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Received July 26, 1978

The α-D-arabinonucleosides of cytosine (**6**) and 5-fluorouracil (**9**) were prepared from the 2,3,-5-tri-*O*-benzoyl-D-arabinofuranosyl halides, in keeping with the *trans* rule. The 2′-*O*-methyl-β-D-arabinonucleosides of 5-fluorouracil (β-**14**) and adenine (β-**21a**) were prepared from 3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-α-D-arabinofuranosyl chloride, although in both cases a lesser amount of the α-anomer was also found. Reaction of 3,5-di-*O*-(4-chlorobenzoyl)-2-deoxy-2-(methylthio)-α-D-arabinofuranosyl chloride, prepared in four steps from methyl 2,3-anhydro-α-D-ribofuranoside (**15**), with *N*-benzoyladenine gave slightly more of the β- than the α-arabinonucleoside **20b**. The β-anomer was converted to 9-[2-deoxy-2-(methylthio)-β-D-arabinofuranosyl]adenine. Only 1-α-D-arabinofuranosylcytosine (**6**) proved to be cytotoxic.

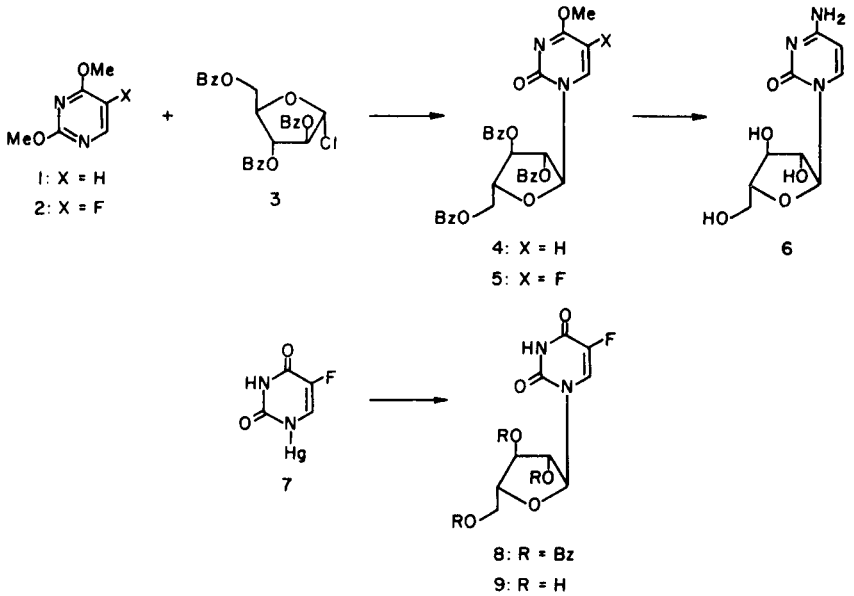
*J. Heterocyclic Chem.*, **16**, 353 (1979).

The anticancer and antiviral activity of 1-β-D-arabinofuranosylcytosine (ara-C) (1) and 9-β-D-arabinofuranosyladenine (ara-A) (2) has led to a great deal of interest in the synthesis and evaluation of other arabinonucleosides. For example, the α-anomer of ara-A and 9-α-D-arabinofuranosyl-8-azaadenine have been found to have antiviral but no anticancer activity (3). They are more cytotoxic than their β-anomers (3), a fact that has been attributed to their metabolism—they are phosphorylated but not deaminated (4,5). In this work, we have undertaken the synthesis and evaluation of additional α-arabinosides and also arabinonucleosides substituted at $C_2'$ by the methoxy (6) and methylthio group.

Reaction of 2,3,5-tri-*O*-benzoyl-D-arabinofuranosyl chloride (**3**) with 2,4-dimethoxypyrimidine (**1**) gave 1-(2,3,5-tri-*O*-benzoyl-D-arabinofuranosyl)-4-methoxypyrimidin-2-one (**4**), presumed on the basis of the *trans* rule (7) to be the α-anomer. Treatment of **4** with methanolic ammonia removed the benzoyl groups and displaced the 4-methoxy group, giving 1-D-arabinofuranosylcytosine (**6**). The signal in the pmr spectrum from the anomeric proton of **6** appeared at about 5.73 ppm, upfield from that of the β-anomer (6.05 ppm) (8) and overlapping with the signal from $H_5$. The anomeric carbon in the $^{13}C$ nmr spectrum of **6** appeared downfield from that of the β-anomer, confirming the assignment of the *trans*- or α-configuration of **6** (9).

Reaction of **3** with 2,4-dimethoxy-5-fluoropyrimidine (**2**) was less satisfactory, giving a low yield of nucleoside. Coupling of the corresponding glycosyl bromide with 5-fluorouracil mercury (**7**) (10) in refluxing toluene proved superior for the production of **8** and led, after basic removal of the benzoyl groups, to a 47% yield of 1-α-D-arabinofuranosyl-5-fluorouracil (**9**) (11), the identity of which was again established by pmr (13).

Reaction of 3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-α-D-arabinofuranosyl chloride (**10**) with 2,4-dimethoxy-5-fluoropyrimidine (**2**) neat gave a complex reaction mixture

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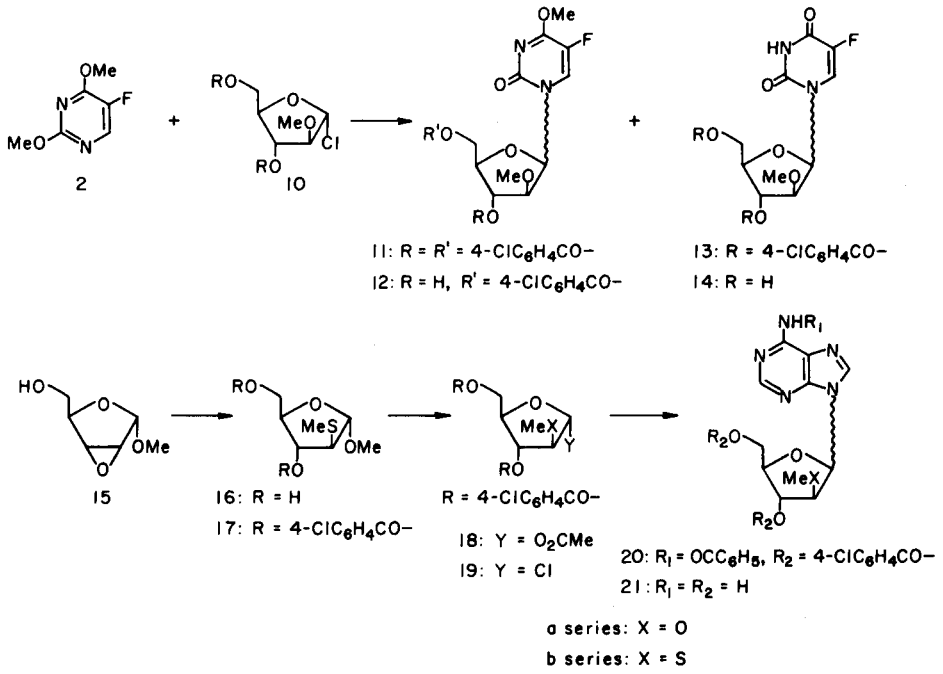


of **2**, α- and β-**11**, **12**, α- and β-**13**, and α- and β-**14** resolved by hplc (14). The two major components of the mixture were the anomers of **11**; separation by silica gel chromatography established the ratio as 5β to 1α. The structures were confirmed by elemental analyses and pmr data. The anomeric proton of the β-anomer appears as a doublet of doublets at 6.29 ppm downfield from a singlet of the α-anomer at 6.08. In addition, the signal from the methoxy group of the β(*cis*)-anomer appears upfield from that of the methoxy group of the α(*trans*)-anomer, the upfield shift of signal from the *cis*-anomer being due to the anisotropic effect of the pyrimidine ring (15). The β-anomer (β-**11**) was converted to the uracil β-**13** by treatment with chloroform saturated with hydrochloric acid. Deacylation was accomplished with methanolic sodium methoxide to give 1-(2-*O*-methyl-β-D-arabinofuranosyl)-5-fluorouracil (β-**14**) in 31% overall yield.

The synthesis of 2′-*O*-methyl-9-β-D-arabinofuranosyladenine (β-**21a**) was accomplished by the reaction of 3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-α-D-arabinofuranosyl chloride (**10**) with 6-benzamidopurine in ethylene chloride containing molecular sieve followed by removal of the blocking groups of **20a** by treatment with methanolic sodium methoxide. A small amount of the α-anomer (α-**21a**) was also isolated and identified by its pmr spectrum, although it could not be crystallized and freed of the β-anomer. In this case also, the signal from the anomeric proton of the β (*cis*) appears downfield from that of the α *(trans)* and the methoxy group signal of the β, upfield from that of the α (15).

The approach to synthesis of 2′-deoxy-2′-(methylthio)-arabinonucleosides was modeled after that used for the 2′-*O*-methylarabinonucleosides. As anticipated, opening the epoxide ring of methyl 2,3-anhydro-α-D-ribofuranoside (**15**) with methanolic sodium methylmercaptide gave a good yield of methyl 2-deoxy-2-(methylthio)-α-D-arabinofuranoside (**16**), reaction occurring exclusively at C-2. The structure of **16** was confirmed by mass spectral and pmr data. Preparation of the blocked sugar **17** was carried out in high yield by reaction of **16** with 4-chlorobenzoyl chloride in pyridine. Acetolysis of **17** at -20° with a mixture of acetic acid, acetic anhydride, and sulfuric acid proceeded poorly giving a 24% yield of an anomeric mixture (3.5 α to 1 β) of the 1-*O*-acetoxy compound **18b**. Reaction of **18b** with ether-hydrogen chloride gas at -70° gave the chloro sugar **19b** as a syrupy product, the pmr spectrum of which showed it to be mostly the α-anomer. Coupling of the highly unstable chloro sugar **19b** with 6-benzamidopurine as described for the 2-*O*-methyl sugar **10** gave the blocked nucleosides **20b** as an anomeric mixture. Without purification, **20b** was deacylated with methanolic sodium methoxide to give an 8% yield of pure cyrstalline β-**21b** along with a 6% yield of α-**21b**. As in the case of the 9-(2′-*O*-methyl-D-arabinofuranosyl)adenines, in the pmr spectra the signal from the anomeric proton of the β appears downfield from that of the α, and the signal from the *S*-methyl group of the β appears upfield from that of the α (15). The low yield of nucleosides (14% *vs.* 35% with **10**) appears to be due to decomposition of the chloro sugar **19b** during the reaction.

Of the compounds described herein, only the α-anomer of ara-C was cytotoxic to H. Ep.-2 cells in culture ($ED_{50}$ =

10 μg./ml.), and it was inactive against L1210 leukemia *in vivo* at 200 mg./kg. (given on days 1,5, and 9).

## EXPERIMENTAL

All evaporations were carried out *in vacuo* with a rotary evaporator. All solvents were dried over Linde 4A molecular sieve, and samples were normally dried *in vacuo* over phosphorus pentoxide at room temperature (unless otherwise stated) for 16 hours. Analtech precoated (250 μm.) silica gel G(F) plates developed in chloroform-methanol (ratio specified for each compound) were used for the tlc analyses; the spots were detected by irradiation with a Mineralight and by charring after spraying with saturated ammonium sulfate. Brinkmann 2-mm. silica gel 60F-254 preparative tlc plates (8 in. x 8 in.) were used for preparative tlc purification. Melting points were determined with a Mel-Temp apparatus and are uncorrected. The uv absorption spectra were determined in 0.1 *N* hydrochloric acid (*p*H 1), *p*H 7 phosphate buffer, and 0.1 *N* sodium hydroxide (*p*H 13) with a Cary 17 spectrophotometer; the maxima are reported in nm ($\epsilon \times 10^{-3}$). The nmr spectra were determined with a Varian XL-100-15 spectrometer with tetramethylsilane as an internal reference; chemical shifts (δ in ppm) quoted in the case of multiplets are measured from the approximate center. Mass spectral data were obtained with a Varian MAT 311A instrument equipped with a combination EI/FI/FD ion source.

1-α-D-Arabinofuranosylcytosine (**6**).

A solution of 10.5 mmoles of 2,3,5-tri-*O*-benzoyl-D-arabinofuranosyl chloride (**3**) and 1.47 g. (10.5 mmoles) of 2,4-dimethoxypyrimidine (**1**) in 200 ml. of acetonitrile containing 5 g. of Linde 4A molecular sieve was stirred and refluxed for 6 hours, filtered, and evaporated to dryness *in vacuo*. A chloroform solution of the residue was dried over magnesium sulfate and evaporated to dryness to give 4-methoxy-1-(2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl)-2-(1*H*)pyrimidinone (**4**) as a cream-colored glass. It was used without further purification; $^1$H nmr (deuteriochloroform): δ 3.97 (s, $OCH_3$), 4.70 (m, $H_5'$) 5.06 (m, $H_4'$), 5.76 (m, $H_3'$), 5.94 (d, $H_5$), 6.06 (t, $H_2'$), 6.23 (d, $J_{1',2'}$ = 2.5 Hz, $H_1'$), 7.3-8.2 (broad m, phenyl), 7.7 (d, $J_{5,6}$ = 7 Hz, $H_6$).

A solution of the blocked nucleoside in 100 ml. of methanol saturated at 0° with ammonia was heated in a stainless steel bomb at 100° for 20 hours, then evaporated to dryness *in vacuo*. The syrupy residue was purified by preparative tlc (3:1 chloroform-methanol). The product was obtained by extraction with methanol. It was recrystallized from methanol, yield 640 mg. (25%), m.p. 158-160°; uv: *p*H 1, 280 (13.4), *p*H 7, 271 (8.50), *p*H 13, 272 (9.05); $^1$H nmr (DMSO-$d_6$): δ 3.5 (m, $2H_5'$), 3.8-4.2 (m, $H_2'$, $H_3'$, $H_4'$), 4.96 (t, $O_5'$H), 5.40 (d, $O_3'$H or $O_2'$H), 5.62 (d, $O_2'$H or $O_3'$H), 5.7 ($H_1'$), 5.76 (d, $H_5$), 7.15 (broad s, $NH_2$), 7.64 (d, $J_{5,6}$ = 7 Hz, $H_6$).

*Anal.* Calcd. for $C_9H_{13}N_3O_5 \cdot 1/3H_2SO_4$: C, 39.05; H, 4.86; N, 15.32. Found: C, 39.27; H, 4.76; N, 15.26.

To a hot solution of 176 mg. (0.7 mmole) of α-ara-C (**6**)·$1/3H_2SO_4$ in 20 ml. of water was added 1 mmole of picric acid. Cooling produced a crystalline precipitate of the picrate of α-ara-C that was collected by filtration, yield 210 mg. (64%).

The analytical sample was obtained by recrystallization from water, m.p. 87-88°.

*Anal.* Calcd. for $C_{15}H_{16}N_6O_{12}$: C, 38.14; H, 3.41; N, 17.79. Found: C, 38.03; H, 3.47; N, 17.54.

1-α-D-Arabinofuranosyl-5-fluorouracil (**9**).

To an azeotropically dried suspension of 2.32 g. (7.05 mmoles) of 5-fluorouracil mercury (**7**) in 350 ml. of toluene was added 7.40 g. (14.1 mmoles) of 2,3,5-tri-*O*-benzoyl-α-D-arabinofuranosyl bromide. The resulting suspension was refluxed for 30 minutes, then filtered, and evaporated to dryness *in vacuo*. A solution of the residue in 100 ml. of ethyl acetate was washed twice with 50 ml. of 30% aqueous potassium iodide solution, then 50 ml. of water, dried over magnesium sulfate, and evaporated to dryness *in vacuo*, giving 1-(2,3,5-tri-*O*-benzoyl-D-arabinofuranosyl)-5-fluorouracil (**8**) as a yellow glass.

A solution of the blocked nucleoside in 21 ml. of 1*N* methanolic sodium methoxide was refluxed for 45 minutes, deionized with Amberlite IR-120 (H) ion-exchange resin, and evaporated to dryness *in vacuo*. The residue was purified by preparative tlc (3:1 chloroform-methanol). The product was obtained by extraction with methanol, yield 968 mg. (53%). The analytical sample of **9** was obtained by recrystallization from methanol, yield 710 mg. (39%), m.p. 108-110°; rotation $[\alpha]_D^{26}$ + 20.0 ± 0.6° (c 0.24 in water); uv: *p*H 1, 269 (8.65), *p*H 7, 269 (8.12), *p*H 13, 270(6.65); $^1$H nmr (DMSO-$d_6$): δ 3.5 (m, $2H_5'$), 3.9 (m, $H_3'$), 4.2 (m, $H_2'$ and $H_4'$), 5.73 (d of d, $J_{1'2'}$ = 3.7 Hz, $J_{HF}$ = 1.7 Hz, $H_1'$), 8.02 (d, $J_{HF}$ = 7 Hz, $H_6$).

*Anal.* Calcd. for $C_9H_{11}FN_2O_6$: C, 41.23; H, 4.23; N, 10.68. Found: C, 40.98; H, 4.27; N, 10.43.

$^1$H nmr of β-anomer (13) (DMSO-$d_6$): δ 3.7 (m, $H_4'$ and $2H_5'$), 3.9 (m, $H_3'$), 4.1 (m, $H_2'$), 5.1 (t, $O_5'$-H), 5.5 (d, $O_3'$-H), 5.6 (d, $O_2'$-H), 5.96 (d of d, $J_{1'2'}$ = 4.4 Hz, $J_{HF}$ = 1.8 Hz, $H_1'$), 7.95 (d, $J_{HF}$ = 7.6 Hz, $H_6$), 11.77 (broad s, NH).

The Reaction of 3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-α-D-arabinofuranosyl Chloride (**10**) with 5-Fluoro-2,4-dimethoxypyrimidine (**2**).

A mixture of 1.00 mmole of 3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-α-D-arabinofuranosyl chloride (**10**) and 474 mg. (3.00 mmoles) of 5-fluoro-2,4-dimethoxypyrimidine (**2**) was heated in an 80° oil bath for 8 hours. The resulting fusion product was examined by hplc and then purified by preparative tlc (99:1 chloroform-methanol). Two major (and several minor) products were obtained. The slower moving band was extracted with methanol to give the β-anomer (β-**11**) as a tlc-homogeneous syrup, yield 230 mg. (41%). The analytical sample was obtained by crystallization of a small sample from methanol, m.p. 144-145°; $^1$H nmr (deuteriochloroform): δ 3.32 (s, $OCH_3$ of sugar), 4.06 (s, $OCH_3$ of pyrimidine), 4.22 (d, $H_2'$), 4.51 (m, $H_4'$), 4.7 (m, $2H_5'$), 5.42 (d, $H_3'$), 6.29 (d of d, $J_{1',2'}$ = 3.6 Hz, $J_{H_1',F}$ = 1.6 Hz, $H_1'$), 7.84 (d, $J_{H,F}$ = 6 Hz, $H_6$), 7.3-8.1 (m, phenylene).

*Anal.* Calcd. for $C_{25}H_{21}Cl_2FN_2O_8$: C, 52.92; H, 3.73; N, 4.94. Found: C, 52.87; H, 3.44; N, 4.74.

The faster moving band was extracted with methanol to give the α-anomer (α-**11**) as a syrup, yield 51 mg. (9%). The analytical sample was obtained as a crystalline solid from ethanol, m.p. 152-153°; $^1$H nmr (deuteriochloroform): δ 3.65 (s, $OCH_3$ of sugar), 4.05 (s, $OCH_3$ of pyrimidine), 4.22 (s, $H_2'$), 4.61 (m, $2H_5'$), 4.91 (m, $H_4'$), 5.44 (s, $H_3'$), 6.08 (s, $H_1'$), 7.3-8.1 (m, phenyl and $H_6$).

*Anal.* Calcd. for $C_{25}H_{21}Cl_2FN_2O_8$: C, 52.92; H, 3.73; N, 4.94. Found: C, 53.21; H, 3.77; N, 4.76.

1-(2-*O*-Methyl-β-D-arabinofuranosyl)-5-fluorouracil (β-**14**).

A solution of 984 mg. (1.73 mmoles) of 5-fluoro-4-methoxy-1-[3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-β-D-arabinofuranosyl]-2(1*H*)pyrimidinone (β-**11**) in 25 ml. of chloroform saturated at 0° with hydrogen chloride gas was kept at room temperature for 20 hours, then evaporated to dryness *in vacuo*, giving 1-[3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-β-D-arabinofuranosyl]-5-fluorouracil (β-**13**) as a colorless syrup.

A solution of the syrup in 28 ml. of 0.11 *N* methanolic sodium methoxide was refluxed for 45 minutes, deionized with Amberlite

IR-120 (H) ion-exchange resin, and evaporated to dryness *in vacuo*. The white solid thus obtained was recrystallized from ethanol, yield 232 mg., m.p. 184-185°. A second crop was obtained from the filtrate, yield 104 mg. [total yield 336 mg. (70%)]; tlc (9:1 chloroform-methanol); uv: *p*H 1, 268 (9.12), *p*H 7, 268 (8.62), *p*H 13, 269 (7.24); $^1$H nmr (DMSO-$d_6$): δ 3.29 (s, $OCH_3$ of sugar), 3.64 (m, $H_4'$ and $2H_5'$), 3.88 (t, $H_2'$), 4.05 (t, $H_3'$), 6.11 (d of d, $J_{1',2'}$ = 5.5 Hz, $J_{H,F}$ = 1.8 Hz, $H_1'$), 8.05 (d, $J_{H,F}$ = 6.5 Hz, $H_6$).

*Anal.* Calcd. for $C_{10}H_{13}FN_2O_6$: C, 43.48; H, 4.74; N, 10.14. Found: C, 43.63; H, 4.46; N, 10.00.

2′-*O*-Methyl-9-β-D-arabinofuranosyladenine (β-**21a**).

A mixture of 2.0 mmoles of 3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-α-D-arabinofuranosyl chloride (**10**) and 480 mg. (2.0 mmoles) of *N*-benzoyladenine in 40 ml. of ethylene chloride containing 5 g. of Linde 4A molecular sieve was stirred and refluxed for 11 days, filtered, and evaporated to dryness *in vacuo* to give *N*-benzoyl-9-[3,5-di-*O*-(4-chlorobenzoyl)-2-*O*-methyl-D-arabinofuranosyl]adenine (**20a**) as an orange glass. The material was used in the next step without further purification; $^1$H nmr (deuteriochloroform): δ 3.33 (s, $OCH_3$), 4.14 (d, $H_2'$), 6.69 (d, $J_{1',2'}$ = 4.0 Hz, $H_1'$).

A solution of the blocked nucleoside in 56 ml. of 0.11 *N* methanolic sodium methoxide was refluxed for 30 minutes, deionized with Amberlite IR-120 (H) ion-exchange resin, and filtered. Evaporation of the filtrate gave an orange glass that was crystallized from methanol as a white solid (β-**21a**), yield 96 mg. Another crop was obtained by purification of the filtrate by preparative tlc (3:1 chloroform-methanol). The β-anomer was obtained from the faster moving band. Extraction with methyl alcohol gave a white solid, yield 75 mg., total yield 171 mg. (30%), m.p. 219-220°; uv: *p*H 1, 257 (14.7); *p*H 7, 258 (15.1), *p*H 13, 258 (15.2); $^1$H nmr (DMSO-$d_6$): δ 3.12 (s, $OCH_3$), 3.67 (m, $2H_5'$), 3.74 (m, $H_4'$), 4.04 (t, $H_2'$), 4.32 (m, $H_3'$), 5.04 (t, $O_5'H$), 5.86 (d, $O_3'H$), 6.41 (d, $J_{1',2'}$ = 5.0 Hz, $H_1'$), 7.25 (s, $NH_2$), 8.16 and 8.21 (2s, $H_2$, $H_8$).

*Anal.* Calcd. for $C_{11}H_{15}N_5O_4$: C, 46.97; H, 5.38; N, 24.90. Found: C, 47.02; H, 5.50; N, 25.20.

The α-anomer (α-**21a**) was obtained from the slower moving band. It was contaminated with about 20% β-anomer and would not crystallize, yield 32 mg. (< 5%); $^1$H nmr (DMSO-$d_6$): δ 3.33 (s, $OCH_3$), 3.5 (m, $H_4'$ and $2H_5'$), 4.2 (m, $H_3'$), 4.48 (t, $H_2'$), 6.03 (d, $J_{1',2'}$ = 4.0 Hz, $H_1'$), 7.30 (s, $NH_2$), 8.2 and 8.36 ($H_2$ and $H_8$).

Methyl 2-Deoxy-2-(methylthio)-α-D-arabinofuranoside (**16**).

A solution of methyl 2,3-anhydro-α-D-ribofuranoside (**15**, 1.8 g., 12.3 mmoles) in 5 *N* sodium methylmercaptide (9 ml.) was refluxed for 18 hours. The solution was carefully neutralized in the cold with concentrated hydrochloric acid and evaporated to dryness. The residue was evaporated with acetonitrile, then extracted into warm acetonitrile (2 x 50 ml.). The solution was dried over magnesium sulfate, evaporated to dryness, and dried *in vacuo*, yield 2.4 g. (100%); $^1$H nmr (deuteriochloroform): δ 2.20 (s, $SCH_3$), 3.07 (m, $H_2$), 3.42 (s, $OCH_3$), 3.81 (broad s, $2H_5$), 4.02 (broad s, $H_3$, $H_4$), 4.90 (d, $J_{1,2}$ = 2.1 Hz, $H_1$). Assignments of $H_2$ and $H_3$ verified by spin-decoupling.

Methyl 2-Deoxy-2-(methylthio)-3,5-di-*O*-(4-chlorobenzoyl)-α-D-arabinofuranoside (**17**).

A solution of methyl 2-deoxy-2-(methylthio)-α-D-arabinofuranoside (**16**, 2.4 g., 12.4 mmoles) in pyridine (25 ml.) was chilled in an ice bath while 3.2 ml. (25.0 mmoles) of 4-chlorobenzoyl chloride was added dropwise. The solution was then kept at room temperature for 20 hours before it was poured over 100 ml. of ice and saturated aqueous sodium bicarbonate solution. The mixture was extracted with 100 ml. of chloroform, and the chloroform extract was washed with 100 ml. each of aqueous sodium bicarbonate, ice-cold dilute sulfuric acid, and water. After drying over magnesium sulfate, the solution was evaporated to dryness *in vacuo* to give the product as a light yellow syrup, yield 5.33 g. (91%); tlc (3:1 cyclohexane-ethyl acetate); $^1$H nmr (deuteriochloroform): δ 2.25 (s, $SCH_3$), 3.34 (m, $H_2$), 3.44 (s, $OCH_3$), 4.60 (m, $H_4$ and $2H_5$), 5.04 (d, $J_{1,2}$ = 2 Hz, $H_1$), 5.38 (m, $H_3$). Assignments of $H_1$, $H_2$, and $H_3$ verified by spin-decoupling.

1-*O*-Acetyl-2-deoxy-2-(methylthio)-3,5-di-*O*-(4-chlorobenzoyl)-D-arabinofuranose (**18b**).

A solution of methyl 2-deoxy-2-(methylthio)-3,5-di-*O*-(4-chlorobenzoyl)-α-D-arabinofuranoside (**17**, 5.33 g., 11.3 mmoles) in 73.5 ml. of acetic anhydride, 147 ml. of acetic acid, and 0.59 ml. of concentrated sulfuric acid was kept at -20° for 20 hours before it was poured into 100 ml. of ice water. The mixture was stirred for 30 minutes and extracted with two 50-ml. portions of chloroform. The chloroform extract was washed with saturated aqueous sodium bicarbonate solution, then water, dried over magnesium sulfate, and evaporated to dryness *in vacuo* to give 1.97 g. of a dark syrup. The syrup was purified by preparative tlc (3:1 cyclohexane-ethyl acetate). Two major components were obtained. The faster traveling material was an unknown weighing 285 mg. The product was the slower moving material, yield 1.34 g. (24%). It was found to be a mixture of anomers, 3.5 α to 1 β: $^1$H nmr (deuteriochloroform): δ 2.04 (s, $CH_3CO_2$ of β), 2.11 (s, $CH_3CO_2$ of α), 2.21 (s, $SCH_3$ of β), 2.32 (s, $SCH_3$ of α), 3.46 (d, $H_2$ of α), 3.63 (d of d, $H_2$ of β), 4.4-4.9 (m, $2H_5$ and $H_4$ of α and β), 5.40 ($H_3$ of α), 5.65 (d of d, $H_3$ of β), 6.33 (s, $H_1$ of α), 6.50 (d, $J_{1,2}$ = 6 Hz, $H_1$ of β).

2-Deoxy-2-(methylthio)-3,5-di-*O*-(4-chlorobenzoyl)-D-arabinofuranosyl Chloride (**19b**).

A solution of 1.34 g. (2.68 mmoles) of 1-*O*-acetyl-2-deoxy-2-(methylthio)-3,5-di-*O*-(4-chlorobenzoyl)-D-arabinofuranose (**18b**) in 100 ml. of ether was chilled to -70° and saturated with anhydrous hydrogen chloride. The solution was kept for 4 days at -70° and then evaporated to dryness *in vacuo* to give the product as a purple syrup. It was used without purification; $^1$H nmr (deuteriochloroform): δ 2.08 (s, acetyl), 2.32 (s, $SCH_3$), 3.79 (d, $H_2$ of α), 4.75 (m, $H_4$ and $2H_5$), 5.41 (d, $H_3$), 6.30 (s, $H_1$ of α), 6.57 (d, $H_1$ of β).

*N*-Benzoyl-9-[3,5-di-*O*-(4-chlorobenzoyl)-2-deoxy-2-(methylthio)-D-arabinofuranosyl]adenine (**20b**).

A solution of 2.7 mmoles of 3,5-di-*O*-(4-chlorobenzoyl)-2-deoxy-2-(methylthio)-D-arabinofuranosyl chloride (**19b**) and *N*-benzoyladenine (745 mg., 2.7 mmoles) in 80 ml. of ethylene chloride containing 5 g. of Linde 4A molecular sieve was stirred at ambient temperature for 11 days, treated with 5 g. more of molecular sieve, refluxed for 18 hours, filtered, and then evaporated to dryness *in vacuo*. The residue was a brown syrup, yield 1.14 g. (62%); tlc (3:1 cyclohexane-ethyl acetate). The product was used in the next step without further purification.

9-[2-Deoxy-2-(methylthio)-β-D-arabinofuranosyl]adenine (β-**21b**).

A solution of crude *N*-benzoyl-9-[3,5-di-*O*-(4-chlorobenzoyl)-2-deoxy-2-(methylthio)-D-arabinofuranosyl]adenine (**20b**, 1.14 g., 1.68 mmoles) in 30 ml. of 0.17 *N* methanolic sodium methoxide was refluxed for 1 hour, deionized by stirring with Amberlite IR-120 (H) ion-exchange resin, and then evaporated to dryness *in vacuo*. The dark, gummy residue was dissolved in 20 ml. of water, and the solution was washed with chloroform (50 ml.). Chilling the aqueous solution produced 54 mg. of a dark cyrstalline

solid, which was recrystallized from methanol to give the β-anomer as a white solid, yield 42 mg. (8%); m.p. 188-190°; tlc (5:1 chloroform-methanol); uv: *p*H 1, 259 (14.5); *p*H 7 and *p*H 13, 260 (15.6); $^1$H nmr (DMSO-$d_6$): δ 1.94 (s, SMe), 3.75 (m, $H_2'$, $H_4'$, and $2H_5'$), 4.3 (m, $H_3'$), 5.14 (t, $O_5'H$), 5.75 (d, $O_3'H$), 6.49 (d, $J_{1',2'}$ = 6.0 Hz, $H_1'$), 7.24 (s, $NH_2$), 8.16 and 8.27 (2s, $H_2$ and $H_8$).

*Anal.* Calcd. for $C_{11}H_{15}N_5O_3S \cdot H_2O$: C, 41.90; H, 5.43; N, 22.21. Found: C, 42.08; H, 5.37; N, 22.14.

Purification of the aqueous filtrate by preparative tlc gave 12 mg. of an unknown material and 30 mg. (6%) of material that appears to be the α-anomer (α-**21b**); ms: 297 $(M)^+$, 250 $(M - SMe)^+$, 136 $(adenine + 2)^+$; uv: *p*H 1, 257 (10.3), *p*H 7, 260 (10.3), *p*H 13, 259 (10.5); $^1$H nmr (DMSO-$d_6$): δ 2.02 (s, SMe), 3.6 (m, $H_4'$ and $2H_5'$), 4.1 (m, $H_2'$ and $H_3'$), 4.85 (broad s, OH), 6.05 (m, $H_1'$ and OH), 7.3 (broad s, $NH_2$), 8.18 and 8.42 (2s, $H_2$ and $H_8$).

Acknowledgment

This investigation was supported by the Division of Cancer Treatment, National Canter Institute, National Institutes of Health, Department of Health, Education, and Welfare, Contract NO1-CM-43762. The authors are indebted to Dr. W. C. Coburn Jr., and Mrs. Martha C. Thorpe, who interpreted the nmr data, and to other members of the Molecular Spectroscopy Section of Southern Research Institute, who performed most of the microanalytical and spectral determinations reported.

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