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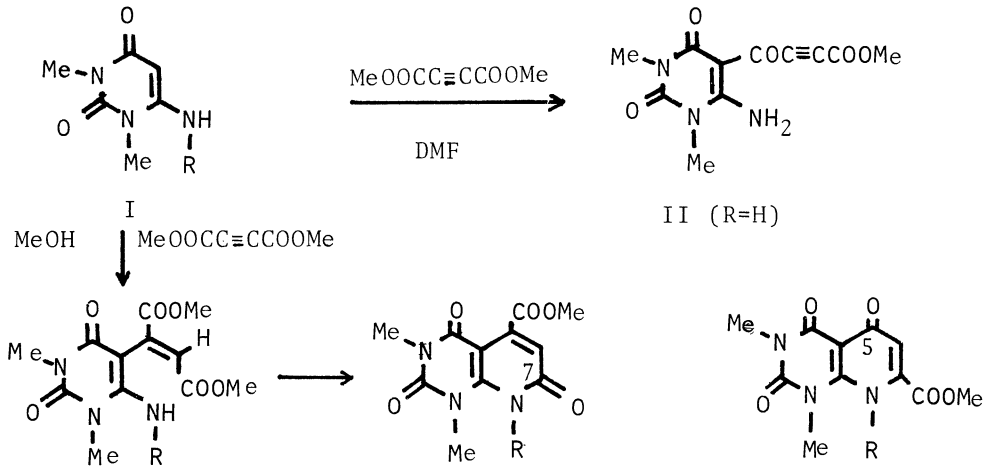
A Novel Synthesis of 5-Oxo- and 7-Oxo-pyrido[2,3-d]pyrimidines[1)]

Haruo OGURA and Masakazu SAKAGUCHI
School of Pharmaceutical Sciences, Kitasato University
Shirogane, Minato-ku, Tokyo 108

5-Oxo- (VI) and 7-oxo-pyrido[2,3-d]pyrimidines (IV) were synthesized from 6-amino-1,3-dimethyluracil derivatives (I) with dimethyl acetylenedicarboxylate or diketene. Analogously, 5-oxothiopyrano[2,3-d]pyrimidine (VIII) was obtained from VII and diketene.

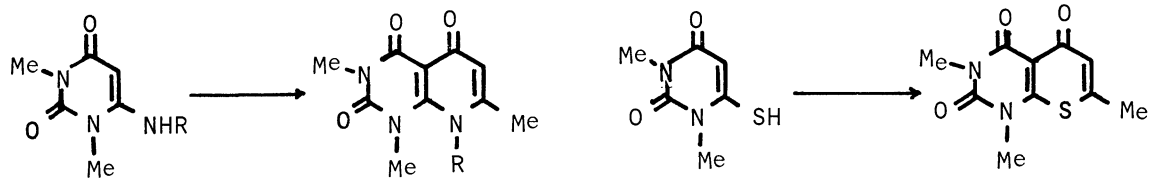
Recently, Shim et al.[2)] reported that the reaction of various N-alkyl-6-aminouracils (I) with dimethyl acetylenedicarboxylate in dimethylformamide gave 6-amino-5-(methoxycarbonyl-2-propinoyl)uracils (II) and they could not obtain cyclized pyrido[2,3-d]pyrimidines. In this communication we describe the reaction of 6-amino-1,3-dimethyluracil and its 6-substituted amino derivatives (Ia,b,c,d) with dimethyl acetylenedicarboxylate in methanol to obtain cyclized compounds.



a: R=H b: R=Me c: R=C_6H_5 d: R=$CH_2C_6H_5$

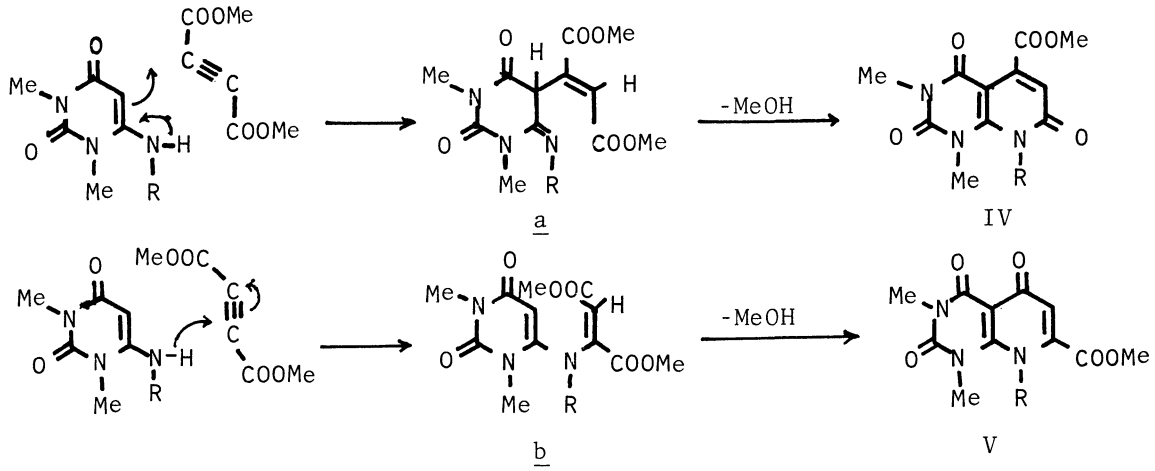
Treatment of Ia with dimethyl acetylenedicarboxylate in MeOH at room temperature gave an open-chain intermediate (IIIa) in 24% yield, cyclization of which by heating in dimethylformamide produced 1,3-dimethyl-5-methoxycarbonyl-2,4,7-trioxopyrido[2,3-d]pyrimidine (IVa). Heating of Ia with dimethyl acetylenedicarboxylate under reflux in MeOH gave the cyclized 7-oxo compound (IVa) in 71%

yield, and a small amount of 5-oxo compound (Va). 5-Oxo compounds (Va,b,c) show a typical band in nmr spectrum at 6-H, δ 7.13, 7.08, and 7.42 ppm, respectively. This value differs from that of 7-oxo compounds (IVa,b,c) which appear at δ 6.42, 6.65, and 6.34 ppm, respectively.



I VI VII VIII

On the other hand, reaction of Ia,b,c,d with diketene gave single compounds, 5-oxopyrido[2,3-d]pyrimidines (VIa,b,c,d), and 7-oxo compound was not obtained. Compound VIa was also obtained from Ia and ethyl acetoacetate. The reaction of 1,3-dimethyl-6-mercaptouracil (VII) with diketene gave 5-oxothiopyrano[2,3-d]-pyrimidine (VIII). From nmr spectra of these compounds (VIa,b,c,d, and VIII), 6-H appeared at δ 6.46, 6.97, 6.29, 6.50, and 6.76 ppm and this value coincides with that of 5-oxo compound.



a IV

b V

These reaction mechainisms may be represented by the sequence shown in above. An intermolecular proton transfer from amino group may take two routes, and this produced the intermediates a and b with an olefinic group attached to the C-1 position (a) or to the amino group (b). These intermediates underwent cyclization to 7-oxo or 5-oxo compound (IV or V). It is interesting that this result is different from the reaction of 2-amino-benzothiazole, benzoxazole, and benzimidazole with dimethyl acetylenedicarboxylate.[3)]

References

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2) J. L. Shim, R. Niess, and A. D. Broom, J. Org. Chem., 37, 578 (1972).
3) H. Ogura, M. Kawano, K. Kikuchi, and T. Itoh, Abstr. Papers, 3rd Int. Congr. Heterocyclic Chem., 506 (1971).

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