Diethyl Diacetylmaleate (2). To **3** (0.10 g, 0.39 mmol) dissolved in CCl_4 (3 mL) was added concentrated H_2SO_4 (0.2 g), and the mixture was agitated for 2 min. Water (7 mL) was added, and the CCl_4 layer was washed three times with water and dried over anhydrous Na_2SO_4. After evaporation of the solvent, a viscous liquid was obtained in quantitative yield: bp 119–122 °C (0.5 mm); NMR (CCl_4–Me_4Si) δ 1.28 (t, 6 H, J = 7.7 Hz), 2.40 (s, 6 H), 4.2 (q, 4 H, J = 7.7 Hz); IR (mineral oil) 1725, 1605 (strong), 1418, 1390, 1380, 1305, 1280 (sh), 1210, 1090, 1025, 940, 900, 845, 780, 777 (sh), 740 cm^{-1}; MS *m/e* (rel intensity) 256 (25), 210 (36), 209 (93), 183 (54), 182 (100), 154 (25), 89 (86), 44 (100). Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.31; H, 6.32.

Diethyl Diacetylfumarate (1). This compound was prepared in 10% yield by the method of Tronov et al.:[4] mp 94 °C (lit.[1] 95.5–96 °C); NMR (CCl_4–Me_4Si) δ 1.28 (t, 6 H, J = 7.7 Hz), 2.40 (s, 6 H), 4.2 (q, 4 H, J = 7.7 Hz); IR (mineral oil) 1728, 1635 (weak), 1450, 1415, 1360, 1300 (sh), 1250, 1100, 1050, 1025, 950, 800 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_6$: C, 56.24; H, 6.29. Found: C, 56.02; H, 6.13.

Registry No.—**1**, 69622-58-8; **2**, 69622-59-9; **3**, 2049-86-7; sodium ethyl acetoacetate, 19232-39-4; ethyl 2-chloroacetoacetate, 609-15-4.

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S-Nucleoside Photorearrangement. Access to Pyridine Pseudonucleosides

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Among the naturally occurring pseudonucleosides (*C*-nucleosides),[1] a few examples of pyridine *C*-nucleosides are known.[2] An understanding of the behavior of this structure type is relevant in light of the recently observed antibiotic character of pyridine nucleosides.[3] We report on the synthesis of pyridine *C*-nucleosides via an application of the thionucleoside photorearrangement.[4]

Preliminary experiments established that the (benzylthio)pyridines **1a** and **4a**[5] undergo photorearrangement to give the *C*-benzyl isomers. Thus, irradiation of **1a** afforded a mixture which on treatment with diazomethane gave 3-benzyl-2-(methylthio)pyridine (**2a**) and 5-benzyl-2-(methylthio)pyridine (**3a**) in yields of 26 and 14%, respectively. The structural assignments for the isomers **2a** and **3a** are based on NMR data. The H-6 proton in the isomer **3a** is a broad singlet (8.2 ppm), while the H-6 proton in **2a** is a quartet centered at 8.14 ppm with $J_{5,6}$ = 5 Hz and $J_{4,6}$ = 2 Hz, respectively. Similarly, irradiation of **4a** and subsequent methylation of the photoproducts gave 3-benzyl-4-(methylthio)pyridine (**5a**, 30%), the structure of which was evident from inspection of its NMR spectrum. This spectrum shows H-2 as a singlet (8.18 ppm) and the two other ring protons as doublets ($J_{5,6}$ = 5 Hz) centered at 8.30 (H-6) and 6.95 ppm (H-5), respectively.

Reaction of 2-mercaptopyridine (**1b**) with 1,2,3,5-tetra-*O*-acetyl-D-ribofuranose (BF_3:Et_2O, dichloroethane, 0 °C) yielded the thionucleoside **1c** (85%). A β configuration is proposed for **1c** from consideration of the method of synthesis.[6] Irradiation of **1c** afforded a mixture of pyridinethiones and nucleoside **6c** (5%). Deacetylation of the latter (NaOMe–MeOH) gave the known β nucleoside **6** (R = ribofuranosyl).[7] The other constituents of the mixture were separated and characterized after methylation (CH_2N_2), deoxyacetylation, and treatment with 2,2-dimethoxypropane (acetone, TsOH). Two anomeric pairs of isomeric pyridine pseudonucleoside acetonides **2d** (9%) and **3d** (5%) were obtained. Inspection of the spectral data (MS, UV, NMR) indicated that derivatives **2d** and **3d** were disubstituted pyridines resulting from a photoinduced migration of the ribosyl moiety from sulfur toward C-3 and C-5, respectively. In addition to the *S*-methyl signals, the NMR spectra of the two anomers **2d** display three quartets due to H-4, H-5, and H-6 with the following coupling constants: $J_{5,6}$ = 5.0 Hz, $J_{4,5}$ = 7.6 Hz, and $J_{4,6}$ = 1.75 Hz. In the case of derivatives **3d**, the lowest field signals are due to H-6 and appear as doublets with a small coupling constant ($J_{4,6}$ < 2.6 Hz).

To establish the configuration at C-1′[8] of the four isomeric pseudonucleosides, we have used a combination of the three following criteria:[9] (i) the chemical shift differences for the acetonide methyls ($\Delta\delta_{CH_3}$),[10] (ii) the respective chemical shifts for the anomeric protons,[11] and (iii) the signal pattern (multiplet or triplet) of the H-4′ proton.[12] Although application to pseudonucleosides of these criteria devised in the nucleoside series might be hazardous, they do give in our case, where both the α and β anomers are available, good evidence to make a reasonable configurational assignment. In fact, the differences of chemical shift ($\Delta\delta_{CH_3}$) due to the acetonide methyls were 0.18 and 0.09 ppm for the α-**2d** and β-**2d** anomers, respectively. Expectedly, the H-1′ signal for the α anomer **2d** is found at lower field than that for the β anomer, and the H-4′ signal appears as a triplet in the case of the α derivative and as a multiplet in the other. For compounds **3d** the acetonide methyl resonance criterion could not be used as the methyl shift difference was higher than 0.15 ppm for both anomers. The tentative attribution has been made on the basis of the H-1′ and H-4′ criteria. Thus, the amorphous compound **3d**, which exhibits H-1′ at 4.82 ppm and H-4′ as a multiplet, was given the β configuration while its crystalline isomer, which shows H-1′ at 5.02 ppm and H-4′ as a triplet, favors an α configuration. For the β and α anomers the $\Delta\delta_{CH_3}$ values were 0.24 and 0.18 ppm, respectively.

As nucleoside **6c** was obtained as the β anomer, it would suggest that the photorearrangement takes place with retention of chirality at C-1′. In the cases of the C-3 and C-5

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pyridine pseudonucleosides, anomerization probably occurs prior to methylation.

Treatment of 4-mercaptopyridine (**4b**) with 1,2,3,5-tetra-O-acetyl-D-ribofuranose gave the thionucleoside **4c** as a 2:1 mixture of β and α anomers.[13] In the case of the β anomer, the H-1′ resonance (5.38 ppm) occurs at higher field than that in the case of the α anomer (6.08 ppm).[14] An anomeric mixture of **4c** was irradiated, and the resulting photoproducts were treated with diazomethane to give a pair of acetylated pseudonucleosides **5c** (yield 5%). In analogy to the spectrum of derivative **5a** and in accord with structure **5c**, the NMR spectrum of the mixture displays in addition to the SMe resonance a signal pattern typical of a 3,4-disubstituted pyridine. Deoxyacetylation and reaction with 2,2-dimethoxypropane provided a mixture of pseudonucleosides **5d**. The $\Delta\delta_{CH_3}$ values for the methyl resonances were found to be 0.09 and 0.27 ppm, and the H-1′ chemical shifts were 5.18 and 5.08 ppm for the α and β anomers, respectively. From this mixture only β-**5d** could be isolated as a spectrally pure compound.

Experimental Section

The ^{1}H NMR spectra ($CDCl_3$) were recorded on Varian EM-360L or Bruker HX-90 spectrometers with tetramethylsilane as an internal standard. Chemical shifts are expressed as δ, parts per million, downfield from the standard. Ultraviolet spectra were measured in EtOH (95%) solution on a Bausch and Lomb "Spectronic 505" spectrophotometer. High- and low-resolution mass spectra were obtained with an A.E.I. MS 50 instrument. Melting points were determined on a Kofler apparatus and are uncorrected. Thin-layer chromatography was performed on Schleicher and Schüll silica gel "F 1500 LS 254" plates.

Irradiation of 2-(Benzythio)pyridine (1a). 2-(Benzylthio)pyridine (**1a**;[5] 201 mg, 1 mmol) in 100 mL of 2-butanol was irradiated at room temperature under nitrogen during 2.5 h in a quartz vessel with a Hanau TQ 150 lamp. The solvent was evaporated under reduced pressure, and the residue was treated with diazomethane in methanol to give, after silica gel column chromatography (elution with hexane–acetone, 95:5), 130 mg of a mixture whose four constituents were separated on silica gel preparative TLC (benzene–ether, 1:1) to provide 2-(benzylthio)pyridine (**1a**; 40 mg), 3-benzyl-2-(methylthio)-pyridine [**2a** (oil); 36 mg (26%); MS *m/e* 215 ($M^{+\cdot}$); UV λ_{max} 254, 293 nm; NMR δ 8.14 (q, 1, H-6), 7.06 (m, 5, C_6H_5), 7.4–6.7 (m, 2, H-4 and H-5), 3.90 (s, 2, CH_2), 2.52 (s, 3, CH_3S)], 5-benzyl-2-(methylthio)-pyridine [**3a** (oil); 19 mg (14%); MS *m/e* 215 ($M^{+\cdot}$); UV λ_{max} 253, 299 nm; NMR δ 8.20 (s, 1, H-6), 7.10 (m, 5, C_6H_5), 7.4–6.9 (m, 2, H-3 and H-4), 3.85 (s, 2, CH_2), 2.50 (s, 3, CH_3S)], and 2-(methylthio)pyridine [1 (R = CH_3); 22 mg (15%)].

Irradiation of 4-(Benzylthio)pyridine (4a). 4-(Benzylthio)-pyridine (**4a**;[5] 90 mg, 0.9 mmol) in 50 mL of 2-butanol was irradiated as above during 1 h. The photoproduct mixture was methylated (diazomethane, methanol) to yield, after silica gel column chromatography (elution with a hexane–acetone gradient), 4-(benzylthio)pyridine (**4a**; 4 mg), 4-(methylthio)pyridine [**4** (R = CH_3); 11 mg], and 3-benzyl-4-(methylthio)pyridine [**5a** (oil); 35 mg (40%); MS *m/e* 215 ($M^{+\cdot}$); UV λ_{max} 263 nm; NMR ($CDCl_3$) δ 8.30 (d, J = 5 Hz, 1, H-6), 8.18 (s, 1, H-2), 7.20 (m, 5, C_6H_5), 6.95 (d, J = 5 Hz, 1, H-5), 4.00 (s, 2, CH_2), 2.40 (s, 3, CH_3S)].

2-[(2′,3′,5′-Tri-*O*-acetyl-β-D-ribofuranosyl)thio]pyridine (1c). A solution of 2-mercaptopyridine [1 (R = H); 222 mg, 2 mmol] 1,2,3,5-tetra-*O*-acetylribose (450 mg, 1.4 mmol), and BF_3:Et_2O (1 mL) in dichloroethane (30 mL) was stirred at 0 °C during 45 min. After addition of methanol (2 mL) and solid sodium bicarbonate (4.5 g), the solution was filtered. The reaction product was purified on a column of silica gel; elution with $CHCl_3$–methanol (99:1) gave 486 mg of 2-[(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)thio]pyridine [**1c** (oil)]: 95%; MS *m/e* 369 ($M^{+\cdot}$) UV λ_{max} 245 nm (ϵ 6000), 285 (4400); NMR δ 8.30 (d, 1, H-6), 7.43 (t, 1, H-4), 7.10 (d, 1, H-3), 6.90 (t, 1, H-5), 6.10 (d, J = 4 Hz, 1, H-1′), 5.6–5.2 (m, 2, H-2′ and H-3′), 4.5–4 (m, 3, 2 × H-5′ and H-4′), 2.10 (s, 9, CH_3CO).

Irradiation of 2-[(2′,3′,5′-Tri-*O*-acetyl-β-D-ribofuranosyl)-thio]pyridine (1c). A *t*-BuOH solution (200 mL) of **1c** (490 mg, 1.33 mmol) was irradiated under the above conditions. After 2 h the solvent was evaporated under reduced pressure and the residue was chromatographed on a column of silica gel to give three fractions (A, B, and C).

Fraction A (eluted with hexane–acetone, 9:1) afforded 180 mg of pure starting material **1c**.

Fraction B (eluted with hexane–acetone, 8:2) consisted of a mixture (85 mg) of 2-mercaptopyridine (**1b**) and 1-*N*-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)pyridine-2-thione (**6c**).

Fraction C (eluted with hexane–acetone, 6:4) consisted of a mixture (56 mg) of pseudonucleosides.

Fraction B was treated with diazomethane in methanol, and the products were separated on preparative TLC (hexane–ethyl acetate, 1:1) to give 5 mg of 1-*N*-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosyl)pyridine-2-thione [**6c** (oil)]: 5%; MS *m/e* 369 ($M^{+\cdot}$); NMR δ 8.18 (d, 1, H-6), 7.62 (d, 1, H-3), 7.19 (q, 1, H-4), 6.96 (d, J = 1.5 Hz, 1, H-1′), 6.70 (t, 1, H-5), 5.56 (d, 1, H-2′), 5.20 (d, 1, H-3′), 4.50 (m, 1, H-4′), 4.46 (m, 2, 2 × H-5′), 2.19, 2.17, and 2.05 (3×) (s, 3, CH_3CO).

Deoxyacetylation of **6c** (48 mg) was accomplished by treatment with NaOMe in methanol followed by neutralization with Amberlite IR 120 (H^+) to give the free nucleoside **6** (R = ribosyl): 25 mg; mp 169–170 °C (from methanol) (lit.[7] 165–166 °C); MS *m/e* 243 (M^+); UV λ_{max} 360 nm (ϵ 13 000), 285 (2000).

Treatment of **6** (R = ribosyl) (21 mg) with 2,2-dimethoxypropane in acetone in the presence of TsOH gave, after purification on silica gel preparative TLC ($CHCl_3$–MeOH, 9:1) **6d**: 23 mg; MS *m/e* 283 ($M^{+\cdot}$); NMR δ 8.52 (d, 1, H-6), 7.64 (d, 1, H-3), 7.16 (q, 1, H-4), 7.15 (d, 1, H-1′), 6.67 (t, 1, H-5), 4.80 (m, 2, H-2′ and H-3′), 4.33 (m, 2, 2 × H-5′), 1.64 and 1.36 (s, 2 × 3, 2 × CH_3).

Fraction C was treated in methanol with an excess of diazomethane. The reaction product was dissolved in dry methanol (5 mL), and to this solution was added NaOMe (5 mg). After being stirred overnight at room temperature, the solution was neutralized with Amberlite IR 120 (H^+) and evaporated. The residue was treated with 2,2-dimethoxypropane (1 mL) and TsOH (4 mg) in acetone (10 mL). After 1 h methanol (0.2 mL) was added and the clear solution was stirred with an excess of sodium bicarbonate and filtered on a column of Celite. The resulting acetonides were separated on preparative TLC ($CHCl_3$–MeOH, 9:1) to give fractions I, II, and III. The less polar material (fraction I) consisted of an anomeric mixture (28 mg) whose constituents were isolated by preparative silica gel TLC (hexane–ethyl acetate, 1:1) to provide the amorphous 2-(methylthio)-3-(2′,3′-isopropylidene-β-D-ribosyl)pyridine [β-**2d** (16 mg)] and 2-(methylthio)-3-(2′,3′-isopropylidene-α-D-ribosyl)pyridine (α-**2d**), mp 52–54 °C (8 mg).

β-**2d** ($C_{14}H_{19}NO_4S$): $M^{+\cdot}$ found 297.1036; UV λ_{max} 250 nm (ϵ 8000), 292 (3700); NMR δ 8.40 (br d, 1, H-6), 7.60 (br d, 1, H-4), 7.00 (q, 1, H-5), 5.06 (d, J = 3.8 Hz, 1, H-1′), 4.73 (m, 2, H-2′ and H-3′) 4.12 (m, 1, H-4′), 3.90 (m, 2, 2 × H-5′), 2.59 (s, 3, CH_3S), 2.10 (br s, 1, OH), 1.64 and 1.36 (2×) (s, 3, CH_3).

α-**2d** ($C_{14}H_{19}NO_4S$): $M^{+\cdot}$ found 297.1034; UV λ_{max} 249 nm (ϵ 7000), 290 (3700); NMR δ 8.40 (br d, 1, H-6), 7.78 (br d, 1, H-4), 7.04 (q, 1, H-5), 5.25 (d, J = 4.1 Hz, 1, H-1′), 5.08 (q, 1, H-2′), 4.78 (d, 1, H-3′), 4.37 (t, 1, H-4′), 3.79 (m, 2, 2 × H-5′), 2.61 (s, 3, CH_3S), 1.60 (br s, 1, OH), 1.37 and 1.28, (2×) (s, 3, CH_3).

Fractions II and III contained the amorphous 2-(methylthio)-5-(2′,3′-isopropylidene-β-D-ribosyl)pyridine [β-**3d** (7 mg)] and 2-(methylthio)-5-(2′,3′-isopropylidene-α-D-ribosyl)pyridine [α-**3d**], mp 87–89 °C (9 mg), respectively.

β-**3d** ($C_{14}H_{19}NO_4S$): $M^{+\cdot}$ found 297.1035; UV λ_{max} 254 nm (ϵ 9000), 296 (3800); NMR δ 8.46 (br s, 1, H-6), 7.44 (d, 1, H-4), 7.16 (d, 1, H-3), 4.82 (d, J = 4.1 Hz, 1, H-1′), 4.74 (q, 1, H-2′), 4.50 (q, 1, H-3′), 4.16 (m, 1, H-4′), 3.88 (d, 2, 2 × H-5′), 2.55 (s, 3, CH_3S), 2.00 (br s, 1, OH), 1.61 and 1.35 (2×) (s, 3, CH_3).

α-**3d** ($C_{14}H_{19}NO_4S$): $M^{+\cdot}$ found 297.1040; UV λ_{max} 254 nm (ϵ 9200), 295 (3800); NMR δ 8.40 (br s, 1, H-6), 7.57 (d, 1, H-4), 7.16 (d, 1, H-3), 5.02 (br s, 1, H-1′), 4.78 (m, 2, H-2′ and H-3′), 4.32 (t, 1, H-4′), 3.75 (d, 2, 2 × H-5′), 2.55 (s, 3, CH_3S), 1.80 (br s, 1, OH). 1.47 and 1.29 (2 ×) (s, 3, CH_3).

4-[(2′,3′,5′-Tri-*O*-acetyl-D-ribofuranosyl)thio]pyridine (4c). To an acetonitrile (30 mL) solution of 4-mercaptopyridine (**4b**, 306 mg, 2.7 mmol) and 1,2,3,5-tetra-*O*-acetyl-D-ribofuranose (636 mg, 2 mmol) was added BF_3:Et_2O (1 mL). This mixture was stirred for 6 h at room temperature. The reaction product was extracted with chloroform after neutralization with a saturated sodium bicarbonate solution and purified by silica gel column chromatography (elution with $CHCl_3$–MeOH, 995:5) to give 4-[(2′,3′,5′-tri-*O*-acetyl-D-ribofuranosyl)thio]pyridine [**4c** (oil)] as an anomeric mixture (485 mg, 66%). **4c**: MS *m/e* 369 ($M^{+\cdot}$); UV 257 nm (ϵ 9100); NMR δ 8.48 (d, J = 6.5 Hz, 2, H-2 and H-6), 7.31 (d, J = 6.5 Hz, 2, H-3 and H-5), 6.67 (d, J = 5.5 Hz, 0.4, α H-1′), 5.35 (d, 0.6, β H-1′), 5.44–5.35 (m, 2, H-2′ and H-3′), 4.44–4.10 (m, 3, 2 × H-5′ and H-4′), 2.10 (s, 9, CH_3CO).

Irradiation of 4-[(2′,3′,5′-Tri-*O*-acetyl-D-ribofuranosyl)-thio]pyridine (4c). A 2-butanol (200 mL) solution of **4c** (369 mg, 1 mmol) was irradiated as above in two quartz vessels (100 mL) at room temperature under nitrogen atmosphere during 1 h. The solvent was evaporated under reduced pressure and the residue was treated with

a methanolic solution of diazomethane. The reaction mixture was chromatographed on a column of silica gel. Elution with hexane–ethyl acetate (4:6) provided **4c** (169 mg) and 4-(methylthio)-3-(2′,3′,5′-tri-*O*-acetyl-D-ribofuranosyl)pyridine [**5c** (11 mg, 5%)] as an anomeric mixture. **5c**: MS *m/e* 384 [$(M + 1)^+$·], 323 [$(M - 60)^+$·]; NMR δ 8.90 (d, 1, H-6), 8.47 (s, 1, H-2), 6.96 (d, 1, H-5), 5.50–5.07 (m, 3, H-1′, H-2′, and H-3′), 4.40–4.10 (m, 3, H-4′ and 2 × H-5′), 2.46 (s, 3, CH_3S), 2.12, 2.08, and 2.05 (3 ×) (s, 3, CH_3CO).

Treatment of compound **5c** (24 mg) with $NaOCH_3$ in methanol followed by neutralization with Amberlite IR 120 (H^+) gave an anomeric mixture of pseudonucleosides which after reaction with 2,2-dimethoxypropane gave the corresponding mixture of acetonide derivatives **4d**. Purification of the β isomer was accomplished by silica gel preparative TLC ($CHCl_3$–MeOH, 9:1) to give 3-(2′,3′-*O*-isopropylidene-β-D-ribofuranosyl)-4-(methylthio)pyridine [β-**5d** (12 mg)] as an amorphous solid. β-**5d** ($C_{14}H_{19}NO_4S$): M^+· found 297.1030; UV λ_{max} 264 nm (ϵ 11 000); NMR δ 8.50 (s 1, H-2), 8.39 (d, J = 5.5 Hz, 1, H-6), 7.07 (d, J = 5.5 Hz, 1, H-5), 5.08 (d, J = 4 Hz, 1, H-1′), 4.78 (m, 2, H-2′ and H-3′), 4.13 (m, 1, H-4′), 3.96–3.73 (m, 2, 2 × H-5′), 2.45 (s, 3, CH_3S), 1.63 and 1.36 (2 ×) (s, 3, CH_3).

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Registry No.—1 (R = CH_3), 18438-38-5; **1a**, 51290-79-0; **1b**, 2637-34-5; **1c**, 69493-87-4; **2a**, 69493-88-5; α-**2d**, 69493-89-5; β-**2d**, 69502-45-0; **3a**, 69493-90-9; α-**3d**, 69493-91-0; β-**3d**, 69493-92-1; **4** (R = CH_3), 22581-72-2; **4a**, 51290-78-9; **4b**, 4556-23-4; α-**4c**, 69493-93-2; β-**4c**, 69493-94-3; α-**4d**, 69493-95-4; β-**4d**, 69493-96-5; **5a**, 69493-97-6; α-**5c**, 69493-98-7; β-**5c**, 69493-99-8; β-**5d**, 69494-00-4; **6** (R = ribosyl), 54606-57-4; **6c**, 69494-01-5; **6d**, 69494-02-6; 1,2,3,5-tetra-*O*-acetyl-D-ribofuranose, 28708-32-9.

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Preparation of α-Substituted β-Alanine Derivatives from 5-Substituted Uracils and Dihydrouracils

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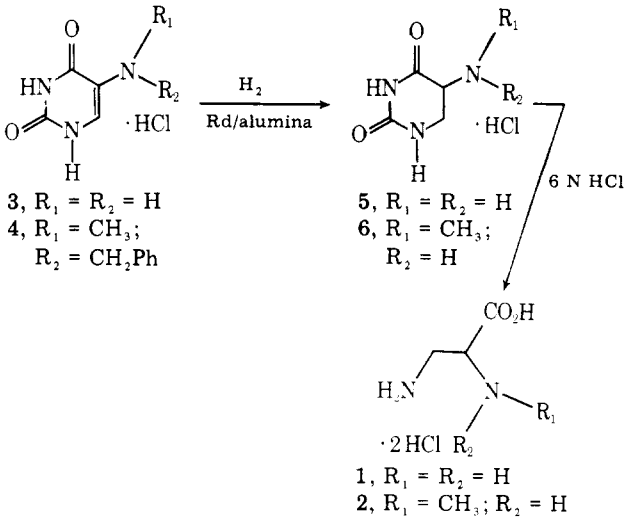
In the course of synthesizing new cyclic analogues of creatine to examine the substrate specificity of the enzyme creatine kinase, we needed reasonable quantities of both 2,3-diaminopropanoic acid (**1**) and 2-(methylamino)-3-aminopropanoic acid (**2**). Compound **1** is available commercially at high cost and can be prepared as the dihydrobromide from 2,3-dibromopropanoic acid and ammonia, but the yield is only 40–50% and high temperatures and pressure are required.[3]

Scheme I



2-(Methylamino)-3-aminopropanoic acid (**2**) was first reported[4] as one of the hydrolysis products of deoxytheobromine (3,7-dimethyl-2-oxo-1,6-dihydropurine).[5] This synthetic procedure, which first requires the reduction of theobromine to deoxytheobromine,[5] suffers from low yields and, in our hands, poor reproducibility.

Martin et al.[6] also report a synthesis of **2**, in this case from the condensation of diethyl (*N*-methyl-*N*-acetylamino)malonate[7] and *N*-(bromomethyl)phthalimide[8] followed by acid-catalyzed hydrolysis of the condensation product. A 30% yield was reported for these final two steps.[6]

An alternative method for the synthesis of compounds **1** and **2** is presented in Scheme I.

Compound **3**, 5-aminouracil, is commercially available, and **4**, 5-(*N*-benzyl-*N*-methylamino)uracil[9] is easily prepared in high yield from commercially available 5-bromouracil. The hydrogenation steps are nearly quantitative for **3** and **4**. The acid-catalyzed hydrolyses of **5** and **6** each give 1 equiv of ammonium chloride as a coproduct along with the dihydrochloride of the corresponding diamino acid. The two products are easily separated by means of ion exchange chromatography on a strongly basic anion exchange resin. The amino acid and chloride ion bind tightly to the column, and the ammonia is eluted with water. The amino acid can then be removed from the column by elution with an acidic solution, e.g., 1.0 N HCl or 1.0 N HCO_2H.

The overall method should be directly applicable to the preparation of a variety of 2-(alkylamino)-3-aminopropanoic acids from other 5-substituted aminouracils, which in turn are easily prepared from 5-bromouracil and the appropriate amine.[9] Also, any 5-substituted uracil derivative in which the 5-substituent is stable to the hydrogenation and acid-catalyzed hydrolysis conditions potentially could be converted to the corresponding α-substituted β-alanine derivative. Some β-substituted β-alanine derivatives have been prepared from their corresponding 6-substituted dihydrouracils in good yields using similar methods to those we describe here, although convenient starting materials are not commercially available and not all of the 6-substituted dihydrouracils examined gave the expected β-alanine derivatives.[10]

We have extended this procedure to obtain reasonably high

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