A Novel Method for the Synthesis of 7-Pteridones

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Summary Reaction of triethyl phosphonoacetate with various 4-amino-5-nitrosopyrimidines gives the corresponding 7-pteridones.

We have recently reported² a new synthesis of 6-substituted pteridines from the reaction of 4-amino-5-nitrosouracil with various amine salts. We now describe a novel method for the synthesis of 7-pteridones by the reaction of triethyl phosphonoacetate³ with various 4-amino-5-nitrosopyrimidines.

Like the carbonyl function, the N=O group of a nitrosocompound possesses some electrophilic character and it is therefore expected to undergo many reactions characteristic of aldehydes and ketones. The reactions of nitrosocompounds with various amines,⁴ with active methylenes,⁵ and with triphenylphosphine alkenes⁶ have been reported. When a 4-amino-5-nitrosopyrimidine reacts with previously base-treated triethyl phosphonoacetate (1), depending on the reaction conditions, 7-oxo-7,8-dihydropteridine or its 8-ethyl substituted derivative is obtained in good yield.[†]

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The reaction probably involves initial attack by the ylide on the nitroso-group to form a betaine intermediate which decomposes spontaneously to the corresponding unsaturated ester and diethyl phosphate. The unsaturated ester may undergo cyclization with the 4-substituted amino-group to give the lactam product[‡] which upon ethylation, at higher temperature, may lead to the corrresponding Nethylated derivative.§

Thus, reaction of 4,6-diamino-5-nitroso-2-phenylpyrimidine (2a) with a freshly prepared excess of (1) at 50° for 10 min gave 4-amino-7-hydroxy-2-phenylpteridine (3a)

[†] In contrast to nitrosoalkanes and nitrosolbenzene,⁶ nitrosopyrimidines show a certain stability in the strongly basic medium even at high temperature.

[‡] According to a recently reported calculation by N. Bodor, M. J. S. Dewar, and A. J. Harget, J. Amer. Chem. Soc., 1970, 92, 2929, the lactam tautomer is favoured over the corresponding hydroxy-tautomer.

[§] The u.v. spectrum of the lactam is expected to be similar to that of its N-alkylated product, but different from that of its O-alkylated derivatives. This similarity was observed in all the lactams, and their corresponding ethylated products, obtained.

(88%) m.p. >340°. Reaction of (1) and (2a) at 150° for



15 min gave (3a) (4%) and (3b) (74%) m.p. 280-283°. Treatment of (3a) in aqueous ethanolic potassium hydroxide solution with ethyl iodide gave (3b).

Similarly (2b) at 60° gives (3c) (82%) m.p. 305-307°.7 At 150°, (2b) gave (3d) (77%) m.p. 240-242°. Likewise, treatment of (2c) and (2d) with (1) at 160° gave (3e) (74%)m.p. 241-243°, and (3f) (71%) m.p. 180-182°, respectively.

Satisfactory analytical figures, molecular weights (massspectrometric) and i.r., n.m.r., and u.v. spectra were obtained for all products.

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