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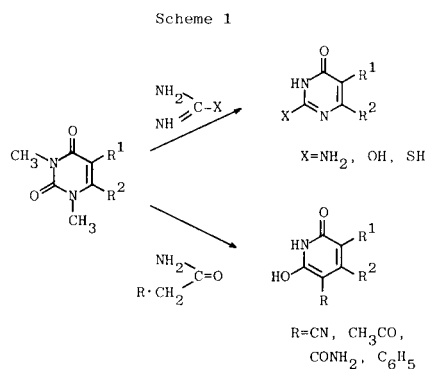
Reaction of 5-formyl-1,3-dimethyluracil with some active methylene compounds in the presence of base causes novel ring transformations to give the *p*-hydroxybenzoates and the nicotinate.

J. Heterocyclic Chem., 17, 413 (1980).

Sir:

It is well known that uracils undergo ring transformation to pyrazolones and isoxazolones by reaction with hydrazine and hydroxylamine, respectively (1). These reactions have been employed extensively for the chemical modification of nucleic acids (2). Certain uracil derivatives also react with other nucleophiles, such as amines and hydroxide anion for conversion into imidazole, pyridine, and 1,3,5-triazepine ring systems (3).

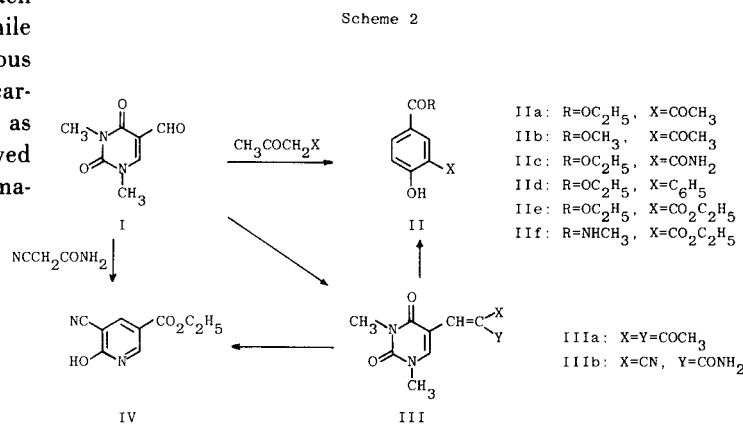
Recently, we have reported (4) that reaction of uracils with 1,3-ambident nucleophiles causes the ring transformation to pyrimidines or pyridines. These reactions involve the direct displacement of N₁-C₂-N₃ portion of the uracil by N-C-N or C-C-N fragment of the employed nucleophile (Scheme 1). In this connection, the reaction of various uracil derivatives with C-C type of nucleophiles was carried out. When 5-formyl-1,3-dimethyluracil (I) was used as the uracil and various active methylene compounds served as the nucleophile, we have found a novel ring transformation of the uracil into the benzene ring system.



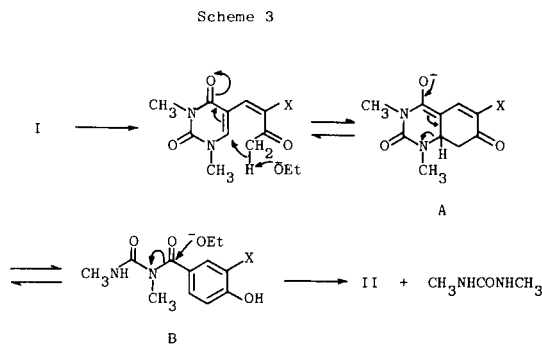
Thus, compound I was refluxed with acetylacetone in ethanolic sodium ethoxide (5) for 2 hours, followed by neutralization of the reaction mixture with concentrated hydrochloric acid, to give the known (6,7) ethyl 3-acetyl-4-hydroxybenzoate (IIa) (55%) and 1,3-dimethylurea. The use of sodium methoxide instead of sodium ethoxide resulted in the formation of the methyl benzoate (IIb) (8). Similar treatment of I with acetoacetamide and phenylacetone afforded the corresponding benzoates IIc (9) and II d (10) in 61% and 18% yields, respectively. When ethyl acetoacetate was used as a nucleophile under the same

conditions, the ring transformation did not occur cleanly. However, the reaction with this reagent in the presence of potassium hydroxide proceeded smoothly to yield two transformation products IIe (11) and II f in 37% and 12% yields, respectively.

The benzoate IIa was also obtained from the intermediate IIIa which was synthesized by condensation of I and acetylacetone in the presence of piperidine-acetic acid with separating water as the benzene azeotrope. The condensate IIIa was refluxed in ethanolic sodium ethoxide affording the conversion product IIa in 71% yield.



On the basis of the isolation of 1,3-dimethylurea from the reaction mixture and the fact that the Knoevenagel product IIIa is converted to the benzoate IIa under ring transformation conditions, the mechanism shown in Scheme 3 is suggested as a plausible route. After forma-



tion of the condensation product III, abstraction of a proton from the active methyl group of III in basic medium would be accompanied by intramolecular cyclization to afford the bicyclic intermediate *A*. Subsequent scission of the N₁-C₆ bond to an ureido benzoate *B* would be followed by attack of an ethoxide anion on the carbonyl group of *B* giving the ethyl benzoate II and 1,3-dimethylurea.

When cyanoacetamide, a C-C-N type of nucleophile, was employed as the active methylene compound in the above reaction, ethyl 5-cyano-6-hydroxynicotinate (IV) was obtained in 46% yield. Compound IV was also prepared from the intermediate IIIb (12) by refluxing with sodium ethoxide in 77% yield. This reaction would proceed by a similar reaction mechanism for the transformation of I to II.

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(5) The molar ratio of the uracil I, nucleophile and sodium ethoxide is 1:4:3.

(6) All compounds reported herein gave satisfactory elemental analyses and spectral data.

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(12) Compound IIIb was prepared from I and cyanoacetamide in a similar manner for the preparation of IIIa, but its geometry has not been determined.