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SYNTHESIS OF 2- (AND 6-) -DITHIAN-2-YLURACIL NUCLEOSIDES AND THEIR CONVERSION INTO NUCLEOSIDE DERIVATIVES*

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ABSTRACT

Addition of 2,2′-anhydro-[1-(3-*O*-acetyl-5-*O*-trityl-β-D-arabinofuranosyl)uracil] (**1**) to excess 2-litho-1,3-dithiane (**2**) in oxolane at −78° gave 2-(1,3-dithian-2-yl)-1-(5-*O*-trityl-β-D-arabinofuranosyl)-4(1*H*)pyrimidinone (**3**), O^2,2′-anhydro-5,6-dihydro-6-(*S*)-(1,3-dithian-2-yl)-5′-*O*-trityluridine (**4**), and 2-(1,4-dihydroxybutyl)-1,3-dithiane (**5**) in yields of 15, 30, and 10% respectively. The structure of **3** was proved by its hydrolysis in acid to give 2-(1,3-dithian-2-yl)-4-pyrimidinone (**6**) and arabinose, and by desulfurization with Raney nickel to yield the known 2-methyl-1-(5-*O*-trityl-β-D-arabinofuranosyl)-4(1*H*)-pyrimidinone (**7**). Detritylation of **3** without glycosidic cleavage could only be effected by prior acetylation to 1-(2,3-di-*O*-acetyl-5-*O*-trityl-β-D-arabinofuranosyl)-2-(1,3-dithian-2-yl)-4(1*H*)-pyrimidinone (**8**) which, after treatment with acetic acid at room temperature for 65 h followed by the action of sodium methoxide gave 2-(1,3-dithian-2-yl)-1-β-D-arabinofuranosyl-4(1*H*)-pyrimidinone (**10**) in 45% yield. Detritylation of **4** in boiling acetic acid gave 5,6-dihydro-6-(*S*)-(1,3-dithian-2-yl)-1-β-D-arabinofuranosyluracil (**12**) and 3-[(*S*)-1-(1,3-dithian-2-yl)]propionamido-(1,2-dideoxy-β-D-arabinofurano)-[1,2-*d*]-2-oxazolidinone (**13**) in 10 and 90% yields, respectively. When **12** was kept in water or methanol for 7 days, quantitative conversion into **13** occurred. Acid hydrolysis of **12** afforded arabinose and 5,6-dihydro-6-(1,3-dithian-2-yl)uracil (**14**), which was desulfurized with Raney nickel to the known 5,6-dihydro-6-methyluracil (**15**). Treatment of **13** with trifluoroacetic anhydride–pyridine yielded 77% of the cyano derivative **17**. Similar dehydration of 3-(*R*)-1-methylpropionamido-(1,2-dideoxy-β-D-arabinofurano)-[1,2-*d*]-2-oxalidinone (**18**), obtained by desulfurization of **13**, gave 60% of the nitrile **19**. Hydrogenation of **19** over platinum oxide in acetic anhydride gave the acetamide derivative **20** in 95% yield. Nitrobenzoylation of **13** gave 3-[(*S*)-1-(1,3-dithian-2-yl)]cyanomethyl-3,5-di-*O*-*p*-nitrobenzoyl-(1,2-dideoxy-β-D-arabinofurano)-[1,2-*d*]-2-oxazolidinone (**22**), which was converted in 37% yield by treatment with methyl iodide in dimethyl sulfoxide into the aldehyde **24**, characterized as the semicarbazone **25**. The purification of **5** and its characterization as 2-(1,4-di-*O*-*p*-nitrobenzoylbutyl)-1,3-dithiane (**27**) is described.

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INTRODUCTION

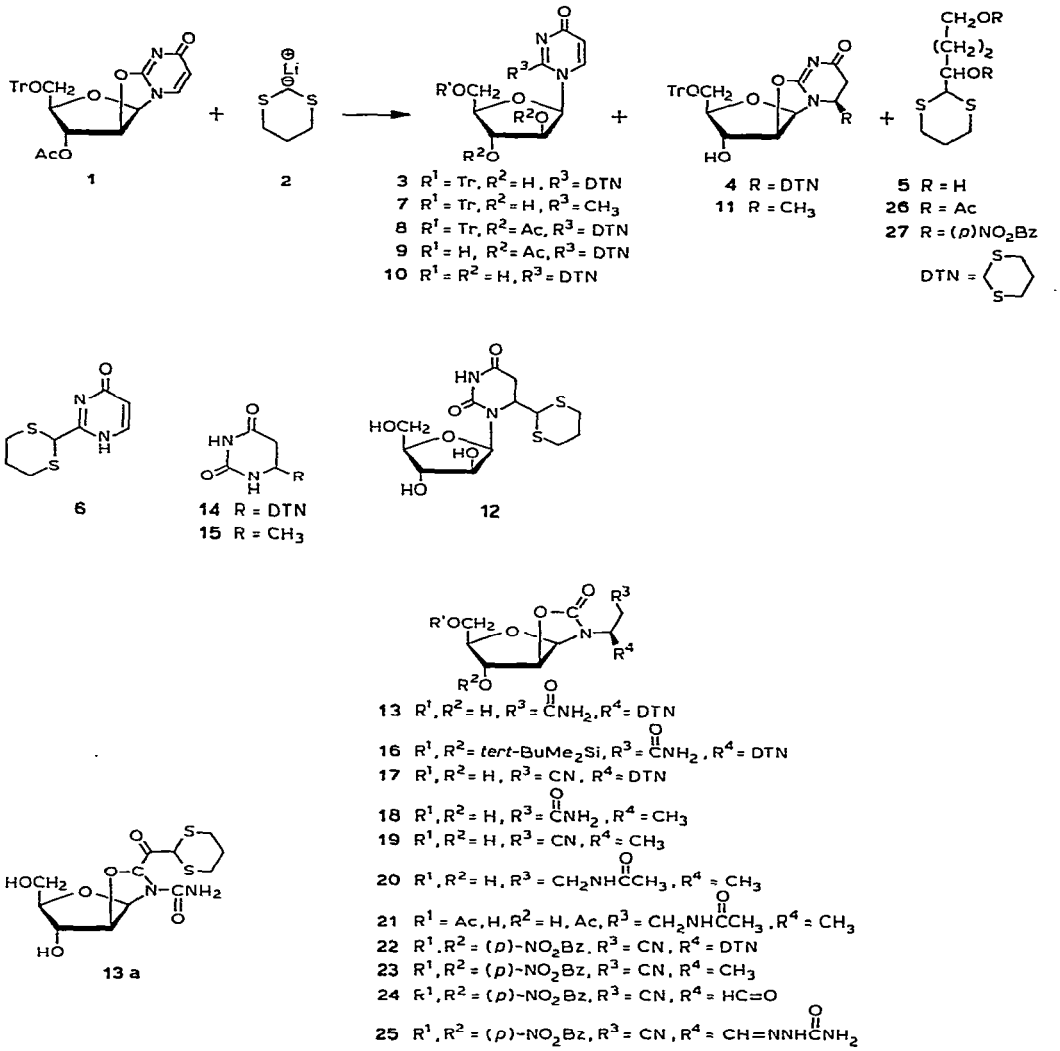
The use of lithiated 1,3-dithianes as nucleophilic, acylating agents is well known. In recent years the reaction has been successfully applied to carbohydrates by both Paulsen's and Gero's groups to give a variety of branched-chain sugars. Thus, 2-lithio-1,3-dithiane is known[2] to react nucleophilically with 2-keto[2], 3-keto[2,3], halo[4], anhydro[5], and aldehydo[6] sugars.

This laboratory has for some time been concerned with the synthesis of branched-chain glycosyl α-amino acids[7-10] (and nucleosides thereof), and the use of lithiated 1,3-dithiane suggested a new route to these α-amino acids via the formyl functionality that may be generated from the cyclic thioacetal after carbon–carbon bond-formation. Moreover, reports of the isolation[11] and synthesis[12] of N^3-(3-L-amino-3-carboxypropyl)uridine 5′-monophosphate from *Escherichia coli* tRNA prompted us to extend our synthetic studies on glycosyl α-amino acid to include nucleosidic-base derivatives of this type, in an effort to form analogs of biological interest. We thus report herein the first examples of pyrimidine modifications of an anhydrouridine nucleoside by the dithianyl anion.

RESULTS AND DISCUSSION

Reaction of [1-(3-*O*-acetyl-5-*O*-trityl-β-D-arabinofuranosyl)-2,2′-anhydro-uracil][13] (**1**) with an excess of 2-lithio-1,3-dithiane[1] (**2**) in oxolane at −78° gave two major products (**3**, 15% and **4**, 30%), which were isolated chromatographically, together with a minor, low molecular-weight compound (**5**), obtained from a mixture of several components of high R_F values.

Compound **3** was characterized as 2-(1,3-dithian-2-yl)-1-(5-*O*-trityl-β-D-arabinofuranosyl)-4(1*H*)-pyrimidinone, that is, as the product arising from attack of the dithianyl anion on C-2 of the anhydronucleoside with concomitant generation of an arabinofuranosyl group. Such displacement-additions at C-2 of anhydronucleosides by a variety of nucleophiles (OH^-, NH_2, SH^-) are well known[14-16]. The n.m.r. spectrum of **3** in dimethyl sulfoxide-d_6 showed two D_2O-exchangeable protons as doublets at δ 5.71 and 5.92 attributable to the secondary hydroxyl groups at C-2′ and C-3′ (the 3′-OH group simply resulting from hydrolysis of the acetate group of **1** under the basic conditions of the reaction). Moreover, H-1″ (namely, SC*H*S) gave rise to a sharp singlet at δ 5.46, downfield from its usual position of δ ~4.3, possibly because of its proximity to the unsaturated imine group. The mass spectrum of **3** showed a prominent peak at *m/e* 375 arising from glycosyl C–N cleavage. When **3** was heated for 10 min in 80% aqueous acetic acid, hydrolysis of both the glycosidic linkage and the 5′-trityl group occurred, yielding (*a*) D-arabinose, (*b*) 2-(1,3-dithian-2-yl)-4-pyrimidinone (**6**), whose structure was readily verified by n.m.r. and chemical analysis, and (*c*) triphenylmethanol. Further proof of structure of **3** came from its desulfurization with Raney nickel in ethanol to give the known 2-methyl-1-(5-*O*-trityl-β-D-arabinofuranosyl)-4(1*H*)-pyrimidinone[14] (**7**).



Detritylation of **3** to give the free nucleoside was hampered by the extreme acid-lability of the glycosyl C–N bond. The use of dilute mineral or acetic acid, even at room temperature, always resulted in cleavage of the aglycon. As the presence of electron-withdrawing groups at C-2′ and C-3′ has been observed to decrease the ease of hydrolysis of the glycosidic linkage in nucleosides[17], compound **3** was acetylated in acetic anhydride–pyridine to give the 2′,3′-di-*O*-acetyl-5′-*O*-trityl derivative **8**, which was then stirred in 80% aqueous acetic acid for 65 h at room temperature, yielding the detritylated compound **9**, isolated by column chromatography on silica gel, with minimal hydrolysis of the glycosylic bond.

Treatment of the diacetate **9** with methanolic sodium methoxide then gave the completely deprotected, amorphous nucleoside analog 2-(1,3-dithian-2-yl)-1-β-D-

arabinofuranosyl-4(1*H*)-pyrimidinone (**10**). The elemental analysis and high-resolution mass spectrum of **10** agreed with the formula $C_{13}H_{18}N_2O_5S_2$, and its n.m.r. spectrum in dimethyl sulfoxide-d_6 clearly indicated the three D_2O-exchangeable hydroxyl resonances as two doublets (at δ 5.52 and 5.83) and a triplet (at δ 5.15).

The second, major product formed in the reaction of **1** and **2** was O^2,2′-anhydro-5,6-dihydro-6-(*S*)-(1,3-dithian-2-yl)-5′-*O*-trityluridine (**4**) arising from 1,4 Michael-type addition of the dithianyl anion to the α,β-unsaturated carbonyl system of the anhydronucleoside **1**. The unsubstituted 1,3-dithianyl anion generally undergoes only 1,2-addition to α,β-unsaturated carbonyl systems[18,19], so that this reaction with anhydronucleoside **1** constitutes, to our knowledge, the first such 1,4-addition*.

The n.m.r. spectrum of **4** showed, in addition to the trityl and dithianyl groups, only one D_2O-exchangeable hydroxyl proton (at δ 5.50) and, significantly, disappearance of the low-field H-5 and H-6 doublets of the pyrimidine ring, with generation of a two-proton multiplet in the δ 2.64–3.26 region (H-5), obscured by the large dithiane resonances. Also, the H-1′ and H-2′ resonances (at δ 6.25 and 5.18 respectively), and their coupling constant of 5.0 Hz agreed with the formulated O^2,2′-anhydro structure. These values correspond closely to those obtained by Hall and coworkers[21] for various C-5 and C-6 substituted O^2,2′-anhydro-5,6-dihydronucleosides. The i.r. spectrum of **4** also showed absorbances characteristic of a O-C=N-C=O system[21] [1702 (m), 1595 (vs), and 1460 (s) cm^{-1}].

In order to obtain clearer n.m.r. evidence for the presence of two protons at C-5, compound **4** was desulfurized with Raney nickel in ethanol to give the 6-methyl derivative **11**. The 100-MHz n.m.r. spectrum of compound **11** in dimethyl sulfoxide-d_6 showed a 3-proton doublet at δ 1.27 with a coupling constant (J_{6,CH_3}) of 6.4 Hz attributed to the methyl group, whereas H-5 resonated as a two-proton doublet at δ 2.26 ($J_{5,6}$ 7.0 Hz) and H-6 as a one-proton multiplet at δ 3.70. These assignments were verified by decoupling experiments and firmly established the position of the dithianyl group at C-6 of compound **4**.

When, in an attempt at detritylation, compound **4** was boiled in 80% aqueous acetic acid for 10 min, two compounds (**12** and **13**) were unexpectedly produced and were chromatographically separated on a weakly acidic cation-exchange resin. The faster-migrating component (**12**) obtained crystalline in 5% yield was shown to be 5,6-dihydro-6-(*S*)-(1,3-dithian-2-yl)-1-β-D-arabinofuranosyluracil, that is, the compound arising from detritylation and hydrolysis of the O^2,2′-anhydro linkage of **4**. Acidic hydrolysis of O^2-2′-anhydronucleosides to give nucleosides having the arabino configuration is well known[22].

That compound **12** did not possess an anhydro structure was shown by the presence in its n.m.r. spectrum, taken in dimethyl sulfoxide-d_6, of one primary hydroxyl resonance (at δ 4.85) and two secondary hydroxyl resonances (at δ 5.60 and 5.36), as well as a low-field (δ 10.31), D_2O-exchangeable N*H* resonance. The

*The dithianyl anion **2** is known to exhibit a 1,4-addition to nitroalkenes[20]. Furthermore, various 2-substituted 1,3-dithianyl anions, such as 2-lithio-2-methoxycarbonyl-1,3-dithiane, give exclusively the 1,4-addition products with α,β-unsaturated carbonyl derivatives[19]. For a general review of dithiane chemistry, see ref. 19.

u.v. spectrum of **12** in methanol showed a maximum at 245 nm, the position of absorption of the dithiane ring[23], but there was no absorption above this value. The i.r. spectrum of **12** no longer displayed the characteristic anhydro-dihydro pattern seen in **4** but rather, closely resembled that of dihydrouridine, as prepared by the method of Levene and LaForge[24], which exhibited peaks at 3400 (OH), 1710 (C=O), 1690 (C=O), and 1600 cm^{-1} (C=N of tautomer). The mass spectrum of **12** showed an intense peak at *m/e* 133 corresponding to M^+-[5,6-dihydro-6-(*S*)-(1,3-dithian-2-yl)uracil]. No typical anhydronucleoside fragmentation-patterns were observed[25]. Furthermore, compound **12** was cleaved under fairly mild acidic conditions (M hydrochloric acid, 4 h, 60°) to give arabinose and the corresponding 6-dithianyldihydrouracil (**14**). Compound **14** was unambiguously characterized by its conversion with Raney nickel into the known[26] 6-methyldihydrouracil (**15**). The *N*-glycosyl bond of 5,6-dihydropyrimidine nucleosides has been observed to be much more sensitive to acid hydrolysis than that of the corresponding unsaturated nucleosides[27].

Compound **13**, the second and major (90%) product formed by acid treatment of **4**, had an i.r. spectrum which, from the previous discussion, discounted an O^2,2′-anhydro structure: two carbonyl-stretching peaks [at 1680 cm^{-1} (amide) and 1740 cm^{-1} (lactone)], as well as a possible amide II peak at 1615 cm^{-1} were observed. The proton-decoupled, ^{13}C-n.m.r. spectrum of **13** in D_2O corroborated the i.r. evidence of the presence of two carbonyl groups; two weak singlets at δ 177.0 and 159.8 were attributed to carbonyl groups of a primary amide and a carbamate group, respectively, based on correlations with the known ^{13}C resonances of these groups in other molecules[28]. The ^1H-n.m.r. spectrum of **13** in dimethyl sulfoxide-d_6 showed the resonance of a primary hydroxyl proton as a triplet at δ 4.70, but that of only one secondary hydroxyl proton (δ 5.66), both of which exchanged rapidly with D_2O, together with two broad, one-proton singlets at δ 6.86 and 7.51 which, however, exchanged slowly with D_2O. These two broad peaks were assigned to the two magnetically non-equivalent protons of a primary amide group, based on i.r. data obtained from the product of the following experiment. When compound **13** was treated with two equiv. of *tert*-butyldimethylsilyl chloride in *N*,*N*-dimethylformamide–pyridine for 24 h, the free hydroxyl groups were selectively silylated to give **16**, the i.r. spectrum of which clearly revealed amide N–H stretching vibrations, previously buried by the intense hydroxyl absorptions (at 3420 and 3230 cm^{-1}) in the spectrum of **13**. These primary amide protons gave resonances in the n.m.r. spectrum of **16** as they had in that of **13**, that is, as two broad, slowly exchangeable, low-field, one-proton singlets. Thus, compound **13** was formulated as 3-[(*S*)-1-(1,3-dithian-2-yl)]propionamido-(1,2-dideoxy-β-D-arabinofurano)-[1,2-*d*]-2-oxazolidinone and would seem to arise, after initial acidic cleavage of the anhydro ring of **4**, from intramolecular attack at C-2 of the dihydropyrimidine ring of **12** by the C-2′ hydroxyl group, displacing the amide group and producing the 2-oxazolidinone structure of **13**.

An alternative structure for **13**, which would arise from scission of the 3,4 bond of **12** with concomitant lactonization, is **13a**. In fact, much evidence exists that this

bond rather than the 2,3 bond of dihydropyrimidines and dihydropyrimidine nucleosides is cleaved under a variety of conditions to give β-ureido acids[27,29]. However, the absence of a ureido group in compound **13** was demonstrated in the following two experiments. Firstly, compound **13** did not give a positive test with *p*-(dimethylamino)benzaldehyde, a reagent known to react selectively with ureido derivatives of pyrimidines and pyrimidine nucleosides[30]. Secondly, treatment of **13** with trifluoroacetic anhydride–pyridine in anhydrous 1,4-dioxane, conditions known to dehydrate primary amides to the corresponding nitriles in high yield[31], followed by hydrolytic processing of the mixture, gave compound **17** as a crystalline solid, the i.r. spectrum of which clearly showed nitrile absorption at 2260 cm^{-1} together with the single carbonyl absorption of the urethane structure at 1740 cm^{-1}. Although the possibility that a ureido functionality might also dehydrate to the corresponding *N*-cyano derivative has not been dismissed, such cyano groups absorb in the i.r. in the 2000 cm^{-1} region[32]. Thus, assuming that the hydrolysis of the anhydronucleoside **4** proceeds through the opened arabinonucleoside **12**, then the tendency of the dihydropyrimidine ring of **12** to cleave as it does in acidic media is no doubt attributable to the presence of the *cis* 2′-hydroxyl group, which can participate in scission of the nearby 2,3 bond but not of the more distant 3,4 bond.

To simplify the n.m.r. spectrum of **13**, the latter was desulfurized with Raney nickel in water to give the syrupy, non-fluorescent methyl derivative **18**. The n.m.r. spectrum of compound **18** showed the expected doublet for the methyl group at δ 1.18, and the C-2 protons of the propionamide group resonated as a sharp doublet at δ 2.43 showing a coupling constant ($J_{1,2}$) of 7.0 Hz.

The primary amide group of **18**, like that of **13**, was dehydrated by using trifluoroacetic anhydride–pyridine to give 3-(*R*)-1-methylcyanoethyl-(1,2-dideoxy-β-D-arabinofurano-[1,2-*d*]-2-oxazolidinone (**19**). The i.r. spectrum of **19** showed the expected nitrile absorption at 2260 cm^{-1} and a carbonyl absorption at 1740 cm^{-1}, while in the n.m.r. spectrum the two amide protons, seen at δ 6.80 and 7.44 in the spectrum of **18**, were no longer visible. These results are completely consistent with those obtained in the transformation of compound **13** into **17**. In addition, the n.m.r. data showed a downfield shift of 0.49 p.p.m. of the H-2 resonance in proceeding from the amide **18** to the (more electronegative) nitrile group of **19**. This is possible only if C-2 and the nitrile group are adjacent, so that **13** (rather than **13a**) must be the correct structure.

To confirm chemically the presence of a nitrile group in **19**, the latter was hydrogenated over platinum oxide in acetic anhydride. The nitrile was thus converted in 33% yield to the *N*-acetyl derivative **20**, isolated by chromatography on silica gel. The i.r. spectrum of **20** showed the appropriate carbonyl absorption of the *N*-acetyl group at 1640 cm^{-1}, together with that of the 2-oxazolidinone group at 1740 cm^{-1}. No nitrile peak could be seen. The n.m.r. spectrum of **20** verified the presence of an acetamido group; a broad one-proton singlet, slowly exchangeable with D_2O, was observed at δ 7.88, and the acetate-proton signal appeared at δ 1.81 as a sharp singlet. The C-2 protons, now adjacent to the newly-formed 3-methylene group instead of to

the highly electronegative, nitrile functionality, showed an expected upfield shift (to δ 1.72). The proton resonances of the arabinofuranose moiety of **20** were essentially identical with those of the starting material **19**. Although chemical analysis of **20** showed the presence of 1.5 mol of water of hydration, a high-resolution mass spectrum of the material substantiated the assigned chemical formula of $C_{12}H_{20}N_2O_6$. Furthermore, a base peak in the mass spectrum at 114.0890 arising from the acetamidobutane fragment was further proof that the dihydrouracil ring of **4** had undergone 2,3-cleavage during acid hydrolysis.

A considerable amount (36%) of material of higher R_F value was also obtained from chromatography of the hydrogenation products of **19**, and was identified by n.m.r. spectroscopy as a mixture of the 3′- and 5′-acetates (**21**) of the acetamide **20**. These two monoacetates could not be separated by chromatography, and no further attempts were made to purify them. Formation of these *O*-acetylated by-products was prevented by hydrogenating a solution of compound **19** in ethanol and acetic anhydride and by shortening the reaction period to 2 h, to give **20** as the sole product, obviating the use of chromatography for purification.

All attempts to detritylate the anhydrodihydronucleosides **4** and **11** without causing simultaneous hydrolysis of the anhydro ring and the dihydropyrimidine ring were unsuccessful. Among the methods tried were hydrogenolysis over palladium catalysts[33], hydrolysis with either ferric chloride in dichloromethane[34], hydrogen chloride gas in anhydrous chloroform[35], or strongly acidic, cation-exchange resins and reduction with lithium in liquid ammonia[35]. That the acid lability of the anhydro ring of compound **4** is a function of the position of attachment of the dithianyl moiety in the dihydro structure rather than of any assistance imparted by the sulfur atoms of that moiety was shown by submitting the 6-methyl tritylated derivative **11**, in which the sulfur atoms are absent, to the same hydrolytic conditions used with compound **4**, namely, boiling for 10 min under reflux in 80% aqueous acetic acid. Only compound **18**, resulting from both anhydro and pyrimidine ring-cleavage, was formed. Curiously enough, none of the compound analogous to **12**, in which the dithianyl group is replaced by methyl, was isolated, indicating an inhibiting influence of the dithianyl group upon the hydrolysis of the dihydropyrimidine ring. Nevertheless, the ease with which this ring could be opened was demonstrated when a solution of the arabinonucleoside **12** in methanol or water was kept for 7 days or more at room temperature; total conversion into compound **13** occurred.

Although the exact geometry at C-6 of compound **4** has not yet been unequivocally determined, it would be expected that, as Paulsen has shown[3], the large dithianyl anion **2** would approach from the less-sterically hindered side of a molecule. As this would correspond to the exo side of **1**, then the *S* isomer of **4** should result[37]. No diastereomeric mixtures of compound **4** and its derivatives **12**, and **16–19** could be detected by n.m.r. or chromatography. Compound **12** had a strong, positive, c.d. spectrum displaying a maximum at 245 nm, which corresponds to the position of absorption of the dithianyl group[23]. This result would suggest that compound **12** and by inference its precursor **4**, are single isomers.

As our original purpose in introducing the dithianyl group into nucleosides was the further derivatization to α-amino acids, formylation of this group was the next crucial step. Toward this end, it was decided to protect the free hydroxyl and amide groups of compound **13** in order to prevent complicating side-reactions in any subsequent hydrolyses of the thioacetal. However, when **13** was *p*-nitrobenzoylated with an excess of *p*-nitrobenzoyl chloride in pyridine at room temperature, a single, crystalline product was formed (**22**) whose n.m.r. spectrum showed only two benzoate groups instead of the expected three. No D_2O-exchangeable protons were observed. The i.r. spectrum of **22** revealed that, just as in the case of the treatment of **13** with trifluoroacetic anhydride–pyridine, dehydration of the primary amide to give the nitrile derivative had occurred. This supposition was verified by removal of the *p*-nitrobenzoyl groups of **22** with methanolic sodium methoxide to give a compound identical to the unprotected nitrile **17** previously obtained directly from **13**. Similarly, when the methyl derivative **15** was *p*-nitrobenzoylated, 3-(*R*)-1-methylcyanoethyl-(1,2-dideoxy-3,5-di-*O*-*p*-nitrobenzoyl-β-D-arabinofurano)-[1,2-*d*]-2-oxazolidinone (**23**) was isolated. Such dehydrations of primary amides by acyl halides have been well documented[38].

When compound **17** was boiled for 1 h in M sodium hydroxide, the cyano group was hydrolyzed back to the primary amide to give compound **13**. For convenience, direct formylation of the dithianyl group of the dibenzoyl nitrile derivative **22** was attempted. However, it was found that **22** was completely inert to traditional mercuric chloride–mercuric oxide S–S acetal hydrolysis[39], and such other reagents as copper(II) chloride[40], *N*-bromo (and chloro) succinimide[41], and ceric ammonium nitrate[4,42] led to extensive decomposition of starting material. Finally, treatment of compound **22** with methyl iodide in dimethyl sulfoxide (a variation of Fétizon's methyl iodide–acetone procedure[43]) for 3 h at 55–60° led to complete alkylative hydrolysis to the aldehyde **24**. which was characterized as its semicarbazone **25** by n.m.r., i.r., and elemental analysis*.

Attempts to produce the 2-formyl derivative from the protected arabino pyrimidinone **8** by similar methods have thus far met with failure because of the extreme lability of the sugar–base linkage.

A third mode of addition of the dithiane anion **2** to the anhydronucleoside **1**, wherein the anion attacks at C-2′ of the sugar ring, displacing the anhydro bond, had also been envisaged; however, no such product was isolated from the reaction. Investigation of a mixture of material of higher R_F value obtained from the chromatography in which **3** and **4** were isolated did show some decomposition-product (**5**), possibly arising from attack at C-2′ by the dithiane anion. The identification of **5** as 2-(1,4-dihydroxybutyl)-1,3-dithiane was established as follows: the mixture of sugar components was acetylated (acetic anhydride–pyridine) and the crude material, consisting of both detritylated and tritylated fluorescent-charring components (R_F

*D. H. R. Barton and co-workers have subsequently informed us in a personal communication that benzeneseleninic anhydride[44] effectively generates the aldehyde **24** from the 1,3-dithianyl compound **22**.

0.30, 0.37 respectively, t.l.c. on silica gel with 10:1 benzene–ethyl acetate) was chromatographed on silica gel. Only the compound having R_F 0.30 (**26**, syrup) was observed by n.m.r. to contain the dithianyl moiety. Furthermore, only two acetate groups were observed, superposed on four hydrocarbon resonances. The mass spectrum showed a molecular weight of only 292, which, after subtraction of the masses of 1,3-dithiane and two acetates, left a skeleton of mass 54, accountable only by a four-carbon chain. Deacetylation of **26** in ammonia-saturated methanol and purification of the single product (**5**) generated by chromatography revealed by n.m.r. in dimethyl sulfoxide-d_6 that there was present a primary and a secondary hydroxyl group (δ 4.38 t, 4.68 d, D_2O-exchangeable). Finally, *p*-nitrobenzoylation of syrupy **5** gave a crystalline product (**27**) amenable to analysis. Decoupling n.m.r. experiments on **27** in chloroform-*d* showed that, when the C-2 and C-3 hydrocarbon protons were irradiated, the C-4 methylene group, previously a triplet at δ 4.45, collapsed to a singlet, whereas H-1 proton, a multiplet before irradiation (δ 5.44–5.68), collapsed to a sharp doublet showing a coupling constant equal to that of the S-C*H*-S proton (6.0 Hz).

If C-1 of **5**, **26**, and **27** corresponds to C-2′ of the anhydronucleoside **1**, then this formulation implies that the dithiane anion does indeed attack at this position. However, the fact that **26** and **27** show no optical activity (the sole chiral center being C-1), means that the dithiane must react with an already-fragmented species rather than with the intact nucleoside **1**; reaction with the latter would give rise to chirality at C-1 of **27** as anion attack would occur from the α-face (SN2 displacement), followed by fragmentation. It is also possible that compound **5** is the result of reaction of the 1,3-dithianyl anion with the oxolane used as the reaction solvent for **1** and **2**.

The 1,3-dithianyl nucleoside analogues **10**, **12**, and **13** are being tested for biological activity.

EXPERIMENTAL

General method. — ^{1}H-N.m.r. spectra were determined in chloroform-*d* or dimethyl sulfoxide-d_6 with tetramethylsilane as the standard (δ = 0) by using a Varian XL-100 or Bruker 270 spectrometer. Coupling constants are first order. Carbon-13 n.m.r. spectra were determined in deuterium oxide with tetramethylsilane as the internal standard by using a Varian CFT-20 spectrometer. Optical rotations were measured at ambient temperature with a Perkin–Elmer Model 141 automatic polarimeter. The c.d. measurements were performed on a Jasco J-20 automatic recording spectropolarimeter at room temperature and i.r. spectra were recorded on a Perkin–Elmer 337 or 727B spectrometer. All melting points were measured on a Leitz microscope heating stage, Model 350, and are corrected. Mass spectra were determined on a HMS-9 spectrometer. Column chromatography was performed on t.l.c. grade Silica Gel H without binder (Merck) under a pressure of 4-8 lb. in^{-2} and flow rates of 70–140 $mL.h^{-1}$, and t.l.c. on Silica Gel G was used to monitor all reactions. Solutions were evaporated under diminished pressure. Chemical analyses

were performed by Mr. P. Borda of the Microanalytical Laboratory of the University of British Columbia.

Synthesis of 2-(1,3-dithian-2-yl)-1-(5-O-trityl-β-D-arabinofuranosyl)-4(1H)-pyrimidinone (**3**), O^2,*2'-anhydro-5,6-dihydro-6-*(S)-(*1,3-dithian-2-yl*)-*5'-O-trityluridine*(**4**), *and 2-(1,4-dihydroxybutyl)-1,3-dithiane* (**5**). — To a solution of 1,3-dithiane (1.5 g, 12.5 mmol) (dried by azeotroping with toluene) in dry oxolane (tetrahydrofuran) (20 mL) was added, under nitrogen at −78°, 1-butyllithium in hexane (7.78 mL of a 1.6M solution). The solution was stirred for 10 min, allowed to warm to −20° and stirred for an additional 2 h. The temperature was then lowered again to −78° before adding a solution of anhydronucleoside **1** (1.2 g, 2.5 mmol) in oxolane (20 mL) slowly by syringe. A yellow precipitate formed immediately and the mixture was stirred at −78° for an additional h, whereupon water (0.5 mL) in oxolane (5 mL) was slowly added. Stirring was continued for 30 min at −78° before the mixture was allowed to attain room temperature. The solution, made neutral with dilute hydrochloric acid, was then extracted with chloroform (5 × 40 mL), the combined organic extracts were dried (magnesium sulfate), and the solvents evaporated, leaving a crude, orange syrup (1.8 g). Chromatography of this syrup on silica gel (200 g) with 9:1 benzene–ethanol as eluent solvents gave **3** (183 mg, 15%), m.p. 155–156°, $[\alpha]_D^{23}$ +38.8° (*c* 1.3, methanol); R_F 0.10; ν_{max}^{KBr} 3380 (OH), 1725 (C=O), 1635 (C=N), and 1600 cm^{-1} (C=C); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.74–2.20 (m, 2 H, SCH_2CH_2), 2.95–3.21 (m, 4 H, SCH_2CH_2), 3.42 (m, H-5'), 3.80–4.51 (m, 3 H, H-2',3',4'), 5.46 (s, 1 H, SCHS), 5.71 (d, 1 H, OH, exchangeable with D_2O), 5.73 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-5), 5.92 (d, 1 H, OH, exchangeable with D_2O), 6.31 (d, 1 H, $J_{1',2'}$ 5.0 Hz, H-1'), 7.31–7.46 (m, 15 H, Ar), and 7.91 (d, 1 H, H-6); mass spectrum: *m/e* 375 (M^+ − base).

Anal. Calc. for $C_{32}H_{32}N_2O_5S_2 \cdot H_2O$: C, 63.36; H, 5.61; N, 4.62. Found: C, 63.13; H, 5.52; N, 4.49.

The faster-migrating compound **4** was isolated as a non-crystallizable glass (392 mg, 30%), $[\alpha]_D^{23}$ −109.3° (*c* 0.66, chloroform); R_F 0.15; $\nu_{max}^{CHCl_3}$ 3350 (OH), 1702 (C=O), 1595 (C=N), and 1460 cm^{-1}; n.m.r. (100 MHz, $CDCl_3$): δ 1.80–2.38 (m, 2 H, SCH_2CH_2), 2.64–3.26 (m, 6 H, SCH_2, H-5), 3.88–4.05 (m, 1 H, H-6), 5.18 (d, 1 H, $J_{1',2'}$ 5.0 Hz, H-2'), 5.50 [s (broad), 1 H, OH, exchangeable with D_2O], 6.25 (d, 1 H, H-1'), and 7.18–7.58 (m, 15 H, Ar).

Anal. Calc. for $C_{32}H_{32}N_2O_5S_2$: C, 65.31; H, 5.44; N, 4.76. Found: C, 65.31; H, 5.64; N, 4.58.

Compound **5** (212 mg) was obtained after chromatography as part of a mixture, R_F 0.20–0.40.

Acid hydrolysis of 3 to give arabinose, 2-(1,3-dithian-2-yl)-4-pyrimidinone (**6**), *and triphenylmethanol.* — A solution of **3** (20 mg) in methanol (2 mL) and 80% aqueous acetic acid (0.5 mL) was boiled for 10 min under reflux. The mixture was observed (t.l.c., 5:1 ethyl acetate–ethanol) to contain a high R_F (0.90), fluorescent compound (triphenylmethanol, yellow when the t.l.c. plate was sprayed with 50% sulfuric acid and heated), a fluorescent, non-charring component (**6**, R_F 0.70), and a charring, nonfluorescent material (arabinose, R_F 0.10). The latter was identified by

paper chromatography (No. 1 Whatman, descending elution with water-saturated 1-butanol) of the degradation mixture against authentic arabinose (R_F 0.11, alkaline silver nitrate detection). Addition of aqueous ethanol to the mixture caused crystallization of the 2-substituted base component **6** (1 mg), m.p. 210–215° (dec.); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.87–2.12 (m, 2 H, SCH_2CH_2), 2.68–3.44 (m, 4 H, SCH_2), 4.92 (s, 1 H, SCHS), 6.31 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-5), 8.11 (d, 1 H, H-6), and 12.51 [s (broad), 1 H, NH, exchangeable with D_2O].

Anal. Calc. for $C_8H_{10}N_2OS_2$: C, 44.85; H. 4.67, N, 13.08. Found: C, 44.60; H, 4.99; N, 13.28.

2-Methyl-1-(5-O-trityl-β-D-arabinofuranosyl)-4-(1H)-pyrimidinone (**7**). — Freshly activated Raney nickel (100 mg) in ethanol (2 mL) was added to a solution of compound **3** (42 mg) in ethanol (5 mL). The mixture was boiled under reflux for 1 h, by which time t.l.c. of the mixture on silica gel with 5:1 ethyl acetate–ethanol as developer showed complete disappearance of **3** and formation of a single, new compound of lower R_F value. The mixture was then filtered, the nickel washed repeatedly with hot ethanol, and the collected filtrate and washings evaporated, leaving a clear syrup (26 mg). Addition of ethanol to the syrup afforded white crystals of **7** (26 mg, 33%), m.p. 234–235° (lit.[14] m.p. 238–239°), $[\alpha]_D^{25}$ −40.4° (*c* 0.65, *N,N*-dimethylformamide) [lit.[14] $[\alpha]_D^{25}$ −43.2° (*c* 0.22, *N,N*-dimethylformamide)]; n.m.r. (100 MHz, Me_2SO-d_6): δ 2.39 (s, 3 H, CH_3), 3.83–4.33 (m, 3 H, H-2′,3′,4′), 5.67 (d, 1 H, OH, exchangeable with D_2O), 5.64 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-5), 5.79 (d, 1 H, OH, exchangeable with D_2O), and 6.02 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-6); mass spectrum: *m/e* 375 (M^+ — base), 241 (M^+ — Ph_3C).

Anal. Calc. for $C_{29}H_{28}NO_5 \cdot C_2H_5OH$: C, 70.18; H, 6.41; N, 5.28. Found: C, 70.21; H, 5.97; N, 5.30.

1-(2,3-Di-O-acetyl-5-O-trityl-β-D-arabinofuranosyl)-2-(1,3-dithian-2-yl)-4(1H)-pyrimidinone (**8**). — A solution of the nucleoside **3** (2.04 g) in pyridine (20 mL) and acetic anhydride (5 mL) was maintained for 12 h at 0°, by which time t.l.c. on silica gel with 9:1 benzene–ethanol as developer showed a single product (R_F 0.43). The solvents were removed by three azeotropic evaporations of xylene and the residual syrup was chromatographed on silica gel (200 g) with 10:10:1 benzene–ethyl acetate–ethanol as eluent, yielding the diacetate **8** as a white foam (2.33 g, 100%); $[\alpha]_D^{25}$ +45.1° (*c* 1.62, chloroform); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.90 (s, 3 H, Ac), 2.11 (s, 3 H, Ac), 2.98–3.20 (m, 4 H, SCH_2), 3.39–3.52 (m, 2 H, H-5′), 4.16–4.36 (m, 1 H, H-4′), 5.34–5.50 (pseudo-t, 1 H, H-3′), 5.63 (s, 1 H, SCHS), 5.68–5.82 (pseudo-t, 1 H, H-2′), 5.91 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-5), 6.53 (d, 1 H, $J_{1',2'}$ 5.6 Hz, H-1′), 7.23–7.53 (m, 15 H, Ar), and 7.83 (d, 1 H, H-6).

Anal. Calc. for $C_{36}H_{36}N_2O_7S_2$: C, 64.29; H, 5.36; N, 4.17. Found: C, 64.58; H, 5.50; N, 4.11.

1-(2,3-Di-O-acetyl-β-D-arabinofuranosyl)-2-(1,3-dithian-2-yl)-4(1H)-pyrimidinone (**9**). — A solution of **8** (1.24 g) in 80% aqueous acetic acid (35 mL) was stirred for 65 h, whereupon evaporation of the solvents and chromatography of the resulting syrup on silica gel (60 g) with 9:1 benzene–ethanol as developer yielded the de-

tritylated compound **9** as a white glass (356 mg, 45%), $[\alpha]_D^{25}$ +48.3° (*c* 1.0, chloroform); R_F 0.13; n.m.r. (100 MHz, Me_2SO-d_6): δ 1.91 (s, 3 H, Ac), 2.12 (s, 3 H, Ac), 2.94–3.22 (m, 4 H, SCH_2), 3.64–3.82 (m, 2 H, H-5'), 3.98–4.16 (m, 1 H, H-4'), 5.20–5.31 (pseudo-q, 2 H, H-3', O*H*, partly exchanges with D_2O), 5.55 (s, 1 H, SC*H*S), 5.68–5.82 (pseudo-t, 1 H, H-2'), 6.12 (d, 1 H, $J_{5,6}$ 8.0 Hz, H-5), 6.51 (d, 1 H, $J_{1',2'}$ 5.8 Hz, H-1'), and 8.04 (d, 1 H, H-6).

Anal. Calc. for $C_{17}H_{22}N_2O_7S_2 \cdot 0.5H_2O$: C, 46.47; H, 5.24; N, 6.38. Found: C, 46.68; H, 5.23; N, 6.10.

*2-(1,3-Dithian-2-yl)-1-β-*D*-arabinofuranosyl-4(1*H*)-pyrimidinone* (**10**). — To a solution of the diacetate **9** (290 mg, 0.67 mmol) in anhydrous methanol (15 mL) was added a 0.04M solution of sodium in methanol (70 μL). The mixture was stirred for 1 h at room temperature, made neutral with Bio-Rex 70 (H^+) weakly-acidic cation-exchange resin, and evaporated to give a white foam (237 mg, 100%); $[\alpha]_D^{23}$ +82.1° (*c* 1.1, methanol); ν_{max}^{KBr} 3350 (OH), 1725 (C=O), 1625 (C=N), and 1600 cm^{-1} (C=C); λ_{max}^{MeOH} 245 nm (ε 15,700); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.55–2.29 (m, 2 H, SCH_2CH_2), 2.91–3.21 (m, 4 H, SCH_2), 3.57–3.79 (m, 3 H, H-4',5'), 3.79–4.05 (m, 1 H, H-3'), 4.37 (q, 1 H, H-2'), 5.15 (t, 1 H, CH_2OH, exchangeable with D_2O), 5.41 (s, 1 H, SC*H*S), 5.52 (d, 1 H, CHO*H*, exchangeable with D_2O), 5.83 (d, 1 H, -CHO*H*, exchangeable with D_2O), 6.00 (d, 1 H, $J_{5,6}$ 7.5 Hz, H-5), 6.24 (d, 1 H, $J_{1',2'}$ 5.2, H-1'), and 8.01 (d, 1 H, H-6); mass spectrum *m/e* 347.0741 (M^+).

Anal. Calc. for $C_{13}H_{18}N_2O_5S_2$: C, 45.09; H, 5.20; N, 7.91. Found: C, 44.80; H, 5.45; N, 7.91.

*O^2,2'-Anhydro-5,6-dihydro-6-*R*-methyl-5'-O-trityluridine* (**11**). — A mixture of compound **4** (1 g) and freshly activated Raney nickel (2 g) in ethanol (50 mL) was boiled for 2 h under reflux. The nickel was removed by filtration, washed copiously with ethanol, and the combined filtrate and washings evaporated. The solid residue was crystallized from ethanol to yield a white powder (340 mg, 41%), m.p. 245–247°, $[\alpha]_D^{23}$ −101.1° (*c* 0.8, methanol); ν_{max}^{KBr} 3350 (OH), 1700 (C=O), 1570 (C=N), and 1450 cm^{-1}; n.m.r. (100 MHz, Me_2SO-d_6): δ 1.26 (d, 3 H, J_{6,CH_3} 6.0 Hz, CH_3), 2.20 (d, 1 H, $J_{4',5'a}$ 1.5 Hz, H-5a'), 2.28 (s, 1 H, 5-b'), 2.82–3.16 (septet, 2 H, $J_{5a,5b}$ 14.5 Hz, $J_{5a,6}$ 5.0 Hz, $J_{5b,6}$ 6.0 Hz, H-5), 3.39 (broad s, 1 H, O*H*, exchangeable with D_2O), 3.60–3.84 (pseudo-q, 1 H, H-6), 4.15–4.28 (m, 1 H, H-4'), 4.33 (broad s, 1 H, H-3'), 5.11 (d, 1 H, $J_{1',2'}$ 5.6 Hz, H-2'), 6.05 (d, 1 H, H-1'), and 7.38 (s, 15 H, Ar). Irradiation of the multiplet at δ 3.60 collapsed the doublets at δ 2.20 and 1.26 to singlets.

Anal. Calc. for $C_{29}H_{28}N_2O_5$: C, 71.90; H, 5.79; N, 5.79. Found: C, 71.80; H, 5.87; N, 5.75.

5,6-Dihydro-6-(S)*-(1,3-dithian-2-yl)-1-β-*D*-arabinofuranosyluracil* (**12**) *and 3-[*(S)*-1-(1,3-dithian-2-yl)]propionamido-(1,2-dideoxy-β-*D*-arabinofurano)-[1,2-d]-2-oxazolidinone* (**13**). — A solution of the tritylated anhydronucleoside **4** (2 g) in 80% aqueous acetic acid (50 mL) was boiled for 10 min under reflux, cooled and diluted with water (50 mL). The resulting precipitate of triphenylmethanol was filtered off and washed copiously with water. The filtrate and collected washings were then

evaporated, the residual syrup dissolved in water, and the solution washed twice with ether to remove residual triphenylmethanol. The water layer was concentrated and applied to a column (3 × 30 cm) of Bio-Rex 70 (H^+) cation-exchange resin that was eluted with water. The first fractions yielded the detritylated nucleoside **12** (50 mg, 10%) as a solid that was recrystallized from aqueous methanol; m.p. 245–247°, $[\alpha]_D^{23}$ +11.4° (*c* 0.25, methanol); R_F 0.42 (silica gel, 5:1 ethyl acetate–ethanol); ν_{max}^{KBr} 3400 (OH), 1710 (C=O), 1690 (C=O), and 1600 cm^{-1}; λ_{max}^{MeOH} 245 nm (ε 1700); c.d. (*c* 3.5 × 10^{-4}, methanol) $\Delta\varepsilon_{250}$ +4.80; n.m.r. (100 MHz, Me_2SO-d_6): δ 1.47–2.21 (m, 2 H, SCH_2CH_2), 2.59–3.01 (m, 6 H, SCH_2, H-5), 3.47–3.73 (m, 3 H, H-5′,6), 3.76–3.90 (m, 1 H, H-4′), 3.93–4.15 (m, 2 H, H-2′,3′), 4.76 (d, 1 H, $J_{1',6}$ 4.0 Hz, SCHS), 4.85 (t, 1 H, CH_2OH, exchangeable with D_2O), 5.60 (d, 1 H, CHOH, exchangeable with D_2O), 5.99 (d, 1 H, $J_{1',2'}$ 5.0 Hz, H-1′), and 10.31 (s, 1 H, NH, exchangeable with D_2O); mass spectrum: *m/e* 245 (M^+ — dithiane), 133 (M^+ — base).

Anal. Calc. for $C_{13}H_{20}N_2O_6S_2$: C, 42.85; H, 5.49; N, 7.69. Found: C, 42.90; H, 5.68; N, 7.78.

Further elution of the chromatography column with water gave the detritylated 2-oxazolidinone derivative **13** (0.5 g, 90%), which was crystallized from aqueous methanol, m.p. 185–188°, $[\alpha]_D^{25}$ −32.3° (*c* 0.65, methanol); R_F 0.23 (silica gel, 5:1 ethyl acetate–ethanol); ν_{max}^{KBr} 3400 (OH), 1740 (carbamate), 1680 (amide), and 1615 cm^{-1} (amide II); λ_{max}^{MeOH} 225 (ε 3500), 232 (3000), and 245 nm (1500); c.d. (*c* 1.92 × 10^{-4}, methanol) $\Delta\varepsilon_{226}$ +2.41; ^{1}H-n.m.r. (100 MHz, Me_2SO-d_6): δ 1.73–2.13 (m, 2 H, SCH_2CH_2), 2.55–3.19 (m, 6 H, $-CH_2C{=}O$, SCH_2), 3.25–3.58 (m, 2 H, H-5′), 3.63–3.90 (m, 1 H, $-CHCH_2C{=}O$), 3.14 (d, 1 H, $J_{1,1''}$ 10.6 Hz, SCHS), 4.15 (broad s, 1 H, H-3′), 4.37–4.61 (m, 1 H, H-4′), 4.68 (d, 2 H, $J_{1',2'}$ 5.8 Hz, H-2′), 4.70 [t (partly buried under H-2′), 1 H, CH_2OH, exchangeable with D_2O], 5.66 (d, 1 H, CHOH, exchangeable with D_2O), 5.80 (d, 1 H, H-1′), 6.86 (broad s, 1 H, NH, exchanges slowly with D_2O), and 7.51 (broad s, 1 H, NH, exchanges slowly with D_2O); ^{13}C-n.m.r. (D_2O): δ 177.0 (amide), 159.8 (carbamate), and 90.5 (anomeric); mass spectrum: *m/e* 227 (M^+ — dithiane).

Anal. Calc. for $C_{13}H_{20}N_2O_6S_2$: C, 42.85; H, 5.49; N, 7.69. Found: C, 42.78; H, 5.66; N, 7.87.

Acid hydrolysis of **12** *to give arabinose and 5,6-dihydro-6-*(S)-(*1,3-dithian-2-yl*)-*uracil* (**14**). — A suspension of nucleoside **12** (5 mg) in M hydrochloric acid (1 mL) was stirred for 4 h at 70°. The mixture was then cooled and the white precipitate formed was filtered off. The precipitate was washed several times with water and shown to be the free base **14** (2 mg, 62%), m.p. 260–261°, $[\alpha]_D^{23}$ +22.7° (*c* 0.1, methanol); ν_{max}^{KBr} 3420 (OH of tautomeric form), 3230 (NH), 1720 (broad, C=O), and 1600 cm^{-1} (C=N of tautomer); λ_{max}^{MeOH} 245 nm (ε 700); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.48–2.18 (m, 2 H, SCH_2CH_2), 2.58–2.98 (m, 6 H, H-5, SCH_2), 3.63–3.92 (m, 1 H, H-6), 4.24 (d, 1 H, $J_{1',6}$ 6.0 Hz, H-1′), 7.61 (broad s, 1 H, NH, exchangeable with D_2O), and 10.01 (broad s, 0.5 H, NH, exchangeable with D_2O).

Anal. Calc. for $C_8H_{12}N_2O_2S_2$: C, 41.38; H, 5.17; N, 12.07. Found: C, 41.38; H, 5.31; N, 12.20.

The filtrate was spotted on Whatman No. 1 paper against D-arabinose, the paper eluted in the descending manner with water-saturated 4:1 1-butanol–acetic acid, and the chromatogram developed by spraying with alkaline silver nitrate solution, which revealed two spots of identical R_F value (0.31).

5,6-Dihydro-6-methyluracil (**15**). — A solution of the dithianyl derivative **14** (12 mg) in *N,N*-dimethylformamide (1 mL) was heated for 2 h at 80° in the presence of freshly activated Raney nickel (50 mg) in ethanol (3 mL). The nickel was then removed by filtration and washed with hot *N,N*-dimethylformamide. Evaporation of the combined filtrate and washings left an off-white solid (5 mg, 75%) that was crystallized from methanol, m.p. 218° (lit.[26] 217–218°); ν_{max}^{KBr} 3200 (NH,OH), 1725 (C=O), 1695 (C=O), 1605 cm^{-1} (C=N of tautomer); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.12 (d, 3 H, J_{6,CH_3} 6.0 Hz, CH_3), 2.10–2.62 [octet (partially obscured by Me_2SO], ~2 H, $J_{5a,5b}$ 16 Hz, $J_{5,6}$ 5.6 Hz, H-5), 3.50–3.68 (m, 1 H, H-6), 7.52 (broad s, 1 H, N*H*, exchangeable with D_2O), 9.96 (broad s, 1 H, N*H*, exchangeable with D_2O).

Di-silylation of **13** *to give 3-*[(S)-*1-*(*1,3-dithian-2-yl*)]*propionamido-3,5-di-*O-*tert-butyldimethylsilyl-*(*1,2-dideoxy-β-*D-*arabinofurano*)-[*1,2-d*]-*2-oxazolidinone* (**16**). — A solution of the dihydroxy derivative **13** (44 mg, 0.12 mmol) and *tert*-butylchlorodimethylsilane (50 mg, 0.3 mmol) in anhydrous *N,N*-dimethylformamide (2 mL) and pyridine (0.5 mL) was stirred for 24 h under nitrogen. Water (0.5 mL) was then added to the mixture and stirring of the solution was continued for 15 min. The solution was then evaporated to dryness, the residue dissolved in chloroform (30 mL) and washed with water (2 × 15 mL). Drying of the chloroform solution with sodium sulfate followed by evaporation left a syrup (97 mg), which was chromatographed on silica gel (15 g) with 1:1 benzene–ethyl acetate as developer, yielding **16** as a white glass (53 mg, 75%); $[\alpha]_D^{23}$ −50.9° (*c* 1.4, chloroform); $\nu_{max}^{CHCl_3}$ 3420 and 3540 (NH_2), 1760 (carbamate), 1695 (amide carbonyl), and 1598 cm^{-1} (amide II); n.m.r. (100 MHz, $CDCl_3$): δ 0.04 (s, 6 H, 2 × CH_3), 0.10 (s, 3 H, CH_3), 0.12 (s, 3 H, CH_3), 0.88 (s, 18 H, 2 × *tert*-Bu), 1.84–2.20 (m, 2 H, SCH_2CH_2), 2.40–3.42 (m, 6 H, SCH_2, $CH_2C{=}O$), 3.52–3.68 (m, 2 H, H-5′), 3.82–3.98 (m, 1 H, NC*H*), 4.07 (d, 1 H, $J_{1,2''}$ 10 Hz, SC*H*S), 4.40 (broad s, 1 H, H-3′), 4.49–4.60 (m, 1 H, H-4′), 4.69 (d, 1 H, $J_{1',2'}$ 6.0 Hz, H-2′), 5.79 (d, 1 H, H-1′), and 5.68–6.30 (broad d (partly buried under H-1′), 2 H, NH_2, exchangeable with D_2O).

Anal. Calc. for $C_{25}H_{48}N_2O_6S_2Si_2$: C, 50.68; H, 8.11; N, 4.73. Found: C, 50.85; H, 8.08; N, 4.81.

Dehydration of **13** *to give 3-*[(S)-*1-*(*1,3-dithian-2-yl*)]*cyanoethyl-*(*1,2-dideoxy-β-*D-*arabinofurano*)-[*1,2-d*]-*2-oxazolidinone* (**17**). — To a suspension of the amide **13** (43 mg, 0.12 mmol) in anhydrous 1,4-dioxane (3 mL) and pyridine (0.08 mL, 8 eq.) at 0° was added trifluoroacetic anhydride (0.14 mL, 8 eq.). The mixture was then stirred for 2 h at room temperature by which time all starting material had dissolved. Methanol (1 mL) was added to the solution and the latter stirred for 30 min before the solvents were evaporated off. The residual syrup was dissolved in a small quantity of water, applied to a column (11 × 1.5 cm) of Bio-Rex 70 (H^+) resin and eluted with water, yielding the nitrile **17** (32 mg, 77%) as a syrup that was

crystallized and recrystallized from chloroform; m.p. 184–185°, $[\alpha]_D^{23}$ −40.2° (*c* 0.99, methanol); ν_{max}^{KBr} 3400 (OH), 2260 (C≡N), and 1740 cm^{-1} (C=O); n.m.r. 100 MHz, Me_2SO-d_6): δ 1.72–2.10 (m, 2 H, SCH_2CH_2), 2.60–3.65 (m, 8 H, SCH_2, H-5′, CH_2CN), 3.77–4.01 (m, 1 H, H-4′), 3.99 (d, $J_{1,2}$- 11.0 Hz, SCHS), 4.01 (broad s, 1 H, H-3′), 4.45–4.71 (m, 1 H, -$CH$$CH_2CN$), 4.82 (t, 1 H, CH_2OH, exchangeable with D_2O), 4.79 (dd after addition of D_2O, $J_{1',2'}$ 6.0, $J_{2',3'}$ 1.5 Hz, H-2′), 5.74 (d, 1 H, -CHO*H*, exchangeable with D_2O), and 5.86 (d, 1 H, H-1′).

Anal. Calc. for $C_{13}H_{18}N_2O_5S_2$: C, 45.09; H, 5.20; N, 8.09. Found: C, 44.57; H, 5.26; N, 7.91.

3-(R)-1-Methylpropionamido-(1,2-dideoxy-β-D-arabinofurano)-[1,2-d]-2-oxazolidinone (**18**). — Freshly activated Raney nickel (1.7 g) in water (5 mL) was added to a solution of the dithianyl compound **13** (314 mg) in water (10 mL) and the mixture was heated for 4 h at 75°. The mixture was then filtered, the nickel washed copiously with water, the filtrate and collected washings concentrated, and the residual syrup passed through a column (2.7 × 18 cm) of Bio-Rex 70 (H^+) cation-exchange resin (water elution), yielding **18** as a clear syrup (190 mg, 85%). The material could not be crystallized, though it was shown to be pure by paper chromatography (R_F 0.36, descending elution on Whatman No. 1 paper with water-saturated 1-butanol); $[\alpha]_D^{23}$ −78.8° (*c* 1.1, methanol); ν_{max}^{film} 3375 (OH), 1740 (carbamate), 1670 (amide carbonyl), and 1625 (amide II); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.18 (d, 3 H, J_{1,CH_3} 6.0 Hz, CH_3) 2.43 (d, 2 H, $J_{1,2}$ 7.0 Hz, -CH_2C=O), 3.28–3.43 (octet, 2 H, $J_{5a,5b'}$ 12.0 Hz, $J_{4',5a'}$ 6.0 Hz, $J_{4',5b'}$ 7.0 Hz, H-5′), 3.80–4.14 (m, 2 H, H-4′, -$CH$$CH_3$), 4.18 (broad s, 1 H, H-3′), 4.67 (d, 1 H, $J_{1',2'}$ 5.0 Hz, H-2′), 4.89 (t, 1 H, CH_2OH, exchangeable with D_2O), 5.62 (d, 1 H, CHO*H*, exchangeable with D_2O), 5.81 (d, 1 H, H-1′), 6.86 (broad s, 1 H, N*H*, exchanges slowly with D_2O), and 7.44 (broad s, 1 H, N*H*, exchanges slowly with D_2O); mass spectrum: *m/e* 152 (M^+ — base).

Anal. Calc. for $C_{10}H_{16}N_2O_6 \cdot 0.5H_2O$: C, 44.60; H, 6.32; N, 10.41. Found: C, 44.50; H, 6.30; N, 10.46.

Dehydration of **18** *to give 3-(R)-1-methylcyanoethyl-(1,2-dideoxy-β-D-arabinofurano-[1,2-d]-2-oxazolidinone* (**19**). — Compound **18** (41 mg) was treated with pyridine–trifluoroacetic anhydride in exactly the same manner used in the conversion of the amide **13** into the nitrile **17**, yielding **19** as a syrup (23 mg, 60%); $[\alpha]_D^{23}$ −67.5° (*c* 1.2, methanol); ν_{max}^{KBr} 3390 (OH), 2230 (C≡N), and 1740 cm^{-1} (C=O); n.m.r. (270 MHz, Me_2SO-d_6): δ 1.35 (d, 3 H, J_{1,CH_3} 6.75 Hz, CH_3), 2.92 (octet, 2 H, $J_{2a,2b}$ 15.3, $J_{1,2a}$ 7.5 $J_{1,2b}$ 6.7 Hz, CH_2CN) 3.27–3.44 (m, 2 H, H-5′), 3.95 (broad t, 1 H, $J_{4',5'}$ 5.75 Hz, H-4′), 4.07 (q, 1 H, $CHCH_3$), 4.24 (s, 1 H, H-3′), 4.77 (d, 1 H, $J_{1',2'}$ 5.0 Hz, H-2′), 5.03 (d, 1 H, -CH_2OH, exchangeable with D_2O), 5.85 (d, 1 H, -CHO*H*, exchangeable with D_2O), and 5.89 (d, 1 H, H-1′).

Anal. Calc. for $C_{10}H_{14}N_2O_5$: C, 49.59; H, 5.79; N, 11.57. Found: C, 49.35; H, 5.55, N, 11.26.

Hydrogenation of **19** *to give 3-(R)-1-methylacetamidopropyl-(1,2-dideoxy-β-D-arabinofurano)-[1,2-d]-2-oxazolidinone* (**20**) *and 3-(R)-1-methylacetamidopropyl-[3-O-acetyl-(and 5-O-acetyl)-1,2-dideoxy-β-D-arabinofurano]-[1,2-d]-2-oxazolidinone*

(**21**). — A solution of compound **19** (28 mg) in anhydrous acetic anhydride (3 mL) was hydrogenated at 55 lb.in.$^{-2}$ for 20 h at room temperature in the presence of platinum oxide (21 mg) as catalyst. The catalyst was then removed by filtration and washed copiously with methanol. The filtrate and collected washings were evaporated, traces of acetic anhydride being removed azeotropically with *p*-xylene. The crude residue was chromatographed on silica gel with 5:1 ethyl acetate–ethanol. A minor component having R_F 0.26 was first eluted and appeared to be an inseparable, syrupy mixture of the 3′-*O*- and 5′-*O*-acetyl acetamido derivatives (**21**, 14 mg, 36%); ν_{max}^{film} 3320 (OH), 1750 (carbamate), 1650 (amide carbonyl), and 1555 cm^{-1} (amide II); n.m.r. (270 MHz, Me_2SO-d_6): δ 1.80 (s, NAc), 2.02 (s, -CH_2OAc), 2.08 (s, CHO*Ac*), and 7.86 (broad s, N*H*, exchangeable with D_2O). The ratio of 5′-acetate to 3′-acetate was ~2:1.

Further elution of the chromatography column gave the acetamido compound **20** as a syrup (11 mg, 33%); $[\alpha]_D^{23}$ −78.8° (*c* 0.52, methanol); R_F 0.16; ν_{max}^{film} 3320 (OH), 1740 (carbamate), 1640 (amide carbonyl), and 1560 (amide II); n.m.r. (270 MHz, Me_2SO-d_6): δ 1.18 (d, 3 H, J_{1,CH_3} 6.0 Hz, $CHCH_3$), 1.72 (m, 2 H, N-CH_2CH_2), 1.81 (s, 3 H, N*Ac*), 3.03 (t, 2 H, $J_{2,3}$ 6.8 Hz, $NHCH_2$), 3.18–3.32 (m, 2 H, H-5′), 3.70 (broad q, 1 H, CH_3CH), 3.90 (broad t, 1 H, H-4′), 4.22 (broad s, 1 H, H-3′), 4.71 (d, 1 H, $J_{1',2'}$ 5.5 Hz, H-2′), 4.96 (t, 1 H, -CH_2OH, exchanges with D_2O), 5.67 (d, 1 H, -CHO*H*, exchanges with D_2O), 5.79 (d, 1 H, H-1′), and 7.88 (broad s, 1 H, N*H*, exchanges slowly with D_2O).

Anal. Calc. for $C_{12}H_{20}N_2O_6 \cdot 1.5\ H_2O$: C, 45.71; H, 7.30; N, 8.88. Found: C, 45.80; H, 6.79; N, 8.40. Mol. wt. by mass spectrometry 288.1328; $C_{12}H_{20}N_2O_6$ (M^+) requires 288.1321; base peak 114.0890; $C_6H_{12}NO$ requires 114.0919.

Hydrogenation of a solution of compound **19** (31 mg) in anhydrous methanol (3 mL) and acetic anhydride (0.5 mL) at 55 lb.in.$^{-2}$ for 2 h at room temperature in the presence of platinum oxide (23 mg) followed by removal of the catalyst by filtration and removal of the solvents from the filtrate by evaporation of xylene, gave compound **20** (35 mg, 95%), with no observable formation of *O*-acetyl derivatives **21**.

Detritylation of compound **11** *to give* **18**. — A solution of compound **11** (94 mg) in 80% aqueous acetic acid (10 mL) was boiled for 10 min under reflux, the mixture cooled, and the solvents were evaporated off at room temperature. The residue was suspended in water and washed twice with ether. Evaporation of the water fraction left a syrup (50 mg) that was applied to a column (1.5 × 11 cm) of Bio-Rex 70 (H^+) resin and eluted with water, yielding compound **18** as a clear syrup (26 mg, 52%).

*3-[(S)-1-(1,3-Dithian-2-yl)]cyanoethyl-(1,2-dideoxy-3,5-di-*O*-p-nitrobenzoyl-β-*D*-arabinofurano)-[1,2-*d*]-2-oxazolidinone* (**22**). — To a solution of compound **13** (285 mg) in anhydrous pyridine (10 mL) was added at room temperature freshly recrystallized *p*-nitrobenzoyl chloride (458 mg, 3 equiv.) in pyridine (5 mL). The solution was stirred for 2 h, water (1 mL) added, and the mixture stirred for another h. The solvents were then evaporated off, the residue was dissolved in chloroform (60 mL) and the latter washed successively with 4% hydrochloric acid (2 × 30 mL), saturated, aqueous sodium hydrogencarbonate (2 × 30 mL), and water (3 × 30 mL).

The chloroform layer was dried with sodium sulfate and evaporated, leaving a crude solid (517 mg) that was chromatographed on silica gel (30 g). Elution with 3:1 chloroform–ethyl acetate yielded the diester **22** as a solid (422 mg, 85%) after removal of solvents. Compound **22** was recrystallized from acetonitrile–water; m.p. 201–202°, $[\alpha]_D^{23}$ −42.9° (*c* 1.3, chloroform); n.m.r. (100 MHz, $CDCl_3$): δ 1.90–2.10 (m, 2 H, SCH_2CH_2), 2.40–3.30 (m, 6 H, SCH_2, $-CH_2C{=}O$), 4.02–4.38 (m, 2 H, $-CHCH_2C{=}O$, SCHS), 4.64 (broad s, 2 H, H-4′,5′), 5.23 (d, 1 H, $J_{1',2'}$ 6.0 Hz, H-2′), 5.70 (s, 1 H, H-3′), 5.90 (d, 1 H, H-1′), and 8.25 (m, 8 H, Ar); $\nu_{max}^{CHCl_3}$ 2260 (CN), 1780 (carbamate), 1740 (ester), 1615, and 1535 cm^{-1} (NO_2).

Anal. Calc. for $C_{27}H_{24}N_4O_{11}S_2$: C, 50.31; H, 3.73; N, 8.70. Found: C, 50.17; H, 3.69; N, 8.66.

Conversion of compound **22** *into compound* **17**. — To a solution of compound **22** (190 mg) in anhydrous methanol (25 mL) and oxolane (3 mL) was added with stirring under nitrogen a solution of 0.1M sodium in methanol (20 μL). After one h, the mixture was made neutral with Bio-Rex 70 (H^+) resin, the resin removed by filtration, and the filtrate evaporated. The residue was suspended in water (30 mL) and washed with ether (3 × 20 mL). The water layer was then evaporated leaving a solid (**17**, 90 mg, 88%) that was crystallized from ethanol–water; m.p. 186–186.5°, $[\alpha]_D^{24}$ −44.2° (*c* 0.94, methanol); ν_{max}^{KBr} 3400 (OH), 2260 (C≡N), 1740 cm^{-1} (C=O); n.m.r. (100 MHz, Me_2SO-d_6): 1.72–2.10 (m, 2 H, SCH_2CH_2), 2.60–3.65 (m, 8 H, SCH_2, H-5′, CH_2CN), 3.77–4.01 (m, 1 H, H-4′), 3.99 (d, J_{1,CH_3} 11.0 Hz, SCHS), 4.01 (broad s, 1 H, H-3′), 4.45–4.71 (m, 1 H, $-CHCH_2CN$), 4.79 (dd after addition of D_2O, 1 H, $J_{1',2'}$ 6.0 Hz, $J_{2',3'}$ 1.5 Hz, H-2′), 4.82 [t (partly buried by H-2′), 1 H, CH_2OH, exchangeable with D_2O], 5.74 (d, 1 H, CHOH, exchangeable with D_2O), and 5.86 (d, 1 H, H-1′); mass spectrum: *m/e* 346 (M^+) and 315 ($M^+ - CH_2OH$).

Anal. Calc. for $C_{13}H_{18}N_2O_5S_2 \cdot H_2O$: C, 42.86; H, 5.49; N, 7.69. Found: C, 42.88; H, 4.93; N, 7.52.

Conversion of compound **17** *into compound* **13**. — A suspension of compound **17** (31 mg) in M sodium hydroxide (3 mL) was boiled under reflux for 5 min, by which time t.l.c. on silica gel with 5:1 ethyl acetate–ethanol as developer showed consumption of all starting material (R_F 0.56) and formation of a major product having R_F 0.26. The mixture was made neutral with Bio-Rex 70 (H^+) resin, the latter was removed by filtration, the filtrate evaporated, and the residual syrup was applied to a column of Bio-Rex 70 (H^+) resin and eluted with water, yielding compound **13** (12 mg, 40%) identical by n.m.r. and i.r. spectrum with that obtained from compound **4**.

3-(R)-1-Methylcyanoethyl-(1,2-dideoxy-3,5-di-O-p-nitrobenzoyl-β-D-arabino-furano)-[1,2-d]-2-oxazolidinone (**23**). — To a solution of compound **18** (60 mg) in anhydrous pyridine (3 mL) was added *p*-nitrobenzoyl chloride (214 mg, 5 equiv.) in pyridine (2 mL). The solution was stirred for 2 h, by which time t.l.c. of the mixture with silica gel (2:1 benzene–ethyl acetate as developer) showed consumption of all starting material and formation of a single component having R_F 0.37. Water (0.5 mL) was added to the solution, and the latter stirred for another h. The mixture was then evaporated, the residue dissolved in dichloromethane (60 mL), and succes-

sively washed with 4% hydrochloric acid (2 × 30 mL), saturated aqueous sodium hydrogencarbonate (2 × 30 mL) and water (3 × 30 mL). The organic layer was dried with sodium sulfate and evaporated, leaving a yellow glass (146 mg) that was chromatographed on silica gel (15 g). Elution with 3:1 benzene–ethyl acetate gave **23** as a white glass (124 mg, 98%). A first crystallization of this glass from ethyl acetate-dichloromethane–hexane gave off-white powder, m.p. 81–82°. Recrystallization from the same solvents resulted in crystals melting at 86–87°, $[\alpha]_D^{23}$ −45.2° (*c* 0.8, chloroform); $\nu_{max}^{CHCl_3}$ 2260 (C≡N), 1780 (carbamate), 1740 (ester carbonyl), 1615, and 1537 cm^{-1} (NO_2); n.m.r. (100 MHz, $CDCl_3$): δ 1.52 (d, 3 H, $J_{1,CH3}$ 7.0 Hz, C*H*$_3$), 2.56–3.04 (octet, 2 H, $J_{2a,2b}$ 17.0 Hz, $J_{1,2}$ 5.8 Hz, -C*H*$_2$C=O), 4.10–4.32 (pseudo-q, 1 H, -C*H*CH$_3$), 4.46–4.70 (m, 3 H, H-4′, H-5′), 5.23 (d, 1 H, $J_{1',2'}$ 5.5 Hz, H-2′), 5.70 (s, 1 H, H-3′), 6.10 (d, 1 H, $J_{1',2'}$ 5.5 Hz, H-1′), and 8.30 (m, 8, Ar). Irradiation of the quartet at δ 4.10 collapsed the octet at δ 2.56 to two doublets having J_{gem} 16.0 Hz and the doublet at δ 1.52 to a singlet; mass spectrum: *m/e* 373.0952 ($M^+ - O_2NC_6H_4CO_2H$).

Anal. Calc. for $C_{24}H_{30}N_4O_{11}$: C, 53.33; H, 3.70; N, 10.37. Found: C, 53.31; H, 3.60; N, 10.06.

3;(R)-*1-aldehydocyanomethyl-(1,2-dideoxy-3,5-di*-O-p-*nitrobenzoyl-β*-D-*arabino-furano*)-[*1,2*-d]-*2-oxazolidinone* (**24**) (as the semicarbazone **25**). — A mixture of **22** (43 mg and barium carbonate (47 mg) in dimethyl sulfoxide (4 mL) and water (0.5 mL) was heated for 15 min at 55°. The mixture was cooled and methyl iodide (1 mL) was added. Heating of the mixture at 55° was resumed for 3 h after which time it was cooled, diluted with acetone (20 mL), and the mixture evaporated to one-half its volume to remove the excess of methyl iodide. More acetone (20 mL) was added to precipitate the barium salts, the mixture was filtered, and the filtrate evaporated. A solution of the residue in chloroform was washed with water and the chloroform layer was dried with sodium sulfate and evaporated, leaving an orange syrup (**24**); n.m.r. (100 MHz, Me_2SO-d_6): δ 9.45 (d, *J* 14.0 Hz, *H*-C=O). Without further purification, the foregoing syrup was dissolved in methanol (2 mL), to which was added pyridine (0.5 mL) and 0.5M aqueous semicarbazide hydrochloride (0.4 mL). The mixture was evaporated, the residue dissolved in water, the solution extracted with ethyl acetate, and the organic extract dried with sodium sulfate and evaporated, leaving a crude solid (41 mg) from which the semicarbazone **25** (15 mg) 37% from **22** was obtained pure by two recrystallizations from ethyl acetate–methanol; m.p. 192–194°, $[\alpha]_D^{23}$ −86.9° (*c* 0.35, 9:1 methanol–ethyl acetate); n.m.r. (100 MHz, Me_2SO-d_6): δ 3.10–3.28 (m, 2 H, -CH$_2$C=O), 4.40–4.60 (m, 2 H, H-5′), 4.65–4.96 (m, 2 H, H-4′, -C*H*CH$_2$C=O), 5.49 (d, 1 H, $J_{1',2'}$ 6.0 Hz, H-2′), 5.68 (s, 1 H, H-3′), 6.10 (d, 1 H, H-1′), 6.37 (broad s, 2 H, N*H*$_2$, exchangeable with D_2O), 7.23 (d, 1 H, $J_{1,CH}$ 3.0 Hz, C*H*=N), 8.20–8.50 (m, 8 H, Ar), and 10.23 (broad s, 1 H, N-N*H*, exchangeable with D_2O); ν_{max}^{KBr} 3450 (NH), 2270 (C≡N), 1765 (carbamate), 1735 (ester C=O), 1690 (NHC=O), 1585 (HC=N-), 1615, and 1535 cm^{-1} (NO_2).

Anal. Calc. for $C_{25}H_{21}N_2O_{12}$: C, 49.10; H, 3.44; N, 16.04. Found: C, 48.98; H, 3.30; N, 15.68.

2-(1,4-Di-O-acetylbutyl)-1,3-dithiane (**26**). — The mixture of unidentified sugars **5** (258 mg) obtained by chromatography of the mixture from reaction of **1** and **2** was acetylated in pyridine (3 mL) and acetic anhydride (2 mL) for 16 h at 5°. The reagents were removed by three azeotropic evaporations with xylene and the residual syrup chromatographed on silica gel (60 g). Elution with 10:1 benzene–ethyl acetate yielded a fluorescent, detritylated material (**26**) as a syrup (97 mg) after evaporation of solvents, $[\alpha]_D^{23}$ 0° (*c* 0.92, chloroform); R_F 0.30; n.m.r. (100 MHz, $CDCl_3$): δ 1.53–1.98 (m, 6 H, CH_2CH_2, SCH_2CH_2), 2.04 (t, 3 H, Ac), 2.10 (s, 3 H, Ac), 2.58–3.08 (m, 4 H, SCH_2), 3.92–4.15 (m, 3 H, CH_2O-, SCHS), and 5.08–5.30 (m, 1 H, -CHO); $\nu_{max}^{CHCl_3}$ 1735 (ester) and 1740 cm^{-1} (ester); mass spectrum: *m/e* 292 (M^+), 232 ($M^+ - CH_3CO_2H$), 172 ($M^+ - 2CH_3CO_2H$), 119 (dithiane).

Anal. Calc. for $C_{12}H_{20}O_4S_2$: C, 49.32; H, 6.85. Found: C, 49.01; H, 6.72.

2-(1,4-Dihydroxybutyl)-1,3-dithiane (**5**). — A solution of the diacetate **26** (43 mg) in ammonia-saturated methanol (15 mL) was maintained for 36 h at 4° after which time evaporation of the solvents left a clear syrup (33 mg) consisting of a single component of R_F 0.25 (t.l.c. silica gel, 9:1 benzene–ethanol). The syrup was chromatographed on silica gel (5 g) with 9:1 benzene–ethanol as eluent, yielding pure **5** (24 mg, 78%); $[\alpha]_D^{23}$ 0° (*c* 1.2, chloroform); n.m.r. (100 MHz, Me_2SO-d_6): δ 1.10–2.19 (m, 6 H, CH_2CH_2, SCH_2CH_2), 2.73–2.93 (m, 4 H, SCH_2), 3.39 (broad s, 2 H, -CH_2O-), 3.50–3.73 (m, 1 H, -CHO-), 4.15 (d, 1 Y, $J_{1,2}$ 5.0 Hz, SCHS), 4.38 (t, 1 H, CH_2OH, exchangeable with D_2O), and 4.98 (d, 1 H, -CHOH, exchangeable with D_2O).

Anal. Calc. for $C_8H_{16}O_2S_2$: C, 46.15; H, 7.69. Found: C, 45.74; H, 7.55.

2-(1,4-Di-O-p-nitrobenzoylbutyl)-1,3-dithiane (**27**). — The pure dihydroxy compound **5** (12 mg) in dry pyridine (1.5 mL) was treated, under anhydrous conditions, with *p*-nitrobenzoyl chloride (50 mg) for 1 h, and then water (0.5 mL) was added. The mixture was stirred for 1 h, the solvents were evaporated off, and the residue dissolved in chloroform (25 mL) and washed successively with 4% hydrochloric acid (2 × 15 mL), saturated aqueous sodium hydrogencarbonate (2 × 15 mL), and water (2 × 15 mL). The chloroform layer was then dried with sodium sulfate and evaporated, leaving a crude syrup (28 mg) that was chromatographed on silica gel (5 g). Elution with 10:1 benzene–ethyl acetate gave pure **27** as a syrup (18 mg, 61%) that was crystallized from carbon tetrachloride–hexane (m.p. 72–75°) and recrystallized from acetonitrile–water as yellow prisms, m.p. 105–107°, $[\alpha]_D^{23}$ 0° (*c* 1.0, chloroform); n.m.r. (100 MHz, $CDCl_3$): δ 1.80–2.35 (m, 6 H, CH_2CH_2, SCH_2CH_2), 2.72–3.02 (m, 4 H, SCH_2), 4.27 (d, 1 H, $J_{1,2}$ 6.0 Hz, SCHS), 4.45 (t, 2 H, $J_{3,4}$ 6.2 Hz, -OCH_2-), 5.44–5.68 (m, 1 H, CHO), and 8.10–8.40 (m, 8 H, Ar); mass spectrum: *m/e* 506 (M^+).

Anal. Calc. for $C_{22}H_{22}N_2O_8S_2$: C, 52.17; H, 4.35; N, 5.53. Found: C, 52.20; H, 4.38; N, 5.49.

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