# Pyrido[2,3-*d*]pyrimidine Nucleosides. Synthesis via Cyclization of C-5-Substituted Cytidines

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*Received July 11, 1981*

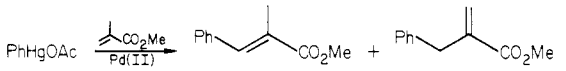
A route to pyrido[2,3-*d*]pyrimidine nucleosides was developed by starting from cytidine. The two key steps in the synthesis were the palladium-mediated coupling of an $\alpha,\beta$-unsaturated ester at the C-5 postion of 5-(chloromercuri)cytidine followed by ultraviolet light catalyzed ring closure between N-4 and the ester function. In this way cytidine was transformed in three steps to 3-$\beta$-D-ribofuranosyl-2,7-dioxopyrido[2,3-*d*]pyrimidine (**4**) when the ester was methyl acrylate. The same sequence of steps from 2'-deoxycytidine and methyl methacrylate led to 3-$\beta$-D-(2'-deoxyribofuranosyl)-6-methyl-2,7-dioxopyrido[2,3-*d*]pyrimidine (**10**). The organopalladium intermediate derived from 5-(chloromercuri)cytidine coupled to acrylonitrile to give, after reduction of an intermediate palladium complex by sodium borohydride, (5-(2-cyanoethyl)cytidine (**5**). Hydrolysis of **5** in 1 M NaOH proceeds rapidly via cyclization at N-4 to give 5-(2-carboxyethyl)cytidine (**7**).

During the course of our studies on the palladium-facilitated coupling reaction of 5-(chloromercuri)cytidine (**1**) with terminal olefins we discovered a photochemically initiated transformation leading to a fluorescent nucleoside analogue. (*E*)-5-[2-(Methoxycarbonyl)ethenyl]cytidine (**2**) when visualized under short-wave UV light on thin-layer chromatographic plates was transformed to a bright violet fluorescent product. On the basis of analytical and spectral data we have assigned this product the structure 3-$\beta$-D-ribofuranosyl-2,7-dioxopyrido[2,3-*d*]pyrimidine (**4**).[1] Although somewhat limited in scope, the present methodology provides a unique route to pyrido[2,3-*d*]pyrimidine nucleosides. Our interest in these compounds stems from their potential as fluorescent probes in biochemical studies on proteins utilizing uridine and its derivatives as substrates, in allosteric control, or as coenzymes. Leonard and co-workers have recently synthesized stretched-out fluorescent analogues of adenosine (*lin*-benzoadenosine)[2] and guanosine (*lin*-benzoguanosine).[3] *lin*-Benzoadenosine and its 5'-mono-, di-, and triphosphates have demonstrated utility as dimensional probes of the enzyme binding sites of adenine nucleotides.[2,4] Nucleoside **4** may be considered in the same light. The 7-oxo, NH-8, and N-1 of **4** define the same pattern of binding capabilities as O-2, NH-3, and O-4 of uridine, but dimensionally more remote from the ribose group. Analogues based on uridine-derived coenzmes such as UDP sugars may prove particularly interesting as fluorescent biochemical probes.

Nucleoside **4** and related oxo-substituted pyrido[2,3-*d*]pyrimidine nucleosides may also be of interest because of their structural relationship to 4-oxopyrido[2,3-*d*]pyrimidine and 2,4-dioxopyrido[2,3-*d*]pyrimidine which have demonstrated activity against Walker muscular tumor in rats.[5]

The routes to pyrido[2,3-*d*]pyrimidines most resembling those described here are those via cyclization between $\alpha,\beta$-acetylinic carbonyl compounds and aminopyrimidines,[6,7] and intramolecular cyclization of methyl 4-aminopyrimidine-5-propionate[8] and 4-aminopyrimidine-5-propionitriles.[9,10] The contribution described herein represents an exceptionally mild method for introduction of side chains into aminopyrimidines to give intermediates which may be cyclized to pyrido[2,3-*d*]pyrimidines. 5-(Chloromercuri)cytidine[11] (**1**) reacts with $Li_2PdCl_4$ and methyl acrylate in methanol within a few hours at room temperature to give (*E*)-5-[2-(methoxycarbonyl)ethenyl]cytidine (**2**, Scheme I). The stereochemistry of the double bond was established by the magnitude of the coupling constant (16 Hz) of two vicinal vinyl protons. The ultraviolet spectrum of **2** [$\lambda_{max}$ 313 nm ($\epsilon$ 12 600)] strongly supported the proposed structure. In comparison to (*E*)-5-[2-(methoxycarbonyl)ethenyl]uridine[12] the $\lambda_{max}$ of **2** was shifted 13 nm to longer wavelength, and the extinction coefficient was significantly lower.

In contrast to the reaction with methyl acrylate, 5-(chloromercuri)deoxycytidine and methyl methacrylate gave initially two major products (Scheme II). The identity of the two products was anticipated on the basis of results of Heck.[13] When an arylpalladium species generated from phenylmercuric acetate was coupled with methyl methacrylate in acetonitrile, methyl 2-benzylacrylate was formed in 72% yield and methyl (*E*)-2-methyl-3-phenylacrylate in 28% yield. More recently




Heck and co-workers[14] found that the coupling reaction between methyl methacrylate, bromobenzene and a tri-*o*-tolylphosphine complex of Pd(0) gave methyl (*E*)-2-

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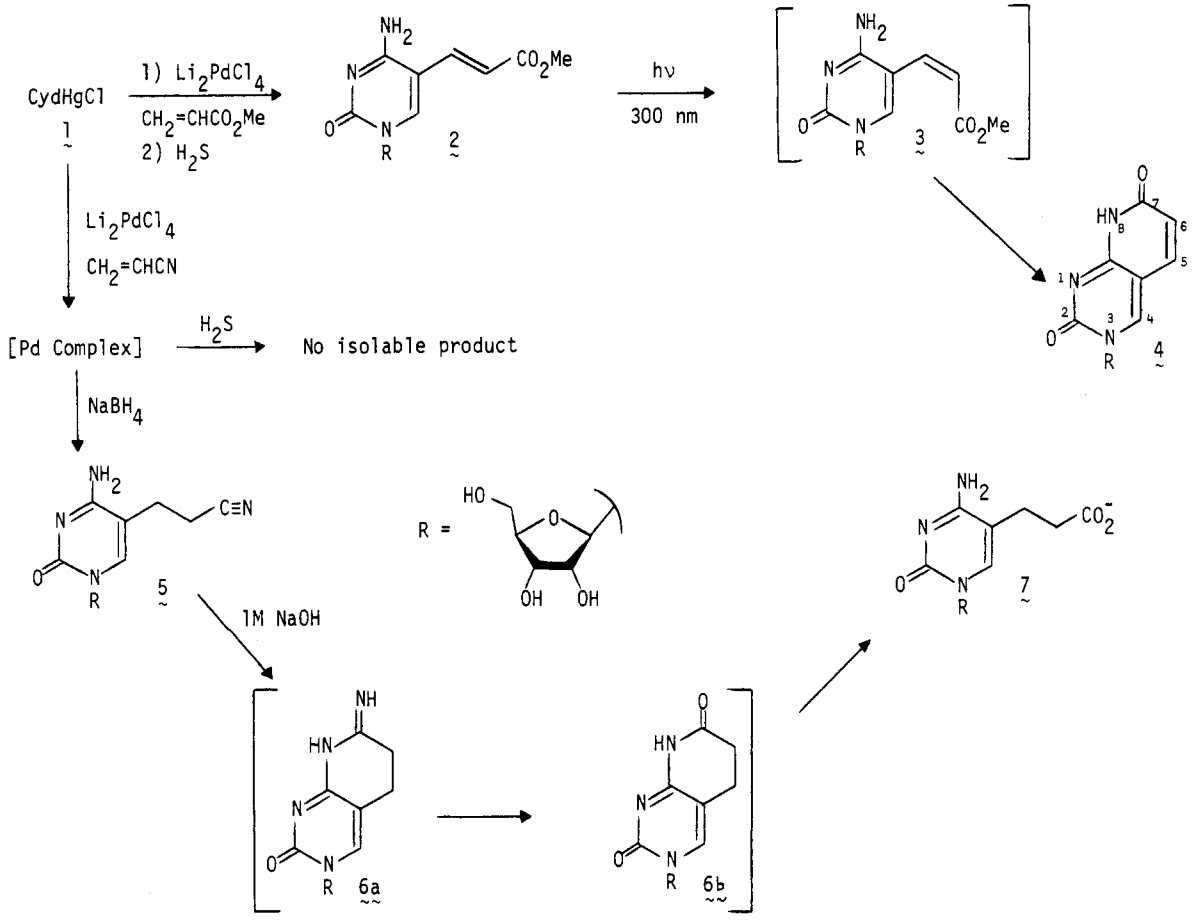
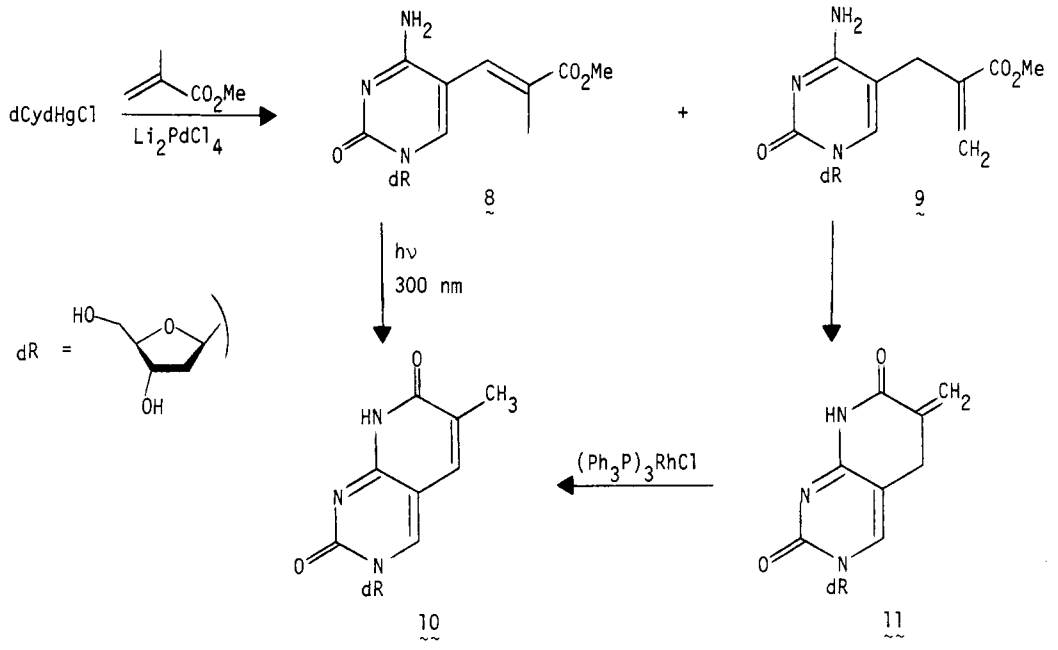
**Scheme I**




**Scheme II**




methyl-3-phenylacrylate and methyl 2-benzylacrylate in yields of 86% and 8%, respectively. With iodobenzene and no triarylphosphine catalyst the yields were 78% and 19%.

The relative yield of the two products from the reaction of 5-(chloromercuri)deoxycytidine with methyl methacrylate could not be determined accurately because of the instability of one of the products. Separation by chromatography on Bio-gel P-2 led to the appearance of a third product. The first of these to elute from the column was 5-[2-(methoxycarbonyl)-2-propen-1-yl]-2′-deoxycytidine (**9**), followed by (*E*)-5-[2-(methoxycarbonyl)-1-propenyl]-2′-deoxycytidine (**8**) and finally 3-β-D-(2′-deoxyribofuranosyl)-5,6-dihydro-6-methylene-2,7-dioxopyrido[2,3-*d*]pyrimidine (**11**). The intramolecular cyclization of **9** to **11** occurs too readily to allow isolation of pure **9**. Only **8** could be purified sufficiently to be characterized unambiguously by spectroscopy and analysis. During purification attempts nucleoside **9** slowly underwent

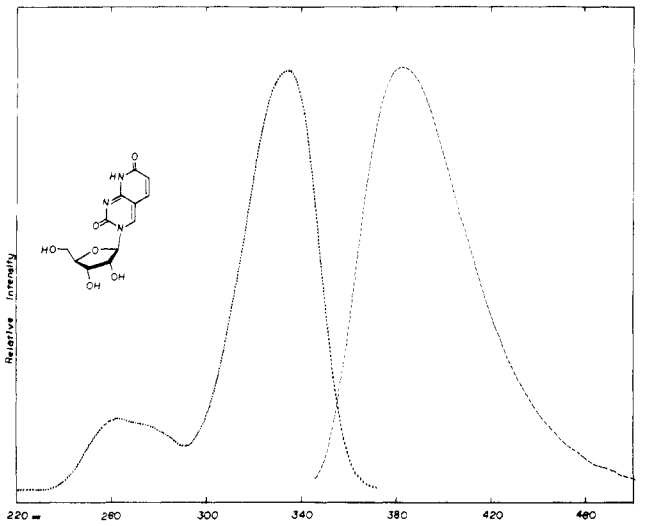



**Figure 1.** Fluorescence excitation and emission spectra of **4** in aqueous solution: excitation (···), emission (- - -).

transformation to **11**, which subsequently polymerized on being allowed to stand in solution. Their stabilities were sufficient for characterization by $^1H$ and $^{13}C$ NMR. No evidence could be found for the product of intramolecular cyclization between N-4 and the $\beta$-carbon of the acrylic ester of **9**.

The stereochemistry of **8** was postulated on the basis of $^1H$ NMR shifts. The proton cis to the methoxycarbonyl group in methyl acrylate falls at $\delta$ 6.38, and in methyl methacrylate it falls at $\delta$ 6.10. The methyl group causes an upfield shift of 0.28 ppm. In contrast the trans protons fall respectively at $\delta$ 5.82 and 5.77. The olefinic proton on nucleoside **2** is cis to the methoxycarbonyl group and falls at $\delta$ 7.62. If nucleoside **8** were to have the same stereochemistry (olefinic C–H cis to $CO_2Me$), its signal would predictably be found at approximately 7.34 ppm. Experimentally it was observed at 7.22 ppm.

The additional methyl group is furthermore responsible for the large shift in the ultraviolet maximum (Table I). As expected, in neutral solution, **2** has a strong absorption band at significantly longer wavelength ($\lambda_{max}$ 313 nm) than that for cytidine ($\lambda_{max}$ 276 nm). In contrast **8** shows only a shoulder at significantly shorter wavelength ($\lambda_{sh}$ 292 nm). These results directly paralleled those observed for cinnamic acid and $\alpha$-methylcinnamic acid. The former absorbs at 272 nm and the latter at 256 nm.

Irradiation of **2** at 300 nm in aqueous solution led to formation of a single product with $\lambda_{max}$ = 330 nm and a fluorescence emission mamimum at 385 nm (Figure 1). On the basis of the $^1H$ NMR spectra the two olefinic protons were retained but were now stereochemically *cis* to one another ($J$ = 9 Hz). The only structure compatible with this and other spectral and analytical data was structure **4**. Although various tautomeric forms of **4** are possible, we have tentatively assigned it the structure with N-8 protonated.

The mechanism for the transformation of **2** to **4** is suggested by the work of others. Zimmer and co-workers[15] have produced coumarins and quinolones by essentially this pathway, light-induced trans to cis isomerization followed by intramolecular ring closure of the carbonyl carbon with a suitably situated amino or hydroxy group. In our case only the amino-substituted derivative (cytosines) cyclized successfully. (*E*)-5-[2-(Methoxycarbonyl)-ethenyl]uridine did not react on irradiation or heating. pH or solvent did not influence the reaction.

Like **2**, nucleoside **8** readily ring closed to the pyrido-[2,3-*d*]pyrimidine (**10**). It may be surmised that the transformation would be possible with many other structural variations in the sugar and minor modification of the methyl acrylate side chain.

In an attempt to widen the scope of the synthesis, we investigated the reaction of 5-(chloromercuri)cytidine (**1**) with acrylonitrile. It was envisaged that 3-$\beta$-D-ribofuranosyl-2-oxo-7-aminopyrido[2,3-*d*]pyrimidine could thereby by produced. However, the initial step of the sequence failed. (*E*)-5-(2-Cyanoethenyl)cytidine was not a product when **2** was treated with acrylonitrile and lithium palladium chloride in either methanol or *N*,*N*-dimethylformamide. Since this coupling reaction had worked well on mercuritubercidin,[16] the results were mystifying. Apparently the coupling reaction takes place, but a palladium complex is formed which does not cleave with $H_2S$ to a methanol-soluble product. When the workup was done with $NaBH_4$, to reduce soluble mercuric and palladium ions, the isolated product was 5-(2-cyanoethyl)cytidine (**5**). In no other previous reaction had the $NaBH_4$ workup reduced an olefinic bond.[12] These results suggest the intermediacy of some palladium complex stabilized by the nitrile functional group. The assigned structure and presence of the nitrile group was confirmed by a band at 2240 $cm^{-1}$ in the infrared spectrum and a peak at 122.62 ppm in the proton-decoupled $^{13}C$ spectrum.

The cyanoethyl side chain has previously been demonstrated to ring close to an adjacent amino function to give 5,6-dihydropyrido[2,3-*d*]pyrimidines.[9,10] When **5** was subjected to similar reaction conditions, we were unable to isolate the dihydropyrido[2,3-*d*]pyrimidine. In aqueous sodium hydroxide (0.1–1.0 M) at room temperature **5** is rapidly hydrolyzed to 5-(2-carboxyethyl)cytidine (**7**, Scheme I). Participation by N-4 facilitates the rapid hydrolysis. Base-catalyzed nitrile and amide hydrolysis normally requires far harsher conditions. However, the intramolecular ring closure is entropically favorable and must lead initially to base-labile cyclic intermediates which rapidly degrade to **7** under the reaction conditions. We can at best speculate about the identity of the cyclic intermediates. Compounds **6a** and/or **6b** may be intermediates. The changes in the ultraviolet spectrum on treatment of **5** with 0.1 N NaOH are at present the only evidence for this speculation. The $\lambda_{max}$ at 277 nm does not change. However, a shoulder rapidly appears at 310 nm,[18] reaches 30% of the height of the 277-nm peak within 1 h, and then slowly decreases until the spectrum ($\lambda_{max}$ 277 nm) matches that exhibited before base treatment. Isolation of the product upon completion of the UV spectrum transformation cycle showed it to be the single pure substance 5-(2-carboxyethyl)cytidine (**7**). We were unable to find basic reaction conditions that would allow isolation of a cyclic intermediate. The lability of N-acylated cytidines is well documented because of the importance of the functionality as a protecting group.[17] Preliminary experiments show that the pyrido[2,3-*d*]pyrimidine nucleoside **4** can be further modified at C-6 by electrophilic reagents ( bromination). Creation of far more complex molecules via a second cycle of organopalladium coupling is thus

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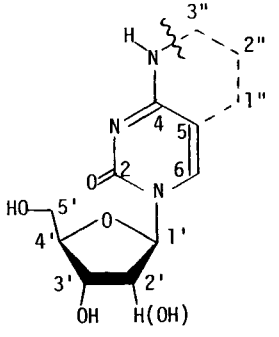
(18) The $\lambda_{max}$ of $N^4$-acetylcytidine at pH 12.0 is 306 nm. Van Montagu, M.; Stockx, J. *Arch. Intern. Physiol. Biochim.* **1965**, *73*, 158.

**Table I. Ultraviolet Absorption Spectra Maxima**

| compd | $\lambda_{max}$, nm ($\epsilon$) neutral[a] | $H^+$ | $OH^-$ |
|---|---|---|---|
| 2 | 313 (12 600), 274 (14 400) | 314 (12 000), 270 (15 400) | 299 (10 600), 269 (13 900) |
| 4 | 330 (17 200), 250 (15 400) | 330 (17 200), 250 (15 300) | |
| 5[b] | 276 (8200) | 287 (12 400) | 277 (8500) |
| 8 | 292 sh (11 700), 273 (14 100), 220 (20 300) | 295 (11 900), 267 (12 700), 248 sh (10 200) | 285 sh (10 000), 260 (12 600), 243 (12 400) |
| 9 | 279 | 287 | *c* |
| 10 | 334 (15 300), 250 (16 100) | 334 (15 200), 249 (15 700) | 336 (15 200), 316 sh (11 500), 252 (11 000) |
| 11 | 307 | 307 | 314, 279 |

[a] UV spectra were obtained in aqueous solution at neutral pH, in 0.136 N HCl ($H^+$), and in 0.136 N NaOH ($OH^-$). [b] Slowly decomposes to 7 in aqueous base. [c] Decomposes to 11 in aqueous base.

**Table II. $^{13}C$ NMR Spectral Data[a]**




| carbon | nucleoside 2 | 4 | 5 | 7 | 8 | 9 | 10 | 11 | 5-EtC |
|---|---|---|---|---|---|---|---|---|---|
| C-2 | 153.92 | 159.13 | 159.24 | 158.51 | 155.99 | 158.93 | 158.71 | 158.53 | 159.35 |
| C-4 | 166.63 | 169.28 | 166.97 | 166.19 | 167.76 | 166.95 | 172.44 | 169.23 | 167.31 |
| C-5 | 101.06 | 101.67 | 107.30 | 109.63 | 101.43 | 107.02 | 101.85 | 105.13 | 112.17 |
| C-6 | 141.95 | 145.80 | 142.27 | 140.40 | 141.86 | 142.53 | 143.81 | 142.29 | 139.66 |
| C-1′ | 89.97 | 91.10 | 92.35 | 91.83 | 87.44 | 89.31 | 87.11 | 89.31 | 92.48 |
| C-2′ | 74.49 | 74.56 | 76.54 | 75.87 | 42.05 | 41.82 | 42.05 | 42.09 | 76.35 |
| C-3′ | 68.34 | 67.95 | 71.23 | 70.52 | 70.47 | 72.51 | 69.62 | 72.24 | 71.20 |
| C-4′ | 82.25 | 84.12 | 85.99 | 85.74 | 85.31 | 88.21 | 88.20 | 89.31 | 85.74 |
| C-5′ | 59.60 | 59.44 | 62.64 | 62.64 | 61.21 | 63.19 | 60.72 | 63.10 | 62.43 |
| C-1″ | 136.71 | 137.60 | 18.50 | 25.29 | 130.43 | 31.21 | 133.30 | 29.63 | 13.35 |
| C-2″ | 114.47 | 117.85 | 25.14 | 37.42 | 127.57 | 137.96 | 125.50 | 134.41 | 22.01 |
| C-3″ | 163.13 | 163.73 | 122.62 (C≡N) | 182.52 ($CO_2^-$) | 163.56 | 170.94 | 164.24 | 163.65 | |
| other | 51.28 ($OCH_3$) | | | | 51.89 ($OCH_3$), 14.22 ($CH_3$) | 54.71 ($OCH_3$), 130.37 (=$CH_2$) | 15.72 ($CH_3$) | 129.12 (=$CH_2$) | |

[a] Spectra of compounds 2, 4, 8, and 10 were run in $Me_2SO$-$d_6$ and are referenced to external $Me_4Si$. Compounds 5, 7, 9, 11, and 5-ethylcytidine (5-EtC) were run in $D_2O$.

conceivable although not of demonstrated interest in nucleoside chemistry.

## Experimental Section

Proton magnetic resonance spectra ($^1$H NMR) were taken on either a Varian EM-360 60-MHz instrument or a Fourier transform NMR JEOL Model PS100. Sodium 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propionate was employed as the internal reference for spectra run in $D_2O$. $^{13}$C NMR were also obtained on the latter instrument. Ultraviolet spectra were measured on a Cary 17 spectrometer in water with pH extremes obtained by diluting 22 mL of stock solution in distilled water to 25 mL with either 1.0 N HCl or 1.0 N NaOH. Fluorescence spectra were determined on a Perkin-Elmer MPF-2A. Infrared spectra were obtained on a Beckman IR-8 in solid KBr. Low-resolution mass spectra were obtained on a Model 3200 Finnigan mass spectrometer at 70 eV, and high-resolution spectra were obtained on a Du Pont 492H instrument. Photochemical transformations were carried out in a Rayonet RPR-204 preparative reactor with four RUL 3000-Å lamps. Column chromatography was done on E. Merck silica gel (70–230 mesh) and on Bio-Gel P-2. Analytical thin-layer chromatography was carried out on precoated plastic-backed silica gel 60 sheets (E. Merck AG; 3.5 × 11 cm). Solvent systems were as follows: I, acetonitrile–*n*-butanol–0.1 M ammonium acetate–concentrated $NH_4OH$ (1:6:2:1 v/v); II, acetonitrile–0.1 M ammonium acetate–concentrated $NH_4OH$ (7:2:1 v/v); III, 1-butanol–methanol–concentrated $NH_4OH$–$H_2O$ (60:20:1:20 v/v). All solvents and reagents were reagent grade. Cytidine and 2′-deoxycytidine were purchased from Sigma Chemical Co. Water was deionized and then distilled through glass. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tn, and by the microanalytical laboratory at the University of California at Berkeley. Melting points were taken on a Büchi 510 melting point apparatus and are uncorrected.

**(*E*)-5-[2-(Methoxycarbonyl)ethenyl]cytidine (2).** Methyl acrylate (4 mL, 44 mmol) was added to a suspension of 5-chloromercuricytidine (1; 1.9 g, 4 mmol) stirring in 0.1 M $Li_2PdCl_4$ in methanol (42 mL, 4.2 mmol) at room temperature. After 8 h the reaction mixture was worked up by filtration to remove Pd(0), and hydrogen sulfide gas was bubbled into the filtrate for a few minutes. The precipitated metal sulfides were removed by vacuum filtration through Celite. The filtrate was concentrated to leave a syrup, then diluted with $H_2O$ (15 mL), and neutralized by the addition of Bio-Rad AG3-X4A (free form) resin which was filtered and washed with $H_2O$. the combined filtrates (25 mL) were applied on a column of Bio-Gel P-2 (2.7 × 114 cm), and the product was eluted with water. On concentration of the solution containing **2** (last of three UV-absorbing fractions), white crystals (553 mg, 42%) were obtained. Analytically pure material was obtained by recrystallization from $H_2O$: mp 220–221 °C dec; $^1$H-NMR ($Me_2SO$-$d_6$-$D_2O$) δ 8.71 (s, 1 H), 7.62 (d, 1 H, $J$ = 16 Hz), 6.26 (d, 1 H, $J$ = 16 Hz), 5.78 (br s, 1 H), 3.96 (m, 2 H), 3.68 (s, 3 H); TLC (system II) $R_f$ 0.42, dark spot which rapidly becomes fluorescent on exposure to UV (254 nm) light. Anal. Calcd for $C_{13}H_{17}O_7N_3$: C, 47.71; H, 5.24; N, 12.84. Found: C, 47.65; H, 5.23; N, 12.79.

**3-β-D-Ribofuranosyl-2,7-dioxopyrido[2,3-*d*]pyrimidine (4).** A solution of **2** (162 mg, 0.5 mmol) in $H_2O$ (200 mL) was irradiated at 300 nm for 20 min in a 5.6 × 30 cm Kimax vessel. A cold-finger-type insert created a pathlength of 0.6 cm. Stirring was achieved by slowly bubbling through nitrogen from a Teflon tube inserted to the bottom of the vessel. On concentration of the solution, slightly yellow crystals (123 mg, 84%) separated. Recrystallization from $H_2O$–EtOH afforded an analytically pure sample: mp 240 °C (gradual decomposition); $^1$H NMR ($Me_2SO$-$d_6$, $D_2O$) δ 9.05 (s, 1 H), 7.58 (d, 1 H, $J$ = 9 Hz), 6.19 (d, 1 H, $J$ = 9 Hz), 5.81 (s, 1 H), 4.02 (m, 3 H), 3.70 (m, 2 H); mass spectrum, *m/e* (relative intensity) 295 (1, molecular ion), 164 (34, B + 2 H), 163 (77, B + 1 H), 135 (60), 134 (11), 133 (8), 121 (17), 119 (17), 108 (13), 107 (57) (40 peaks at *m/e* < 100 showed a relative intensity of 10 or greater); TLC $R_f$ 0.25 (system I), 0.36 (System II), 0.41 (System III). Anal. Calcd for $C_{12}H_{13}O_6N_3$·0.5$H_2O$: C, 47.39; H, 4.64; N, 13.81. Found: C, 47.60; H, 4.74; N, 13.76.

**5-(2-Cyanoethyl)cytidine (5).** To a suspension of **1** (1.909 g, 4.0 mmol) in 0.1 M $Li_2PdCl_4$ in DMF (45 mL, 4.5 mmol) was added acrylonitrile (2 mL). The solution was stirred at room temperature for 6 days and worked up by adding 100 mL of $H_2O$ and then solid sodium borohydride in small portions until precipitation of Pd(0) and Hg(0) was complete. The filtrate was lyophilized to a viscous liquid and chromatographed first on Bio-Gel P-2, eluting with $H_2O$, and then silica gel with a solvent gradient from 25% MeOH–$CHCl_3$ to 45% MeOH–$CHCl_3$. The resulting solid (377 mg, 32%) was a single product by $^1$H NMR and TLC. Recrystallization from water gave analytically pure product melting at 220–221 °C dec: $^1$H NMR ($D_2O$) 7.85 (s, 1 H), 5.89 (br s, 1 H), 4.17 (m, 3 H), 3.87 (narrow m, 2 H), 2.73 (s, 4 H, $CH_2CH_2CN$); IR (KBr) 2240 cm$^{-1}$ (C≡N). Anal. Calcd for $C_{12}H_{16}N_4O_5$: C, 48.64; H, 5.44; N, 18.91. Found: C, 48.60; H, 5.54; N, 18.82.

**5-(2-Carboxyethyl)cytidine (7).** A solution of **5** (0.7 g, 2.37 mmol) in 1 M aqueous NaOH (30 mL) was stirred at room temperature for 2 h. The product was isolated by neutralizing with dilute HCl, lyophilizing, and chromatographing on Bio-Gel P-2 ($H_2O$ elution). Lyophilization gave white crystalline **7** (220 mg, 30%). Analytically pure product mp (235–236 °C) was obtained by recrystallization from aqueous ethanol: $^1$H NMR ($D_2O$) 7.59 (s, 1 H), 5.80 (d, 1 H, $J$ = 3 Hz) 4.11 (m, 3 H), 3.76 (m, 2 H) 2.42 (m, 4 H). Anal. Calcd for $C_{12}H_{17}N_3O_7$·3$H_2O$: C, 39.02; H, 6.28; N, 11.38. Found: C, 38.68; H, 5.92; N, 11.40.

**(*E*)-5-[2-(Methoxycarbonyl)-1-propenyl]-2′-deoxycytidine (8) and 5-[2-(Methoxycarbonyl)-2-propen-1-yl]-2′-deoxycytidine (9).** The procecure described above for the reaction of **1** with methyl acrylate was followed with 5-(chloromercuri)-2′-deoxycytidine and methyl methacrylate. $^1$H NMR analysis of the crude product prior to chromatography indicated a mixture of nucleosides **8** and **9** (~1:2). Chromatography on Bio-Gel P-2 eluting with water resulted in the isolation of **8** in 12% yield while the yield of **9** varied because of its partial transformation to nucleoside **11**. Compounds **9** and **11** were only partially characterized ($^{13}$C NMR, $^1$H NMR, and qualitative UV) because their instability precluded complete purification. Nucleoside **8**: mp 197–200 °C dec.; $^1$H NMR ($Me_2SO$-$d_6$–$D_2O$) δ 8.05 (s, 1 H), 7.22 (narrow m, 1 H), 6.17 (t, 1 H, $J$ = 6.5 Hz), 4.24 (m, 1 H), 3.9 (m, 1 H), 3.55 (m, 2 H), 2.1 (m, 2 H), 1.93 (d, 3 H, $J$ < 1 Hz). Anal. Calcd for $C_{14}H_{19}N_3O_6$·0.5$H_2O$: C, 50.29; H, 6.03; N, 12.57. Found: C, 50.18; H, 6.17; N, 12.55.

Nucleoside **9**: $^1$H NMR ($D_2O$) heterocycle and side-chain protons at δ 7.79 (s, 1 H), 6.34 (m, 1 H), 5.72 (m, 1 H), 3.80 (s, 3 H), 3.38 (s, 2 H); TLC $R_f$ 0.49 (system II); 0.47 (system III).

Nucleoside **11**: $^1$H NMR ($D_2O$) δ 8.16 (s, 1 H), 6.27 (narrow m, 1 H), 6.18 (t, 1 H, $J$ = 6.5 Hz), 5.80 (narrow, 1 H), 4.47 (m, 1 H), 4.12 (m, 1 H), 3.86 (m, 2 H), 3.71 (narrow m, 2 H), 2.45 (m, 2 H); TLC $R_f$ 0.50 (system II), 0.54 (system III).

**3-β-D-(2′-Deoxyribofuranosyl)-6-methyl-2,7-dioxopyrido[2,3-*d*]pyrimidine (10).** An aqueous solution of **8** was irradiated at 300 nm as described above for the preparation of **4** to give, after recrystallization from water, a white solid which darkened but did not melt on heating to 300 °C: $^1$H NMR ($Me_2SO$-$d_6$) δ 8.77 (s, 1 H), 7.44 (narrow m, 1 H), 6.10 (t, 1 H, $J$ = 6.5 Hz), 5.28 (d, 1 H, $J$ = 5 Hz), 5.09 (t, 1 H, $J$ = 5 Hz), 4.22 (m, 1 H), 3.90 (m, 1 H), 3.66 (m, 2 H), 2.27 (m, 2 H), 1.98 (s, 3 H). Anal. Calcd for $C_{13}H_{15}N_3O_5$: C, 53.24; H, 5.16; N, 14.33. Found: C, 53.21; H, 5.16; N, 14.29.

**Acknowledgment.** We express our appreciation to M. Schweickert and J. L. Ruth for helpful discussions. This work was supported by Grant No. CA 21493 awarded by the National Cancer Institute, whom we gratefully acknowledge.

**Registry No.** 1, 65523-07-1; 2, 81244-97-5; 4, 81206-83-9; 5, 81206-84-0; 7, 81206-85-1; 8, 81206-86-2; 9, 81206-87-3; 10, 81206-88-4; 11, 81206-89-5; methyl acrylate, 96-33-3; acrylonitrile, 107-13-1; 5-(chloromecuri)-2′-deoxycytidine, 65523-09-3; methyl methacrylate, 80-62-6; 5-ethylcytidine, 56367-98-7.