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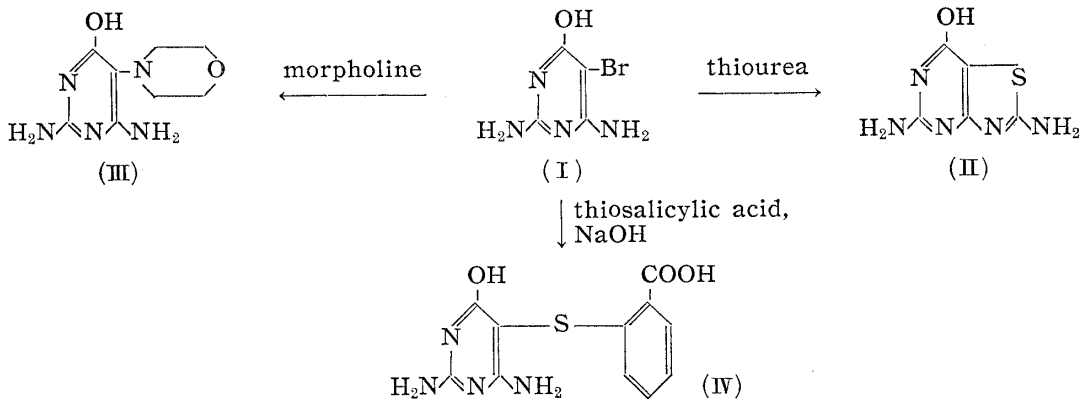
A New Synthesis of 2,5-Diamino-7-hydroxythiazolo[4,5-*d*]pyrimidine and a New Aspect on the Reactivity of 5-Bromopyrimidines

Only one method has so far been published on the synthesis of thiazolo[4,5-*d*]-pyrimidine series.[1] In the course of the investigation of nucleophilic displacement of 5-bromopyrimidines, the writer found a new reaction to yield 2,5-diamino-7-hydroxy-thiazolo[4,5-*d*]pyrimidine (II) in a good yield.



2,6-Diamino-4-hydroxy-5-bromopyrimidine (I), m.p. 244° (decomp.), was added to a solution of thiourea in ethanol, and after refluxing for half an hour the solid was separated and treated with alkali. To this solution, diluted acetic acid was gradually added and light yellow crystals precipitated, m.p. >300°, U.V. λ_{max} (in 0.1*N* NaOH) 271, 345 mμ (log ε 3.94, 3.61) (*Anal.* Calcd. for $C_5H_5ON_5S \cdot 2H_2O$: C, 27.40; H, 4.15; N, 31.95. Found: C, 27.20; H, 4.21; N, 31.59). Yield, 91.3%.

This compound was confirmed to be 2,5-diamino-7-hydroxythiazolo[4,5-*d*]pyrimidine (II) through the comparison of I.R. spectrum and analytical data with those of the authentic sample prepared by the method of Maggiolo, *et al.*[1]

It has been generally concluded in pyrimidine chemisry that halogens at C-5 of pyrimidines are quite stable and difficult to displace by nucleophilic reagents[2,3] except in a few examples.[4] Above-mentioned 2,6-diamino-4-hydroxy-5-bromopyrimidine (I) was reported to be entirely inactive for popular nucleophilic reagents,[3] but from the experiments recently carried out by the writer it became clear that this 5-bromopyrimidine (I) reacts smoothly with morpholine or thiosalicylic acid to give 2,6-diamino-4-hydroxy-5-morpholinopyrimidine (III), m.p. >300°, U.V. λ_{max} (in 0.1*N* NaOH) 269 mμ (log ε 4.00), I.R. λ_{max} 1116 cm^{-1} (C-O-C) (*Anal.* Calcd. for $C_8H_{13}O_2N_5 \cdot H_2O$: C, 42.00; H, 6.62; N, 30.59. Found : C, 42.45; H, 6.96; N, 30.83), or 2,6-diamino-4-hydroxy-5-(2-carboxy-phenylthio)pyrimidine (IV), m.p. >300°, U.V. λ_{max} (in 0.1*N* NaOH) 262 mμ (log ε 3.24)

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(*Anal.* Calcd. for $C_{11}H_{10}O_3N_4S$: C, 47.50; H, 3.59; N, 20.12; S, 11.52. Found : C, 47.54; H, 3.68; N, 19.98; S, 11.10), respectively.

These results suggest the possibility of the use of 5-bromopyrimidines for the syntheses of new derivatives of amino- or hydroxy-pyrimidines. The details of these reactions and further examples in other pyrimidines will be published later.

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Synthesis of the Ethynylated Steroids
(Studies on Acetylenic Compounds)

Recently, several works on the alkylated steroids bearing methyl group at the 1-,[1] 2-,[2] 4-,[3] 6-,[4] 7-,[5] 11-,[6] 14-,[7] or 16-[8] position have been reported. Some of these alkylated steroids, especially, 6- and 16-methyl compounds are significant in enhancing hormonal activity as compared with the mother steroids.

Considering that 17-ethynylated steroid is more important in variety of its actions, the following steroids ethynylated at 6-, 7-, or 16-position have been prepared from the corresponding oxosteroids.

Addition of 16-oxo-5-androstene-3β,17α-diol 3-methyl ether[9] to lithium acetylide (LiC≡CH) in liquid ammonia and subsequent stirring at -40° for 5 hr. yielded 16α-ethynyl-5-androstene-3β,16β,17α-triol 3-methyl ether (I) of m.p. 191~194°, $[\alpha]_D^{22}$ −66°(in $CHCl_3$), which was converted into 16,17-acetonide by the action of acetone and hydrochloric acid at room temperature.

Analogously 7ξ-ethynyl-5-cholestene-3β,7ξ-diol 3-acetate (III) of m.p. 152.5~154°, $[\alpha]_D^{25}$ −104.3°(in $CHCl_3$), was prepared from 7-oxocholesterol[10] by the action of lithium acetylide and subsequent acetylation.

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