REACTION OF 6-AMINO-1,3-DIMETHYLURACILS WITH ETHOXYMETHYLENEMALONONITRILE

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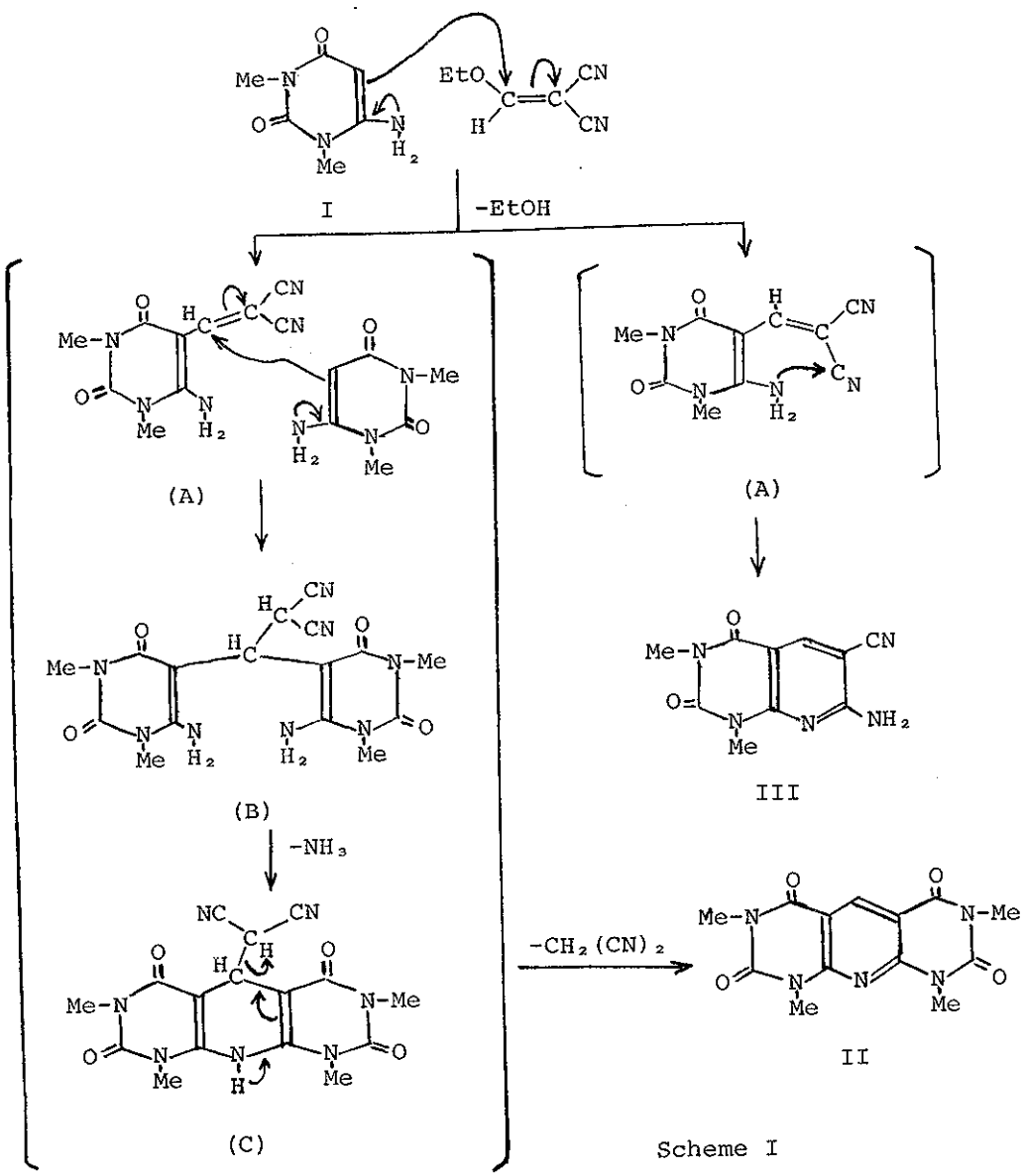
Treatment of 6-amino-1,3-dimethyluracil with ethoxymethylenemalononitrile (EMMN) afforded 1,3,7,9-tetramethylpyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8-(1H,3H,7H,9H)-tetrone and 7-amino-6-cyano-1,3-dimethylpyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione. On the other hand, reaction of 6-hydrazino-1,3-dimethyluracil with EMMN gave 6-(3-amino-4-cyanopyrazol-2-yl)-1,3-dimethyluracil.

The synthesis of fused heterocyclic compounds by the reaction of ethoxymethylenemalononitrile (EMMN) with various types of amines is known.[1-3]

We have recently described new synthetic approaches to 4-oxoquinazolines and 3,3'-biquinazoline-4,4'-diones by cyclization of o-aminobenzamide derivatives using EMMN as a one-carbon reagent.[4] In connection with these finding, we investigated the reaction of 6-amino-1,3-dimethyluracils with this reagent.

Heating of 6-amino-1,3-dimethyluracil (I) (0.032 mol) with EMMN (0.016 mol) in acetic acid (40 ml) under reflux for 6 hr gave 1,3,7,9-tetramethylpyrido[2,3-d:6,5-d']dipyrimidine-2,4,6,8-(1H,3H,7H,9H)-tetrone (II) (19%)[5] and 7-amino-1,3-dimethyl-



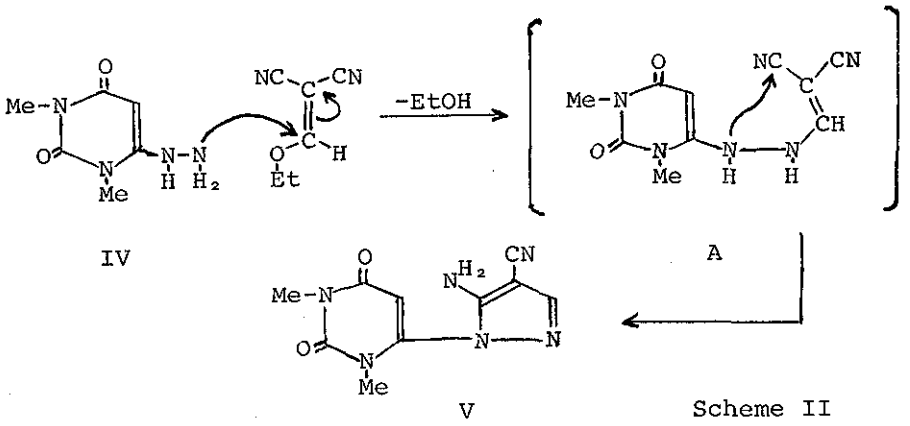
Scheme I

pyrido[2,3-d]pyrimidine-2,4(1H,3H)-dione (III) (22%)[6], which were isolated[7] by concentration of the reaction mixture and addition of water. The structures of (II) and (III) were confirmed by the satisfactory spectral data and elemental analyses.[8]

As depicted in the scheme I, this reaction can be rationalized by the initial formation of intermediary 6-amino-5-(2,2-dicyanovinyl)-1,3-dimethyluracil (A) by the electrophilic attack of EMMN on the electron-rich 5-position of (I). This intermediate could then react with another molecule of (I) to give 2,2-dicyano-1,1-bis(6-amino-1,3-dimethyluracil-5-yl)ethane intermediate (B). Subsequent intramolecular cyclization accompanying elimination of ammonia to intermediate (C), followed by loss of malononitrile would yield (II).

On the other hand, the formation of (III) can be explained by usual intramolecular cyclization of (A).

Next, heating of 6-hydrazino-1,3-dimethyluracil (IV) with an equivalent amount of EMMN in ethanol under reflux for 6 hr afforded 6-(3-amino-4-cyanopyrazol-2-yl)-1,3-dimethyluracil (V), mp 282-283° (DMF-H_2O), in 69% yield. The spectral data [IR (KBr) cm^{-1} 3200, 3220, 3320 and 3380 (N-H), 2220 (C≡N), 1650sh, 1655sh and 1720 (C=O), 1630 (C=N), NMR δ (DMSO-d_6) 2.92 (3H, s, N-Me), 3.19 (3H, s, N-Me), 5.92 (1H, s, C^5-H), 7.22 (2H, s, NH_2), 7.86 (1H, s, C^5-H of pyrazole), Mass (m/e) 246 (M^+)] were in good agreement with the assigned structure. This reaction probably proceeds through the initial formation of intermediate 6-[2-(2,2-dicyanovinyl)hydrazino)-1,3-dimethyluracil (A), followed by intramolecular cyclization (Scheme II).



Scheme II

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7 Precipitated crystals were filtered by suction, and recrystallized from DMF-EtOH to give II. The mother liquid was concentrated in vacuo and the precipitated crystals were filtered off. Recrystallization from DMF-H_2O gave III.

8 The compounds (II) and (III) were identical in thier IR spectra with the authentic samples prepared by the reported procedure.[5,6]

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