A New Pteridine Synthesis

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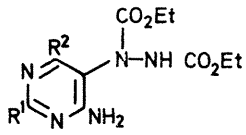
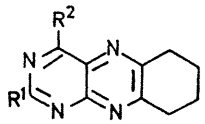
Summary The reaction of 6-amino-5-(1,2-diethoxycarbonylhydrazino)pyrimidines with enamines represents a convenient method for the preparation of pteridines.

THE reaction of 6-amino- and -hydrazino-pyrimidines, unsubstituted at C-5,with diethyl azodicarboxylate gives the corresponding 5-(1,2-diethoxycarbonylhydrazino)-derivatives, which have been used for the preparation of aza-pteridines and purines.[1] We have found that these 6-amino-5-(1,2-diethoxycarbonylhydrazino)pyrimidines are also attractive intermediates for the synthesis of pteridines. Thus, fusion of 5-(1,2-diethoxycarbonylhydrazino)-2,4,6-triaminopyrimidine (I)[1] with an excess of morpholinocyclohexene at 250° for 20 min, followed by dilution with ether, led to 70% of 2,4-diaminocyclohexa[*g*]pteridine (IV)† (m.p. > 350°), whose structure was established by its

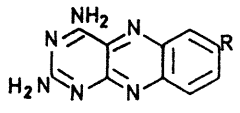
† Satisfactory analytical and spectral data were obtained for all products.



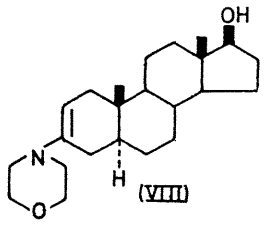
(I) $R^1 = R^2 = NH_2$
(II) $R^1 = NH_2, R^2 = OH$
(III) $R^1 = MeS, R^2 = NH_2$



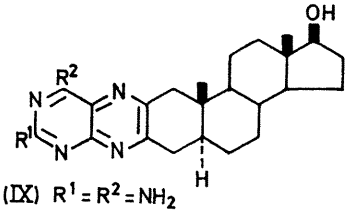
(IV) $R^1 = R^2 = NH_2$
(V) $R^1 = NH_2, R^2 = OH$
(VI) $R^1 = MeS, R^2 = OH$
(VII) $R^1 = MeS$ $R^2 = NH_2$



(XI) R = H
(XII) R = Cl



(VIII)



(IX) $R^1 = R^2 = NH_2$
(X) $R^1 = NH_2, R^2 = OH$

synthesis by the alternative routes[2,3] consisting of treatment of 5-nitroso-2,4,6-triaminopyrimidine[2] or 5-*p*-nitrophenylazo-2,4,6-triaminopyrimidine[3] with morpholinocyclohexene. Similarly, heating 2,6-diamino-5-(1,2-diethoxycarbonylhydrazino)-4-hydroxypyrimidine (II)[1] with morpholinocyclohexene gave 89% of 2-amino-4-hydroxycyclohexa[*g*]pteridine (V) (m.p. > 350°). 4,6-Diamino-5-(1,2-diethoxycarbonylhydrazino)-2-methylthiopyrimidine (III)[1] and morpholinocyclohexene yielded 68% of 4-hydroxy-2-methylthiocyclohexa[*g*]pteridine (VI) (m.p. 248°) and 21% of 4-amino-2-methylthiocyclohexa[*g*]pteridine (VII) (m.p. 285°). This new pteridine synthesis has been extended to the preparation of steroidal pteridines. Heating (I) with 17β-hydroxy-5α-androstan-3-one morpholine enamine (VIII) (m.p. 170°), prepared from androstanolone and morpholine, gave 98% of 2,4-diaminoandrostano-[2,3-*g*]pteridine (IX) (m.p. 331°). Similarly, (II) with (VIII) led to 95% 2-amino-4-hydroxyandrostano[2,3-*g*]pteridine (X) (m.p. > 330°). The structure of these steroidal pteridines was confirmed by the Isay's pteridine synthesis from 17β-hydroxyandrostane-2,3-dione[4] (m.p. 107°) and the corresponding 5,6-diaminopyrimidines.

The 6-amino-5-(1,2-diethoxycarbonylhydrazino)pyrimidines also proved to be useful intermediates for alloxazine (benzopteridine) synthesis. Thus, fusion of (I) with an excess of aniline or *p*-chloroaniline in the presence of a small amount of concentrated hydrochloric acid at 200° for 20 min gave 2,4-diamino-2,4-deoxyalloxazine (XI) (m.p. > 350°) and 7-chloro-2,4-diamino-2,4-deoxyalloxazine (XII) (m.p. > 350°) in 25 and 35 yields, respectively.

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[2] J. Weinstock, R. Y. Dunoff, J. E. Carevic, J. G. Williams, and A. J. Villani, *J. Medicin. Chem.*, 1968, **11**, 618.
[3] E. C. Taylor and F. Yoneda, unpublished result.
[4] G. Ohta, T. Takegoshi, K. Ueno, and M. Shimizu, *Chem. and Pharm. Bull.* (*Japan*), 1965, **13**, 1445.