A NEW RING CONTRACTION OF PTERIDINE 5-OXIDES TO PURINES AND A 7-DEAZAPURINE BY THE 1,3-DIPOLAR CYCLOADDITION REACTION

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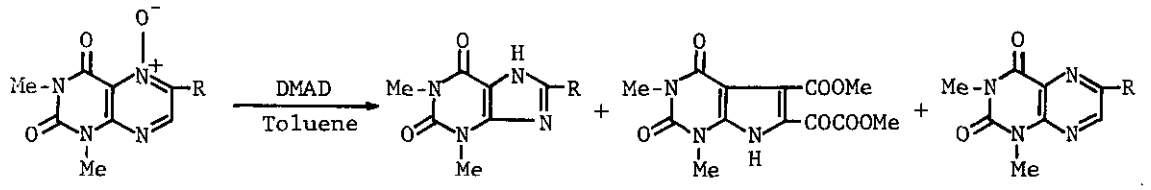
Abstract —— The 1,3-dipolar cycloaddition reaction of pteridine 5-oxides with dimethyl acetylenedicarboxylate resulted in a new ring contraction of the pyrazine moiety to give purines and a 7-deazapurine.

We have previously reported that the 1,3-dipolar cycloaddition reaction of pyrimido[5,4-e]-as-triazine 4-oxides with acetylenic esters causes a ring transformation of the as-triazine moiety to give 9-deazapurines.[1] Subsequently, we have also reported that the reaction of a thiazolo[5,4-d]pyrimidine 3-oxide with dimethyl acetylenedicarboxylate (DMAD) results in the ring transformation of the thiazole moiety to yield a 9-deazapurine via a pyrimido[4,5-b][1,4]thiazine.[2] On the basis of these findings, we have now investigated the ability to undergo 1,3-dipolar cycloaddition reaction of pteridine 5-oxides, and have found that the pyrazine moiety undergoes a new ring contraction to furnish purines and a 7-deazapurine. Heating of the pteridine 5-oxide (Ia)[3] (0.001 mol) with DMAD (0.003 mol) in toluene (10 ml) at 120°C for 60 h resulted in the formation of the purine (IIa[4]: mp >300°C; 15%) and the 7-deazapurine (III: mp 241°C; 10%) along with the deoxygenated pteridine (IVa[5]: mp 260°C; 37%). The reaction was equally applicable to



Ia-c IIa-c III IVa-c

a: R=C_6H_5; b: R=4-Cl-C_6H_4; c: R=4-MeO-C_6H_4

other pteridine 5-oxides (Ib-c)[6] to give (IIb-c),[4] III, and (IVb-c)[5] in similar ratio of yields. Generally, IIa-c were readily precipitated out from the reaction solution, while III and IVa-c were isolated by the fractional crystallization of the filtrate from EtOH.

The characterization of II and IV was based on the spectral comparison with those of authentic samples,[4,5] while that of III was derived from the following data. ^{1}H NMR (DMSO-d_6)δ: 3.18 (N-Me), 3.48 (N-Me), 3.78 (O-Me), 3.81 (O-Me), 13.07 (NH, D_2O exchangeable); IR (KBr) cm^{-1}: 1750, 1710, 1650sh, 1640 (CO), 3230 (NH); UV λmax (EtOH) nm (log ε): 254 (3.42), 360 (3.63); MS m/z: 323 (M^+), 264 (M^+-59), 232 (M^+-91). In particular, the mass spectrum unequivocally suggested that the methoxycarbonyl and methoxalyl groups are attached at the positions 5 and 6, respectively,[7] since the isomeric 9-deazapurine exhibits similar fragment pattern.[8] Although the definite mechanism for the ring contraction is not clear at present, it is apparent that the reaction would involve 1,3-dipolar cycloaddition process since the treatment of IVa-c with DMAD under the same conditions resulted in the quantitative recovery of the starting materials. To our knowledge, the chemical conversion of pteridines to purines has two precedents,[9] however, the ring contraction of pteridines to 7-deazapurines has not hitherto been reported.

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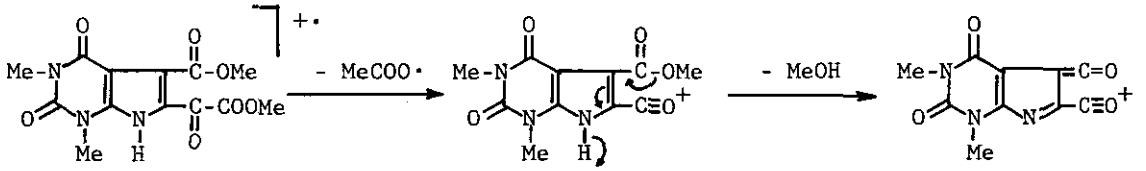
REFERENCES AND NOTES

1. K. Senga, M. Ichiba, and S. Nishigaki, J. Org. Chem., 44, 3830 (1979).
2. K. Senga, M. Ichiba, H. Kanazawa, and S. Nishigaki, J. Chem. Soc., Chem. Commun., 1981, 278.
3. W. Pfleiderer and W. Hutzenlaub, Chem. Ber., 106, 3149 (1973).
4. K. Senga, K. Shimizu, and S. Nishigaki, Chem. Pharm. Bull., 25, 495 (1977).
5. K. Senga, Y. Kanamori, and S. Nishigaki, Heterocycles, 6, 693 (1977).
6. These compounds were prepared according to the reported procedure[3]: Ib, mp 243-245°C; Ic, mp 263-265°C.

7. The principal fragment path of III is as follows:



m/z 323 (M^+) m/z 264 (M^+-59) m/z 232 (M^+-91)

8. 6-Methoxalyl-7-methoxycarbonyl-1,3-dimethylpyrrolo[3,2-d]pyrimidine-2,4(1H,3H)-dione[1]: MS m/z 323 (M^+), 264 (M^+-59), 232 (M^+-91).

9. W. Hutzenlaub, H. Yamamoto, G.B. Barlin, and W. Pfleiderer, Chem. Ber., 106, 3203 (1973); A. Nagel and H.C. van der Plas, Chem. Pharm. Bull., 23, 2678 (1975).

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