Pyrimidinylalkylthiols, Furo[2,3-*d*]pyrimidines and Derivatives (1a)

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Several pyrimidinylalkylthiols and furo[2,3-*d*]pyrimidines and their derivatives have been prepared as potential radiation-protection agents.

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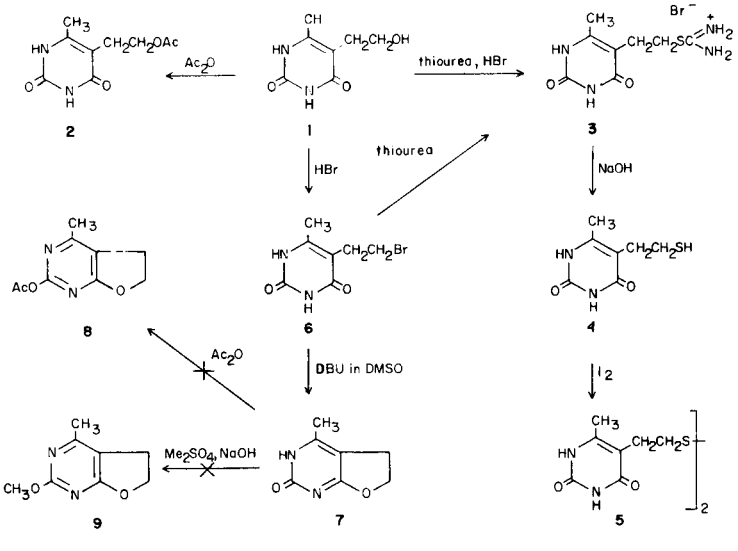
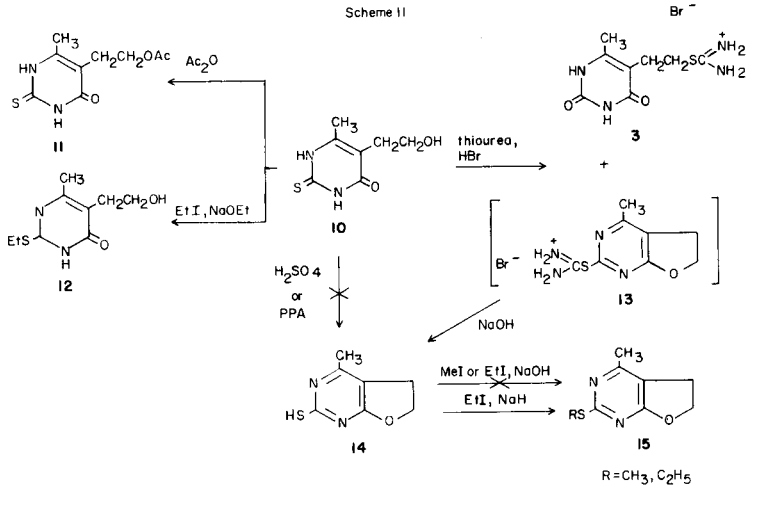
A great variety of organic compounds, primarily containing nitrogen and sulfur, have been shown to be active radiation-protection agents (2,3). Recently, several heterocyclic alkylthiols (pyrimidines and pyridines) (3-5) and glucosamines (6) have been prepared and screened as radiation-protection agents with varying degrees of success. As a continuation of our earlier work concerning the preparation of pyridylalkylthiols and their derivatives for

Scheme I



Scheme II



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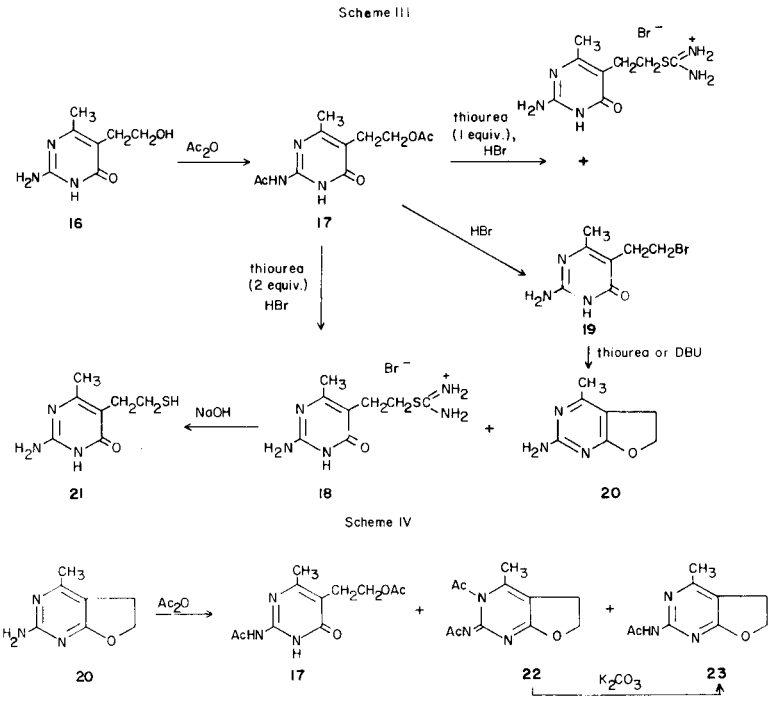

antiradiation screening (3), we now report the preparation of pyrimidinylalkylthiols, furo[2,3-*d*]pyrimidines and derivatives thereof as potential radiation-protection agents. The synthetic routes leading to the desired compounds are outlined in Schemes I-IV.

Compound **1**, the starting material for the synthetic sequence outlined in Scheme I, was prepared as reported in the literature (7), and could be acetylated in refluxing acetic anhydride to give **2**. Treatment of **1** with thiourea in the presence of hydrogen bromide gave the thiouronium bromide **3**, which could be hydrolyzed in base to give the ethylthiol derivative **4**. Subsequent reaction of **4** with iodine in methanol gave the disulfide **5**. 5-(2-Bromoethyl)-6-methyluracil (**6**) was prepared by treatment of **1** with hydrogen bromide. Compound **6** gave the thiouronium bromide **3** on treatment with thiourea in refluxing ethanol, and also produced the ring closed furo[2,3-*c*]pyrimidine derivative **7** on reaction with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) in DMSO.

DBU was originally introduced as a superior reagent for the introduction of double bonds by the removal of hydrogen halides (8). It was later reported as a useful cyclizing reagent for the synthesis of pyrroles (9) and oxazoles (10), and most recently has been shown to be an effective reagent for the formation of esters from acids and alkyl halides (11). This last reaction parallels the cyclization reaction used to obtain **7**.

In an attempt to acetylate **7** in refluxing acetic anhydride for four hours, only the starting material could be isolated. The attempted methylation of **7** with dimethyl sulfate in aqueous sodium hydroxide also proved unsuccessful in obtaining the methoxyfuro[2,3-*d*]pyrimidine **9**; again, only starting material could be isolated from the reaction mixture. These results parallel the obstacles encountered in the acylation and *O*-alkylation of hydroxypyrimidines (12a).

Scheme II outlines the chemical transformations carried out with the thiouracil **10**, which was prepared according to the literature (7). The *O*-acylation and *S*-acylation of **10** were carried out in refluxing acetic anhydride and in ethyl iodide/sodium ethoxide in refluxing ethanol, respectively, to give **11** and **12**. Reaction of **10** with thiourea in refluxing aqueous hydrogen bromide gave a mixture of products, from which **3** could be isolated and characterized. The major product of this reaction could not be purified after repeated recrystallizations. This product was assumed to have the structure **13**; on reaction of the crude **13** with aqueous sodium hydroxide, compound **14** was obtained.

Compound **14** could not be *S*-alkylated with either methyl iodide or ethyl iodide in ethanolic sodium hydroxide. However, alkylation was accomplished with ethyl iodide and sodium hydride in *N,N*-dimethylformamide (DMF) to give **15** (R = Et). These results parallel the difficulty in the *S*-alkylation of 4-hydroxy-2-mercaptopyrimidine with alkyl halides in the presence of sodium hydroxide (12b). Compound **14** could also not be prepared *via* **10** on treatment with either sulfuric acid or polyphosphoric acid. In both cases, only a mixture of unidentified products was obtained.

Scheme III outlines the chemical transformations performed on the diacylated compound **17**, prepared from **16** (13) by reaction in refluxing acetic anhydride. Treatment of **17** with one equivalent of thiourea in refluxing aqueous hydrogen bromide gave a mixture of the thiouronium bromide **18** and the bromoethylpyrimidine **19**. This same reaction, when carried out with two equivalents of thiourea, yielded a mixture of **18** and the ring closed furo[2,3-*d*]pyrimidine **20**. Compound **20** could also be generated by reaction of **19** with additional thiourea or with DBU in DMF. Compound **19** was the sole product obtained in the reaction of **17** with refluxing hydrogen bromide. Compound **18** was further hydrolyzed to **21** by treatment with base.

Scheme IV outlines the results obtained in the reaction of **20** with acetic anhydride. Three products were isolated from this reaction mixture, namely, the previously discussed **17**, and two furo[2,3-*d*]pyrimidines **22** and **23**. Compound **22** could also be hydrolyzed in potassium carbonate to give the deacylated **23**.

EXPERIMENTAL

All melting points were taken on a Mel-Temp apparatus and are uncorrected. Ir spectra were taken on an IRA-2 JASCO spectrophotometer. Nmr spectra were recorded on a JNM-FX-100 JEOL instrument using TMS as the internal standard. Mass spectra were recorded on a JMS-01 SG JEOL spectrometer.

2-[5-(1,2,3,4-Tetrahydro-6-methyl-2,4-dioxopyrimidinyl)]ethyl Acetate (**2**).

A mixture of 3.0 g (0.0176 mole) of **1** (7) and 20 ml of acetic anhydride was refluxed for 4 hours and allowed to stand overnight. The resulting crystals were collected by filtration, washed with water and air dried to give 3.4 g of **2** (91% yield). Recrystallization from methanol gave colorless needles, m.p. 241-244°; ir (potassium bromide): ν max 1648 (C=O), 1708 (C=O), 1725 cm^{-1} (C=O); nmr (DMSO-d_6): δ 1.96 (3H, s), 2.05 (2H, t, J = 8 Hz), 3.94 (3H, t, J = 8 Hz), 10.54 (1H, s), 10.83 ppm (1H, s); uv (ethanol): λ max nm (log ϵ) 266 (3.97); ms: m/e 169 (M^+ - 43).

Anal. Calcd. for $C_9H_{12}N_2O_4$: C, 50.94; H, 5.70; N, 13.20. Found: C, 50.79; H, 5.67; N, 13.42.

2-[5-(1,2,3,4-Tetrahydro-6-methyl-2,4-dioxopyrimidinyl)]ethylthiouronium Bromide (**3**).

A mixture of 6.0 g. (0.0353 mole) of **1**, 2.7 g (0.0355 mole) of thiourea and 40 ml of 47% hydrogen bromide was refluxed for 3 hours. After cooling with ice water, the resulting crystals were collected by filtration, washed with water and acetone, and air dried to give 9.0 g (83% yield) of the thiouronium salt **3**, m.p. 290-294°. Recrystallization from water gave colorless needles, m.p. 292-293° dec; ir (potassium bromide): ν max 1650 (C=O), 1693 cm^{-1} (C=O); uv (ethanol): λ max nm (log ϵ) 270.

Anal. Calcd. for $C_8H_{13}BrN_4O_2S$: C, 31.07; H, 4.24; N, 18.12; S, 10.37. Found: C, 31.30; H, 4.26; N, 18.00; S, 10.58.

2-[5-(1,2,3,4-Tetrahydro-6-methyl-2,4-dioxopyrimidinyl)]ethanethiol (**4**).

A mixture of 7.0 g (0.175 mole) of sodium hydroxide in 100 ml of water and 22.0 g (0.071 mole) of thiouronium bromide **3** was heated on the steam bath for 1 hour under an atmosphere of nitrogen. After cooling, the reaction mixture was filtered and the filtrate was acidified with acetic acid. The resulting precipitate was collected by filtration to give 11.9 g (90% yield) of **4**, m.p. 252-256°. Recrystallization from methanol gave 9.1 g (69% yield) of **4** as colorless plates, m.p. 258-261° [lit. (14) mp 310°]; ir (potassium bromide): ν max 1660 (C=O), 1720 (C=O), 2530 cm^{-1} (SH); nmr (DMSO-d_6): δ 2.10 (3H, s), 2.28-2.66 (5H, the signal at 2.39 ppm disappeared upon addition of deuterium oxide), 10.54 (1H, s), 10.84 ppm (1H, s); uv (ethanol): λ max nm (log ϵ) 268 (4.00); ms: m/e 186 (M^+).

Anal. Calcd. for $C_7H_{10}N_2SO_2$: C, 45.14; H, 5.41; N, 15.05; S, 17.22. Found: C, 45.09; H, 5.41; N, 15.11; S, 17.35.

Bis[2-[5-(1,2,3,4-Tetrahydro-6-methyl-2,4-dioxopyrimidinyl)]ethyl]-disulfide (**5**).

To a solution of 1.0 g (5.4 mmoles) of **4** in 80 ml of methanol, was added 0.68 g (2.7 mmoles) of iodine at room temperature, and the solution was stirred for 1 hour. The resulting crystals were collected by filtration and washed with methanol and water, and finally air dried, giving 1.0 g of colorless needles, mp 328-330° dec (quantitative yield). Compound **5** was only sparingly soluble in the usual organic solvents. Recrystallization from DMF gave the disulfide as colorless crystals, mp 329-330° dec; ir (potassium bromide): ν max 1660 (C=O), 1726 cm^{-1} (C=O); nmr (trifluoroacetic acid): δ 2.43 (6H, s), 2.95 ppm (8H, s); uv (ethanol): λ max nm (log ϵ) 269, sparingly soluble in ethanol.

Anal. Calcd. for $C_{14}H_{18}N_4O_4S_2$: C, 45.39; H, 4.89; N, 15.13; S, 17.31. Found: C, 45.18; H, 4.85; N, 15.22; S, 17.24.

5-(2-Bromoethyl)-6-methylpyrimidine-2,4-(1*H*,3*H*)dione (**6**).

A mixture of 11.0 (0.0647 mole) of **1** and 60 ml of 47% hydrogen bromide was refluxed for 3 hours. After cooling, the resulting precipitate was collected by filtration, washed successively with water and 5% sodium bicarbonate and air dried, giving 14.1 g of **6** (94% yield). Recrystallization from a large volume of methanol gave colorless plates, mp 274-277°; ir (potassium bromide): ν max 1658 (C=O), 1720 cm^{-1} (C=O); nmr (DMSO-d_6): 2.10 (3H, s), 2.76 (2H, t, J = 8 Hz), 3.49 (2H, t, J = 8 Hz), 11.66 (1H, s), 11.96 (1H, s).

Anal. Calcd. for $C_7H_9BrN_2O_2$: C, 36.07; H, 3.89; N, 12.02. Found: C, 36.49; H, 3.94; N, 12.38.

5,6-Dihydro-4-methylfuro[2,3-*d*]pyrimidin-2-(3*H*)one (**7**).

To a solution of 6.9 g (0.03 mole) of **6** in 20 ml of DMSO, was added 4.5 g of DBU. The mixture was stirred at room temperature for 3 hours and then allowed to stand overnight. The resulting crystals were collected by filtration and washed with water to give 3.5 g (79% yield) of the cyclized compound **7** as colorless plates, mp > 350°. Recrystallization from methanol gave colorless fine plates (2.1 g, 47% yield), mp > 360°; ir (potassium bromide): ν max 1672 cm^{-1} (C=O); nmr (DMSO-d_6): δ 2.10 (3H, s), 2.96 (2H, t, J = 8 Hz), 4.60 (2H, t, J = 8 Hz), 10.46-11.08 ppm (1H, d); uv (ethanol): λ max nm (log ϵ) 287 (3.79).

Anal. Calcd. for $C_7H_8N_2O_2$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.26; H, 5.33; N, 18.08.

Preparation of **3** *via* **6**.

A mixture of 1.0 g (4.29 mmoles) of **3**, 0.33 g (4.34 mmoles) of thiourea and 20 ml of ethanol was refluxed for 2 hours. After cooling, the resulting crystals were collected by filtration to give colorless crystals, mp 288-289° dec (1.2 g, 91% yield). Recrystallization from water gave 0.85 g (64%) of **3** as colorless fine needles, mp 289-290° dec. Compound **3** was found to be identical with that prepared *via* compound **1** by mixed mp and ir spectral data.

2-[5-(1,2,3,4-Tetrahydro-6-methyl-4-oxo-2-thioxopyrimidinyl)]ethyl Acetate (**11**).

A mixture of 1.0 g (5.4 mmoles) of **10** (7) and 10.0 ml of acetic anhydride was refluxed for 6 hours and then allowed to stand at room temperature overnight. The resulting crystals were collected by filtration, washed with water and air dried to give 1.0 g (82% yield) of **11**. Recrystallization from methanol gave colorless prisms, mp 202-203°; nmr (DMSO-d_6): δ 1.96 (3H, s), 2.12 (3H, s), 2.56 (2H, t, J = 7 Hz), 4.00 (2H, t, J = 7 Hz), 12.11 (1H, s), 12.34 ppm (1H, s).

Anal. Calcd. for $C_9H_{12}N_2O_3S$: C, 47.37; H, 5.30; N, 12.28. Found: C, 47.53; H, 5.28; N, 12.51.

2-[5-(3,4-Dihydro-2-ethylthio-6-methyl-4-oxopyrimidinyl)]ethanol (**12**).

A mixture of 9.3 g (0.05 mole) of **10**, 8.0 g (0.051 mole) of ethyl iodide and sodium ethoxide [1.2 g (0.052 mole) of sodium in 60 ml of absolute ethanol], was refluxed for 4 hours. The reaction mixture was then evaporated to dryness under reduced pressure. The residue was triturated with water and acidified with acetic acid, and then extracted with chloroform. The usual work-up of the chloroform extracts gave 8.9 g of pale yellow crystals, mp 149-153°. Recrystallization from ethanol gave compound **12** as colorless fine needles, mp 154-155° (6.1 g, 57% yield) [lit. (7) mp 156-157°].

Reaction of **10** with Thiourea and Hydrogen Bromide.

A mixture of 15 g (0.0806 mole) of **10**, 6.2 g (0.0816 mole) of thiourea and 100 ml of 47% hydrogen bromide was refluxed for 7 hours. The reaction mixture was evaporated to dryness under reduced pressure and acetone was added to the residue. This mixture was allowed to stand for 1 hour. The resulting crystals were collected by filtration, yielding 19.0 g of product. These crystals were washed successively with methanol and were air dried to give 5.0 g (18% yield) of colorless crystals. Recrystallization from water gave 3.8 g (14% yield) of **3**, which was shown to be identical with the previously prepared sample by mixed mp and spectral data.

The methanolic solution from the above procedure was evaporated to dryness under reduced pressure to give 13.5 g of yellow crystals. These crystals were shown to be a mixture of several products (3-4 spots) by tlc. Compound **13** could not be purified further.

5,6-Dihydro-4-methyl-2-thiofuro[2,3-*d*]pyrimidine (**14**).

To a solution of 1.6 g of sodium hydroxide in 30 ml of water was added 3.9 g of the crude compound **13**. The resulting mixture was heated on a water bath for 1 hour. After cooling, the reaction mixture was acidified with acetic acid. The crystals which separated were collected by filtration to give 1.6 g of pale yellow crystals, mp 279-285° dec. Recrystalliztaion twice from methanol gave 0.6 g of yellow crystals, mp 286-290° dec. This product showed only one spot on tlc; nmr (trifluoroacetic acid): δ 2.55 (3H, s), 3.47 (2H, t, J = 8 Hz), 3.93 ppm (2H, t, J = 8 Hz); uv (ethanol): λ max nm (log ϵ) 224 (s, 3.90), 273 (3.86), 316 (3.99); ms: m/e 168 (M^+).

Anal. Calcd. for $C_7H_8N_2OS$: C, 49.98; H, 4.79; S, 19.06. Found: C, 49.93; H, 4.74; S, 19.17.

5,6-Dihydro-4-methyl-2-ethylthiofuro[2,3-*d*]pyrimidine (R = Et) (**15**).

Sodium hydride (0.34 g of a 50% dispersion in oil, 7.08 mmoles) was washed with anhydrous ether, and suspended in 20 ml of freshly distilled DMF. To this suspension was added 1.0 g of **14** in 10 ml of DMF. After this mixture was stirred at room temperature for 30 minutes, 1.8 g (0.0115 mole) of ethyl iodide was added with stirring. The reaction mixture changed from a yellow to red-brown in color after being stirred for 2 hours. The solvent was then removed *in vacuo* and a small portion of water was added to the resulting residue. This mixture was then acidified with acetic acid. The resulting acidic solution was extracted with ether and the extracts were washed with water and dried over sodium sulfate. The solvent was removed to give a yellow oil, which was chromatographed on a column of silica gel. Eluting with acetone-benzene (1:9) gave 0.3 g of **15** as a yellow oil; nmr (deuteriochloroform): δ 1.38 (3H, t, J = 8 Hz), 2.30 (3H, s), 3.08-3.48 (4H, m), 4.52 ppm (2H, q, J = 7 Hz); ms: m/e 196 (M^+); uv (ethanol): λ max nm (log ϵ): 225 (3.94), 242 (s, 3.62).

Anal. Calcd. for $C_9H_{12}N_2OS$: C, 55.07; H, 6.16; S, 16.34. Found: C, 54.68; H, 6.26; S, 16.58.

The picrate of **15** had mp 165-168° and was obtained as yellow needles from methanol.

Anal. Calcd. for $C_{15}H_{15}N_5O_8S$: C, 42.35; H, 3.55; N, 16.47; S, 7.54. Found: C, 42.21; H, 3.49; N, 16.45; S, 7.64.

2-[5-(2-Acetylamino-3,4-dihydro-6-methyl-4-oxopyrimidinyl)]ethyl Acetate (**17**).

A mixture of 15 g (0.0888 mole) of **16** (13) and 100 ml of acetic anhydride was refluxed for 6 hours. The reaction mixture was allowed to stand at room temperature for 24 hours, and the resulting crystals were collected by filtration and washed with water to give the crude **17**. Recrystallization from methanol gave 14.9 g of colorless needles, mp 198-200° (66.4% yield); ir (potassium bromide): ν C=O 1645, 1692, 1735 cm^{-1}; nmr (deuteriochloroform): δ 2.03 (3H, s), 2.32 (6H, s), 2.83 (2H, t, J = 7 Hz), 4.20 (2H, t, J = 7 Hz), 11.20-11.88 ppm (2H, broad).

Anal. Calcd. for $C_{11}H_{15}N_3O_4$: C, 52.17; H, 5.97; N, 16.59. Found: C, 52.19; H, 6.03; N, 16.71.

Reaction of **17** with Thiourea (1 Equivalent) and Hydrogen Bromide.

A mixture of 5.0 g (0.0198 mole) of **17**, 1.5 g (0.0197 mole) of thiourea and 40 ml of 47% hydrogen bromide was refluxed for 4 hours; the excess hydrogen bromide was removed by distillation *in vacuo*. To the resulting gummy residue, acetone was added and the solution was allowed to stand at room temperature for 2 hours with occasional shaking. The resulting crystals were collected by filtration giving 4.0 g of colorless crystals. These crystals were dissolved in water and the resulting solution was neutralized with 10% aqueous sodium bicarbonate. The crystals which separated were collected by filtration to give 2.2 g of crude 2-[5-(2-amino-3,4-dihydro-6-methyl-4-oxopyrimidinyl)]ethylthiouronium bromide (**18**), mp 239-244°. Recrystallization from water gave colorless needles, mp 255-257° (1.7 g, 27.9% yield); ir (potassium bromide): ν max 1660 (C=O), 3200 (NH_2), 3320 cm^{-1}; uv (ethanol): λ max nm (log ϵ) 392 (3.97).

Anal. Calcd. for $C_8H_{14}BrN_5OS$: C, 31.17; H, 4.58; N, 22.72; S, 10.40. Found: C, 30.95; H, 4.61; N, 22.49; S, 10.70.

The acetone layer from the above procedure was evaporated to dryness. The resulting residue was dissolved in water and neutralized with 10% aqueous sodium carbonate. The crystals which separated were collected by filtration to give 1.4 g of 2-amino-5-(2-bromoethyl)-6-methylpyrimidin-4-(3*H*)one (**19**). Recrystallization from methanol gave 0.7 g of colorless needles, mp 246-248° (15.3% yield); ir (potassium bromide): ν max 1640 (C=O), 3250, 3340 cm^{-1} (NH_2); nmr (DMSO-d_6): δ 2.34 (3H, s), 3.14 (2H, t, J = 8 Hz), 4.83 (2H, t, J = 8 Hz), 7.62-8.62 (2H, broad), 12.02-13.42 ppm (1H, broad).

Anal. Calcd. for $C_7H_{10}BrN_3O$: C, 36.22; H, 4.34; Br, 34.43; N, 18.11. Found: C, 35.87; H, 4.27; Br, 34.21; N, 18.12.

Reaction of **17** with Thiourea (2 Equivalents) and Hydrogen Bromide.

A mixture of 8.0 g (0.0316 mole) of **17**, 4.8 g of thiourea and 60 ml of 47% hydrogen bromide was refluxed for 4 hours; the excess hydrogen bromide was then removed *in vacuo*. Acetone was added to the residue; the resulting crystals were collected by filtration and washed with acetone giving 10.8 g of product. The crystalline product was dissolved in water and the aqueous solution was neutralized with 10% sodium carbonate. The crystals which separated were collected by filtration giving 6.0 g (58.6% yield) of the thiouronium salt **18**, mp 255-257°, as colorless needles. This compound was identical to an authentic sample prepared as has been described, by mixed melting point and ir spectral analysis.

The acetone layer from the above procedure was evaporated to dryness. Water was added to this residue and the resulting solution was neutralized with 10% sodium carbonate. The crystals which separated were collected by filtration to give 0.65 g of **20** (13.6% yield), as a colorless powder, mp >360°. Recrystallization from methanol gave a colorless powder, mp >360°; ir (potassium bromide): ν max 3160 (NH_2), 3320 cm^{-1}; nmr (DMSO-d_6): δ 2.11 (3H, s), 2.97 (2H, t, J = 8 Hz), 4.47 (2H, t, J = 8 Hz), 6.25 (2H, s). Compound **20** was identical with an authentic sample (13) by ir spectral comparison.

Anal. Calcd. for $C_7H_9N_3O$: C, 55.61; H, 6.00; N, 27.80. Found: C, 55.29; H, 5.97; N, 27.79.

Preparation of **19** *via* Reaction of **17** with Hydrogen Bromide.

A mixture of 6.8 g (0.0269 mole) of **17** and 60 ml of 47% hydrogen bromide was refluxed for 4 hours. The reaction mixture was then condensed *in vacuo*; the resulting residue was dissolved in water and was then made alkaline with 10% sodium carbonate. The crystals which formed were collected by filtration to give 5.8 g of colorless crystals, mp 237-241°. Recrystallization from methanol gave 4.1 g (65.8% yield) of **19** as colorless needles, mp 246-248°. This compound was identical to an authentic sample prepared as has been described, by mixed melting

point and ir spectral analysis.

Preparation of **20** *via* **19**.

Method A.

A solution of 0.4 g (1.72 mmoles) of **19**, 0.14 g (1.84 mmoles) of thiourea and 20 ml of ethanol was refluxed for 2 hours. The solvent was evaporated *in vacuo*; the residue was dissolved in water and then made alkaline with 10% sodium carbonate. The resulting precipitate was collected by filtration to give 0.25 g of a colorless powder (96% yield), mp >360°. Recrystallization from methanol gave a colorless powder, mp >360°. This compound was shown to be identical to that previously prepared by comparison of spectral data.

Method B.

To a warm solution of 1.15 g of **19** (4.96 mmoles) in 30 ml of DMF, was added 0.75 g (5.0 mmoles) of DBU. The solution was allowed to stand at room temperature for 3 hours. The crystals which formed were collected by filtration to give 0.7 g (94% yield) of **20**, mp >360°. This product was identical to an authentic sample of **20** by a comparison of spectral data.

2-[5-(2-Amino-3,4-dihydro-6-methyl-4-oxopyrimidinyl)]ethanethiol (**21**).

A mixture of 2.0 g (6.49 mmoles) of **18** and 0.6 g of sodium hydroxide in 10 ml of water was heated on a steam bath under an atmosphere of nitrogen for 1 hour. After cooling, the reaction mixture was acidified with acetic acid. The crystals which formed were collected by filtration, and washed with water and acetone, to give 1.1 g of colorless powder, mp 265-268°. Recrystallization from a large amount of methanol gave 0.8 g (67% yield) of 21 as colorless needles, mp 270-273° [lit. (14) mp 288-292°].

Anal. Calcd. for $C_7H_{11}N_3OS$: C, 45.38; H, 5.99; N, 22.68; S, 17.31. Found: C, 44.99; H, 5.97; N, 22.56; S, 17.01.

Reaction of **20** with Acetic Anhydride.

A mixture of 1.3 g (8.61 mmoles) of **20** and 10 ml of acetic anhydride was refluxed for 3.5 hours and excess acetic anhydride was then removed *in vacuo*. The residual solid (1.9 g) was dissolved in ethyl acetate and the insoluble materials were collected by filtration to give 0.2 g of colorless crystals. Recrystallization from methanol gave 0.1 g (4.6% yield) of colorless needles, mp 198-200°. This product was identical with the authentic previously prepared **17**.

The ethyl acetate solution was condensed *in vacuo*. The resulting residue was chromatographed over a column of silica gel using chloroform as the eluent, giving the diacetyl compound **23**. Recrystalization of this product from ethyl acetate gave 0.8 g (40% yield) of colorless fine needles, mp 174-176°; ir (potassium bromide): ν max 1710 (C=O), 1720 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.31 (6H, s), 2.45 (3H, s), 3.25 (2H, t, J = 8 Hz), 4.77 ppm (2H, t, J = 8 Hz); ms: m/e 235 (M^+); uv (ethanol): λ max nm (log ϵ) 229 (s, 3.74), 263 (3.77).

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.51; N, 17.86. Found: C, 56.11; H, 5.58; N, 17.76.

The second product resulting from column chromatography was 2-Acetylamino-5,6-dihydro-4-methylfuro[2,3-*d*]pyrimidine (**23**). Recrystallization of this product from ethyl acetate gave 0.2 g (12% yield) of colorless needles, mp 138-139°; ir (potassium bromide): ν max 1662 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.35 (3H, s), 2.49 (3H, s), 3.16 (2H, t, J = 9 Hz), 4.68 (2H, t, J = 9 Hz), 8.01-8.61 (1H, broad); ms: m/e 193 (M^+); uv (ethanol): ν max nm (log ϵ) 245 (4.10), 293 (3.92).

Anal. Calcd. for $C_9H_{11}N_3O_2$: C, 55.95; H, 5.74; N, 21.75. Found: C, 55.89; H, 5.74; N, 21.55.

Hydrolysis of **22**.

To a solution of 1.0 g of potassium carbonate dissolved in a mixture of 15 ml of water and 10 ml of ethanol, was added 1.0 g (4.26 mmoles) of **22**. The mixture was stirred at room temperature for 2 hours, and then acidified with acetic acid and extracted with chloroform. The extracts were dried over sodium sulfate. Evaporation of the solvent gave 0.5 g of colorless crystals, mp 136-138°. Recrystallization from ethyl acetate gave **23** as colorless needles, mp 138-139°. This product was identical to the previously prepared **23** by mixed melting point and a comparison of spectral data.

REFERENCES AND NOTES

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