, it is not possible to say whether one or more *chlorodimethyl-lupinines* had been formed (Found: N, 6·3. $C_{12}H_{22}NCl$ requires N, 6·5%).

*Chlorolupinine Methiodide.*—A solution of lupinine (12·6 g.) in benzene (40 c.c.) was refluxed with phosphorus pentachloride (9 g.) for 1¾ hours and cooled, and a little ice added, followed by potassium hydroxide (230 c.c., *d* 1·25). The mixture was well shaken, the benzene layer separated, the extraction repeated, and the extract dried over solid potassium hydroxide over-night. Fractionation gave 12·3 g. of chlorolupinine as a colourless oil, b. p. 88—92°/1 mm.,

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* This method was employed for all the fusions with potassium hydroxide in a vacuum recorded in this paper.

and 0·8 g., b. p. up to 120°/1 mm. When chlorolupinine (15 g.), acetone (7·5 c.c.), and methyl iodide (6 c.c.) were mixed and cooled, the solution rapidly set to a crystalline mass. After warming on the water-bath for 30 minutes, the solid was collected (27·5 g., m. p. 193—195°), and recrystallised from ethyl alcohol (35 c.c.), giving 24 g. of well-formed prisms, m. p. 204° (Found: C, 40·6; H, 6·6. $C_{11}H_{21}NClI$ requires C, 40·1; H, 6·4%).

*ψ-Anhydrolupinine.*—Chlorolupinine methiodide (6·5 g.) was dissolved in water (30 c.c.), silver oxide (5 g.) added, the mixture well shaken for 2 hours, and the filtered solution reduced to a small bulk by heating on the water-bath under diminished pressure. The evaporation to dryness was completed with a free flame, leaving a colourless very deliquescent mass, which, on being heated with a free flame, or in a metal-bath to 280°, under 1 mm. pressure, gave 2·8 g. of slightly damp distillate. This was dissolved in ether, dried with potassium carbonate, and distilled, giving 2·6 g. of a colourless mobile oil, b. p. 63°/0·5 mm., with a geranium-like odour when fresh. $[\alpha]_D$ in acetone $-35·3°$ (Found: C, 79·3; H, 11·3. $C_{10}H_{17}N$ requires C, 79·4; H, 11·3%). *ψ-Anhydrolupinine* is lighter than and slightly soluble in water, very alkaline to litmus, and slowly turns brown in contact with the air, although quite stable when sealed up out of contact with the air. Its cold acetone solution reduces potassium permanganate, and the base is unchanged after being heated for 12 hours at 100° with 15% hydrochloric acid. The *picrate* was prepared in ether–ethyl alcoholic solution, and after recrystallisation from ethyl alcohol gave canary-yellow plates, m. p. 154° (Found: C, 50·6; H, 5·4. $C_{10}H_{17}N,C_6H_3O_7N_3$ requires C, 50·5; H, 5·3%). Anhydrolupinine picrate forms deep yellow prisms, m. p. 94°.

The *chloroplatinate* forms deep orange prisms from ethyl alcohol–water (9 : 1) containing a trace of hydrogen chloride and melts at 210° (decomp.) [Found: C, 33·85; H, 4·8; Pt, 27·6; *M*, 149. $(C_{10}H_{17}N)_2,H_2PtCl_6$ requires C, 33·7; H, 5·0; Pt, 27·4%; *M*, 151].

*α- and β-ψ-Anhydrolupinine Methiodides.*—ψ-Anhydrolupinine (5 g.), acetone (12 c.c.), and methyl iodide (2·5 c.c.) were mixed and kept over-night. The resulting solid (8·5 g., m. p. 195—200°) was separated by fractional crystallisation from acetone into *α-ψ-anhydrolupinine methiodide*, colourless prismatic plates, m. p. 172° (Found: C, 45·3; H, 6·9. $C_{10}H_{17}N,MeI$ requires C, 45·05; H, 6·8%), and *β-ψ-anhydrolupinine methiodide*, colourless prisms, m. p. 263° (Found: C, 44·7; H, 6·6%). Anhydrolupinine methiodide when prepared in and recrystallised from acetone melts at 189—190° (Willstätter and Fourneau, *loc. cit.*, give m. p. 180°). The above α-methiodide (2·2 g.) was refluxed with silver chloride for 2 hours, and the resulting methochloride decomposed by heating under 1 mm. pressure, thus regenerating 0·6 g. of ψ-anhydrolupinine, as proved by conversion into the picrate. This base (0·3 g.) gave 0·45 g. of mixed methiodides, m. p. 200—205°, which were separated into the α- and β-forms by treatment with acetone.

*ψ-Anhydromethyl-lupinine Methiodide.*—The above α-methiodide (m. p. 172°) (1·5 g.) was dissolved in water (10 c.c.), silver oxide (1 g.) added, and the mixture shaken for 2 hours and worked up as usual, giving 0·6 g. of base, b. p. 60°/1 mm., of which 0·3 g. gave 0·5 g. of crystals, m. p. 168—170°. After three crystallisations from acetone a pure *methiodide* was obtained, m. p. 186—187° (Found: C, 47·0; H, 7·3. $C_{12}H_{22}NI$ requires C, 46·9; H, 7·2%). The same methiodide resulted when a mixture of the α- and β-methiodides was used in the above reaction.

*ψ-Anhydrodihydrolupinine.*—ψ-Anhydrolupinine (3·2 g.) was reduced in acetic acid solution with hydrogen and palladium chloride and gave 2 g. of a colourless oil, b. p. 58—59°, $[\alpha]_D$ in acetone +21·7° (Found: C, 78·6; H, 12·4; N, 9·2. $C_{10}H_{19}N$ requires C, 78·4; H, 12·4; N, 9·1%). The base is quite stable in the air, and forms a *picrate*, yellow prisms (from ethyl alcohol), m. p. 176—177° (Found: C, 50·6; H, 5·8. $C_{10}H_{19}N,C_6H_3O_7N_3$ requires C, 50·2; H, 5·7%). Treatment of the base (3·5 g.) with acetone (7 c.c.) and methyl iodide (1·5 c.c.) gave 6·15 g. of mixed methiodides, m. p. 250—280° (decomp.). Extraction with acetone left a residue which when recrystallised from ethyl alcohol–acetone (1 : 1) gave colourless prisms of *α-ψ-anhydrodihydrolupinine methiodide*, m. p. 310—312° (decomp.) (Found: C, 45·0; H, 7·7. $C_{11}H_{22}NI$ requires C, 44·7; H, 7·5%). The cold acetone extract gave a crystalline deposit, m. p. 220—240°, but all attempts to isolate a second form of the methiodide in a pure state have failed.

*Anhydromethyl-lupinine.*—Chlorolupinine methiodide (8·25 g.), water (30 c.c.), and silver oxide (6·2 g.) were stirred on the steam-bath for 7 hours and the liquid was filtered, reduced to small bulk on the water-bath under diminished pressure, and to dryness from an oil-bath at 130°/12 mm.; a colourless oil then passed over. Small amounts of water were added to the residue, and the evaporation to dryness was repeated as long as any oil came over. The oil was extracted with ether, dried over potassium carbonate, and distilled, giving 2·65 g. of a colourless oil, b. p. 63°/1 mm., $[\alpha]_D$ in acetone − 46·8° (Found: C, 80·0; H, 11·9; N, 8·6. $C_{11}H_{19}N$ requires C, 80·0; H, 11·5; N, 8·5%). *Anhydromethyl-lupinine* has a slight fishy odour, is very much more stable than anhydrolupinine, and is but slightly soluble in water and faintly alkaline to litmus. It is not reduced by sodium amalgam in boiling alcohol, but its solution in cold acetone rapidly reduces potassium permanganate. When it is heated on the water-bath with hydrochloric acid (15%), a complex reaction occurs, and together with other products an isomeric base, $C_{11}H_{19}N$, is obtained, the *methiodide* of which forms colourless plates, m. p. 219° (Found: C, 47·1; H, 7·35. $C_{11}H_{19}N,MeI$ requires C, 46·9; H, 7·2%).

The *picrate* of anhydromethyl-lupinine, prepared in, and recrystallised from, methyl alcohol, forms bright yellow prisms, m. p. 162—163° (Found: C, 51·6; H, 5·6. $C_{11}H_{19}N,C_6H_3O_7N_3$ requires C, 51·8; H, 5·65%). The *chloroplatinate* crystallises in well-formed old-gold prisms, decomp. 210° [Found: C, 36·0; H, 5·75; Pt, 26·1; *M*, 169·3. $(C_{11}H_{19}N)_2,H_2PtCl_6$ requires C, 35·7; H, 5·5; Pt, 26·3%; *M*, 165].

*Methiodide.* When the base (1·1 g.) in acetone (2 c.c.) and methyl iodide (0·5 c.c.) were left over-night, 1·95 g. of crystalline solid, m. p. 184—186°, formed. This was recrystallised from ethyl alcohol–acetone (1 : 6), giving thin colourless prisms, m. p. 191—192° (Found: C, 46·7; H, 7·3. $C_{11}H_{19}N,MeI$ requires C, 46·9; H, 7·2%). An attempt to carry out the Hofmann degradation on this methiodide gave a high-boiling base, probably through polymerisation.

*Anhydrodihydromethyl-lupinines.*—The catalytic reduction of the above anhydromethyl-lupinine (3 g.) was carried out as in the previous case, and gave 1·5 g. of a colourless oil, b. p. 60°/1 mm. (Found: C, 78·85; H, 12·7; N, 8·3. $C_{11}H_{21}N$ requires C, 79·0; H, 12·6; N, 8·3%). A second treatment failed to effect further reduction of the base, which only slowly reduced potassium permanganate in cold acetone.

*α- and β-Picrates.* A solution of picric acid (0·54 g.) in methyl alcohol (4 c.c.) was added to the basic mixture (0·4 g.) and 0·475 g. of stout yellow prisms was collected after 3 hours. Recrystallisation from methyl alcohol gave the α-form as six-sided prisms, m. p. 145—146° (Found: C, 51·3; H, 5·9. $C_{11}H_{21}N,C_6H_3O_7N_3$ requires C, 51·5; H, 6·1%). On standing, the partly evaporated initial mother-liquor deposited 0·15 g. of prisms, m. p. 113—120°, and recrystallisation from methyl alcohol gave the β-*form* as six-sided prisms, m. p. 132° (Found: C, 51·5; H, 6·2%). When picrate formation was carried out in ethyl alcohol–ether, bright yellow, apparently homogeneous prisms were obtained, m. p. 115—130°, which remained unchanged after four recrystallisations from ethyl alcohol.

*Anhydrodihydromethyl-lupinine Methiodides.*—A solution of the basic mixture (1·5 g.) in acetone (2 c.c.) and methyl iodide (0·5 c.c.) was left for 24 hours and the precipitate was then collected and washed three times with small amounts of acetone and finally with ether (filtrate A); 1 g., m. p. 170—180°, remained. Recrystallisation from ethyl acetate and then from acetone gave the *α-meth-*

*iodide*, m. p. 195—196° (Found: C, 46·7; H, 7·8. $C_{11}H_{21}N$,MeI requires C, 46·6; H, 7·7%).

Filtrate A on dilution with ether gave 1·6 g. of crystalline precipitate, m. p. 100—110°, and two recrystallisations from ethyl acetate gave the pure β-*methiodide*, m. p. 145—146° (Found: C, 46·7; H, 7·9%). The mother-liquor from the β-form slowly deposited a small amount of a third *methiodide*, which crystallised from acetone in stout prisms, m. p. 199—200°, depressed to 180—185° on admixture with the α-form (Found: C, 47·2; H, 7·9%).

N-*Piperidyl-lupinine.*—Chlorolupinine (5·5 g.), piperidine (6 g.), sodium acetate (2·7 g.), and copper powder (0·2 g.) were heated in a sealed tube for 10 hours at 200°. Water (15 c.c.) and then potassium hydroxide (15 c.c., *d* 1·25) were added, the mixture was extracted with ether, and the extract was dried with potassium carbonate and fractionated, giving 1·2 g. of piperidine, 2·2 g., b. p. up to 115°/1 mm., and 5·5 g., b. p. 128—130°/1 mm. (Found for the last fraction: C, 76·4; H, 12·0. $C_{15}H_{28}N_2$ requires C, 76·3; H, 11·9%). N-*Piperidyl-lupinine* is a colourless, very stable oil, lighter than and almost insoluble in water, and strongly alkaline to litmus. It gives a light orange precipitate in the sulphur–hydrogen sulphide reaction, and slowly decolorises a cold acetone solution of potassium permanganate.

*The dimethiodide.* The base (1·2 g.) in acetone (5 c.c.) and methyl iodide (1 c.c.) gave 2·4 g. of *dimethiodide*, m. p. 305—310°, which separated as colourless, well-formed prisms, m. p. 324° (decomp.), from ethyl alcohol–water (4 : 1) (Found: C, 39·4; H, 6·5. $C_{15}H_{28}N_2$,2MeI requires C, 39·2; H, 6·6%).

*Methylsparteine.*—Sparteine methiodide (α- or α′-) was fused with potash in a vacuum as above, and the product from 12 g. redistilled at 135—136°/1 mm. (7 g.) (Found: C, 77·4; H, 11·2; N, 11·3. $C_{16}H_{28}N_2$ requires C, 77·4; H, 11·3; N, 11·3%). $[\alpha]_D$ (in alcohol, 2·64% solution) − 16·3°. The base (1 g.) and mercuric chloride (3·4 g.) in dilute hydrochloric acid gave the mercurichloride (3·2 g.; calc., 3·6 g.), m. p. 170°, raised to 179—182° by recrystallisation from hydrochloric acid (*d* 1·09).

The *methiodide* was obtained when the base (2 g.) in acetone (2·5 c.c.) and methyl iodide (2 c.c.) were kept over-night (1·3 g., m. p. 242° with decomp.). Recrystallisation from water gave irregular prisms with half a molecule of water of crystallisation, not lost by heating for 3 hours at 120°; m. p. 247° (decomp.) (Found: C, 51·1, 51·1; H, 7·7, 8·0. $C_{16}H_{28}N_2$,MeI,$\frac{1}{2}H_2O$ requires C, 51·1; H, 8·0%). Mixed with the monomethiodide of α-methylsparteine, it melted at 232°.

Oxysparteine was prepared by a method essentially the same as that of Schöpf, but was purified by distillation in a vacuum; it then had b. p. 204°/9 mm., m. p. 86—87° after recrystallisation from light petroleum, and $[\alpha]_D$ in ethyl alcohol $-10{\cdot}4°$ (Found: C, 72·3; H, 9·7; N, 11·5. Calc. for $C_{15}H_{24}ON_2$: C, 72·6; H, 9·7; N, 11·3%). The picrate melts at 185° (Schöpf gives 183° and Ahrens, *Ber.*, 1891, **24**, 1095, 176—178°). The methiodide (15 g., m. p. 228°) was obtained when oxysparteine (10 g.), acetone (10 c.c.), and methyl iodide (7 c.c.) were gently heated on the water-bath over-night. Recrystallised from methyl alcohol, it formed colourless needles (12·5 g.), m. p. 231° (Ahrens, *Ber.*, 1892, **25**, 3067, gives 191—193°) [Found: I (ionic), 32·8. Calc. for $C_{16}H_{27}ON_2I$: I, 32·5%].

*The methosulphate.* Oxysparteine (2·5 g.), acetone (10 c.c.), and methyl sulphate (1·25 g.), when refluxed gently over-night, gave 2·7 g. of colourless plates, m. p. 179° after recrystallisation from alcohol–ether (Found: C, 54·0; H, 8·5. $C_{17}H_{30}O_5N_2S$ requires C, 54·5; H, 8·0%).

*α-Methyloxysparteine.*—Oxysparteine methiodide (10 g.) when submitted to the Hofmann degradation gave a colourless viscous oil (5·8 g., b. p. 225—227°/18 mm.) which rapidly solidified, and crystallised from light petroleum as colourless prisms, m. p. 85—87° (Found: C, 73·3; H, 10·0. $C_{16}H_{26}ON_2$ requires C, 73·2; H, 10·0%). The same base was obtained when a solution of oxysparteine methosulphate (7 g.) in absolute ethyl alcohol (50 c.c.) was refluxed with sodium amalgam (50 g. of 4%) for 5 hours.

The *picrate*, prepared in and recrystallised from ethyl alcohol, formed golden-yellow needles, decomp. 248° (Found: N, 14·25. $C_{16}H_{26}ON_2,C_6H_3O_7N_3$ requires N, 14·3%).

*α-Methyloxysparteine methosulphate* (1·7 g.; m. p. 265°) was formed when methyl sulphate (0·6 c.c.) and the base (1·5 g.) were heated gently in acetone (5 c.c.) on the water-bath over-night. It crystallised from alcohol in small colourless prisms, m. p. 268° (Found: C, 55·95; H, 8·6; S, 8·5. $C_{18}H_{32}O_5N_2S$ requires C, 55·7; H, 8·2; S, 8·2%).

*β-Methyloxysparteine.*—Oxysparteine methiodide (3 g.) was fused with potash as usual, the distillation being carried out as slowly as possible to avoid the formation of a mixture of the α- and β-bases which can only be separated with difficulty. The product from four such experiments was redistilled, giving 6 g., b. p. 210—215°/1 mm., which solidified on being rubbed with light petroleum and, after recrystallisation from this solvent, melted at 86° alone and at 62° when mixed with the α-base. $[\alpha]_D + 55{\cdot}8°$ (Found: C, 73·0; H, 10·1; N, 10·6. $C_{16}H_{26}ON_2$ requires C, 73·2; H, 10·0; N, 10·7%). The same compound is produced when the α-base (1 g.) is fused with potash (3 g.) in the usual manner.

The *picrate* forms dendritic clusters from alcohol and has m. p. 237°, after softening at 229° (Found : N, 14·25. $C_{16}H_{26}ON_2,C_6H_3O_7N_3$ requires N, 14·3%).

*The methiodide.* The β-base (5 g.), acetone (7 c.c.), and methyl iodide (2·5 c.c.) were heated in a sealed tube in a boiling water-bath for 4 hours. After cooling, the solid was rubbed with acetone, collected (7·8 g.), and recrystallised from water, giving 6·5 g. of colourless needles, m. p. 247°, containing two molecules of water of crystallisation (Found : loss at 120°, 7·8. Loss of $2H_2O$ requires 8·2%. Found for dried material : C, 50·5; H, 7·55. $C_{17}H_{29}ON_2I$ requires C, 50·5; H, 7·2%).

*Dimethyloxysparteine Methiodide.*—The Hofmann degradation of the above methiodide (5 g.) gave 2·3 g. of a yellow viscous oil with a green fluorescence, b. p. 195—210°/1 mm. This oil (3·5 g.) in acetone (2·5 c.c.) was cooled and treated with methyl iodide (3·5 c.c.); heat was developed and 3·5 g. of crystalline *methiodide* rapidly separated, m. p. 186°. Recrystallisation from methyl alcohol–acetone gave pale yellow prisms, m. p. 194° [Found : C, 51·7; H, 7·5; I (ionic), 30·6. $C_{18}H_{31}ON_2I$ requires C, 51·7; H, 7·4; I, 30·3%]. The acetone mother-liquor from this methiodide deposited on standing a further 0·4 g. of solid, m. p. 232—235°, which, after recrystallising from water, melted at 247° alone or mixed with β-methyloxysparteine methiodide.

*The Action of Cyanogen Bromide on Methyloxysparteine.*—α-Methyloxysparteine (5 g.) in acetone (10 c.c.) was cooled and treated with cyanogen bromide (2·5 g.), and the mixture kept over-night. The crystalline product (3 g.) on fractional crystallisation from methyl alcohol was separated into an *addition product* of one molecule of base and two molecules of cyanogen bromide, decomp. 244° (Found : C, 45·65, 45·5; H, 6·1, 5·9. $C_{18}H_{26}ON_4Br_2$ requires C, 45·6; H, 5·55%), and a *compound*, m. p. 202°, forming large colourless prisms and having the composition of methyloxysparteine in which the methyl group is replaced by cyanogen (Found : C, 70·6, 70·4; H, 8·5, 8·5. $C_{16}H_{23}ON_3$ requires C, 70·3; H, 8·5%).

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