280. *Strychnine and Brucine. Part XXXVIII. Exhaustive Methylation of* N(b)-*Methyl*chano*dihydro*neo*strychnidine and its Dihydro-derivative.*

By O. Achmatowicz.

The first stage of the Hofmann degradation of dihydrostrychnidine-A has already been described and affords two *des*-bases, namely, the *des*-base-D and methyl*chano*dihydro*neo*strychnidine. The present paper deals with the exhaustive methylation of the latter base, resulting in the formation of two *desaza*strychnidines and trimethylamine. At the second stage two *des*-bases were isolated, the isomerism depending on the position of an ethylene linkage. The eliminations in the dihydro-series of bases have also been studied.

This and the two following memoirs are concerned with investigations on the Hofmann degradation of dihydrostrychnidine-A and dihydrobrucidine and, although our studies along these lines are not yet completed, it is necessary, in view of the work of Leuchs (*Ber.*, 1937, **70**, 2455), to place the results on record.

The present communication contains the description of experiments on the exhaustive methylation of methyl*chano*dihydro*neo*strychnidine, which is one of the two isomeric methyl-*des*-bases formed on thermal decomposition of methyldihydrostrychnidinium-A carbonate (Achmatowicz and Robinson, J., 1934, 581) or on Emde degradation of either methylstrychnidinium or methyl*neo*strychnidinium salts (Perkin, Robinson, and Smith, *ibid.*, p. 574). The paper also includes an account of experiments on the Hofmann degradation of methyldihydro*chano*dihydrostrychnidine, which is a methyl-*des*-base produced from methylstrychnidinium chloride by catalytic degradation-reduction process (Achmatowicz, *Roczn. Chem.*, 1933, 25) or by direct catalytic hydrogenation of methyl*chano*dihydro*neo*strychnidine (Perkin, Robinson, and Smith, *loc. cit.*). The paper is concluded by the description of two cases of stereoisomerism, and two pairs of stereoisomeric substances are described.

The highest yields of the *N*(*b*)-ring-fission products were obtained on heating methyl*chano*dihydro*neo*strychnidine dimetho-salts with sodium methoxide. Unfortunately, the crude decomposition product was a complex mixture, very readily soluble in the usual solvents, and it was impossible to resolve it into components by simple crystallisation. The separation was achieved by a chemical method and the following substances were obtained: (*a*) a base, $C_{22}H_{28}ON_2$, m. p. 143—144°, identified as methyl*chano*dihydro*neo*strychnidine, (*b*) a base, $C_{23}H_{30}ON_2$, m. p. 113—114°, (*c*) a base, $C_{23}H_{30}ON_2$, m. p. 73—74°, and (*d*) a substance, $C_{24}H_{32}O_2N_2$, m. p. 130—131°.

The base (*b*) contains $-N(b)Me_2$ and two double bonds, as demonstrated by hydrogenation to a tetrahydro-derivative (amorphous, probably a mixture of stereoisomerides; analysed as the methiodide, m. p. 263—264°) in presence of palladised charcoal in dilute acetic acid solution.

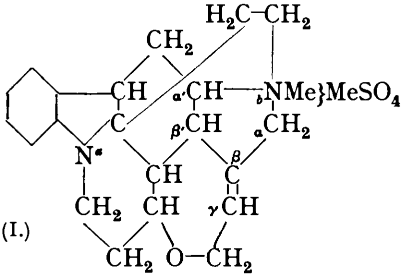
The yield of the base (*c*) was very small (about 0·3 g. from 1 kg. of dihydrostrychnidine) and consequently the investigation of the substance is not so complete as could be desired. The base (*c*) is isomeric with the base (*b*) and also contains $-N(b)Me_2$ and two unsaturated linkages. These facts show that both substances are dimethyl-*des*-bases and, for reasons given below, the base (*b*) is designated N(b)N(b)-*dimethyl*desbisneo*strychnidine* and the isomeride (*c*) is termed N(b)N(b)-*dimethyl*desneo*strychnidine*.

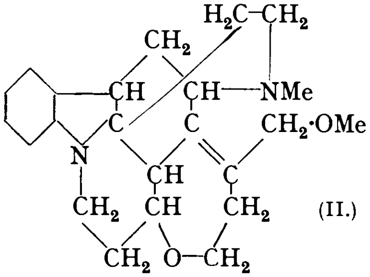
When *dimethyl*desneo*strychnidine methochloride* was heated with sodium methoxide, free dimethyl*desbisneo*strychnidine was obtained in theoretical yield. The reverse change, dimethyl*desbisneo*strychnidine methochloride ⟶ dimethyl*desneo*strychnidine, could not be effected (see following paper). On the other hand, catalytic hydrogenation of dimethyl*desneo*strychnidine gave a tetrahydro-base which was found to be identical with the hydrogenation product of dimethyl*desbisneo*strychnidine (the methiodides were compared). These experiments reveal two important facts: (i) the difference between the isomeric dimethyl*desneo*strychnidine and dimethyl*desbisneo*strychnidine consists in the position of one (or, less probably, of both) of the unsaturated bonds, and (ii) one of the ethylenic linkages of dimethyl*desneo*strychnidine is capable of migration.

The substance (*d*) contains a methoxy-group, two methyl groups attached to nitrogen, and one double bond; it is termed methoxy-*N*(*b*)*N*(*b*)-dimethyldihydro*chano*dihydro*bisneo*strychnidine. When it was hydrogenated in dilute hydrochloric acid solution in presence of platinum-black, two stereoisomeric dihydro-derivatives were formed: one of them, designated *methoxy*-N(b)N(b)-*dimethyldihydro*chano*tetrahydrostrychnidine*, has m. p. 131—132°, and the other, termed allo*methoxy*-N(b)N(b)-*dimethyldihydro*chano*tetrahydrostrychnidine*, melts at 113—114°. When methoxydimethyldihydro*chano*tetrahydrostrychnidine was treated successively with boiling 30% (by vol.) sulphuric acid, sodium iodide, and silver chloride, elimination of methyl alcohol took place and a quaternary chloride, identical with methyldihydro*chano*dihydrostrychnidine methochloride, was obtained. Methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine, under similar conditions, unexpectedly gave a quaternary chloride, isomeric, but not identical, with methyl*chano*dihydro*neo*strychnidine methochloride. The new quaternary chloride, on heating with sodium methoxide, yielded dimethyl*desbisneo*strychnidine.

The decomposition of methyldihydro*chano*dihydrostrychnidine dimetho-salts by sodium methoxide gives rise to the following products: (i) a base, $C_{22}H_{30}ON_2$, m. p. 177—178°, identified as methyldihydro*chano*dihydrostrychnidine, (ii) a base, $C_{23}H_{32}ON_2$ (amorphous; analysed as the *methiodide*, m. p. 299—301°), termed *N*(*b*)*N*(*b*)-dimethyl*des*dihydrostrychnidine-D, (iii) a base, $C_{23}H_{32}ON_2$ (amorphous; analysed as the *methiodide*, m. p. 177—178°), termed *N*(*b*)*N*(*b*)-dimethyl*des*dihydro*bisneo*strychnidine, and (iv) a substance, $C_{24}H_{34}O_2N_2$, m. p. 131—132°, identical with *methoxydimethyldihydro*chano*tetrahydrostrychnidine*. It is very likely that dimethyl*des*dihydrostrychnidine-D and dimethyl*des*dihydro*bisneo*strychnidine are dihydro-derivatives of dimethyl*desbisneo*strychnidine and dimethyl*desneo*strychnidine; it is of importance that rearrangement of the double linkage does not take place with either of the dimethyl*des*dihydro-bases as in the case of dimethyl*desneo*strychnidine. This fact gives a clue to the position of the labile double bond in dimethyl*desneo*strychnidine; this position must be different from that occupied by the double bond in the dimethyl*des*dihydro-bases.

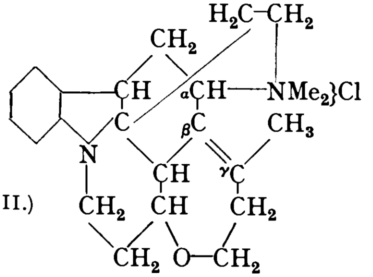
The conversion of methyl*chano*dihydro*neo*strychnidine methochloride into methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine presents certain analogies to the change: strychnidine methosulphate (I) ⟶ methoxymethyldihydro*neo*strychnidine (II) (Clemo, Perkin, and Robinson, J., 1927, 1589; Achmatowicz, Perkin, and Robinson, J., 1932, 487) and may be explained in a similar manner. When methyl*chano*dihydro*neo*strychnidine methochloride (III) is subjected to the action of sodium methoxide, a ring-fission occurs at N(b) and at the same time the double bond shifts to a new position. It is very unlikely that it should return to the position which it occupies in strychnidine (I), because the *neo*-position is believed to be the more stable. It is also highly improbable that :CMe in (III) might become :C=CH₂. But no theoretical objections to the third alternative are evident, *viz.*, that the ethylenic linkage moves from the *neo*-position (βγ) in (III) to the αβ-position. In this case methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine would have the structure (IV). It is evident that this formula is in accord with the fact that dilute sulphuric acid acts on methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine to yield a quaternary hydrogen sulphate, isomeric, but not identical, with the corre-


(I.)

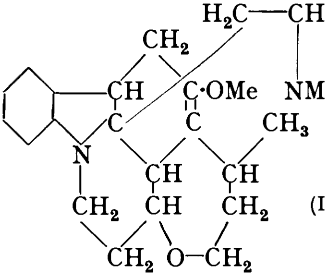

(II.)

sponding salt of methyl*chano*dihydro*neo*strychnidine. If, on the other hand, we take into consideration the fact that this salt may be converted into dimethyl*desbisneo*strychnidine, we come to the conclusion that one of the unsaturated linkages in this base also occupies the αβ-position. The transformation of dimethyl*desneo*strychnidine methochloride into dimethyl*desbisneo*strychnidine is analogous to the conversion of strychnidine methosulphate into *neo*strychnidine (Clemo, Perkin, and Robinson, *loc. cit.*), which is accompanied by migration of the double bond to the *neo*-position; hence one of the ethylenic linkages (the labile) in dimethyl*desneo*strychnidine is located in the same position which it occupies in methyl*chano*dihydro*neo*strychnidine, *i.e.*, in the *neo*-position. This implies that when both rings at N(b) are opened, the *neo*-arrangement becomes less stable and acquires a tendency towards isomerisation.

(III.)

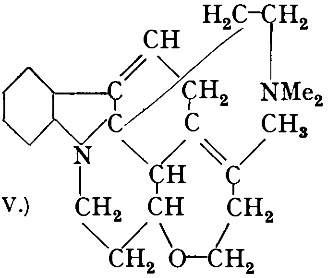


(IV.)

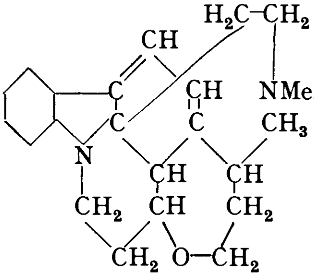


In accordance with the view that strychnine and brucine are substituted γ-phenylpropylamines, Hofmann elimination would be expected to give rise to substituted *iso*-propenylbenzenes. This indicates the position of the second double bond in dimethyl*desneo*strychnidine and dimethyl*desbisneo*strychnidine, and the bases receive formulæ (V) and (VI) respectively (compare, however, the discussion in the preceding paper).

(V.)



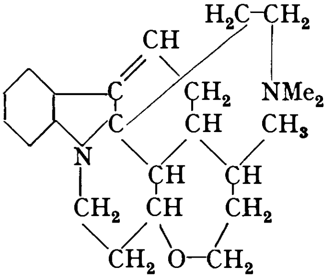
(VI.)

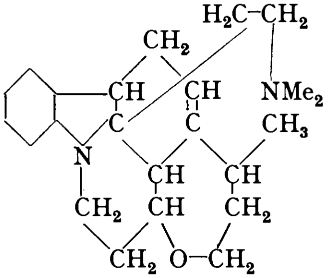


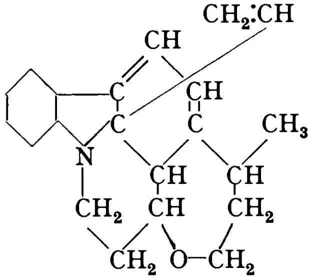
One of the double bonds in dimethyl*desneo*strychnidine occupies the same position as in *neo*strychnidine, hence the prefix *neo*. The position of one of the unsaturated linkages in dimethyl*desbisneo*strychnidine differs from that in strychnidine by two migrations, consequently some different prefix had to be introduced and *bisneo* is proposed. For the same reason the methoxy-derivative is designated methoxydimethyldihydro*chano*-dihydro*bisneo*strychnidine, and it is evident that in the reduced series both prefixes should be dropped.

We shall now consider the decomposition products in the dihydro-series. Here the position, as could be anticipated, is somewhat different. Methyldihydro*chano*dihydrostrychnidine has no double bonds, and therefore no isomerisation is involved in the decomposition of its dimetho-salts into methoxydimethyldihydro*chano*tetrahydrostrychnidine (analogy to the change: dihydrostrychnidine methochloride ——> methoxymethyltetrahydrostrychnidine). For the same reason dilute sulphuric acid acts on the latter base to reconstitute methyldihydro*chano*dihydrostrychnidine hydrogen sulphate, but not to give an isomeric salt, as in the case of methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine (analogy to the transformation: methoxymethyltetrahydrostrychnidine ——> dihydrostrychnidine). It is also clear that dimethyl*des*dihydrostrychnidine-D and dimethyl*des*dihydro*bisneo*strychnidine are normal products of the second stage of Hofmann elimination. One of these bases (presumably the isomeride D) probably has the structure (VII), based on the γ-phenylpropylamine conception. But the position of the double bond in the other base cannot be located with certainty; however, it is almost certain that it is not in the *neo*-position, because neither of the two dimethyl*des*dihydro-bases, as already stated, is capable of rearrangement of the type: dimethyl*desneo*strychnidine methochloride ⟶ dimethyl*desbisneo*strychnidine. If dimethyl*des*dihydrostrychnidine-D possesses formula (VII), and if both bases are normal products of Hofmann elimination, dimethyl*des*dihydro*bisneo*strychnidine should be represented by the formula (VIII) (hence the prefix *bisneo*).

On inspecting the formulæ of various degradation products (see also the following paper) of dihydrostrychnidine, it will be noticed that formula (VI), representing dimethyl*desbisneo*strychnidine, contains a peculiar arrangement, namely, a conjugated system of two double bonds, attached to the benzene nucleus. On the basis of Robinson's theory as to the influence of unsaturated groups on colour reactions in the strychnidine series, dimethyl*desbisneo*strychnidine, if it really does contain such an arrangement in proximity to N(a), might be expected to give unusual colour reactions. Actually, the dilute aqueous acid–ferric reaction of this base is unique, for, whereas substances of the strychnidine, dihydrostrychnidine and *neo*strychnidine type usually give a pink coloration, changing to eosin-red, dimethyl*desbisneo*strychnidine gives an intense bordeaux coloration, changing slowly to dark brown. This reaction is so sensitive that it was necessary to reduce the amount of the base to 1/10 of that used in the standard test (Achmatowicz and Robinson, J., 1934, 581); under these conditions the colour develops somewhat more slowly, but it is reddish-purple and remains so for days. When the conjugated arrangement of double bonds is not present, the eosin-red colour may again be observed. Thus, for instance, dimethyl*desneo*strychnidine (V) and tetrahydro(dimethyl*desbisneo*strychnidine) give a typical strychnidine reaction, but methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine (IV) and both of its dihydro-derivatives give a yellow coloration with a faint, transient pinkish tinge. Unexpectedly, dimethyl*des*dihydrostrychnidine-D gave the strychnidine type colour effect, whereas the dilute aqueous acid–ferric reaction of the isomeric dimethyl*des*dihydro*bisneo*strychnidine was negative.


(VII.)


(VIII.)


(IX.)

The isomerisation of dimethyl*desneo*strychnidine into dimethyl*desbisneo*strychnidine suggests that the latter possesses a more stable arrangement than the former. In the light of our hypothesis this isomerisation, as well as the transformation methyl*chano*dihydro*neo*strychnidine dimethochloride ⟶ dimethyl*desbisneo*strychnidine, is a result of the tendency of the double bonds to acquire a conjugated arrangement: there are numerous examples in the literature of this kind of isomerisation.

The realisation of the final stage of the Hofmann degradation has been accomplished with dimethyl*desbisneo*strychnidine and again the most favourable yields of the degradation products were obtained when the dimetho-salts of the base were taken. The reaction was accompanied by evolution of a considerable amount of trimethylamine, identified as hydrochloride and platinichloride. Of the three degradation products, one was identified with dimethyl*desbisneo*strychnidine, and the other two were isolated as methiodides. These salts are isomeric and have the composition $C_{21}H_{23}ON,MeI$. One of them, designated desaza*strychnidine-a methiodide*, has m. p. 154—156° and the other, termed desaza*strychnidine-b methiodide*, melts at 104—105°.

Free *desaza*strychnidine-a (amorphous) was prepared by thermal decomposition of the methochloride; in contrast to all known strychnidine derivatives, it is only sparingly soluble in dilute acids; it is precipitated from solutions in more concentrated acids as the free base, on dilution with water. When subjected to catalytic hydrogenation, it takes up three molecules of hydrogen (in accordance with theory), but the hexahydro-derivative has not, as yet, been prepared in crystalline form, and is probably a mixture of stereoisomerides.

If we accept the " conjugated bond system " hypothesis advanced in this memoir, *desaza*strychnidine-a should be represented by formula (IX), since this base is one of the only two known dihydrostrychnidine degradation products giving a reddish-purple coloration in the dilute aqueous acid–ferric test. Here, again, the reddish-purple coloration is no longer observed after hydrogenation and hexahydro*desaza*strychnidine-a gives under standard conditions a stable eosin-red coloration, typical of strychnidine. The latter colour effect is also given by *desaza*strychnidine-b, whence it must be supposed that this base does not possess a conjugated double bond system. The properties and the structure of *desaza*strychnidine-b are discussed in the following paper.

As stated above, methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine, on catalytic hydrogenation, yields two isomeric dihydro-derivatives. They are undoubtedly stereoisomerides, and, so far as the writer is aware, it is for the first time in the strychnine series that two stereoisomeric substances have been obtained in one and the same process and isolated in a pure state. Formation of another pair of stereoisomerides was observed when methyl*chano*dihydrostrychnidine in dilute hydrochloric acid solution was hydrogenated in presence of platinum-black or palladised charcoal. Two dihydro-derivatives were isolated: the already known methyldihydro*chano*dihydrostrychnidine, m. p. 177—178° (compare Perkin, Robinson, and Smith, *loc. cit.*), and a new one, termed allo-N(b)-*methyldihydro*chano*dihydrostrychnidine*, m. p. 117—118°. The isomerides of both pairs show a rather great difference in m. p. (methoxydimethyldihydro*chano*tetrahydrostrychnidine has m. p. 131—132°, and the *allo*-isomeride melts at 113—114°); however, this is not an obstacle, since analogy may be found in other groups of substances, for example, *cis*-β-decalol has m. p. 105°, whereas the *trans*-isomeride melts at 75° (Hückel, *Annalen*, 1925, **441**, 1; 1926, **451**, 109), and *cis-trans-trans-trans*-androsterone melts at 182—183°, whereas *trans-cis-trans-trans*-androsterone has m. p. 150—151° (Ruzicka and coll., *Helv. Chim. Acta*, 1934, **17**, 1395). Methoxydimethyldihydro*chano*tetrahydrostrychnidine and the *allo*-isomeride have the same crystallographic structure, but the crystals of the other pair of isomerides are different.

EXPERIMENTAL.

Derivatives of N(b)-*Methyl*chano*dihydro*neo*strychnidine*.—The experiments were carried out with methyl*chano*dihydro*neo*strychnidine, m. p. 143—144°, produced by thermal decomposition of methyldihydrostrychnidinium-A carbonate. *The methiodide* was prepared by direct union of the components at room temperature, but, contrary to previous observations (Perkin, Robinson, and Smith, J., 1934, 574), it had little tendency for crystallisation. It could be crystallised only from much boiling benzene, from which it separated in colourless needles, m. p. 208—210° (Found in a crystalline specimen, dried at 104°: C, 57·4; H, 6·8. Found in an amorphous specimen, dried at 104°: C, 57·5; H, 6·7; I, 26·2. $C_{23}H_{31}ON_2I$ requires C, 57·7; H, 6·5; I, 26·6%). The methochloride, prepared by means of silver chloride from the amorphous modification of the methiodide, formed a brown horny mass, freely soluble in water or methyl alcohol. The *dimethiodide* was produced by heating the components for 12 hours in a sealed tube at 130°; the semicrystalline dimethiodide, which remained after evaporation of the excess of methyl iodide, was sufficiently pure for analysis and for further purposes (Found in material dried at 104°: C, 46·1, 46·3; H, 5·8, 5·7; I, 40·7. $C_{24}H_{34}ON_2I_2$ requires C, 46·5; H, 5·5; I, 41·0%). The derivative was moderately readily soluble in water or methyl alcohol and had little tendency for crystallisation. The dimethochloride formed a brown horny mass, freely soluble in water.

The Action of Sodium Methoxide on N(b)-*Methyl*chano*dihydro*neo*strychnidine Metho- and*

Dimetho-salts.—The decomposition of these salts by sodium methoxide gave rise to a mixture of exactly the same substances, but the best yields of the *N*(*b*)-ring-fission products were obtained from the dimethochloride. The experiments were carried out under various conditions and a variety of methods was applied for the separation of the decomposition products. The following is a brief description of a typical procedure.

A mixture of methyl*chano*dihydro*neo*strychnidine dimethochloride (5 g., previously dried in a vacuum) with methyl-alcoholic sodium methoxide (30 c.c. of 25%) is heated in an open flask, first on the steam-bath and subsequently on a sand-bath, until the temperature reaches 130—135°. At 105—110° the mixture begins to froth and the flask is frequently shaken. The yellowish melt is allowed to cool, diluted with ice-water, washed, and dried in a vacuum (or the melt is mixed with water and exhaustively extracted with benzene, and the dried extract evaporated to dryness in a vacuum). The dry product (about 4 g.) is dissolved in boiling methyl alcohol (15 c.c.) and left in an ice-chest. After several hours methyl*chano*dihydro*neo*strychnidine (0·9 g.), m. p. 141—143°, crystallises; the methyl-alcoholic mother-liquor is twice concentrated and two fresh crops (0·3 g. and 0·2 g.) of the same base, m. p. 137—140°, are obtained. The base, recrystallised from methyl alcohol, has m. p. 143—144°, not depressed by pure methyl*chano*dihydro*neo*strychnidine. The dark-coloured methyl-alcoholic filtrate is diluted with methyl alcohol (10 c.c.), and methyl iodide (1 c.c.) added. Heat is evolved and shortly a slightly coloured, crystalline precipitate (0·4 g.), m. p. 295—300°, is formed (crop 1). The filtrate is concentrated to half its volume; after 2—3 days crop 2, m. p. 290—300°, separates (0·2 g.). The residue is diluted with methyl alcohol (5 c.c.) and poured into boiling water (50 c.c.), and the mixture digested until methyl alcohol is boiled away. The liquid is allowed to cool and the clear aqueous solution (A) is filtered from the gummy precipitate (B). The latter is ground with boiling water and the cold washings are added to the solution (A). This is now evaporated to half its volume; after several days crop 3 (0·65 g.), m. p. 260—290°, is deposited. The concentration is repeated three times and affords crops 4, 5, and 6 (0·6 g., 0·2 g., and 0·3 g.), m. p. 250—265° (crystallisation at this stage is slow and formation of the last three crops usually takes about 3 weeks). The remaining aqueous solution is evaporated, the residue mixed with (B) and freshly precipitated silver chloride (from 3 g. of silver nitrate), and the whole heated for 4 hours on a water-bath. The filtrate from the silver salts is evaporated to dryness and a brown horny solid (C) is obtained (0·2 g.). The silver salts are dried at room temperature and extracted with benzene and the dried extract is evaporated in a vacuum; this operation furnishes product (D) (0·4 g.).

Crops 1 and 2 are repeatedly crystallised from water and the aqueous mother-liquors are used for crystallisation of crops 3—6. Finally two substances are obtained: *N*(*b*)*N*(*b*)-dimethyl*desbisneo*strychnidine methiodide (1·4 g.), m. p. 310—312°, and *N*(*b*)*N*(*b*)-dimethyl*desneo*strychnidine methiodide (0·25 g.), m. p. 263—265°.

The amorphous solid (C) was proved to be identical with methyl*chano*dihydro*neo*strychnidine methochloride; it (collected from several preparations) was heated with sodium methoxide and the decomposition product, worked up as previously described, was resolved into the same substances as those obtained by decomposing methyl*chano*dihydro*neo*strychnidine dimethochloride.

Repeated crystallisation of the product (D), first from methyl alcohol and subsequently from light petroleum (b. p. 60—65°), furnished methoxy-*N*(*b*)*N*(*b*)-dimethyldihydro*chano*dihydro*bisneo*strychnidine (0·3 g.), m. p. 129—130°, along with an oily halogen-free product (0·7 g.), which has not been examined.

N(b)N(b)-*Dimethyl*desbisneo*strychnidine methiodide* crystallises from water or methyl alcohol in long, colourless, fragile, prismatic needles, m. p. 310—312° (Found in air-dried material: C, 58·5, 58·4; H, 6·7, 6·8. $C_{24}H_{33}ON_2I$ requires C, 58·5; H, 6·7%). It is very sparingly soluble in water (0·25 in 100 at 17°; 1·6 in 100 at 100°), and dissolves sparingly in methyl alcohol.

The *methochloride* separates from a concentrated aqueous solution in long colourless needles containing $7H_2O$. The air-dried heptahydrate, on rapid heating in a capillary tube, shrinks and partly melts at 53—55°; on further heating, it crystallises and melts again at 235—237°; dried at 60°, it gives the monohydrate, m. p. 235—237° without previous shrinking. The anhydrous salt is obtained by drying the hepta- or the mono-hydrate at 104°, and is somewhat hygroscopic (Found in air-dried material: loss at 60°, 20·2; loss at 104°, 23·6. $C_{24}H_{33}ON_2Cl,7H_2O$ requires $6H_2O$, 20·4; $7H_2O$, 24·0%. Found in material dried at 104°: C, 72·0, 72·1; H, 8·4, 8·5. $C_{24}H_{33}ON_2Cl$ requires C, 71·9; H, 8·2%).

N(b)N(b)-*Dimethyl*desbisneo*strychnidine.*—Free *dimethyl*desbisneo*strychnidine* was obtained by the action of heat on the methochloride just described. The base crystallises from acetone in stout colourless plates (Fig. 1), m. p. 113—114° (Found in air-dried material: C, 79·0, 78·9; H, 8·7, 8·7; N, 7·8, 7·9; Me as NMe, 9·0, 8·8. $C_{23}H_{30}ON_2$ requires C, 78·9; H, 8·6; N, 8·0; 2Me as NMe, 8·6%); it is readily soluble in the simple alcohols, chloroform or benzene, dissolves moderately readily in acetone, and is sparingly soluble in light petroleum (b. p. 60—65°). A solution of the base (0·5—0·1 mg.) in 0·1% hydrochloric acid (5 c.c.), on addition of ferric alum solution (5 c.c. of 0·25%), slowly develops a reddish-purple coloration, which intensifies on standing and becomes brown on warming. The same colour effects are produced by the methochloride and methosulphate of the base. Dimethyl*desbisneo*strychnidine instantly combines with methyl iodide with evolution of heat and formation of a methiodide, identical with dimethyl*desbisneo*strychnidine methiodide, described above. The identity was established by m. p., by mixed m. p. (310—312° in both cases), and by analysis (Found in air-dried material: C, 58·6; H, 6·9%).

The *methosulphate*, prepared by direct union of the components in a benzene solution at room temperature, forms colourless tablets, m. p. 227—229°, readily soluble in water and fairly soluble in methyl alcohol (Found in a specimen dried at 104°: C, 63·2; H, 7·9. $C_{25}H_{36}O_5N_2S$ requires C, 63·0; H, 7·6%).

The dimethiodide. Dimethyl*desbisneo*strychnidine (4·1 g.), dissolved in dry benzene (40 c.c.), was mixed with methyl sulphate (6 c.c.) and refluxed for 6 hours on a water-bath. The semi-crystalline, yellow product was dissolved in water (30 c.c.), basified with ammonia (no precipitate), heated to boiling, and mixed with aqueous sodium iodide (5 g. in 10 c.c. of water). The *dimethiodide*, which was precipitated, was thrice recrystallised from water, forming minute colourless plates (4·7 g.), m. p. 273—275° (Found in air-dried material: loss at 104°, 2·7. $C_{25}H_{36}ON_2I_2,H_2O$ requires H_2O, 2·8%. Found in a specimen dried at 104°: C, 47·1, 47·0; H, 5·9, 6·0; I, 39·7. $C_{25}H_{36}ON_2I_2$ requires C, 47·3; H, 5·7; I, 40·1%). It is sparingly soluble in water or in the simple alcohols and has the power of retaining water of crystallisation.

The related *dimethochloride* separates from a concentrated aqueous solution as a hexahydrate, which forms yellowish needles, discoloring at 104°. Kept over sulphuric acid, it loses $3H_2O$, forming a trihydrate; the anhydrous salt is obtained when the hydrates are dried at 104°. The hexahydrate, on slow heating in a capillary tube, shrinks at 70—75°; when it is heated rapidly, it melts at 75—80°; the melt, on further heating, crystallises at 110—120° and melts again at 242—244°. This is also the m. p. of the trihydrate and the anhydrous salt (Found in air-dried material: loss at 104°, 18·8. $C_{25}H_{36}ON_2Cl_2,6H_2O$ requires $6H_2O$, 19·3%. Found in material dried over sulphuric acid: C, 59·4; H, 8·3; Cl, 14·0. $C_{25}H_{36}ON_2Cl_2,3H_2O$ requires C, 59·4; H, 8·4; Cl, 13·5%. Found in a specimen dried at 104°: C, 66·3; H, 8·3. $C_{25}H_{36}ON_2Cl_2$ requires C, 66·5; H, 8·0%). When the dry dimethochloride was heated in a test-tube over a free flame, methyl chloride was given off and pure dimethyl*desbisneo*strychnidine was formed, m. p. 113—114° after recrystallisation from acetone.

Catalytic Hydrogenation of N(b)N(b)-*Dimethyl*desbisneo*strychnidine in the Presence of Platinum-black.*—The base (0·9 g.) was dissolved in 5% hydrochloric acid (15 c.c.) and hydrogenated in the presence of platinum-black (from 0·1 g. of platinum oxide, prepared by Adams's method) at room temperature. Absorption of the gas ceased after about 65 minutes, 123 c.c. (at N.T.P.) having been taken up (calc. for 4H, 115 c.c.). The filtered solution was basified with ammonia and the semi-solid precipitate was thrice extracted with petroleum (b. p. 65—70°); a quaternary ammonium chloride was not detected in the aqueous layer. The extract was dried, filtered, and evaporated to dryness in a vacuum. The slightly coloured residue (0·9 g.) was readily soluble in the usual solvents and, despite numerous attempts, could not be prepared in a crystalline state. In order to establish its composition, it was subjected to the action of methyl iodide; interaction took place at room temperature to yield a *methiodide*, which after three crystallisations from water formed minute colourless needles, m. p. 261—263° (Found in a specimen dried at 104°: C, 58·3, 58·0; H, 7·3, 7·5. $C_{24}H_{37}ON_2I$ requires C, 58·1; H, 7·5%). The examination of the mother-liquor with the aim of isolating a presumed stereoisomeric methiodide is in progress.

N(b)N(b)-*Dimethyl*desneo*strychnidine methiodide* is moderately readily soluble in methyl alcohol and readily in ethyl alcohol; it separates from an aqueous solution in soft, silky, colourless needles, m. p. 263—267° (Found in a specimen dried at 104°: C, 58·3, 58·4; H, 6·8, 6·8. $C_{24}H_{33}ON_2I$ requires C, 58·5; H, 6·7%).

The related *methochloride* is very readily soluble in water or methyl alcohol; it separates from an aqueous solution as a polyhydrate, forming colourless, glistening needles. Unlike the heptahydrate of the isomeric dimethyl*desbisneo*strychnidine methochloride, it becomes opaque on standing (2—3 days) in the air and the long, transparent needles are transformed into a white, sandy powder, consisting of a monohydrate; when the latter is dried at 60°, it loses $\frac{1}{2}H_2O$; the anhydrous salt is formed at 104°, and is hygroscopic. The polyhydrate melts at 58—60° to a colourless oil, which on further heating crystallises at about 120° and melts again at 271—273°; this is also the m. p. of the other hydrates and of the anhydrous salt (Found in air-dried material: loss at 60°, 1·8; loss at 104°, 4·6. $C_{24}H_{33}ON_2Cl,H_2O$ requires $0·5H_2O$, 2·1; $1H_2O$, 4·3%. Found in a specimen dried at 104°: C, 72·0; H, 8·5. $C_{24}H_{33}ON_2Cl$ requires C, 71·9; H, 8·2%).

*The Conversion of Dimethyl*desneo*strychnidine Methochloride* * *into Dimethyl*desbisneo*strychnidine*.—Dimethyl*desneo*strychnidine methochloride (80 mg.) was mixed with methyl-alcoholic sodium methoxide (1 c.c. of 25%) and heated for 2 hours in an open flask on a water-bath. The cold product was mixed with ice-water (5 c.c.) and exhaustively extracted with light petroleum (b. p. 45—50°). The extract was dried, filtered, and left for slow evaporation of the solvent. The crystalline residue (50 mg.), after being twice recrystallised from light petroleum (b. p. 35—40°), was identified as dimethyl*desbisneo*strychnidine by m. p., by mixed m. p., by comparison of crystals (microphotographs), and by analysis (Found in air-dried material: C, 78·8; H, 8·8%).

N(b)N(b)-*Dimethyl*desneo*strychnidine*.—When dimethyl*desneo*strychnidine methochloride (70 mg.) was cautiously melted in a small test-tube over a free flame, no decomposition occurred; the cold melt, after being recrystallised from acetone, had m. p. 271—273°, not depressed by the initial methochloride. When, however, the methochloride (100 mg.) was gently heated for a short time a few degrees above the m. p., methyl chloride was given off and free dimethyl*desneo*strychnidine was formed. The product was thrice recrystallised from light petroleum (b. p. 30—40°) and minute colourless plates (Fig. 2), m. p. 73—74°, were obtained (Found in air-dried material: C, 78·7, 78·9; H, 8·9, 8·9; N, 8·2, 8·3; Me as NMe, 9·0. $C_{23}H_{30}ON_2$ requires C, 78·9; H, 8·6; N, 8·0; 2Me as NMe, 8·6%). *Dimethyl*desneo*strychnidine* is very sparingly soluble in light petroleum, readily soluble in the simple alcohols, acetone or ethyl acetate, and dissolves very readily in chloroform or benzene. The dilute aqueous acid–ferric reaction of this substance (standard conditions) is of strychnidine type, although the colour develops more slowly and is less intense. When dimethyl*desneo*strychnidine was hydrogenated on a semi-micro-scale in presence of platinum-black, 4H were taken up, but the reduction product has not been isolated (see following paper). Dimethyl*desneo*strychnidine readily combines with methyl iodide, yielding a methiodide identical with dimethyl*desneo*strychnidine methiodide described on p. 1478 (m. p. and mixed m. p. 263—267°).

Methoxy-N(b)N(b)-*dimethyldihydro*chano*dihydro*bisneo*strychnidine* crystallises from methyl alcohol or light petroleum (b. p. 65—70°) in stout colourless plates (Fig. 3), m. p. 129—130° (Found in air-dried material: C, 75·7, 75·5; H, 8·9, 8·9; N, 7·5; OMe, 8·7; Me as NMe, 9·1. $C_{24}H_{32}O_2N_2$ requires C, 75·4; H, 8·9; N, 7·3; OMe, 8·1; 2Me as NMe, 7·9%); it is readily soluble in chloroform, benzene and acetone, but dissolves sparingly in methyl alcohol or light petroleum. It was recovered (95%) unchanged after being heated for 12 hours with excess of methyl iodide in a sealed tube at 110°. Unlike methoxymethyldihydro*neo*strychnidine (Clemo, Perkin, and Robinson, J., 1927, 1589), it is not oxidised by methyl iodide in methyl-alcoholic or acetone solution, even on prolonged boiling; neither does it become purple on standing in the air and its methyl-alcoholic mother-liquor remains colourless. A solution of the base (10 mg.) in 0·1% hydrochloric acid (5 c.c.), on addition of ferric alum solution (5 c.c. of 0·25%), slowly becomes pinkish-yellow; this colour changes to yellow on standing.

The Action of Boiling Dilute Sulphuric Acid on Methoxy-N(b)N(b)-*dimethyldihydro*chano-*dihydro*bisneo*strychnidine*.—Methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine is not attacked by boiling 10% (by vol.) sulphuric acid during 3 hours and only a slight change occurs when 20% sulphuric acid is used. Under the following conditions the reaction was complete. A solution of the base (0·5 g.) in 30% sulphuric acid (10 c.c.) was refluxed for 6 hours. The cold liquid was diluted with ice, rendered alkaline with ammonia at 0° (slight turbidity), filtered, and mixed with solid sodium iodide (1 g.). The brown oily iodide which was precipitated was washed with water (the washings and the alkaline filtrate were combined and evaporated to

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* Owing to lack of material, all the experiments with dimethyl*desneo*strychnidine and its methochloride described in this paper were carried out on a semi-micro-scale. When this part of the investigations was completed, it was found that dimethyl*desneo*strychnidine is also formed, but in a better yield, from the *des*-base-D (see following paper). It was therefore possible to repeat on a macro-scale the whole cycle of transformations of this base and all the results now described were confirmed.

a small bulk in a vacuum; a further small quantity of the same iodide was obtained) and heated for 3 hours with silver chloride (from 1 g. of silver nitrate) and water (25 c.c.). The filtrate from the silver salts was evaporated to dryness and the brownish glassy residue was decomposed by sodium methoxide as described on p. 1477. The decomposition product was worked up by the usual method, but no methyl*chano*dihydro*neo*strychnidine could be isolated. When the methyl-alcoholic solution was mixed with methyl iodide, it became warm and almost instantly a crystalline precipitate was deposited; this was recrystallised from water. It was proved to be identical with dimethyl*desbisneo*strychnidine methiodide by m. p., mixed m. p. (310—312° in both cases), and by conversion into free dimethyl*desbisneo*strychnidine (thermal decomposition of the related methochloride).

*Catalytic Hydrogenation of Methoxy-*N(b)N(b)*-dimethyldihydro*chano*dihydro*bisneo*strychnidine. Formation of Two Stereoisomeric Dihydro-bases: Methoxy-*N(b)N(b)*-dimethyldihydro*chano*tetrahydrostrychnidine and* allo*Methoxy-*N(b)N(b)*-dimethyldihydro*chano*tetrahydrostrychnidine.*—This experiment was carried out (i) in presence of palladised charcoal and (ii) in presence of platinum-black; in both cases the same result was obtained and the following is the description of the experiment with platinum-black. Methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine (0·57 g.) was dissolved in 5% hydrochloric acid (10 c.c.) and agitated in hydrogen in presence of platinum-black (from 0·05 g. of platinum oxide) at 17°. Absorption of the gas ceased after 50 minutes, 35 c.c. (at N.T.P.) having been taken up (calc. for 2H, 34 c.c.). The filtered solution was basified with ammonia (caseous precipitate) and exhaustively extracted with benzene. The colourless residue left after distillation of the solvent in a vacuum was repeatedly crystallised from methyl alcohol and two products were obtained: *methoxydimethyldihydro*chano*tetrahydrostrychnidine* (0·12 g.), m. p. 131—132°, and an oily fraction (0·41 g.). The identity of the former was proved by m. p., by mixed m. p. (no depression), by comparison of crystals (microphotographs), and by analysis (Found: C, 75·1; H, 9·6. $C_{24}H_{36}O_2N_2$ requires C, 75·0; H, 9·4%). A description of this substance (prepared in a different way) is given below.

The oily fraction was very readily soluble in the usual organic solvents; it was dissolved in ether (10 c.c.) and left in an open test-tube for slow evaporation of the solvent. After about 3 weeks allo*methoxydimethyldihydro*chano*tetrahydrostrychnidine* began to crystallise; the collected crystals were three times recrystallised from light petroleum, giving finally minute colourless plates (85 mg.), m. p. 113—114° (Found: C, 75·1; H, 9·6%). The base is readily soluble in chloroform or benzene, moderately readily soluble in methyl alcohol, and dissolves sparingly in light petroleum.

N(b)*-Methyldihydro*chano*dihydrostrychnidine Dimetho-salts.*—These derivatives are semi-crystalline in the crude state and fail to crystallise on "recrystallisation"; they are all fairly soluble in water or methyl alcohol. The only salt which was analysed was the *dimethiodide*, produced by direct union of the components in a sealed tube at 130° (Found in a specimen dried at 104°: C, 46·1, 46·0; H, 6·2, 6·1; I, 40·4. $C_{24}H_{36}ON_2I_2$ requires C, 46·3; H, 5·8; I, 40·9%).

The Decomposition of N(b)*-Methyldihydro*chano*dihydrostrychnidine Metho- and Dimetho-salts by Means of Sodium Methoxide.*—The behaviour of the salts of both series is analogous to that of the corresponding salts of methyl*chano*dihydro*neo*strychnidine: for instance, (i) the methochloride, treated with sodium methoxide, gives methyldihydro*chano*dihydrostrychnidine together with a minute quantity of *N*(*b*)-ring-fission products; (ii) the dimethochloride under similar conditions also gives methyldihydro*chano*dihydrostrychnidine, but the yield of the degradation products is better (much worse, however, compared with methyl*chano*dihydro*neo*strychnidine dimethochloride). The separation of the decomposition products was carried out as described previously, but it occupied a longer time and at one point the procedure was somewhat different, namely, when the methyl-alcoholic mother-liquor (which remained after isolation of methyldihydro*chano*dihydrostrychnidine) was mixed with methyl iodide, the first substance which crystallised (after several days) was methoxydimethyldihydro*chano*tetrahydrostrychnidine (and not a methiodide, as in the previous case). The decomposition products (from 5 g. of dried dimethochloride) were: (a) *N*(*b*)-methyldihydro*chano*dihydrostrychnidine (3·3 g.), m. p. 177—178°, identified in the usual way; (b) *N*(*b*)*N*(*b*)-dimethyl*des*dihydrostrychnidine-D methiodide (0·4 g.), m. p. 299—301°; (c) *N*(*b*)*N*(*b*)-dimethyl*des*dihydro*bisneo*strychnidine methiodide (0·2 g.), m. p. 177—178°; and (d) methoxy-*N*(*b*)*N*(*b*)-dimethyldihydro*chano*tetrahydrostrychnidine (0·15 g.), m. p. 131—132°.

N(b)N(b)*-Dimethyl*des*dihydrostrychnidine-D methiodide* crystallises from aqueous or methyl-alcoholic solution in soft colourless needles, m. p. 299—301° (Found in air-dried material:

C, 58·5, 58·4; H, 7·3, 7·2; I, 26·1. $C_{24}H_{35}ON_2I$ requires C, 58·3; H, 7·1; I, 25·7%); it is very sparingly soluble in water and dissolves moderately readily in methyl alcohol.

The related methochloride separates from a concentrated aqueous solution in minute colourless plates, m. p. 225—227°. When it was cautiously heated for a few minutes at a temperature a few degrees above the m. p., methyl chloride was given off and free dimethyl*des*dihydrostrychnidine-D was formed in good yield. This substance was also obtained when the methochloride was heated with sodium methoxide. The base, despite numerous attempts, could not be prepared in a crystalline state; however, the decomposition product from both preparations was homogeneous, since it gave with methyl iodide a methiodide, m. p. 299—301° (yield, 90%), which was found to be identical with dimethyl*des*dihydrostrychnidine-D methiodide described above. Ferric alum solution gives with dimethyl*des*dihydrostrychnidine-D (standard conditions) a pink coloration, changing to eosin-red.

N(b)N(b)-*Dimethyl*des*dihydro*bisneo*strychnidine methiodide* is moderately readily soluble in water or methyl alcohol and separates from both solvents in colourless plates, m. p. 177—178° (Found in material dried at 104°: C, 58·2, 58·4; H, 7·4, 7·2. $C_{24}H_{35}ON_2I$ requires C, 58·3; H, 7·1%).

The corresponding methochloride forms a brown horny mass, freely soluble in water. When it was heated (as in the preceding experiment), methyl chloride was given off and free dimethyl*des*dihydro*bisneo*strychnidine was formed. This base was also obtained by decomposing the methochloride with sodium methoxide. Dimethyl*des*dihydro*bisneo*strychnidine is amorphous and combines (on gentle heating) with methyl iodide to yield a methiodide, m. p. 177—178°, identical with dimethyl*des*dihydro*bisneo*strychnidine methiodide. The identity was established by mixed m. p. A solution of the base in dilute hydrochloric acid (standard conditions) remains almost colourless on addition of ferric alum or ferric chloride solution.

Methoxy-N(b)N(b)-*dimethyldihydro*chano*tetrahydrostrychnidine* crystallises from methyl alcohol or light petroleum (b. p. 65—70°) in stout colourless plates (Fig. 4), m. p. 131—132° (the m. p. is considerably depressed on admixture with methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine). It is readily soluble in chloroform, benzene or acetone and dissolves sparingly in methyl alcohol or light petroleum (Found in air-dried material: C, 74·8, 74·9; H, 9·5, 9·6; N, 7·5; OMe, 8·4; Me as NMe, 7·6. $C_{24}H_{36}O_2N_2$ requires C, 75·0; H, 9·3; N, 7·3; OMe, 8·1; 2Me as NMe, 8·0%). Methoxydimethyldihydro*chano*tetrahydrostrychnidine does not combine with methyl iodide at 110° (12 hours), and was recovered unchanged after boiling for 3 hours with 20% (by vol.) sulphuric acid. The colour reaction of the base, under standard conditions, is similar to that of methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine.

The Action of Boiling Dilute Sulphuric Acid on Methoxy-N(b)N(b)-*dimethyldihydro*chano*tetrahydrostrychnidine. Formation of* N(b)-*Methyldihydro*chano*dihydrostrychnidine Hydrogen Sulphate.*—A solution of methoxydimethyldihydro*chano*tetrahydrostrychnidine (0·5 g.) in dilute sulphuric acid (10 c.c. of 40% by vol.) was refluxed for 6 hours. The cold liquid was worked up as in the case of methoxydimethyldihydro*chano*dihydro*bisneo*strychnidine and the quaternary chloride, which was finally obtained, was submitted to the action of sodium methoxide (under the usual conditions). The decomposition product was washed, dried, and recrystallised from methyl alcohol; methyldihydro*chano*dihydrostrychnidine thus obtained (yield, 70%) had m. p. 177—178°, not depressed by an authentic specimen. The mother-liquor was not examined.

The Action of Methyl-alcoholic Sodium Methoxide on N(b)N(b)-*Dimethyl*desbisneo*strychnidine Dimethochloride. Elimination of Trimethylamine and Formation of Two Isomeric Bases:* desaza-*Strychnidine-a and* desaza*Strychnidine-b.*—A solution of dimethyl*desbisneo*strychnidine dimethochloride (5 g., previously dried at 104°) in methyl alcohol (15 c.c.) was mixed with methyl-alcoholic sodium methoxide (30 c.c. of 25%) and heated until the temperature reached 130°. Evolution of trimethylamine began at about 105° and the gas was passed into dilute hydrochloric acid and identified by conversion into the hydrochloride, m. p. 272—274°, and the platinichloride, m. p. 240—242°. The cold, grey decomposition product was mixed with ice-water and exhaustively extracted with benzene (thrice, 75 c.c. in all) and the dried and filtered extract was evaporated to dryness in a vacuum. The dark residue was dissolved in boiling acetone (10 c.c.) and left in an ice-chest. After 12 hours dimethyl*desbisneo*strychnidine, m. p. 113—114°, crystallised, and a further small quantity of this base was obtained on concentrating the filtrate. Separation of other decomposition products could not be accomplished by simple crystallisation, and was achieved by the following method. The final acetone mother-liquor was evaporated to dryness, the residue dissolved in hydrochloric acid (10 c.c. of 25%) and diluted with water (100 c.c.), and the milky liquid exhaustively extracted with benzene. The extract was washed with aqueous sodium bicarbonate, dried, filtered, and evaporated to dryness in a vacuum (product A). The aqueous layer was rendered alkaline with ammonia (turbidity) and extracted with benzene, the extract evaporated to dryness in a vacuum, and the residue crystallised from acetone; the product thus isolated was pure dimethyl*desbisneo*strychnidine, m. p. 113—114° (total yield, 2·4 g.).

The product A (1·2 g.) was dissolved in methyl iodide (20 c.c.) and refluxed for 12 hours on a water-bath. The residue, after evaporation of the excess of methyl iodide, crystallised when rubbed with acetone, but the collected crystals were sticky and again by simple crystallisation it was impossible to get an analytically pure substance. The methylation product was dissolved in a mixture of equal volumes of methyl alcohol and acetone (15 c.c.) and precipitated by addition of ether (150 c.c.); the semi-solid precipitate was dissolved in acetone and a fresh portion of ether added. This operation was repeated until a dry (not sticky) product (B) was obtained (4—5 times). The ethereal solutions were combined and evaporated to dryness; the residue (C) was examined separately.

The product B (0·9 g.) had m. p. 132—146° and, as was later established, consisted of *desaza*strychnidine-a methiodide and *desaza*strychnidine-b methiodide. Preliminary separation of these substances was achieved by washing the mixture with much acetone, in which the former was very sparingly soluble and the latter moderately readily. *desaza*Strychnidine-a methiodide thus purified had m. p. 150—152°; two further crystallisations from water raised the m. p. to 154—155° (constant).

The residue C (0·3 g.), after many unsuccessful attempts had been made to crystallise it, was refluxed with methyl iodide. After about 2 hours the solution began to deposit crystals and the heating was discontinued. The product was almost colourless and, after being washed with acetone, had m. p. 152—154°, not depressed by *desaza*strychnidine-a methiodide.

desaza*Strychnidine-a methiodide* is very sparingly soluble in acetone and sparingly soluble in water, but dissolves readily in the simple alcohols. A hot saturated solution of the salt solidifies, on cooling, to a snow-white crystalline mass of a polyhydrate. This, on standing in the air for 1—2 days, is transformed into a hard crust containing $3{\cdot}5H_2O$. When the latter hydrate is dried over sulphuric acid in a high vacuum at room temperature for 5—6 days, it loses $3H_2O$, forming a hemihydrate. The anhydrous salt could not be prepared in a pure state, as both hydrates, on drying at 90—100°, split off methyl iodide. In a quantitative experiment, 4·596 mg. of the hemihydrate, heated at 104° in a high vacuum for 4 hours, lost 1·447 mg. or 31·5%, whereas $C_{22}H_{26}ONI,0{\cdot}5H_2O$, losing MeI and $0{\cdot}5H_2O$, requires a loss of 33·1%, or, losing MeI, requires a loss of 31·9%. The dried residue gave the following figures: C, 80·0; H, 7·7, whereas $C_{21}H_{23}ON$ requires C, 82·7 and H, 7·6%. The air-dried methiodide melts at 96—98°; on further heating, the liquid solidifies at about 110° and melts again at 154—155°. The product, dried at room temperature in a high vacuum, melts at 98—101° (Found in air-dried material: loss over sulphuric acid in a high vacuum at room temperature, 10·8. $C_{22}H_{26}ONI,3{\cdot}5H_2O$ requires $3H_2O$, 10·6%. Found in a specimen dried over sulphuric acid in a high vacuum at room temperature: C, 58·2, 58·2; H, 6·1, 6·1; N, 3·2, 3·4. $C_{22}H_{26}ONI,0{\cdot}5H_2O$ requires C, 58·0; H, 5·8; N, 3·1%).

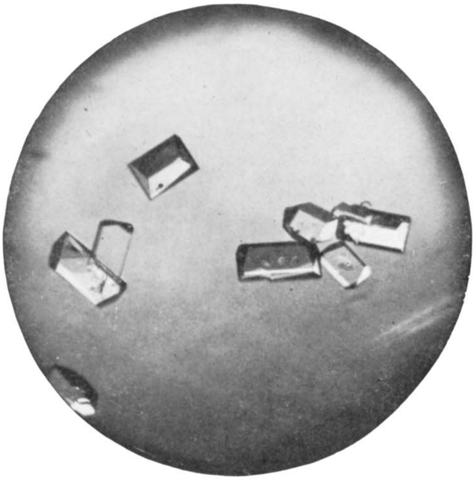
The related methochloride, prepared in the usual way, forms a slightly yellow, thick oil which, in contrast with all known quaternary chlorides of strychnine or brucine bases, is sparingly soluble in water.

desaza*Strychnidine-a.*—*desaza*Strychnidine-a methochloride (0·1 g.) was mixed with methyl-alcoholic sodium methoxide (3 c.c. of 25%) and heated in an open flask on a rapidly boiling water-bath. The cold product was diluted with water and *desaza*strychnidine-a was extracted with light petroleum (20 c.c.). The base forms a colourless thick oil, readily soluble in most organic solvents except methyl alcohol. A solution of the base (1—2 mg.) in dilute hydrochloric acid (5 c.c. of 0·1%, mixed with 3 drops of 25% hydrochloric acid) slowly becomes reddish-purple on addition of ferric alum solution (5 c.c. of 0·25%); on standing or more quickly on heating, the colour changes to brown and yellow. *desaza*Strychnidine-a is sparingly soluble in dilute acids; solutions in more concentrated acids deposit the free base on dilution with water. *desaza*Strychnidine-a does not combine with methyl iodide in the cold, but when it is refluxed with an excess of this reagent for 2 hours, the methiodide, m. p. 154—155°, is obtained in theoretical yield.

desaza*Strychnidine-b methiodide* crystallises from water in minute colourless needles, m. p. 104—105°, very readily soluble in methyl alcohol and moderately readily in acetone or water. It separates from an aqueous solution as a monohydrate, which loses water of crystallisation on being dried over sulphuric acid in a high vacuum at room temperature; at 104° the salt undergoes decomposition (Found in air-dried material: loss over sulphuric acid at room

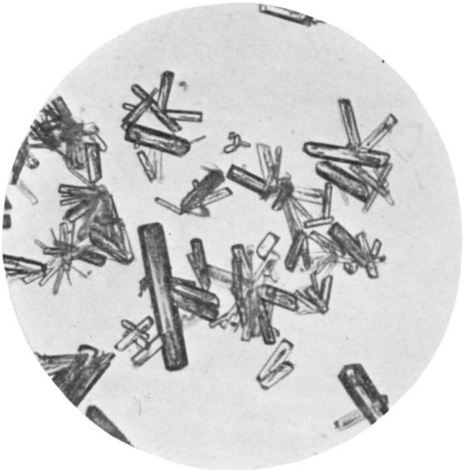
PART XXXVIII.

FIG. 1.



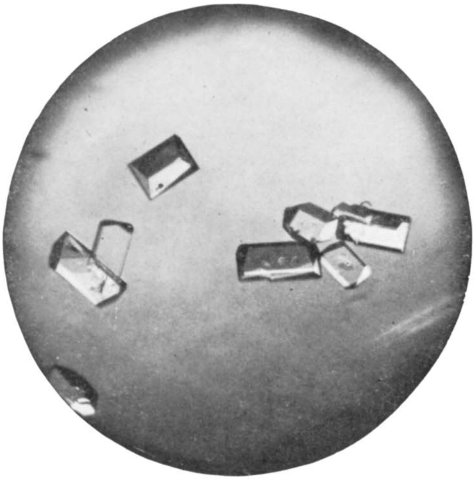
N(b)N(b)-*Dimethyl*desbisneo*strychnidine*, *m. p.* 113—114° (*from acetone*).

FIG. 2.



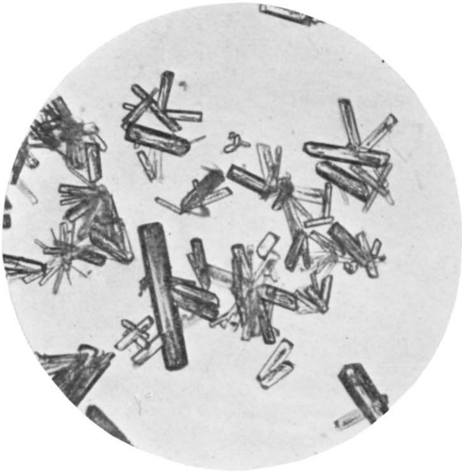
N(b)N(b)-*Dimethyl*desneo*strychnidine*, *m. p.* 73—74° (*from ethyl alcohol*).

FIG. 3.



Methoxy-N(b)N(b)-*dimethyldihydro*chano*dihydro*-bisneo*strychnidine*, *m. p.* 129—130° (*from light petroleum*).

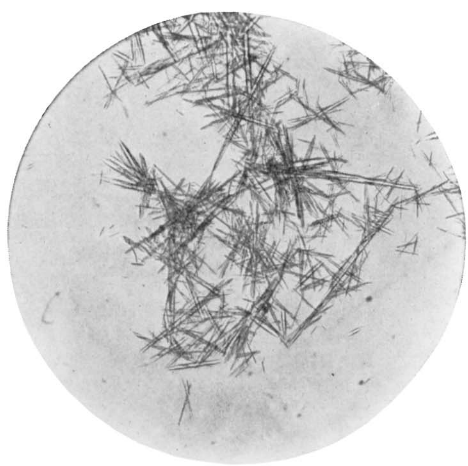
FIG. 4.



Methoxy-N(b)N(b)-*dimethyldihydro*chano*tetrahydrostrychnidine*, *m. p.* 131—132° (*from light petroleum*).

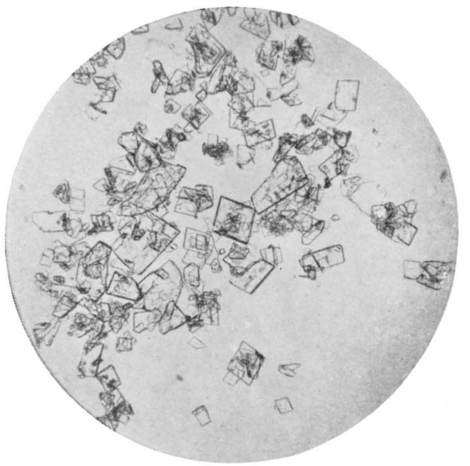
[*To face p.* 1482.

FIG. 5.



N(b)-*Methyldihydro*chano*dihydrostrychnidine*, *m. p.* 177—178° (*from methyl alcohol*).

FIG. 6.



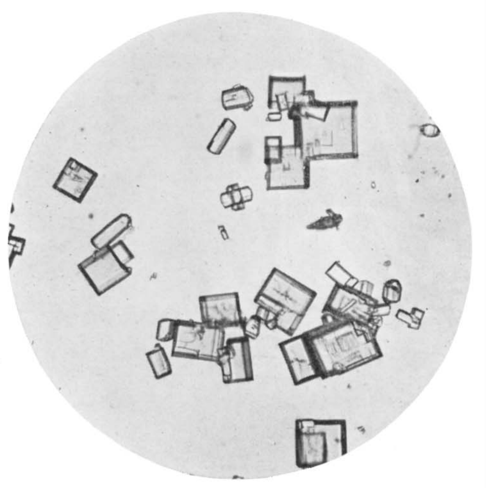
allo-N(b)-*Methyldihydro*chano*dihydrostrychnidine*, *m. p.* 117—118° (*from methyl alcohol*).

PART XXXIX.

FIG. 1.

N(b)N(b)-*Dimethyl*des*strychnidine*-D, *m. p.* 156—157° (*from ethyl alcohol*).

FIG. 2.



desaza*Strychnidine-b*, *m. p.* 109—110° (*from ethyl alcohol*).

temperature in a high vacuum, 3·9. $C_{22}H_{26}ONI,H_2O$ requires H_2O, 4·0%. Found in a specimen dried as just stated: C, 59·5, 59·6; H, 6·2, 6·2; N, 3·5, 3·2; I, 27·6. $C_{22}H_{26}ONI$ requires C, 59·1; H, 5·8; N, 3·1; I, 28·4%). Free *desaza*strychnidine-b is described in the following paper.

Catalytic Hydrogenation of N(b)-*Methyl*chano*dihydro*neo*strychnidine. Formation of Two Stereoisomeric Dihydro-bases*: N(b)-*Methyldihydro*chano*dihydrostrychnidine and* allo-N(b)-*Methyldihydro*chano*dihydrostrychnidine*.—Methyl*chano*dihydro*neo*strychnidine (14 g., m. p. 143—144°) was dissolved in 25% acetic acid (100 c.c.) and shaken with hydrogen in presence of platinum-black (from 1 g. of platinum oxide and 100 c.c. of water) at 17—19°. After 4 hours the volume of hydrogen absorbed was 940 c.c. (at N.T.P.; calc. for 2H, 933 c.c.); absorption then ceased. The reduction product was precipitated from the filtered liquid by means of ammonia (grey, voluminous precipitate) and extracted with benzene. The colourless residue (14 g.), after distillation of the solvent in a vacuum, gave on repeated crystallisation from methyl alcohol methyldihydro*chano*dihydrostrychnidine (total yield, 4·6 g.), m. p. 177—178° (Fig. 5) (compare Perkin, Robinson, and Smith, J., 1934, 579; Achmatowicz, *Roczn. Chem.*, 1933, 25).

allo-N(b)-*Methyldihydro*chano*dihydrostrychnidine*.—The methyl-alcoholic mother-liquor was evaporated to dryness in a vacuum. The very readily soluble residue, after many attempts to induce it to crystallise had failed, was dissolved in ether (200 c.c., though 20 c.c. suffice to dissolve the product) and left in an open flask for slow evaporation of the solvent. After 5 weeks allo*methyldihydro*chano*dihydrostrychnidine* began to crystallise and, on addition of ether (15 c.c.) and rubbing, solidified to a hard crystalline mass. This was ground and washed with ether and thrice recrystallised from methyl alcohol. *allo*Methyldihydro*chano*dihydrostrychnidine (yield, 8·8 g.) formed colourless plates (Fig. 6), m. p. 117—118° (Found in air-dried material: C, 78·2, 78·3; H, 8·9, 8·9. $C_{22}H_{30}ON_2$ requires C, 78·1; H, 8·8%). When pure, it has a great tendency for crystallisation and may be crystallised from various solvents (methyl alcohol, acetone, ethyl acetate, benzene, petroleum); it is moderately readily soluble in methyl alcohol, light petroleum or ether and dissolves very readily in chloroform, benzene or acetone. The base was recovered unchanged (95%) after being heated for 4 hours on a water-bath with an excess of freshly distilled acetic anhydride and fused anhydrous sodium acetate. It readily combines with methyl iodide and, in common with other bases of the *chano*-series, yields a methiodide having no tendency for crystallisation.

Both isomeric dihydro-bases were also formed when the hydrogenation was carried out on a smaller scale in presence of palladised charcoal.

The author expresses his sincere gratitude to Professor Robert Robinson, F.R.S., for his constant interest and encouragement during the prosecution of this and previous researches on the *Strychnos* alkaloids. He is also indebted to Docent K. Lindenfeld of Warsaw for preparing the microphotographs and for carrying out the micro-analyses.

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