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Synthesis of Pyrimidines and Condensed Pyrimidines

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A new one-step synthesis of pyrimidines and condensed pyrimidines by heating carboxamides or cyclic lactams with formamide in the presence of POCl_3 in a sealed tube is described.

This paper provides the full version of the new one-step synthesis of pyrimidine and condensed pyrimidine compounds published in a previous communication.¹⁾

4-Aminopyrimidine (**1a**) was obtained when a mixture of acetamide and formamide (FA) was heated in the presence of POCl_3 at 120 °C in a sealed vessel for 12 hr. The structure was established by comparing its IR spectrum with that of an authentic material.

Several workers have already reported the one-step synthesis of pyrimidines. Davies *et al.*^{2a)} reported syntheses of 4-amino-5-arylpyrimidines in yields of 4—54%, by heating arylacetonitriles and FA under nitrogen flow. However, under these conditions, aliphatic nitriles and FA did not react. Tsatsaronis and Kehayoglov^{2b)} also

obtained 4-amino-5-arylpyrimidines in yields of 7—54% by the reaction of tris(formylamino)methane with substituted acetonitriles, acetamides, and the corresponding esters. But the yield of 4-amino-5-methylpyrimidine was only 1.8%. Bredereck *et al.*³⁾ obtained purine in 19% yield by heating aminoacetonitrile and FA. Loader and Timmons⁴⁾ obtained benzo[f]quinazoline by heating β -naphthylamine and FA in the presence of POCl_3 in a yield of 3.5%. Yamada and Okamoto⁵⁾ also obtained purine by heating FA alone for 28 hr in 20.5% yield.

Experiments designed to maximize the yield of **1a** showed that the best yields were obtained when the reaction was carried out between 120—160 °C (Fig. 1), with the optimum reaction time being 12—20 hr (Fig.

1) K. Morita, S. Kobayashi, H. Shimadzu, and M. Ochiai, *Tetrahedron Lett.*, **1970**, 861.

2) a) W. H. Davies, and H. A. Piggott, *J. Chem. Soc.*, **1945**, 347; W. H. Davies, A. W. Johnson, and H. A. Piggott, *ibid.*, **1945**, 352. b) G. C. Tsatsaronis, and A. H. Kehayoglov, *J. Org. Chem.*, **35**, 438 (1970).

3) H. Bredereck, H. Ulmer, and H. Waldman, *Chem. Ber.*, **89**, 12 (1956).

4) C. E. Loader, and C. J. Timmons, *J. Chem. Soc., C*, **1967**, 1343.

5) H. Yamada, and T. Okamoto, *Chem. Pharm. Bull.* **20**, 632 (1972).

2). Although the yield did not change significantly as the molar ratio of FA to acetamide varied, maximum yield was obtained when this ratio was between 2:1 and 3:1 (Fig. 3). The final and most crucial factor varied in this study of reaction conditions was the condensing agent (Table 1). Of the several condensing agents tested, POCl_3 and PCl_5 proved to be effective, with POCl_3 giving higher yields of **1a**. The best

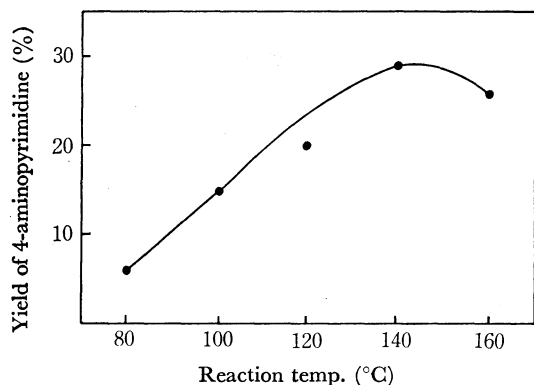


Fig. 1. Effect of reaction temperature on the yield of 4-aminopyrimidine (**1a**).
Mol. ratio: CH_3CONH_2 : FA: POCl_3 = 1: 2: 3
Reaction time: 5 hr

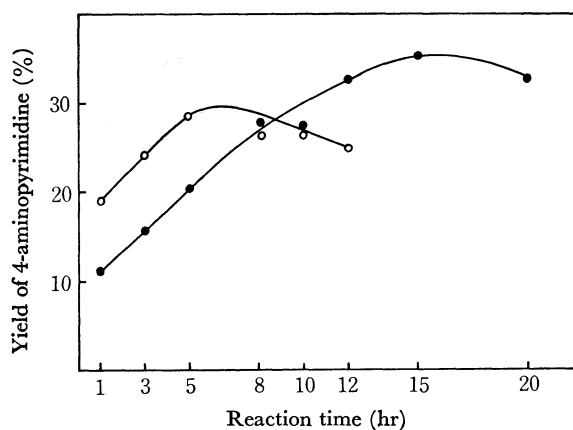


Fig. 2. Effect of reaction time on the yield of 4-aminopyrimidine (**1a**).
Mol. ratio: CH_3CONH_2 : FA: POCl_3 = 1: 2: 3
Reaction temp.: ●—●: 120 °C; ○—○: 140 °C

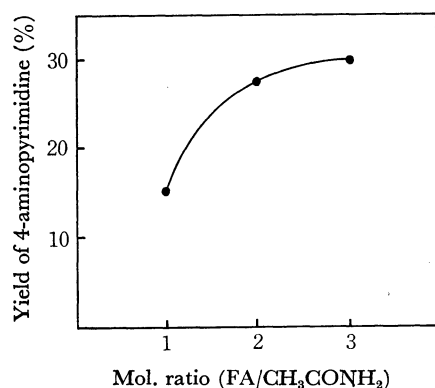


Fig. 3. Effect of mol. ratio (FA to CH_3CONH_2) on the yield of 4-aminopyrimidine (**1a**).
Reaction temp.: 140 °C Reaction time: 5 hr

TABLE 1. EFFECT OF CONDENSING AGENTS ON THE YIELD OF 4-AMINOPYRIMIDINE (**1a**)

Reagent	Yield of 4-aminopyrimidine (%)
POCl_3	34
PCl_5	9
PCl_3	trace
$\text{H}_3\text{C}-\text{C}_6\text{H}_4-\text{SO}_2\text{Cl}$	0
$\text{H}_3\text{CSO}_2\text{Cl}$	0
SOCl_2	0

Reaction temp.: 120 °.
Reaction time: 12 hr.
Mol. ratio: CH_3CONH_2 : H_2NCHO : reagent (1: 2: 3).

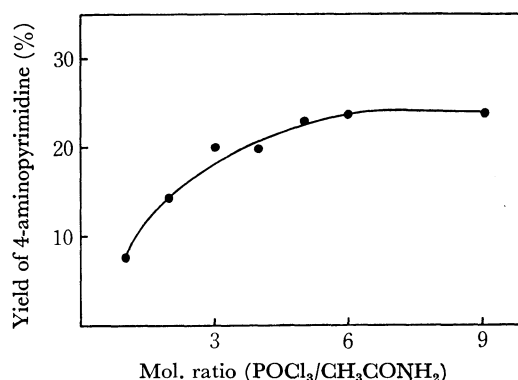


Fig. 4. Effect of mol. ratio (POCl_3 to CH_3CONH_2) on the yield of 4-aminopyrimidine (**1a**).
Reaction temp.: 120 °C, Reaction time: 10 hr
Mol. ratio (FA/ CH_3CONH_2): 2

POCl_3 to acetamide ratio was between 3 and 9 (Fig. 4). The isolated yield of **1a** was 32% when a mixture of acetamide, FA and POCl_3 (molar ratio 1: 2: 3) was heated in a sealed tube at 120 °C for 12 hr.

When acetic acid and ethyl acetate were used instead of acetamide, **1a** was also obtained in yields of 13 and 12%, respectively. In these cases, acetamide is thought to be formed in the reaction media *via* acid-amide exchange reaction and then similarly converted to **1a**. Acetic chloride and acetic anhydride also gave **1a** although the yields diminished significantly, as shown in Table 2.

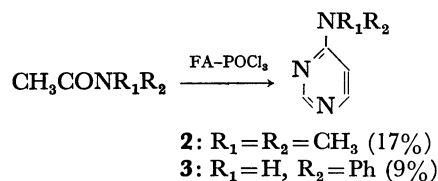
One-Step Synthesis of 4-(Substituted amino)pyrimidines. Although the reaction mechanism of this novel one-step synthesis is far from clear, it is worthwhile to note that

TABLE 2. YIELDS OF 4-AMINOPYRIMIDINE (**1a**) FROM ACETIC ACID DERIVATIVES

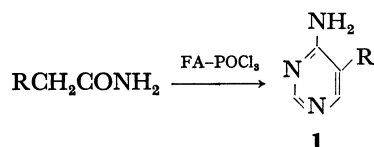
R	Yield of 4-aminopyrimidine (%)
NH_2	34
OH	13
OCH_2CH_3	12
Cl	4.7
OCOCH_3	3.5

Reaction temp.: 120°.
Reaction time: 12 hr.

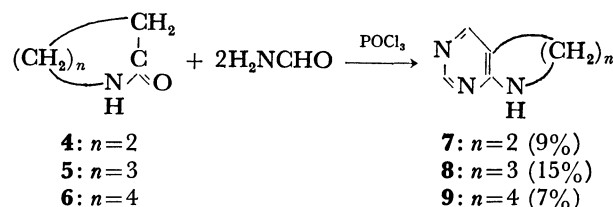
two nitrogen atoms on a pyrimidine nucleus originate from FA, as shown in the following examples. *N,N*-Dimethylacetamide, when treated with FA-POCl₃, gave 4-(dimethylamino)pyrimidine (2). Similarly, acetanilide gave 4-anilinoypyrimidine (3).



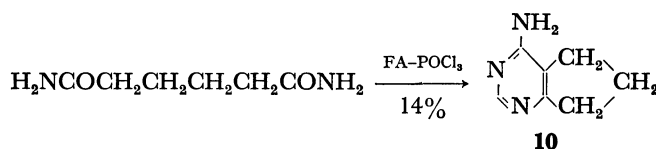
One-Step Synthesis of 4-Amino-5-alkylpyrimidines. In other attempts to generalize the one-step synthesis, propionamide and stearamide were treated with FA-POCl₃. The product isolated from the propionamide experiment was the anticipated 4-amino-5-methylpyrimidine (1b). Similarly, stearamide gave 4-amino-5-hexadecylpyrimidine (1i). Other aliphatic carboxamides could be used and the same class of compounds was obtained, as shown in Table 3. Thus, these reactions furnish a convenient one-step synthesis of 4-amino-5-alkylpyrimidines, as illustrated by the general equation:



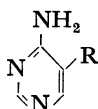
One-Step Synthesis of Condensed Pyrimidines. Cyclic lactams could also be the substrates of this novel one-step synthesis. Thus, α-pyrrolidone (4), δ-valerolactam (5), and ε-caprolactam (6) gave 5,6-dihydro-7H-pyrrolo-[2,3-d]pyrimidine (7), 5,6,7,8-tetrahydropyrido[2,3-d]-pyrimidine (8) and 5,6,7,8-tetrahydro-9H-pyrimido[4,5-b]azepine (9), respectively.



When adipamide was treated with FA-POCl₃, the isolated product was white and crystalline, and its analysis agreed with the formula C₇H₉N₃. Its NMR spectrum was consistent with the structure of 4-amino-6,7-dihydro-5H-cyclopenta[d]pyrimidine (10).



The UV characteristics were also in accord with the values described in literature.⁹⁾ A plausible reaction mechanism for the formation of 10 is as follows:

TABLE 3. ANALYTICAL AND SPECTRAL DATA OF 4-AMINOPYRIMIDINES: 

Compd.	R	Mp (°C)	Recrystn solvent	Yield (%)	Formula	Analysis (%)					
						Calcd			Found		
						C	H	N	C	H	N
1a	H-	149—151 ^{a)}	—	32	C ₄ H ₅ N ₃	50.51	5.30	44.19	50.53	5.30	43.79
1b	CH ₃ -	170—173 ^{b)}	CHCl ₃	28	C ₅ H ₇ N ₃	55.03	6.47	38.51	54.56	6.23	37.45
1c	CH ₃ CH ₂ -	160—162 ^{c)}	EtOH	16	C ₆ H ₉ N ₃	58.51	7.37	34.12	58.08	7.37	34.01
1d ^{e)}	CH ₃ CH ₂ CH ₂ -	162	EtOAc	24	C ₇ H ₁₁ N ₃	61.28	8.08	30.63	61.37	8.17	30.23
1e ^{f)}	CH ₃ (CH ₂) ₂ CH ₂ -	103—105	EtOAc	17	C ₈ H ₁₃ N ₃	63.54	8.67	27.79	63.54	8.71	27.54
1f ^{g)}	CH ₃ (CH ₂) ₄ CH ₂ -	119	Benzene	18	C ₁₀ H ₁₇ N ₃	66.99	9.57	23.44	67.04	9.85	23.13
1g ^{b)}	CH ₃ (CH ₂) ₆ CH ₂ -	125—126	n-Hexane	16	C ₁₂ H ₂₁ N ₃	69.52	10.21	20.27	69.22	10.43	19.07
1h ^{h)}	CH ₃ (CH ₂) ₁₂ CH ₂ -	118—119	EtOH	27	C ₁₈ H ₃₃ N ₃	74.17	11.41	14.42	74.16	11.36	14.23
1i ^{j)}	CH ₃ (CH ₂) ₁₄ CH ₂ -	113—114	EtOH	21	C ₂₀ H ₃₇ N ₃	75.18	11.67	13.15	75.09	11.97	13.13

a) Lit.⁹⁾ mp 151°. MS: Mol wt 95 (100%).

b) Lit.⁷⁾ mp 176°. MS: Mol wt 109 (100%).

c) Lit.⁹⁾ mp 163°. MS: Mol wt 123 (100%).

d) NMR Spectra were determined in d₆-DMSO. NMR Signals for singlet are designated as s, triplet as t, and multiplet as m.

e) NMR (δ): 0.89 (t), 1.10—1.85 (m), 2.35 (M), 6.63 (s), 7.87 (s), 8.23 (s); ratio: 3: 2: 2: 2: 1: 1.

f) NMR (δ): 0.91 (t), 1.10—1.80 (m), 2.43 (M), 5.69 (s), 7.70 (s), 8.05 (s); ratio: 3: 4: 2: 2: 1: 1.

g) NMR (δ): 0.89 (t), 1.05—1.90 (m), 2.42 (M), 5.45 (s), 8.07 (s), 8.47 (s); ratio: 3: 8: 2: 2: 1: 1.

h) NMR (δ): 0.89 (t), 1.30 (s), 2.43 (M), 5.41 (s), 8.10 (s), 8.32 (s); ratio: 3: 12: 2: 2: 2: 1.

i) NMR (δ): 0.89 (t), 1.27 (s), 2.42 (M), 5.60 (s), 8.03 (s), 8.36 (s); ratio: 3: 24: 2: 2: 1: 1.

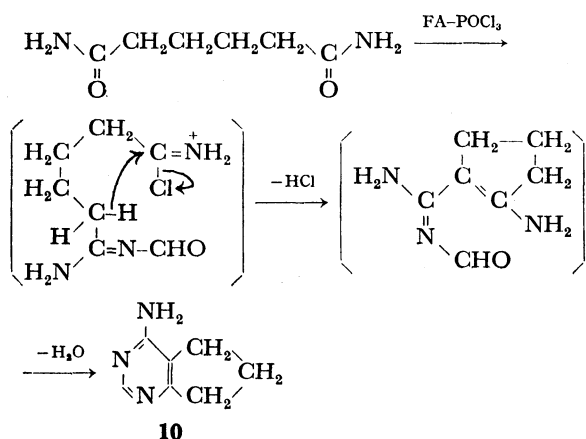
j) NMR (δ): 0.87 (t), 1.29 (s), 2.43 (M), 5.15 (s), 8.10 (s), 8.52 (s); ratio: 3: 28: 2: 2: 1: 1.

6) E. Büttner, *Ber. Deutsch. Chem. Ges.* **36**, 2227 (1903).

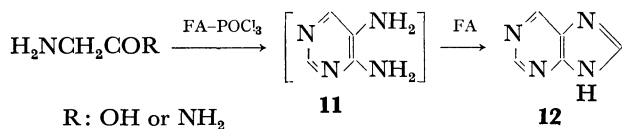
7) O. Gerngrass, *ibid.*, **38**, 3394 (1905).

8) A. V. Merkat, *ibid.*, **52**, 369 (1919).

9) L. O. Ross, L. Goodman, and B. R. Baker, *J. Amer. Chem. Soc.*, **81**, 3108 (1959).



Glycinamide, when treated with FA-POCl₃, did not give 4,5-diaminopyrimidine (**11**); instead, purine (**12**) was obtained in 7% yield. From the above arguments it is clear that the reaction proceeded *via* intermediary formation of **11**.



Glycine itself also yielded purine when treated under the same conditions. Here again, the conversion of glycine to glycinamide could be the first step in this reaction, as in the case of the formation of 4-amino-pyrimidine from acetic acid.

Further Aspects of This One-Step Synthesis. With the hope of ultimately employing the present reaction as a practical synthetic tool, we tried to synthesize a hitherto unknown diazaisolog (**16**) of the antidepressant drug, 5-(3-dimethylaminopropyl)-10,11-dihydro-5H-dibenz[*b,f*]azepine¹⁰ (**17**), which is clinically used ex-

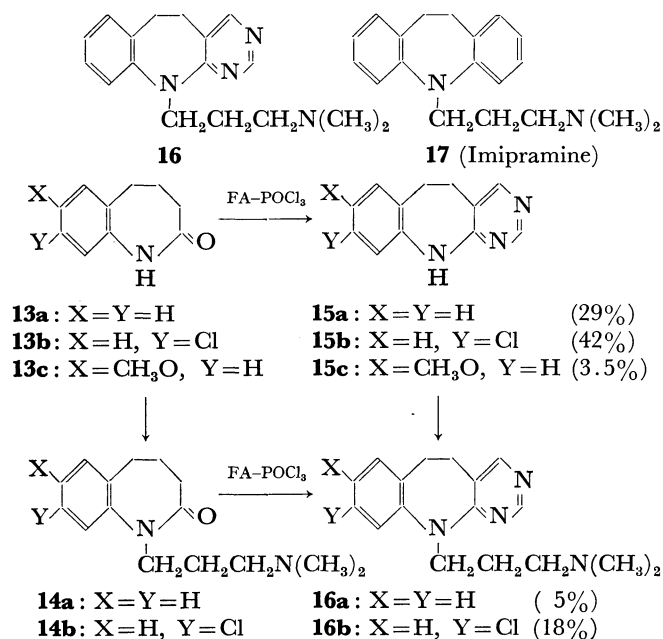


Chart 1

tensively. The results are shown in Chart 1. Interestingly, 5,6-dihydro-11H-dibenz[2,3]azepino[7,6-*d*]-pyrimidine (**15a**) and 9-chloro-5,6-dihydrobenz[2,3]-azepino[7,6-*d*]pyrimidine (**15b**) were obtained from homohydrocarbostyryl (**13a**) and 8-chloro-homohydrocarbostyryl (**13b**) in 29 and 42% yields, respectively. Similarly, **16a** and **16b** were obtained from **14a** and **14b** as shown in Chart 1.

Both **16a** and **16b** showed weak antidepressant activities; the biological effects of these compounds will be described elsewhere.

Experimental

Mps were taken in open capillaries and are uncorrected. NMR spectra were recorded for solns in CDCl₃ or in *d*₆-DMSO (internal TMS standard), using a Varian A-60 spectrophotometer. Mass spectra (70 eV) were recorded on a Hitachi RMU-6D double focusing spectrometer and UV spectra on a Hitachi recording spectrophotometer.

Reactants. **13a**, **13b**, and **13c** were prepared by reported procedures.¹¹ All other reactants were obtained from commercial sources and purified by distillation or recrystallization where necessary.

General Procedure. To a mixture of carboxamides (0.01 mol) and FA (0.02 mol) in a stainless steel vessel (30 ml), POCl₃ (0.03 mol) was added under dry ice-acetone cooling. After being closed tightly, the vessel was heated at 120 °C for 12 hr. Then water (15 ml) was added to dissolve the reaction mixture. After neutralization with aqueous NaOH, the products were extracted with 3 × 5 ml EtOAc, dried over Na₂SO₄, filtered and evaporated. Column chromatography of the residue on silica gel using CHCl₃: acetone: EtOH (70:30:3) as solvent, yielded the products.

The following compounds were prepared by the general procedure unless otherwise stated.

4-Dimethylaminopyrimidine (2). *N,N*-Dimethylacetamide (0.87 g, 0.01 mol) yielded 0.21 g of **2**; mp *ca.* 40 °C (lit.¹²) *ca.* 40 °C); NMR (δ) CDCl₃: 3.10 (s, 6H), 6.30 (broad s, 1H), 8.20 (broad s, 1H), 8.55 (broad s, 1H). Found: C, 58.35; H, 7.32; N, 34.01%.

4-Anilinopyrimidine (3). Acetanilide (1.35 g, 0.01 mol) gave 0.15 g of **3**; mp 139–142 °C (lit.¹³) 142–143 °C); NMR (δ) CDCl₃: 6.75 (dd, *J*=3 and 10 Hz, 1H), 7.20–7.50 (m, 5H), 8.25 (d, *J*=10 Hz, 1H), 8.52 (broad s, 1H), 8.66 (s, 1H). Found: C, 70.21; H, 5.31; N, 24.29%.

*5,6-Dihydro-7H-pyrrolo[2,3-*d*]pyrimidine (7).* α-Pyrrolidone (0.85 g, 0.01 mol) yielded 0.11 g of **7**; mp 113–114 °C; NMR (δ) CDCl₃: 2.86–3.36 (m, 2H), 3.54–3.92 (m, 2H), 6.24 (broad s, 1H), 7.96 (s, 1H), 8.34 (s, 1H); UV (mμ) λ_{max} (ε) H₂O (pH 1): 266 (10700); H₂O (pH 11): 250 (7560), 284 (4180). Found: C, 59.32; H, 5.89; N, 34.51%. Calcd for C₆H₇N₃: C, 59.48; H, 5.82; N, 34.69%.

*5,6,7,8-Tetrahydropyrrodo[2,3-*d*]pyrimidine (8).* δ-Valerolactam (0.99 g, 0.01 mol) gave 0.19 g of **8**; mp 106–108 °C; NMR (δ) CDCl₃: 1.65–2.15 (m, 2H), 2.5–2.9 (m, 2H), 3.3–3.6 (m, 2H), 6.64 (broad s, 1H), 7.94 (s, 1H), 8.35 (s, 1H); UV (mμ) λ_{max} (ε) H₂O (pH 1): 262 (12100), H₂O (pH 11): 247 (9730), 286 (4750). Found: C, 62.38; H, 6.62; N, 30.92%. Calcd for C₇H₉N₃: C, 62.20; H, 6.71; N, 31.09%.

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12) D. J. Brown, and L. N. Short, *ibid.*, **1953**, 331.

13) W. Winkelmann, *J. Prakt. Chem.*, **115**, 292 (1927).

10) W. Schindler, and F. Häfliger, *Helv. Chim. Acta*, **37**, 472 (1954).

5,6,7,8-Tetrahydro-9H-pyrimido[4,5-b]azepine (9).

ϵ -Caprolactam (1.13 g, 0.01 mol) gave 0.11 g of **9** after recrystallization from *n*-hexane; mp 99.5–101 °C; mol wt 149 (100%) (mass); NMR (δ) CDCl_3 : 1.6–2.1 (m, 4H), 2.5–2.9 (m, 2H), 3.2–3.5 (m, 2H), 5.85 (broad s, 1H), 8.04 (s, 1H), 8.40 (s, 1H); UV ($m\mu$) λ_{max} (ϵ) H_2O (pH 1): 274 (11500); H_2O (pH 11): 251 (7640), 282 (5210). Found: C, 64.16; H, 7.24; N, 28.10%. Calcd for $\text{C}_8\text{H}_{11}\text{N}_3$: C, 64.40; H, 7.43; N, 28.17%.

4-Amino-6,7-dihydro-5H-cyclopenta[d]pyrimidine (10).

Adipamide (1.44 g, 0.01 mol) yielded 0.19 g of **10**; mp 231–234 °C (lit.⁹) 235–238 °C; mol wt 135 (100%) (mass); NMR (δ) d_6 -DMSO: 1.65–2.35 (m, 2H), 2.45–2.95 (m, 4H), 6.55 (broad s, 2H), 8.20 (s, 1H); UV ($m\mu$) λ_{max} (ϵ) H_2O (pH 11): 238 (10800), 266 (5640) [lit.⁹] H_2O (pH 13) 237 (8610), 266 (5370). Found: C, 61.94; H, 6.67; N, 30.98%.

Purine (12). Following the general procedure, 1.10 g of glycineamide hydrochloride (0.01 mol) was reacted with FA-POCl_3 . Chromatography on Amberlite CG-120 and silica gel [$\text{MeOH}:\text{CHCl}_3$ (1:1)] yielded 0.09 g of **12**. The IR spectra agreed well with that of an authentic sample.

5,6-Dihydro-11H-benz[2,3]azepino[7,6-d]pyrimidine (15a).

1,3,4,5-Tetrahydro-2H-1-benzazepin-2-one (**13a**, 1.61 g, 0.01 mol) gave 0.57 g of **15a**; mp 168–170.5 °C; NMR (δ) d_6 -DMSO: 3.02 (s, 4H), 6.75–7.35 (m, 4H), 8.13 (broad s, 1H), 8.15 (s, 1H), 8.57 (s, 1H). Found: C, 72.67; H, 5.53; N, 21.15%. Calcd for $\text{C}_{12}\text{H}_{11}\text{N}_3$: C, 73.07; H, 5.62; N, 21.31%.

9-Chloro-5,6-dihydro-11H-benz[2,3]azepino[7,6-d]pyrimidine (15b).

8-Chloro-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (**13b**, 1.96 g, 0.01 mol) gave 0.97 g of **15b**, mp 177–178 °C; NMR (δ) CDCl_3 : 3.00 (s, 4H), 6.8–7.2 (m, 3H), 8.15 (broad s, 1H), 8.21 (s, 1H), 8.61 (s, 1H). Found: C, 62.00; H, 4.35; N, 18.44; Cl, 15.47%. Calcd for $\text{C}_{12}\text{H}_{10}\text{N}_3\text{Cl}$: C, 62.21; H, 4.35; N, 18.14; Cl, 15.30%.

8-Methoxy-5,6-dihydro-11H-benz[2,3]azepino[7,6-d]pyrimidine (15c).

7-Methoxy-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (**13c**, 1.91 g, 0.01 mol) yielded 0.08 g of **15c**; mp 145–146 °C; NMR (δ) CDCl_3 : 2.99 (s, 4H), 3.79 (s, 3H), 6.6–6.9 (m, 2H), 6.85 (s, 1H), 8.05 (broad s, 1H), 8.15 (s, 1H), 8.53 (s, 1H). Found: C, 68.80; H, 5.56; N, 18.30%. Calcd for $\text{C}_{13}\text{H}_{13}\text{ON}_3$: C, 68.70; H, 5.77; N, 18.49%.

11-(3-Dimethylaminopropyl)-5,6-dihydro-11H-benz[2,3]azepino[7,6-d]pyrimidine (16a).

1-(3-Dimethylaminopropyl)-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (**14a**, 2.46 g, 0.01 mol) gave a yellow powder of **16a** (0.14 g); NMR (δ) CDCl_3 : 1.6–2.1 (m, 2H), 2.12 (s, 6H), 2.2–2.35 (m, 2H), 3.00 (s, 4H), 4.22 (t, $J=11$ Hz, 2H), 7.0–7.3 (m, 4H), 8.20 (s, 1H), 8.52 (s, 1H).

The dihydrochloride was prepared and recrystallized from EtOH-ether; mp 233–234 °C. Found: C, 57.49; H, 7.20;

N, 16.06; Cl, 19.99%. Calcd for $\text{C}_{17}\text{H}_{22}\text{N}_4 \cdot 2\text{HCl}$: C, 57.47; H, 6.81; N, 15.77; Cl, 19.96%.

9-Chloro-11-(3-dimethylaminopropyl)-5,6-dihydro-11H-benz[2,3]azepino[7,6-d]pyrimidine (16b).

Method 1: Following the general procedure, 8-chloro-1-(3-dimethylaminopropyl)-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (**14b**, 2.81 g, 0.01 mol) gave 0.57 g of **16b**; mp 93–94 °C; NMR (δ) CDCl_3 : 1.5–2.0 (m, 2H), 2.15 (s, 6H), 2.25–2.45 (m, 2H), 2.97 (s, 4H), 4.18 (t, $J=12$ Hz, 2H), 7.05–7.3 (m, 3H), 8.11 (s, 1H), 8.61 (s, 1H).

The dihydrochloride was prepared and recrystallized from EtOH-ether; mp 234–235 °C. Found: C, 51.92; H, 5.78; N, 14.41; Cl, 26.96%. Calcd for $\text{C}_{17}\text{H}_{21}\text{N}_4\text{Cl} \cdot 2\text{HCl}$: C, 52.39; H, 5.95; N, 14.37; Cl, 27.29%.

Method 2: To a solution of 9-chloro-5,6-dihydro-1H-benz[2,3]azepino[7,6-d]pyrimidine (**15b**, 1.16 g, 0.005 mol) and 3-dimethylaminopropylchloride (1.83 g, 0.015 mol) in 4 ml of DMSO, 0.43 g of NaH (54% in mineral oil) in 6 ml of DMSO was added with stirring under nitrogen. After being stirred for 4 hr at room temperature, the reaction mixture was poured into 30 ml of water and extracted with 2×20 ml ether. The usual work up and chromatography on basic alumina using benzene: ethyl acetate (1:1) as solvent yielded 0.62 g of **16b**.

The following compounds (**14a** and **14b**) were prepared by this method.

1-(3-Dimethylaminopropyl)-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (14a).

1,3,4,5-Tetrahydro-2H-1-benzazepin-2-one (**13a**, 16.1 g, 0.1 mol) gave a yellow oil of **14a** which did not crystallize (17.4 g); NMR (δ) CDCl_3 : 1.5–2.0 (m, 2H), 2.14 (s, 6H), 2.15–2.35 (m, 4H), 2.35–2.45 (m, 2H), 2.6–2.9 (m, 2H), 3.90 (t, $J=11$ Hz, 2H), 7.1–7.3 (m, 4H). Found: C, 73.21; H, 9.18; N, 11.55%. Calcd for $\text{C}_{15}\text{H}_{22}\text{ON}_2$: C, 73.13; H, 9.00; N, 11.37%.

8-Chloro-1-(3-dimethylaminopropyl)-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (14b).

8-Chloro-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (**13b**, 45.0 g, 0.23 mol) gave a yellow oil of **14b** (44.3 g); NMR (δ) d_6 -DMSO: 1.4–1.9 (m, 2H), 2.10 (s, 6H), 2.1–2.4 (m, 6H), 2.45–2.8 (m, 2H), 3.82 (t, $J=12$ Hz, 2H), 7.25 (d, 2H), 7.43 (broad s, 1H). Found: C, 63.73; H, 7.64; N, 9.46; Cl, 12.37%. Calcd for $\text{C}_{15}\text{H}_{21}\text{ON}_2\text{Cl}$: C, 64.16; H, 7.54; N, 9.98; Cl, 12.63%.

The hydrochloride was recrystallized from EtOH-ether; mp 160–161 °C. Found: C, 56.77; H, 7.15; N, 8.82; Cl, 22.12%. Calcd for $\text{C}_{15}\text{H}_{21}\text{ON}_2\text{Cl} \cdot \text{HCl}$: C, 56.80; H, 6.99; N, 8.83; Cl, 22.35%.

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