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SYNTHESIS OF PYRIMIDO[4,5-d]PYRIMIDINES

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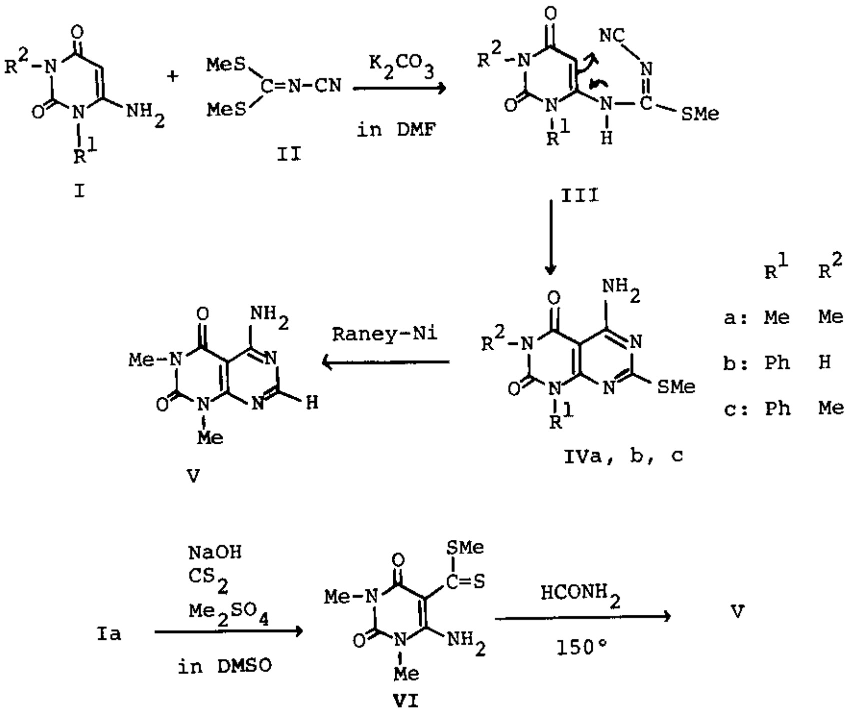
Abstract — 5-Aminopyrimido[4,5-d]pyrimidine-2,4(1H,3H)-diones were synthesized by the reaction of 6-aminouracil with dimethyl cyanoimidodithiocarbonate in the presence of potassium carbonate in dimethylformamide in good yields.

Many pyrimidopyrimidines were initially synthesized for a study of biological activity or physical properties because of close structural relationship of these systems to the quinazolines$^{1)}$. We now wish to report synthsis of 5-aminopyrimido[4,5-d]pyrimidine-2,4(1H,3H)-diones by the reaction of 1,3-dialkyl-6-aminouracils with dimethyl cyanoimidodithiocarbonate (II)^{2}.
Condensation of 6-amino-1,3-dimethyluracil (Ia) with II in the presence of potassium carbonate in dimethylformamide on a steam bath for 4-5 hr gave a fused pyrimidine, 5-amino-1,3-dimethyl-7-methylthiopyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione (IVa), colorless needles, mp 236°, in 72% yield. Raney-nickel desulfurization of IVa on a steam bath in ethanol afforded 5-amino-1,3-dimethylpyrido-[4,5-d]pyrimidine-2,4(1H,3H)-dione (V), colorless needles, mp 268°, which was also synthesized by treatment of methyl 6-amino-1,3-dimethyluracil-5-dithiocarboxylate (VI) with formamide at 150° for 5 hr in 45% yield.^{3} Compound VI was prepared by the reaction of Ia with carbon disulfide and dimethyl sulfate in the presence of sodium hydroxide in dimethylsulfoxide at room temperature. In the same method, other 5-aminopyrimido[4,5-d]pyrimidine-2,4(1H,3H)-dione derivatives (IVb, c) were obtained by the reaction of Ib, c with II in good yields.



Yields and Physical Properties of IV and V

IVa: Yield 72%, mp 236°. IRν_{max}^{KBr}cm^{-1}: 3360(NH), 1710, 1650(CO). UVλ_{max}^{EtOH}nm(log ε): 239(4.56), 281(4.22), 292(4.21). NMR(in $CDCl_3$+CF_3COOH)δ: 2.72(3H, s, SMe), 3.44(3H, s, NMe), 3.66(3H, s, NMe), 9.50(2H, broad, NH_2).

IVb: Yield 67%, mp 329° . IRν_{max}^{KBr}cm^{-1}: 3360(NH), 1700(CO). UVλ_{max}^{EtOH}nm: 240, 282.

IVc: Yield 38%, mp 257°. IRν_{max}^{KBr}cm^{-1}: 3380, 3280(NH), 1700, 1645(CO). UVλ_{max}^{EtOH}nm (log ε)δ:240(4.54), 283(4.23).

V: Yield 45%, mp 268°. IRν_{max}^{KBr}cm^{-1}: 3360(NH), 1700, 1650(CO). UVλ_{max}^{EtOH}nm(log ε): 236(4.58), 294(3.74). NMR(in CF_3COOH)δ: 3.52(3H, s, NMe), 3.78(3H, s, NMe), 8.72(1H, bs, NH), 8.85(1H, s, 7-H), 9.73(1H, bs, NH).

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