**1,3,2′,6′-Tetra-*N*-(benzyloxycarbonyl)-2″,3″,5″-tri-*O*-benzoyl-6,3′,4′-tri-*O*-benzylribostamycin (9).** A mixture of **4** (0.23 g, 0.2 mmol), mercuric cyanide (0.16 g, 0.62 mmol), Drierite (2.0 g), and anhydrous chloroform (5 mL) was stirred 16 h at 25 °C. A solution of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride[7] (0.19 g, 0.39 mmol) in 3 mL of chloroform was added, and the mixture was stirred 72 h at reflux. It was filtered through Celite and concentrated to dryness. The solid residue was purified by chromatography on a silica gel column with benzene–ethyl acetate as solvent and then recrystallized from chloroform–hexane to give 0.11 g (35%) of **9** as white solid: mp 132–135 °C; $[\alpha]^{26}_{546}$ +43.4° (*c* 1.0, $CHCl_3$); IR (KBr) 1720 (benzoate), 1710, 1700, 1695 (NHCO I), 1520 $cm^{-1}$ (NHCO II); NMR ($CDCl_3$) $\delta$ 4.17 (benzyl), 5.40 and 5.60 (anomeric protons), 6.9–8.15 (aromatic).

Anal. Calcd for $C_{91}H_{88}N_4O_{21}$: C, 69.45; H, 5.63; N, 3.56. Found: C, 69.37; H, 5.53; N, 3.88.

**Ribostamycin (10).** A solution of sodium methoxide, prepared from 10 mg of sodium and 10 mL of dry methanol, was treated with **9** (25 mg). After 3.5 h the mixture was neutralized with acetic acid and concentrated under reduced pressure. The residual solid was dissolved in 20 mL of 50% aqueous dioxane, treated with 10% palladium-on-carbon (50 mg) and 2 mL of acetic acid, and shaken with hydrogen for 48 h. The mixture was filtered through Celite and concentrated. TLC of the residue showed that hydrogenolysis was incomplete. The hydrogenation was repeated as described above, except that the solvent was only water. A workup in the same manner gave a solid that was purified by chromatography on Amberlite IR-C-50 ($NH_4^+$) with 0–0.5 M ammonium hydroxide as the solvent, followed by chromatography on Amberlite IR-400 ($OH^-$) with water as the solvent. These procedures gave 1.52 mg (21%) of **10** as a white solid that was identical with an authentic sample from Mieji Laboratories in IR absorption spectrum and TLC in the systems chloroform–methanol–28% ammonium hydroxide–water (1:4:2:1) and the upper phase of chloroform–methanol–28% ammonium hydroxide (1:1:1).

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**Registry No.** 1·$H_2SO_4$, 28002-70-2; **2**, 58096-78-9; **4**, 78763-85-6; **6**, 66787-83-5; **7**, 78763-86-7; 8·$2H_2CO_3$, 78763-88-9; **9**, 78763-89-0; **10**, 25546-65-0; 2,3,5-tri-*O*-acetyl-D-4-thioribofuranosyl chloride, 59042-15-8; carbobenzyloxy chloride, 501-53-1; 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride, 5991-01-5.

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## Synthesis of 2′-Deoxynucleosides by Deoxygenation of Ribonucleosides

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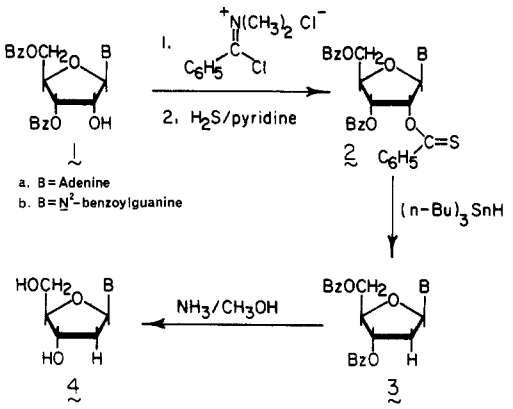
A recent communication by Robins and Wilson[2] prompts us to report an alternative method for the conversion of ribonucleosides to 2′-deoxyribonucleosides that may offer certain advantages when applied to the synthesis of analogues of naturally occurring 2′-deoxyribonucleosides.

One of the major drawbacks in the direct synthesis of 2-deoxyribofuranosyl derivatives of synthetic analogues of the naturally occurring purine bases is the formation of a mixture of anomers upon condensation of the heterocyclic base with an appropriately protected derivative of 2-deoxyribofuranose.[3] On the other hand, synthesis of the corresponding ribofuranosyl derivatives proceeds with high stereoselectivity to give almost exclusively the desired $\beta$ anomer, an effect which is generally attributed to the intramolecular participation of the acyl protecting group employed on the 2-hydroxyl group of the sugar.[4] It was our purpose to utilize the stereoselectivity in the condensation step to provide the desired $\beta$ anomer and then to deoxygenate selectively at the 2′-position.

Scheme I




Selective deoxygenation of nucleosides has been difficult to realize in the past. Most approaches have relied upon intramolecular displacement of a derivatized 2′-hydroxyl group followed by reductive ring opening[5] or upon ring opening of a bridged intermediate by halide ion followed by reductive dehalogenation.[6] In order to develop a general, efficient procedure for 2′-deoxygenation under reasonably mild conditions, we selected homolytic cleavage of the 2′-carbon–oxygen bond via tri-*n*-butyltin hydride reduction of a thioester derivative as demonstrated by Barton et al.[7] Ribonucleosides suitably protected by acyl groups on the 3′- and 5′-hydroxyls were prepared by regioselective deacylation of fully acylated nucleosides with hydroxylaminium acetate in dry pyridine according to the method of Ishido et al.[8] This approach seems particularly appropriate for the synthesis of unnatural nucleoside analogues, since fully acylated nucleosides generally result from most ribosidation procedures applied to heterocyclic bases and since direct removal of only the 2′-*O*-acyl group avoids the necessity for total deprotection followed by introduction of a new protection scheme. Additionally, the demonstrated applicability of the selective deprotection method to both purine and pyrimidine ribonucleosides makes it an effective, general step in the synthesis of 3′,5′-diprotected ribonucleosides suitable for use in subsequent deoxygenation procedures. Whether the observed selectivity in the 2′,3′,5′-tri-*O*-acyl cleavage to the 3′,5′-di-*O*-acyl ribonucleoside is due to the conversion of the

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2′,5′-di-O-acyl nucleoside into the 3′,5′ isomer upon chromatography[8] or to preferred crystallization of the 3′,5′-di-O-acyl nucleoside from an equilibrating mixture of isomers in solution, as suggested by observations of acyl migration in such systems,[9] is not clear. Nevertheless, 3′,5′-di-O-acyl derivatives are generally isolable in 60–75% yields from the fully acylated nucleosides.

3′,5′-Di-O-benzoyl ribonucleosides 1 obtained in this manner from fully benzoylated nucleosides were thiobenzoylated under the mildest conditions possible so as to minimize further acyl migration[9] before reaction (Scheme I). Treatment of the 3′,5′-di-O-benzoyl ribonucleoside with the chloroiminium chloride derived from N,N-dimethylbenzamide and phosgene, followed by hydrogen sulfide/pyridine,[7] gave the 3′,5′-di-O-benzoyl-2′-O-thiobenzoyl ribonucleosides 2 in 75–80% yields. Reductive cleavage of these thiobenzoates with tributylstannane in refluxing toluene under conditions of inverse addition afforded the 2′-deoxy-3′,5′-di-O-benzoyl nucleosides 3 in 85–90% yields. The absence of detectable amounts of the 3′-deoxy-2′,5′-di-O-benzoyl nucleosides in the reaction mixtures indicates that acyl migration is sufficiently slow to allow derivatization of the 2′-hydroxyl of 1 exclusively. Examples are provided in the Experimental Section for the conversion of 3′,5′-di-O-benzoyladenosine (**1a**) to 2′-deoxy-3′,5′-di-O-benzoyladenosine (**3a**) in 73% overall yield and of $N^2$,3′-O,5′-O-tribenzoylguanosine (**1b**) to 2′-deoxy-$N^2$,3′-O,5′-O-tribenzoylguanosine (**3b**) in 66% overall yield. Final ammonolysis to the deoxyribonucleosides 4 is amply documented. The general composite method outlined in Scheme I is particularly applicable to the synthesis of derivatives and analogues of the naturally occurring 2′-deoxyribonucleosides when fully acylated precursors are available.

## Experimental Section

3′,5′-Di-O-benzoyl ribonucleosides 1 were prepared as previously described.[8] Melting points were determined with a Büchi capillary melting point apparatus and are uncorrected. $^1$H NMR spectra were recorded on a Varian EM-390 spectrometer using $Me_4Si$ as an internal standard. Reactions were monitored by TLC on Merck f-254 precoated silica gel plates with 15% methanol in chloroform as the developing solvent. Column chromatography was performed on Brinkman 0.05–0.2-mm silica gel. High-resolution mass spectra were obtained on a Varian MAT 731 spectrometer, coupled with a 620i computer and a STATOS recorder.

**3′,5′-Di-O-benzoyl-2′-O-thiobenzoyladenosine (2a).** A solution of N,N-dimethylbenzamide (0.8 g, 5.4 mmol) in dry dichloromethane (20 mL) was treated with condensed phosgene (4 mL), the solution was stirred overnight, and the solvent and excess phosgene were removed in vacuo. The residue was dissolved in dry dichloromethane (20 mL), and 3′,5′-di-O-benzoyladenosine (**1a**; 0.11 g, 0.23 mmol) was added as a solid. The mixture was stirred for 12 h, pyridine (3 mL) was added, and hydrogen sulfide was bubbled through the mixture for 10 min. The resulting solution was washed with water (2 × 20 mL), 2 N sulfuric acid (2 × 20 mL), and saturated aqueous sodium bicarbonate, dried over sodium sulfate, and evaporated in vacuo. The residue was dissolved in chloroform and chromatographed on silica gel. Elution with chloroform gave N,N-dimethylthiobenzamide. Further elution with 2% methanol in chloroform gave **2a** as a yellow glass: 110 mg (82%); $^1$H NMR ($CDCl_3$, $D_2O$ added) δ 4.93 (m, 3 H, H-4′,5′,5″), 6.56 (m, 1 H, H-3′), 6.65 (d, 1 H, H-1′, $J_{1',2'}$ = 6 Hz), 6.93 (dd, 1 H, H-2′, $J_{1',2'}$ = 6 Hz, $J_{2',3'}$ = 6 Hz), 7.3–7.8 (br m, 10 H, 2 $C_6H_5$), 8.1–8.4 (br m, 6 H, H-8 and $C_6H_5$), 8.53 (s, 1 H, H-2); $C_{31}H_{25}N_5O_6S$.

**2′-Deoxy-3′,5′-di-O-benzoyladenosine (3a).** To a solution of 3′,5′-di-O-benzoyl-2′-O-thiobenzoyladenosine (**2a**; 132 mg, 0.22 mmol) in refluxing toluene (25 mL) was added a solution of tri-n-butyltin hydride (0.15 mL) in toluene (25 mL) dropwise over a period of 2 h. The mixture was heated at reflux for an additional 30 min and then was allowed to stand at room temperature for 12 h. Solvent was removed in vacuo, and the residue was dissolved in chloroform and chromatographed on silica gel. Elution with a 0–4% methanol gradient in chloroform afforded 2′-deoxy-3′,5′-di-O-benzoyladenosine (**3a**) as a glass (94 mg, 89%), identical with an authentic sample by TLC and NMR: $^1$H NMR ($CDCl_3$) δ 2.87 (ddd, 1 H, H-2′, $J_{1',2'}$ = 8 Hz, $J_{2',3'}$ = 4 Hz, $J_{2',2''}$ = 14 Hz), 3.25 (dd, 1 H, H-2″, $J_{1',2''}$ = 9 Hz, $J_{2',2''}$ = 14 Hz), 4.85 (br m, 3 H, H-4′,5′,5″), 6.03 (br m, 1 H, H-3′), 6.23 (br s, 2 H, $NH_2$), 6.74 (dd, 1 H, H-1′), 7.5–7.9 (br m, 6 H, $C_6H_5$ and H-8), 8.1–8.5 (br m, 5 H, $C_6H_5$), 8.58 (s, 1 H, H-2); $C_{24}H_{21}N_5O_5$.

**2′-O-(Thiobenzoyl)-$N^2$,3′-O,5′-O-tribenzoylguanosine (2b).** A solution of N,N-dimethylbenzamide (1.4 g, 9.3 mmol) in dry dichloromethane (40 mL) was treated with condensed phosgene (4 mL) with stirring under nitrogen for 18 h. Solvent and excess phosgene were removed in vacuo, and the residue was dissolved in dry dichloromethane (20 mL). $N^2$,3′-O,5′-O-Tribenzoylguanosine (**1b**; 330 mg, 0.55 mmol) was added as a solid. The mixture was stirred for 24 h, pyridine (4 mL) was added, and hydrogen sulfide was bubbled through the mixture for 10 min. The mixture was stirred for an additional hour, washed with water (2 × 20 mL), 2 N sulfuric acid (2 × 20 mL), and saturated aqueous sodium bicarbonate (2 × 20 mL), dried over sodium sulfate, and evaporated in vacuo. The residue was dissolved in chloroform and chromatographed on silica gel. Elution with chloroform gave N,N-dimethylthiobenzamide. Further elution with 2% methanol in chloroform afforded 2′-O-(thiobenzoyl)-$N^2$,3′-O,5′-O-tribenzoylguanosine (**2b**) as a yellow glass: 306 mg (79%); $^1$H NMR ($CDCl_3$) δ 5.0 (br m, 3 H, H-4′,5′,5″), 6.50 (m, 1 H, H-3′), 6.9–7.1 (br m, 2 H, H-1′,2′), 7.3–8.5 (br m, 21 H, $4C_6H_5$ and H-8), 10.1 (br s, 1 H, $N^2H$); high-resolution field-desorption mass spectrum calcd for $C_{38}H_{29}N_5O_6S$ m/e 715.1736, obsd 715.1731.

**2′-Deoxy-$N^2$,3′-O-tribenzoylguanosine (3b).** A solution of 2′-O-(thiobenzoyl)-$N^2$,3′-O,5′-O-tribenzoylguanosine (**2b**; 294 mg, 0.41 mmol) in toluene (40 mL) was heated to reflux. A solution of tri-n-butyltin hydride (0.15 g) in toluene (40 mL) was added dropwise over the period of 2 h with stirring under nitrogen. The reaction was cooled, and the solvent was removed in vacuo. The residue was dissolved in chloroform and chromatographed on silica gel. Elution with chloroform to remove nonpolar materials was followed by elution with 2% methanol in chloroform to give 2′-deoxy-$N^2$,3′-O,5′-O-tribenzoylguanosine (**3b**) as a glass, 201 mg (85%). The product crystallized from methanol: mp 125–127 °C; $^1$H NMR ($CDCl_3$) δ 2.65 (ddd, 1 H, $J_{1',2'}$ = 7 Hz, $J_{2',2''}$ = 14 Hz, $J_{2',3'}$ = 3 Hz, H-2′), 3.18 (dd, 1 H, $J_{2'',3'}$ = 7 Hz, H-2″), 4.55 (br m, 2 H, H-4′,5′), 4.87 (dd, 1 H, $J_{5',5''}$ = 13 Hz, $J_{4',5''}$ = 8 Hz, H-5″), 5.77 (m, 1 H, H-3′), 6.15 (dd, 1 H, H-1′), 7.2–8.2 (br m, 16 H, $3C_6H_5$ and H-8); $C_{31}H_{25}N_5O_7 \cdot CH_3OH$ (C, H, N); high-resolution chemical-ionization mass spectrum calcd for $C_{31}H_{26}N_5O_7$ (M + $H^+$) m/e 580.1832, obsd 580.1826.

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**Registry No.** **1a**, 62374-24-7; **1b**, 62374-25-8; **2a**, 78763-65-2; **2b**, 78763-66-3; **3a**, 20838-22-6; **3b**, 78763-67-4; N,N-dimethylbenzamide, 611-74-5.

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# Synthetic Applications of 2-Phenylselenenyl Enones. 2. Synthesis of Dihydrojasmone and *cis*-Jasmone

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2,3-Dialkylated cyclopentanones and cyclopentenones encompass a broad class of important, naturally occurring substances. Perhaps the best known and most often synthesized members of this class of compounds are two

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