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NOVEL RING-TRANSFORMATION REACTIONS OF 5-FORMYLURACIL DERIVATIVES

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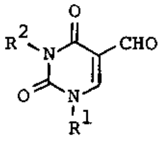
Our recent works have demonstrated that reactions of uracils with 1,3-ambident nucleophiles cause facile ring-transformations to pyrimidines or pyridines. These ring-transformations are formally regarded as the displacement of the urea moiety (N_1-C_2-N_3) of the uracil ring by the N-C-N or C-C-N chain of the employed nucleophile.

The present paper describes further novel ring-transformations by the reaction of 5-formyluracil derivatives (1) with ambident nucleophiles possessing the C-C-C, C-C-N, or N-N chain.

5-Formyl-1,3-dimethyluracil (1b) was allowed to react with acetylacetone in ethanolic sodium ethoxide to give ethyl 3-acetyl-4-hydroxybenzoate (2a). Similar treatment of (1b) with α-substituted acetones (C-C-C type nucleophile) such as acetoacetamide, ethyl acetoacetate, and phenylacetone afforded the corresponding 4-hydroxybenzoates (2b-d). On the other hand, treatment of (1b) with cyanoacetamide (C-C-N type nucleophile) gave ethyl 5-cyano-6-hydroxynicotinate.

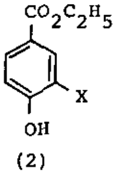
Cheng et al.* reported the reaction of 5-formyluracil (1a) with hydrazine hydrate (N-N type nucleophile) in the presence of acetic acid gave 4-ureidomethylene-1H-5-pyrazolone (4). Our structure proof, however, clearly showed that the Cheng's compound (4) should be revised to 4-ureidocarbonylpyrazole (3a). Thus, the reaction of (1) with hydrazine derivatives (NH_2NHR; R=H or CH_3) under the Cheng's conditions provided a convenient preparative methods of various ureidocarbonylpyrazoles (3).

The reaction sequence for the present ring-transformations is accounted for by involvement of the initial condensation of the aldehyde group in (1) with ambident nucleophiles followed by nucleophilic attack at position 6 of the uracil ring.



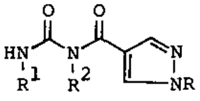
(1)

a; $R^1 = R^2 = H$
b; $R^1 = R^2 = CH_3$
c; $R^1 = CH_3, R^2 = C_2H_5$



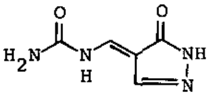
(2)

a; X= $COCH_3$
b; X= $CONH_2$
c; X= $CO_2C_2H_5$
d; X= C_6H_5



(3)

a; $R^1 = R^2 = R = H$
b; $R^1 = R^2 = CH_3$, R= H
c; $R^1 = CH_3$, $R^2 = C_2H_5$, R= H
d; $R^1 = R^2 = R = CH_3$
e; $R^1 = CH_3$, $R^2 = C_2H_5$, R= CH_3



(4)

* C.C.Cheng et al., J.Org.Chem.,**33**,892(1968).