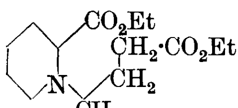
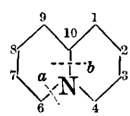
455. *The Lupin Alkaloids. Part VI.*

By G. R. Clemo, G. R. Ramage, and R. Raper.

In Parts IV and V (J., 1931, 437, 3190) the preparation of nor-lupinane " A " from lupinine was recorded. " A " was compared with the isomeric octahydropyridocoline " B " (II), as synthesised from the dicarboxylic ester (I) by the Dieckmann and subsequent reactions, and shown to be different. This result could arise from " A " and " B " being structurally different, or from their being stereoisomerides of the *cis-trans* decalin types (cf. Hückel, *Annalen*, 1925, **441**, 1). Although dipole-moment measurements indicate the non-planar nature of the three valencies of nitrogen in the ammonias, it is an outstanding fact that no such compounds have yet been resolved, and the balance of recorded opinion (cf. Meisenheimer, *Ber.*, 1924, **57**, 1744; Jackson and Kenner, J., 1928, 573; Clemo, Ormston, and Ramage, J., 1931, 3185) inclines to the view that the three nitrogen valencies are coplanar in ring systems. If this were true for the system (II), it could not exist in two forms.


(I.)



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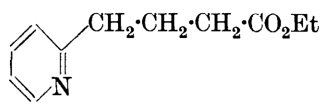
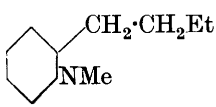
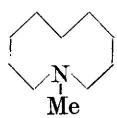


(III.)

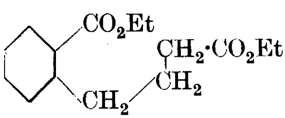
The stereoisomeric possibility has, however, always been kept in mind, and formed the basis of the work described in Part V (p. 3192) with *cis*- and *trans*-hexahydroquinolinic acids. When, therefore, evidence was found pointing to the existence of two forms of pyrrocoline (see succeeding paper), the case for two forms of (II) was strengthened, and it became necessary to see if a second form could be synthesised. Success was attained eventually in the early summer by subjecting ethyl γ-2-pyridylbutyrate (III) to a combined Bouveault and nuclear reduction, followed by halogenation and abstraction of hydrogen halide; an octahydropyridocoline was thus obtained which gave derivatives identical with those of " A."

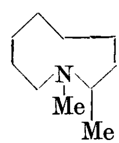
The Hofmann reaction on the methiodide of " A," followed by catalytic reduction, gives a mixture of three isomeric bases, $C_{10}H_{21}N$, two of which, " C " and " D," can be separated conveniently as picrolonates, m. p.'s 153° and 167° respectively, and the third " E " as its picrate, m. p. 196—197°. The second picrolonate occurs as either acicular prisms or stout prisms with dome-shaped ends, both melting at 167°, whilst the former is usually obtained as stout rhombs, m. p. 153°, which are transformed completely after two recrystallisations into monoclinic prisms, m. p. 147°. The pure bases regenerated from the 153° and 167° picrolonates give picrates, m. p. 88° and 94°, and methiodides, m. p. 164° and 168°, respectively, and " E " gives a picrolonate, m. p. 129°, and a methiodide, m. p. 263°. A similar treatment of the methiodide of " B " gave two of these isomerides, " D " and " E." The ring system (II) can normally undergo the Hofmann degradation in two ways by fission at either *a* or *b* with the formation, after reduction, of 1-methyl-2-*n*-butylpiperidine (IV) and 1-methyl*cyclo*azadecane (V). The former

(IV.) 



(V.)

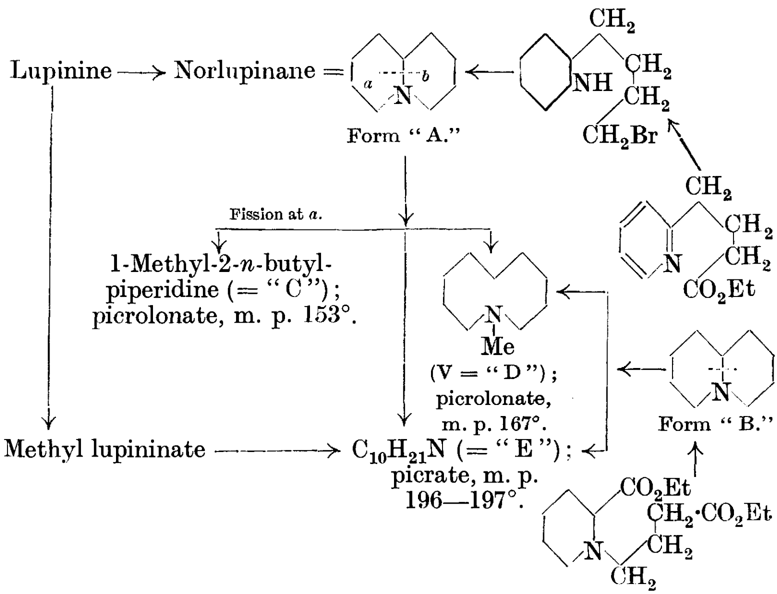
(VI.) 



(VII.)

base has been prepared by condensing α-picoline with propaldehyde, 2-β-hydroxybutylpyridine being formed, replacing the hydroxy-group by chlorine, eliminating hydrogen chloride, and reducing the ring and side chain in one operation to give 2-*n*-butylpiperidine by use of the platinum oxide catalyst of Adams and Shriner (" Organic Synthesis," VIII, 92). This was *N*-methylated by the method of Hess (*Ber.*, 1917, **50**, 1386) and gave a picrolonate, m. p. 153°, changing to 147°, identical with that obtained from " A," and the picrate and methiodide of the synthetic base were identical with those already described.

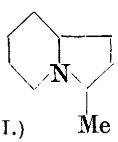
Since it is extremely unlikely that anomalous reactions have occurred in the syntheses of both " A " and " B," it is probable that " D " is (V), and, since it and " E " are obtained from both " A " and " B," these would seem to be structurally identical stereoisomerides. To account for the formation of " E," we are driven to the conclusion that either (V) can exist in stereoisomeric forms, an improbable view not supported by the examination of models, or else that, while " A " undergoes fission at both *a* and *b*, " B " breaks at *b* only, and in both cases (V), at the moment of formation, partially undergoes isomeric change, yielding possibly (VII). The base " E " is assumed to have the abnormal structure, since its formation from methyl lupininate methiodide as subsequently described involves the unusual loss of a carbomethoxy-group. Another alternative is that " A " and " B " are *cis*- and *trans*-forms of (VIII), but, as remarked already, this dual abnormality is not likely, and, further, it would not account for inactive norlupinane being formed from active norlupinene by reduction (cf. Part V, p. 3196). When the methiodide of either " A " or " B " is converted into its methochloride and the latter decomposed by vigorous heating, the original base is recovered in each case. It seems definite, therefore, that (II) exists in *cis*- and *trans*-forms which are stable and, as yet, non-interconvertible.

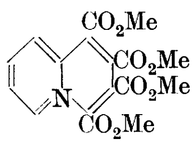


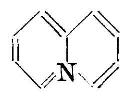
The literature does not afford any direct help as to whether the *cis*- or the *trans*-form is likely to be formed in the Dieckmann reaction on (I), since the parallel reactions with the ester (VI) with the eventual production of a decalin do not appear to have been investigated. An examination of models of the *cis*- and *trans*-modifications of (II) shows that the *cis* may assume a very compact form, which would lead to an almost strainless tricyclic system by uniting carbon atoms 3 and 7.

These results are taken to prove, therefore, that lupinine has either the *cis*- or the *trans*-octahydropyridocoline ring system and eliminate the two other possibilities emanating from the work of Karrer and co-workers (*Helv. Chim. Acta*, 1928, **11**, 1062). They do not establish the position of the $CH_2{\cdot}OH$ side chain of lupinine, which Karrer places at 1, and further synthetical work is in hand to settle this point, and also the additional problem of attaching the extra 5 carbon atoms and 1 nitrogen atom to lupinine to give sparteine and lupanine.

This paper had already been drafted (it has been held back in order to elucidate the structure of " E ") when that of Diels and Alder (*Annalen*, 1932, **498**, 1, 16) came to hand in which they describe the preparation of (IX) from pyridine and acetylenedicarboxylic ester. On hydrolysis this is stated to give (X), and finally (II) by reduction. A table is included of the derivatives prepared here from " A " and " B," but Diels only describes a picrate, m. p. 203°,


(VIII.)


(IX.)


(X.)

of his base. If this is derived from (II), it may be a mixture of the two forms melting at 194° and 213° respectively, since we have recorded such mixtures melting at about 200°. Winterfeld and Holschneider (*Annalen*, 1932, **499**, 109) also have published a synthesis of " A." The m. p.'s of their derivatives are in excellent agreement with those we have recorded (Parts IV and V) for norlupinane * and (in this paper) for synthetic " A." Their method involves heating with phosphorus pentabromide at 150° and is thus more likely to give abnormal results than the synthesis of " B," in which the only vigorous treatment is the Clemmensen reduction; it is noteworthy that refluxing with concentrated hydrochloric acid is a feature common to the work of Winterfeld and our preparations of " A," " B," and norlupinane, and, if ring crumpling has occurred

* See correction, *J.*, Feb., 1932, vi.

as a result, it might be expected that each process would give the same end product.

Until the position of the lupinine side chain is fixed it is not possible to formulate the curious chemistry shown by some of its derivatives; *e.g.*, the production of ψ-anhydrolupinine (Parts II and III). Further, it has been found that methyl lupininate gives two isomeric methiodides, α and β, and that the Hofmann degradation of these leads to the somewhat remarkable loss of the carbomethoxy-group and the formation of two $C_{10}H_{19}N$ bases. That produced from the α-methiodide does not seem to be reduced by palladium and hydrogen under conditions usually successful in this work, but it is reduced by platinum and hydrogen to the $C_{10}H_{21}N$ base "E," which is also formed by the reduction of the $C_{10}H_{19}N$ base from the β-methiodide with palladium and hydrogen. This base "E" loses its nitrogen as trimethylamine after two Hofmann reactions, giving an unstable hydrocarbon, and is therefore monocyclic and different from either (IV) or (V). When its methochloride is distilled, a small proportion of "E" is recovered, but the bulk isomerises to an open-chain tertiary base, $NMe_2{\cdot}C_9H_{18}Cl$. The methiodide of this on treatment with silver oxide gives trimethylamine and an oil which appears to be 9-hydroxy-Δ^1-nonene, since on oxidation it readily gives suberic acid. This result bears out the contention that "E" is either (V) or (VII). The former would give only suberic acid, but the latter could give in addition pimelic and ζ-keto-octoic acid.

A slight alteration in the conditions described in Part IV (p. 439) for the preparation of norlupinene leads to the production of *iso*-norlupinene, which is also easily reducible to norlupinane "A." The existence of two isomeric $C_9H_{15}N$ bases must depend on the position of the double bond and is additional evidence against the attachment of the lupinine side chain to C_{10}. Norlupinene gives a perbromide containing 4 atoms of bromine, from which dibromo-norlupinane is easily prepared. The *iso*-base, however, gives a perbromide with 3 atoms of bromine and so far it has not been possible to convert it into dibromonorlupinane. Attempts to break the ring system (II) by using cyanogen bromide in ether or acetone have so far not been successful, and the only definite result obtained by us has been the curious formation of norlupinane hydrobromide. This result is of interest because Diels and Alder (*loc. cit.*) used the same reaction and claim to have obtained 2-*n*-butylpiperidine, although the derivatives obtained therefrom do not agree with those previously recorded for the base.

In Part V (p. 3195) it is stated that a small fraction of an oil, giving the analytical results required for hydroxy-norlupinane, is produced in the preparation of norlupinene. This fraction has now yielded 10% of a crystalline hydroxynorlupinane. It may be that the oil contains a possible stereoisomeric form of the hydroxy-compound, but the whole mechanism of the formation of the norlupinenes is too uncertain to allow of any deduction in this connexion.

EXPERIMENTAL.

Base "A."—*2-Crotylpyridine.* 2-β-Hydroxy-*n*-butylpyridine (6 g.) (Löffler and Plöcker, *Ber.*, 1907, **40**, 1312) and PCl_5 (8 g.) were refluxed for 90 min. in C_6H_6. The mixture was cooled and made alkaline with 40% NaOH aq., the C_6H_6 extract separated and dried, and the solvent removed under reduced press. The residue, refluxed with methyl-alc. KOH (30 c.c., 3·5*N*) and worked up as for octahydropyridocoline "A" (below), gave crotylpyridine (4 g.), b. p. 92—93°/16 mm. (Found: N, 10·6. Calc.: N, 10·5%). The compound has been previously prepared, but only in 10% yield, from 2-β-hydroxy-*n*-butylpyridine by treatment with conc. HCl (Madzdorff, *Ber.*, 1890, **23**, 2711) or with conc. H_2SO_4 and AcOH (Löffler and Plöcker, *loc. cit.*). The m. p.'s of the picrates, chloroaurates, and chloroplatinates of these bases and ours are different. This variation must be due to mixtures of either geometrical or structural isomerides, but all are reduced to the following compound.

2-n-*Butylpiperidine.* The above unsaturated base (5·0 g.) and platinum oxide catalyst (0·1 g.) in EtOH containing 1 equiv. of HCl (60 c.c.) were shaken for 12 hr. in H (55 lb./sq. inch), a further quantity of catalyst (0·1 g.) being added after 8 hr. The solution was decanted, treated with charcoal, and concentrated; on cooling, the hydrochloride of 2-*n*-butylpiperidine (5·6 g.) separated, m. p. 176—178°, raised to 182° by one recrystn. (Found: N, 8·2. Calc.: N, 7·9%). The free base (3·4 g. from 5 g. of the hydrochloride) had b. p. 75°/14 mm. and gave a picrolonate, m. p. 182°, dark yellow prisms from EtOH (Found: C, 56·2; H, 6·85. Calc. for $C_9H_{19}N,C_{10}H_8O_5N_4$: C, 56·3; H, 6·7%).

1-*Methyl*-2-n-*butylpiperidine.* A mixture of 2-*n*-butylpiperidine hydrochloride (1·2 g.) or the free base (1 g.), CH_2O (0·8 g., 40%), HCO_2H (0·4 g.), and H_2O (2 c.c.) was heated for 8 hr. at 130—140°. The solution was basified with NaOH and steam-distilled, and an ethereal extract of the distillate dried and fractionated, giving 1-*methyl*-2-n-*butylpiperidine* (0·8 g.), b. p. 78—80°/15 mm. (Found: N, 9·1. $C_{10}H_{21}N$ requires N, 9·0%). The picrolonate (Found: C, 56·95; H, 6·8%), picrate, and methiodide (Found: C, 44·6; H, 8·3%) were identical with those of (IV) and the *chloroaurate* crystallised from aq. EtOH in yellow prisms, m. p. 90° (Found: Au, 40·0. $C_{10}H_{21}N,HAuCl_4$ requires Au, 39·8%).

Ethyl pyridine-2-carboxylate. The following method, adapted from that used by McElvain and Adams (*J. Amer. Chem. Soc.*, 1923, **45**, 2744) for the isomeric 3-carboxylic acid, is a considerable improvement on Wibaut's process (*Rec. trav. chim.*, 1926, **45**, 657). Pyridine-2-carboxylic acid hydrochloride (12 g., cryst. from EtOH) and purified $SOCl_2$ (30 c.c.) were refluxed for 2 hr. on the water-bath, the excess of $SOCl_2$ removed under slightly reduced press., abs. EtOH (20 c.c.) added to the cooled solid residue, and the mixture refluxed for 3 hr. before being evaporated to dryness. After basification with sat. K_2CO_3 aq. and fractionation, ethyl pyridine-2-carboxylate (9·0 g., b. p. 123°/14 mm.) was obtained as a colourless oil (Found: N, 9·2. Calc.: N, 9·3%).

Ethyl β-2-pyridoylpropionate. Ethyl pyridine-2-carboxylate (10 g.) and ethyl succinate (11 g.) in C_6H_6 (20 c.c.) were added to NaOEt (from 2 g. Na) and refluxed for 1 hr. before removal of the solvent. H_2O (10 c.c.) was added, and the unchanged ester extracted with C_6H_6. The aq. solution was heated on the water-bath for 6 hr. with conc. HCl (12 c.c.) and for a further 6 hr. after addition of more HCl aq. (5 c.c.) and then evaporated to dryness. The material extracted from the residue by EtOH was esterified with alc. HCl, the EtOH removed, and the residue made alkaline with K_2CO_3 aq. and extracted with Et_2O. Fractionation gave some unchanged ester (partly due to hydrolysis by HCl) and *ethyl β-2-pyridoylpropionate* (4·5 g.), a pale yellow oil, b. p. 135—140°/0·2 mm. (Found: N, 7·1. $C_{11}H_{13}O_3N$ requires N, 6·8%). The *picrolonate*, light brown prisms from EtOH, had m. p. 104° (Found: N, 14·8. $C_{11}H_{13}O_3N,C_{10}H_8O_5N_4$ requires N, 14·9%).

Ethyl γ-2-pyridylbutyrate (III). A mixture of the above ester (4·0 g.), amalgamated Zn (20 g.), and conc. HCl (15 c.c.) was refluxed for 6 hr. and for a further period after addition of more HCl aq. (15 c.c.). The liquid was decanted from the Zn and evaporated to dryness, H_2O added to the residue, and excess of H_2S passed into the solution while it was gradually made alkaline with NaOH. The filtrate from the ZnS was acidified with HCl aq. and evaporated to dryness, and on extraction, esterification, and working up as described above, *ethyl γ-2-pyridylbutyrate* was obtained as a colourless oil (2 g.), b. p. 145—150°/18 mm., 100°/0·2 mm. (Found: C, 68·2; H, 8·2; N, 7·5. $C_{11}H_{15}O_2N$ requires C, 68·4; H, 7·8; N, 7·25%).

4-Keto-octahydropyridocoline. The above ester (2·5 g.) was refluxed for 6 hr. with HCl aq. (10 c.c., 1 : 1), the solution evaporated to dryness, and the residue kept in a vac. desiccator. Na (6 g.) was added to the acid hydrochloride dissolved in dry EtOH (25 c.c.), further EtOH being added to dissolve unused Na during heating on the water-bath. The solution, after cooling, was treated with conc. HCl till acid, filtered, and evaporated to dryness, and the residue esterified. The solvent was removed from the resulting Et_2O extract, the residue heated to about 250° and then distilled in vac., giving a partly basic oil (0·9 g.). This was made just acid to Congo-red with HCl aq. and extracted with $CHCl_3$; *4-keto-octahydropyridicoline* was then obtained as a non-basic oil (0·6 g.), b. p. 146°/20 mm. (Found: N, 9·1. $C_9H_{15}ON$ requires N, 9·15%).

*δ-2-Piperidyl-*n*-butyl alcohol.* Ethyl γ-2-pyridylbutyrate (3·5 g.) in dry EtOH (30 c.c.) was poured on molten Na (10 g.) and heated on the water-bath while further EtOH was added to effect solution. After acidification with conc. HCl the filtrate was taken to dryness, and the residue made alkaline with NaOH aq. (10%) and extracted with $CHCl_3$. Distillation gave a basic oil * (1·5 g., up to 155°/20 mm.). This was treated as above with HCl aq., and extracted with $CHCl_3$. From the extract, 4-keto-octahydropyridocoline (0·35 g.) was isolated; the residue obtained by evaporating the acid solution to dryness, after basification and extraction with $CHCl_3$, gave *δ-2-piperidyl-*n*-butyl alcohol* as a viscous, strongly basic oil (0·8 g.), b. p. 149°/17 mm. (Found: N, 9·1. $C_9H_{19}ON$ requires N, 8·9%).

Octahydropyridocoline "A." The above basic oil * (1·5 g.) (or the pure base prepared from it) and PBr_5 (3·0 g.) in dry C_6H_6 (10 c.c.) were heated for 2 hr. on the water-bath and cooled, and excess of NaOH aq. (40%) added. The C_6H_6 solution was separated, and removal of the solvent left a semi-solid residue which was refluxed for 30 min. with methyl-alc. KOH (8 c.c., 3·5*N*).

The distillate from steam-distillation was acidified and taken to dryness, and the residue basified with K_2CO_3 aq. and extracted with Et_2O. Fractionation gave *octahydropyridocoline* " *A* " as a colourless oil (0·3 g.) basic to litmus, b. p. 72°/16 mm. (Found: N, 10·0. $C_9H_{17}N$ requires N, 10·1%). The base and S in Et_2O give a light orange ppt. on treatment with H_2S. The picrate, m. p. 194°, methiodide, m. p. 335°, and chloroaurate, m. p. 167°, are all identical with the corresponding derivs. of norlupinane (compare J., 1931, 440, 3196). The *picrolonate* of this base, or of norlupinane, crystallised from EtOH in yellow prisms, m. p. 245° (Found: C, 56·65; H, 6·3. $C_9H_{17}N,C_{10}H_8O_5N_4$ requires C, 56·5; H, 6·2%), whereas octahydropyridocoline " B " gave a *picrolonate*, m. p. 191°, yellow prisms from EtOH (Found: N, 17·5. $C_9H_{17}N,C_{10}H_8O_5N_4$ requires N, 17·4%).

The Hofmann degradation of " A." Bases " C," " D," and " E." To norlupinane (3·55 g.) in acetone (10 c.c.), MeI (3 c.c.) was added. After 12 hr., 7·5 g. of cryst. solid were obtained, m. p. 335° (decomp.). This was dissolved in H_2O (20 c.c.) and shaken with Ag_2O (4 g.) for 2 hr., and the filtered solution evaporated to dryness under reduced press. The resulting cryst. ammonium hydroxide was heated under 20 mm. press., and the damp distillate dissolved in Et_2O, dried over K_2CO_3, and fractionated; 3·05 g. of base passed over at 45—48°/1 mm. This was dissolved in AcHO (30 c.c.) and reduced by stirring with palladised charcoal (0·2 g.) in H. After filtration, and addition of HCl aq. (2 c.c.) and a fragment of Zn, the solution was evaporated to dryness, the cryst. residue dissolved in a few c.c. of H_2O, basified (KOH), and extracted 3 times with Et_2O. The extract, dried over K_2CO_3, was fractionated, giving 2·55 g., b. p. 43—45°/1 mm. (Found: C, 77·5; H, 13·4; N, 8·8. $C_{10}H_{21}N$ requires C, 77·4; H, 13·5; N, 9·0%). A solution of picrolonic acid (0·075 g.) in EtOH (1·5 c.c.) was added to the basic mixture (0·05 g.). The reddish solution deposited yellow prisms (0·04 g.), m. p. 167°, after standing over-night. When recryst., either yellow acicular prisms or stout prisms with dome-shaped ends separated, m. p. 167° (Found: C, 57·1; H, 7·1. $C_{10}H_{21}N,C_{10}H_8O_5N_4$ requires C, 57·3; H, 6·95%). When the filtrate from the 0·04 g. was left for 48 hr., 0·05 g. of reddish-brown rhombic prisms, m. p. 153°, was deposited: this was easily separated by hand picking from a further small amount of the first form. This picrolonate of " C " was recrystallised from EtOH, giving stout rhombs, m. p. 153° (Found: C, 57·1; H, 7·2%), but two further recrystns. gave monoclinic prisms, m. p. 147° (Found: C, 57·3; H, 6·9%). These were reconverted into the stout rhombs by seeding under suitable conditions. " C," regenerated from the picrolonate, gave a *picrate*, yellow prisms from EtOH, m. p. 88° (Found: C, 49·8; H, 6·6. $C_{10}H_{21}N,C_6H_3O_7N_3$ requires C, 50·0; H, 6·3%), and a methiodide, colourless prisms from acetone, m. p. 164°.

The sparingly sol. picrate of " E " (0·01 g.) was obtained from the basic mixture (0·07 g.) in a small vol. of EtOH as yellow prisms, m. p. 196°, identical with the compound prepared subsequently from methyl lupininate. The regenerated base " E " gave a picrolonate, m. p. 129°, and a methiodide, m. p. 261° (decomp.).

The Hofmann Degradation of " B."—The pure recryst. methiodide (0·9 g.) —prepared from " B " (0·75 g.) as regenerated from its picrate—was treated with Ag_2O and gave 0·35 g. of a basic mixture, b. p. 43°/1 mm. This, reduced with palladised charcoal and H in AcHO, gave 0·24 g., b. p. 49°/1 mm.

Picrolonates of " D " and " E."—When picrolonic acid (0·05 g.) in EtOH

(1 c.c.) was added to this basic mixture (0·03 g.) and left over-night, 0·015 g. of yellow prisms separated, m. p. 154—155°, raised to 166—167° on recrystn. from EtOH. The mother-liquor after a further 24 hr. deposited 0·01 g. of prisms, m. p. 124°, raised to 128° on recrystn.

Picrate of " E."—Picric acid (0·05 g.) in EtOH–Et_2O was added to the basic mixture (0·03 g.); yellow prisms (0·05 g.) separated at once, m. p. 178—180°, raised to 197° by recryst. from EtOH.

(In the prep. of pure " B " considerable quantities of its picrate were prepared, but careful fractionation failed to reveal the presence of the picrate of " A " in the mother-liquors.)

The Action of Cyanogen Bromide on " A " and " B."—When " A " (0·1 g.) in Et_2O or acetone (1 c.c.) was added to CNBr (0·1 g.) in Et_2O, a cryst. ppt. quickly separated (0·1 g.); recryst. from acetone–EtOH, it formed long colourless prisms, m. p. 283° (Found: C, 48·9; H, 8·0. $C_9H_{17}N,HBr$ requires C, 49·1; H, 8·2%). A similar expt. with " B " gave scarcely any cryst. ppt.

Methyl Lupinate α- and β-Methiodides.—Methyl lupininate (10 g.) was dissolved in EtOH (10 c.c.) and acetone (30 c.c.), and MeI (8 c.c.) added. A cryst. ppt. quickly separated, which was collected after 4 hr. (13·4 g.) and recrystallised from EtOH, giving colourless plates, m. p. 240° (decomp.). On concentration of the EtOH–acetone filtrate and addition of MeI (1 c.c.), hard prisms slowly separated (1·3 g.), m. p. 165—168°, raised to 170° by recryst. from acetone–EtOH (Found: C, 42·7; H, 6·75; N, 4·3. $C_{12}H_{22}O_2NI$ requires C, 42·5; H, 6·5; N, 4·1%).

The Hofmann Degradation of the α- and β-Methiodides.—The α-methiodide (8 g.) in H_2O (30 c.c.) was either shaken in the cold or refluxed for 2 hr. with Ag_2O (6 g.); evaporation of the filtrate then left an ammonium hydroxide which was only decomposed by strong heating under 20 mm. press. The wet distillate was dried with K_2CO_3 in Et_2O and fractionated, giving 2·6 g., b. p. 48°/1 mm., and 0·2 g., b. p. 95°/1 mm. approx. (Found for 1st fraction: C, 78·75; H, 12·7; N, 9·3. $C_{10}H_{19}N$ requires C, 78·4; H, 12·4; N, 9·1%). The second fraction has not yet been fully investigated. The *picrate* of the first fraction formed yellow needles from EtOH, m. p. 179° (Found: C, 50·4, 50·3; H, 5·4, 5·8. $C_{10}H_{19}N,C_6H_3O_7N_3$ requires C, 50·3; H, 5·8%). The *methiodide* (3·7 g.), m. p. 253—255°, was obtained from the base (2 g.) in acetone; recryst. from acetone–EtOH, it formed long colourless prisms, m. p. 258—259° (decomp.) (Found: C, 45·1; H, 7·55; N, 5·0. $C_{10}H_{19}N,MeI$ requires C, 44·7; H, 7·5; N, 4·8%). After this methiodide (6 g.) had been dissolved in H_2O (25 c.c.) and treated with Ag_2O (3 g.), decomp. of the ammonium hydroxide in the usual way gave 2·6—2·9 g. of base, b. p. 65°/1 mm., from which about 4·8 g. of an amorphous mixture of low- and indefinite-melting methiodides were obtained with Et_2O–MeI. Treatment with Ag_2O (2 g.) gave, after decomp. and extraction with HCl aq., 1 g. of a colourless non-basic oil, b. p. 25—26°/1 mm. This hydrocarbon polymerises readily on standing.

Reduction of the α-$C_{10}H_{19}N$ Base.—The base (1 g.) was shaken for 6 hr. in EtOH (10 c.c.) containing an equiv. of HCl with Pt-black (0·1 g.) in H (3 atm.). On working up, 0·65 g. of the base " E " was obtained, b. p. 48°/1 mm. (Found: C, 77·7; H, 13·8; N, 9·1. $C_{10}H_{21}N$ requires C, 77·4; H, 13·5; N, 9·0%). *Picrate*: long canary-yellow prisms from EtOH, m. p. 196—197° (Found: C, 50·0; H, 6·5. $C_{10}H_{21}N,C_6H_3O_7N_3$ requires C, 50·0; H, 6·2%). *Picrolonate*: compact, light brown prisms from EtOH, m. p.

129—130° (Found: C, 57·3; H, 7·2. $C_{10}H_{21}N,C_{10}H_8O_5N_4$ requires C, 57·3; H, 6·9%). *Methiodide*: long colourless prisms, m. p. 263—265° (Found: C, 44·9; H, 8·15. $C_{10}H_{21}N$,MeI requires C, 44·4; H, 8·15%).

Treatment of the β-methiodide of methyl lupininate (2 g.) with Ag_2O as for the α-isomeride above gave 0·4 g., b. p. 45°/1 mm., and 0·15 g., b. p. 95°/1 mm. (also not fully investigated; it gave a picrate, m. p. 117°) (Found for the first fraction: N, 9·3. $C_{10}H_{19}N$ requires N, 9·1%). This β-base gives a picrate, m. p. 145°, raised to 148—149° by recrystn. from EtOH (Found: C, 50·5; H, 5·9. $C_{10}H_{19}N,C_6H_3O_7N_3$ requires C, 50·3; H, 5·8%). Reduction of the β-base gave "E," as proved by its giving identical picrate and methiodide.

Distillation of the Methochloride of "E."—The methiodide of "E" (2·4 g.) was refluxed for 1 hr. in H_2O (15 c.c.) with AgCl (from $AgNO_3$, 3 g.), and the filtered solution taken to dryness. The colourless solid residue was carefully heated under 1 mm. press., and the oily distillate dried in Et_2O and fractionated, giving "E" (0·15 g.), and 0·71 g., b. p. 90°/1 mm. approx. This gave a methiodide, colourless plates, m. p. 91°, from acetone–Et_2O (Found: C, 41·2; H, 8·1. $C_{12}H_{27}NClI$ requires C, 41·45; H, 7·8%). This methiodide (3·8 g.) in H_2O (30 c.c.) was refluxed for 3 hr. with Ag_2O (12 g.), the filtered solution evaporated, and the residue distilled. The distillate was treated with dil. HCl, and the non-basic portion extracted with Et_2O and distilled, giving 0·6 g., b. p. 97—104°/15 mm. (Found: C, 75·7; H, 12·5. $C_9H_{18}O$ requires C, 76·05; H, 12·7%). This compound (0·4 g.) in acetone (10 c.c.) was stirred at 0° with $KMnO_4$ (2 g. excess). The H_2O extract of the MnO_2 on acidification gave 0·15 g., m. p. 120—130°, which, on extraction with Et_2O–C_6H_6, gave colourless needles, m. p. 138°, raised to 140° by recrystn., and not depressed by admixture with authentic suberic acid (Found: C, 55·1; H, 8·3; equiv., 88, 89. Calc. for $C_8H_{14}O_4$: C, 55·1; H, 8·0%; equiv., 87).

iso*Norlupinene.*—Aminonorlupinane (1·54 g.) in *N*-HCl (20 c.c.) was diazotised at 0° with *N*-$NaNO_2$ (10 c.c.). The solution was left for 5 min., heated for 1—2 min. on the water-bath, and then rapidly evaporated from the water-bath under reduced press.—the usual method for evaporns. in these two papers. Five such batches were dissolved in a small vol. of H_2O, made strongly alkaline with KOH, and extracted 3 times with Et_2O, and the dried extracts fractionated, giving 4·75 g., b. p. 43—47°/1 mm., and 1·7 g. up to 95°/1 mm. On redistillation of the 1st fraction, 4·5 g. passed over at 43—45°/1 mm. (Found: C, 78·9; H, 10·95. $C_9H_{15}N$ requires C, 78·8; H, 10·9%). The *picrolonate* after one crystn. from EtOH had m. p. 189° (Found: C, 56·9; H, 6·0. $C_9H_{15}N,C_{10}H_8O_5N_4$ requires C, 56·9; H, 5·7%). On recrystn. a few times from EtOH, in which the compound became markedly less sol., the m. p. rose to 229—230°, small acicular prisms being obtained, identical with the *picrolonate* of norlupinene (Found: C, 57·3; H, 5·5. $C_9H_{15}N,C_{10}H_8O_4N_5$ requires C, 56·9; H, 5·7%). The *picrate* of *iso*norlupinene formed long yellow prisms from EtOH, m. p. 147° (Found: C, 48·6; H, 5·2. $C_9H_{15}N,C_6H_3O_7N_3$ requires C, 49·2; H, 4·9%). The m. p. of this compound also rises on repeated crystn., but the change to norlupinene is not so regular as for the picrolonate.

On refractionation of some of the combined 1·7 g. fractions, the distillate obtained partly solidified (10%), and then formed colourless prisms, m. p. 109°, from light petroleum (Found: C, 69·3; H, 11·1; N, 8·8. $C_9H_{17}ON$ requires C, 69·7; H, 11·2; N, 9·0%).

The Action of Bromine on (a) *Norlupinene and* (b) iso*Norlupinene.*—(a) To norlupinene (1 g.) in AcHO (5 c.c.), a solution of Br in AcHO (1 g. in 1 c.c.) was added so long as a ppt. separated. The orange solid was collected, washed with H_2O and EtOH, dried (1·8 g.), and crystallised rapidly in small portions from EtOH; long orange prisms, m. p. 175° with softening at 170°, were formed (Found : N, 2·9. $C_9H_{15}NBr_4$ requires N, 3·1%). If the orange EtOH solution is heated on the water-bath for 1·5 hr., it becomes almost colourless : when the EtOH is removed and the residue made alkaline, extraction with Et_2O and distillation give a solid, which forms colourless prisms, m. p. 84—85°, from light petroleum (Found : C, 36·2; H, 5·05; N, 4·9. $C_9H_{15}NBr_2$ requires C, 36·3; H, 5·05; N, 4·7%).

(b) To *iso*norlupinene (0·4 g.) in AcHO (1 c.c.), Br (1·3 g.) in AcHO (1·3 c.c.) was added. The solid was washed with H_2O and EtOH and dried (1·15 g.). When cryst. in portions from EtOH, yellow prisms were obtained, m. p. 156—157° (Found : C, 28·7; H, 4·0. $C_9H_{15}NBr_3$ requires C, 28·7; H, 3·9%).

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