NEW SYNTHESIS OF FUSED PYRIMIDINES BY THE USE OF 6-METHYLURACIL DERIVATIVES

Shigeo Senda, Kosaku Hirota, Tatsuji Asao, and Yoshihiro Yamada
Gifu College of Pharmacy, Mitahora, Gifu 502, Japan

Reaction of 5-substituted 6-methyluracils with nucleophiles and the synthetic utility for the fused pyrimidines were investigated.

When 5-nitro-1,3,6-trimethyluracil (1) was treated with potassium cyanide, 6-cyano-5-nitro-1,3,6-trimethyl-5,6-dihydrouracil (4) was obtained as a diastereoisomeric mixture. Hydrazinolysis of (1) afforded 5-methyl-4-nitropyrazol-3-ones. On reaction of 6-bromomethyl-1,3-dimethyl-5-nitrouracil (2) with potassium cyanide, 6-cyano-1,3-dimethyl-5-nitrocyclothymine was obtained. Treatment of (2) with excess methylhydrazine afforded 1,3-dimethyluracil-6-carboxaldehyde methylhydrazone. We suggested that the mechanism for these reactions of (1) and (2) with nucleophiles such as potassium cyanide and hydrazines involves the nucleophilic addition to the C-6 position as a key step.

On the other hand, by refluxing (2) with various primary amines in ethanol effeciently ring closure occurred to give 2-substituted pyrazolo[4,3-d]pyrimidin-1-oxides. In the case of 6-bromomethyl-1,3-dimethyl-5-formyluracil (3), an analogous reaction with primary amines led to the formation of 6-substituted pyrrolo[3,4-d]-pyrimidines in good yields. Treatment of (3) with hydrazines gave 7-substituted pyrimido[4,5-d]pyrimidines.