pendicular to the fibre axis, and without postulating what is essentially a 'backbone spacing' of 4·65 A. as a repeat of 5·2 A. along the fibre axis.

We are indebted to Dr. A. Elliott for very helpful discussions, and to Drs. S. G. Waley and J. Watson for help with the synthetic work.

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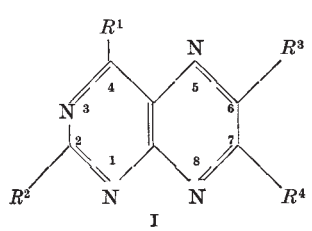
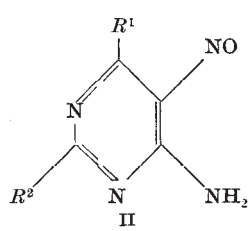
A New Synthesis of Pteridines

There is a growing biological interest in derivatives of pteridine (I: R^1, R^2, R^3, R^4 = H) as a source of antagonists for folic acid (I: R^1 = OH; R^2 = NH_2; R^4 = H; R^3 = .CH_2.NH.C_6H_4.CO.NHCH(COOH).CH_2CH_2COOH-*p*), since this vitamin plays an important part in the growth of certain bacteria and normal and malignant tissue. Thus, Hertz[1] has reported that abnormal growth in the chick genital tract evoked by stilbœstrol was inhibited by methyl folic acid (*I*: R^1 = OH; R^2 = NH_2; R^4 = CH_3; R^3 = .CH_2.NH.C_6H_4.CO.NHCH(COOH).CH_2CH_2-COOH-*p*), which is a powerful antagonist (Martin *et al.*[2]), an effect which was reversed by giving folic acid. Little *et al.*[3] and Woll[4] have reported inhibition of growth of the Rous chicken sarcoma by means of antagonists, and Bass and Freeman[5] found that the inhibition of a lymphoma (lymphoma 6C3HED) in the mouse by mustard gas was to some extent prevented by giving folic acid. Meyer[6] claims a favourable clinical effect in acute leukæmia with methylpteroic acid (I: R^1 = OH; R^2 = NH_2; R^4 = H; R^3 = CH_2.N(CH_3)C_6H_4COOH-*p*). Other antagonists of simple structure are reported by Daniel *et al.*[7].

Hitherto, pteridines have been synthesized essentially by condensation between the appropriate 4:5-diaminopyrimidine and a suitable structure containing adjacent carbon atoms (which are to take up positions 6 and 7 (I)), with substituents R^3 and R^4. Where R^3 and R^4 are different, a mixture of isomers may be formed, leading in some cases to a relatively poor yield of a compound of undetermined structure. The precise positioning of a substituent in the 6 or 7 position is important since (I) (R^1 = OH; R^2 = NH_2; R^4 = OH; R^3 = .CO.NH.C_6H_4.CO.NH.-CH(COOH)CH_2CH_2.COOH-*p*) is a much more potent antagonist than the isomer with R^3 and R^4 substituents interchanged (Woolley and Pringle[8]).

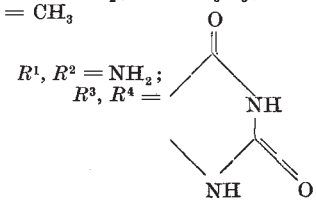
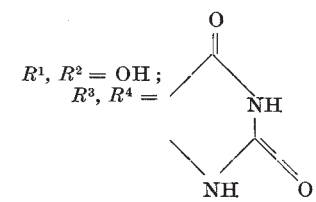


I



II

It therefore appeared desirable to seek a new method of synthesis which would avoid the disadvantage of isomer formation and ambiguity about the structure of the product, and it has now been found that 5-nitroso-4-aminopyrimidines (II) condense readily with ketones (III) and related ring structures, which contain suitably active and adjacent methylene and carbonyl groups, to yield pteridines of type (I). The new route involves two fewer stages than the existing method, when, as is often the case, the diaminopyrimidine and the diketone are made from (II) and (III) respectively. The following compounds of type (I) have been made by condensation in acetic acid solution at 100–160° C.

Substituents	Melting point or absorption spectrum			
R^1, R^2 = NH_2; R^3, R^4 = C_6H_5	282° *			
R^1, R^2 = NH_2; R^3 = C_6H_5; R^4 = CH_3	330°			
	Maxima		Minima	
	λ	log ε	λ	log ε
R^1, R^2 = NH_2; R^3, R^4 = 	264	4·11	294	3·59
	369	4·34		
R^1, R^2 = OH; R^3, R^4 = 	280	4·2	275	4·16
	388	4·3	322	3·4

* Previously made by Mallette *et al.*, *J. Amer. Chem. Soc.*, **69**, 1814 (1947).

This work will be reported elsewhere later in more detail. Where melting points are not applicable, purity has been established by ultra-violet absorption spectra, for which I thank Dr. Tudor S. G. Jones.

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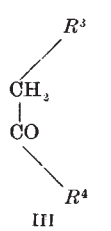
[2] Martin *et al.*, *Arch. Biochem.*, **12**, 318 (1947).
[3] Little *et al.*, *Trans. New York Acad. Sci.*, (ii), **10**, 91 (1948).
[4] Woll, *Trans. New York Acad. Sci.*, (ii), **10**, 83 (1948).
[5] Bass and Freeman, *J. Nat. Cancer Inst.*, **7**, 171 (1946).
[6] Meyer, *Trans. New York Acad. Sci.*, (ii), **10**, 99 (1948).
[7] Daniel *et al.*, *J. Biol. Chem.*, **169**, 689 (1947).
[8] Woolley and Pringle, *J. Biol. Chem.*, **174**, 327 (1948).

Hydroxylamine Assay of Penicillin

In order to obtain a satisfactory chemical method for the determination of penicillin which might be applied throughout the penicillin production process from fermenter broth to final product, the hydroxylamine method of Staab, Ragan and Binkley[1], which was modified by Ford[2] to include the assay of broth, was investigated in these laboratories.



III

The coloured compound produced by the reaction of the hydroxamic acid and the ferric chloride was found to be much more stable in *n*-butanol solution than in aqueous solution, although the very rapid fall in colour intensity, described by Ford,