Pyrimidines. 24. Analogues and Derivatives of 2-Amino-5-bromo-6-phenyl-4(3*H*)-pyrimidinone (ABPP)

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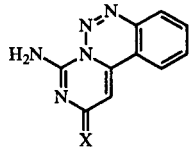
Received December 11, 1992

Dedicated to the memory of Roland K. Robins

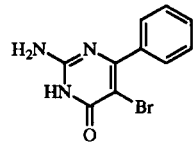
Preparation of a number of derivatives of 2-amino-5-bromo-6-phenyl-4(3*H*)-pyrimidinone (ABPP) including the 2-dialkylaminoalkylamino-, 2-hydroxyalkylamino-, 2-ethoxycarbonylamino- and 2-alkylaminocarbonylamino- groups substituted on the pyrimidine ring as well as preparation of 1-(alkylaminoalkyl)-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidines and 3,5-dioxo-7-phenyl-1,2,3,5-tetrahydroimidazo-[1,2-*a*]pyrimidines with or without the bromo-substitution are reported.

J. Heterocyclic Chem., **30**, 1273 (1993).

In an attempt to synthesize some pyrimido[1,6-*c*][1,2,3]-benzotriazines **1**, Brown and Stevens prepared several pyrimidine intermediates [1]. Among these compounds, 2-amino-5-bromo-6-phenyl-4(3*H*)-pyrimidinone (ABPP, 2), was subsequently found to induce high levels of interferons in the serum of mice upon intraperitoneal, subcutaneous or oral administration [2]. In addition, this 6-phenylpyrimidinone was also reported to possess antiviral [3,4] and antitumor activity against B16 melanoma [3,5].



1 X = O, NH



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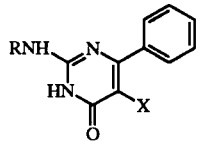
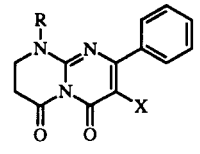
A number of analogues of ABPP with the modifications at the 5-halo and 6-aryl positions [6] as well as a series of *N*-substituted derivatives [7] were prepared for screening of interferon-inducing antiviral activity and diuretic, hypotensive and antiinflammatory properties. In connection with our continuing exploration in uncovering novel antineoplastic agents, some selected derivatives of ABPP (**3**), the cyclized tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidines **4** and 1,2,3,5-tetrahydroimidazo[1,2-*a*]pyrimidines **5** were prepared in this laboratory.

Treatment of ABPP with 2-bromoethanol in 2-propanol, in the presence of potassium carbonate, yielded 5-bromo-2-hydroxyethylamino-6-phenyl-4(3*H*)-pyrimidinone (**3a**). The corresponding 2-(2-dimethylamino)ethylamino- **3b** and 2-(3-diethylamino)propylamino- **3c** derivatives, isolated as their hydrochloride salts, were prepared from ABPP with 2-dimethylaminoethyl chloride and 3-dimethylaminopropyl chloride, respectively. Using pyridine as both a solvent and an acid scavenger, the 2-ethoxycarbonylamino derivative of ABPP was prepared from both ABPP (to give **3d**) and the corresponding 5-unsubstituted analogue (to give **3e**). Diethylaminocarbonyl chloride in pyridine also converted ABPP to the 2-diethylaminocarbonylamino derivative **3f**. Both compounds **3d** and **3e** were further converted to the substituted amides **3g-3i** with appropriate amines.

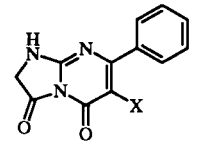
Both ethyl bromopropionate and ethyl bromoacetate, in the presence of potassium carbonate, not only condensed with ABPP and the unbrominated analogue but also underwent further cyclization to form 4,6-dioxo-8-phenyl-



3a X = Br, R = $(CH_2)_2$-OH
b X = Br, R = $(CH_2)_2$-$N(CH_3)_2$•HCl
c X = Br, R = $(CH_2)_3$-$N(CH_3)_2$•HCl
d X = Br, R = $CO_2C_2H_5$
e X = H, R = $CO_2C_2H_5$
f X = Br, R = CO-$N(C_2H_5)_2$
g X = Br, R = $CONH(CH_2)_2$-OH
h X = Br, R = $CONH(CH_2)_2$-$N(CH_3)_2$
i X = H, R = $CONH(CH_2)_2$-$N(CH_3)_2$



4a X = Br, R = H
b X = H, R = H
c X = Br, R = $(CH_2)_2$-$N(CH_3)_2$•HCl
d X = Br, R = $(CH_2)_3$-$N(CH_3)_2$•HCl
e X = H, R = $(CH_2)_2$-$N(CH_3)_2$•HCl
f X = H, R = $(CH_2)_3$-$N(CH_3)_2$•HCl
g X = Br, R = CH_2-$CO_2C_2H_5$
h X = H, R = CH_2-$CO_2C_2H_5$
i X = Br, R = CH_2-CO_2H



5a X = Br,
b X = H

2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidines **4**, (X = Br, H) and 3,5-dioxo-7-phenyl-1,2,3,5-tetrahydroimidazo-[1,2-*a*]pyrimidines **5**, (X = Br, H), respectively. Position-1 of compounds **4** can be further derivatized by reacting with appropriate alkyl halides in the presence of potassium carbonate.

In contrast to general *O*-alkylation reactions, the *N*-alkylation reactions of compounds of this type are rather critical and depend on many factors including relative amount of reactants, rate of addition, type of solvent, reaction temperature and method of purification. These are provided in the following section.

EXPERIMENTAL

5-Bromo-2-hydroxyethylamino-6-phenyl-4(3*H*)-pyrimidinone (**3a**).

To a suspension of 1.33 g (5 mmoles) of 2-amino-5-bromo-6-phenyl-4(3*H*)-pyrimidone (**2**, ABPP) [1] and 2.07 g (15 mmoles) of anhydrous potassium carbonate in 50 ml of 2-propanol was added dropwise, with stirring, a solution of 1 g (8 mmoles) of 2-bromoethanol dissolved in 20 ml of 2-propanol at 75-80°. The addition took 5 hours. The reaction mixture was then stirred at 75-80° for another 15 hours and evaporated under reduced pressure to almost dryness. To the residue was added 16 ml of water. The resulting suspension was heated to boiling and 2-propanol was added dropwise, with stirring, into the suspension until a complete solution was achieved. A small amount of insoluble impurity was removed by filtration. The filtrate was chilled at 0° overnight and the resulting precipitate was collected by filtration to give 0.63 g of crude product. Recrystallization from a mixture of water and 2-propanol (1:1) gave 0.53 g (35% yield) of white crystals, mp 216-218°; uv (methanol): λ max 201 (log ε 4.17), 235 (log ε 4.17) and 310 nm (log ε 3.86); ms: 310 (M^+).

Anal. Calcd. for $C_{12}H_{12}BrN_3O_2$: C, 46.47; H, 3.90; N, 13.55. Found: C, 46.29; H, 3.90; N, 13.18.

5-Bromo-2-[(2-dimethylamino)ethylamino]-6-phenyl-4(3*H*)-pyrimidinone Hydrochloride (**3b**).

To a suspension of 1.31 g (5 mmoles) of ABPP and 2.76 g (20 mmoles) of anhydrous potassium carbonate in 40 ml of 2-propanol was added dropwise, with stirring, a solution of 1.25 g (10 mmoles) of 2-dimethylaminoethyl chloride hydrochloride in a 5:4 (60 ml) mixture of dimethylformamide and 2-propanol at 75-85°. The slow addition took 5 hours. After which the mixture was stirred at that temperature for an additional 16 hours (no starting material was present at that time, as evidenced by tlc) and cooled to 0° overnight. The reaction mixture was filtered and the solids washed with 2-propanol. The filtrate and washings were combined and evaporated under reduced pressure to *ca* 6 ml. The resulting light brown liquid was dropped into a solution of 75 ml of absolute ethanol containing 1 ml of concentrated hydrochloric acid whereupon a precipitate formed. This acid mixture was heated to boiling. Water was slowly added to the boiling mixture until all solids dissolved. The solution was allowed to cool overnight. The resulting white crystals were collected by filtration, washed with a small amount of absolute ethanol and ether to give, after drying, 0.83 g (45% yield) of **3b**, mp 241-242°.

Anal. Calcd. for $C_{14}H_{17}BrN_4O\cdot HCl$: C, 45.00; H, 4.86; N, 14.99. Found: C, 45.30; H, 4.78; N, 15.00.

In a similar manner, 5-bromo-2-[(3-dimethylamino)propylamino]-6-phenyl-4(3*H*)-pyrimidinone hydrochloride (**3c**) was prepared from 1.33 g (5 mmoles) of ABPP, 0.95 g (6 mmoles) of 3-dimethylaminopropyl chloride hydrochloride and 1.66 g (12 mmoles) of potassium carbonate. The yield of **3c**, after recrystallized from 1-butanol, was 48% (0.93 g), mp 246-247° dec.

Anal. Calcd. for $C_{15}H_{19}BrN_4O\cdot HCl$: N, 14.45. Found: N, 14.24.

5-Bromo-2-ethoxycarbonylamino-6-phenyl-4(3*H*)-pyrimidinone (**3d**).

A mixture of 1.33 g (5 mmoles) of ABPP and 50 ml of dry pyridine was heated with stirring. After a solution was achieved, it was cooled in an ice bath. To this was added dropwise, with stirring, 0.58 g (5.3 mmoles) of ethyl chloroformate in 150 ml of toluene. The addition took 25 minutes. The mixture was stirred at 0° for 2 hours, at room temperature for 3.5 hours, then at 100° for 30 minutes. It was evaporated to dryness. To the residue was added 50 ml of water. The solid was carefully pulverized and filtered. The resulting solid was added to 20 ml of 6*N* hydrochloric acid and the mixture was evaporated to dryness. The residue was recrystallized from benzene to give 0.55 g (33% yield) of **3d**, mp 198°.

Anal. Calcd. for $C_{13}H_{12}BrN_3O_3$: C, 46.17; H, 3.55; N, 12.43. Found: C, 46.21; H, 3.69; N, 12.30.

2-Ethoxycarbonylamino-6-phenyl-4(3*H*)-pyrimidinone (**3e**).

This compound was prepared in an analogous manner as described for **3d** from 9 g (48 mmoles) of 2-amino-6-phenyl-4(3*H*)-pyrimidinone [6], 15.6 g (144 mmoles) of ethyl chloroformate and 150 ml of dry pyridine. After the purification process and recrystallization from ethanol, 6.4 g (51% yield) of **3e** was obtained, mp 217-218°.

Anal. Calcd. for $C_{13}H_{13}N_3O_3$: C, 60.22; H, 5.05; N, 16.21. Found: C, 60.57; H, 5.29; N, 16.17.

5-Bromo-2-[(diethylaminocarbonyl)amino]-6-phenyl-4(3*H*)-pyrimidinone (**3f**).

A mixture of 1.33 g (5 mmoles) of ABPP in 50 ml of dry pyridine was heated until a clear solution was obtained. With stirring, a solution of 1.36 g (10 mmoles) of diethylcarbamyl chloride in 15 ml of toluene was added dropwise to the pyridine solution in one hour. The resulting solution was stirred at room temperature overnight. Its volume was reduced to 15 ml under reduced pressure then poured into 100 ml of water with stirring. After chilling at 0° for 2 hours, the precipitated solid product was collected by filtration. It was washed with water, dried and recrystallized from 2-propanol to give 0.8 g (44% yield) of pure **3f** as white needles, mp 139-140°.

Anal. Calcd. for $C_{15}H_{17}BrN_4O_2$: C, 49.33; H, 4.69; N, 15.34. Found: C, 49.45; H, 4.84; N, 15.45.

5-Bromo-2-[(2-hydroxyethyl)aminocarbonylamino]-6-phenyl-4(3*H*)-pyrimidinone (**3g**).

A mixture of 1.69 g (5 mmoles) of **3d** and 50 ml of dry dioxane was stirred until all solids dissolved. To the solution was added 0.62 g (10 mmoles) of ethanolamine. The mixture was refluxed for 25 hours and cooled overnight. The resulting precipitate was collected by filtration, washed with dioxane and ether. The crude product, which contained a small amount of ABPP, was purified by dissolving in 9*N* hydrochloric acid. The acidic solution was poured into 300 ml of water. The resulting precipitate was collected by filtration, washed with water and recrystallized from a

mixture of dimethylformamide and ethanol (1:5) to give 0.95 g (54% yield) of pure **3g**, mp 220-221°.

Anal. Calcd. for $C_{13}H_{13}BrN_4O_3$: C, 44.21; H, 3.71; N, 15.86. Found: C, 44.40; H, 3.53; N, 15.73.

5-Bromo-2-[(2-dimethylaminoethyl)aminocarbonylamino]-6-phenyl-4(3*H*)-pyrimidinone (**3h**).

To a stirred solution of 1.69 g (5 mmoles) of **3d** in 70 ml of toluene was added 0.88 g (10 mmoles) of *N,N*-dimethylethylenediamine. The mixture was refluxed for 15 hours, after which it was evaporated to dryness under reduced pressure. To the residue was added 50 ml of 2-propanol. The mixture was boiled for 10 minutes and cooled to room temperature. The resulting solids were separated by filtration and washed with ether. The crude product (1.42 g) was suspended in 30 ml of ethanol and heated to boiling. To the boiling mixture was added dropwise, with stirring, dimethylformamide until a complete solution was obtained. The solution was cooled at 0° overnight. The resulting finely powdered crystals were collected by filtration, washed with ether and dried to give 1.1 g (58% yield) of **3h**, mp 203-204°.

Anal. Calcd. for $C_{15}H_{18}BrN_5O_2$: C, 47.38; H, 4.77; N, 18.42. Found: C, 47.24; H, 4.90; N, 18.24.

2-[(2-Dimethylaminoethyl)aminocarbonylamino]-6-phenyl-4(3*H*)-pyrimidinone (**3i**).

This compound was prepared in a manner similar to that for the preparation of **3h** from 5.1 g (20 mmoles) of the pyrimidinecarboxylic ethyl ester **3e**, 3.53 g (40 mmoles) of *N,N*-dimethylethylenediamine and 150 ml of toluene. Compound **3i** was obtained in 58% yield (3.5 g), mp 230-231°; ms: 301 (M^+).

Anal. Calcd. for $C_{15}H_{19}N_5O_2$: C, 59.78; H, 6.36; N, 23.24. Found: C, 59.80; H, 6.31; N, 23.27.

7-Bromo-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine (**4a**).

To a stirred mixture of 1.31 g (5 mmoles) of ABPP, 1.43 g (11 mmoles) of potassium carbonate and 50 ml of 2-propanol heated at 75° was added dropwise, in 6 hours, a solution of 1.45 g (8 mmoles) of ethyl 3-bromopropionate in 20 ml of 2-propanol. After which the mixture was stirred for an additional 18 hours at 75°. It was then cooled at 0° and the solid was collected by filtration. The crude product was washed well with a large amount of water until the *p*H of the filtrate was 7. The remaining solid was air-dried (1.42 g) then dissolved in 50 ml of boiling dimethylformamide. The solution was cooled and to it was added 20 ml of ethanol. After overnight standing the precipitated white solids were collected by filtration and washed with 100 ml of ether to give, after drying at 130° under reduced pressure for 6 hours, 1.32 g (79% yield) of **4a**. The product initially melted at 270-271°, which resolidified at higher temperature and remelted at 291° dec; ms: 320 (M^+), indicating that the product was the monohydrate of the product rather than the uncyclized 5-bromo-2-[(2-carboxyethyl)-amino]-6-phenyl-4(3*H*)-pyrimidinone.

Anal. Calcd. for $C_{13}H_{10}BrN_3O_2 \cdot H_2O$: C, 46.17; H, 3.58; N, 12.43. Found: C, 46.30; H, 3.50; N, 12.68.

4,6-Dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine (**4b**).

This compound was prepared in a similar fashion as for the preparation of **4a** from 0.94 g (5 mmoles) of 2-amino-6-phenyl-4(3*H*)-pyrimidinone [6], 1.12 g (8 mmoles) of potassium carbonate, 1.45 g (8 mmoles) of ethyl 3-bromopropionate and 70 ml of 2-propanol. The yield of **4b** was 31% (0.38 g), mp 300-301°.

Anal. Calcd. for $C_{13}H_{11}N_3O_2$: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.50; H, 4.70; N, 17.30.

7-Bromo-1-(2-dimethylaminoethyl)-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine Hydrochloride (**4c**).

To a mixture of 1.64 g (5 mmoles) of **4a** in 50 ml of 2-propanol containing 1.66 g (12 mmoles) of potassium carbonate heated at 80° was added dropwise, with stirring, 0.86 g (6 mmoles) of 2-dimethylaminoethyl chloride hydrochloride in a mixture of 10 ml of dimethylformamide and 10 ml of 2-propanol. After the addition, which took five hours, the mixture was stirred at 75-85° for another 16 hours. The reaction mixture was filtered while hot and the solids were washed with 30 ml of hot 2-propanol. The combined filtrate and washings were evaporated to dryness. To the residue was added 75 ml of 95% ethanol, then acidified with concentrated hydrochloric acid to *p*H 1. The mixture was heated to boiling and filtered. The filtrate was evaporated to dryness and the residue recrystallized from 1-butanol to give 0.8 g (35% yield) of **4c**, mp 263° dec.

Anal. Calcd. for $C_{17}H_{19}BrN_4O_2 \cdot HCl \cdot H_2O$: C, 45.80; H, 4.98; N, 12.57. Found: C, 45.89; H, 4.82; N, 12.44.

7-Bromo-1-(3-dimethylaminopropyl)-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine Hydrochloride (**4d**).

This compound was prepared in a similar manner as that for the preparation of **4c** from 1.69 g of **4a**, 1.66 g of potassium carbonate, 50 ml of 2-propanol and 0.95 g of 3-dimethylaminopropyl chloride hydrochloride in 20 ml of dimethylformamide. After recrystallized from 1-butanol, 0.93 g (41% yield) of **4d** was obtained, mp 246-247° dec.

Anal. Calcd. for $C_{18}H_{21}BrN_4O_2 \cdot HCl \cdot 1/2H_2O$: C, 48.01; H, 5.15; N, 12.44. Found: C, 47.90; H, 5.43; N, 12.36.

1-(2-Dimethylaminoethyl)-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine Hydrochloride (**4e**).

This compound was similarly prepared from 1.21 g of 2-amino-6-phenyl-4(3*H*)-pyrimidinone, 1.96 g of potassium carbonate, 85 ml of 2-propanol and 1.01 g of 2-dimethylaminoethyl chloride hydrochloride in 20 ml of dimethylformamide. The yield of **4e** was 56% (1.14 g), mp 221-222° dec.

Anal. Calcd. for $C_{17}H_{20}N_4O_2 \cdot HCl \cdot 1/4H_2O$: C, 57.79; H, 6.13; N, 15.95. Found: C, 57.72; H, 6.33; N, 15.95.

1-(3-Dimethylaminopropyl)-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine (**4f**).

This compound was similarly prepared from 1.21 g of 2-amino-6-phenyl-4(3*H*)-pyrimidinone, 1.66 g of potassium carbonate, 50 ml of 2-propanol and 0.95 g of 3-dimethylaminopropyl chloride hydrochloride in 20 ml of dimethylformamide. The yield of **4f** was 35% (0.65 g), mp 197-198°.

Anal. Calcd. for $C_{18}H_{21}N_4O_2 \cdot HCl \cdot 1/2H_2O$: C, 58.14; H, 6.23; N, 15.07. Found: C, 57.87; H, 6.56; N, 14.98.

7-Bromo-1-ethoxycarbonylmethyl-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine (**4g**).

To 1.64 g (2.5 mmoles) of **2** and 1.4 g (10 mmoles) of potassium carbonate in 50 ml of dioxane heated at 90-100° was added dropwise 1.69 g (10 mmoles) of ethyl bromoacetate in 20 ml of dioxane. After the addition was complete (which took 5 hours), the mixture was stirred at the same temperature for another 18

hours. Analysis (tlc) of the reaction mixture indicated that some starting material was still present. To the mixture was thus added an additional 0.7 g (5 mmoles) of potassium carbonate and 0.84 g (5 mmoles) of ethyl bromoacetate in 10 ml of dioxane at 90-100° at a comparable rate. Stirring was continued for 6 hours. The mixture was cooled to room temperature and filtered. The filtrate was evaporated to dryness and the residue recrystallized from 2-propanol to give 1.24 g (63% yield) of pure **4g**, mp 187-188°.

Anal. Calcd. for $C_{17}H_{16}BrN_3O_4$: C, 50.26; H, 3.97; N, 10.34. Found: C, 50.14; H, 4.01; N, 10.25.

1-Ethoxycarbonylmethyl-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine (**4h**).

This compound was prepared in a similar manner as described for the preparation of **4g** except that the temperature of addition was kept at 80°. From 1.44 g of 2-amino-6-phenyl-4(3*H*)-pyrimidinone, 3.32 g of potassium carbonate in 60 ml of dioxane and 4.0 g of ethyl bromoacetate in 20 ml of dioxane there was obtained, after recrystallization from ethanol, 1.4 g (72% yield) of **4h**, mp 158.5-159.5°.

Anal. Calcd. for $C_{17}H_{17}N_3O_4$: C, 62.37; H, 5.24; N, 12.84. Found: C, 62.19; H, 5.36; N, 12.88.

7-Bromo-1-carboxymethyl-4,6-dioxo-8-phenyl-2,3,4,6-tetrahydro-1*H*-pyrimido[1,2-*a*]pyrimidine (**4i**).

One g of **4g** and 0.9 g of potassium carbonate in 50 ml of water was refluxed for two hours. The mixture was filtered and the filtrate was acidified with 6*N* hydrochloric acid. The resulting white solid product was collected by filtration and washed with ether (0.87 g). It was recrystallized from 100 ml of 60% ethanol to give 0.60 g (65% yield) of **4i** as white crystals, mp 236° dec.

Anal. Calcd. for $C_{15}H_{12}BrN_3O_4$: C, 47.64; H, 3.20; N, 11.11. Found: C, 47.42; H, 3.38; N, 10.94.

6-Bromo-3,5-dioxo-7-phenyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]-pyrimidine (**5a**).

To a refluxed mixture of 1.31 g (5 mmoles) of **2**, 1.43 g (11 mmoles) of potassium carbonate and 50 ml of 2-propanol was added dropwise (8 hours), 0.92 g (5.5 mmoles) of ethyl bromoacetate in 20 ml of 2-propanol. After the addition the mixture was refluxed and stirred continuously for another 12 hours. It was evaporated to dryness under reduced pressure. The resulting white powder was dissolved in 60 ml of water and acidified with 6*N* hydrochloric acid to *p*H 1. The precipitated white solid was collected by filtration and thoroughly washed with water. It was recrystallized from a mixture of ethanol and dimethylformamide to give 0.85 g (57% yield) of **5a**, mp 233-234°; ms: 306 (M^+).

Anal. Calcd. for $C_{12}H_8BrN_3O_2$: C, 47.08; H, 2.63; N, 13.73. Found: C, 46.95; H, 2.60; N, 13.48.

3,5-Dioxo-7-phenyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyrimidine (**5b**).

This compound was similarly prepared from 5.61 g (30 mmoles) of 2-amino-6-phenyl-4(3*H*)-pyrimidinone, 5.4 g (39 mmoles) of potassium carbonate in 250 ml of 2-propanol with 6.63 g (39 mmoles) of ethyl bromoacetate in 20 ml of 2-propanol. The yield, after recrystallization from dimethylformamide-water (5:2) was 59% (4.0 g). The white crystals melted at 294-295° dec.

Anal. Calcd. for $C_{12}H_9N_3O_2 \cdot 1/2H_2O$: C, 61.01; H, 4.27; N, 17.79. Found: C, 61.10; H, 4.19; N, 17.96.

Acknowledgments.

The authors thank the Wesley Foundation for the financial support of this study (Grant No. 8704020). They also thank the M-H-W Laboratories, Phoenix, AZ for conducting the elemental analyses and to Katherine Cheng for characterization of these compounds.

REFERENCES AND NOTES

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[1] T. B. Brown and M. F. G. Stevens, *J. Chem. Soc., Perkin Trans. I*, 1023 (1975).

[2] W. Wierenga, H. I. Skulnick, D. A. Stringfellow, S. D. Weed, H. E. Renis and E. E. Eidson, *J. Med. Chem.*, **23**, 237 (1980).

[3] D. A. Stringfellow, *Prog. Cancer Res. Ther.*, **16**, 215 (1981).

[4] J. D. Nelson and C. Grassi, eds, Current Chemotherapy and Infectious Diseases, American Association for Microbiology, Washington, D.C., 1980, p 1401 and p 1411.

[5] L. Milas, E. M. Hersh, D. A. Stringfellow and N. Hunter, *J. Nat. Cancer Inst.*, **68**, 139 (1982).

[6] H. I. Skulnick, S. D. Weed, E. E. Eidson, H. E. Renis, W. Wierenga and D. A. Stringfellow, *J. Med. Chem.*, **28**, 1864 (1985).

[7] H. I. Skulnick, J. H. Ludens, M. G. Wendling, E. M. Glenn, N. A. Rohloff, R. J. Smith and W. Wierenga, *J. Med. Chem.*, **29**, 1499 (1986).