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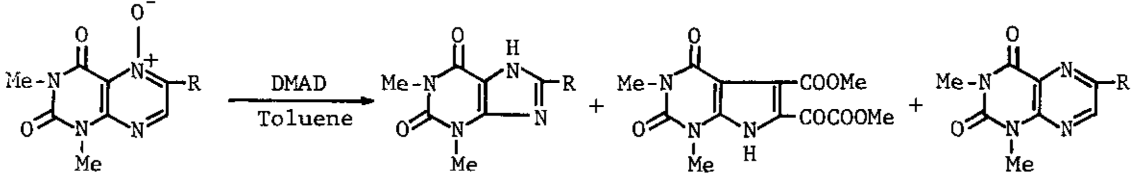
Abstract —— The 1,3-dipolar cycloaddition reaction of pteridine 5-oxides with dimethyl acetylenedicarboxylate resulted in a new ring contraction of the pyrazine moiety to give purines and a 7-deazapurine.

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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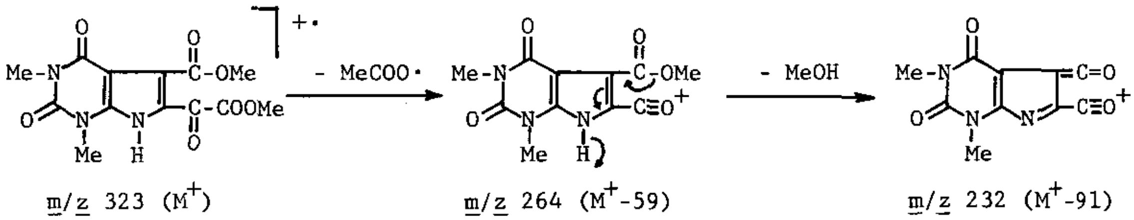
6. These compounds were prepared according to the reported procedure[3]: Ib, mp 243-245°C; Ic, mp 263-265°C.

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



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).

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