Synthesis of Phidolopin, 7-(4-Hydroxy-3-nitrobenzyl)-1, 3-dimethyl-xanthine from the Briozoan Phidolopora Pacifica. Kosaku Hirota*, Keiko Kubo, Yukio Kitade, Yoshifumi Maki

Phidolopin, 7-(4-hydroxy-3-nitrobenzyl)-1,3-dimethylxanthine recently isolated from a marine organism, shows antifungal and antialgal activities. A total synthesis of phidolopin was accomplished. Thus, 2-nitro-\( p \)- cresol was treated with \( \text{MeOCH}_2\text{Cl} \) to afford a \( O \)-protected cresol (1). Bromination of (1) with NBS in the presence of \( a,a' \)-azobis-\( \text{iso} \)-butyronitrile gave the corresponding benzyl bromide (2). Theophylline was alkylated with the benzyl bromide (2) followed by the deprotection of a methoxy-methyl group under acidic conditions resulted in the formation of phidolopin, which was identical with natural phidolopin. Its 9-regioisomer was also synthesized.

Pyrimidines. 52. Synthesis of Pyrido (2, 3-\( d \)) pyrimidine-2, 4-diones and Pyrido (2, 3-\( d \): 6, 5-\( d \)) dipyrimidine-2, 4, 6, 8-tetrones. Kosaku Hirota*, Yukio Kitade, Shigeo Senda

Reactivities of 5-dimethylaminomethylene-6-imino-1,3-dimethyluracil hydrochloride (1) toward a variety of active methylene compounds were investigated. Treatment of (1) with malononitril, cyanoacetamide, ethyl cyanoacetate, acetylacetone, and diethyl malonate in the presence of triethylamine gave the corresponding pyrido(2,3-\( d \)) pyrimidines. Reaction of (1) with barbituric acids and 2-thiobarbituric acid resulted in the formation of pyrido(2,3-\( d:6,5- d \)) dipyrimidine-2,4,6,8-tetronel derivatives, which were also prepared by the reaction of 6-amino-1,3-dimethyluracil with barbituric acids.


Reaction of 5-bromo-6-methyluracil derivatives possessing a phenyl or \( p \)-substituted phenyl group at the 1-position of the uracil ring, with methylamine and hydrazine hydrate causes novel ring transformations to give 1-aryldyhdantoins and 4-ureidopyrazol-3-ones, respectively. The latter conversion into the pyrazoline is a double transformation via a hydantoin intermediate. Reaction mechanisms for the ring transformations are discussed.