NEW SYNTHESSES OF A PTERIDINE


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The reaction of 6-amino-1,3-dimethyl-5-phenylazouracil (I), 6-amino-1,3-dimethyl-5-nitrosouracil (II), or 6-hydrazino-1,3-dimethyl-5-nitrosouracil (III) with dimethyl acetylenedicarboxylate offers new synthetic route to a pteridine [6,7-bis(methoxycarbonyl)-1,3-dimethylumazine: IV].

The traditional synthetic route to pteridines involves the condensations of (a) 4,5-diaminopyrimidines with 1,2-dicarbonyl compounds (Isay reaction); (b) 4-amino-5-nitrosopyrimidines with active methylene compounds (Timmis reaction); (c) 2-aminopyrazine-3-carboxamides with one-carbon reagents. We now report three new synthetic approaches to pteridine by the reaction of 6-amino-1,3-dimethyl-5-phenylazouracil (I), 6-amino-1,3-dimethyl-5-nitrosouracil (II), or 6-hydrazino-1,3-dimethyl-5-nitrosouracil (III) with dimethyl acetylenedicarboxylate (DMAD).

Method A Refluxing of I (0.003 mol) with DMAD (0.0039 mol) in dimethylformamide (DMF: 3 ml) for 7 hr, followed by concentration of the reaction mixture and addition of chilled methanol caused the separation of 6,7-bis(methoxycarbonyl)-1,3-dimethylumazine (IV: mp 154-156°) in 60% yield. The structure of IV was confirmed by the satisfactory elemental analysis and spectral data. This reaction presumably proceeds through the initial formation of the Michael-type adduct [A], followed by cyclization to [B] and subsequent aromatization by the loss of aniline. To our knowledge, this is the first example in which 4-amino-5-phenylazopyrimidine was used directly in the synthesis of pteridine nucleus (Scheme I).

* Dedicated to Professor Tetsuji Kametani on the occasion of his retirement from Tohoku University.
Method B  We next investigated the utility of the nitroso group which would possess similar reactivity to the phenylazo group as an origin for N-5 in the synthesis of pteridine. Thus, refluxing of II (0.003 mol) with DMAD (0.0039 mol) in DMF (3 ml) for 7 hr, followed by treatment as described in Method A provided IV in 27% yield. This reaction can be explained by assuming the initial formation of the Michael-type adduct [C], followed by cyclization to [D] and subsequent aromatization accompanying dehydration (Scheme II).
Method C  In connection with our recent studies on the synthesis of fused pyrimidines from III, we also examined the reaction of III with DMAD and found that the product is surprisingly the unexpected IV. Thus, refluxing of III (0.002 mol) with DMAD (0.0026 mol) in methanol (3 ml) for 10 hr, followed by cooling caused the separation of IV in 41% yield. This reaction is envisioned as proceeding through the Michael-type adduct [E], followed by cyclization to [F] and subsequent N-N bond fission to [G]. The nucleophilic attack of the amino group at the C-5 of the uracil nucleus in G resulted in the elimination of hyponitrous acid to give [H] and whose aromatization would then yield IV (Scheme III).

Scheme III

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REFERENCES

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