Synthesis of Pyrido[2,3-*d*]pyrimidine-2,4-diones

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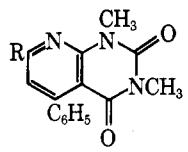
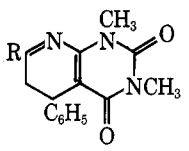
Pyrido[2,3-*d*]pyrimidine-2,4-diones were prepared by the acid- and base-catalyzed condensation of 6-amino-1,3-dimethyluracil with α,β-unsaturated carbonyl compounds. The reaction was carried out successfully with benzalacetophenone, benzalpinacolone, benzalacetone, cinnamaldehyde, crotonaldehyde, methyl vinyl ketone, and 3-penten-2-one. The intermediate dihydropyridine was isolated only in the condensation with benzalpinacolone in acetic acid. In all other examples air oxidation probably occurred and formed the pyridine. Disproportionation of the dihydropyridine to the pyridine and tetrahydropyridine occurred to a minor extent with the product from benzalacetophenone.

The reaction of 6-amino-1,3-dimethyluracil with α,β-unsaturated carbonyl compounds was investigated under a variety of conditions as a method for the preparation of pyrido[2,3-*d*]pyrimidine-2,4-diones. Condensations of this type have been reported only with dibenzoylethylene.[1]

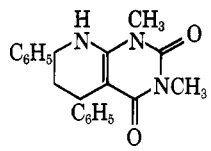
The condensation reaction with benzalacetophenone and benzalpinacolone in the presence of sodium ethoxide gave good yields of the corresponding pyrido[2,3-*d*]pyrimidine-2,4-diones (**1a, 1b**), and poor yields of the desired pyridines



1a, R = C_6H_5
b, R = $C(CH_3)_3$
c, R = H



2a, R = C_6H_5
b, R = $C(CH_3)_3$



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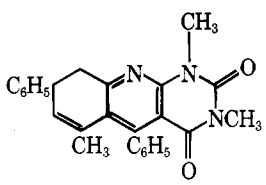
with methyl vinyl ketone, 3-penten-2-one, and benzalacetone.

The expected intermediate **2** from the first two examples was not isolated but is apparently oxidized by air to the pyridines **1a** and **1b.** Disproportionation of **2a** to the pyridine **1a** and the tetrahydro derivative **3** is a minor reaction and was observed only with the phenyl derivative **2a.** Proofs for the structures were the NMR and ir spectra and elemental analyses.

Benzalacetone using sodium ethoxide as the condensing agent gave as the main product **4** which results from the con-



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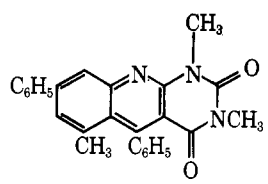

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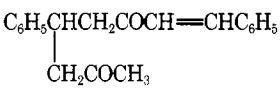
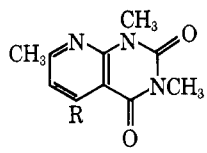
densation of the amine with the dimer of benzalacetone resulting from a Michael addition of benzalacetone to itself. This



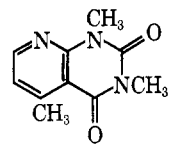
compound (**4**) was converted by sulfur to the quinoline derivative **5.** The NMR and mass spectral data were in agreement with these formulations.

Methyl vinyl ketone, 3-penten-2-one, and benzalacetone were converted to the corresponding pyridines **6** in better yields than those obtained using sodium ethoxide by heating with the amine in acetic acid at 100 °C.

The acetic acid method was also suitable for the preparation of the 5-phenyl derivative **1c** from cinnamaldehyde but was



6a, R = H
b, R = CH_3
c, R = C_6H_5



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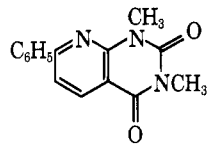

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not a general method for the preparation of pyridopyrimidines since it gave the dihydro derivative **2b** as the main product when benzalpinacolone was used. The structure was demonstrated by dehydrogenation with chloranil to the corresponding pyridine **1b.** The NMR spectrum was likewise in agreement with this formulation and showed 12 lines for the ABX system involving the hydrogens on the 5 and 6 carbons.

The dihydro derivative **2b** is stable to air oxidation in acetic acid in contrast to the dihydro derivative of **6b.** The reaction of 6-amino-1,3-dimethyluracil with 3-penten-2-one in acetic acid under nitrogen gave a mixture of compounds which, by TLC analysis on silica gel using chloroform as the solvent, contained the pyridine **6b** and two other compounds. Attempts to isolate and characterize these compounds by chromatography and fractional crystallization from methanol were not successful. Evidence for the presence of the dihydro derivative was obtained by heating the mixture further in acetic acid exposed to air; the yield of the pyridine **6b** obtained was twice that present in the original mixture.

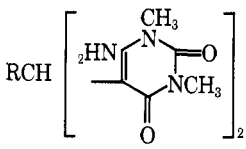
The use of trifluoroacetic acid as a solvent in the condensation reaction was investigated only with benzalacetone and gave **4** as the product instead of the pyridopyrimidine **6c.** Further studies using this acid were therefore not pursued.

Hydrochloric acid as a condensing agent was also studied using crotonaldehyde and cinnamaldehyde. This acid had been used successfully[2] for the conversion of crotonaldehyde and 5-amino-1,3-dimethyluracil to the pyrido[3,2-*d*]pyrimidine. The product formed from 6-amino-1,3-dimethyluracil and crotonaldehyde was the 1,3,5-trimethyl derivative **7.** This formulation was based on the NMR spectrum; the coupling constant for the 6,7 hydrogens was 5 Hz in contrast to a coupling constant of 8 Hz for the 5,6 hydrogens in the 1,3,7-trimethyl derivative **6a.** The related hydrogens in 4-methylquinoline (5 Hz) and 2-methylquinoline (8 Hz) show similar coupling constants. Further evidences for these structures were the ^{13}C NMR spectra. The chemical shift for the 7-methyl group in **6a** (25.15 ppm) was further downfield than that for the 5-methyl group in **7** (22.40 ppm). The tetramethyl derivative **6b** gave shifts of 22.13 and 24.57 ppm for these two groups.

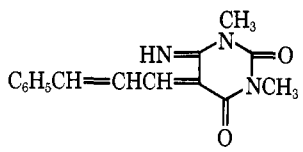
Cinnamaldehyde under these conditions gave the 5-phenyl derivative **1c** in a smaller yield than that obtained using acetic

acid. The reaction in hydrochloric acid was accompanied by a considerable amount of tar.

The condensation of 6-amino-1,3-dimethyluracil with benzalacetophenone, benzalacetone, and cinnamaldehyde in ethanol under neutral conditions was also investigated since the amine reacts with dibenzoylethylene under these conditions and forms a pyrrolo[2,3-*d*]pyrimidine-2,4-dione.[1] No reaction occurred, however, between the amine and either benzalacetophenone or benzalacetone in alcohol at reflux for 24 h. The corresponding reaction with cinnamaldehyde gave **9a**. This aldehyde behaved differently if heated with the



9a, R = $C_6H_5CH{=}CH$
b, R = C_6H_5



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amine at 250 °C in the absence of a solvent and formed the 7-phenyl derivative **8**. The structure assignment was based on its NMR spectrum. The coupling constant for the 5,6 hydrogens was 9 Hz in contrast to a coupling constant of 5 Hz for the 6,7 hydrogens in **1c**. In addition the phenyl group in **8** showed the characteristic splitting found for benzylidene structures. The cinnamylidene derivative **9a** is probably a precursor for the 7-phenyl derivative **8**. The loss of 6-amino-1,3-dimethyluracil by a reverse Michael reaction would form the 5-cinnamylidene derivative of the amine **10**. Cyclization of **10** followed by air oxidation would form **8**.

The formation of the pyridines must occur by a 1,4 addition of the amine at the 5 position to the unsaturated carbonyl system followed by cyclization and air oxidation. Such an involvement of the enamine structure was demonstrated by the behavior of 6-amino-1,3-dimethyluracil with benzaldehyde; the condensative at 190 °C or in acetic acid gave **9b**.

Experimental Section

Melting points are not corrected. Infrared spectra were recorded on a Perkin-Elmer Model 137B spectrophotometer. NMR spectra were obtained with Varian A-60 and Bruker HX-90E nuclear magnetic resonance spectrometers. Mass spectra were obtained with a Hitachi RMU6E spectrometer.

Condensation of Benzalacetophenone with 6-Amino-1,3-dimethyluracil. A solution of benzalacetophenone (2.08 g), 6-amino-1,3-dimethyluracil (1.55 g), and sodium ethoxide (0.68 g) in absolute ethanol (118 ml) was heated at reflux for 17 h. The solution on cooling gave 1.81 g (53%) of 1,3-dimethyl-5,7-diphenylpyrido[2,3-*d*]pyrimidine-2,4-dione (**1a**), mp 250–255 °C. Two crystallizations gave a sample melting at 250–252 °C: ir (Nujol) 5.87, 6.01 μ (C=O); NMR (CF_3COOH) δ 3.53 (s, 3 H, NCH_3), 4.08 (s, 3 H, NCH_3), 7.2–8.0 (m, 11 H, 2 C_6H_5, CH).

Anal. Calcd for $C_{21}H_{17}O_2N_3$: C, 73.47; H, 4.96; N, 12.24. Found: C, 73.48; H, 5.03; N, 12.43.

Concentration of the filtrate gave 0.26 g of solid which from its infrared spectrum proved to be a mixture of **1a** and its tetrahydro derivative (**3**). The resulting filtrate was evaporated to dryness and the solid obtained was extracted with benzene. The benzene extract was discarded and the remaining solid was treated with water and filtered, yield 0.67 g. Two crystallizations from ethanol gave the tetrahydro derivative (**3**) melting at 262–264 °C: ir (Nujol) 3.23 (NH), 6.03 μ (C=O); NMR ($CDCl_3$) 1.7–3.2 (m, 2 H, CH_2), 3.12 (s, 3 H, NCH_3), 3.33 (s, 3 H, NCH_3), 3.8–4.5 (m, 2 H, 2CH), 4.93 (broad s, 1 H, NH), 7.1 (s, 5, C_6H_5), 7.28 (s, 5, C_6H_5).

Anal. Calcd for $C_{21}H_{21}O_2N_3$: C, 72.83; H, 6.07; N, 12.14. Found: C, 72.89; H, 5.84; N, 12.29.

1,3-Dimethyl-7-*tert*-butyl-7-phenylpyrido[2,3-*d*]pyrimidine-2,4-dione (1b). Benzalpinacolone under similar conditions to those given for the preparation of **1a** gave an 81% yield of **1b** melting at 120–128 °C. Two recrystallizations from ethanol gave a sample melting at 139–142 °C: ir (Nujol) 5.75, 6.02 μ (C=O); NMR ($CDCl_3$) δ 1.43 [s, 9, $C(CH_3)_3$], 3.35 (s, 3, NCH_3), 3.78 (s, 3, NCH_3), 7.07 (s, 1, CH), 7.20–7.53 (m, 5, C_6H_5).

Anal. Calcd for $C_{19}H_{21}N_3O_2$: C, 70.56; H, 6.50; N, 13.00. Found: C, 70.89; H, 6.56; N, 13.21.

1,3,7-Trimethylpyrido[2,3-*d*]pyrimidine-2,4-dione (6a). A solution of methyl vinyl ketone (4 ml) and 6-amino-1,3-dimethyluracil (7.7 g) in acetic acid (100 ml) was heated on a steam bath for 21 h. Removal of the acetic acid under reduced pressure followed by the addition of water gave 1.92 g (18.7%) of a solid melting at 153–158 °C. Sublimation followed by two crystallizations from ethanol gave white crystals melting at 157.5–159 °C: ir (Nujol) 5.86, 5.98 μ (C=O); NMR ($CDCl_3$) δ 2.60 (s, 3, CH_3), 3.43 (s, 3, NCH_3), 3.64 (s, 3, NCH_3), 7.03 [d, 1, 6-H (J = 8 Hz)], 8.20 [d, 1, 5-H (J = 8 Hz)], 25.15 (7-CH_3), 28.27 (1-CH_3), 29.25 (3-CH_3); *m/e* 205.

Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.54; H, 5.37; N, 20.49. Found: C, 58.41; H, 5.62; N, 20.59.

Using sodium ethoxide as the reagent in ethanol gave only trace amounts of this compound.

1,3,5,7-Tetramethylpyrido[2,3-*d*]pyrimidine-2,4-dione (6b). 3-Penten-2-one using the directions given for the preparation of **6a** gave a 61% yield of a solid melting at 155–165 °C. Sublimation under reduced pressure followed by crystallization from ethanol gave white crystals of **6b** melting at 178–180 °C: ir (Nujol) 5.89, 6.02 μ (C=O); NMR ($CDCl_3$) δ 2.52 (s, 3 H, 7-CH_3), 2.73 (s, 3 H, 5-CH_3), 3.40 (s, 3 H, NCH_3), 3.64 (s, 3 H, NCH_3), 6.79 (s, 1 H, 6-H), 22.29 (5-CH_3), 24.73 (7-CH_3), 28.21 (1-CH_3), 29.93 (3-CH_3).

Anal. Calcd for $C_{11}H_{13}N_3O_2$: C, 60.27; H, 5.94; N, 19.17. Found: C, 60.19; H, 5.42; N, 19.55.

Fractional crystallization of the compounds present in the alcohol filtrate from ethyl acetate gave 0.165 g of a sample melting at 188–193 °C. The NMR spectrum indicated that this sample was probably a mixture of the dihydro and tetrahydro derivative of **6b**. The amount obtained was insufficient to allow further separation and characterization.

The same reaction when carried out under nitrogen gave a 58% yield of a solid which, when chromatographed upon silica gel using chloroform, gave three distinct bands. The first of these was the pyridine **6b** and amounted to 35% of the total product. The second band upon workup also gave the pyridine **6b**. The third fraction gave an oil which could not be obtained crystalline.

Fractional crystallization from methanol gave fractions which always contained the pyridine **6b**.

The above mixture (1 g) when heated in acetic acid (15 ml) at 100 °C in air for 18 h gave 0.7 g of the pyridine **6b**.

The use of sodium ethoxide as a condensing agent gave a 19% yield of **6b**.

5-Phenyl-1,3,7-trimethylpyrido[2,3-*d*]pyrimidine-2,4-dione (6c). A solution of the amine (1.55 g) and benzalacetone (1.46 g) in acetic acid (50 ml) was heated at reflux for 17 h. Removal of the acetic acid followed by the addition of water gave a gum which when triturated with ethanol gave a solid (0.23 g, 8%) melting at 170–173 °C. Crystallization from ethanol gave a sample melting at 185–187 °C. Purification by sublimation followed by crystallization from methanol gave white crystals melting at 187–189 °C: ir (Nujol) 5.87, 6.02 μ (CO); NMR ($CDCl_3$) δ 2.60 (s, 3 H, 7-CH_3), 3.33 (s, 3 H, NCH_3), 3.75 (s, 3 H, NCH_3), 6.89 (s, 1 H, 6-H), 7.1–7.6 (m, 5 H, C_6H_5).

Anal. Calcd for $C_{16}H_{15}N_3O_2$: C, 68.32; H, 5.33; N, 14.95. Found: C, 68.45; H, 5.79; N, 15.03.

The ethanol filtrate upon evaporation gave a solid which upon sublimation under reduced pressure gave 0.33 g (12%) of **6c**.

5-Phenyl-1,3-dimethylpyrido[2,3-*d*]pyrimidine-2,4-dione (1c). **A.** The amine (3.1 g) and cinnamaldehyde (2.5 ml) were heated in acetic acid (50 ml) on a steam bath for 21 h. Removal of the acetic acid followed by addition of water gave a gum which was dissolved in hot ethanol. The pale brown solid (0.68 g, 12.8%) obtained melted at 171–178 °C. Sublimation under reduced pressure followed by recrystallization from ethanol gave white crystals melting at 184–186 °C: ir (Nujol) 5.84, 5.93 μ (CO); NMR ($CDCl_3$) δ 3.34 (s, 3, CH_3N), 3.73 (s, 3, CH_3N), 6.99 [d, 1, 6-H (J = 5 Hz)], 7.08–7.62 (m, 5, C_6H_5), 8.62 [d, 1, 7-H (J = 5 Hz)].

Anal. Calcd for $C_{15}H_{13}N_3O_2$: C, 67.42; H, 4.87; N, 15.73. Found: C, 66.96; H, 4.85; N, 15.58.

An additional 1.0 g (19%) of **1c** was obtained by vacuum sublimation of the tarry materials obtained from the ethanol filtrate.

B. The amine (2.0 g) and cinnamaldehyde (2 ml) were heated at reflux in 6 N hydrochloric acid (40 ml) for 30 min. The resulting solution was decanted from the tar formed, poured into water, and neutralized with ammonia. The resulting solid (0.55 g, 16%) melting at 140–170 °C was recrystallized from ethanol, mp 182–184 °C. The ir spectrum was identical with that of **1c** formed using acetic acid as a solvent. The tar from this preparation when heated in a sublimator under reduced pressure gave an additional 0.33 g (5%) of **1c**.

5-Phenyl-7-*tert*-butyl-5,6-dihydropyrido[2,3-*d*]pyrimidine-2,4-dione (2b). The amine (3.1 g) and benzalpinacolone (3.76 g) were heated in acetic acid (100 ml) on a steam bath for 23 h. Removal of the acetic acid followed by the addition of water gave a waxy solid (5.32 g). Trituration with ethanol gave a white solid (3.35 g, 51%) melting at 210–215 °C. Recrystallization from ethyl acetate gave white crystals melting at 215–219 °C: ir (Nujol) 5.90, 6.07 μ (CO); NMR ($CDCl_3$) δ 1.0 [s, 9, $(CH_3)_3C$], 2.32, 2.61 [2, d, 1, B-H (J_{BX} = 9 Hz)], 2.87, 3.15 [2 d, 1, A-H (J_{AX} = 2 Hz)], 3.37 (s, 3, NCH_3), 3.63 (s, 3, NCH_3), 4.16, 4.31 [2 d, 1, X-H (J_{AX} = 2 Hz)], 6.93–7.5 (m, 5, C_6H_5).

Anal. Calcd for $C_{19}H_{23}N_3O_2$: C, 70.15; H, 7.08; N, 12.92. Found: C, 69.85; H, 7.43; N, 12.74.

The dihydropyridine **2b** (0.162 g) and chloranil (0.14 g) in benzene (10 ml) were heated at reflux for 24 h. The resulting solution was cooled and the hydroquinone (0.044 g) which crystallized was filtered. The benzene filtrate was evaporated to dryness. Addition of ethanol gave 0.03 g of **1b** melting at 136–139 °C.

1,3,5-Trimethylpyrido[2,3-*d*]pyrimidine-2,4-dione (7). The amine (7.75 g) and crotonaldehyde (5 ml) were treated with 6 N hydrochloric acid (77.5 ml) using the directions given for 5-amino-1,3-dimethyluracil.[2] The resulting solution was filtered from the tar and the hydrochloric acid was removed under reduced pressure. Treatment with water and basification with ammonium hydroxide was followed by extraction with methylene chloride. Removal of the solvent gave an oil which was dissolved in hot ethanol. Cooling gave crystals (1.52 g, 14%) melting at 130–142 °C. An additional 0.16 g (1.5%) was obtained by concentration of the aclohol filtrate. Sublimation under reduced pressure gave a sample melting at 159–160.5 °C: ir (Nujol) 5.88, 6.05 μ (CO); NMR ($CDCl_3$) δ 2.79 (s, 3, CH_3), 3.42 (s, 3, NCH_3), 3.66 (s, 3, NCH_3), 6.97 [d, 1, 6-H (J = 5 Hz)], 8.42 [d, 1, 7-H (J = 5 Hz)], 22.40 (7-CH_3).

Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.54; H, 5.37; N, 20.49. Found: C, 58.75; H, 5.49; N, 20.93.

The tar obtained in this preparation when heated in a sublimator under vacuum gave an additional 0.87 g (8.5%) of **7**. The residue from this sublimation was a white solid (1.59 g) melting at 319–315 °C. The insolubility of this compound in organic solvents prevented the elucidation of its structure.

7-Phenylpyrido[2,3-*d*]pyrimidine-2,4-dione (8). A mixture of the amine (2.0 g) and cinnamaldehyde (2 ml) was heated at 250 °C under nitrogen for 30 min. The red glass obtained was dissolved in hot ethanol and the resulting solution upon cooling gave a solid (0.88 g, 25%) melting at 178–183 °C. Sublimation (vacuum) followed by two recrystallizations from ethanol gave white crystals melting at 186–187.5 °C: ir (Nujol) 5.85, 6.01 μ (CO); NMR ($CDCl_3$) δ 3.44 (s, 3, NCH_3), 3.76 (s, 3, NCH_3), 7.32–7.63 (m, 3, *m,p*-ArH), 7.60 [d, 1, 6-H (J = 9 Hz)], 7.92–8.28 (m, 2, *o*-ArH), 8.46 [d, 1, 7-H (J = 9 Hz)].

Anal. Calcd for $C_{15}H_{13}N_3O_2$: C, 67.42; H, 4.87; N, 15.73. Found: C, 67.37; H, 5.03; N, 15.85.

Condensation of Benzalacetone with 6-Amino-1,3-dimethyluracil. A. A solution of amine (1.55 g), benzalacetone (1.46 g), and sodium ethoxide (0.68 g) in absolute ethanol (130 ml) was heated at reflux for 23 h. Removal of the ethanol followed by the addition of water gave a solid (2.23 g) melting at 140–170 °C. Treatment with methanol gave a solid (0.48 g, 12%) melting at 193–198 °C. Recrystallization from methanol gave pale yellow crystals of **4** melting at 197–199 °C: ir (Nujol) 5.87, 6.05 μ (CO); NMR ($CDCl_3$) δ 1.85 (s, 3, CH_3), 1.95–3.05 (m, 2 H, CH_2), 3.27 (s, 3, NCH_3), 3.79 (s, 3, NCH_3), 3.83–3.86 (m, 1, CH), 6.31 [d, 1, =CH (J = 5.8 Hz)], 6.47–6.83 (m, 3, aromatic H), 6.83–7.62 (m, 7 H, aromatic); *m/e* 409.

Anal. Calcd for $C_{26}H_{23}N_3O_2$: C, 75.91; H, 6.08; N, 10.21. Found: C, 75.64; H, 5.70; N, 10.11.

The methanol filtrate was evaporated to dryness and the residue was sublimed under reduced pressure. The solid (0.72 g) obtained, upon fractional crystallization from ethanol, gave **4** (0.05 g) and **6c** (0.31 g).

B. The amine (1.55 g) and benzalacetone (1.46 g) were dissolved in trifluoroacetic acid (10 ml) and the solution was allowed to stand for 65 h at room temperature. Addition of water to the solution followed by extraction with methylene chloride gave a solid which after recrystallization from ethanol gave **4** (0.91 g, 22% melting at 191–196 °C.

1,3,6-Trimethyl-5,8-diphenyl-1,2,3,4-tetrahydropyrimido[4,5-*b*]quinoline-2,4-dione (5). The dihydro compound **4** (0.82 g) was heated with sulfur (0.064 g) at 225–230 °C until the evolution of hydrogen sulfide ceased. The resulting product was dissolved in benzene and chromatographed upon silica gel using benzene as an eluent. Removal of the benzene gave **5** (0.55 g) melting at 198–203 °C. Sublimation under reduced pressure followed by two crystallizations from ethyl acetate gave pale yellow crystals melting at 207–209 °C: ir (Nujol) 5.84, 5.98 μ (CO); NMR ($CDCl_3$) δ 2.55 (s, 3, 9-CH_3), 3.31 (s, 3, NCH_3), 3.72 (s, 3, NCH_3), 6.6–7.25 (m, 11, aromatic H's and 8-H), 7.87 [broad s (meta coupling), 1, 6-H]; *m/e* 407.

Anal. Calcd for $C_{26}H_{21}O_2N_3$: C, 76.85; H, 4.93; N, 10.34. Found: C, 76.72; H, 5.18; N, 10.24.

3-Phenyl-1,1-bis(6-amino-1,3-dimethyluracil-5)-2-propene (9a). The amine (1.55 g) and cinnamaldehyde (1.25 ml) were heated under reflux in absolute ethanol (100 ml) under nitrogen for 24 h. Removal of the solvent followed by the addition of methanol gave 1.33 g (31%) of **9a**. Two crystallizations from methanol gave a sample which melted partially at 202 °C, resolidified completely at 208 °C, and then melted at 281 °C with gas evolution: ir (Nujol) 2.90, 3.07 (NH_2), 3.2 (CH=CH), 5.91, 6.01 (C=O), 10.2 μ (CH=CH); NMR (Me_2SO-d_6) δ 3.22 [s, 6, 2 N $(CH_3)_2$], 3.42 [s, 6, 2 N $(CH_3)_2$], 5.08 (m, 1, >CH), 6.1–6.66 (m, 2, CH=CH), 7.33 (s, 5, C_6H_5), 7.48 [s, 4, 2 NH_2 (exchanges with D_2O)].

Anal. Calcd for $C_{21}H_{24}N_6O_4$: C, 59.43; H, 5.66; N, 19.81. Found: C, 59.52; H, 5.66; N, 19.91.

Phenylbis(6-amino-1,3-dimethyluracil-5)methane (9b). A. The amine (1.0 g) and benzaldehyde (1 ml) were heated at 190 °C for 30 min. Trituration of the product with methanol gave a solid (1.0 g, 39%) which after recrystallization from methanol gave white crystals of **9b**: mp softens at 283 °C and melts at 289 °C with decomposition; ir (Nujol) 2.92, 3.11 (NH_2), 5.92, 6.06 μ (CO); NMR (Me_2SO-d_6) δ 3.24 (s, 6, 2 NCH_3), 3.40 (s, 6, 2 NCH_3), 5.70 (s, 1, CH), 7.24 (s, 5, C_6H_5), 7.52 [s, 4, 2 NH_2 (exchanges with D_2O)].

Anal. Calcd for $C_{19}H_{22}N_6O_4$: C, 57.29; H, 5.53; N, 21.11. Found: C, 57.26; H, 5.82; N, 20.98.

B. The amine (1.55 g) and benzaldehyde (1 ml) were heated in acetic acid (40 ml) at 100 °C for 16 h. Removal of the acetic acid followed by the addition of methanol gave 1.24 g (31%) of **9b**.

Registry No.—**1a,** 59796-99-5; **1b,** 59797-00-1; **1c,** 59797-01-2; **2b,** 59797-02-3; **3,** 59797-03-4; **4,** 59797-04-5; **5,** 59797-05-6; **6a,** 59797-06-7; **6b,** 59797-07-8; **6c,** 59797-08-9; **7,** 59797-09-0; **8,** 17789-35-4; **9a,** 59797-10-3; **9b,** 13191-76-9; benzalacetophenone, 94-41-7; 6-amino-1,3-dimethyluracil, 6642-31-5; benzalpinacolone, 538-44-3; methyl vinyl ketone, 78-94-4; 3-penten-2-one, 625-33-2; benzalacetone, 122-57-6; cinnamaldehyde, 104-55-2; chloranil, 118-75-2; crotonaldehyde, 4170-30-3; 5-amino-1,3-dimethyluracil, 49738-24-1.

References and Notes

(1) Y. Tamura, T. Sakaguchi, T. Kawasaki, and Y. Kita, *Heterocycles*, **3**, 183 (1975). This publication appeared while the present study was under investigation.
(2) W. J. Irwin and D. G. Wibberley, *J. Chem. Soc. C*, 1745 (1967).