VanSickle, Mona Quesada, and Rae Miller for their assistance in the preparation of this manuscript and Jack Hinkley for large-scale preparations of starting materials.

Registry No. 4, 93202-00-7; 5, 33359-02-3; 6, 115340-68-6; 7, 93201-97-9; 8, 115340-69-7; 9, 93201-99-1; 12, 115340-70-0; 13, 35011-47-3; 14, 115340-71-1; 18, 93201-98-0; 19, 115340-72-2; 20, 93233-10-4; 2-amino-4-(benzylamino)pyrimidin-6-one, 60308-49-8; (*S*)-methylpseudothiourea sulfate, 14527-26-5; methoxycarbonyl isothiocyanate, 35266-49-0; dicyclohexylcarbodiimide, 538-75-0.

Synthesis of 5-Substituted Uracils, Uridines, and 2'-Deoxyuridine Analogues[1]

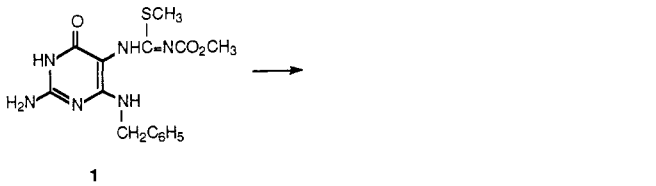
Ji-Wang Chern, Dean S. Wise, William Butler, and Leroy B. Townsend*

Department of Medicinal Chemistry, College of Pharmacy, and Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109-1065

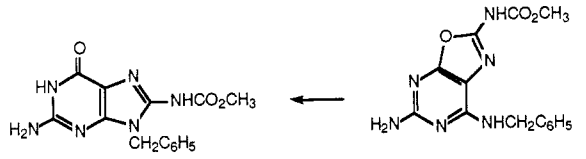
Received January 12, 1988

Reactions of 5-aminouracil (**4**), 5-aminouridine (**19a**), and 2'-deoxy-5-aminouridine (**19b**) with methoxycarbonyl isothiocyanate afforded 5-[1-[3-(methoxycarbonyl)thioureido]]uracil (**5**), 5-[1-[3-(methoxycarbonyl)thioureido]]uridine (**20a**), and 5-[1-[3-(methoxycarbonyl)thioureido]]-2'-deoxyuridine (**20b**) in near quantitative yields. Treatment of compound **5** or **20a** with 1 equiv of methyl iodide furnished 5-[1-[3-(methoxycarbonyl)-*S*-methylpseudothioureido]]uracil (**6**) and 3-methyl-5-[1-[3-(methoxycarbonyl)-*S*-methylpseudothioureido]]uridine (**21**), respectively. Compound **5** reacted with alcohols, amines, and ethanethiol in the presence of dicyclohexylcarbodiimde (DCC) to afford several 5-[1-[3-(methoxycarbonyl)-*O*-alkylpseudoureido]]uracils, 5-[1-[3-(methoxycarbonyl)guanidino]]uracil (**15**), and 5-[1-[3-(methoxycarbonyl)-*S*-ethylpseudothioureido]]uracil (**17**), respectively. Similar, reactions with **20a** resulted in the formation of 5-[1-[3-(methoxycarbonyl)-*O*-ethylpseudoureido]]uridine (**22**), 5-[1-[3-(methoxycarbonyl)ureido]]uridine (**23**), and 5-[1-[3-(methoxycarbonyl)-*S*-ethylpseudothioureido]]uridine (**24a**). The synthesis of 5-[1-[3-(methoxycarbonyl)-*S*-ethylpseudothioureido]]-2'-deoxyuridine (**24b**) was accomplished by the treatment of compound **20b** with ethanethiol in the presence of DCC. The ^{1}H NMR and ^{13}C NMR spectra of these compounds and the X-ray crystallography of compounds **13** and **17** are discussed.

Recently we reported that methyl 9-benzylguanine-8-carbamate (**2**) may be readily formed from either 2-amino-4-(benzylamino)-5-[1-[3-(methoxycarbonyl)-*S*-methylpseudothioureido]pyrimidin-6-one (**1**) or methyl 6-amino-4-(benzylamino)oxazolo[5,4-*d*]pyrimidine-2-carbamate (**3**)[2] via a short-lived carbodiimide intermediate.[3]



1



2 **3**

In connection with these studies,[2,3] it was considered that possibly a pyrimidine or pyrimidine nucleoside that contained a 5-[1-[3-(methoxycarbonyl)-*S*-methylpseudoureido]] group or a nucleoside with a methyl oxazolo[5,4-*d*]pyrimidine-2-carbamate aglycon might have good potential for biological activity due to the reactivity of these systems toward nucleophiles. This paper describes our synthetic efforts in this area.

5-Aminouracil (**4**) was reacted with methoxycarbonyl isothiocyanate[4] to furnish 5-[1-[3-(methoxycarbonyl)thioureido]]uracil (**5**) in near quantitative yield. Treatment of **5** with 1 equiv of methyl iodide gave a modest yield of 5-[1-[3-(methoxycarbonyl)-*S*-methylpseudothioureido]]-uracil (**6**). Treatment of **5** with dicyclohexylcarbodiimide (DCC), under conditions which in our previous studies[2,3] readily furnished oxazolo[4,5-*d*]pyrimidines from a series of 4-amino-5-thioureidopyrimidin-6-ones, effected no reaction in this case. Performing the reaction under high-temperature conditions afforded a complex mixture. To determine the influence of DMF on the course of this reaction, the reaction of **5** with DCC was repeated with methanol as the solvent at reflux temperature. In this case, only a single product was isolated from this reaction. The spectral data for this compound exhibited: (1) a UV spectrum with an absorption pattern very similar to that observed for **3** and (2) a ^{1}H NMR spectrum that contained, in addition to the expected peak at δ 3.8 (singlet) for the methyl moiety of the methoxycarbonyl group, an additional peak at δ 3.6 (singlet), which was suggestive of another methyl group. A methanol adduct at the C-6 position of the pyrimidine ring of the desired compound **8**, such as compound **9**, was ruled out since the chemical shift for the C-6 proton of this compound was at δ 7.58, which would suggest that the uracil ring system in this compound was still a conjugated system. In addition the ^{13}C NMR spectra of this compound revealed that the chemical shift of the carbon atoms of the uracil ring system remained relatively

(1) (a) Presented in Part at the Tenth International Congress of Heterocyclic Chemistry, University of Waterloo, Ontario, Canada, August 11-16, 1985, Abstract No. P1-23. (b) Chern, J.-W.; Wise, D. S.; Townsend, L. B. *Heterocycles* **1985**, *23*, 2197.

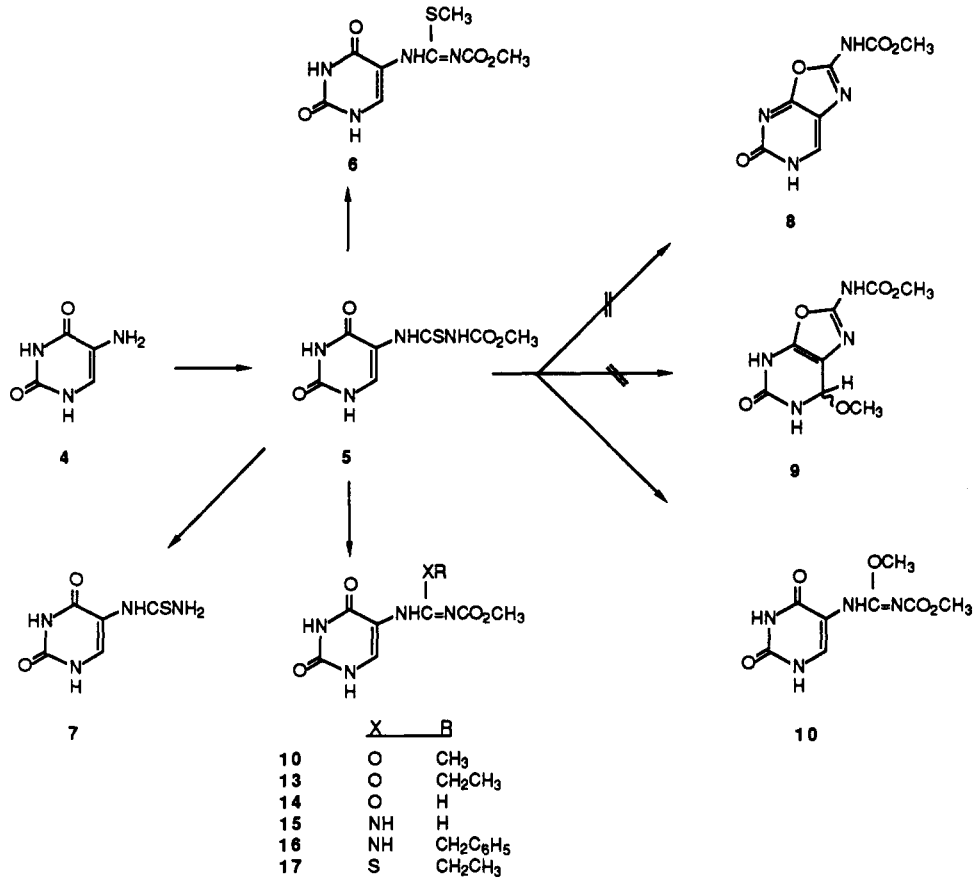
(2) Chern, J.-W.; Wise, D. S.; Townsend, L. B. *J. Heterocycl. Chem.* **1984**, *21*, 1245.

(3) Chern, J.-W.; Lee, H. Y.; Wise, D. S.; Townsend, L. B. *J. Org. Chem.*, preceding paper in this issue.

(4) Lamon, R. W. *J. Heterocycl. Chem.* **1968**, *5*, 837.

0022-3263/88/1953-5622$01.50/0 © 1988 American Chemical Society

Scheme I



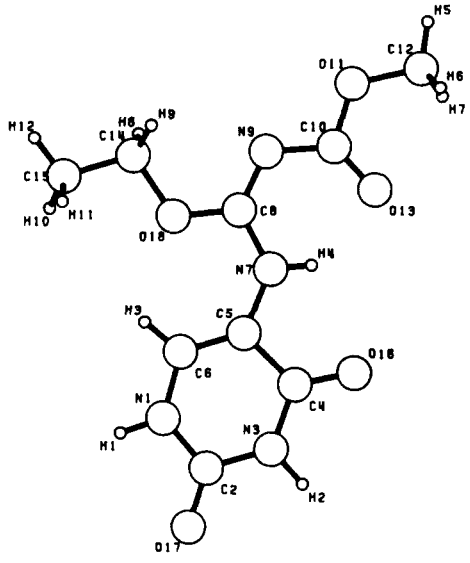
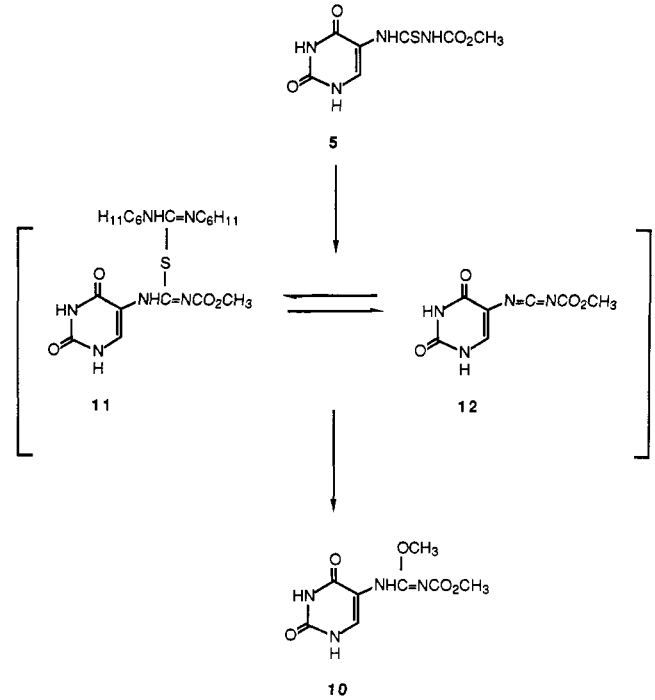


Figure 1. Projection view of compound **13**.

unchanged when compared to the chemical shifts of the carbon atoms of the starting material **5**, 5-(1-thioureido)-uracil (**7**), or with values reported in other uracil systems.[5] The mass spectrum of the product exhibited a peak at $M^+ - 32$, indicative of the loss of MeOH. Thus, we have assigned the structure of this product as 5-[1-[3-(methoxycarbonyl)-*O*-methylpseudoureido]]uracil (**10**).

The formation of compound **10** most likely occurs through an initial attack of the thione moiety at the relatively electron deficient carbon atom of DCC to form the intermediate **11**.[6] *N,N′*-Dicyclohexylthiourea may then be eliminated from **11** by either a direct intermolecular displacement by methanol to furnish **10**, or by abstraction of a proton from the methoxycarbonyl pseudothiourea side chain of **11** to form the methoxycarbonyl carbodiimide intermediate **12**. A nucleophilic attack of methanol on



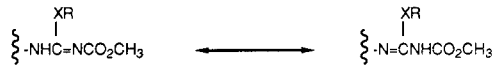
(5) (a) Levy, G. C. *Carbon-13 Nuclear Magnetic Resonance Spectroscopy*; Wiley-Interscience: New York, 1972; p 126. (b) Tarpley, A. R., Jr.; Goldstein, J. H. *J. Am. Chem. Soc.* **1971**, *93*, 3573.

(6) Wragg, R. T. *Tetrahedron Lett.* **1970**, 3931.

12 would also lead to the formation of **10**. This facile conversion of a thiourea derivative into an *O*-alkylpseudoureido derivative in alcohol without the aid of a catalyst or base has not been previously reported.

To study the scope of this reaction, **5** was reacted with DCC in the presence of water, ethanol, benzylamine, ammonia, and ethanethiol (Scheme I). Treatment of **5** with DCC in ethanol at reflux temperature furnished 5-[1-[3-(methoxycarbonyl)-*O*-ethylpseudoureido]]uracil (**13**) in 67% yield. The reaction of **5** with DCC in an ethanol–water mixture (80:20) afforded a 56% yield of 5-[1-[3-(methoxycarbonyl)ureido]uracil (**14**) and 14% of compound **13**. To eliminate the formation of **13**, the reaction of **5** with DCC was carried out in a tetrahydrofuran–water mixture (80:20). In this case, only compound **14** was obtained in an 86% yield. 5-[1-[3-(Methoxycarbonyl)-guanidino]]uracil (**15**) was isolated in 77% yield from the reaction of **5** with DCC in a sealed bottle containing DMF saturated with ammonia at room temperature. The structure of **15** was established by a direct comparison with **15** that had been prepared by a reaction of 5-aminouracil with 1-(methoxycarbonyl)-*S*-methylpseudothiourea. The treatment of **5** with DCC in dry tetrahydrofuran (THF) in the presence of benzylamine afforded 5-[1-[3-(methoxycarbonyl)-*N*-benzylguanidino]]uracil (**16**) in 71% yield. The treatment of **5** with ethanethiol in the presence of DCC at room temperature proved to be a somewhat sluggish reaction, furnishing after 4 days 5-[1-[3-(methoxycarbonyl)-*S*-ethylpseudothioureido]]uracil (**17**) in only a 12% yield along with a large amount of recovered starting material. The poor yield of this reaction was most likely due to the poor solubility of **5** in DMF at room temperature.

The 5-substituted side chain of the compounds obtained in the above series may exist in two tautomeric forms, either A or B. The UV spectra of the compounds with



A B

an *O*-alkyl- or *S*-alkylpseudoureido or guanidino side chain all exhibited a hypsochromic shift to longer wavelengths in acidic, neutral, and basic solutions compared to the starting material. However, the magnitude of the shift was less in the examples with an *S*-alkylpseudothioureido side chain possibly indicating that the *O*-alkylpseudoureido and guanidino derivatives exist in a more conjugated system than those of the *S*-alkylpseudothioureido series of compounds. This suggests that the *O*-alkylpseudoureido and guanidino side chain uracil derivatives may be predominantly in the B form while the *S*-alkylpseudothioureido side chain compounds most likely exist predominantly in the A form.

An X-ray crystallographic study of compounds **13** and **17** (Figures 1 and 2) was carried out, and the determined structures are in agreement with our ^{1}H NMR structure assignments. Single crystals of **13** were grown from ethanol. Crystals of **17** were grown by evaporation of an ethanol and water mixture. Data was collected with a Syntex $P2_1$ diffractometer. Lattice parameters were determined from a least-squares refinement of 15 reflection settings obtained from an automatic centering routine.

Intensity data were obtained with Mo K_α radiation monochromatized from a graphite crystal whose diffraction vector was parallel to the diffraction vector of the sample. Three standard reflections were measured every 50 reflections. The data were reduced by procedures previously described.[7] An absorption correction was not necessary.

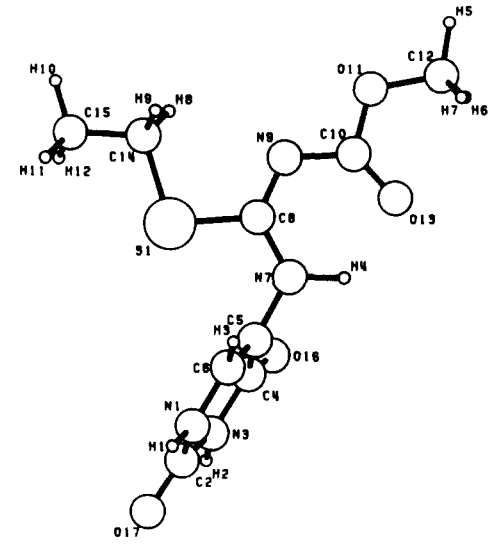


Figure 2. Projection view of compound **17**.

The structures were solved using MULTAN.[7] The function $\sum w(|F_o| - |F_c|)^8$ was minimized where $|F_o|$ and $|F_c|$ are the absolute values of the observed and calculated structure factor amplitudes. In the least-squares refinement, the agreement indices $R = \sum[|F_o| - |F_c|]/\sum|F_o|$ and $R_w = [\sum w(|F_o| - |F_c|)^2/\sum w|F_o|^2]^{1/2}$ were used. The atomic scattering factors are from ref 8. Positions for all hydrogen atoms connected to carbon atoms were calculated and added as fixed.

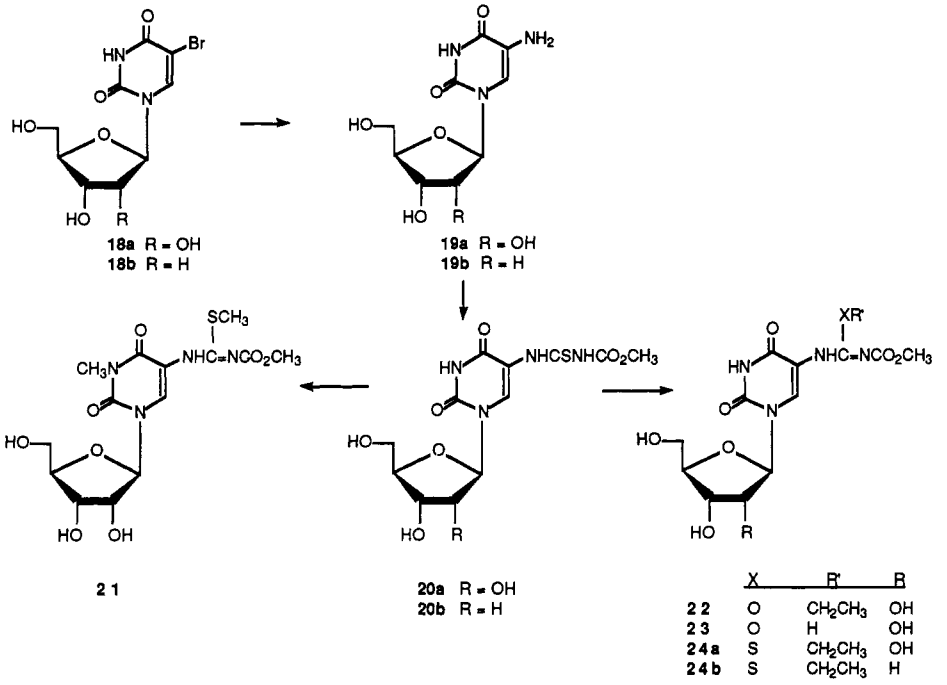
Figures 1 and 2 show the structures of **13** and **17**, respectively. Both of these compounds have a hydrogen atom on N7 and none on N9. Both have hydrogen bonds between H4 and O13. In each compound, the ring and its attached atoms are planar within 0.1, and the rest of the atoms (excluding hydrogen atoms) are planar within 0.3. The main structural difference between **13** and **17** is the orientation of the ring with respect to the rest of the structure. The angle between the ring plane and the C8–N9–C10 plane is 9.0° (6) in **13** and 82.4° (4) in **17**. Because of this, the distance from H4 to O16 in **13** is 2.35 Å while it is greater than 3.5 Å in **17**. The near planarity of **13** and lack of planarity in **17** is apparently due to the relative size of the oxygen and sulfur atoms attached to C8. The inability of **17** to attain planarity would appear to explain the observed differences in UV spectra of **13** and **17**. The planarity of **13** allows it to possess extended conjugation in solution, while this would not be the case for **17**.

With these interesting results we initiated a study of our targeted 5-[1-[3-(methoxycarbonyl)-*S*-alkylpseudothioureido]]uridines and the corresponding 2′-deoxyuridine derivatives. 5-Aminouridine (**19a**), prepared by treatment of 5-bromouridine (**18a**) with liquid ammonia in a sealed steel vessel, was treated with methoxycarbonyl isothiocyanate to furnish 5-[1-[3-(methoxycarbonyl)thioureido]]uridine (**20a**) in good yield. During the course of the treatment of compound **20a** with 1 equiv of methyl iodide and potassium carbonate in DMF, one product, in

(7) Computations were carried out on an Amdahl 5860 computer. Computer programs used during the structural analysis were from the SHELX program package by George Sheldrick, Institute Fur Anorganische Chemie der Universitat Gottingen, Federal Republic of Germany. Other programs used include ORTEP, a thermal ellipsoidal drawings program by C. K. Johnson, PLUTO78, a structure plotting program by S. Motherwell, and the direct methods program MULTAN78 by P. Main.

(8) *The International Tables for X-Ray Crystallography*; Ibers, J. A., Hamilton, W. C., Eds.; Kynoch: Birmingham, England, 1974; Vol. IV, Tables 2.2 and 2.3.1.

Scheme II



addition to the starting material, was observed by thin-layer chromatography. Only by adding one more equivalent of methyl iodide could the starting material be totally converted into product.

The ^{1}H NMR spectrum of **21** (see Figure 3) exhibited, in addition to the methoxycarbonyl methyl signal at δ 3.6 (singlet), another set of peaks centered at δ 3.18 (doublet), which integrated for three protons. Chemical analysis indicated the presence of an additional methyl group, and this peak was assigned to a methyl group at N3 of the uracil ring. That dimethylation had occurred and that only one product spot was observed on TLC indicates that methylation of the heterocyclic ring nitrogen is very facile. In addition to the split signal for the N3-methyl group, the signal for the anomeric proton of the ribose moiety was observed as a pseudotriplet (doublet of doublets) centered at δ 5.84, while the NH of the *S*-methylpseudothioureido side chain appeared as a pair of peaks at δ 9.84 (major) and at δ 9.67 (minor) in an approximate 94% (δ 9.84) to 6% (δ 9.67) ratio determined by integration (at 22 °C). Heating the sample to 51 °C effected a change in the ratio of the areas of these two peaks to 32:68, respectively. Upon cooling, the ratio of isomers returned to the original ratio of the mixture. The signal for the proton at C6 was also observed as a pair of peaks at δ 7.47 and 8.31. These unexpected patterns in the ^{1}H NMR spectrum are presumably related to a tautomerization phenomena of the *S*-methylpseudothioureido side chain between structures A and B.

The synthesis of 5-[1-[3-(methoxycarbonyl)-*O*-ethylpseudoureido]]uridine (**22**) was accomplished in 67% yield by the treatment of **20a** with DCC in anhydrous ethanol at reflux temperature (Scheme II). Treatment of **20a** with DCC in aqueous THF at reflux temperature led to the formation of 5-[1-[3-(methoxycarbonyl)ureido]]uridine (**23**) in 70% yield. Also, the reaction of **20a** with DCC in the presence of ethanethiol in DMF at room temperature afforded a 62% yield of 5-[1-[3-(methoxycarbonyl)-*S*-ethylpseudothioureido]]uridine (**24a**).

To prepare the ethylthio-2′-deoxy derivative, 5-bromo-2′-deoxyuridine (**18b**) was obtained by treatment of 2′-deoxyuridine with bromine–water. Compound **18b** was

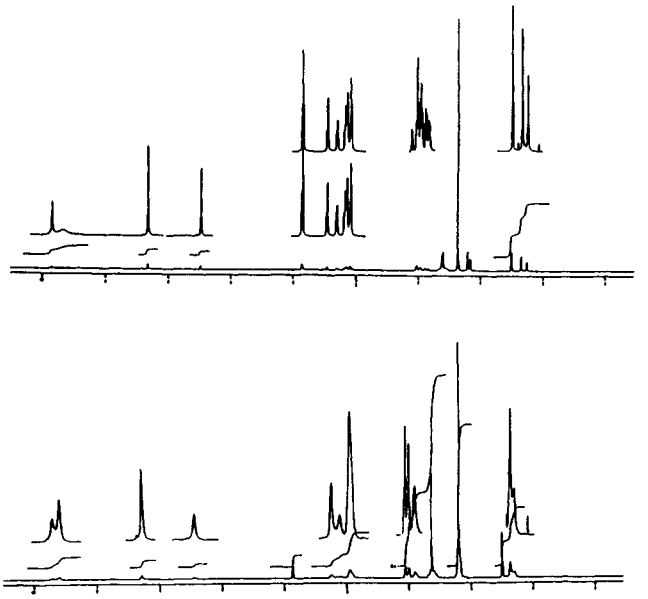


Figure 3. (Top) ^{1}H NMR (360 MHz, DMSO-d_6) spectrum of 3-methyl-5-[1-[3-(methoxycarbonyl)-*S*-methylpseudoureido]]-uridine (**21**) at 22 °C. (Bottom) ^{1}H NMR (360 MHz, DMSO-d_6) spectrum of **21** at 51 °C.

then treated with liquid ammonia to furnish crude 5-amino-2′-deoxyuridine (**19b**). Without purification, **19b** was condensed with methoxycarbonyl isothiocyanate, generated in situ, which resulted in a 94% crude yield of 5-[1-[3-(methoxycarbonyl)thioureido]]-2′-deoxyuridine (**20b**). The crude **20b** was treated with DCC in the presence of ethanethiol in DMF at room temperature to furnish an 84% yield of 5-[1-[3-(methoxycarbonyl)-*S*-ethylpseudothioureido]-2′-deoxyuridine (**24b**).

Structure assignments for these compounds were made on the basis of UV, ^{1}H NMR, and ^{13}C NMR spectral data and elemental analysis.

Experimental Section

General Methods. Proton nuclear magnetic resonance (^{1}H

NMR) spectra were obtained by using a Varian EM-360 (60 MHz) or Bruker Wm 360 (360 MHz) spectrometer. Carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a JEOL FX-90Q or Bruker Wm 360 spectrometer (90.56 MHz). The chemical shifts are reported in ppm (δ) downfield from internal Me_3Si in DMSO-d_6. The following abbreviations were used to designate the multiplicity of individual signals: s = singlet, br = broad singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. Melting points are uncorrected and were determined on a Thomas-Hoover capillary melting point apparatus. The ultraviolet spectra were recorded on a Hewlett-Packard UV 8450 spectrometer. The infrared spectra were recorded on a Perkin-Elmer 281 spectrophotometer. Mass spectra data were obtained on a Finnigan Model 4023 GC/MS with use of electron ionization. Elemental analysis were obtained from M-H-W Laboratories, Phoenix, AZ. Thin-layer chromatography (TLC) was performed with Analtech silica gel GHLF plates (250 μm). Tetrahydrofuran (THF) was freshly distilled from sodium. Dimethylformamide (DMF) was vacuum distilled from calcium oxide and then stored over molecular sieves (3A).

5-[1-[3-(Methoxycarbonyl)thioureido]]uracil (5). Methyl chloroformate (0.53 mL, 6.9 mmol) was added to a mixture of potassium thiocyanate (0.67 g, 6.9 mmol) in acetonitrile (15 mL), and the reaction mixture was heated in an oil bath at 70 °C for 30 min. The mixture was then cooled to 5 °C in an ice bath, and the potassium chloride was removed by filtration. The filtrate was added to a suspension of 5-aminouracil (**4**, 0.44 g, 3.5 mmol) in acetonitrile (35 mL), and the suspension was heated at reflux in an oil bath for 2 h. The mixture was cooled to room temperature, and the solid that had separated was collected by filtration and washed with water (10 mL) and then methanol (4 mL). The sample was dried over sodium hydroxide at the reflux temperature of toluene to afford compound **5** (0.8 g, 94%): mp >300 °C; IR (KBr) 1780 cm^{-1}; UV λ_{max} (MeOH) 259 nm (ϵ 2200), 311 (ϵ 1000), (pH 1) 259 (ϵ 2000), (pH 11) 260 (ϵ 1600); ^1H NMR (DMSO-d_6) δ 3.4 (s, 3 H), 8.9 (s, 1 H), 10.9 (d, 1 H, J = 6 Hz, NH, D_2O exchangeable), 11.4 (s, 1 H, NH, D_2O exchangeable), 11.65 (s, 1 H, NH, D_2O exchangeable), 11.75 (s, 1 H, NH, D_2O exchangeable); ^{13}C NMR δ 53.0, 113.7, 131.1, 149.4, 160.7, 153.9, 176.1. Anal. Calcd for $C_7H_8N_4SO_4$ (244.23): C, 34.43; H, 3.30; N, 22.94. Found: C, 34.54; H, 3.36; N, 23.11.

5-[1-[3-(Methoxycarbonyl)-*S*-methylpseudothioureido]]uracil (6). Methyl iodide (0.26 mL, 4.1 mmol) was added to a suspension of **5** (1.0 g, 4.1 mmol) and anhydrous potassium carbonate (0.57 g, 4.1 mmol) in DMF (50 mL). While the reaction was stirred at room temperature, the mixture initially dissolved slowly to effect a clear solution and then it turned again into a cloudy suspension. After 12 h, the solid that had separated was collected by filtration and dissolved in water (25 mL). To this solution was added 0.2 g of activated charcoal. The mixture was filtered, and a fine white crystalline material was formed by slowly adding glacial acetic acid to the filtrate to adjust the pH to 7. The solid was collected by filtration, and the crude product was recrystallized by reprecipitation with 10% potassium carbonate solution and glacial acetic acid to furnish compound **6** (0.4 g, 40%): mp >300 °C; IR (KBr) 3380, 3200, 3120, 3060, 2950, 2790, 1710, 1500, 1325, 1070, 820 cm^{-1}; UV λ_{max} (MeOH) 246 nm (ϵ 1500), (pH 1) 248 (ϵ 1200), (pH 11) 292 (ϵ 900); ^1H NMR (DMSO-d_6) δ 2.3 (s, 3 H, CH_3), 3.6 (s, 3 H), 7.65 (s, 1 H), 9.2–12.2 (br, 3 H, NH, D_2O exchangeable). Anal. Calcd for $C_8H_{10}N_4O_4S$ (258.256): C, 37.21; H, 3.90; N, 21.69. Found: C, 37.18; H, 4.00; N, 21.71.

5-(1-Thioureido)uracil (7). A mixture of **5** (1.0 g, 4.01 mmol) in 10% sodium hydroxide solution (20 mL) was allowed to stir at room temperature for 24 h. To the solution was added activated charcoal (0.3 g), and the mixture was heated on a hot plate for 30 min. The mixture was filtered, and the filtrate was adjusted to pH 5. After cooling, the white solid was collected and washed with water to afford compound **7** (0.58 g, 76%). An analytical sample was recrystallized from sodium hydroxide solution and glacial acetic acid: mp >300 °C. Anal. Calcd for $C_5H_6N_4O_2S \cdot {}^3/_4H_2O$ (199.69): C, 30.07; H, 3.78; N, 28.04. Found: C, 30.24; H, 3.95; N, 27.89.

5-[1-[3-(Methoxycarbonyl)-*O*-methylpseudoureido]]uracil (10). A suspension of **5** (1.0 g, 4.0 mmol) and DCC (2.53 g, 12 mmol) in methanol (50 mL) was heated at reflux in an oil bath. After 12 h, the solvent was removed in vacuo (water pump) on a rotary evaporator at 50 °C. The residue was suspended in boiling toluene (100 mL) for 15 min, and the solid was then collected by filtration to afford pure **10** (0.71 g, 72%). An analytical sample of **10** was prepared by suspending the compound in boiling methanol, collecting the solid by filtration, and drying the solid over potassium hydroxide at the reflux temperature of toluene: mp >360 °C with softening at 240 °C and then resolidified and changed color to deep brown; IR (KBr) 3210, 3180, 3070, 2950, 1785, 1765, 1710, 1660, 1610, 1365, 1180 cm^{-1}; UV λ_{max} (MeOH) 288 nm (ϵ 1100), (pH 1) 261 (ϵ 900), (pH 11) 291 (1000); ^1H NMR (DMSO-d_6) δ 3.6 (s, 3 H), 3.8 (s, 3 H, CH_3O), 7.58 (s, 1 H), 10.2 (s, 1 H, NH, D_2O exchangeable), 11.28 (br, 2 H, D_2O exchangeable); mass spectrum, m/z (relative intensity) 242.02 (M^+, base), 224 (4.41), 210 (47.88), 197.1 (3.59), 179.0 (4.73), 167.0 (11.17), 153.0 (13.62), 141.1 (28.97), 125.1 (22.52), 110.04 (10.80). Anal. Calcd for $C_8H_{10}N_4O_5$ (242.191): C, 39.67; H, 4.16; N, 23.13. Found: C, 39.90; H, 4.21; N, 23.37.

5-[1-[3-(Methoxycarbonyl)-*O*-ethylpseudoureido]]uracil (13). A suspension of **5** (1.0 g, 4.0 mmol) and DCC (2.87 g, 13.9 mmol) in anhydrous ethyl alcohol (75 mL) was heated at reflux in an oil bath. After 15 h the reaction was complete, as ascertained by TLC. The mixture was cooled to room temperature and allowed to stand for 4 h. The white precipitate was collected by filtration and discarded. The filtrate was allowed to stand at 5 °C for 12 h, and the precipitate that formed was collected. The filtrate was evaporated to dryness, and the resulting residue was combined with the precipitate. The crude product was stirred in boiling toluene (30 mL) for 10 min and then collected by filtration and washed with ethyl ether (20 mL) to afford compound **13** (0.75 g, 67%): mp >360 °C, softened at 215 °C and then resolidified and changed color to deep brown; R_f 0.29 (methanol/methylene chloride, 5/95, v/v); IR (KBr) 3540, 3120, 3030, 1710, 1660, 1615, 1440, 1275, 1080 cm^{-1}; UV, λ_{max} (MeOH) 252 (ϵ 1100), 289 (ϵ 1300), (pH 1) 261 (ϵ 1000), (pH 11) 291 (ϵ 1300); ^1H NMR (DMSO-d_6) δ 1.25 (t, 3 H, CH_3), 3.6 (s, 3 H), 4.3 (q, 2 H, CH_2), 7.55 (s, 1 H), 10.3 (s, 1 H, NH, D_2O exchangeable), 11.3 (br, 2 H, D_2O exchangeable); ^{13}C NMR δ 55.1, 111.3, 131.9, 149.9, 160.6, 160.8, 163.0; mass spectrum, m/z (relative intensity) 256.2 (M^+, base), 224.1 (19.05), 209.1 (4.89), 197.1 (10.36), 181.1 (10.40), 166.1 (2.53), 153.1 (100), 127.1 (28.05), 110 (76.34). Anal. Calcd for $C_9H_{12}N_4O_5 \cdot H_2O$ (274.218): C, 39.42; H, 5.14; N, 20.43. Found: C, 39.71; H, 4.90; N, 20.75.

5-[1-[3-(Methoxycarbonyl)ureido]]uracil (14). A suspension of **5** (1.0 g, 4.0 mmol) and DCC (2.97 g, 14.4 mmol) in 75% aqueous ethyl alcohol (50 mL) was heated at reflux in an oil bath. After 15 h, water (30 mL) was added to the mixture, and it was heated for another 15 min. The mixture was cooled to room temperature and allowed to stand for 4 h. The solid was collected by filtration, suspended in boiling toluene (30 mL) for 10 min, and then filtered and dried in vacuo (water pump) over sodium hydroxide at 70 °C for 12 h to furnish compound **14** (0.31 g). A second crop of compound **14** (0.21 g) was obtained from the mother liquor after it stood at 5 °C for 18 h. The total yield of compound **14** was 0.52 g (56%). The second filtrate was then allowed to stand at 5 °C for 2 days, and the white solid was collected by filtration to obtain compound **13** (0.15 g, 14%). An analytical sample of **14** was obtained by recrystallization from 75% aqueous ethanol and drying in vacuo over potassium hydroxide at the reflux temperature of toluene for 24 h: mp >360 °C, softening at 275 °C and then color changed to brown; UV λ_{max} (EtOH) 286 (ϵ 900), (pH 1) 279 (ϵ 700), (pH 11) 286 (ϵ 700); ^1H NMR (DMSO-d_6) δ 3.7 (s, 3 H), 8.0 (s, 1 H), 9.9 (s, 1 H, NH, D_2O exchangeable), 10.7 (br, 2 H, D_2O exchangeable), 11.6 (s, 1 H, D_2O exchangeable); ^{13}C NMR δ 52.8, 113.2, 126.6, 149.5, 150.2, 154.9, 160.5; mass spectrum, m/z (relative intensity) 228.2 (M^+, base), 209.2 (1.00), 197.2 (2.94), 185.2 (0.38), 167.2 (3.74), 153.3 (69.37), 146.2 (5.32), 127.2 (100), 110.1 (43.05). Anal. Calcd for $C_7H_8N_4O_5$ (228.164): C, 36.85; H, 3.53; N, 24.56. Found: C, 36.77; H, 3.74; N, 24.35.

5-[1-[3-(Methoxycarbonyl)guanidino]]uracil (15). Method 1. A suspension of **5** (0.5 g, 2.05 mmol) and DCC (1.45 g, 7.64 mmol) in DMF (75 mL) saturated with ammonia was allowed to stir at room temperature in a sealed glass vessel. After 30 min, a clear solution was effected, which became cloudy after 1 day. After 4 days, the solid was collected by filtration and washed first with methanol (10 mL) and then with water (10 mL) to afford compound **15** (0.75 g, 77%). An analytical sample was prepared

by the suspension of **15** in boiling 50% aqueous methanol with stirring for 20 min. The sample was collected by filtration and dried in vacuo (water pump) over potassium hydroxide at the reflux temperature of toluene for 24 h: mp >360 °C; IR (KBr) 3330, 3250, 3180, 1710, 1440 cm^{-1}; UV λ_{max} (MeOH) 292 nm (ϵ 1200), (pH 1) 264 (ϵ 1000), (pH 11) 289 (ϵ 1100); ^1H NMR (DMSO-d_6) δ 3.5 (s, 3 H), 7.7 (br, 2 H, NH_2, D_2O exchangeable), 8.1 (s, 3 H), 8.3–12 (br, 3 H, NH + OH, D_2O exchangeable); ^{13}C NMR δ 51.4, 112.7, 131.7, 149.9, 159.8, 161.2, 163.6; mass spectrum, m/z (relative intensity) 227.1 (9.23), 209.1 (0.89), 195.1 (5.46), 185.1 (0.75), 166.1 (1.77), 152.0 (9.28), 135.1 (5.93), 127.0 (27.36), 109.0 (3.46), 44.0 (100). Anal. Calcd for $C_7H_9N_5O_4 \cdot H_2O$ (245.18): C, 34.29; H, 4.52; N, 28.56. Found: C, 34.30; H, 4.55; N, 28.69.

Method 2. A solution of 1-(methoxycarbonyl)-*S*-methylpseudothiourea was generated in situ by adding an aqueous 10% sodium hydroxide solution dropwise to a stirred mixture of *S*-methylpseudothiourea sulfate (2.2 g, 7.9 mmol), methyl chloroformate (1.2 mL, 15.8 mmol), and water (15 mL) in an ice bath in order to adjust the pH of the solution to pH 8. The pH of the solution was then adjusted to 5 by the addition of glacial acetic acid. 5-Aminouracil (**4**) (1.0 g, 7.87 mmol) was added to this solution, and the mixture was heated at 85 °C for 4 h in an oil bath. The mixture was cooled to room temperature, and the white solid was collected by filtration and then recrystallized by dissolving the crude product in warm 10% hydrochloric acid solution and reprecipitation by the addition of a mixture of ammonium hydroxide and hydrazine (v/v, 3/1) to afford compound **15** (1.62 g, 91%): mp >360 °C; ^1H NMR (DMSO-d_6) δ 3.5 (s, 3 H, CH_3), 7.7 (br, 2 H, NH_2, D_2O exchangeable), 8.1 (s, 1 H, H-6), 8.3–12 (br, 3 H, NH + OH, D_2O exchangeable); the UV (methanol) and ^{13}C NMR spectra were the same as those obtained from the product prepared by method 1. Anal. Calcd for $C_7H_9N_5O_4 \cdot H_2O$ (245.18): C, 34.29; H, 4.52; N, 28.56. Found: C, 34.37; H, 4.41; N, 28.25.

5-[1-[3-(Methoxycarbonyl)-*N*-benzylguanidino]]uracil (16). A suspension of **5** (0.5 g, 2.0 mmol), DCC (0.84 g, 4.0 mmol), and benzylamine (2 mL, 18.3 mmole) in freshly distilled anhydrous THF was heated at reflux temperature in an oil bath. After 15 h, the mixture was evaporated to dryness in vacuo (water pump), and the residue was stirred in boiling toluene for 15 min. The solvent was then decanted, and 50% aqueous methanol (30 mL) and glacial acetic acid were added to the residue. The solution was allowed to stand at room temperature for 12 h. The solid was collected by filtration and washed with water (10 mL) and then ethyl ether (5 mL) to give compound **16** (0.16 g). The filtrate was allowed to stand at 5 °C for 2 days to obtain an additional 0.3 g of compound **16**. The total yield of compound **16** was 0.46 g (71%). An analytical sample was prepared by recrystallization from 50% aqueous methanol with a few drops of glacial acetic acid. The sample was dried over sodium hydroxide at the reflux temperature of toluene for 24 h: mp 136–138 °C; R_f 0.44 (methanol/chloroform, v/v, 1/9); IR (KBr) 3520, 3380, 3160, 3040, 2950, 2820, 1725, 1660, 1590, 1440, 1120, 800 cm^{-1}; UV λ_{max} (MeOH): 263 nm (ϵ 800), (pH 1) 266 (ϵ 1000), (pH 11) 291 (ϵ 1000); ^1H NMR (DMSO-d_6) δ 3.5 (s, 3 H), 4.42 (d, 2 H, CH_2), 7.3 (s, 5 H, Ar H), 7.6 (s, 1 H), 9.5 (br, 1 H, NH, D_2O exchangeable), 10–11.6 (br, 2 H, D_2O exchangeable); ^{13}C NMR δ 43.5, 51.6, 110.0, 126.6, 126.8, 128.1, 139.5, 140.4, 151.0, 160.1, 161.9, 163.6; mass spectrum, m/z (relative intensity) 317 (M^+, base), 299, 281 (1.65), 271 (11.88), 253 (4.06), 209 (21.38), 197 (50.96), 181 (2.28), 149 (12.13), 135 (100), 110 (1.57). Anal. Calcd for $C_{14}H_{15}N_5O_4 \cdot H_2O$ (335.305): C, 50.15; H, 5.11; N, 20.89. Found: C, 50.33; H, 5.25; N, 20.88.

5-[1-[3-(Methoxycarbonyl)-*S*-ethylpseudothioureido]]uracil (17). A suspension of **5** (0.89 g, 3.06 mmol), DCC (2.25 g, 11.0 mmol), and ethanethiol (2.5 mL, 33.18 mmol) in DMF (50 mL) was allowed to stir at room temperature. After 12 days, the solvent was removed in vacuo (oil pump) by rotary evaporation. The residue was stirred with boiling toluene (100 mL) and filtered. The solid was found (by TLC) to contain both starting material and compound **17**. The crude product was then suspended in boiling methanol (50 mL), and the undissolved solid was removed by filtration. The methanol filtrate, containing pure **17**, was rotary evaporated, and the resulting residue was added to 75% aqueous methanol (30 mL). The mixture was heated to reflux, and after the solid was completely dissolved, activated charcoal was added to the solution, and the mixture was filtered. The filtrate was allowed to stand at room temperature for 12 h to afford compound **17** (120 mg, 15%): mp 180–185 °C; R_f 0.35 (methanol/chloroform, v/v, 5/95); IR (KBr) 3450, 3390, 3020, 2390, 2840, 1780, 1720, 1660, 1440 cm^{-1}; UV λ_{max} (EtOH) 248 nm (ϵ 1700), (pH 1) 252 (ϵ 1300), (pH 11) 293 (ϵ 1100); ^1H NMR (DMSO-d_6) δ 1.2 (t, 3 H, CH_3), 2.95 (q, 2 H, CH_2), 3.6 (s, 3 H), 7.6 (s, 1 H), 9.11 (br, 3 H, NH, D_2O exchangeable); ^{13}C NMR δ 14.1, 25.0, 52.3, 111.6, 139.4, 150.5, 160.8, 170.5; mass spectrum, m/z (relative intensity) 271.1 (M^+, base), 240.0 (24.08), 210.0 (14.22), 198.0 (10.45), 179.0 (75.73), 169.0 (18.98), 153.0 (23.62), 139.0 (39.22), 134.0 (58.15), 110.0 (7.67), 81.0 (30.86), 74.0 (100), 59.0 (56.23). Anal. Calcd for $C_9H_{12}N_4O_4S$ (272.283): C, 39.70; H, 4.44; N, 20.58. Found: C, 39.87; H, 4.52; N, 20.52.

5-[1-[3-(Methoxycarbonyl)thioureido]]uridine (20a). Methyl chloroformate (0.32 g, 4.10 mmol) was added to a suspension of potassium thiocyanate (0.4 g, 4.10 mmol) in acetonitrile (12 mL), and the mixture was stirred in an oil bath at 65 °C for 30 min. The mixture was chilled in an ice bath for 1 h, potassium chloride was removed by filtration, and 5-aminouridine (**19a**, 0.5 g, 2.06 mmol) was added to this pale yellow filtrate. The mixture was heated at reflux in an oil bath for 2 h. After the mixture was cooled to room temperature, the solid was collected by filtration and air-dried for 3 h. The solid was then placed in an oven at 60 °C in vacuo (water pump) for 12 h to furnish compound **20a** (0.67 g, 92%). An analytical sample was prepared by recrystallization from 80% aqueous methanol: R_f 0.53 (methanol/chloroform, v/v, 2/8); mp 214–215 °C, at 207 °C changed color to brown; IR (KBr) 3480, 3400, 3190, 2980, 2820, 1690, 1565, 1470, 1270, 1230, 1060 cm^{-1}; UV λ_{max} (MeOH) 261 nm (ϵ 2400), 312 (ϵ 800), (pH 1) 260 (ϵ 2100), (pH 11) 267 (ϵ 1900); ^1H NMR (DMSO-d_6) δ 3.55 (t, 2 H, H-5'), 3.72 (s, 3 H), 3.84 (q, 1 H, H-4'), 3.91 (q, 1 H, H-3'), 3.99 (q, 1 H, H-1'), 4.95 (t, 1 H, 5'-OH), 5.18 (d, 1 H, 3'-OH, J = 5.1 Hz), 5.43 (d, 1 H, 2'-OH, J = 5.6 Hz), 5.85 (d, 1 H, H-1', J = 5.2 Hz), 11.48 (s, 1 H, NH), 9.16 (s, 1 H), 11.65 (s, 1 H, NH, D_2O exchangeable), 11.91 (s, 1 H, NH, D_2O exchangeable); ^{13}C NMR δ 53.02, 61.63, 70.23, 73.50, 84.77, 87.96, 114.52, 130.3, 148.9, 153.85, 159.6, 176.66. Anal. Calcd for $C_{12}H_{16}N_4O_8S \cdot {}^1/_4H_2O$ (376.794): C, 37.40; H, 4.44; N, 14.54. Found: C, 37.37; H, 4.61; N, 14.58.

3-Methyl-5-[1-[3-(methoxycarbonyl)-*S*-methylpseudothioureido]]uridine (21). Methyl iodide (0.11 mL, 1.6 mmol) was added to a suspension of **20a** (0.3 g, 0.8 mmol) and anhydrous potassium carbonate (0.2 g, 0.87 mmol) in dry DMF (15 mL). The suspension was allowed to stir at room temperature for 24 h, and the solvent was then removed in vacuo (oil pump) on a water bath at 55 °C. The residue was dissolved in methanol (10 mL) and filtered, and the filtrate was allowed to stand at 0 °C for 10 h. The colorless crystals were collected by filtration and dried in vacuo (water pump) at 70 °C for 12 h. This crude product was recrystallized from 90% aqueous methanol to give compound **21** (0.21 g, 65%): mp 148–149 °C; IR (KBr) 3350, 3090, 2960, 1715, 1680, 1565, 1440, 1265, 1200 cm^{-1}; UV λ_{max} (MeOH) 247 nm (ϵ 1300), (pH 1) 249 (ϵ 1200), (pH 11) 236 (ϵ 1300). Anal. Calcd for $C_{14}H_{20}N_4O_8S$ (404.398): C, 41.58; H, 4.99; N, 13.85. Found: C, 41,37; H, 4.95; N, 13.79.

5-[1-[3-(Methoxycarbonyl)-*O*-ethylpseudoureido]]uridine (22). A mixture of **20a** (0.5 g, 1.33 mmol) and DCC (0.323 g, 4.0 mmol) in anhydrous ethyl alcohol (50 mL) was heated at reflux in an oil bath for 5 h. The mixture was allowed to stand at room temperature for 4 h. The solid was collected by filtration to give compound **22** (120 mg). The mother liquor was evaporated to dryness, boiling toluene was added to the residue with stirring, and then the solvent was decanted. This process was repeated two more times. The syrupy residue was recrystallized from 70% aqueous ethanol to obtain compound **22** (0.23 g). The total yield of compound **22** was 0.35 g (67%): mp 220–221 °C; IR (KBr) 3530, 3400, 3290, 2980, 1690, 1660, 1640, 1610, 1450, 1280, 1090 cm^{-1}; UV λ_{max} (MeOH) 251 nm (ϵ 1100), 289 (ϵ 1300), (pH 1) 268 (ϵ 1000), (pH 11) 258 (ϵ 1200), 287 (ϵ 1200); ^1H NMR (DMSO-d_6) δ 1.26 (t, 3 H, CH_2CH_3), 3.58 (m, 2 H, H-5'), 3.62 (s, 3 H), 3.86 (q, 1 H, H-4'), 3.97 (q, 1 H, H-3'), 4.03 (q, 1 H, H-2'), 4.33 (q, 2 H, CH_2CH_3), 5.12 (t, 1 H, 5'-OH), 5.14 (d, 1 H, 3'-OH, J = 4.75 Hz), 5.40 (d, 1 H, 2'-OH, J = 5.79 Hz), 5.86 (d, 1 H, H-1', J = 5.71 Hz), 8.06 (s, 1 H), 10.30 (s, 1 H, NH, D_2O exchangeable), 11.87 (s, 1 H, NH, D_2O exchangeable); ^{13}C NMR δ 14.04, 52.23, 61.01, 64.15, 70.11, 73.68, 87.82, 112.42, 130.40, 149.2, 159.6, 160.25, 163.07. *Anal.*

Calcd for $C_{14}H_{20}N_4O_9$ (388.33): C, 43.30; H, 5.19; N, 14.43. Found: C, 43.59; H, 5.12; N, 14.18.

5-[1-[3-(Methoxycarbonyl)ureido]]uridine (23). A mixture of **20a** (0.5 g, 1.33 mmol) and DCC (0.32 g, 4 mmol) in THF (25 mL) and water (3 mL) was heated at reflux in an oil bath. After 16 h, the solvent was removed in vacuo (water pump) at 60 °C, and the residue was stirred in boiling toluene (50 mL). The toluene was decanted, and the resulting residue was recrystallized twice from 50% aqueous methanol to afford compound **23** (0.34 g, 70%): mp 248–249 °C; UV λ_{max} (MeOH) 288 nm (ϵ 900), (pH 1) 283 (ϵ 800), (pH 11) 283 (ϵ 700); ^{1}H NMR (DMSO-d_6) δ 3.67 (t, 2 H, H-5′), 3.71 (s, 3 H), 3.84 (q, 1 H, H-4′), 3.90 (q, 1 H, H-3′), 4.01 (q, 1 H, H-2′), 4.92 (t, 1 H, 5′-OH), 5.16 (d, 1 H, 3′-OH, J = 4.97 Hz), 5.41 (d, 1 H, 2′-OH, J = 5.0 Hz), 5.85 (d, 1 H, H-1′, J = 5.54 Hz), 8.35 (s, 1 H), 9.85 (s, 1 H, NH), 10.56 (s, 1 H, NH, D_2O exchangeable), 11.86 (s, 1 H, NH, D_2O exchangeable). Anal. Calcd for $C_{12}H_{16}N_4O_9$ (360.28): C, 40.00; H, 4.48; N, 15.55. Found: C, 39.74; H, 4.70; N, 15.27.

5-[1-[3-(Methoxycarbonyl)-*S*-ethylpseudothioureido]]uridine (24a). A mixture of **20a** (2.0 g, 5.3 mmol), DCC (3.3 g, 15.9 mmol), and ethanethiol (6 mL) in anhydrous DMF (20 mL) was allowed to stir at room temperature for 3 days. The solvent was removed in vacuo (oil pump) at 40 °C. Hot toluene (50 mL) was added to the sticky residue, and the mixture was stirred. The toluene was decanted, and the process was repeated two times. The sticky residue was recrystallized from 50% aqueous methanol to obtain compound **24a** (1.6 g, 65%): mp 200–201 °C dec; IR (KBr) 3500, 3200–3400, 3080, 2960, 1730, 1710, 1670–1690, 1630, 1550, 1440–1470, 1050, 800 cm^{-1}; UV λ_{max} (MeOH) 250 nm (ϵ 1800) (pH 1) 261 (ϵ 1600), (pH 11) 248 (ϵ 2100); ^{1}H NMR (DMSO-d_6) δ 1.2 (t, 3 H, SCH_2CH_3), 2.95 (q, 2 H, SCH_2CH_3), 3.55 (m, 2 H, H-5′), 3.59 and 3.60 (2 s, 3 H), 3.86 (q, 1 H, H-4′), 3.95 (q, 1 H, H-3′), 4.00 (q, 1 H, H-2′), 5.05 (t, 1 H, 5′-OH), 5.12 (q, 1 H, 3′-OH), 5.41 (d, 1 H, 2′-OH, J = 5.65 Hz), 5.77 (t, 1 H, H-1′), 7.42 and 8.19 (2 s, 1 H), 9.70 and 9.91 (2 s, 1 H, NH, D_2O exchangeable), 11.28 and 11.73 (2 s, 1 H, NH, D_2O exchangeable); ^{13}C NMR (contains both tautomers) δ 13.96, 14.24, 24.80, 25.09, 52.25, 52.33, 60.62, 60.77, 69.58, 69.80, 73.71, 74.03, 84.46, 85.00, 87.98, 88.20, 112.37, 123.10, 128.50, 138.37, 149.77, 150.00, 152.51, 153.40, 159.95, 159.09, 161.10. Anal. Calcd for $C_{14}H_{20}N_4O_8S$ (404.254): C, 41.60; H, 4.95; N, 13.86. Found: C, 41.50; H, 4.99; N, 13.75.

5-[1-[3-(Methoxycarbonyl)thioureido]]-2′-deoxyuridine (20b). A mixture of 5-bromo-2′-deoxyuridine (**18b**, 4.4 g, 14.33 mmol) in liquid ammonia (50 mL) in a sealed steel vessel was heated at 50 °C in an oil bath for 58 h. The reaction vessel was cooled to 0 °C, and the excess ammonia was allowed to evaporate at room temperature. The yellow syrup residue was stored in a desiccator over concentrated sulfuric acid for 4 days in vacuo (water pump) to remove excess ammonia. To the crude residue was added water (20 mL), and the solution was concentrated in vacuo at 10 mL. Methoxycarbonyl isothiocyanate (57.32 mmol) in acetonitrile (60 mL) was added, and a solid started to precipitate after 5 min. The mixture was heated at 70 °C for 3 h. The solid was collected by filtration and dried over phosphorus pentoxide in vacuum for 3 days to furnish crude compound **20b** (5.09 g, 94%). An analytical sample was recrystallized from 50% aqueous methanol: mp 216.5–217.5 °C; IR (KBr) 3540, 3460, 3160, 3030, 2820, 1690 (C=O), 1670 (C=O), 1570, 1480, 1430, 1285, 1045 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 2.08 (m, 1 H, H-2′), 2.18 (m, 1 H, H-2′), 3.52 (m, 2 H, H-5′), 3.74 (s, 3 H), 3.80 (q, 1 H, H-4′), 4.22 (q, 1 H, H-3′), 4.93 (t, 1 H, 5′-OH), 5.33 (d, 1 H, 3′-OH, J = 4.12 Hz), 6.22 (t, 1 H, H-1′), 9.25 (s, 1 H), 11.48 (s, 1 H, NH, D_2O exchangeable), 11.73 (s, 1 H, NH, D_2O exchangeable), 11.91 (s, 1 H, NH, D_2O exchangeable); ^{13}C NMR δ 39.23, 61.93, 70.54, 84.46, 87.39, 114.6, 129.8, 148.7, 153.91, 159.71, 176.45. Anal. Calcd for $C_{12}H_{16}N_4O_7S\cdot H_2O$ (378.345): C, 38.10; H, 4.76; N, 14.81. Found: C, 38.23; H, 4.77; N, 14.91.

5-[1-[3-(Methoxycarbonyl)-*S*-ethylpseudothioureido]]-2′-deoxyuridine (24b). A mixture of **20b** (0.23 g, 0.64 mmol) and ethanethiol (0.8 mL) in anhydrous DMF (20 mL) was allowed to stir at room temperature for 4 h. The solvent was removed in vacuum at 40 °C. To the sticky residue was added hot toluene (about 60 °C), and the residue was rubbed for 10 min. The solid that had formed was filtered and washed with hot toluene. The solid was then recrystallized from 50% aqueous methanol (23 mL) to obtain compound **24b** (0.21 g, 84%): mp 204–205 °C dec; IR (KBr) 3490, 3440, 3210, 3080, 2940, 1730, 1675, 1275, 1375, 1050 cm^{-1}; UV λ_{max} (MeOH) 249 nm (ϵ 1500), (pH 1) 257 (ϵ 1200), (pH 11) 246 (ϵ 1700); ^{1}H NMR (DMSO-d_6) δ 1.21 (t, 3 H, SCH_2CH_3), 2.11 (m, 2 H, H-2′), 2.84 and 2.93 (2 q, 2 H, SCH_2CH_3), 3.54 (m, 2 H, H-5′), 3.59 and 3.60 (2 s, 3 H), 3.79 (q, 1 H, H-4′), 4.21 (m, 1 H, H-3′), 5.04 (t, 1 H, H-5′), 5.26 (d, 1 H, 3′-OH, J = 4.19 Hz), 6.16 (m, 1 H, H-1′), 7.35 and 8.16 (2 s, 1 H), 9.87 (s, 1 H, NH, D_2O exchangeable), 11.73 and 11.78 (2 s, 1 H, NH, D_2O exchangeable); ^{13}C NMR (contains both tautomers) δ 13.78, 14.34, 24.96, 25.26, 40.18, 52.51, 61.39, 70.52, 84.55, 84.81, 87.35, 87.72, 112.49, 123.36, 128.35, 149.60, 149.86, 152.68, 153.76, 160.13, 161.28. Anal. Calcd for $C_{14}H_{20}N_4O_7S$ (388.255): C, 43.31; H, 5.16; N, 14.43. Found: C, 43.19; H, 5.14; N, 14.50.

Acknowledgment. These investigations were supported by funds from the Filariasis component of the UNDP/World Bank/WHO Special Program for Research and Training in Tropical Diseases (ID-800134 and 820177). J.-W. Chern received a fellowship from National Science Council of the Republic of China in Taiwan. We are also grateful to Deanna Vansickle and Mona Quesada for their assistance in the preparation of this manuscript.

Registry No. **4**, 932-52-5; **5**, 102971-15-3; **6**, 116888-36-9; **7**, 77296-62-9; **10**, 102971-16-4; **13**, 116888-37-0; **14**, 116888-38-1; **15**, 116888-39-2; **16**, 116888-40-5; **17**, 116888-41-6; **18b**, 59-14-3; **19a**, 2149-76-0; **20a**, 116888-42-7; **20b**, 116910-05-5; **21**, 116888-43-8; **22**, 116888-44-9; **23**, 116888-45-0; **24a**, 116888-46-1; **24b**, 116910-06-6; $MeSC(NH)NH_2\cdot H_2SO_4$, 14527-76-5; $PhCH_2NH_2$, 100-46-9; EtSH, 917-59-9; MeOCONCS, 35266-49-0.

Supplementary Material Available: Detailed X-ray crystal data (molecular packing figures, tables of fractional coordinates, thermal parameters, bond distances, bond angles, etc.) (8 pages). Ordering information is given on any current masthead page.