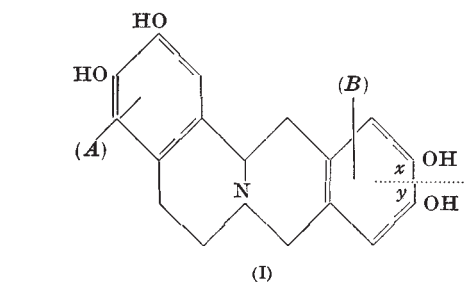
LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. No notice is taken of anonymous communications

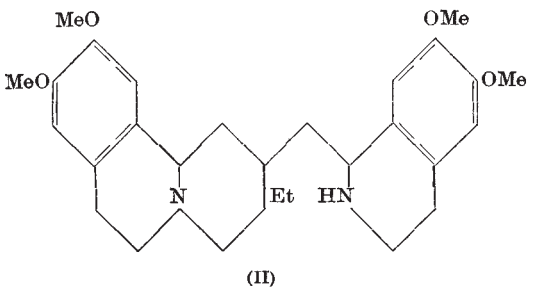
Structure and Biogenesis of Emetine

In making favourable comment on Woodward's ingenious suggestion respecting the biogenesis of strychnine[1], the hope was expressed that further speculation of a similar kind would be based on a comparable "degree of coincidence". The remarkable development mentioned below certainly meets this requirement. It provides an outstanding example of interaction of results in two fields, strengthening theoretical conclusions in both of them.

I noticed that (excluding consideration of the methylation of phenolic hydroxyls) emetine could be constructed from three molecules of dihydroxyphenylalanine and one of the formaldehyde equivalent, assuming a fission of one aromatic nucleus on Woodward's lines. Following these quite closely, it will be noted that the hydroxyl in the meta position to the side-chain of the amino-acid becomes an aldehyde group; that in the para position is found in the alkaloid in a state of oxidation equivalent to that of an alcohol. Postulating exactly the same circumstances in the case of the stages leading, on this hypothesis, to emetine, we arrive without ambiguity at a single formula (II). Thus the *nor*-pseudotetrahydroberberine (I) represents the familiar *nor*-laudanosine of the Winterstein – Trier hypothesis condensed with formaldehyde or its equivalent. What has long been known[2] about emetine proves that our next stage cannot be the degradation of the *A*-nucleus. If we assume the oxidative degradation of the *B*-nucleus, as indicated by the dotted line, and so that *x* becomes a formyl group, and the chain beginning with *y* is fully reduced, and later that the new aldehyde condenses in the usual manner with dihydroxyphenylalanine (decarboxylated at some stage) to an *iso*quinoline derivative, then, after O-methylation, emetine would be (II).



(I)



(II)

No special importance was attached to this speculation until, in the course of a discussion with Dr. M. J. S. Dewar, he wrote down formula (II) as the most likely interpretation of results described in three recent communications[3] on the subject of the chemistry of emetine. Of these, the work of Späth, and of Pailer, solves the problem of the arrangement of carbon atoms in the chain connecting the *iso*quinoline nuclei; that of Karrer and his co-workers supplies a detail which indicates the relation of this carbon skeleton to the tertiary nitrogen.

Thus the constitution (II) appears to be firmly established by these recently disclosed experiments, and by the earlier investigations. It is surely significant that, without knowledge of the recent publications, the same constitution was deduced by applying Woodward's theory of biogenesis of strychnine to a complex member of the *iso*quinoline group.

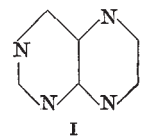
R. Robinson

Dyson Perrins Laboratory,
University, Oxford.
Sept. 5.

[1] Woodward, R. B., *Nature*, **162**, 155 (1948).
[2] Carr, F. H., and Pyman, F. L., *J. Chem. Soc.*, **105**, 1591 (1914); Späth, E., and Leithe, W., *Ber.*, **60**, 688 (1927).
[3] Späth, E., *Monatsh.*, **78**, 348 (1948). Pailer, M., *ibid.*, **79**, 127 (1948). Karrer, P., Eugster, C. H., and Rüttner, O., *Helv. Chim. Acta*, **31**, 1219 (1948).

A Synthesis of Pteridine

Although many derivatives of pteridine, both natural and synthetic, are known, the parent substance pteridine (I) does not appear to have been described. This substance has now been prepared by the condensation of 4 : 5-diaminopyrimidine with glyoxal bisulphite.



I

4 : 5-Diaminopyrimidine has been described by Isay[1], but it is more readily available by a slightly modified procedure. 2-Chloro-4-amino-5-nitropyrimidine, m.p. 232° (Isay, *loc. cit.*, gives m.p. 217°), is hydrogenated in methanol over a nickel catalyst to give 2-chloro-4 : 5-diaminopyrimidine. m.p. 232° (found: C, 33·3; H, 3·7; N, 38·7; Cl, 24·6. $C_4H_5N_4Cl$ requires C, 33·2; H, 3·5; N, 38·8; Cl, 24·5 per cent). Catalytic dehalogenation over palladium on charcoal in the presence of barium oxide gives 4 : 5-diaminopyrimidine, m.p. 204°, which forms a crystalline nitrate decomposing without melting above 260° (found: C, 27·8; H, 4·0; N, 40·0. $C_4H_7O_3N_5$ requires C, 27·7; H, 4·1; N, 40·5 per cent). Reaction of the diaminopyrimidine in aqueous solution with glyoxal bisulphite gives pteridine which crystallizes from alcohol in pale yellow plates, m.p. 140° (found: C, 54·3; H, 2·9; N, 42·9. $C_6H_4N_4$ requires C, 54·5; H, 3·05; N, 42·4 per cent).

Pteridine is soluble in water and alcohol and readily sublimes *in vacuo*. Its ultra-violet absorption spectrum in aqueous solution at *p*H 5·8 shows a sharp maximum at 299 mμ with $\varepsilon = 7{,}890$ (Beckmann spectrophotometer), and in neutral or alkaline solution it shows a violet-blue fluorescence in the ultra-

violet. It forms a picrate m.p. 117·5° (found: C, 35·9; H, 2·8; N, 24·6. $C_{12}H_7O_7N_7.2H_2O$ requires C, 36·2; H, 2·8; N, 24·7 per cent), and an oxalate which decomposes without melting above 128° (found: C, 37·5; H, 3·5. $C_8H_6O_4N_4.2H_2O$ requires C, 37·2; H, 3·9 per cent).

W. G. M. JONES

Imperial Chemical Industries, Ltd.,
Research Laboratories,
Hexagon House, Manchester 9.
Aug. 10.

[1] *Ber.*, **39**, 250 (1906).

Chemical Assay of Streptomycin *B* (Mannosido – Streptomycin)

MORRIS[1] has recently described the use of a new reagent (0·2 per cent anthrone, a reduction product of anthroquinone, in 95 per cent sulphuric acid) for quantitative determination of carbohydrates. We have found that it can be used not only for distinguishing streptomycin *B* (a mannoside) from streptomycin *A*, but also for estimating the amount of the former present in a mixture. The glucosamine moiety, present in both molecules, apparently does not react with the reagent. Results obtained are in accord with those calculated from biological and chemical assays, making the accepted assumption about the relative biological activities of the two streptomycins.

It is hoped to publish elsewhere details of the analytical procedure, with some typical results.

W. B. EMERY
A. D. WALKER

Fermentation Division,
Glaxo Laboratories, Ltd.,
Barnard Castle,
Co. Durham.
July 30.

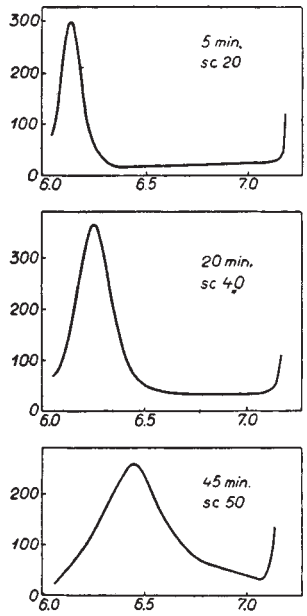
[1] Morris, *Science*, **107**, 254 (1948).

Molecular Weight of Malt-Amylase

IN an earlier investigation[1], the molecular weight of α-amylase from pig's pancreas[2,3] was found to be 45,000, as calculated from the values[4] $s_{20} = 4{\cdot}50\ S$, $D = 8{\cdot}05 \times 10^{-7}$ C.G.S. and $V_{20} = 0{\cdot}70$. At this Institute a new method for the isolation of amylase from malt has been developed[5]. It was shown that by repeated purification of the albumin fraction from malt a preparation was obtained with high α-amylase and β-amylase activity. Therefore it was assumed that the amylase activity of malt is localized in the albumin fraction. By ultracentrifugation of the albumin fraction, only one peak was obtained. It must be stated here that malt-amylase is more polydisperse than α-amylase from pancreas.

A determination of the molecular weight was carried out on an amylase preparation with a saccharification activity[6] of 45,000 and a dextrinizing activity[7] of 57,400, calculated for the dry substance. The determination was carried out in a buffer solution with a concentration of 0·2 *M* sodium chloride, 0·03 *M* primary sodium phosphate and 0·02 *M* secondary sodium phosphate, *p*H 7.

Ultracentrifuge measurement. The accompanying sedimentation diagrams were obtained by centrifuging at 65,000 r.p.m.



Sedimentation curves for malt-amylase. In Table 1 the sedimentation constants for different concentrations are shown

Table 1

Conc. of amylase (per cent)	$s_{20}S$
0·19	4·62
0·28	4·44
0·31	4·96
0·32	4·22
0·41	4·76
0·45	4·12
0·75	4·69
1·00	4·44
1·05	4·39

The sedimentation constant is evidently independent of the concentration. An average value of the sedimentation constant is $s_{20} = 4{\cdot}52\ S$.

Diffusion measurement. The determination of the diffusion constant was carried out in exactly the same way as for α-amylase from pancreas[1]. The resulting values of the diffusion constant are shown in Table 2.

Table 2

Diffusion time (sec.)	34,440	79,020	99,960	129,420	Average value
D_m	6·96	6·70	6·70	6·59	6·74
D_A	6·42	6·20	6·29	6·36	6·32

The agreement between D_m and D_A is good. The average value of $D = 6{\cdot}53 \times 10^{-7}$ C.G.S. is used in the following. The value $V_{20} = 0{\cdot}69$ was kindly determined by Prof. C. Drucker. Using these values, the molecular weight of malt-amylase is 54,000. Evidently this value is of the same order of magnitude as that for α-amylase from pancreas. It is an interesting fact that the amylase activity is associated with molecules with about the same molecular weight in both the plant and animal kingdom.

CARL-ERIK DANIELSSON

Institute of Physical Chemistry,
University of Uppsala. May 24.

[1] Danielsson, C.-E., *Nature*, **160**, 899 (1947).
[2] Meyer, K. H., Fischer, E. H., and Bernfeld, P., *Experientia*, **2**, 362 (1946); *Helv. Chim. Acta*, **30**, 64 (1947).
[3] Fischer, E. H., "La purification et l'isolement de l'α-amylase de pancréase". Thèse No. 1094 (Genève, 1947).
[4] Svedberg, T., and Pedersen, K. O., "The Ultracentrifuge" (Oxford, 1940).
[5] Danielsson, C.-E., and Sandegren, E., *Acta Chem. Scand.*, **1**, 917 (1947).
[6] Windisch, W., and Kolbach, P., *Woch. Brau.*, **42**, 139 (1925).
[7] Ehrnst, L. E., Yakish, G. J., and Olson, W., *Cereal Chem.*, **16**, 724 (1939).