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THE NEW SYNTHESIS OF URACIL AND 1,3-DIMETHYLURACIL

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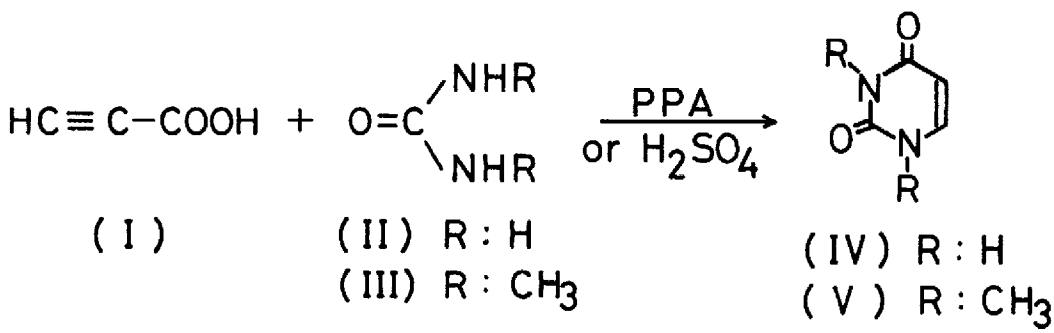
The syntheses of uracil from malic acid and urea with sulfuric acid (yield, 50-55%)[1] and with polyphosphoric acid (PPA) (yield, 20%)[2] were reported. The synthesis of uracil from maleic aicd and urea with PPA was also reported (yield, 20%)[3].

In this paper, new syntheses of uracil (IV) and 1,3-dimethyluracil (V) from propiolic acid (I) and urea (II) [or N,N'-dimethylurea (III)] with PPA are described.



(I) (II) R : H (III) R : CH_3 (IV) R : H (V) R : CH_3

Uracil (IV): A mixture of (I), (175.1 mg, 2.5 mmol) and (II), (150.2 mg, 2.5 mmol) was heated in PPA (4.0 g) at 85°C with occasional stirring. After 4 hr of heating, 8 ml of water was added to the reaction mixture under cooling. The precipitated white crystals (IV) were collected by filtration [171 mg, 61% yield, Found: C, 42.77; H, 3.76; N, 25.09%. Calcd. for $C_4H_4N_2O_2$: C, 42.85; H, 3.60; N, 25.00%. λ_{max}= 259.5 nm (log ε =4.94) at pH 2, 259.5 nm (4.93) at pH 5.5,

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284 nm (4.81) at pH 12]. The filtrate was diluted to 25 ml. A portion of the solution (10 μl) was spotted on a filter paper (Toyo-roshi, No.527) and was developed paper chromatographically using a solvent composed of t-butylalcohol/methylethylketone/water/concentrated aqueous ammonia (4:3:2:1). The (IV) was detected as a dark spot by irradiation of ultraviolet light (R_f:0.40). The spot of (IV) was cut off and was extracted with 20 ml of 0.01 N HCl. The absorbance of the extract was determined at 259.5 nm and the yield of (IV) in the filtrate was determined as 14 %. The total yield of (IV) was 75 %.

On the other hand, the reaction of (I), (2.5 mmol) and (II), (2.5 mmol) in sulfuric acid (5 ml) at 100-105°C for 7 hr gave (IV) in a 59 % yield. However, no (IV) was found in the reaction mixture of (I) and (II) with orthophosphoric acid.

1,3-Dimethyluracil (V): A mixture of (I), (2.5 mmol) and (III), (2.5 mmol) was heated with PPA (4.0 g) at 85°C for 4 hr, and then 8 ml of cold water was added to the reaction mixture. The (V) was separated by paper chromatography (R_f:0.90) and the yield was determined by spectrophotometry as in the case of (IV) (71 %). In order to isolate (V), 10 ml of water was added to the reaction mixture started with (I), (3.0 mmol) and (II), (3.0 mmol) with PPA (10 g). The solution was placed on the Dowex 50 column (H type, 50~100 mesh, 2.5 x 28 cm) and was eluted with water. First, the PPA was eluted and then fractions containing (V) were collected. The solution was treated with activated charcoal, and was evaporated to dryness under reduced pressure. The crude yellow crystals (V), (350 mg) were recrystallized from ethanol-ether to white crystals [m.p. 120.5-121.5°C, Found: C, 51.53; H, 5.77; N, 20.23%. Calcd. for $C_6H_8N_2O_2$: C, 51.41; H, 5.76; N, 19.99%. λ_{max}= 266 nm (log ε = 3.92) at pH 2 ~ 11].

References

1. D. Davidson and O. Baudisch, J. Amer. Chem. Soc., 48, 2379 (1926).
2. S. W. Fox and K. Harada, Science, 133, 1923 (1961).
3. K. Takemoto and Y. Yamamoto, Synthesis, 1971, 154.