182. *Strychnine and Brucine. Part L. Experiments with Pseudostrychnine, Dihydropseudostrychnine, and* neo*Strychnine.*

By K. H. Pausacker and Sir Robert Robinson.

Pseudostrychnine (hydroxystrychnine) condenses with nitromethane to *nitromethylstrychnine* and with *p*-nitrophenylhydrazine and 2 : 4-dinitrophenylhydrazine to substituted *arylhydrazones* of *sec.*-pseudostrychnine.

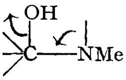
*neo*Strychnine is reduced by zinc and dilute hydrochloric acid to dihydrostrychnine under conditions whereby strychnine remains unchanged. *neo*Strychnine combines with acetic anhydride with formation of a neutral *product*, $C_{23}H_{28}O_5N_2$.

Dihydropseudostrychnine methyl ether is converted by Raney nickel in boiling xylene into *neo*strychnine. In the same way pseudostrychnine methyl ether yields a *hydroxy*neo*strychnine* (or possibly a homologue, see below) reduced by zinc and hydrochloric acid or by catalytic hydrogenation to a new x-*hydroxydihydrostrychnine* (or a homologue). The latter base is changed by Raney nickel into *neo*strychnine. Pseudostrychnine reacts with phosphorus trichloride, and the *product*, isolated after solution in aqueous ammonia and acidification, has the composition $C_{21}H_{23}O_5N_2P$. This is a very stable substance, unaffected by hot dilute acids and alkalis. It does not form a hydrochloride but yields an abnormal *perchlorate*, $2C_{21}H_{23}O_5N_2P,HClO_4,H_2O$. On catalytic reduction it absorbs four atoms of hydrogen.

*neo*Strychnine (but not strychnine) reacts with phosphoric acid and with phosphorous acid to form *substances* $C_{21}H_{23}O_5N_2P$ and $C_{21}H_{27}O_6N_2P$ (probably $C_{21}H_{23}O_4N_2P,2H_2O$) respectively. Each of these absorbs two atoms of hydrogen on catalytic reduction. The nature of these substances is not clear but they are possibly substituted amides of phosphoric and phosphorous acids.

THE pseudostrychnine of Warnat (*Helv. Chim. Acta*, 1931, **14**, 997) had m. p. 268° (decomp.), and the work of Blount and Robinson (*J.*, 1932, 2307) was carried out with material of the same Swiss origin. Leuchs and Räck (*Ber.*, 1940, **73**, 734), following Leuchs (*Ber.*, 1937, **70**, 1543) and Leuchs and Tessmar (*ibid.*, p. 2369), oxidised strychnine by atmospheric oxygen in the presence of Fehling's solution and obtained an isomeride, m. p. 233°. This was stated to be convertible into Warnat's pseudostrychnine by simple solution in dilute hydrochloric acid and precipitation with ammonia. Nevertheless it was found (Leuchs, Grünow, and Tessmar, *Ber.*, 1937, **70**, 1701) that the isomeride, m. p. 233°, was more resistant to catalytic hydrogenation in acid solution than that of m. p. 263°, though the same dihydro-derivative was obtained. This suggests a slow transformation and reduction by way of the substance of m. p. 263°. On these grounds as well as from the different rotatory powers there seems to be little doubt but that the isomerism is real. Unfortunately we do not yet know whether the underlying cause is stereochemical or structural and it may be a source of confusion that many experiments on pseudostrychnine have been recorded without any statement of the m. p. of the material employed.

The base employed in the present investigations had m. p. 235° and was prepared by the method of Leuchs and Räck (*loc. cit.*) before that described in the previous part of this series (Bailey and Robinson, this vol., p. 703) had been discovered. The condensation reactions of pseudostrychnine on the one hand, and its conversion into derivatives of *sec.*-pseudostrychnine (such as the neutral *N*-nitroso- and *N*-acetyl derivatives) on the other, show that the base is a typical carbinol-amine, ⁚C(OH)·N⁚, and it is thus an analogue of cotarnine. Yet there are contrasts : as one example, cyanohydrocotarnine is easily decomposed into its generators by mineral acids, but cyanodihydrostrychnine is very stable to hot hydrochloric acid. These divergences do not obscure the general correspondence of reaction type and are probably due to the circumstance that the stereochemical configuration of pseudostrychnine does not permit a large displacement from the carbinol-amine to the unsaturated quaternary ammonium structure. The arrows in the annexed expression may represent the full transfer of two electrons in cotarnine, but it is now suggested that only a small fraction of such a transfer is possible in the pseudostrychnine molecule. The hypothesis of small alternating displacements allows us to envisage a reaction mechanism in such a case which is fully analogous to that postulated when a large displacement may be assumed.



Hope and Robinson found that cotarnine condensed with the greatest readiness with nitromethane, 2 : 4-dinitrotoluene, and 2 : 4 : 6-trinitrotoluene in alcoholic solution (*J.*, 1911, **99**, 2114). Pseudostrychnine undergoes no condensation under these conditions, doubtless because the ethyl ether is formed and is much less reactive than the corresponding derivative of cotarnine. The condensation of pseudostrychnine with nitromethane, used also a solvent, occurs, however, and the product is *anhydropseudostrychninenitromethane*.

Although the imino-group of *sec.*-pseudostrychnine has been recognised by the preparation of *N*-substituted derivatives, the carbonyl group of this substance has hitherto not been directly characterised.

We now find that the p-*nitrophenylhydrazone* and the 2 : 4-*dinitrophenylhydrazone* can be obtained.

N-*Acetyl*-sec.-*pseudostrychnine* also affords a p-*nitrophenylhydrazone*. Hydrolysis of *N*-acetyl-*sec.*-pseudostrychnine by means of hot dilute hydrochloric acid gives pseudostrychnine.

Interesting results were obtained in studying the action of Raney nickel on pseudostrychnine derivatives. Dihydropseudostrychnine methyl ether is better obtained by hydrogenation of pseudostrychnine methyl ether in the presence of platinic oxide than by the method of Leuchs and Räck (*Ber.*, 1940, **73**, 811) which depended on reduction of pseudostrychnine followed by condensation with methanol. Reversal of the order of the processes avoids the formation of strychnine by hydrogenolysis.

When dihydropseudostrychnine methyl ether was refluxed with Raney nickel in xylene, *neo*strychnine was produced in good yield. This result does not demonstrate a close structural relation between the two substances as, for example, in the formation of a double bond by simple elimination of methanol, though it is clearly consistent with that hypothesis. Similar treatment of pseudostrychnine methyl ether furnished a base, the analyses of which point to the formula $C_{22}H_{24}O_3N_2$, though $C_{21}H_{22}O_3N_2$ is not definitely excluded. But the base does not contain a methoxyl group or a methylimino-group, and if methyl were attached to carbon the eventual transformation to *neo*strychnine would be hard to explain. For these reasons the formula $C_{21}H_{22}O_3N_2$ must be entertained, and we regard the base provisionally as x-*hydroxy*neo*strychnine*. The *neo*-double-bond character is evinced by the behaviour on coupling with *p*-nitrobenzenediazonium chloride in acid solution.

On catalytic reduction, a volume of hydrogen corresponding to two atoms is absorbed, and the product is $C_{21}H_{24}O_3N_2$ ($C_{22}H_{26}O_3N_2$?). The same substance is obtainable by reduction with zinc and dilute hydrochloric acid, and it is noteworthy that *neo*strychnine (but not strychnine) can be reduced to dihydrostrychnine in the same way. This is even a convenient method of preparation of dihydrostrychnine. The reduced base, $C_{21}H_{24}O_3N_2$, is tentatively considered to be x-*hydroxydihydrostrychnine*. On treatment with Raney nickel in boiling xylene, it was converted into *neo*strychnine.

The base $C_{21}H_{24}O_3N_2$ is not identical with the isomeric dihydropseudostrychnine and hence the position *x* may denote one of the carbon atoms of the strychnine double bond. If that supposition is justified the substance might be a primary or secondary alcohol, and another isomeride, which has been isolated and which will be described in the next part of the series, comes into consideration for the former possibility. Its properties are quite different from those of *x*-hydroxydihydrostrychnine. Furthermore *neo*strychnine is now known (see Part LI) to contain the group $\colon\mathrm{N(b){\cdot}CH{=}C}\colon$, and hence the *x*-hydroxy*neo*strychnine cannot be formulated with a hydroxyl group on the β-carbon atom. As it is clearly improbable that a hydroxyl group has been introduced into some position unrelated to the strychnine unsaturation, the most plausible hypothesis is that *x*-hydroxy*neo*strychnine contains the group $\colon\mathrm{N(b){\cdot}CH{=}C{\cdot}CH(OH){\cdot}CH_2}$. We know that an oxidation–reduction process may involve the two carbon atoms joined to N(b), and hence the mechanism may be: $\colon\mathrm{C(OH){\cdot}\dot{N}(b){\cdot}CH_2{\cdot}\dot{C}{=}CH{-}} \longrightarrow \colon\mathrm{CH{\cdot}\dot{N}{\cdot}CH(OH){\cdot}\dot{C}{=}CH{-}} \longrightarrow \colon\mathrm{CH{\cdot}\dot{N}{\cdot}CH{=}\dot{C}{\cdot}CH(OH){\cdot}}$, the last step by allyloid rearrangement.

Attempts to bring about a ring-fission of *neo*strychnine, $\colon\mathrm{N{-}CH{=}C}\colon \longrightarrow \colon\mathrm{NH\ CHO{\cdot}CH}\colon$, have been continued, but the system shows unusual stability. Failure with acids under varied conditions has already been reported. In the presence of hydroxylamine or *p*-nitrophenylhydrazine some indications of hydrolysis have been obtained and the same is true of the Schotten–Baumann benzoylation. A definite reaction with formation of a neutral product occurs on long treatment with acetic anhydride at 100°. The base adds the elements of the reagent and the product may contain $\colon\mathrm{N(b){\cdot}COMe\ Me{\cdot}CO{\cdot}O{\cdot}CH{=}C}\colon$. Its investigation has not yet been completed. In the course of the benzoylation experiments the formation of much benzoic anhydride was noted. It was then found that benzoic anhydride can be prepared by shaking benzoyl chloride with aqueous sodium hydroxide in the presence of quite small quantities of pyridine. The method is convenient for the preparation of the anhydrides of aromatic acids.

An attempt to dehydrate pseudostrychnine by means of phosphorus trichloride led to the eventual formation of an acidic *substance*, $C_{21}H_{23}O_5N_2P$, which was at first thought to be a phosphinic acid. It is now regarded as a phosphinamide: $\colon\mathrm{N(b){\cdot}C(OH)}\colon \longrightarrow \colon\mathrm{N{\cdot}PO_2H\ CO}\colon$. The four hydrogen atoms absorbed on catalytic reduction are presumably taken up by the carbonyl group and the strychnine double bond. The carbonyl group could not be detected by the formation of derivatives.

*neo*Strychnine affords similar *products* with both phosphorous and phosphoric acids. These furnish *dihydro*-derivatives ($\mathrm{CHO} \longrightarrow \mathrm{CH_2{\cdot}OH}$?), and the power to form *p*-nitrophenylhydrazones (colour-reaction test) is lost after the reduction. All attempts to hydrolyse these substances were unsuccessful. A curious point in regard to the product from *neo*strychnine and phosphoric acid is that it has the composition $C_{21}H_{23}O_5N_2P$ and not the expected $C_{21}H_{25}O_6N_2P$ (for $\mathrm{N{\cdot}CH{=}C} \longrightarrow \mathrm{NPO_3H_2,\ CHO{\cdot}CH}$). The Otto reaction is exhibited [N(a)·CO present] and loss of the cyclic ether oxygen is unlikely; hence the groups present may be $\colon\mathrm{N(b){\cdot}PO_2,\ CHO{\cdot}CH}\colon$ or $\colon\mathrm{N(PO_2H){\cdot}O{\cdot}CH}\colon\mathrm{C}\colon$.

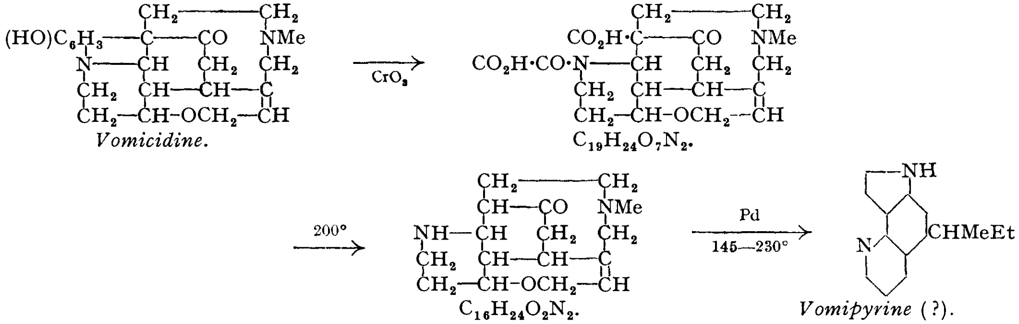
Of miscellaneous observations the following may be mentioned. (*a*) Kotake, Sakan, and Kusumoto (*Sci. Papers Inst. Phys. Chem. Res. Tokyo*, 1939, **35**, 415) found that the action of ozone on strychnine furnished pseudostrychnine.

Ozonisation of *neo*strychnine, however, affords the neutral ketone, $C_{21}H_{22}O_4N_2$, first prepared by Kotake and Yokayama (*ibid.*, 1937, **31**, 329) by oxidation of *neo*strychnine with permanganate.

(*b*) A *dibenzylidene* derivative (+ H_2O) can be obtained from strychninonic acid. Doubtless one benzylidene group is vicinal to N(a)·CO·, but it is not probable that the second indicates a methylene group adjacent to the carbonyl. It may well be that the groups introduced are $\colon\mathrm{N(a){\cdot}CO{\cdot}C(}\colon\mathrm{CHPh){\cdot}}$ and $\colon\mathrm{N(b){-}CHPh{-}\underset{\cdot}{\dot{C}}{-}CO{\cdot}CO_2H}$. This theory involves hydrolysis of the α-keto-amide structure and is thus H_2O more than a dibenzylidene derivative; the ring bridged by the benzylidene group would be five-membered.

(*c*) Some years ago, one of us suggested to Professor H. Wieland that vomicine is constituted like *N*-methylchanopseudostrychnine (*N*-methyl-*sec.*-pseudostrychnine) with, of course, a phenolic hydroxyl group in the *o*-position to N(a).

That hypothesis was rejected by Professor Wieland (letter dated May 15th, 1939),* but it still seems much more probable than the view advanced by him that vomicine contains $^-O\cdot CH_2$ N(b):. All experience shows that such acetal-like structure are readily hydrolysed by acids. Since the extra carbon atom is analytically recognisable as present in NMe, the Wieland hypothesis is the only good alternative to the preferred postulation of an actual NMe in vomicine. The additional oxygen must then be in a carbonyl or cyclic ether group; the latter theory introduces many difficulties, but the former is feasible on account of the weak carbonyl character and the stability of *N*-methyl-*sec.*-pseudostrychnine. This view also provides a ready explanation of the facile decarboxylation of certain carboxylic acids (such as the intermediate for vomipyrine) obtained by the oxidative degradation of the aromatic nucleus (Wieland and Horner, *Annalen*, **1937**, **528**, 73).



Vomicidine. $C_{19}H_{24}O_7N_2$. $C_{16}H_{24}O_2N_2$. *Vomipyrine* (?).

It should be further noted that the acid $C_{19}H_{24}O_7N_2$ probably exists in a betaine form, $CO_2^-\cdot\dot{C}\cdot C(OH)\cdot\dot{N}Me^+$ (second line from the top of the formula), and thus would neither exhibit carbonyl reactions nor be so unstable as a normal β-ketonic acid.

EXPERIMENTAL.

Pseudostrychnine, m. p. 235°, was used throughout (Found: C, 71·8; H, 6·3; N, 8·2. Calc. for $C_{21}H_{22}O_3N_2$: C, 72·0; H, 6·3; N, 8·0%); it was prepared by the method of Leuchs and Räck (*loc. cit.*).

Anhydropseudostrychninenitromethane.—A mixture of pseudostrychnine (0·5 g.) and nitromethane (10 c.c.) was heated for 3 hours on the steam-bath. The excess of nitromethane was evaporated under diminished pressure and the residue crystallised from aqueous alcohol; the *compound* formed pale yellow needles, m. p. 170° with frothing (Found: C, 65·7; H, 6·1. $C_{22}H_{23}O_4N_3,0{\cdot}5H_2O$ requires C, 65·7; H, 6·0%).

sec.-*Pseudostrychnine* p-*Nitrophenylhydrazone.*—A mixture of pseudostrychnine (0·35 g.), *p*-nitrophenylhydrazine (0·15 g.), and pyridine (3 c.c.) was refluxed for 1½ minutes. The tar precipitated by water gave crystals from aqueous alcohol. After several recrystallisations (charcoal) the fine yellow needles had m. p. 235° (Found: C, 67·1; H, 6·0. $C_{27}H_{27}O_4N_5$ requires C, 66·8; H, 5·6%). The alcoholic solution developed a crimson coloration on the addition of sodium hydroxide. The p-*nitrophenylhydrazone* is stable towards yellow mercuric oxide in boiling alcoholic solution.

The corresponding 2 : 4-*dinitrophenylhydrazone* was prepared in a like fashion. It formed orange needles, m. p. 166° (decomp.) (Found: C, 58·8; H, 4·9. $C_{27}H_{26}O_6N_6,H_2O$ requires C, 59·1; H, 5·1%). This derivative was also not oxidisable by means of mercuric oxide.

N-*Acetyl*-sec.-*pseudostrychnine.*—The crude substance (0·51 g.) was refluxed for 1·25 minutes with *p*-nitrophenylhydrazine (0·15 g.) in acetic acid (2 c.c.). The *product* crystallised from aqueous alcohol (charcoal) as slender, light yellow needles, m. p. 187° (decomp.) (Found: C, 63·4; H, 5·6. $C_{29}H_{29}O_5N_5,H_2O$ requires C, 63·8; H, 5·7%). The alcoholic alkali colour reaction was the same as that of the *p*-nitrophenylhydrazone of pseudostrychnine. *N*-Acetylpseudostrychnine (0·5 g.) was hydrolysed by means of boiling 2N-hydrochloric acid (20 c.c.). 0·4 G. of pseudostrychnine, m. p. 235°, was obtained on basification of the filtered solution with ammonia. The m. p. was not depressed on admixture with an authentic specimen.

Dihydropseudostrychnine Methyl Ether.—Pseudostrychnine methyl ether (2·0 g.), m. p. 191·3°, was hydrogenated in methanol (100 c.c.) at the ordinary temperature and pressure in the presence of platinic oxide (0·1 g.). 152 C.c. of hydrogen (calc., 143 c.c.) were absorbed. Concentration of the filtered solution gave the dihydro-derivative (2·0 g.), m. p. 196—199°, and 197—199° when mixed with a specimen, m. p. 198—199°, prepared according to Leuchs (*loc. cit.*).

A mixture of this substance (0·6 g.), Raney nickel sediment (1·3 c.c.), and xylene (80 c.c.) was distilled

---

* *Added June 18th*, 1948.—Professor Wieland has now concurred in the vomicine formula, and a joint communication on vomicine chemistry is in preparation. He has disclosed that vomipyrine contains NMe, and hence the formula suggested must be modified to contain NMe in the pyrrole ring, and also *iso*butyl is reduced to propyl or *iso*propyl.

until 30 c.c. had been collected; it was then protected from moisture and refluxed for 12 hours. The isolated base (0·4 g., m. p. 218—220°) was crystallised from alcohol; it then had m. p. 224—225° and m. p. 226—227° when mixed with pure *neo*strychnine, m. p. 227°. The characteristic coupling with *p*-nitrobenzenediazonium chloride was noted.

*neo*Strychnine, m. p. 226—227°, had $[\alpha]_D^{18°}$ + 215° (*c*, 1·2 in chloroform) and $[\alpha]_D^{18°}$ + 90° (*c*, 1·2 in acetic acid).

Action of Raney Nickel on Pseudostrychnine Methyl Ether.—The ether (3·3 g.), Raney nickel sediment (3·5 c.c.), and xylene (120 c.c.) were employed and the process carried out as with the dihydro-derivative. The isolated base (2·5 g., m. p. 125° with frothing) was readily soluble in most organic solvents and crystallised from aqueous alcohol in slender needles, m. p. 130° with frothing (Found : C, 67·6; H, 6·7; OMe, 0·0; NMe, a trace. Found in material dried at 100° in a high vacuum: C, 72·4; H, 6·3. $C_{22}H_{24}O_3N_2,1·5H_2O$ requires C, 67·3; H, 6·9. $C_{22}H_{24}O_3N_2$ requires C, 72·5; H, 6·6. $C_{21}H_{22}O_3N_2,1·5H_2O$ requires C, 66·8; H, 6·7. $C_{21}H_{22}O_3N_2$ requires C, 72·0; H, 6·3%).

This product was obtained after dissolution in dilute hydrochloric acid and basification with ammonia. When, however, the xylene solution and chloroform washings were evaporated under reduced pressure, the residue could be crystallised from light petroleum (b. p. 100—120°) in anhydrous form, m. p. 116° (Found : C, 72·3; H, 6·8; OMe, 0·0%). Both specimens gave a yellow precipitate on coupling with *p*-nitrobenzenediazonium chloride. The form first described (0·2 g.) in 2N-hydrochloric acid (5 c.c.) was treated with a diazo-solution from *p*-nitroaniline (0·3 g.). After 10 minutes the solid was collected and crystallised several times from aqueous alcohol. It separated as light yellow needles, m. p. 240° (decomp.) (Found : C, 63·4; H, 5·8. $C_{28}H_{29}O_6N_5$ requires C, 63·3; H, 5·5. $C_{27}H_{27}O_6N_5$ requires C, 62·7; H, 5·3%). The substance gives the usual red coloration in alcoholic alkali. Neither this x-*hydroxy*neo*strychnine* (?) nor its dihydro-derivative (below) showed any signs of reaction with methanol.

x-*Hydroxydihydrostrychnine* (?).—(A) The above *x*-hydroxy*neo*strychnine (0·5 g.) in water (13 c.c.), N-hydrochloric acid (1·5 c.c.), and N-acetic acid (1·5 c.c.) was hydrogenated at the ordinary temperature and pressure in presence of platinic oxide (0·05 g.). In 1½ hours, 41 c.c. of hydrogen were absorbed (calc. for 2H, 43 c.c.). The isolated *base* (0·5 g., m. p. 112° with frothing) crystallised from aqueous alcohol in long, white needles, m. p. 114° (frothing) (Found : C, 66·8; H, 7·5. $C_{22}H_{26}O_3N_2,1·5H_2O$ requires C, 67·1; H, 7·4. $C_{21}H_{24}O_3N_2,1·5H_2O$ requires C, 66·5; H, 7·2%).

(B) The same base was obtained by hydrogenation at 60° in the presence of palladised charcoal.

(C) *x*-Hydroxy*neo*strychnine (0·05 g.) in warm 2N-hydrochloric acid (2·5 c.c.) was reduced by the addition of zinc dust (0·2 g.) during 15 minutes followed by heating on the steam-bath for ½ hour. A faint pink coloration indicated the formation of a small quantity of a strychnidine-type base. After filtration, precipitation with ammonia, and crystallisation from aqueous alcohol, needles, m. p. 114° with frothing, were obtained. The m. p. was the same on admixture with the analysed specimen.

x-Hydroxydihydrostrychnine does not react with *p*-nitrobenzenediazonium chloride in acid solution. When treated with Raney nickel in boiling xylene (9 hours) under the usual conditions, it was converted into *neo*strychnine, white prisms from alcohol, m. p. 222° and m. p. 224° on admixture with an authentic specimen, m. p. 224°. The characteristic reaction with *p*-nitrobenzenediazonium chloride was observed.

Reduction of neo*Strychnine.*—Zinc dust (1·0 g.) was gradually added during 10 minutes to a hot solution of *neo*strychnine (0·5 g., m. p. 224°) in 2N-hydrochloric acid (25 c.c.) and the mixture then heated for 1 hour on the steam-bath. The isolated base (0·5 g., m. p. 213°) crystallised from aqueous methanol in long, white needles, m. p. 217—218°, and 218° on admixture with dihydrostrychnine, m. p. 219°. The product gave no precipitate when *p*-nitrobenzenediazonium chloride was added to its acid solution. The formation of strychnine by reduction of pseudostrychnine under similar conditions shows that the double bond of the base cannot be reduced in this way, although some strychnidine is always produced. Using amalgamated zinc dust and dilute hydrochloric acid it was possible to isolate strychnidine from the products of the reaction.

Similarly the reduction of *neo*strychnine with amalgamated zinc dust and 4N-hydrochloric acid afforded dihydrostrychnidine-A, mixed with dihydrostrychnine. If the process can be improved so as to make it complete, details will be submitted; it is not yet a satisfactory method of preparation.

Derivatives of Pseudostrychnine and neo*Strychnine containing Phosphorus.*—(A) *Anhydropseudostrychninephosphorous acid.* A mixture of pseudostrychnine (5 g.), phosphorus trichloride (5 c.c.), and chloroform (50 c.c.) was refluxed for an hour. Next day the solution was evaporated under diminished pressure (steam-bath) and excess of dilute ammonia added to the residue. Acidification of the filtered solution with hydrochloric acid gave the crude product (4·0 g.). It crystallised from water, in which the substance is sparingly soluble, in white prisms containing phosphorus but free from chlorine. On being heated the substance darkens at 280°, shrinks at 295°, and decomposes vigorously at 315° (Found in material dried at 100°/15 mm. : C, 60·5; H, 5·9; N, 6·8. $C_{21}H_{23}O_5N_2P$ requires C, 60·9; H, 5·6; N, 6·8%). The *acid* exhibits a strong Otto reaction (violet) and dissolves in aqueous sodium hydrogen carbonate with effervescence. It remained unchanged after refluxing with dilute hydrochloric acid or aqueous sodium hydroxide. When sodium iodide was added before precipitation with hydrochloric acid the same product was obtained, but if perchloric acid was used to acidify the ammoniacal solution an abnormal *perchlorate* resulted. The sparingly soluble derivative crystallised from water in colourless needles, m. p. 266° (decomp.), $[\alpha]_D^{13°}$ − 21° (*c*, 2·0 in 2N-ammonia) (Found in material dried at 100° in a high vacuum : C, 53·1; H, 5·6; N, 6·3; Cl, 3·9. $2C_{21}H_{23}O_5N_2P,HClO_4,H_2O$ requires C, 53·3; H, 5·2; N, 5·9; Cl, 3·7%). A similar substance was obtained from dihydropseudostrychnine when it was treated in like manner and the ammoniacal solution acidified with 2N-perchloric acid. The white solid *perchlorate* crystallised from water in microscopic needles which darken from 230°, shrink at 330°, and decompose vigorously at 350° (copper block) (Found in material dried at 100°/15 mm. : C, 54·2; H, 5·8. $2C_{21}H_{25}O_5N_2P,HClO_4$ requires C, 54·0; H, 5·5%). Owing to its unexpected solubility in water, the free acid could not be isolated in this instance and acidification of the ammoniacal solution with hydrochloric acid gave no precipitate.

The interaction of pseudostrychnine with phosphoryl chloride or phosphorus pentachloride did not give rise to isolable compounds.

(B) *Tetrahydroanhydropseudostrychninephosphorous acid.* Anhydropseudostrychninephosphorous acid (0·2 g.) suspended in water (20 c.c.) at 60° was hydrogenated in the presence of platinic oxide (0·03 g.); 26 c.c. (1·93 mol.) of hydrogen were absorbed in 1 hour. The *acid*, obtained on concentrating the filtered solution, crystallised from water in small, white prisms, m. p. 302° (decomp.), $[\alpha]_D^{21°}$ + 67° (*c*, 1·2 in water) (Found in material dried at 100° in a high vacuum: C, 59·5; H, 7·0. $C_{21}H_{27}O_5N_2P,0{\cdot}5H_2O$ requires C, 59·1; H, 6·6%).

(C) *Bisanhydro*neo*strychninephosphoric acid.* A mixture of *neo*strychnine (2·0 g.) and syrupy phosphoric acid (8 c.c.; *d* 1·75) was treated for ½ hour at 150—160°. Water (15 c.c.) was added to the cooled solution and, after it had been kept in the refrigerator for 2 days, colourless crystals (1·0 g.) separated. The *acid* was readily soluble in dilute ammonia and crystallised from a small volume of water in prisms, m. p. 185° (decomp.) (Found in material dried at 100° in a high vacuum: C, 60·5; H, 5·8; N, 7·1. $C_{21}H_{23}O_5N_2P$ requires C, 60·8; H, 5·6; N, 6·8%). The strong Otto reaction was a purple coloration.

The hydrated *dihydro*-derivative, obtained as above by catalytic reduction (PtO_2) at 60° (volume of hydrogen absorbed equivalent to 2H), was readily soluble in water. It crystallised from methanol in short, colourless prisms which shrank at 307—312° and decomposed at 318—320° (Found in material dried at 100° in a high vacuum: C, 58·5; H, 6·1. $C_{21}H_{27}O_6N_2P$ requires C, 58·1; H, 6·3%).

(D) *Anhydro*neo*strychninephosphorous acid.* A mixture of *neo*strychnine (2·0 g.) and phosphorous acid (8 c.c. of molten acid of 100%) was heated for ½ hour at 150—160°. After addition of water (15 c.c.), white crystals (0·7 g.) gradually separated. The *acid* (soluble in ammonia) crystallised from a little water in prisms which shrank at 295° and decomposed at 316° (Found in material dried at 100°/15 mm.: C, 58·5; H, 6·1. $C_{21}H_{27}O_6N_2P$ requires C, 58·1; H, 6·3%). The usual Otto reaction was exhibited.

The *dihydro*-derivative prepared in the usual way (absorption, 1·1 mol.) was very easily soluble in water. It crystallised from methanol as stout needles which shrank at 295° and decomposed from 312°, $[\alpha]_D^{21°}$ + 67° (*c*, 1·2 in water) (Found in material dried at 100°/15 mm.: C, 61·6; H, 6·4. $C_{21}H_{25}O_4N_2P,0{\cdot}5H_2O$ requires C, 61·6; H, 6·5%).

(E) *Colour tests for the carbonyl group.* The compound (3 mg.) was heated at 100° with pyridine (1 c.c.) and *p*-nitrophenylhydrazine (0·5 mg.) for 30 minutes. Alcohol (4 c.c.) and then a few drops of 2N-sodium hydroxide were added.

All oxo-derivatives of strychnine and strychninonic acid gave red colorations; a negative reaction was light brown.

Pseudostrychnine and the anhydro-phosphorous and -phosphoric acids from *neo*strychnine gave positive indications for the carbonyl group. All the hydrogenated compounds and, curiously, anhydropseudostrychninephosphorous acid gave the same result as a blank.

Ozonisation of neo*Strychnine.*—*neo*Strychnine was recovered unchanged after attempted oxidation with atmospheric oxygen in the presence of Fehling's solution. The inactivity of dihydrostrychnine under these conditions has been reported by Prelog and Kočov (*Helv. Chim. Acta*, 1947, **30**, 369), and we have had the same experience.

Ozone (*ca.* 2 mols.) was passed during 1½ hours through a solution of *neo*strychnine (3·3 g.) in chloroform (30 c.c.) cooled in an ice-bath. After addition of water (50 c.c.) the mixture was refluxed for an hour, the chloroform was separated, extracted with dilute sulphuric acid, washed with aqueous ammonia and water, and dried. The oil obtained on removal of the solvent crystallised in contact with methanol (crude, m. p. 225—226°). After recrystallisation from the same solvent it had m. p. 236—237° (lit., 234—235°), and a mixture with an authentic specimen of Kotake's ketone (*loc. cit.*) had m. p. 235—236°. The *p*-nitrophenylhydrazone had m. p. 267—268°, alone or mixed with an authentic specimen (lit., 269—270°).

neo*Strychnine–Acetic Anhydride.*—A mixture of *neo*strychnine (3 g.) and acetic anhydride (30 c.c.) was heated for 20 hours at 100° and the excess of reagent removed from the brown solution by distillation at a low pressure. A solution of the residue in chloroform was repeatedly washed with dilute sulphuric acid (1·8 g. of unchanged bases were recovered on basification). The light brown solid left on removal of the chloroform was readily soluble in solvents, except light petroleum. Its benzene solution was passed through an alumina column, and a white solid was eventually obtained by fractional precipitation with light petroleum (b. p. 80—100°). In this condition it had m. p. 190° with frothing (Found: C, 68·7; H, 6·2. $C_{25}H_{28}O_5N_2$ requires C, 68·8, H, 6·5%). The investigation is incomplete; the *substance* does not afford a base on attempted hydrolysis with boiling dilute sulphuric acid.

Dibenzylidenestrychninonic Acid Hydrate.—A mixture of strychninonic acid (0·4 g.), benzaldehyde (0·3 g.), and alcohol (5 c.c.) was refluxed, and a solution of sodium (0·1 g.) in alcohol (5 c.c.) introduced; refluxing was continued for 15 minutes. The deep orange liquid was evaporated under diminished pressure, water added, and the filtered solution washed several times with ether. Acidification of the aqueous layer gave the *dibenzylidene* derivative as a light yellow solid which crystallised from aqueous dioxan in small, pale yellow needles, m. p. 181—183° (decomp.) (Found in material dried at 15° over phosphoric anhydride: C, 68·7; H, 5·7. Found in material dried at 100° in a high vacuum; C, 71·0; H, 5·4. $C_{35}H_{30}O_7N_2,H_2O$ requires C, 69·1; H, 5·3. $C_{35}H_{30}O_7N_2$ requires C, 71·2; H, 5·1%).

The corresponding *dianisylidene* derivative, prepared similarly, separated from aqueous alcohol as a light yellow solid, m. p. 203° (decomp.) (Found in material dried at 100° in a high vacuum: C, 68·1; H, 5·5. $C_{37}H_{34}O_9N_2$ requires C, 68·3; H, 5·3%).

The authors wish to thank the University of Melbourne for a Travelling Scholarship and the Carnegie Fund for a grant awarded to one of them (K. H. P.).

DYSON PERRINS LABORATORY, OXFORD UNIVERSITY. [*Received, June 24th*, 1947.]